Gastrointestinal SURGICAL EMERGENCIES

American College of Surgeons
International Relations Committee

Editors
Giuseppe Nigri, MD, PhD, FACS, FRCS
Georgios Tsoulfas, MD, PhD, FACS

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Foreword

It gives me great pleasure to see this textbook on "Gastrointestinal Surgical Emergencies" finalized. This book is the product of a broad international collaboration, as reflected by the diverse group of authors, and is intended for surgeons worldwide. I commend the American College of Surgeons (ACS) and the editors for recognizing the importance of surgical education on the global stage and making this text available as a free online resource for all surgeons and surgeons-in-training around the world.

This text offers a practical overview of surgical emergencies of the gastrointestinal system. It draws from diverse surgical practices, patients, resources, and health care systems. It presents a wide variety of treatment algorithms and alternatives based on shared surgical principles. This text equips surgeons to be prepared for gastrointestinal emergencies with the goal of providing safe, effective, efficient, and comprehensive urgent care to the ill and injured.

This effort has been facilitated by the Dr. Pon Fund International Chapter Opportunity Program, named for Pon Satitpunwaycha, MD, FACS, whose generous donation through the International Relations Committee (IRC) has sponsored educational courses by national ACS chapters around the world. This text was inspired by the "ACS Gastrointestinal Surgical Emergencies Course," which was organized by the Italian ACS National Chapter in October 2018 as part of the Italian National Surgical Congress.

I would like to extend my congratulations to Dr. Giuseppe Nigri and Dr. George Tsoulfas, two former International Guest Scholarship recipients, active members of the ACS IRC, and successful academic surgeons in Italy and Greece, respectively. Additionally, I would like to specifically thank Kathleen McCann, Tony Ortiz, and the ACS IRC members who have been instrumental in delivering this comprehensive educational resource.

I feel fortunate to be included among those who have contributed to this effort. The recent pandemic has reminded us that medicine is global. By widely sharing our knowledge, experience, technology, and information, and by building communication and collaboration, we can each learn to provide better care for our individual patients, advance the fields of medicine and surgery, and promote improved health globally. This volume is an important step in that direction.

— **Fabrizio Michelassi, MD, FACS, MEMSE, ESA(Hon), SIC(Hon)**, Lewis Atterbury Stimson Professor of Surgery and Chairman of Surgery at Weill Cornell Medicine and Surgeon-in-Chief at New York-Presbyterian/Weill Cornell Medical Center

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CHAPTER 1
Acute Care Surgery

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Key words:
ACS, throughput, model, training, outcomes

Abstract

Acute care surgery (ACS) is a relatively new surgical specialty forged from the changing landscape of trauma surgery and increasing gaps in the delivery of quality care for the acutely ill and injured patient. The fundamental principle of this specialty is to provide comprehensive, timely, urgent, and emergent general surgical care. ACS models have been steadily adopted with variability in many health care systems globally. The core common components are a dedicated on-call surgeon with no elective responsibilities, an acute care surgery service with resident support, and an allocated operating room for acute care patients. Research has shown improved outcomes with adoption of ACS models regarding patient throughput and clinical outcomes. Acute care surgery imparts a positive financial impact on a hospital contribution margin by increasing the productivity of both acute care and nonacute care surgeons. A curriculum exists to prepare ACS fellows to manage critically ill patients and to operate comfortably in a variety of anatomic regions. Over time the number of fellowship positions has increased, and there is renewed interest among graduating residents in the field of acute care surgery; however, the size of the ACS workforce is at risk. This, in addition to the ever-changing economic landscape, provides ongoing challenges with the growth of the specialty.

Development of the Acute Care Surgery Specialty

Acute care surgery has emerged over the past 20 years as a common care model for both academic and private medical centers. The core elements of acute care surgery include trauma, emergency general surgery, and surgical critical care. In some settings, the scope of practice for the acute care surgery may also include management of acute burn injuries and elective general surgery. The conception of acute care surgery sought to fulfill a vital need of the American public: providing high-quality, timely surgical care to the injured and acutely ill patients.[1] Many professional, economic, and societal forces have forged the development of acute care surgery over the past half century.

The necessity of staffing hospitals with surgeons capable of handling emergencies can be traced back to the genesis of surgical training at Johns Hopkins University at the turn of the 20th century. Dr. William Stewart Halsted wrote, "Every important hospital should have on its resident staff of surgeons at least one who is well and able to deal with any emergency that may arise."[2] The early seeds of the specialty as we currently know it can be traced to the development of trauma centers at safety-net* city and county hospitals in the United States during the 1960s. In this setting, trauma surgeons would routinely and confidently operate on injuries of the neck, chest, abdomen, pelvis, and cardiovascular system. In addition to trauma care, safety-net hospital surgeons frequently provided elective and urgent general surgery care for their facilities. This rich environment of broad surgical practice and strong master surgeon mentorship helped popularize careers in trauma surgery among trainees and young surgeons.[3]

By the 1970s and 1980s, trauma surgery entered a golden age. Trauma surgery made the leap from focusing on the parochial interest of an individual county hospital to the initial development of regional trauma systems in the early 1970s.[4] The American College of Surgeons Committee on Trauma (ACS COT) published its first edition of *Optimal Hospital Resources for Care of the Seriously Injured* in 1976, establishing guidelines for the care of trauma patients.[4] With standardization and regionalization, trauma surgery and trauma systems became recognized as a driver of improved outcomes.[5] At its very core, trauma surgery remained a largely operative specialty at this time. The advent of diagnostic peritoneal lavage in the mid-1960s and popularization throughout this period ensured high frequency of the trauma laparotomy, albeit, frequently, with nontherapeutic results.[6]

By the 1990s, two large seismic shifts were occurring in trauma care. The first was the increased utilization of imaging in the routine evaluation of the trauma patient. Broader access to, and implementation of computed tomography and ultrasound began displacing diagnostic peritoneal lavage as the primary mode of diagnosing intra-abdominal injuries. This greatly decreased unnecessary operations in both blunt and penetrating trauma victims. Moreover, it limited the operative experience and training opportunities of the trauma surgeon.[7] The other crucial change was the evolving epidemiology of trauma. By the late 1990s, the elderly accounted for the increased proportion of trauma patients; penetrating trauma was less common; and the average patient was less severely injured on presentation thanks to improvements in vehicular design, seatbelt laws, airbags, and injury prevention programs.[8] The inevitable result of these epidemiologic shifts was decreased trauma operative volume and increased responsibilities for nonoperative management of patients.[8]

Two landmark studies began sounding the alarm about a potential crisis in trauma surgery in the early 1990s. The first, by Esposito and colleagues, identified a negative attitude toward trauma patients and a preference to not treat them in a large proportion of surgeons surveyed from a Washington statewide sample through the American College of Surgeons.[9] The preference to not treat was driven by a perceived negative practice impact, older age of the provider, and a presumed increased medicolegal risk of trauma care.[9] The other study, by Richardson and Miller, identified an overwhelming negative impression of trauma and a paucity of interest in pursuing a career in trauma surgery on a nationwide survey of surgical trainees postgraduate year 3 (PGY-3) or higher.[10] The authors found that while 81 percent of residents have some interest in trauma care, only 18 percent wished to pursue a career in trauma and 8 percent were interested in trauma fellowship. Barriers to the pursuit of a trauma career included the volume of work with too few operations, other specialty interest, a large volume of overnight call, and "unsavory clientele".[10]

By the early 2000s, trauma surgeons and leaders in the field increasingly identified a growing concern about the future of the profession. The American Association for the Surgery of Trauma (AAST), the Eastern Association for the Surgery of Trauma (EAST), and the Western Trauma Association (WTA) surveyed its members about career satisfaction and perceived incentives, disincentives, and opportunities for change in trauma practice.[11] Among the respondents, nearly 90 percent expressed satisfaction with a career in

*Safety-net hospitals are defined by the Institute of Medicine as institutions that are legally mandated or mission driven to provide a disproportionate amount of care to vulnerable groups, including the uninsured, Medicaid recipients, and other populations including homeless individuals, HIV patients, and those with mental illness. Safety-net hospitals provide care to these populations regardless of their ability to pay. Institute of Medicine (US) Committee on the Changing Market, Managed Care, and the Future Viability of Safety Net Providers, Ein Lewin M, Altman S, eds. *Americas's Health Care Safety Net: Intact but Endangered*. Washington (DC): National Academies Press (US); 2000..

general surgery, while 72 percent were satisfied with their trauma practice. Almost two-thirds of respondents felt trauma surgery was not viable or sustainable in its current form. The vast majority felt trauma surgery should change and could be redesigned to make it more sustainable and viable.[11] The developing crisis in trauma and critical care was further confirmed by an Institute of Medicine Report projecting a shortage of on-call specialists including a 35 percent deficit of intensivists.[12] Reasons cited for specialist surgeon unavailability were lack of reimbursement related to uninsured patients, increased liability and malpractice claims for care of emergency department (ED) patients, disruptions in elective surgical practice, and work-life balance.[13]

With the rising threat to the future trauma surgery practice, the AAST convened the Committee to Develop the Reorganized Specialty of Trauma, Surgical Critical Care, and Emergency General Surgery including an eminent panel of leaders in the field. Their ultimate report, published in 2005[1], laid out a foundation for the new specialty of acute care surgery. This work group identified the challenges to the long-term viability of the profession including decreasing trauma surgical volume, relatively lower compensation for trauma resuscitation over operative work, unappealing work hours, unpredictable schedules, and high stress burden. They proposed a new specialty of acute care surgery, combining trauma, emergency general surgery, and surgical critical care. In combining these fields of practice into one entity, they sought to address these challenges as follows: creating a more desirable operative specialty incorporating wider skills and techniques; giving the acute care surgeon a more controlled lifestyle to improve work-life balance; developing a workforce that is adept at complex operations and a resource to the entire medical staff; and providing in-house care around the clock to both improve patient outcomes and to increase educational opportunities for trainees.[1]

Acute Care Surgery Curriculum

The development of a new training paradigm is essential to the growth and establishment of acute care surgery as a new specialty. The AAST ACS Committee was charged with developing the curriculum, competencies, and fellowship certification criteria that were the basis for the AAST Acute Care Surgery Fellowship.[14] Potential sites for fellowship programs are required to submit an application that, once approved by the committee, are followed with an onsite visit. Reviewers meet with faculty, residents, and administration to determine first, whether the program can support the operative volume required for the ACS fellowship requirements and second, to assess the credibility of the proposed educational structure. Finally, the reviewers determine if there will be a negative impact of the additional fellowship on the existing general surgery residency experience and case numbers. Once accredited, these fellowships require recertification with onsite visits at regular intervals to maintain accreditation.[14,15] Since the first fellowship program opened its doors in 2008, the number of programs has steadily increased to 28 fully accredited programs.[16]

Matriculation to an ACS Fellowship generally follows successful completion of a general surgery residency. The core structure of the AAST fellowship consists of a two-year fellowship with the first year being an ACGME (Accreditation Council for Graduate Medical Education) Surgical Critical Care fellowship with subsequent eligibility for board certification in Surgical Critical Care. The second year of fellowship is an operative year with surgical trauma call responsibilities after which certification through the AAST is possible. To achieve a broad operative experience, rotations on trauma and general surgery, thoracic, vascular, hepatobiliary/transplant, along with electives in neurosurgery, orthopaedics, and endoscopy were recommended in the original curriculum.[14]

Analysis of several factors has shaped the curriculum over time. In 2010 a case log registry was developed in order to track the operative experiences of the ACS fellows. Review of the case log data in 2013 by Dente et al.,[17] showed that the fellows completed on average 200 major cases which were dominated primarily by abdominal cases. Although there was a wide variety in types of cases performed, approximately 50 percent of the fellows failed to meet the operative case types specified by the original curriculum. Specifically, gaps were identified in otolaryngology–head and neck surgery, pediatric surgery, and vascular surgery. Based on this analysis, the curriculum was updated to the operative case requirement from previously elective rotations in thoracic and vascular surgery to required rotations and refinements.[14,16] The rationale for this change was to provide the necessary training and comfort level needed for emergent operations by providing exposure to these anatomic regions in the elective setting. Minimum case log requirements for successful fellowship completion were put in place based on anatomic regions and organ-based management like the American Board of Surgery.[16] The case registry offers the opportunity for real-time analysis by program directors to modulate rotations to meet the requirements of the fellowship. The written exam required of each graduating fellow also plays a role in refining the fellowship curriculum. Analysis of test results has led to the addition of an in-training exam taken prior to the start of the operative year. This pretest allows the program director and trainee to identify areas of weakness and to focus the education and operative experience accordingly.[14, 15] Educational modules tied to the curriculum have also been added to the fellowship training comparable to the computer-based general surgery curriculum. These modules cover the basic educational content but also have maintenance of certification-type test questions as well as expanded education on complex operative techniques more applicable to the ACS fellow level of training.[14, 15]

The impact of these fellowships on surgical training and surgical practice has been a research focus.[18,19] Dinan et al.[18] showed no decrease in the ACGME case log data before and after initiation of an AAST-approved ACS fellowship and specifically demonstrated no change in the number of operative cases performed by chief residents. The ACS fellow was found to have added value to the program in the role of educator. Cothren Burlew et al.,[19] surveyed graduates of the AAST-approved fellowships. Survey results indicated 96 percent of the graduates were practicing acute care surgery, while 2 percent practiced only trauma surgery, and the remaining 2 percent practiced only general surgery. Hospital-based practice (84 percent) and private group (12 percent) were the top two practice settings. Graduates were asked to describe case specifics one year after fellowship completion. Interestingly, the data revealed that 92 percent of the graduates were performing vascular cases, 88 percent were doing thoracic cases, and 70 percent were involved in hepatobiliary cases to some degree. Overall, 93 percent would recommend an ACS fellowship to others with 82 percent relaying the fellowship prepared them well for practice and was worth the time invested. Given the relative infancy of the acute care surgical field compared to other aspects of general surgery, one would expect further refinements to the training model to meet the future needs of the specialty.

The Acute Care Surgery Model

Traditionally, emergency surgical care was provided by a group or department of general surgeons who also managed an elective surgical practice in addition to rotating call responsibilities. This model has many limitations. Call responsibilities could provide interference with elective surgical practice and clinic schedules. Reluctance to perform elective surgery after a busy night on call also impacted elective surgical volumes. Gaps in surgical expertise exist given not all surgeons had the same level of familiarity and skill with specific acute general surgery disease processes.[20] In addition, there was a limited surgical subspecialty workforce that may lead to delays in care and potentially worse outcomes for patients.[21] Adopting an ACS model addresses some of these issues.

An ACS model requires a dedicated team of surgeons that provide comprehensive care for all general surgical and trauma emergencies. Typically, this dedicated team of surgeons provides 24/7 coverage, although some variability may exist depending on the hospital system. This model aims to enhance hospital resources, allowing surgery departments to provide quality care to both elective surgical patients and patients with acute surgical problems.[22]

Vanderbilt University in Nashville, TN, was one of the first hospital systems to implement an ACS model. They identified several components that are essential to the successful implementation of an acute care surgery model. Following are those recommendations.

The service concept

A service concept allows for a multi-disciplinary group of providers to manage patients and improve communication. The service concept also allows for rotation of rested surgical teams which can allow for better attention to complex patients. The service concept allows for patient management to occur around the clock and, if available, a residency team can expedite patient evaluation and management.[22] Daily multi-disciplinary rounds have been shown to shorten length of stay for trauma patients, and there may be similar advantages for the emergency general surgery patient population.[22]

The surgical director

The director implements the mission of the service. The service concept model may involve multiple physicians and caregivers involved in a complex patient's care. The director is critical for ensuring continuity of patient care. The director can oversee the implementation of practice management guidelines and protocols which will help to decrease variability in care.[22]

Hospital support

The emergency department provides a gateway for the emergency general surgery patient into the hospital system. Excellent care in the emergency department can significantly reduce organ failure and mortality. Having an outstanding working relationship with the emergency department provides timely evaluation, resuscitation, and surgical care of the emergency general surgery patient. Developing evidence-based protocols and patient care guidelines jointly with the emergency department can facilitate care.[22] In addition to the emergency department, access to a dedicated acute care surgery operating room will allow for less delays in scheduling urgent and emergent cases. Finally, having a dedicated surgical intensive care unit team has been shown to improve outcomes and decrease hospital cost for emergency general surgery patients.[22] Coordination of care with the surgical intensive care unit team is important because complex patients often require resuscitation and frequent interventions. As with the emergency department, establishing collaborative evidence-based protocols between the acute care service team and the surgical intensive care unit team will provide minimal variability of care and lower hospital costs.[22]

Intrahospital communications

Establishing a dedicated hospital transfer center to coordinate both inhospital consults as well as incoming transfers from other hospitals should allow for decreases in delays of care for the complex acute surgical patient. Previous studies from trauma systems have shown this to improve care. Additionally, an established transport system and aeromedical transport service will allow for the rapid transfer of patients to a higher level of care. Previous research for trauma patients has shown aeromedical transport to improve outcomes.[22]

Service staffing

Finally, it is important to have an appropriately staffed acute care surgery service. Ideally, the key members of this team will include 24/7 faculty coverage, access to both surgical and medical subspecialty consultants, and a fully staffed surgical resident team. Additional team members include physician extenders, case managers, and social workers. These individuals will help to provide a continuum of care for the complex emergency general surgery patient.[22] Access to long-term acute care hospitals and rehabilitation facilities will facilitate discharge planning and hopefully lead to decreased length of stay and better long-term functional outcomes.

In conclusion, Vanderbilt University set the standard for development of an ACS model. The key elements include an ACS service with 24/7 faculty and resident coverage, access to the operating room to allow timely completion of service cases, and an integrated care pathway from the emergency room to the intensive care unit to the discharge destination.[22]

Global Acute Care Surgery

Timely access to emergency general surgery remains a challenge globally with limited-to-no access to surgical resources for most of the world's population.[23] Adaptation of ACS models have been limited for the most part to high-income countries while expanding access to essential surgery remains a priority in low- and middle-income countries.[23] Heterogeneity in the models has been observed, primarily attributable to variations in hospital infrastructure, hospital resources, and discrepancies in the health care environment.[24] Shared common elements, though, are a dedicated surgical service covering nontrauma emergency general surgery, onsite daytime attending who covers emergencies with no elective practice obligations, operating room allocation, and 24/7 resident coverage.[14, 24] One notable difference between the U.S. models and non-U.S. models is the separation of trauma surgery and surgical critical care from the duties of the acute care surgeon.[24] Part of the challenge relates to established frameworks of care delivery that vary in each health care environment. In Europe, for example, trauma surgeons manage visceral and skeletal trauma, whereas, in the U.S., skeletal trauma in managed by orthopaedic surgeons. Whether ACS belongs in the domain of trauma surgery versus gastrointestinal surgery remains debated. Further research is needed to determine the ideal model for each health care system, but key to each model's success is the hospital resource commitment and the presence of a dedicated surgeon for emergency cases.[14]

Advantages of Acute Care Surgery Model

Each year, more than three million patients are admitted to the hospital requiring emergency general surgery care in the United States.[25] These patients represent a high-risk population with frequent poor outcomes compared to elective general surgery patients.[26, 27] They have significantly more comorbidities including diabetes, hypertension, immunosuppression, and chronic obstructive pulmonary disease.[26, 27] Due to acute illness, these patients have physiologic and metabolic derangements and worsening of baseline function. At the time of presentation 12 to 14 percent of these patients will have septic shock.[26, 27] As a result, patients requiring emergency surgery have significantly higher mortality and complication rates compared to elective patients.[27] Traditionally, local general surgeons have provided surgical care for these patients. Over the last decade, an acute care model has been adopted by many institutions, and several studies have demonstrated improvements in costs and quality of patient care.[28-35]

One of the first studies to address cost of patient care in an ACS model was conducted at Loma Linda University Medical Center in Murietta, California. In this study, the authors compared patient outcomes and costs in an acute care model with a traditional care model in patients undergoing appendectomy and cholecystectomy.[28] Researchers found that patients in the acute care model had earlier surgical evaluation, earlier surgical intervention, earlier recovery, and earlier return home.[28]

In addition, this study found significant cost savings between the acute care model and the traditional model. Regarding appendectomy, researchers reported a mean cost savings of $1,024 per patient. For those patients undergoing cholecystectomy, the mean cost savings was $3,225 per patient.[28] The authors clearly demonstrated improvements in care and cost savings for two of the most-performed emergency general surgery operations.

A study by To et al.,[29] was one of the first studies to examine the correlation between patient care models and emergency general surgery outcomes across multiple institutions by utilizing a prospectively collected patient outcomes registry. For their study, To and colleagues analyzed 308,243 patients in the Michigan Surgical Quality Collaborative registry comparing case logs and patient outcomes across 34 hospitals. Patient care models for emergency patients were determined by self-reported survey responses at each site. In their study population, overall mortality for emergency general surgery patients was 4.1 percent, with 11.6 percent mortality for those patients undergoing intestinal resections. The patient care model was found to be a significant

variable for mortality. Notably, facilities with an ACS model were associated with a 31 percent mortality reduction for emergency general surgery cases compared to facilities who had traditional general surgery or hybrid models.

Another advantage to consider is how an ACS model impacts financial profitability for hospital systems. We have seen that an ACS model reduces cost of care and improves patient outcomes. Both factors have been shown to improve hospital contribution margins.[31] Previous studies have shown that an ACS model reduces time from admission to surgery.[32] Since delays of care in emergency general surgery patients have been shown to lead to increased mortality and longer lengths of stay, an ACS model favorably impacts hospital profitability.[33]

Additionally, several institutions have reported on the impact of an ACS service on nonacute care surgeon productivity. Loss of productivity from call was a major concern to non-ACS surgeons when adopting an ACS model. Wake Forest University in Winston-Salem, North Carolina reported their nonacute care surgeons saw elective cases increase by 22 percent, leading to a significant increase in hospital profit.[34] Similarly, the University of Missouri in Colombia, Missouri saw an increase of 94 percent in work RVUs (work relative value units, a scale used by Medicare to assign fees for different physician activities accounting for the time and effort required) and 60 percent increase in operative volume among nonacute care surgeons.[35] Both ACS and non-ACS surgeons reported higher job satisfaction rate crediting the addition of the ACS model on having a positive impact on their practice.

Globally, ACS models have demonstrated decreased operative delays with dedicated operating room resources.[13] In regard to appendicitis, ACS model implementation in New Zealand led to decreased length of stay with an increase in operations performed during daytime hours.[13]

In summary, the adoption of an ACS practice model has led to improvements in patient care and reduction of costs associated with emergency general surgery. The models have also been associated with increased operative volumes and improved job satisfaction for both ACS and non-ACS surgeons. These improvements in patient care and the associated increase in nonacute care surgery volume has led to financial profitability for hospitals. Overall, it appears that the adoption of an ACS model has benefits for patients, surgeons, and hospital systems.

Challenges

Despite the demonstrated advantages, adaptation of ACS models has been disparate. A survey of 1,690 U.S. hospitals in 2015 revealed only 16 percent of the hospitals had an acute care surgery model (increased from 2.1 percent in 2001), with the remainder utilizing a traditional general surgery call rotation model. Hospitals with an ACS model were likely to be urban, to have greater than 500 beds, and to be teaching hospitals.[36] Areas with lower population densities were less likely to have access to facilities with an ACS model. This rural disparity in ACS implementation is further demonstrated by only 7 percent of the graduates of the ACS fellowship programs reporting practice in a rural environment.[19] Regionalization or concentration of acutely ill surgical patients at higher-performing centers with ACS models may be necessary to assure the availability of quality emergency surgical care to less-populated regions.[26, 37]

Staffing and retention remain a major challenge to the future of acute care surgery. The number of general surgeons has not proportionally increased with population growth and demand.[38] The projected shortfall of general surgeons is between 17,100 and 28,700 for the year 2033 largely due to expected attrition from retirement.[38] Specialization after general surgery residency is chosen by 80 percent of residents, leaving a small number of generalists available for providing emergency surgery care. Though the field of trauma surgery has seen a resurgence due to the reorganization of acute care surgery, 10 percent of fellowship spots were unfilled in 2015.[15] Lifestyle, compensation, inadequate staffing, and burnout have been cited as challenges to retention and longevity of the acute care surgeon.[31]

Even with the demonstrated advantages to hospitals and surgical departments, the economic value of the ACS model remains at risk due to an ever-changing economic landscape. In the United States in 2013, trauma and ACS patients accounted for 5 to 6 million admissions per year resulting in $65 -$100 billion in costs for direct patient care.[31] This was estimated to be about 20-30 percent of the total inpatient hospital costs nationwide. These patients are severely ill at presentation requiring operations, procedures, intensive care unit admissions, and longer hospital stays due to complications, which leads to the higher costs of care.[26, 27, 31]

In the United States, reimbursement for these complicated cases remains dependent on payor mix which varies by location. In facilities where the payor mix has a higher percentage of underinsured patients, lack of reimbursement for services rendered may leave the hospital in a financial shortfall. The shift from private payor system to government insurance at the lower reimbursement rate also has repercussions as our population continues to age.[31] Compensation plans for acute care models that rely on

reimbursement for acute care surgeons in these areas will need external funding support to remain revenue-neutral.

With these financial challenges, hospitals may tend to undervalue the overall benefits of the acute care surgery model especially if the only metric for success is reimbursement and RVU generation. Studies have demonstrated that acute care surgery services provide timely care leading to less morbidity and mortality and increase the RVU productivity and reimbursement of the elective surgeons mainly through the offloading of emergency call to focus on the elective insured patients.[14, 29, 32-35] Careful analysis at the institutional level is essential to assess the impact of the acute care surgery model across the hospital and determine what service lines within acute care surgery should be maximized to improve the contribution margin.

Summary

Acute care surgery is a relatively new specialty developed to meet the needs of acutely ill patients and an increasingly nonoperative field of trauma surgery. Acute care models have been adopted globally with the shared components being a dedicated surgeon with no elective responsibilities, a dedicated service with resident and faculty support 24/7, and dedicated operating room resources. Studies have shown significant benefits to quality of care with increased patient throughput, morbidity and mortality with implementation of acute care models, as well as increased profitability and surgeon satisfaction. The growth of the acute care surgery specialty will be further shaped by changing health care economics, projected surgeon shortages, and population health needs.

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CHAPTER 2

Emergency Gastrointestinal Surgery in the Patient with Significant Comorbidities

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Introduction

Elective gastrointestinal surgical procedures carry a low to moderate (1 to 5 percent) risk of perioperative complications, most commonly related to hemodynamic or physiological reactions, blood loss, or infection.[1] The risk of mortality is minimal. Compared to elective surgery, emergent gastrointestinal surgery (EGS) is associated with a significantly higher risk for mortality and morbidity, sometimes reported to be as high as 8-fold. This is due in large part to the fact that patients needing emergent surgery are often in a compromised and critical state due to the acuity of disease with which they are presenting. This risk is further compounded in patients with chronic medical conditions such as coronary artery disease, chronic obstructive pulmonary disease, or diabetes that can further decrease physiologic reserves.

While the life-threatening or time-sensitivity nature of the situation often precludes lengthy preparations for surgery, gathering as much information as possible about an EGS patient's past medical and surgical history is essential to provide the best and safest care possible. While the availability of such information should not delay access to the operating room (OR), failing to obtain a full, even if basic, understanding of a patient's comorbidities will exponentially increase the risk of postoperative morbidity and mortality, and hinder the surgical team efforts to salvage them. Even social history information including any history of alcohol, tobacco, and/or substance use may prove essential for perioperative care given the potential for drug interactions or changes in hemodynamics secondary in the perioperative period. In addition to optimizing perioperative care, understanding the medical, surgical, and social history of EGS patients well helps us better predict their risk of mortality and morbidity. Several newly established risk assessment tools, such as the Emergency Surgery Score (ESS) or the Artificial Intelligence-based POTTER calculator were designed specifically for EGS and can be used as adjuncts in decision-making and helping better counsel the patient and their family.

Women of reproductive age should get a rapid pregnancy test, standard preoperative antibiotic prophylaxis or more broad-spectrum antibiotic therapy should be started in abdominal sepsis, and patients with shock should undergo active resuscitation without delaying the source control aspect of their shock management, i.e. surgical control of hemorrhage or sepsis.

In the following section, we will discuss the challenges the management of EGS with specific medical comorbidities such as liver cirrhosis, pulmonary disease, or cardiac disease.

EGS in the Patient with Liver Cirrhosis

Patients presenting with liver disease are at an incredibly increased risk of morbidity and mortality given the cirrhosis-related cardiovascular and circulatory alterations, the reduced synthetic function leading to coagulopathy and thrombocytopenia, and the decreased hepatic perfusion which makes the liver more susceptible to hypoxemia and hypotension.[2] Cirrhotic changes alter systemic circulation secondarily to portal hypertension which decreases blood flow through the liver. These changes lead to increased cardiac output and decreased systemic vascular resistance. This can be further worsened by arteriovenous shunting and reduced splanchnic flow.[2] Altered synthetic function of the liver can produce profound coagulopathies in patients that can be refractory to corrective therapies and thus make them susceptible to difficult to control and life-threatening hemorrhage. A prothrombin time and International Normalized Ratio (INR) are considered the gold standard to estimate synthetic function.[2] Resuscitation during the perioperative period may also require correction of any coagulopathies secondary to decreased synthetic function. Patients with significant ascites can experience massive fluid shifts during abdominal surgery that result in intraoperative hemodynamic instability due to intravascular hypovolemia. In the immediate postoperative phase, periodic and frequent assessment of the intravascular volume should be performed, and resuscitation with colloids and/or crystalloids will be necessary to reduce further perfusion of the hepatic and renal systems resulting in worsening of the liver and renal function. Once the acute phase of resuscitation resolves, hypervolemia and fluid overload can in turn lead to pulmonary edema, peripheral edema, acute hepatic congestion, and wound complications,[2] and balancing the resuscitation with diuresis is often challenging.

A patient's Model for End-Stage Liver Disease (MELD) score or Child-Pugh classification can be used to predict the risk of perioperative risk in the emergency setting. Mortality rates for patients with advanced increase significantly to 22 percent for Child-Pugh class A, 38 percent for Child-Pugh class B patients, and nearly 100 percent for Child-Pugh class C cirrhosis patients.[3] The MELD score similarly correlates well with perioperative mortality and is considered one of the most precise predictors of perioperative mortality in cirrhotic patients due to its reliance on objective data points with weighted variables.[4] Patients should be monitored closely in the perioperative period as intraoperative changes and insults can cause acute decompensation of an otherwise stable liver disease. The use of narcotics and benzodiazepines should be monitored closely as they can be poorly metabolized in patients with hepatic dysfunction resulting in altered mental status or acute hepatic encephalopathy.[2] The patient's blood glucose should also be monitored closely in patients with

evidence of decompensated cirrhosis as they often have impaired gluconeogenesis which becomes problematic with concurrent depletion of the hepatic glycogen stores during the acute recovery phase.[2]

EGS in the Patient with Pulmonary Disease

Patients with underlying pulmonary disease are at increased risk of developing major cardiopulmonary complications such as acute coronary syndrome, heart failure, pneumonia, and/or respiratory failure following major operative interventions.[5] With the increased prevalence of chronic obstructive pulmonary disease (COPD) within the population, careful attention should be paid to a patient's respiratory mechanics as well as their maintenance and rescue medications, as chronic steroid use can also further increase the risk of complications within this patient population. Patients with COPD will be more prone to exacerbation of bronchial inflammation during instrumentation and are more likely to have bacterial airway colonization which increases the risk of postoperative respiratory infections.[6] Patients with more advanced COPD (e.g. home oxygen dependence, shortness of breath/dyspnea on exertion) and downstream sequelae such as pulmonary hypertension are particularly at risk for decompensation given the risk of right heart failure and ventilator dependence and are thus likely to have the worst prognosis among patients with pulmonary disease.[6]

Postoperatively, key steps are to minimize agents that decrease respiratory drive and to encourage aggressive pulmonary toilet (e.g. deep breathing exercise, incentive spirometry, pulmonary physical therapy) to help prevent and mitigate pulmonary complications. However, inadequate pain control can lead to shallow breathing and fatigue of the respiratory muscles and thus adequate analgesia should also be a priority. In the emergency setting, many patients may need to be placed in the intensive care unit (ICU) and remain intubated. Early extubation and mobilization will help decrease the risk of ventilator dependency and respiratory failure in patients with significant pulmonary comorbidities.

Patients with a heavy smoking history are also often challenging perioperatively after EGS. Smoking is well documented to be a risk factor for postoperative complications including adverse cardiac events, bronchospasm/laryngospasm leading to unplanned ICU admission, and serious wound complications including dehiscence. Patients with a significant smoking history are more prone to having increased airway sensitivity, increased airway secretions, and a decreased ability to clear secretions effectively. In the emergent setting, the abrupt cessation of smoking can cause an acute worsening of these symptoms and thus particular interest should be paid to pulmonary toilet in the perioperative time period.

Emergency Surgery in the Patient with Cardiac Disease

Patients with a history of cardiac disease, specifically ischemic cardiac disease, carry risk of perioperative morbidity and mortality when undergoing major noncardiac operations.[7-8] In the elective surgery setting, patients can often be medically optimized prior to intervention; however, in a patient that is presenting with an indication for EGS, for example, acute mesenteric ischemia, medical optimization is invariably not feasible. A thorough history and physical will elucidate key information about a patient's functional status and general cardiac health. Knowing if a patient is able to perform their own activities of daily living (ADLs) and walk up a flight of stairs with minimal issues can give significant insight into a patient's ability to tolerate a major procedure. Patients with cardiac disease may also be on various forms of anticoagulation or antiplatelet therapy which may significantly increase the risk of perioperative hemorrhage or coagulopathy.[9] It is important to note any significant valvular disease, such as aortic stenosis, as patients may be more sensitive to fluid shifts and preload dependent. Significant hypotension can result in cardiac events in the perioperative period and increase their risk of morbidity or mortality.[9] Patients on anticoagulation can be reversed for brief periods perioperatively to allow safe surgery. The time sensitivity of EGS rarely allows enough time to preoperatively hold anti-platelets agents for enough time. There is no evidence that prophylactic platelet transfusions in those cases are beneficial.

Emergency Surgery in the Patient with Diabetes Mellitus

Patients with uncontrolled diabetes present with significant risk of metabolic derangement and putting them at a significantly increased risk of systemic as well as wound complications. Attempts to lower blood glucose <200 should be made in the perioperative period to decrease the risk of complications.[10] While insulin scales are often sufficient, insulin drips in the intensive care unit might be necessary while longer-acting insulin regimens are adjusted. In cases with difficult to control perioperative hyperglycemia, blood glucose levels should be managed with the assistance of an endocrinologist, if necessary.

Emergency Surgery in the Anticoagulated Patient

As the population ages, surgeons are more commonly encountering anticoagulated patients in needing EGS. Some of the most commonly encountered drugs will be heparin and vitamin K antagonists like warfarin. More recently, direct Factor Xa inhibitors like rivaroxaban and apixaban are being more commonly used. Both heparin and low-molecular weight heparin (LMWH) are readily reversible with protamine sulfate, while coumadin can be reversed with the administration of oral and/or intravenous vitamin

K or prothrombin complex concentrate (PCC). Fresh frozen plasma (FFP) can also be used as an adjunct for reversal. FFPs will not fully correct the induced coagulopathy, especially to INR levels less than 1.6-1.8 and many patients with underlying heart failure may be able to tolerate the associated fluid overload from the large transfused volume. Recombinant factor Xa (Andexxa) can be used to reverse rivaroxoban and apixaban, and idracuizmab (Praxbind) can be used for thrombin inhibitors like dabigatran.[11]

Emergency Surgery in the Immunocompromised Patient

In patients who are immunocompromised due to steroids, adrenal insufficiency might be challenging perioperatively. While the data for the need for stress-dosing are not definitive, surgeons and anesthesiologist should consider it perioperatively. In transplant patients on immunosuppressive medications, the transplant team should be consulted in order to manage the immunosuppression medication regiment, especially if oral intake is jeopardized in the EGS patient, and weigh in on antimicrobial therapy, if necessary.[12]

Emergency Surgery in the Pregnant Patient

A pregnancy test should be performed on all women of child-bearing age given the risk in the perioperative period to both the fetus, particularly in the first trimester, and the mother. Pregnancy-specific risks associated with surgery include preterm labor and delivery, miscarriage, and increased risk of stillbirth. Consultation to obstetrics should be placed to assist with monitoring of the fetus in the perioperative window. If there is a chance of preterm labor and delivery, the neonatal and pediatric teams should be alerted. Having an understanding of the significant physiologic changes associated with each trimester of surgery is also important given the changes in physiologic reserve and the effects those changes will have on both mother and fetus.[13] In general, the guidelines have shifted in the last few years towards management of surgical emergencies (such as acute cholecystitis or appendicitis) in the pregnant patient similarly to the nonpregnant patient, irrespective of the trimester of pregnancy, as the risk of delaying definitive care to the mother and fetus is most often deemed higher than the perioperative risk.

Conclusion

EGS can carry significant risk of perioperative morbidity and mortality. In order to decrease these risks, it is important that medical comorbidities are medically optimized as much as possible without delaying definitive surgical management. Close coordination with the appropriate consulting teams can also reduce the risk of significant perioperative adverse events. Early mobilization, nutrition optimization, and consultation to occupational and physical therapy also play an integral part in improving postoperative outcomes and decreasing the risk of preventable complications.

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CHAPTER 3

Management of Upper Gastrointestinal Bleeding

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Abstract

Upper gastrointestinal bleeding (UGIB) is a common cause for emergency admissions worldwide with substantial mortality, morbidity, and socio-economic costs. Presentation of the patients can vary depending on the intensity of bleeding, and management ranges from sole observation to surgical or interventional radiologic response. Thus, quick initial evaluation and adequate diagnostics are of the utmost importance to identify severe cases and initiate correct management. In most cases endoscopic intervention is sufficient to control hemorrhage. However, in cases of intractable bleeding, escalation of management to interventional radiology and/or even surgery may be necessary. In this chapter, a clinical approach to acute UGIB in adult patients will be presented with solid scientific background. Possible algorithms for initial work-up and treatment will be proposed, integrating recommendations by several societies. Management and work-up of chronical UGIB are excluded.

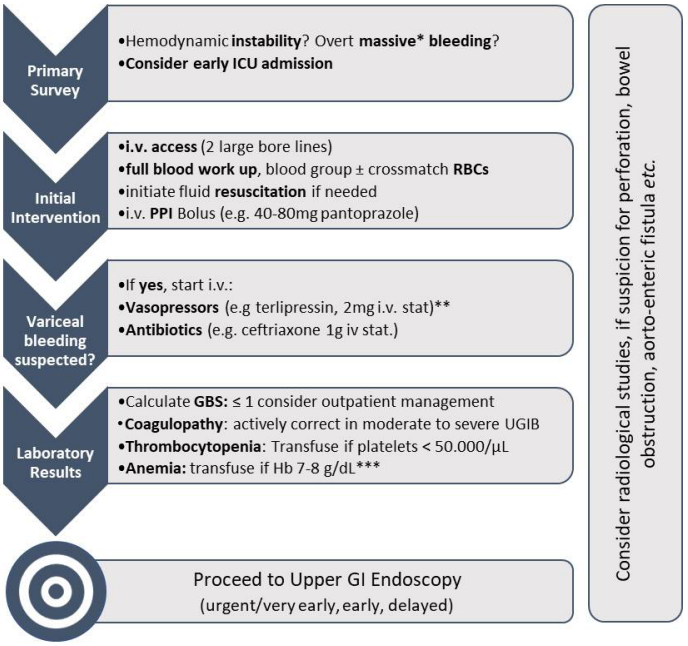
Introduction

Upper gastrointestinal bleeding is a common cause for emergency admission and is defined as bleeding proximal to the ligament of Treitz. Incidence ranges from 40 to 150 per 100,000 per year, while mortality rates are between 2.1 to 10 percent.[1–4] Peptic ulcer disease (PUD), both gastric and duodenal, is the most common cause of UGIB and accounts for about 50 percent of cases.[5–7] One-third of UGIB hospitalizations occur in patients between 45 and 64 years, and another 44 percent in patients between 65 and 84 years.[7] Rarely, significant bleeding can arise from the hepatobiliary and pancreatic system or aorto-enteric fistulae. Apart from chronic diseases (such as hepatic cirrhosis), risk factors for UGIB include Helicobacter pylori infection, intake of non-steroidal anti-inflammatory drugs (NSAID), acetylsalicylic acid as well as other antiplatelet and anticoagulation drugs, and selective serotonin reuptake inhibitors (SSRIs).[8] In the U.S., inhospital costs of UGIB increased from $3.3 billion in 1989 to $7.6 billion in 2009,[1] imposing a substantial economic burden on health care systems.[9] However, hospitalization rates decreased by 21 percent from 81 cases per 100,000 in 2002 to 67 cases per 100,000 in 2012.[7] Patient presentations and complaints range widely from only slight symptoms to severe hypovolemic shock and the need for resuscitation and immediate intervention. Whether patients are initially treated by surgeons or gastroenterologists depends on national, regional, or even local customs.
In the vast majority of cases hemostasis can be achieved endoscopically. If endoscopy fails and the patient's condition is stable, angioembolization may be a good option. Surgical intervention may be necessary in severe cases.

Initial Assessment and Work-Up

Presenting symptoms and severity grades can vary significantly in acute UGIB. Typically, melena (black, tarry stools) and hematemesis (vomiting of [usually coagulated] blood and/or vomiting of black "coffee-ground" material) are the main signs for UGIB.

While some patients may do well on outpatient management and oral PPIs, others will eventually require intensive care, including urgent endoscopy, blood products, and/or surgery. Choosing the right treatment path begins with a type of *primary survey,* including anamnesis, physical examination, and laboratory tests (**Figure 1**).



* overt bleeding: massive hematemesis, lots of juicy melena; **Consider cardiovascular contraindications; *** higher transfusion trigger in severe bleeding and cardio-vascular disease; GBS Glasgow-Blatchford-Scale; RBCs red blood cell; PPI proton pump inhibitor

Figure 1. Initial work-up in acute UGIB

***NB*: Every patient (irrespective of age, comorbidities, and so on) presenting with suspected UGIB should be considered as a potential emergency until bleeding severity is determined.**

Primary Survey

At first contact, several paths (anamnesis, physical examination, laboratory results) can indicate the source and severity of suspected UGIB. Initially, two questions—hemodynamic stability and severity of symptoms—can lead the way for initial triage and, if necessary, emergency intervention. In parallel, resuscitation may be started. Every patient with UGIB should have two large bore intravenous (IV) lines (18 Gauge or bigger).

Is the patient hemodynamically stable?

Depending on duration and severity, an ongoing hemorrhage compromises hemodynamic stability. Blood pressure and heart rate can be used as a simple indicator for blood loss: a heart rate more than 100 bpm *and/or* systolic blood pressure below 100 mm Hg have to be considered as non-stable. Of note, especially in younger patients, **the heart rate usually increases *before* blood pressure is altered and thus may be an early indicator for relevant hemorrhage.**[10] Immediate resuscitation in patients with shock is one of the most important factors to improve outcomes.[11] Initial resuscitation starts with a minimum of two large-bore IV lines (18 Gauge or bigger) and administration of fluids and, if needed (see below), blood products.[12] While there has been extensive discussion on which fluid (crystalloids versus colloids)

should be used, current guidelines recommend the use of crystalloids for initial resuscitation.[12,13] However, lessons learned from damage control resuscitation in trauma surgery show that permissive hypotension limiting crystalloids and delivering higher ratios of plasma and platelets may prevent coagulopathy and improve hemostasis.[14]

***NB:* Normal hemodynamic parameters do not rule out severe bleeding, and not every tachycardia is caused by hemorrhagic shock.**

How severe are the symptoms?

Hematemesis and melena are very "broad" terms that need to be specified:

Hematemesis: Vomiting fresh red blood is an obvious sign of significant bleeding in a short period of time. These patients most probably will need urgent intervention.[15,16] Coffee-ground-like blood, on the other hand, has already been altered by digestive fluids and is more likely associated with smaller amounts, past bleeding, and/or slower blood loss. Many anamnestic factors can facilitate a working diagnosis (for example, serial previous vomiting and Mallory-Weiss syndrome, history of peptic ulcer, chronic liver disease with esophageal varices, and so on). Some patients take pictures of the vomited contents, which can prove helpful and should be looked at. While patients often cannot easily differentiate hematemesis from hemoptysis, simple anamnestic questions (for example, describing the difference between vomiting and coughing: Did you vomit—which equals contraction of the abdominal muscles—or cough?) can point the way. Another possible cause of ostensible hematemesis is swallowed blood from extra-intestinal bleeding sources.

Melena (black, tarry stool) found at digital rectal examination: The more "liquid" the melena, the higher the suspicion of significant bleeding. "Dry" melena may be older and is found in less-severe cases, as even the loss of relatively small amounts of blood (>50 mL) may lead to black stool.[17] Of note, due to the gastrointestinal passage time, melena often persists for a certain time *after* the bleeding has already stopped. Melena can be a "*false friend*" in UGIB. It usually originates from the upper-GI tract, but other sources both *inside* (small bowel distal to Treitz *or* right colon) and *outside* (bleeding from nose or throat; prior oral surgery, and so on) the GI tract are possible. Additionally, some medication (such as oral iron and bismuth) can mimic melena; a simple guaiac test for fecal occult blood (FOB) is usually sufficient to distinguish one from the other.

Hematochezia (passing of blood per rectum) is usually a sign of lower-GI bleeding. *However,* it can occur in very severe cases of UGIB.[18] Patients with hematochezia in UGIB frequently are cold, sweaty, and not stable.

Additional information

Anamnesis

Apart from bleeding manifestation and duration, a focused anamnesis should: (a) aim at features that can lead to a working hypothesis and, (b) evaluate for comorbidities or other risk factors associated with worse outcomes. In patients with shock, initial medical history may be very basic; however, a complete medical history should be obtained once stability is established.[19]

a. Features to establish a working hypothesis include a history of previous UGIB, peptic ulcer disease (+/- Helicobacter pylori), liver disease (+/- known varices), alcohol abuse, abdominal operations (including gastroenteric anastomosis and abdominal aortic graft repair), and any recent endoscopic interventions (for example, bleeding after polypectomy). GI symptoms (vomiting, pain, heart burn, and so on) existing prior to bleeding manifestation can indicate a possible cause. Examples include repeat vomiting for Mallory-Weiss syndrome; alcohol abuse and/or known cirrhosis for variceal bleeding; dys- and/or odynophagia for esophagitis, esophageal ulcerations and/or tumor; and epigastric pain for PUD.
b. Comorbidities that can negatively impact UGIB and need to be taken into account include cardiovascular, pulmonary, and/or renal diseases; coagulopathies; hematological diseases (including anemia, thrombocytopenia); and conditions that predispose for aspiration of gastric content (dementia, stroke, and so on, for example).

Additionally, attention must be paid to complaints suggestive of complications (such as tenderness in gastric perforation; see following). Smoking and drinking habits should also be obtained.

Physical examination

Apart from the observations made at the primary survey, a physical examination should pay special attention to signs and symptoms of additional complications. These include signs of peritonitis (bleeding ulcers may also perforate), bowel obstruction (can mimic coffee-ground-like vomit), and pain patterns suggestive for gastrointestinal ischemia (coffee-ground-like vomit and/or melena by necrosis and bleeding).

Medication

Several drugs increase the risk of gastrointestinal bleeding, including low-dose aspirin and other antiplatelet agents, NSAIDs, anticoagulants, corticosteroids, aldosterone antagonists, and selective serotonin reuptake inhibitors (SSRIs).[6,12,20] A combination of several of these drugs further increases bleeding risk.[20] On the other hand, oral intake of iron or bismuth may lead to dark feces mimicking melena (as mentioned previously).

Laboratory tests

Blood samples must be obtained as early as possible in *every* patient with suspected acute UGIB. These tests include complete blood count, serum chemistry, lactate, and coagulation parameters. If available, point-of-care devices can accelerate results.

Anemia: Hemoglobin (Hb) and hematocrit (HCT) levels at presentation are the most important laboratory parameters for initial evaluation. Although not an independent risk factor for worse outcome,[21] decreased Hb (< 8g/dL) and HCT (<20 percent) at initial assessment are associated with a high likelihood of severe UGIB.[22] These patients are at a higher risk of being in, or developing, hemorrhagic shock. Preexisting coronary heart disease may additionally lead to cardiac hypoxemia due to reduced oxygen carriers and a worse outcome.

***NB:* Hb and HCT can be normal at baseline even in severe bleeding. Patients bleed "whole blood," and hemo-dilution (shifting fluid into the intravasal compartment) may take a while.**

Anemia can also be caused by chronic blood loss or iron deficiency. These patients may be well adapted even with low Hb values. The presence of a microcytic, hypochromic anemia indicates in this direction. However, a chronic anemia patient can still develop acute UGIB![23]

To transfuse or not to transfuse, that is the question. The decision to transfuse red blood cells (RBCs) depends on the clinical scenario and bleeding severity. Several guidelines[12,24,25] propose a restrictive transfusion strategy aiming for a target Hb between 7 g/dL to 9 g/dL. A systemic review by Odutayo et al.,[26] included five RCTs (including more than 1,900 patients both with variceal and nonvariceal UGIB) and reported a reduced risk of mortality (relative risk [RR] 0.65, 95 percent confidence interval (CI) 0.44–0.97, p=0.03) and rebleeding (RR 0.58, 0.40–0.84, p=0.004) when restrictive transfusion protocols were entertained. While there is no conclusive data for patients with preexisting cardiovascular disease (CVD), guidelines recommend adhering to a more liberal transfusion policy to reduce the risk of ischemic events in this population group.[12,24,25,27] However, all studies analyzed by Odutayo et al. excluded patients with massive hemorrhage. Additionally, patients often received very early endoscopy, which calls for caution when interpreting these findings.[28]

***NB*: In an actively bleeding shocked patient, RBC transfusion should be considered irrespective of initial Hb values.**[12,25,27]

In select cases, it might be necessary to treat patients according to massive transfusion protocols.[29]

Thrombocytopenia: An increased risk of GI bleeding has been observed in patients with thrombocytopenia.[30] While diagnostic endoscopy may be performed with a platelet count as low as 20,000/microL,[31] a platelet count below 50,000/microL in patients with UGIB should prompt transfusion.[12,25,32,33] Patients with normal platelet counts inactivated by antiplatelet therapy seem to *not* benefit from platelet transfusion.[34]

Coagulopathy can have many causes and is a known risk factor for a negative outcome. A national audit study including more than 2,700 patients with nonvariceal UGIB observed coagulopathy in 16 percent of admissions and reported a more than fivefold increase of inhospital mortality.[35] In UGIB "medically induced" (therapeutic anticoagulation +/- [dual] antiplatelet therapy) and hepatic coagulopathy are the most common causes encountered.[35] A history of congenital and acquired coagulation disorders (such as hemophilia, [acquired] von Willebrand disease, and so on) in patients presenting with acute UGIB should prompt consultation with a hematologic specialist. Prothrombin time (PT), activated partial thromboplastin time (aPTT), international normalized ratio (INR), and fibrinogen should be obtained.[12,24]

Although no clear cut-off value exists, elevated INR caused by vitamin K antagonist (VKA) should be corrected to 2.5 or below before endoscopy.[36] In stable patients this can be achieved by IV vitamin K administration. In severely bleeding, hemodynamically unstable patients, correction with prothrombin complex concentrates (PCC) or fresh frozen plasma (FFP) in combination with IV vitamin K may be necessary. The 2015 guidelines of the European Society of Gastroenterology (ESGE) recommend the use of PCC (if available) over FFP, as it has a faster onset, less risk of fluid overload, and a similar risk of thrombotic events.[12] At the same time, the preexisting indication for therapeutic anticoagulation should be reconsidered, and the possible negative effects of antagonization in patients with CVD should be discussed with a cardiologist.[25] The onset of new or direct oral anticoagulation (N/DOAC such as Dabigatran/Pradaxa®, Rivaroxaban/Xarelto®, Apixaban/Eliquis®, Edoxaban/Lixiana®) has added another facet to therapeutic anticoagulation in UGIB. There is no clear marker to show the status of anticoagulation with these drugs in a standard coagulation laboratory panel.[37] Depending on the used agent, plasma half-life times range from five to 17 hours, but are significantly prolonged in patients with reduced kidney function.[38] In moderate UGIB with normal renal function, metabolic elimination of DOACs can be awaited. However, massive hemorrhage (especially if accompanied by severely impaired kidney function) calls for active deactivation to improve coagulation. Until recently, administration of PCC and (in extremis) hemodialysis were the only available options.[36,39] In recent years, however, specific antidotes (Idarucizumab/Praxbind® for Dabigatran and Andexanet

alfa/Andexxa® for Rivaroxaban and Apixaban) were FDA-approved with satisfying results in the correction of coagulopathy.[40,41]

Serum chemistry: Several other values included in a comprehensive metabolic panel (CMP) may be of interest to suggest a possible diagnosis or to predict prognosis. ***Elevated liver enzymes*** may indicate chronic liver disease with potential varices and coagulopathy, which need to be taken into consideration for further management. Blood absorption in the small intestine paired with reduced renal perfusion in acute UGIB leads to elevated ***blood urea nitrogen (BUN)*** to creatinine ratio.[42] A BUN to creatinine ratio >30 (or urea to creatinine ratio >100) is suggestive of UGIB. Interestingly, an increase in BUN at 24 hours after admission has been observed to predict a worse outcome in nonvariceal UGIB.[43] ***Lactate*** is a basic metabolic marker easily obtained via (venous) blood gas analysis. Elevated lactate levels (>2 mmol/L) at admission have been shown to be a predictive marker for ICU admission, the need for transfusion, and mortality.[44,45] Shah et al. observed 1.4-fold increased odds for inhospital mortality with every one point increase in lactate levels.[46]

Nasogastric lavage

Nasogastric lavage (NGL) is a bedside procedure that can be performed via a large-bore nasogastric tube flushed with 50 mL of saline solution or water. The appearance of the aspirate can further clarify the bleeding site and its severity. Gross blood suggests active bleeding while brownish coffee-ground-like fluid indicates less severe and/or stopped bleeding. However, unremarkable aspirate on NGL does not definitely rule out UGIB, as more distal bleeding sites (for example, duodenal ulcers) may not have gastric reflux of blood.[47] **NGL has high specificity (95 percent) paired with low sensitivity (44 percent) for UGIB; thus, a negative lavage does not rule out bleeding.**[22] Another rationale behind NGL is to clear the stomach from blood and excess fluid. However, data comparing NGL with medical methods (such as erythromycin, discussed below) have found no benefit in NGL in terms of gastric visualization.[48,49] And while patients with a positive NGL may undergo earlier endoscopy, no advantage in terms of mortality and other clinical outcome factors has been observed.[50]

Based on these results, **guidelines do not recommend the routine use of NGL for diagnostic *and* gastric emptying.**[12, 51]

NGL can, however, be of use in select patient groups (for example, in [unresponsive] patients with a reported, non-observed episode of hematemesis) to gather information and determine whether bleeding is ongoing.

Risk stratification scoring

Several risk stratification tools have been proposed to triage patients in terms of need-for-admission, timing of endoscopy, timing of discharge, and predicting mortality.[52] The most used include the Glasgow-Blatchford Score (GBS), the (pre- and postendoscopic) Rockall Score, and the AIMS65 Score. A global multi-center prospective trial including more than 3,000 patients in six centers compared these three (and one more) scores and found the GBS to be superior in predicting the need for intervention and the likelihood of death. GBS performed well irrespective of regional differences.[53] The AIMS65 score, however, outperforms the GBS in prediction of inhospital mortality.[53,54] As current guidelines recommend the GBS alone as a first stratification tool to assess the likelihood for intervention (admission, endoscopy, blood transfusion), only this score will be addressed here.[12,25,27]

The GBS was published in 2000 and has been validated several times since then.[55–57] It consists of nine items (**Table 1**) cumulating in a score between 0 and 23. A score of ≤1 implies a low risk of intervention and safe outpatient management, which can free resources and save money.[12,24,25,27,58] A GBS >7 has been described as a predictor of the need for endoscopic therapy.[53]

Table 1. Glasgow-Blatchford Score[55,58]

Systolic blood pressure (mm Hg)	
100–109	1
90–99	2
<90	3
Blood urea (mmol/L)	
6.5–8	2
8–10	3
10–25	4
>25	6
Hemoglobin (g/dL) in men	
12–12.9	1
10–11.9	3
<10	6
Hemoglobin (g/dL) in women	
10–11.9	1
<10	6
Other Markers	
Pulse ≥100 (per min)	1
Presentation with melena	1
Presentation with syncope	2
Hepatic disease*	2
Cardiac failure **	2

*Known history, or clinical and laboratory evidence, of chronic or acute liver disease
**Known history, or clinical and echocardiographic evidence, of cardiac failure

While scores such as the GBS can aid clinical decision-making, no single tool has been shown to cover all aspects of risk patterns in UGIB and thus should always be used with care.[52,59]

Preendoscopic management

After initial evaluation and resuscitation, further management depends on the state of the patient and the "working diagnosis."

Medical therapy

Proton pump inhibitors (PPIs): The use of a high-dose PPI therapy is recommended in suspected *nonvariceal* UGIB.[12,24,27,60] However, as discrimination between nonvariceal and variceal bleeding is often not possible preendoscopically, every patient with acute UGIB should receive PPIs.

In a systematic Cochrane review, PPIs have been shown to reduce the need for endoscopic therapy, *but* no significant improvement of outcomes have been found.[61] However, this metanalysis included studies with both variceal and nonvariceal UGIB. In ulcer bleeding alone, PPIs reduce risk of rebleeding, the need for surgery and—in high-risk patients—mortality.[62] In vitro data suggest that acid suppression improves hemostasis and clot formation.[63] Other acid-suppressing drugs, namely H2-receptor antagonists (for example, famotidine, cimetidine) are not as effective as PPIs.[64]

No statistically significant differences have been observed between continuous and intermittent IV application of PPIs after an initial bolus.[65]

Thus an initial IV bolus of 80 mg (for example, pantoprazole or esomeprazole) can be followed by *either* continuous administration of 8 mg per hour *or* repeat bolus of 40 mg every eight to 12 hours.[12,24]

Once diagnosis has been established endoscopically, PPIs should be continued in acid-related hemorrhage (PUD, gastritis, esophagitis, and so on). In cirrhotic patients, however, special attention has to be paid to possible side effects. While PPI therapy seems to be beneficial in terms of rebleeding after an episode of variceal hemorrhage, an increased risk of mortality has been observed, probably due to an increase in spontaneous peritonitis.[66–68]

Erythromycin: Erythromycin (a macrolide antibiotic) has been shown to significantly improve visualization of the stomach in severe UGIB by increasing motility and gastric emptying.[69,70] Thus administration of a single IV dose of 250 mg Erythromycin 30 to 120 minutes prior to endoscopy is recommended. Specific contraindications apart from allergy include prolonged QT interval.[12,24,71] Alternative agents such as metoclopramide have been little studied and should be considered with care due to their possible neurologic side effects.[12]

Tranexamic acid (TXA): Until recently, evidence of a positive effect of TXA on survival and rebleeding was of low quality with equivocal results.[71] However, in 2020 a multicenter, double-blind, placebo-controlled study found no beneficial impact of TXA on survival in acute GI bleeding.[72] Based on these findings, routine use of TXA cannot be recommended.

Additional medical therapy in patients with suspected variceal bleeding, including patients with known cirrhosis, a history of variceal bleeding, and/or indicative findings in laboratory work-up or clinical examination (Caput medusae, jaundice, and so on).

Antibiotics: Patients with cirrhosis and active variceal bleeding are at a high risk of bacterial infection and should have IV antibiotics initiated prior to endoscopy. If the diagnosis is confirmed, therapy should be continued for five to seven days. Therapy should cover a wide bacterial spectrum, especially Gram-negative bacteria. Depending on regional resistance rates and local antimicrobial policies, possible antibiotics include ceftriaxone (for example, 2g/24h) or ciprofloxacin (2x500mg/24h).[24,25]

Vasoconstrictors: Intravenous administration of vasoconstricting agents is recommended as soon as possible in suspected variceal bleeding and should be continued for up to five days after bleeding control.[24,25,73] Terlipressin, Somatostatin, or Octreotid can be used for this purpose. They do not differ significantly in efficacy and risk profile (**Table 2**).[24,74] Care should be paid to possible adverse effects in patients with known ischemic cardiovascular conditions.

Table 2. Initial dose and continuous application rates for vasopressors in variceal hemorrhage

	Terlipressin	Somatostatin	Octreotid
Loading dose (pre-endoscopic)	2 mg IV	250 mcg IV	50 mcg IV
Continuous dose for 5 days	1 mg IV every 6 hours	250 mcg/h	25 mcg/h

Imaging studies

Radiological studies should be entertained when differential diagnoses must be addressed prior to endoscopy. These include bowel obstruction, perforation, and, rarely, aorto-enteric fistulae. In all three indications, endoscopy will not be useful and may even be dangerous to perform. Imaging

modalities vary according to the clinical question and range from plain abdominal X rays to CT scans, including CT angiography.

Radiological interventions such as angioembolization are usually to be considered after a diagnosis is confirmed by endoscopy and endoscopic treatment fails. This step will be addressed later.

Endoscopy

Who? Endoscopy is the main diagnostic and therapeutic procedure in acute UGIB **(Figure 2)**. It should be available on call on a 24/7 basis and offered to every patient.[12]

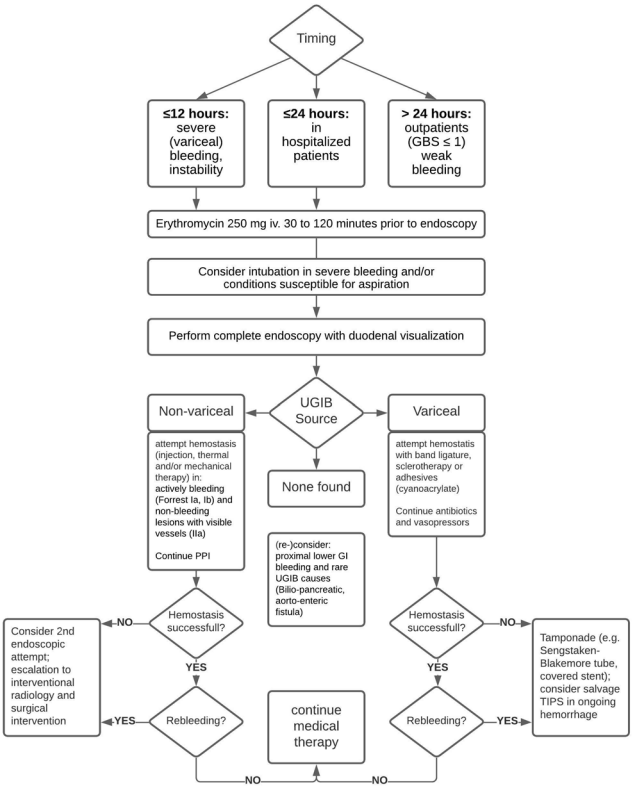


Figure 2. Preendoscopic and further management

When? The timing of endoscopy depends on the bleeding source, severity, symptoms, and state of the patient and is usually defined as very early (≤12 hours), early (≤24 hours), and delayed (>24 hours). In general, most patients hospitalized for acute UGIB should undergo endoscopy within 24 hours.[12,27,51] A recent controlled randomized study found no benefit in terms of mortality and rebleeding between very early and early endoscopy in hemodynamically stable (or successfully stabilized) patients.[75] However, patients with hemodynamic instability *despite* ongoing resuscitation and/or cirrhosis with suspected variceal hemorrhage should receive early or urgent endoscopy within 12 hours of presentation.[12,24,60,73,76,77] Whenever possible, endoscopy should not be performed before measures to stabilize hemodynamics have been employed.[71]

On the other hand, patients with hemodynamic stability and a low GBS score can safely receive delayed endoscopy, in GBS ≤1 even on an outpatient basis.

How? Patients with severe ongoing bleeding (for example, ongoing hematemesis), encephalopathy, or agitation should be intubated for airway protection prior to endoscopy.[12,77] As mentioned above, preendoscopic NGL is not routinely recommended, while a bolus of erythromycin can be given to enhance gastric emptying. Irrespective of intubation or spontaneous breathing, all patients need to be monitored meticulously during intervention and should receive additional oxygen. To improve visualization, it might be necessary to reposition (from left lateral to right lateral) the patient several times during the procedure.

***NB:* A complete gastroscopy (including visualization of the duodenum) should always be performed. Do not stop at the first possible bleeding source. A patient could have severe esophageal varices and still bleed from a duodenal ulcer!**

Endoscopic interventions

Over the years a wide range of endoscopic hemostatic therapies has been developed, which in part can be used individually or combined to achieve hemostasis.

Injection therapy aims at a local tamponade by injecting a certain amount of fluid. Depending on the substance used (**Table 3**), vasoconstriction, tissue sclerosis, and tissue adhesion can be additionally achieved.[78]

Table 3. Substances for injection therapy

Substance	***Additional effect***
Saline + Epinephrine (1:10,000, 1:20,000)	Vasoconstriction
Sclerosing agents (for example, Ethanolamine oleate, Ethanol, Sodium morrhuate)[78]	Tissue injury and subsequent sclerosis. CAVEAT: Tissue necrosis
Adhesives	*Biological*: thrombin, fibrin *Synthetic:* cyanoacrylate glue

Thermal coagulation can be achieved by either contact (bipolar cautery, thermal probes) or noncontact devices (for example, argon plasma coagulation [APC]). The generated heat leads to edema, coagulation, tissue sealing, and indirect activation of the coagulation cascade.[79]

Mechanical therapy uses deployable clips or band ligation devices to directly compress the bleeding site. Clips exist in a variety of lengths and types. Through-the-scope clips are applied via the working channel. Over-the-scope clips (OTSC) are connected to an applicator cap and are deployed after tissue is sucked into the cap. Band ligation devices are usually used to treat varices and hemorrhoids. Like OTSC application, the target tissue is sucked into an applicator cap and the band then deployed via a thread.

Topical therapy using hemostatic sprays has been developed in recent years.[80] These include inorganic (for example, TC-325, Hemospray®, Cook Medical Inc, North Carolina, U.S.) and organic (for example, starch based, EndoClot®, EndoClot Plus Inc, California, U.S.) powders that enhance clotting at the bleeding site. The advantage of this approach is the possibility to spray hemostatics on large areas as well as hard to reach bleeding sites. Treatment efficacy has been reported in several studies.[81,82] Active arterial bleeding may wash away the hemostatic before it can work.

The therapy to use depends on the bleeding source, severity, and the endoscopic skill level available.

Causes of acute UGIB

Bleeding sources are mostly identified at endoscopy. If no lesion can be identified, further diagnostics (in other words, angiography, CT scan) need to be employed.

Nonvariceal hemorrhage

Nonvariceal bleeding sources account for the majority of UGIB. An analysis of a nation-wide inpatient database in the U.S. between 2002 and 2012 found PUD to be the most common source (47 percent) of acute UGIB followed by gastritis (18.1 percent), esophagitis (15.2 percent), Mallory-Weiss Syndrome (6.9 percent), and angiodysplasia (6.2 percent). Other less frequent sources included neoplasms (3.7 percent) and Dieulafoy lesions (1.5 percent).[7]

Nonvariceal lesions can be classified according to Forrest.[83] This classification not only describes appearance and bleeding activity, but also allows a risk estimation for rebleeding (**Table 4**).[84]

Table 4. Forrest classification

Type of hemorrhage	*Risk of rebleeding/ persisting bleeding*[84]
Ongoing bleeding	
F Ia: spurting hemorrhage	Up to 100 percent
F Ib: oozing hemorrhage	10–27 percent
Signs of recent bleeding	
F IIa: nonbleeding visible vessel	Up to 50 percent
F IIb: adherent clot	8–35 percent
F IIc: flat pigmented spot (hematin)	<8 percent
No bleeding	
F III: clean base ulcer	<3 percent

Forrest Ia, Ib, and IIa should receive endoscopic treatment (**Figures 3–7**). Whether or not clot removal (either by flushing or mechanically) should be undertaken in IIb lesions is up for debate.[12,27] The rationale for removal is to identify and treat the underlying cause (for example, visible vessel). While often only used in PUD, the Forrest classification can describe all nonvariceal bleeding sources. Further risk factors for rebleeding are lesion size (>2 cm) and location (lesser curvature, proximal stomach, posterior duodenal wall).[12,24,45,85]

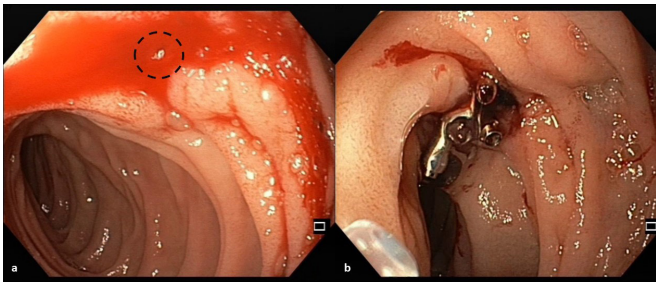


Figure 3. a. Forrest Ia duodenal ulcer (spurting bleeding encircled); b. Hemostasis achieved with clips

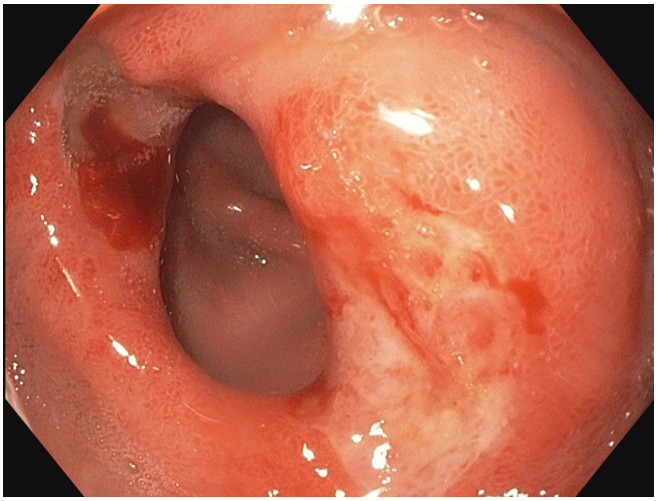


Figure 4. Kissing duodenal ulcers (left Forrest Ib, right III)

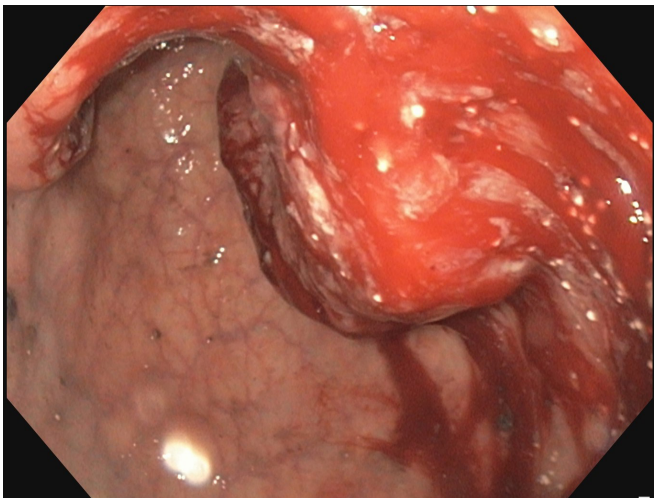


Figure 5. Forrest Ib from a gastric cancer; this patient required acute gastrectomy after failed endoscopic hemostasis and persisting bleeding with hemodynamic instability

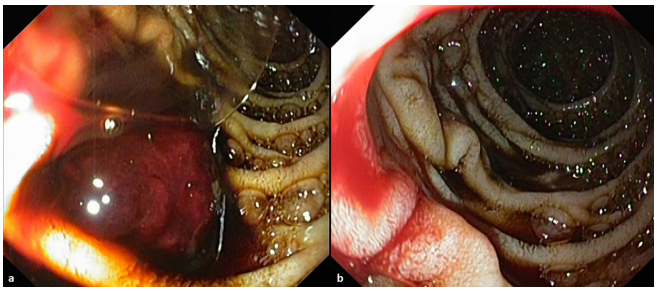


Figure 6. a. Forrest IIb duodenal ulcer; b. Forrest Ib after clot removal by soft flushing

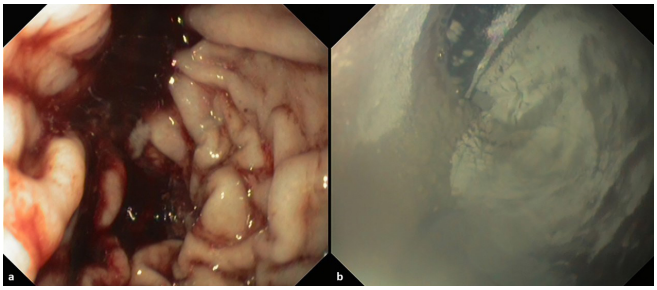


Figure 7. a. Diffuse oozing gastric fundus (Forrest Ib); b. Hemostasis achieved with hemostatic powder

Depending on the identified bleeding source (ulcer, tumor, gastritis, and so on) biopsies should be obtained to identify (pre-)malignancy or infection with H. pylori. In case of presence of the latter, eradication adhering to regional resistance rates should be initiated.

Endoscopic therapy. There is currently no evidence favoring one standard treatment method over the other.[12] However, **injection therapy with epinephrine alone is not recommended due to higher rebleeding risk**[86] and should always be combined with other modalities (sclerosing, mechanical or thermal). If these measures do not stop the bleeding, the guidelines recommend advancing to topical hemostatic powders and/or OTSC.[24,27]

What to do when endoscopy fails? In case of rebleeding after successful initial endoscopic control, a second interventional re-endoscopy should be performed.[12] If bleeding control cannot be achieved by endoscopic means, radiologic intervention and/or surgery should be considered. Selective trans-arterial angioembolization (SAE) has been shown to be effective (in terms of mortality and need for further intervention) in UGIB but produces higher rebleeding rates than surgery (**Figure 8**).[87–89] Prophylactic SAE in high-risk lesion after endoscopic hemostasis has shown no benefit in terms of rebleeding and mortality.[90] For angioembolization, patients should be hemodynamically stable.[85]

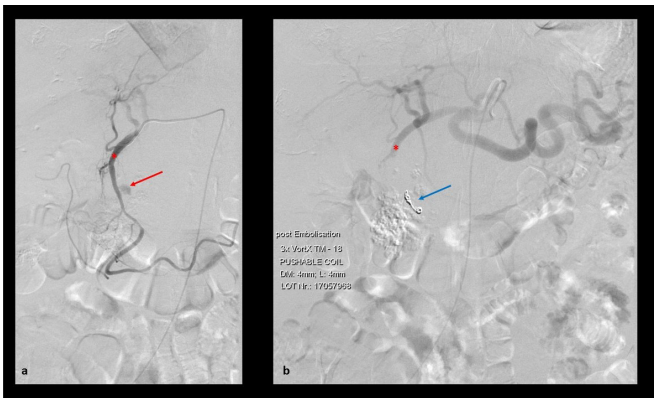


Figure 8. a. Contrast blush (red arrow) from the gastroduoedenal artery (*). b. cessation of bleeding after coiling (blue arrow).

Surgery is necessary in about 2 percent of patients with acute UGIB.[91] It should be entertained if hemostasis cannot be achieved by endoscopy and SAE is not available or has failed. Surgeons should be present at a preoperative endoscopy or receive information on the location of the bleeding source. The 2020 WSES guidelines recommend an open approach in acute UGIB surgery.[85]

The method and extent of surgery depend on bleeding cause, site, and characteristics. Surgery can vary from simple oversewing to extensive resection +/- vessel ligation and/or selective vagotomy. In suspicious lesions a biopsy should be obtained. In the majority of bleeding gastric ulcers simple oversewing of the lesion (+/- previous excision or biopsy) will suffice. Duodenal ulcers, on the other hand, most often occur on the posterior wall, and hemorrhaging may be directly fed by the gastroduodenal artery (GDA). Duodenal lesions have been shown to yield higher mortality and reoperation rates than gastric ulcers.[92] Thus if oversewing of a duodenal ulcer is feasible, a triple ligation of the GDA should be additionally performed. The GDA originates from the common hepatic artery, a branch of the celiac trunk, and passes dorsally to the duodenum. It forms anastomotic connections with the splenic artery (via the right and left gastroepiploic arteries) and the superior mesenteric artery (via the superior and inferior pancreaticoduodenal arteries). Due to this rich anastomotic network, simple ligation of the GDA does not suffice; all three vessels (GDA, right gastroepiploic, and superior pancreaticoduodenal artery) should be ligated (**Figure 9**).[85] Attention must be paid to differentiate with absolute certainty the GDA from the proper hepatic artery prior to ligation to prevent inadvertent disruption of hepatic circulation. Considering vagotomy in peptic ulcer bleeding, an analysis of 775 patients from the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP®) database,[93] found improved mortality (AOR [95 percent confidence interval] 0.39 [0.19–0.80]), but higher morbidity (AOR 1.39 [0.88–2.20]) rates after vagotomy and drainage as compared with local procedures alone.

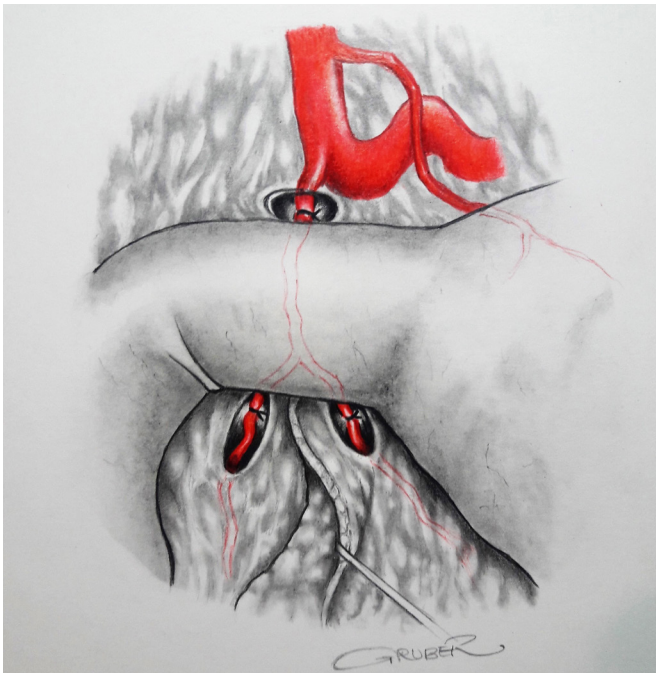


Figure 9. Schematic triple ligation of the gastroduodenal artery and its (anastomotic) branches. *Illustration by Andreas Gruber*

In case of bleeding tumors (**Figure 5**), malignancy of these lesions is highly probable. If possible, hemostasis should be achieved by endoscopy or SAE.[94] Outcomes after emergency resection in bleeding gastric cancer have been shown to be poor both in terms of oncological adequacy and survival rates.[95] Thus, these patients may profit from (semi-) elective resection after preoperative optimization, and emergency operation should be avoided if possible.

Variceal hemorrhage

In the U.S., bleeding esophageal varices account for about 1.8 percent of acute UGIB[7] but yield substantial inhospital mortality rates (up to 15 percent).[96,97] While esophageal varices as a complication of portal hypertension are primarily a case for a gastroenterologist, surgeons may become involved in treating the acutely bleeding patient (**Figure 10**). For this eventuality there are several important aspects to know.

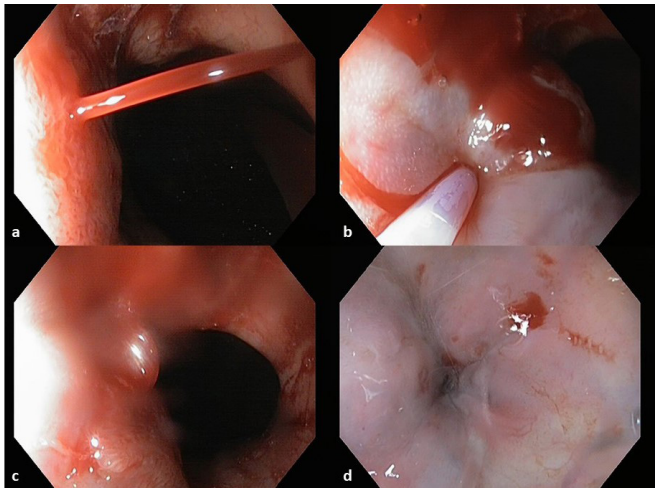


Figure 10. a. Spurting variceal bleeding at gastro-esophageal junction; b. Injection of a sclerosing agent; c. Reduced bleeding intensity after first sclerosing attempt; d. Result after extensive sclerotherapy.

While there are several classifications describing location and bleeding risk, only the location is of interest for our purpose. Varices can occur in various locations of the upper GI tract, including esophagus, gastric fundus, and corpus, as well as the duodenum. This is important to know, as some therapeutic options (for example, Sengstaken-Blakemore tube) do not work in all variceal locations.

Additionally, about 20 percent of patients suspected of variceal hemorrhage do not bleed from varices but from peptic ulcers.[98] Gastroscopy should always screen the complete stomach and the descending part of the duodenum for other bleeding lesions.

In variceal bleeding, band ligation is considered the gold standard, but injection with sclerosing agents or cyanoacrylate are other treatment options.[73,99–101] If bleeding cannot be controlled with these measures or endoscopic expertise is not available, tamponade can be achieved using a Sengstaken-Blakemore tube or special covered stents in esophageal varices and a Linton-Nachlas tube in gastric fundus varices.[73,102] Tamponade can be upheld for up to 24 hours, allowing for stabilization and initiation of further therapy. If bleeding is still ongoing or only moderately controlled, acute trans-jugular intrahepatic portosystemic shunting (TIPS) as a salvage procedure may be an option. This procedure may require the patient be transferred to a specialized center.[73]

Rare bleeding sources

Biliopancreatic hemorrhage includes haemobilia and haemosuccus pancreaticus and manifests through bleeding from the duodenal papilla.

In **haemobilia**, bleeding originates in the hepatobiliary tract and most often occurs after iatrogenic trauma (for example, TIPS, percutaneous transhepatic cholangiography [PTC], endoscopic retrograde cholangiography [ERCP], biopsies, cholecystectomy).[103] Other potential causes include tumors, hepatic trauma, and/or ruptured aneurysms of the hepatic artery. About one-third of patients present with a classical triad of upper abdominal pain, UGIB, and jaundice.[104] Diagnosis of this rare condition is based on bleeding from the duodenal papilla plus a CT angiogram. The treatment of choice in ongoing bleeding is angiographic embolization, although surgical hemostasis (for example, selective ligation of vessels) may be necessary.[104,105]

Haemosuccus pancreaticus describes hemorrhage from the pancreatic duct and occurs in an estimated one in 1,500 cases of GI bleeding.[106] In the majority of cases, ruptured aneurysms (either pseudo or primary) of peripancreatic vessels lead to this condition, often on the base of chronic pancreatitis.[107] Other causes include tumors, arteriovenous malformations, persistent ductal stones, pancreatic trauma, and iatrogenic lesions. Bleeding can occur either into the pancreatic duct or into pseudocysts.[108] Signs and symptoms can include upper abdominal pain, increased pancreatic enzymes, and signs of active or stopped UGIB (melena, anemia, rarely hematemesis). Of note, endoscopically confirmed signs of hemorrhage only occur in 30 to 50 percent of patients.[106,108] Diagnosis thus needs to be confirmed by CT angiography. As in haemobilia, the first line of treatment in persistent bleeding is interventional radiology. Surgery should be entertained if angiographic control fails or is not available in a reasonable time in hemodynamically significant bleeding. The type of surgery depends on the bleeding location and ranges from pseudoaneurysm exclusion to all types of pancreatic resections.[108]

Aorto-enteric fistula are a rare but severe condition with inhospital mortality around 30 percent.[109,110] While spontaneous fistulae have been described, the majority of cases develop as a long-term complication of prosthetic aortic repair.[109] According to a metanalysis including 752 patients, signs of UGIB are present in about 70 percent of cases. About one-third of patients presents with hemodynamical instability, and 39 percent present with signs of sepsis.[110] The usual location of these fistulae lies in the distal duodenum, which is rarely reached by conventional gastroscopy. Diagnosis is thus established by CT angiography and surgical intervention by skilled vascular surgeons is indicated.[110]

Conclusion

Acute upper-GI bleeding is a common cause of hospital admissions worldwide and can be managed endoscopically in most cases. The patient should receive a first evaluation quickly after hospital contact. Risk stratification can help use the available resources. Rare differential diagnosis should be kept in mind when no obvious sign of bleeding can be identified at upper endoscopy.

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CHAPTER 4

Management of Incarcerated and Strangulated Hiatal Hernias

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Abstract

Paraesophageal hernias (PEH) account for 5 percent of all hiatal hernias. While some patients remain asymptomatic and their hernias are diagnosed incidentally, others present with a wide variety of symptoms secondary to gastroesophageal reflux and/or intermittent obstruction.

Rarely, patients present with acute symptoms with incarceration, strangulation, and perforation. In these cases, surgical repair is indicated, often emergently. This procedure can be very challenging, with potential life-threatening complications. The laparoscopic PEH repair is the preferred approach in most patients.

Introduction

Hiatal hernias (HH) are a common finding in the general population, and due to the progressive aging of patients and the epidemic of obesity the number of HH is expected to increase in the future.[1] Interestingly, the real incidence of these hernias is unclear because many patients are asymptomatic, and the HH is often diagnosed incidentally in the context of chest or abdominal imaging for unrelated conditions.

Hiatal hernias occur due to a progressive widening of the diaphragmatic esophageal hiatus and weakening of the phreno-esophageal membrane. Consequently, the stomach and other intra-abdominal organs may herniate through the diaphragmatic hiatus into the mediastinum.

Hiatal hernias are classified into four types:

- Type I "sliding hernia": The esophagogastric junction (EGJ) herniates above the diaphragm into the mediastinum.
- Type II: A portion of the stomach is herniated into the mediastinum alongside a normally positioned (in other words, intra-abdominal) EGJ.
- Type III: The EGJ is above the hiatus and a portion of the stomach is folded alongside the esophagus.
- Type IV: An intra-abdominal organ other than the stomach is additionally herniated through the hiatus.

Type I hernias are the most common and account for up to 95 percent of the total prevalence. Type II, III, and IV hernias are together termed paraesophageal hernias (PEHs) and account for the remaining 5 percent of hiatal hernias.

Clinical Findings

Most patients are asymptomatic, and their hernias are diagnosed incidentally. However, large PEH (type III is the most common) may cause a wide variety of symptoms due to gastroesophageal reflux (heartburn, regurgitation, respiratory problems due to aspiration) or intermittent obstruction (postprandial bloating, dysphagia, epigastric and chest discomfort). Anemia secondary to gastric erosions can also be present.

Rarely, patients may present with acute severe symptoms with incarceration, strangulation, and perforation, and these patients may require emergent surgery.

Preoperative work-up

For an elective repair of a PEH, a barium swallow, an upper endoscopy, and esophageal manometry are often performed to define the anatomy **(Figures 1 and 2)** and esophageal function and to plan the best therapeutic approach.

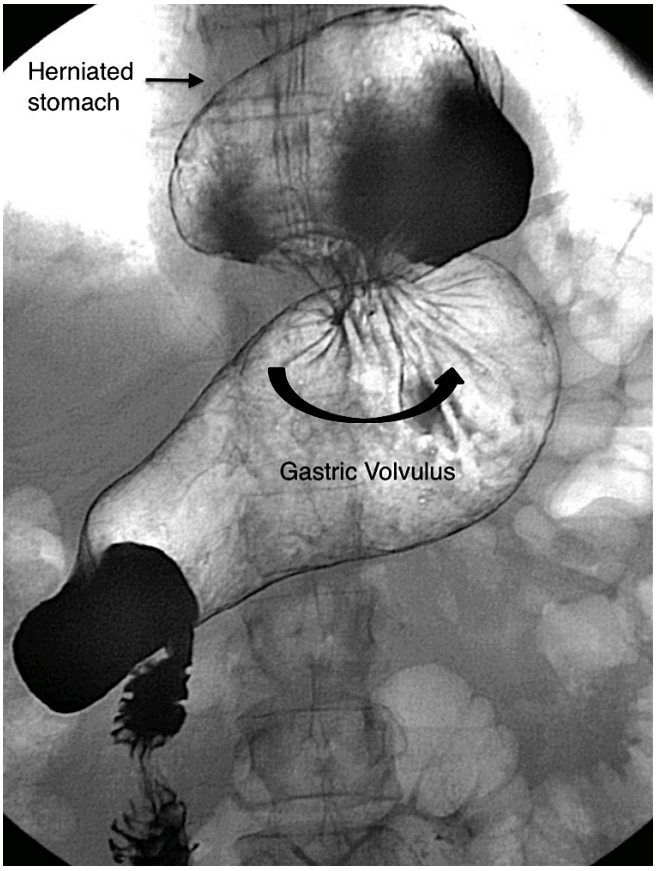

Figure 1. Barium swallow showing a paraesophageal hernia with a gastric volvulus

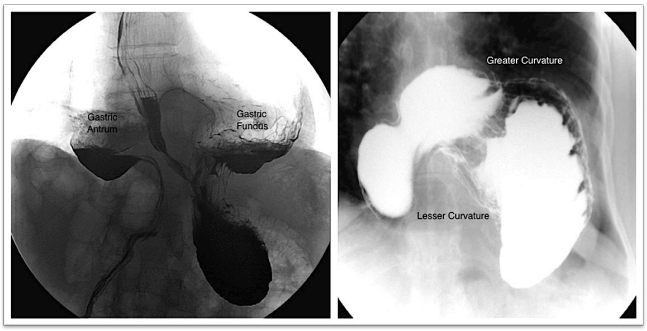

Figure 2. Barium swallow showing herniation of the entire stomach into the posterior mediastinum

However, in emergent situations, an abdominal and chest computed tomography (CT) scan is often the only test that is performed once a cardiac and respiratory cause is excluded by appropriate tests.

Barium esophagram: Key for the diagnosis of PEH and description of its anatomy. The ability to distinguish between different hernia types helps planning the procedure.

Upper endoscopy: It is important to rule out malignancy and determine the presence of esophagitis, Barrett esophagus, gastritis, Cameron ulcers, and/or peptic ulcer disease.

Esophageal manometry: Helps tailoring the operation; in patients with aperistalsis or severely impaired peristalsis we perform a partial fundoplication. If the manometry is not technically feasible (for example, the patient cannot tolerate the catheter or in case of acute presentation), a partial fundoplication is preferred.

Pulmonary function tests and cardiac risk assessment: Patients with PEH are often elderly, and these tests may help in the decision-making and during the perioperative management. Regarding the 24-hour pH monitoring study, it does not add relevant information preoperatively. The operation will undoubtedly alter the anatomy and physiology of the EGJ. Therefore, we believe a fundoplication to prevent reflux should be performed regardless of the presence or not of GERD preoperatively. In addition, it also helps secure the EGJ below the diaphragm.

Abdominal and chest CT scan: This test provides additional information regarding the anatomy of the hernia and may show the herniation of other abdominal organs (type IV hernia).

Surgical Repair of PEH

Historically, surgical repair has been advocated in all patients with PEH, even when asymptomatic, due to the considerable mortality associated with acute hernia incarceration and strangulation. Currently, nonsurgical management is considered a better alternative in asymptomatic or minimally symptomatic patients, because the risk of strangulation is lower than the risk of morbidity associated with the operation. Therefore, surgical repair is indicated mainly for symptomatic PEH.[2]

Traditionally, PEH repair required either a laparotomy or thoracotomy, and these approaches were associated with high morbidity. Since its introduction in 1992, the laparoscopic approach has been increasingly embraced due to its improved postoperative outcomes.[3,4] Nowadays, the vast majority of patients with PEH are managed with a laparoscopic approach.

Laparoscopic PEH Repair

Trocar placement

We use five ports for the procedure: one for the camera, two for the operating surgeon, one for the assistant, and one for the liver retractor. The first port is usually placed in the midline, about 14 cm below the xiphoid process; it also can be placed slightly to the left of the midline to be in line with the esophagus. This port is used for insertion of the scope.

The second port is placed in the left midclavicular line at the same level as port one, and it is used for the insertion of a Babcock clamp for traction, a grasper to hold the Penrose drain while surrounding the esophagus, or for devices used to divide the short gastric vessels. The third port is placed in the right midclavicular line at the same level of the other two ports, and it is used for the liver retractor. The fourth and fifth ports are placed under the right and left costal margins so that their axes and the camera form an angle of approximately 120°. These ports are used for the insertion of dissecting and suturing instruments **(Figure 3)**.

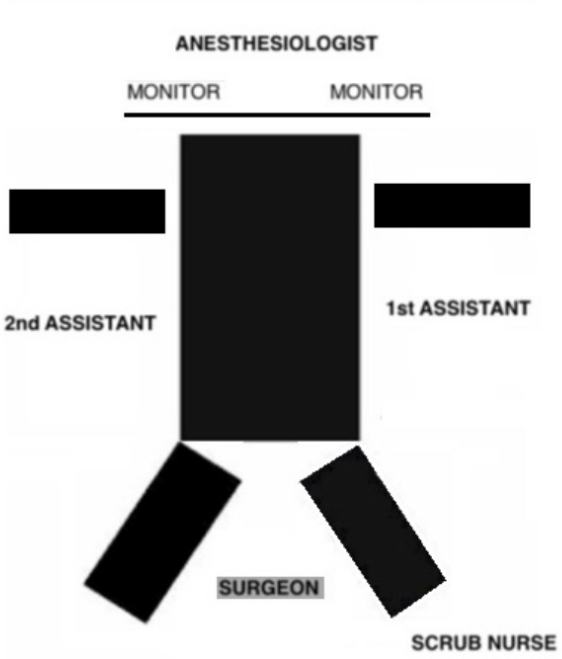

Figure 3. Position of the team (surgeon, assistants, anesthesiologist, and scrub nurse) around the operating table

Dissection and reduction of hernia sac

Reduction of the stomach into the abdominal cavity is done by gently pulling the herniated stomach out of the posterior mediastinum down into the abdomen using a Babcock clamp. This maneuver usually resolves a volvulus. The dissection is started along the greater curvature, the short gastric vessels are divided, and the left pillar of the crus is reached. Excessive force should be avoided during the reduction of the stomach to prevent gastric injury or perforation. Starting the dissection along the greater curvature of the stomach by dividing the short gastric vessels reduces the risk of injury of an accessory left hepatic artery that can occur if the dissection is started over the gastrohepatic ligament (can be challenging to control the resultant bleeding if the arterial gastric stump retracts above the diaphragm into the mediastinum).

The hernia sac is then incised at the junction with the left crus and an anterior and lateral mobilization of the esophagus is performed. Once the initial dissection from the left has been completed and more stomach is reduced, the gastro-hepatic ligament is opened toward the right pillar of the crus, and the esophagus is further dissected in the posterior mediastinum. A posterior window behind the esophagus is created, and a Penrose drain is placed around the esophagus incorporating both the anterior and posterior vagus nerves. The hernia sac is then freed from mediastinal adhesions by blunt dissection. We do not attempt the complete excision of the hernia sac.

Esophageal mobilization

The mediastinal dissection is extended proximally to have at least 3 cm of esophagus below the diaphragm without tension.

It is of note that after extended mobilization of the esophagus in the posterior mediastinum, the presence of a short esophagus is rare. Therefore, esophageal lengthening procedures (for example, stapled wedge gastroplasty) are rarely needed.

Closure of the esophageal hiatus

Proper exposure of the hiatus is obtained by retraction of the esophagus upward and toward the patient's left with the Penrose drain. The closure of the diaphragmatic crura is done with interrupted nonabsorbable sutures. The first stitch is placed about 1 cm posterior to the esophagus. Subsequent stitches are placed below the first one. Usually only posterior sutures are necessary, but sometimes one or two additional stitches anterior to the esophagus are needed to further narrow the hiatus.

As the hiatus is often very large, the closure of the crura can be under tension. If there is considerable tension placed on the closure, a relaxing incision on the right hemidiaphragm (incision just lateral to the right crus) can help approximate the right crus with the left one. If this incision is performed, a mesh patch over the diaphragmatic defect is needed.

There is a point of controversy regarding the use of mesh to reinforce the closure. A nonabsorbable mesh is not recommended due to potential complications such as mesh erosion into the esophagus or the aorta. Biological meshes with absorbable material are a safer alternative, but the efficacy in avoiding recurrence is unfortunately minimal. In 2006, a randomized trial showed a significant reduction of the six-month recurrence rate with the use of a biologic prosthesis as compared with cruroplasty alone (9 versus 24 percent).[5] The same study group, however, later reported a similar five-year recurrence rate between the two groups (54 versus 59 percent).[6]

In 2015, Dr. Watson published the results of a randomized controlled trial of large hiatus hernia, comparing the outcome of the repair with sutures (43 patients), versus absorbable mesh (41 patients), versus nonabsorbable mesh (42 patients).[7] Among the patients, 96 percent were followed up to 12 months, with objective follow-up data in 92.9 percent. The study showed no significant difference for recurrent hiatus hernia. The clinical differences were unlikely to be clinically significant. Overall outcomes after sutured repair were similar to mesh repair. The same group published the five-year follow-up of that trial in 2020.[8] The follow-up showed no advantage for mesh repair, and symptoms outcomes were worse after repair with absorbable mesh. Overall, the results of the long-term follow-up of the initial trial did not support mesh repair for large hiatus hernias.

Another randomized clinical trial published in 2018 compared the laparoscopic hiatal hernia repair using sutures (36 patients) with sutures reinforced with nonabsorbable mesh.[9] At one-year follow-up the recurrence rate and the symptomatic outcome were similar between the two groups. It is important to remember that as shown by Oelschlager and colleagues, most of the recurrences are small asymptomatic sliding hernias that do not need repair.[6] Based on these data and our personal experience, we do not recommend the routine use of mesh. Its use should be reserved for selected patients, such as for patients in whom a tension-free cruroplasty cannot be achieved or for re-do PEH repair.

Fundoplication

The fundoplication is key to either treat gastroesophageal reflux present preoperatively or prevent the development of postoperative reflux secondary to the extensive dissection of the gastroesophageal junction. In addition, the fundoplication helps anchor the stomach below the diaphragm.

The stomach is passed behind the esophagus, and a shoe-shine maneuver is performed to verify sufficient fundic mobilization and to avoid having part of the gastric fundus above the wrap. For a total 360° fundoplication, a 56 French bougie is inserted down the esophagus into the stomach to prevent postoperative dysphagia. Then, the gastric fundus is pulled under the esophagus with two graspers, and the left and right sides of the fundus are wrapped above the esophagogastric junction. A Babcock clamp is used to hold the two sides of the fundus during the placement of the first stitch. A 360º fundoplication is created by placing three stitches of nonabsorbable material at 1 cm intervals to approximate the right and left side of the fundoplication. The length of the anterior portion of the fundoplication should be approximately 2 cm.

The partial posterior 240° fundoplication (Toupet fundoplication) is created by placing six stitches of nonabsorbable material. The right and left sides of the fundus are separately sutured to the right and left side of the esophagus, leaving 120º of the anterior esophageal wall uncovered. This procedure if often preferred when the preoperative esophageal function is unknown because of the emergent nature of the operation, particularly in elderly patients.

Care must be taken to avoid having a wrap under tension. For instance, if the wrap does not remain in the right side after pulling the fundus under the esophagus and retracts back to the left, a partial fundoplication is preferred. Some studies have shown the value of a gastropexy in avoiding a recurrent gastric volvulus and recurrence of the hernia. The anterior gastropexy must be performed starting with sutures of nonabsorbable material between the anterior wall of the stomach and the posterior sheath of the right rectus muscle. It is then extended down toward the left with stitches placed between the anterior gastric wall all the way to the greater curvature and the posterior left rectus sheath. In 2003, Ponsky et al.[10] reported the results of 28 patients with PEH who underwent reduction of the stomach, excision of the sac, fundoplication, and anterior gastropexy. At a follow-up of two years, there were no recurrences.

We do not agree with the use of a gastrostomy as a form of gastropexy. We have seen many cases of acute re-herniation of the stomach, with consequent pulling of the tube out of the stomach and leakage in the posterior mediastinum. In addition, the gastrostomy is uncomfortable and prone to infections and other complications.

Postoperative care

Patients start with clear liquids and then soft diet the morning after the procedure. They are usually discharged after 24 to 48 hours, and they are instructed to avoid meat, bread, and carbonated beverages for the following two weeks. The time to full recovery ranges between two and three weeks.

Urgent and Emergent Surgery

Some patients present with chest and abdominal pain and vomiting. A CT often shows herniation of a good part of the stomach into the chest, with a gastric volvulus. In these patients, we do perform an upper endoscopy to determine if ischemia or bleeding are present. If the test is negative, we do leave a nasogastric tube for decompression. Most of the time, this approach transforms an emergent operation into a semi-elective operation, allowing proper resuscitation and optimization of the patient. Kohler and colleagues reported on 24 patients who presented with acute symptoms due to an intrathoracic stomach.[11] They found that only 12.5 percent of patients required emergency surgery (within 24 hours), while 25 percent were operated on within seven days and 62.5 percent eventually had an elective repair within four weeks. Similarly, Wirshing et al. reported on 38 patients who were admitted for an acute presentation of a herniated stomach.[12] Only 8 percent of patients required emergency surgery, while 92 percent had initially gastric decompression followed by surgery. When compared with other patients who had elective surgery for repair of a PEH, there was no increase in morbidity or mortality.

A minority of patients will present with severe ischemia and/or gastric perforation. In these cases, emergent surgery is indicated. These patients are often quite sick, so the approach needs to be tailored to the physiologic condition and the findings. After reduction of the stomach and resolution of the volvulus, sometimes an area of ischemia and/or a perforation is found along the greater curvature of the stomach. In these cases, this area can be removed using staplers, a gastropexy is done, drains are left, and a feeding jejunostomy is performed. In rare cases the entire stomach is necrotic, which requires a gastrectomy, stapling of the distal stomach, and a cervical esophagostomy (plus a feeding jejunostomy). At a later date, a colon interposition will be used to restore the continuity of the gastrointestinal tract.

Outcome Is Dependent on Surgical Volume and Experience of the Surgeon

A major advantage of delaying the repair of a PEH is the possibility to refer the patient to a high-volume center and an expert surgeon to improve the chances of a successful outcome. In fact, as for other procedures, the relationship between high-volume surgeons/centers and the outcome of the repair of a PEH has been clearly shown.[13,14,15]

Using the National Inpatient Sample (2000–2013), Schlottmann et al. analyzed the impact of surgical volume on perioperative results for 63,812 PEH repairs in the U.S.[13] Surgical volume was categorized as small (fewer than six operations/year), intermediate (six to 20 operations/year), or high (more than 20 operations/year). The findings of this study showed that the rate of laparoscopic procedures was significantly different among groups: small volume, 38.4 percent; intermediate volume, 41.8 percent; and high volume, 67.4 percent ($p<0.001$). Similarly, the surgical morbidity showed an inverse relationship with the volume: small volume, 26.4 percent; intermediate volume, 24.1 percent; and high volume, 12.7 percent ($p<0.0001$). Similar findings were documented in relationship to mortality: low volume, 2.9 percent; intermediate volume, 2.4 percent; high volume, 0.8 percent ($p<0.0001$). In addition, the authors found that during the last decade the rate of PEH repairs in high-volume centers has increased from 65.8 to 94.4 percent.[13] Similar findings were reported by Whealon and colleagues.[14] Finally, Markar and colleagues analyzed 12,441 admissions for acute PEH and found that high-volume centers had a significant

reduction in utilization of emergent surgery (8.8 versus 14.9 percent; p<0.0001), 30-day mortality (5.3 versus 7.8 percent; p<0.0001), and 90-day mortality (9.3 versus 12.7 percent; p<0.0001) when compared with low-volume centers.[15]

Conclusion

The repair of a paraesophageal hernia is a complex operation whose outcome depends on many factors, including the clinical presentation and comorbid condition of the patient, the expertise of the surgeon and the volume of the center, and the emergent versus semi-elective or elective type of operations. The best results are obtained in high-volume centers by experienced foregut surgeons when the operation is not performed emergently, and when ischemia or perforation of the stomach are not present.

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CHAPTER 5

Management of Esophageal Perforation

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Key words:

Esophagus, esophageal, perforation, laceration, management, surgical, conservative

Abstract

Despite being an uncommon event, esophageal perforation is a life-threatening condition and represents a surgical emergency. Rapid diagnosis and early intervention are essential in managing patients and lowering morbidity and mortality. While primary repair remains the gold standard surgical operation to restore esophageal integrity, other options are available. This chapter addresses the topic in a systematic way, discussing operative and nonoperative options for the management of esophageal perforation.

Introduction

Irrespectively of its etiology, esophageal perforation is always a surgical emergency. A diagnostic delay greater than 24 hours after the perforating event nearly doubles the overall mortality rate (14 to 27 percent), regardless of type of repair **(Figure 1)**.[1] Early detection and management are therefore crucial in minimizing the severity of the necrotizing inflammatory process that originates from leakage of esophageal contents into the mediastinum and in restoring the lumen continuity.[2,3] Therefore, clinicians practicing in surgical and acute care disciplines must be knowledgeable about this relatively rare yet clinically significant condition.

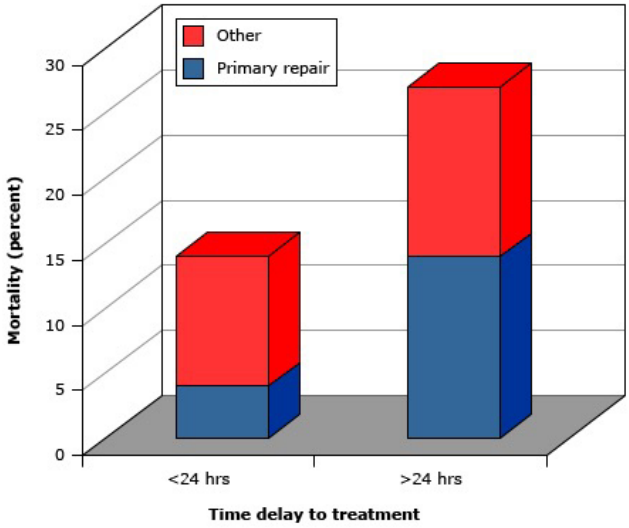

Figure 1. Effect of delay in treatment on overall mortality rates

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Location and Etiology

Even though perforation may occur in any site along the esophagus, physiologic areas of narrowing in the esophageal lumen represent more common sites of rupture. Such areas are the cricopharyngeal muscle (at 14–16 cm from incisors), the broncho-aortic pinch (at 22–24 cm from incisors), and the esophagogastric junction (at 40–45 cm from incisors).[4] As the majority of all perforations iatrogenic in nature occur during endoscopy, care should be taken while introducing the endoscope not to injure the esophagus at Killian triangle (the area described by the oblique inferior constrictor muscle superiorly and the cricopharyngeal muscle inferiorly). This area, in fact, lacks a muscularis layer posteriorly, and thus it is a site of structural weakness.[5-7] Other causes of esophageal rupture include increased intraluminal pressure at sites narrowed by a tumor, a foreign body, or physiologic dysfunction.

The most common causes of esophageal perforation include **(Figure 2)**:[8]

- 61 percent – iatrogenic
- 15 percent – Boearhaave's syndrome (in other words, spontaneous perforation)
- 12 percent – ingestion of foreign body
- 9 percent – trauma
- 2 percent – intraoperative injury
- 1 percent – cancer

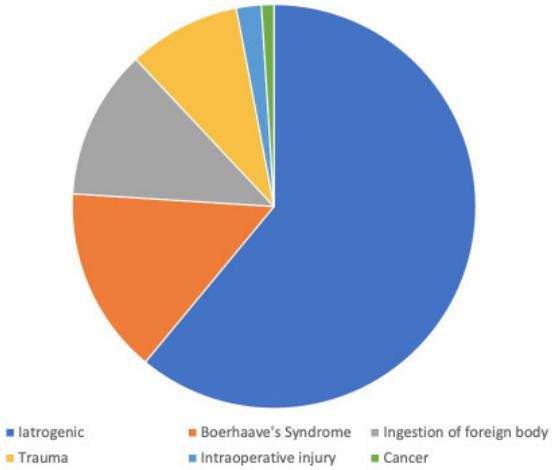

Figure 2. Esophageal perforation: Etiologies

Clinical Presentation, Diagnosis, Injury Grading

Based on the mechanism and site of injury, the clinical presentation of patients with esophageal perforation may vary. The most common symptoms are neck or chest pain (71 percent), followed by fever (51 percent), shortness of breath (24 percent), and subcutaneous emphysema (22 percent).[9] Other symptoms and signs of esophageal injury include dysphagia, odynophagia, hypersalivation, and hematemesis. However, all these symptoms have been reported not to be reliably present, making esophageal perforation a difficult and often delayed diagnosis.[10]

Initial evaluation should be tailored based on the clinical condition of the patient and the mechanism and site of injury. Computed tomography (CT) has been demonstrated to have an overall low sensitivity in detecting esophageal injuries, although indirect findings like periesophageal fluid or pneumomediastinum may be shown.[11] Esophagoscopy used to directly inspect the esophageal lumen and any direct or indirect signs of injury is a better diagnostic tool,[12] with a reported sensitivity ranging from 96 to 100 percent and specificity from 92 to 100 percent.[13-17] If endoscopy is not available or feasible, a contrast esophagram should be performed instead, although with higher rates of false

negatives compared with esophagoscopy, especially for cervical perforations.[18,19] A water-soluble contrast (for example, Gastrografin) must be used in order to avoid iatrogenic mediastinitis due to leak of barium-based contrasts into the mediastinum.

Esophageal injuries are graded according to the American Association for the Surgery of Trauma (AAST) injury-scoring system, as shown in **Figure 3**.[20]

Grade	Injury description
I	Contusion; hematoma; partial thickness laceration
II	Laceration ≤ 50% of circumference
III	Laceration > 50% of circumference
IV	Segmental loss or devascularization of ≤ 2 cm
V	Segmental loss or devascularization of > 2 cm

Figure 3. AATS Esophagus Injury Scale

Initial Management

The initial management strictly depends on the patient's general conditions. Once the diagnosis of esophageal perforation is made by esophagoscopy or esophagography (or it is strongly suspected), the following initial steps should be taken:

- If the patient is unstable, airways must be secured and a large-bore intravenous line must be started for fluid resuscitation with isotonic saline or lactated Ringers solution.
- The patient must remain nil per os (NPO).
- Broad-spectrum, intravenous antibiotics covering both aerobes and anaerobes must be started. Our preferred choice is Piperacillin/tazobactam, although ampicillin/sulbactam or a carbapenem are also acceptable.
- Antifungal coverage with fluconazole is indicated in selected cases: patients on long-term proton pump inhibitors, patients on long-term steroids or immunosuppressive regimens, patients with a known history of esophageal candidiasis, and HIV-positive patients.

Without delay, unstable or very sick patients should be prepared for operative management. This includes transferal to an intensive care unit with hemodynamic monitoring and insertion of a central venous, arterial catheter and Foley catheter. Laboratory evaluation and a chest radiograph should be taken as soon as possible. On the other hand, stable patients can undergo initial nonoperative management, as detailed in the dedicated section of this chapter.

Operative Management

A prompt surgical approach remains the foundation of an effective treatment. Indeed, Asensio et al. performed a multicenter evaluation of patients with penetrating traumas of the cervical esophagus, which showed that patients undergoing lengthy preoperative evaluations had significantly higher rates of postoperative esophageal complications and a significant longer intensive care unit (ICU) length of stay when compared with patients taken directly to the operating room.[21] Therefore, stabilization of the patient in a timely manner is key to achieving a good outcome.

Surgical principles of esophageal perforation treatment are: debridement of devitalized and necrotic material, exposure through a longitudinal incision along the muscle fibers superior and inferior to the perforation, and closure of the wall defect in a two-layer fashion **(Figure 4, A-C)**. The muscular layer is closed with interrupted nonabsorbable suture, while the mucosa is closed with absorbable interrupted sutures. A precise re-approximation prevents narrowing of the lumen. An esophageal bougie also can be placed to avoid narrowing of the lumen. Usage of vascularized tissue to buttress the repair is desirable, as it retains the native esophagus and avoids the need for later reconstructive operations **(Figure 4, D)**.[22] Flap options depend on the location of the rupture: left neck incisions allow for sternocleidomastoid or pectoralis muscle flaps; incisions in the right chest at the 6th or 7th intercostal space allow for usage of the intercostal, latissimus, or serratus muscles, the parietal pleura, the pericardial fat, or the pericardium itself; anddistal intraperitoneal perforations accessed by laparotomic incisions allow for gastric fundoplication. If significant contamination of the periesophageal tissues occur, we recommend placing a closed-suction drain in order to prevent abscess formation over the postoperative course.

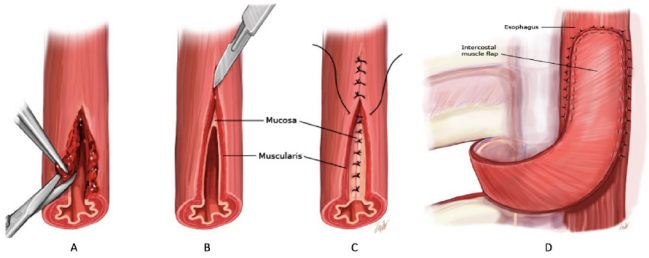

Figure 4. Primary repair of esophageal perforation
A. Mucosal debridement; B. Optimal exposure; C. Two-layer closure; D. Intercostal muscle flap

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Alternatives to Primary Surgical Repair

The only exceptions to performing a primary repair are diffuse mediastinal necrosis, impossibility to reapproximated the two borders of the perforation, presence of esophageal cancer or preexisting severe benign esophageal diseases, and cervical perforation that cannot be surgically addressed with

primary repair.[23] These cases may benefit from one of the following options:

- *Simple drainage*. Surgical drainage as the only surgical act may be suggested in perforations of the cervical esophagus in case the site of perforation is not clearly exposed or visualized. This should not be performed alone in perforation of the thoracic or abdominal esophagus, and additional treatment (in other words, endoscopic stenting, clipping) should be used to address the perforation, as the risk of uncontrolled leak into surrounding spaces would bear a high risk of contamination.
- *Diversion*. This technique consists of diverting the esophagus proximally with a cervical esophagostomy, resecting the remaining esophagus and performing a gastric diversion through a gastrostomy tube and/or a jejunostomy to assure adequate enteral feeding. Surgical diversion is indicated in case the patient is unstable or has preexisting esophageal disease that makes primary repair not feasible. Esophageal reconstruction should be performed in a two-stage approach, a few months later.
- *Stenting*. Endoscopic placement of a covered stent could be appropriate for frail patients with mediastinal sepsis, large esophageal perforations, or multiple comorbidities making surgical risk prohibitive. Sharma et al. reported that stenting options are based on weak evidence.[24] Freeman and colleagues identified four key factors that significantly reduced the effectiveness of esophageal stenting in treating esophageal perforation:[25] injury to the proximal esophagus, injury through the gastroesophageal junction, injury longer than 6 cm, and presence of anastomotic leak associated with a more distal conduit leak. If proceeding with this therapeutic option, we recommend considering stent anchoring[26] and assessing proper placement and adequate seal by contrast esophagography and further monitoring with plain radiographs.
- *Clipping*. Endoscopic clips placement has recently emerged as an option in carefully selected patients,[27,28] in other words, those who present with small defects with a healthy surrounding mucosa and with minimal extraluminal contamination.
- *Vacuum-assisted closure therapy*. Endoscopic vacuum-assisted closure therapy is a recently described option consisting of positioning an open-pored polyurethane sponge and a suction tube connected to a wound drainage system into the opening of the perforation.[29] Favorable outcomes have been reported in patients with spontaneous, iatrogenic, and postoperative esophageal perforation.[30]
- *Esophagectomy*. Esophageal perforations in the presence of esophageal cancer, undilatable strictures, or achalasia should not be treated with a primary repair. These patients, if clinically stable, should undergo esophagectomy.

Postoperative Management

In the postoperative course, patients should be kept NPO for several days, with a decompressive nasogastric tube in place (particularly in thoracic and abdominal injuries). Nutritional support can be provided through a jejunostomy feeding tube. We recommend broad-spectrum antibiotic coverage for seven to ten days. Patients should begin liquid oral intake on postoperative day five to ten, after having obtained an esophagogram demonstrating no leaks.

Nonoperative Management

Minimal esophageal injuries can be addressed with a conservative, nonoperative approach. This usually applies to etiologies such as iatrogenic, emetogenic, or foreign body ingestion, whose defects in the esophageal wall are limited in dimension. Penetrating and blunt esophageal perforations generally preclude a nonoperative approach, with wall defects being more extensive in these cases. Analogously, perforation into the pleural or peritoneal cavity represents a contraindication to conservative management due to difficult control of spillage of leaking contents. Perforation of the cervical esophagus is most commonly considered for conservative management due to the complexity of surrounding surgical structures. Careful patient selection is therefore essential. Conservative care consists of NPO maintenance, intravenous fluid, and broad-spectrum antibiotics during healing for five to seven days. If patients remain clinically stable, contrast esophagography is performed to assess presence of leak. As long as no leak is detected, resumption of oral intake under close monitoring is considered.

Summary

Despite its rarity, esophageal perforation is a life-threatening condition and represents a surgical emergency. Rapid diagnosis and early intervention are essential in managing patients and lowering morbidity and mortality. Primary repair is the gold standard surgical procedure to restore esophageal integrity, but other options are available in cases where such approach is contraindicated.

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CHAPTER 6

Management of Acute Complications following Elective Esophageal Surgery

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Key words:

Esophagectomy, Zenker's diverticulectomy, giant paraesophageal hernia repair, Heller myotomy, perforation, anastomotic leak, conduit ischemia, chylothorax, tracheoesophageal fistula, reherniation

Introduction

The esophagus is a long, 25cm muscular conduit of the upper digestive tract spanning the length of the thorax from the hypopharynx to the gastroesophageal junction. With pathologic processes that may occur along any point in the neck, thorax, or abdomen, surgical approaches vary considerably. We present in this chapter a breadth of potential complications in open and minimally invasive esophageal surgery, with particular focus on diagnosis, prevention, and both conservative and surgical management of these complications.

Esophagectomy

Esophagectomy is the standard curative procedure for resectable esophageal cancer, end-stage achalasia, and a number of other benign conditions that fail traditional surgery. Though esophageal cancer represents only 1 percent of all new cancer cases annually, its high mortality rate contributes to 2.7 percent of all cancer deaths.[1] Treatment approaches vary, but for local and regionally advanced cancers, standard therapy incorporates neoadjuvant chemotherapy or chemoradiotherapy[2] followed by surgical resection. Benign disorders such as end-stage achalasia, perforations, and failed operations for reflux or weight loss may ultimately result in indications for esophagectomy.[3] Whether for benign or malignant indications, esophagectomy is a complex and highly specialized operation with a mortality rate up to 10 percent and higher in some centers. Increasingly, esophagectomy is performed at high-volume and specialized esophageal centers (at least >20 cases per year), which can reduce the mortality rate to the 1 to 3 percent range and decrease postoperative complications and length of hospitalization.[4] These high-volume surgeons and surgical centers tend to concentrate their efforts on a singular surgical approach, which may vary to some degree based on location of the pathology to be resected. Esophageal resections can be tracked by either the STS or ACS NSQIP databases, with 4,321 esophagectomies recorded through the STS database over a three-year period between 2012 and 2014.[5] Both ACS NSQIP and STS data indicate that the most utilized surgical approaches are the Ivor Lewis and transhiatal techniques.[6] More recent analyses have documented that minimally invasive esophagectomy has now surpassed open esophagectomy as the most common surgical approach and that robotic esophagectomy is rising at a very rapid rate.[7] Complication frequency and management decisions vary considerably between surgeons and surgical approaches, but overall morbidity and mortality has deceased considerably in recent years. The most common major complications of esophagectomy include conduit ischemia, anastomotic leak, chylothorax, and fistula.

Conduit ischemia

Conduit ischemia can be the most devastating acute complication in esophagectomy. The preferred initial conduit of choice for creation of a neo esophagus is the tubularized stomach, which relies on the blood supply of the right gastroepiploic artery and arcade. Veeramootoo et al (2009) defined three types of conduit necrosis representing the breadth of postoperative sequelae: Type I, or focal ischemia leading to breakdown at the anastomosis resulting in a simple anastomotic leak; Type II, with concentric conduit tip necrosis requiring possible stenting, reoperation and/or re-anastomosis; and Type III, with complete conduit ischemia requiring conduit resection and bipolar exclusion.[8] Inadequate perfusion can lead to a range of complications depending on severity and duration, from anastomotic leak to fulminant conduit necrosis necessitating emergent surgical management.

Prevention begins with patient selection and identifying patients at high risk for development of conduit ischemia. Comorbid conditions associated with the development of ischemia include diabetes mellitus, peripheral vascular disease, recent or remote history of radiation, hypertension, arrhythmia, malnutrition, and steroid use.[9] Preoperative computerized tomography (CT) imaging can be helpful to evaluate the extent of calcific plaque on the aorta and particularly the presence or absence of celiac artery stenosis.[10] In an attempt to reduce the incidence of conduit ischemia, laparoscopic "ischemic conditioning" of the gastric conduit has been studied. In an ischemic conditioning operation, gastric mobilization is performed, with or without tubularization of the conduit, either during staging laparoscopy or in a separate procedure weeks prior to planned esophagectomy. While in smaller studies it had been shown that ischemic conditioning improved microcirculation of the conduit,[11] larger-scale investigations have not found ischemic conditioning to minimize rates of ischemia or conduit necrosis, and in fact this can lead to more complications during gastric mobilization due to development of adhesions or herniation.[12,13] Many successful intraoperative techniques aimed to promote conduit health have been adopted by high-volume esophageal centers including careful preservation of the gastroepiploic arcade during gastric mobilization, avoidance of grasping or manipulating the greater curvature which will eventually become the conduit ("no-touch technique"), creation of a narrow conduit (<5cm in diameter), careful preservation of orientation, and prevention of twisting.[14] It is also critical to maintain adequate perfusion pressure intraoperatively with the use of crystalloid and colloids, and to avoid vasoconstrictive agents, which may increase the incidence of conduit ischemic events. Additional techniques such as use of Doppler or indocyanine green (ICG) to confirm adequate blood supply after formation of the conduit may be helpful

adjuncts and are used in some centers.[15] The application of near infrared fluorescence imaging with ICG shows promise in identifying the gastric arcade and collateral vessels during conduit formation and may help identify the optimal location for formation of the esophagogastric anastomosis.[16,17]

Tachycardia and atrial fibrillation in the postoperative period may be early warning signs of the development of conduit ischemia. In addition, the change in color, quality, and amount of output from the surgical drain placed adjacent to the anastomosis may provide early indication of anastomotic leak. Decreased urine output, increasing pressor requirements to maintain adequate blood pressure, and persistent fever may be late findings that warrant urgent endoscopic evaluation of the conduit. CRP, as an isolated lab value, may be more useful than white blood cell count in monitoring signs for conduit ischemia. In one study, a continued elevation of CRP served as an indicator of conduit ischemia warranting endoscopic evaluation,[8] though we have not confirmed this in our center and do not use this particular parameter.

If conduit ischemia and/or anastomotic leak is suspected, we perform an upper GI endoscopy for direct visualization of the conduit. If the mucosa is pink and no concerning areas are noted, attention to other sources of systemic illness are sought. If the endoscopy is suspicious for ischemia, the conduit assessment can be supplemented with CT scan with oral and, on occasion, IV contrast. Endoscopic evaluation is highly sensitive in detecting an anastomotic leak and evaluating the overall conduit health and viability. CT scan is useful for detection of intramural, mediastinal and/or intrapleural air, which can be a sign of conduit necrosis and demonstrate intrathoracic collections that may need to be drained. Many surgeons routinely order a gastrografin swallow evaluation prior to initiating PO intake to evaluate conduit health. A swallow study is our standard, but we acknowledge it is not 100 percent sensitive in detection of leak, necrosis, or ischemia.[18] However, we do perform a swallow in all patients following discharge from the ICU and after passing a bedside swallowing test to assess for potential aspiration. If cough is present on the bedside swallow test, or if the patient is experiencing hoarseness, we prefer to delay the swallow or to obtain a modified barium swallow. Regarding leak or conduit assessment, a negative swallow may provide false security, as it may be normal even in advanced conduit ischemia, as contrast remains in the lumen preferentially and necrosis may be present without an associated leak. Routine upper GI endoscopy one week postoperatively is favored by some institutions and provides a safe and reliable way to evaluate conduit health; we perform this if there are any concerns over conduit health or the presence of systemic illness.[19] In summary, no one study provides 100 percent assurance of conduit viability and absence of a leak, thus, experience and a low threshold for endoscopy and other studies is required.

In the event of a large anastomotic dehiscence or if the viability of the gastric conduit is in question, especially in the setting of clinical deterioration, one must consider bipolar exclusion and cervical esophagostomy. This is a major decision and should be undertaken by an experienced member of the surgical team. The timing of this major intervention requires judgement. Waiting too long may lead to overwhelming sepsis, ARDS and even death. Intervening too early, when a conduit may be marginal, but potentially salvageable has obvious negative consequences, but in certain circumstances, it is lifesaving. If indeed the decision is to re-operate for possible conduit resection, the threatened or ischemic conduit is first examined with an on the table endoscopy. If concern remains, then we operate and circumferentially mobilize the conduit in the thorax via a right thoracotomy or thoracoscopic approach and carefully examine it. If the conduit is marginal it may require a second look, again, depending on the condition of the patient. If indeed the surgeon feels the only option is resection, the anastomosis is carefully taken down and separated from the esophagus. In our experience, an immediate reconstruction is generally not advisable for a several reasons. First, the patient may be quite ill and on pressors, and potentially in early multi-organ failure. Secondly, the remaining viable gastric remnant may not be able to be mobilized or reconstructed in a fashion that will allow it to reach the proximal esophagus. Third, if there is a sizeable gastric remnant, bipolar exclusion and returning the marginal gastric conduit to the abdominal cavity may allow a recovery of the marginal component for delayed reconstruction.

If the decision is to proceed with bipolar exclusion, it is important that one carefully handles the proximal esophagus with the goal being to salvage all of the remaining esophagus to create a cervical esophagostomy. We begin our bipolar exclusion in the chest by first mobilizing the proximal esophagus well up into the thoracic inlet and above, staying nearly on the wall of the esophagus. There is a concentrated effort to perform most of the dissection that would be needed in the neck via thoracoscopy or thoracotomy. If this is done carefully, once the surgeon has moved to the cervical incision and divides the omohyoid muscle, it should be easy to retrieve a quarter inch penrose drain encircling the esophagus to deliver the cervical esophagus into the neck. The remaining portion of viable gastric conduit, which many times is of significant length, should be carefully reduced into the abdomen and reassessed with only necrotic areas resected. Every potentially salvageable centimeter of the gastric conduit may become extremely important during subsequent reconstruction. If an adequate gastric remnant remains, with a reasonable amount of proximal esophagus it may be possible to perform a redo gastric pull-up at a later date. Of course, colon interposition or other alternative conduit may be required depending on length issues.

Next, the patient is positioned supine and the abdomen entered via open or laparoscopic approach. The hiatus is dissected circumferentially, and the gastric remnant carefully delivered into the abdomen and examined. If the patient is stable and the degree of necrosis is uncertain, we resect only the clearly non-viable portion and perform a temporary closure and come back for a second look in 24 to 48 hours. It cannot be overemphasized that careful judgement on precisely how much gastric conduit needs to be resected is crucial, as later reconstruction may require every possible viable centimeter that was spared. Once a decision is made on how much gastric conduit is preserved, we place a surgical gastrostomy tube at the tip of the remaining viable gastric conduit for decompression, enteric access, and reconditioning for possible future reconstruction. Once the necrotic conduit is removed and the gastrostomy tube has been inserted in the remaining viable portion, the abdomen, if possible, is closed. If the patient is stable, we proceed the same day with left neck exploration and cervical esophagostomy. If the patients' systemic condition is marginal, the cervical esophagostomy can safely be delayed for 24 to 48 hours. Longer delays can lead to difficulties in mobilizing and retrieving the remaining cervical and high thoracic esophagus.

Regardless of the timing of the cervical esophagostomy, the following is our routine for neck exposure. The medial head of the sternocleidomastoid (SCM) muscle is identified, and a horizontal skin incision is made over the SCM just roughly two fingerbreadths below the cricoid cartilage cephalad to the clavicular head. Platysmal flaps are elevated and monopolar cautery and blunt dissection with a peanut is used along the anterior border of the left SCM. While some surgeons prefer to perform an oblique incision along the SCM border, either skin and platysmal incision will work and the deeper dissection remains the same. Of importance, in the systemically ill patient, the cervical incision location should take into consideration of the potential need for a subsequent tracheostomy. If that is a possibility, we attempt to locate the cervical incision as far away from the subsequent planned trach site as possible. If one has an extremely short esophageal remnant leading to a high spit fistula, and then a tracheostomy is needed, overlapping wound with saliva contamination of the tracheostomy site can be a difficult problem, and can be avoided in most cases with careful incision selection. As the dissection proceeds deeper along the medial border of the SCM, the omohyoid muscle will be seen coursing obliquely and is divided for exposure. After we divide the omohyoid muscle, we transition to bipolar electrocautery or harmonic scalpel to avoid trauma to the recurrent laryngeal nerve. While continuing the dissection deep, the internal jugular vein and carotid artery are identified and retracted laterally, and the middle thyroid vein is ligated. The carotid sheath is retracted laterally after ligation of the inferior thyroid artery and gentle blunt dissection is carried down to the vertebral column. During retraction of the larynx and carotid sheath, we avoid the use of traumatic metal retractors and prefer kittners or finger retraction.

At this point, the cervical esophagus should be easily identified with minimal dissection if an adequate dissection was performed into the thoracic inlet during the thoracoscopic portion of the procedure. When the esophagus is identified and circumferentially mobilized, it can be retracted out of the neck through the incision using the Penrose drain left during the thoracic portion of the procedure. The esophagus is then measured on the left chest to identify the best location for the skin incision for the cervical esophagostomy while maintaining as much viable length as possible for future possible reconstruction. In most patients, the remaining cervical and upper thoracic esophagus will remain viable, and overly aggressive cervical dissection can lead to further ischemia to the remaining esophagus. We generally will preserve all of the remaining proximal esophagus. A subcutaneous tunnel over the fascial layer of the pectoralis muscle is created and the esophagus is passed through the tunnel. The esophagostomy is then matured with interrupted absorbable sutures. The entire area should be irrigated with warm saline solution with antibiotics. During the postoperative period, the cervical esophagostomy should be routinely checked for viability as in rare circumstance there will be distal esophageal tip necrosis requiring revision. Post cervical esophagostomy, we encourage some PO sips of liquids to maintain the swallowing mechanism and to minimize cervical esophageal strictures. Over time, while awaiting reconstruction, dilations may be prudent to avoid excessive scarring of the esophagostomy site as this can lead to loss of some esophageal length if excessive stenosis occurs.

Anastomotic leak

Anastomotic leak is one of the most common causes of morbidity following esophageal reconstruction.[20] Development of this complication can be quite variable in severity ranging from a minor subclinical radiographic finding with little intervention needed, to a more severe leaks with multiple downstream effects including fistula, stricture, sepsis, and death. Risk factors for anastomotic leak, like those for conduit ischemia, include poor surgical technique with intraoperative conduit trauma, the use of preoperative steroids, a low preoperative FEV1, smoking, obesity, and surgical approach. Intraoperative periods of hypotension and blood transfusion are also associated with significantly higher rates of anastomotic leak. In a meta-analysis published in 2020 examining anastomotic leaks after esophagectomy, the overall pooled rate of anastomotic leak was 11 percent among 74,266 esophagectomies performed for esophageal cancer. The incidence of anastomotic leak ranged from 0 to 49 percent based on the included studies

(100), which were published between 1988 to 2018.[9] Analysis of the STS database revealed a similar anastomotic leak rate around 10 percent,[21] allowing for variation among institutions and surgical technique. Many surgeons favor the Ivor Lewis approach to esophagectomy with an intrathoracic anastomosis, citing the lower incidence of anastomotic leak (9.3 versus 12 percent) when compared with transhiatal esophagectomy. Despite this difference in anastomotic leak rate, the overall mortality between these two approaches is similar. In addition, improved leak rates have been claimed by some surgeons; for example, minimally invasive approaches to esophagectomy in some centers have reported comparable to lower incidences of leak (5 percent) when compared to the open approach.[22]

As with conduit ischemia, prevention begins with patient selection, as those with vascular or inflammatory disease, obesity, heart disease, renal failure, cigarette use, and steroid use are at much higher risk of developing anastomotic leak.[21] Technical choices and their impact on development of anastomotic leak have been examined, but few studies exist that are randomized or well controlled. Certain aspects of surgical reconstruction such as type of anastomosis (hand sewn versus stapled) have not been found to make considerable difference in the development of this complication. Similarly, complication rates between end-to-side and end-to-end anastomoses have been equivocal.[23]

In our approach, we focus on certain aspects of our gastric conduit construction and anastomosis in an attempt to prevent anastomotic leak. The gastric conduit is carefully created with preservation of the epiploic arcade, utilizing a "no-touch" technique for the greater curve and any portion of the stomach that is destined to be part of the ultimate conduit. We also take care to prevent any twisting or spiraling as serial staple loads are fired. During these steps, the stomach is grasped at the fundic tip and stretched towards the upper left quadrant of the abdomen as sequential staple loads are applied, which lead to maximizing conduit length (this is especially important for cases where a neck anastomosis is needed).

Once the tubularization is complete, the stomach is advanced into the lower chest through the hiatus. Even at this point, we ensure the staple line is facing the right crus and greater curve vessels oriented to the spleen, to ensure there is no twisting of the conduit. In the setting of neoadjuvant radiation, we create an omental flap based on one or two prominent arcades from the gastroepiploic vessels. While we do not have data to confirm the advantages of the omental flap, this is being studied currently. At this time, we limit the use of an omental flap to radiated patients. It should be noted that creating an omental flap can be challenging, time-consuming and even hazardous to the conduit, the gastroepiploic and the colon. This becomes more technically challenging especially in the obese patient or in the setting of intraabdominal adhesions. We prefer an omental flap that is approximately 3 to 4 centimeters in width and 10 to 15 centimeters in length. Once created, we tack the tip of the omental flap to the fundic tip or our newly created conduit to facilitate easy retrieval in the chest. Bulky omental flaps can be difficult to mobilize into the chest, and on rare occasions can lead to somewhat of a "vascular steal" effect, thus we prefer a modest sized flap.

After completing the laparoscopic steps, we proceed to turn the patient in the left lateral decubitus position, confirm double lumen endotracheal tube placement, and begin with a right thoracoscopy. During the intrathoracic portion of the procedure, after the conduit is properly advanced into the chest, it is opened at the fundic tip and cleaned out with antibiotic irrigation and inspected for orientation, viability and general suitability. Our most common anastomotic approach is the EEA. In most patients, it will be possible to place a 28mm EEA anvil into the lumen of the proximal esophagus and to insert the 28 mm stapler into the lumen of the conduit. If difficulty is encountered with this diameter EEA device, gentle dilations using an empty sponge stick will generally allow the 28 mm to be used. On occasion, a smaller EEA diameter (25mm) may be required in smaller female patients, or in the setting of neoadjuvant radiation, proximal esophageal scarring, or stricture. We avoid 21 mm diameter EEA in adults due to the high recalcitrant stricturing that invariably occurs with this small diameter. Once one is ready to divide the proximal esophagus, it is important to take an additional moment to consider the proximal extent of the tumor, including the tumor's pre-treatment border, and the proximal extent of any Barrett's. At this point we consider the ideal oncologic location of the esophagus division, ideally giving us a proximal margin of 5 centimeters or more. However, this must be taken into context of the length and mobility of the new gastric conduit. In most patients with GE junction tumors, we are able to divide the proximal esophagus well above the azygous affording a good negative proximal tumor margin and allowing the new conduit to easily reach the area. In most cases, we have enough conduit length to resect 6 to 10 centimeters of the tip of the conduit to ensure a negative tumor margin, but also to remove any potentially radiated gastric tip and remove the most ischemic portion.

After we suture the EEA anvil in place in the proximal esophagus, we then pass the EEA handle into the tip of the conduit, and we determine the site of EEA spike exiting the greater curve side of the gastric conduit. Again, we consider the following: where to divide the proximal esophagus, how much conduit to bring into the chest, how much conduit can be easily removed without limiting length, how much tension will be on the anastomosis, etc. The proximal extent of any pathology, cancer, presence of Barrett's esophagus,

and scarring all should be taken into consideration before dividing the esophagus and before deploying the EEA spike out the greater curve side of the conduit. Once these steps are done, and conduit orientation is determined, we carefully exit the spike of the EEA handle end out the back wall of the conduit near the line of the short gastric arteries. Next, we carefully bring this to the EEA anvil, assess orientation and any tension and dock with the EEA anvil in the esophageal end. We then fire the EEA. Once the anastomosis is complete and the EEA is removed, the remaining gastric fundic tip is stapled off, leaving at least one centimeter between staple lines to promote adequate tissue perfusion.

Once the anastomosis is complete, the omental flap (if created) is placed between the conduit and the airway and wrapped around the anastomosis. Conflicting data exist on the efficacy of an omentoplasty in preventing leak;[24,25] however, we feel that in adhering to basic surgical principles, adequate tissue should be placed between the airway and the newly fashioned staple line to prevent fistula. At the conclusion of the procedure, our routine is to place a chest tube near the conduit and a smaller Jackson Pratt drain just posterior to the anastomosis to allow for early diagnosis and proper drainage in the event of an anastomotic leak.

Mean duration between surgery and identification of leak, if it should develop, is around nine days.[26] As with development of conduit ischemia, postoperative patients should be closely monitored for early signs of sepsis such as tachycardia or atrial fibrillation. For patients with a neck anastomosis, induration or drainage at the cervical incision may become apparent. Elevated CRP and drain amylase levels may also indicate anastomotic leak.[27] Change in color, quantity, and quality of surgical drain output are also signs of anastomotic leak. Early endoscopic intervention is a safe and effective way to diagnose and monitor anastomotic leak.[28] At some institutions, routine endoscopy is performed on all post-esophagectomy patients. We favor a close surveillance, with prompt endoscopic evaluation of any patient with clinical suspicion for development of leak. A barium swallow, though nonspecific, is also obtained once the patient is stable, which may identify early anastomotic leaks prior to any symptomatology. The barium swallow also serves as an opportunity to assess the diameter and lie of the new conduit. In In the setting of a cervical anastomotic leak, the cervical incision should be opened to help facilitate additional drainage.

Once the diagnosis of anastomotic leak is made, antibiotic coverage and supportive measures are initiated. In following basic surgical principles, wide drainage of anastomotic leaks may be required to avoid the development of an abscess, empyema and sepsis, and additional drains may need to be placed. In the setting of small, contained leaks, surveillance and close monitoring may suffice. For larger defects, endoscopic surveillance and intervention is often the next step in conservative therapy. Esophageal stenting is widely used and may be successful in sealing up to 70 percent of uncomplicated anastomotic leaks.[29] Endoluminal vacuum therapy, in which a vacuum sponge is endoscopically placed at the site of the anastomotic leak and is connected to suction via a nasogastric tube, has shown promising results in reducing the size of the anastomotic cavity, promoting formation of granulation tissue, and successfully healing leaks.[30] Furthermore, when compared with stent therapy, endoluminal vacuum therapy has been found to have a higher success rate, shorter treatment duration, and should be considered when weighing endoscopic management options.[31] Given the high mortality rate for reoperation, surgery should be reserved for cases in which the leak is being inadequately controlled by drains and in which endoscopic therapies have failed.[32]

Surgical intervention begins with direct endoscopic visualization of the leak. As most small leaks will heal, endoscopic surveillance, wide drainage, and dilation distal to the leak may be sufficient to maintain the inner lumen of the conduit as the path of least resistance. Therefore, we do not recommend primary repair in the setting of small anastomotic leaks. In the setting of a cervical anastomotic leak, the neck incision is opened to allow for drainage of any GI contents. Patients with an intrathoracic anastomotic leak may require a thoracic cavity washout via thoracotomy or VATS with manipulation of the surgical drains to ensure wide drainage. If sepsis persists despite adequate drainage or if the anastomotic leak continues to evolve and worsen in the setting of conduit ischemia, we recommend a bipolar exclusion not only for source control but also to provide the ability for future chances of reestablishing GI continuity. Primary repair in this setting will likely be unsuccessful and should not be attempted especially on a patient in extremis.

Chylothorax

Chylothorax may occur as a complication of any thoracic or mediastinal procedures. The highest incidence of postoperative chylothorax, occurring between 1 and 9 percent of the time, is in the post-esophagectomy population, owing to the location of the dissection plane.[33] Chylothoraces may occur from many areas in the lymphatic system including various points of the thoracic duct and lymph node stations. Chyle leaks may be categorized as a low-output (<500cc of chest tube drainage per day) or high-output (>1L drainage per day) chylothorax, and the treatment of each may vary. A low-output leak may result in spontaneous closure with conservative management. Additional interventions are generally necessary to manage a high-output leaks. If left untreated, a chyle leak may directly lead to development of malnutrition, electrolyte derangements, and immunosuppression, and is associated with significant post-operative morbidity and mortality.[34]

Given the morbidity associated with this complication in the esophagectomy patient, preoperative supplementation to aid in the identification of the thoracic duct has been described. Increased success in identifying the duct during dissection has been demonstrated in studies in which patients have been given milk or other lipid rich enteric feeds intraoperatively, either via NG tube or feeding jejunostomy.[35,36] The increased size and white appearance of the thoracic duct has led to easier identification and lower postoperative incidence of chylothorax. The success in the use of this approach may be variable, however. Overall, the best prevention of chylothorax is careful surgical technique. Careful adherence to the avascular pleural and pericardial planes is critical during esophageal mobilization, as well as avoidance of dissection into the fat posterior to the esophagus and adjacent to the aorta. Due to the variability in thoracic duct anatomy, clips should be liberally applied to any duct-like structures identified posterior to the esophagus during dissection.

Early postoperative chest tube output of greater than 400ccs/day is highly concerning for and predictive of chyle leak. Though a chyle leak is associated with the characteristic presentation of "milky" chest tube output, it is important to recognize that in postoperative patients in which a diet has not been introduced, a chyle leak is likely to appear serous. Pleural fluid analysis is the first step in diagnosis, with a fluid triglyceride level being a both highly sensitive and specific test; >110mg/dl being highly specific for a chyle leak, with a level of less than 50mg/dl associated with chyle leak less than 5 percent of the time. The presence of chylomicrons in pleural fluid is considered diagnostic for a chyle leak.[37]

The first step in conservative management of chylothorax includes dietary restrictions focused on limiting fat intake and avoiding long chain triglycerides. This may be accomplished by implementing a strict NPO diet, relying on specialized tube feeds, or transitioning to total parenteral nutrition. Adequate drainage should be established if not already managed with the existing drains. Long periods of keeping the patient NPO, on TPN should be avoided in most cases of high output leaks as they may attribute to more overall harm. Continued chest-tube output of about 12 or greater ml/kg/day after initiation of medical management has been found to be highly predictive of failure of conservative therapy.[34]

Conservative management will seal the majority of low to moderate flow leaks. However, for high-volume, persistent leaks we prefer early lymphangiography and embolization. Lymphangiography and thoracic duct embolization can be performed via direct CT-guided puncture, microcatheter insertion over a guidewire, and subsequent micro coil embolization.[38] If this is unsuccessful, at a minimum it frequently contributes to the anatomic localization of the leak and will help find the leak site during surgical exploration.

While conservative treatment and/or interventional radiologic (IR) embolization may be very successful in most cases, some patients may continue to leak as the trauma to the lymphatic ducts during the circumferential dissection of the esophagus either in the chest or through the hiatus may be substantial. Nonetheless, medical management and IR-guided embolization should be first utilized in order to identify patients with refractory chyle leaks. In patients with refractory chylothoraces following esophageal surgery, we recommend mass ligation of the thoracic duct. This technique is necessarily employed due to the anatomic variance associated with the thoracic duct and the inability to identify the exact area of injury of the duct during the primary operation. We prefer a minimally invasive approach. In an attempt to identify the injury, the mapping from the lymphangiography may be helpful, and some recommend that patients be given heavy cream mixed with methylene blue through a nasogastric tube once the patient is intubated and positioned in left lateral decubitus position. We have found the films from the lymphangiogram to be most helpful. During surgical exploration, we begin the dissection just above the diaphragm in the right thoracic cavity where the thoracic duct has the least amount of anatomic variance in order to ensure that all tributaries are identified and ligated. In this location, the thoracic duct most frequently lies between the aorta, the previous location of the esophagus and the azygos vein overlying the vertebral column. Once these anatomic landmarks are identified, the visceral pleura is entered sharply posteriorly to the azygos vein. The dissection plane is carried down to the vertebral column and to the aortic adventitia. The plane is then extended to visceral pleura where the esophagus was previously resected. An 0-silk suture is passed along this plane and all this tissue, including the azygos vein, is ligated en masse. If a direct duct injury is identified that area should be inspected and clipped or suture ligated as well. Surgical treatment with VATS or open thoracotomy remains the gold standard and is successful in 67 to 100 percent of cases. It is more successful than chemical pleurodesis alone, [39] though it may be performed as an adjunct at this time. If surgery and other interventions are unsuccessful in controlling the leak, a pleuroperitoneal or pleurovenous shunt may be performed as a last resort along with TPN.

Tracheoesophageal fistula

Tracheoesophageal fistula (TEF) is a rare but devastating complication of esophagectomy. This can occur with the formation of an injury between the esophagus or neo-esophagus and the airway. When this does occur, it will more often be encountered at the middle third of the trachea or the left mainstem bronchus. While the incidence of its development is around 1 percent, the mortality rate associated with this complication is upwards of 57 percent. Higher mortalities will be seen in the setting of delays in diagnosis and treatment, concurrent pneumonias, and for larger fistulous connections.[40]

Development of TEF may be iatrogenic (sharp dissection or thermal injury) or promoted by inflammation or mediastinitis at the membranous airway as a result of anastomotic leak or conduit tip necrosis. Occasionally, misadventures during endotracheal intubation, double lumen tube placement or even intraoperative transesophageal ECHO can lead to TEF. Aggressive surgical dissection with disruption of bronchial arteries leading to segmental airway ischemia has been theorized to contribute to development of TEF. However, aggressive lymph node dissection has not been found to be associated with TEF development.[41] Surgeons should be always aware of the proximity to the airway during esophageal mobilization and employ precision to avoid thermal injuries or harmonic scalpel injuries. Intraoperative indications of an airway injury include difficulty in ventilating the patient due to a loss of tidal volumes or visual identification of a defect or the balloon of the double lumen tube. Tracheoesophageal fistula, should it develop, may also reveal itself in the post-operative period or during follow-up. Concern should be raised with patients that present to the hospital with recurrent pneumonias. Development of aspiration pneumonia and persistent cough (particularly after meals) are clinical signs that may point in the direction of evaluation of TEF. In the presence of a large fistula, a patient may present with frequent choking spells when ingesting liquids leading to inability to tolerate oral intake, or have clinical signs of lower respiratory tract infection including difficulty oxygenating. Plain radiographs may be suggestive of an aspiration pneumonia. CT imaging can also help identify the location of the TEF. A small pocket of air or fluid collection posterior to the airway should raise suspicion for this complication and warrant additional testing. Barium swallow may reveal contrast passage into airway signifying TEF. Follow-up esophagram may also be helpful for post-treatment surveillance. As in other acquired post-esophagectomy complications, the gold standard for diagnosis is direct inspection of the conduit and the airways using endoscopy and bronchoscopy.

Surgical management is the mainstay of this difficult complication. Initial approach focuses on preventing additional pulmonary soilage in two ways: by ensuring the cuff of a tracheal or endotracheal tube lies beyond the fistula, and by creating alternate feeding access (via jejunostomy tube) and preventing reflux (via gastrostomy tube).[42] Endoscopic stenting has not been shown to be a reliable treatment approach and should be considered only for early, very small fistulae without a well-defined passage to the airway.[43] Bipolar exclusion should be considered in cases that have failed prior management. Individual case reports have been described in which ECMO is used for a brief period of time to facilitate tracheal healing by maintaining minimal ventilatory pressures.[44,45] New research in the field of 3D-printed tracheal stents has been promising; in one recent series of six patients treated with segmented Y airway stents, full tracheal healing was obtained after an average of 62 days.[46]

The surgical approach to repair a TEF depends upon its size and location. Conduit takedown with esophageal diversion may be necessary in select cases.[49] If the defect to the airway is small enough, it may be repaired primarily and patched with either an intercostal muscle flap or an omental flap. In some circumstances, the use of adjunct reconstructive materials may be necessary. The use of bioprosthetic materials such as aortic homograft or acellular dermal matrix buttressed with a muscle or omental flap has been described.[47] At our institution we have had success repairing complex tracheal injuries with an aortic homograft or bovine pericardial patch and placement of an overlying muscle flap (personal communication with Dr Doug Mathisen, Mass General Hospital). Larger fistulae may require tracheal resection, particularly those with circumferential damage (such as in the case of sequelae to endotracheal cuff ischemia).[48] Treatment approaches are not uniform, and surgical repair is a complex undertaking best performed by thoracic surgeons experienced in esophageal and tracheal reconstruction.

Heller Myotomy, Pneumatic Dilation, and Per-Oral Endoscopic Myotomy

Achalasia is a progressive disease defined by dysfunctional esophageal peristalsis or aperistalsis frequently accompanied by failure of relaxation of the lower esophageal sphincter (LES) resulting in high LES pressures. Patients typically present with varying degrees of dysphagia, regurgitation, and chest pain depending on the extent of the disease.[50] In the past, achalasia was typically associated with a triad of presenting symptoms including dysphagia, regurgitation and weight loss. However, in a recent study of 100 patients with achalasia, weight loss was only reported in 51 percent of patients with a median weight loss of 20 pounds. However, more patients with type II achalasia reported weight loss (63 percent) and 73 percent of patients with type III achalasia denied having weight loss[51]. While achalasia treatments can offer significant improvement in symptoms in most patients, it is important for patients and physicians to remember that the treatments are not "curative" but are palliative in nature and aim to improve passage of ingested material, reduce complications such as aspiration, and slow disease progression. Hence the need for long-term follow-up and careful dietary discretion on the part of the patient.

Medical and surgical therapies target muscle fibers of the LES, and include calcium channel blockers, botulinum toxin injections, balloon dilation, and surgical myotomy. Pneumatic dilation for achalasia was once a very popular approach in many centers with reasonable results, though surgical therapy (open esophagomyotomy) demonstrated more definitive long-term success.[52] In more recent years, the popularity of pneumatic dilation dwindled and expertise with this approach significantly decreased in many countries with the introduction of laparoscopy. While the open heller myotomy was the standard surgical approach in

many centers for achalasia for decades, laparoscopic heller myotomy was introduced in the early 1990's as a safe and effective approach with a mortality rate of 0.1 percent and significant symptom relief in close to 90 percent of patients treated.[53] Due to high rates of the development of pathologic gastroesophageal reflux post procedurally, Richards landmark study showed that adding a laparoscopic Dor to the myotomy minimized the reflux associated with a myotomy alone.[54] We have had great success with the laparoscopic approach at our institution, with greater than 95 percent of patients reporting symptomatic improvement at long-term follow up. In experienced hands, the laparoscopic heller myotomy proved to not only produce durable results but also a safe operation with a short average hospital stay of 3 days. Our complication rate of 9 percent in our series included esophageal perforations that were recognized and repaired intraoperatively, as well as development of hemothorax (1) and pneumothorax (1).[55] Worldwide, pneumatic balloon dilation, performed endoscopically, remains one of the most popular procedures for achalasia palliation. Treatment efficacy ranges from 40 to 78 percent after five years. Overall, complication rates are comparable with that of heller myotomy.[53] More recently, per oral endoscopic myotomy (POEM) has emerged as an alternative treatment with outcomes comparable to laparoscopic heller myotomy for the dominant complaint of dysphagia, but GERD is seen in over 50 percent of patients post-POEMs. Advantages of POEMs include an incisionless, minimally invasive approach, using a natural orifice technique which is being increasingly requested by patients and adopted by esophageal surgeons. Using an endoscope with CO_2 insufflation, a mucosal incision is created approximately 12cm proximal to the gastroesophageal junction. Next, a submucosal tunnel is created down the esophagus and past the lower esophageal sphincter. Circular muscle fibers are then divided with an endoscopic knife and the mucosal incision is closed with endoscopic clips.[56] Outcomes of this approach are excellent compared to heller myotomy for the dysphagia, however, the development of GERD in over 50 percent of patients cannot be understated and remains the most commonly reported side effect across short-term and medium-term follow-up cohorts.[57] Acute complications are rare, and include most commonly the development of subcutaneous emphysema (7.5 percent) or pneumoperitoneum (6.8 percent).[58, 59] In our experience, we have now performed over 200 POEMs without a single 30-day mortality. However, we have noted a steep learning curve, and limit this procedure to only two surgeons in our group of close to 20 thoracic surgeons due to the concerns of the potential for esophageal perforation in inexperienced hands. We are mentoring other surgeons in our group, and we believe the learning curve requires 20 or more proctored or mentored procedures before a comfort level is reached by the learning surgeon.

Esophageal perforation

Full-thickness perforation may occur up to 10 percent of the time in the course of a surgical myotomy, however, most of these are small 1 to 2 mm tears near the gastric side of the final centimeters of the myotomy and are easily recognized, and easily repaired, and most will be additionally buttressed by the Dor fundoplication. It has also been noted in several studies that these tears tend to occur in the surgeons initial learning experience. Primary repair at the time of injury will not impact long-term success of the operation.[60] In comparison, pneumatic dilation is associated with a perforation rate from 1 to 11 percent[61] depending on the experience of the endoscopist and the definition of the perforation. Transmural perforations are less common and more frequently require surgical intervention to repair. Conservative management for non-transmural perforations has been shown to be possible, but careful selection of these patients requires considerable surgical experience. Full thickness perforation due to POEMs is uncommon (less than 1 percent) and conservative management may be sufficient with careful observation. It is important to keep in mind, however, that a mucosal opening in the esophagus is the intent of the procedure, thus care in the subsequent dissection plane, the final irrigation and mucosal closure must be meticulous to avoid complications. We also study each patient with a barium esophagram afterwards and admit them for 2 to 3 days of observation.

Prevention of perforation in laparoscopic Heller myotomy begins with adequate visualization and surgical experience. The gastroesophageal fat pad and anterior vagus nerve should be mobilized off the anterior esophagus and stomach so that the true GE junction and angle of His is visualized. Only once adequate visualization of intra-abdominal and mediastinal esophagus is obtained should the myotomy be performed. After the longitudinal muscle fibers are identified they can be bluntly separated with atraumatic graspers immediately proximal to the GE junction on the anterior wall of the esophagus until the circular muscle fibers are encountered. The circular fibers are then divided until the submucosal plane is identified. As this is being completed, the mucosa of the distal esophagus will bulge into view and can be avoided. If sharp dissection with an energy device is utilized for the myotomy, care must be taken to minimize any direct contact with the bulging mucosa to avoid a thermal injury. During a laparoscopic or open Heller myotomy, when a full thickness defect is identified, primary repair with a 4-0 suture (we prefer 4-0 PDS) should be performed promptly during surgery. The repair should then be buttressed with omentum or covered by stomach at the time of Dor anti-reflux fundoplication.

To avoid sequelae of a full thickness perforation during POEMs, the endoscopic incisions (mucosotomy and myotomy) must be created carefully and strategically. After a mucosotomy incision has been created and the submucosal plane has been developed, the myotomy should be placed several centimeters distally (ideally at least 4cm distally) to the mucosotomy to ensure there is no direct connection between the lumen of the esophagus and the mediastinum. Careful attention should be paid to the creation of the myotomy by dividing the layer of the circular muscle fibers while sparing the longitudinal muscle fibers, thus preventing full-thickness perforation. During a POEMs procedure, we do not intentionally separate the longitudinal muscle, but this is frequently observed during the POEMs procedure to some degree. Even partial thickness dissections can lead to significant egress of insufflated CO_2 during a POEMs procedure and can lead to the development of acute pneumothorax or pneumoperitoneum. This is not uncommon in the early experience of the operating surgeon and can be minimize by paying close attention to the dissection plane, periodically suctioning out the surrounding area and the stomach and maintaining a high index of suspicion. However, some degree of mediastinal air, subcutaneous emphysema and tracking air into the peritoneal cavity can occur. High peak ventilatory pressures and plateau airway pressures as well as hemodynamic compromise will raise strong suspicion for the development of pneumoperitoneum, gastric dilatation, and/or tension pneumothorax.

Pneumoperitoneum, if minimal, can be safely observed, but in extreme cases can be managed promptly in the operating room via placement of a veress needle, insertion of laparoscopic optical separator, or by a 5 to 10mm decompressive incision via cut-down. A laparoscopic port should remain in place for the duration of the case to provide decompression. Periodic endoscopic suctioning of the gastric bubble should be performed to minimize the effects of gastric dilatation. At the conclusion of the case, laparoscopic decompression sites may be closed primarily without need for drain placement.

Similarly, CO_2 dissection leading to the development of pneumothorax should be addressed with a tube thoracostomy, ideally with 8 French pigtail catheter placement. This pigtail may be removed at the conclusion of the case upon evacuation of air or maintained for 24 hours post-procedurally. In cases of uncertainty in a stable patient, intra-op fluoroscopy or on the table chest X ray may be utilized. Once the myotomy is complete, the mucosotomy is typically reapproximated with endoscopic clips to allow for the mucosal tunnel to collapse and preferential flow down the proper lumen of the esophagus. There is a learning curve to the placement of these clips, and they can be particularly challenging in the setting of esophagitis or in the setting of a relatively normal size diameter of the esophagus.

More dilated esophagi are more amenable to relatively straightforward endoscopic clipping due to the somewhat redundant folds of the mucosa. Endoscopic suturing devices have been described, but at this point in time, we have tried them with some difficulty and we prefer to close with the endoscopic clips (i.e., Resolution 360, Boston Medical; Instinct, Cook Medical).

We perform an immediate post-procedure chest X ray in the recovery unit as an initial measure to identify unrecognized pneumothoraces or significant subcutaneous emphysema. Small, clinically stable pneumothoraces may be observed, and for the most part, subcutaneous emphysema does not require intervention. In our practice, all patients who have undergone laparoscopic Heller myotomy or POEMs procedure undergo a barium swallow prior to diet advancement. This is typically employed 24 to 48 hours post-procedurally. We advise patients and families that rarely a delayed presentation of an esophageal perforation may develop. Thus, if the patient experiences fevers, chest pain, or abdominal pain, or generally does not feel well, we recommend that the patient come in for further evaluation. Plain radiographs may reveal development of pleural effusion which should raise suspicion of intrathoracic perforation. CT scan with oral contrast may be used to assess for intra-mediastinal or intrathoracic collection, but to localize a leak, a barium esophagram is our preferred diagnostic study. Alternatively, endoscopic evaluation for diagnosis and treatment should be performed. Small mucosal perforations (<10mm) that are identified post POEMs barium esophagram may be identified and closed with endoscopic evaluation and additional Endo clips. For larger perforations, or where we are not convinced with Endo clip is enough, we deploy fully covered esophageal stents to manage the leak or operate. Other sequelae such as abscesses or large fluid collections in the abdomen or chest should be drained and controlled image-guided drain placement, depending on the clinical situation and judgement of the surgeon. In the setting of a routine myotomy, POEMS or laparoscopic, we administer 1 to 2 doses of a broad-spectrum antibiotic. If clinically significant leaks are present, we manage them as described above or with additional surgery, and broad-spectrum antibiotic and antifungal coverage should be initiated for seven to 10 days. Exploratory laparoscopy, laparotomy and/or thoracoscopy and thoracotomy are used at the discretion of the surgeon in the case of a clinically significant leak, which should be a rare occurrence.

Zenker's Diverticulectomy

Zenker's diverticulum is an uncommon, acquired condition that affects approximately 0.01 to 0.011 percent of the population and is manifest by an outpouching of esophageal mucosa through Killian's triangle. By definition, this is a "false" diverticulum, and frequently results in significant dysphagia, regurgitation, and aspiration. Exactly why people

develop a Zenker's diverticula is uncertain. What is known is that there is a separation of the muscle fibers posteriorly just superior and posterolateral to the cricopharyngeus, which is generally quite hypertrophic and "bar-like".[62] Gastroesophageal reflux is highly associated with presence of a Zenker's diverticulum, and the associated pathologic reflux up to the level of the upper esophageal sphincter may contribute to forceful upper esophageal sphincter contraction leading initially to a cricopharyngeal bar and cervical dysphagia. Over time, and in what appears to be the minority of cases, a Zenker's diverticulum develops.[63] Open trans-cervical myotomy with diverticulectomy, or diverticulopexy was the preferred treatment approach for several decades. However, in the late 1990's, one of the first natural orifice procedures for disorders of the esophagus was developed and introduced with widespread popularity. This natural orifice approach includes a transoral exposure with a rigid Weerdascope and transoral stapling of the cricopharyngeal septum. Thus, in the transoral procedure, the diverticulum is not removed, but becomes "one" with the esophageal lumen. It is ideal for diverticulae in the 3 cm range and up and has compared favorably to open cervical myotomy.[64] Patient selection for the trans-oral approach may be challenging as those with extensive dental work, cervical spinal disease, hardware, or small mouth orifices make the transoral approach difficult due to exposure problems. In experienced hands, most patients will have a successful outcome with a trans-oral technique, but not all. In cases of significant difficulty, one should convert to open cervical myotomy. The risk of major complications with either technique is low, with a reported overall morbidity of 10.5 percent and a mortality of 0.6 percent. Among a review of 2,826 patients in 41 studies, the most common complications were recurrent laryngeal nerve injury (3.3 percent), leak or perforation (3.3 percent) followed by cervical infection (1.8 percent) and hematoma (1 percent).[65] In our retrospective analysis of over twenty years of patient data including transoral repair of Zenker's diverticulum in 135 patients, our post-operative major complication rate was around 3 percent with a clinically significant leak rate less than 2 percent.[64] Other reported infrequent complications in the literature include emphysema and mediastinitis.[66]

Cervical leak

Cervical leak after myotomy may result in passage of enteric contents from the esophageal lumen into the retropharyngeal space. This complication is particularly worrisome as descending mediastinitis may acutely develop. Rates of mediastinitis vary significantly based on procedural approach, with up to 1 percent of cases of open Zenker's diverticulectomy developing mediastinitis in contrast to 0.2 percent following transoral stapling for Zenker's diverticulectomy.[66] Overall, full thickness injury to the cervical esophagus is a rare occurrence in experienced hands whether using the trans-oral or open approach, with most reports identifying this complication less than one percent of the time.[67, 68]

The trans-oral stapling approach for Zenker's became popular decades ago with the introduction of endoscopic stapling devices. This approach allows for the division of the common septum (cricopharyngeus) and therefore allows for the diverticulum to become incorporated into the true lumen of the esophagus. Additional placement of a traction stitch will allow the surgeon to retract the common septum into the stapler to improve upon stapling the base of the septum and minimizing any residual pouch at the base of the original diverticulum. Even with this approach, it is common to observe a small residual pouch, but as long as there is complete division of the cricopharyngeus bar, the clinical results tend to be good.

The surgical approach to a cervical leak following transoral stapling for Zenker's diverticulum begins with a neck incision to allow for adequate drainage and diversion from the retropharyngeal space. This incision is performed in similar fashion to the cervical exposure to the esophagus as discussed in the surgical approach to esophageal exclusion for ischemia. Once the esophagus and the area in question is identified, it may be primarily repaired in the standard two-layer approach. Wide drainage of the retropharyngeal space is of upmost importance with surgical drains to minimize any risk for descending mediastinitis and sepsis. The skin may be loosely reapproximated to allow for additional drainage of the space.

Liner staplers are also often utilized for open Zenker's diverticulectomy. For very large diverticulae, we prefer to staple them flush with the esophagus with a bougie in place to avoid narrowing the lumen. Open cricomyotomy with diverticulopexy alone remains an option as to not invade the endoluminal plane of the cervical esophagus. With this approach, it is important to try to elevate the base of the diverticular pouch and transfix it to the prevertebral fascia, posterior to the proximal esophagus and pharynx. As a general rule, after most open procedures, we leave a small drain and close the cervical incisions with an interrupted one-layer closure with a minimal amount of skin staples. If any cervical esophageal leak were to develop, drainage could then be easily diverted to the skin and away from the mediastinum. Tight closure of the deeper layers with subcuticular layers may impede leak exit and thus we avoid this. The neck wound tends to heal quite well, especially if Langer's lines are respected.

Patients who undergo surgical treatment for Zenker's diverticulum generally have a short hospital stay. Thus, we do educate patients and families to watch for a delayed cervical leak post-discharge. This may manifest clinically by neck pain, fever, redness and swelling, subcutaneous emphysema, and signs and symptoms of systemic sepsis. If any of these develop, or there is any concern over the general recovery, we advise immediate evaluation. In the setting of a contained leak, there may be no drainage to the

skin, but deeper abscesses and descending mediastinitis can occur in rare cases. A contrast esophagram is our first choice using gastrograffin to rule out leak. If concern remains, we perform a CT with oral and IV contrast to look for signs of leak and mediastinitis or abscess. If the patient is clinically ill, we may go directly to the operating room for endoscopy and wound exploration, but a pre-op CT scan can be invaluable in directing the areas to be explored in the setting of descending mediastinitis and in most centers does not delay the operation significantly. Since the tracking of mediastinitis can be extensive, and may enter deeper places and either pleural cavity, going to the OR without the CT upfront may prove a disadvantage in extreme cases which may require the exploration of the mediastinum, right or left chest and the deeper layers of the neck. Typically, the mediastinitis involves subcutaneous gas and fluid which most frequently tracks into the retropharyngeal space. Once the diagnosis of mediastinitis is made, rapid and experienced surgical intervention can be lifesaving. Diabetics and immunocompromised patients are particularly prone to this problem. While small leaks may be managed with IV antibiotics and NPO, there is no substitute for surgical treatment and wide drainage of the retropharyngeal space and any other involved space.

Giant Paraesophageal Hernia (GPEH) Repair

Giant paraesophageal hernia repair may be performed either electively for symptom management, or semi-urgently for severe unrelenting symptoms or in the setting of gastric volvulus, hemorrhage or gastric ischemia. Acute gastric ischemia with necrosis has a mortality rate of from 30 percent and higher depending upon the degree of systemic sepsis and the delays from necrosis to intervention. The sooner the surgical intervention in this setting, the more likely of a good outcome.[69] Fortunately, only a minority of patients with a GPEH will present emergently with gastric ischemia, volvulus or hemorrhage. When emergency surgery is required the mortality and complications are much higher than if the GPEH is repaired electivley.[70] For decades, open surgery via thoracotomy or laparotomy remained the mainstay of therapy.[71] However, only a few centers of excellence produced consistent, durable hiatal hernia repair and symptom resolution with a low morbidity and mortality. We were one of the first centers to gain experience with a laparoscopic approach to the repair of giant paraesophageal hernia and reported good to excellent short-term outcomes.[72] Other laparoscopic series followed but few reported intermediate to long-term outcomes, and many suffered from significant recurrence rates compared to the standards set by Dr. Pearson's experience (1998). Elective giant paraesophageal hernia repair results in significant symptomatic relief and improved quality of life. In our experience, small radiographic recurrences occur in up to 15 percent of patients, but many of these are associated with modest symptoms and can be managed with medications. Some will progress and require surgical reintervention. In our long-term follow-up, our reoperation rate for laparoscopic GPEH repair was in the 3 to 4 percent range at a median follow-up of 7 years.[73, 74] Overall rates of major complications are low but are highly dependent upon on surgical expertise and on medical comorbidities.[75] Pulmonary complications, such as pneumonia or respiratory failure requiring re-intubation represent one of the most common major complications in both urgent and elective repair populations, followed by postoperative gastric or esophageal leak.[76] Postoperative leaks may develop in 2.2 to 2.5 percent of cases. Risk factors for leaks after GPEH repair include a BMI >35, and in patients who undergo a concomitant Collis gastroplasty to re-establish adequate esophageal length.[73]

Laparoscopic hiatal hernia repair has traditionally been accompanied by an anti-reflux procedure such as a Dor or Nissen fundoplication. To accomplish a durable result, one must achieve adequate, tension-free, intra-abdominal esophageal length (2-3 cm). Next, for a partial wrap, the gastric fundus is mobilized and wrapped either anteriorly (Dor) or posterior (Toupet) around the tension-free segment of intra-abdominal esophagus. Depending on the symptomatology and the motility of the patient's esophagus, the fundoplication can be wrapped in various degrees from a full 360-degree wrap (Nissen) to various degrees of a partial wrap. The laparoscopic Nissen fundoplication is the most common anti-reflux surgery performed in conjunction with repair of a GPEH. This is a well-established approach and is associated with good symptom relief for heartburn and regurgitation symptoms. However, the side effects of a full or partial wrap include gas bloat, dysphagia, and increased flatus especially in the elderly with a higher incidence of esophageal dysmotility. Overall, the laparoscopic repair of a GPEH with a partial or full wrap is safe in experienced hands, and should be associated with a mortality rate of 1 to 2 percent with low morbidity and good symptom control.[77] Gastric or esophageal perforation is the most serious complication with an incidence between 1.5 and 2 percent.[78, 79]

A gastropexy procedure can be employed as an alternative to fundoplication in select patients. Historically, gastropexy was utilized in select patients with high surgical risk, or in the setting of an urgent operation to address gastric volvulus and impending gastric ischemia. First described by Nissen (1956) using an anterior gastropexy technique,[80] some high-volume centers continue to use this technique selectively in urgent cases.[81] Reherniation remains major complication of emergent anterior gastropexy.

We have incorporated gastropexy in selected elective patients with exclusively obstructive symptoms, using a surgical technique to restore normal anatomy and reduce reflux symptoms by reinforcing the LES. In our approach, a series of interrupted horizontal mattress sutures is introduced from the line of the short gastrics to an everted edge of the left hemidiaphragm, fashioned to recreate an intra-abdominal angle of His and normal anatomic lie of the stomach.[82] We have found reherniation to be extremely rare utilizing this anatomic gastropexy technique, and results are comparable to traditional GPEH with partial fundoplication.

Esophageal and gastric perforation

Perforation of the esophagus and/or the stomach during the repair of a giant paraoesophageal can occur due to traction on the distal esophagus or GE junction, or from thermal injury or harmonic scalpel injury during dissection with an energy device. With experience, both of these complications should be rare. The esophagus itself should never be "grasped" with a grasper or a clamp. One can gently retract the esophagus from side to side atraumatically, or if needed, a penrose drain can be placed around the esophagus to facilitate back and forth retraction if needed. If an esophagus perforation is recognized, it can generally be primarily repaired and sutured with a two-layer approach. This may be buttressed with omentum or with the gastric fundus as the fundoplication is created. The stomach is more forgiving, and one may grasp the gastric wall carefully without damaging it. If a gastric perforation is identified, small defects may be primarily repaired as well, or if in a favorable location they can be stapled closed. Following repair, we place a nasogastric tube under direct or laparoscopic visualization to avoid any trauma to the site of repair in the early post-op period. This will allow for adequate gastric decompression to avoid any stress or tension on the repair. Oral intake should be restricted for several days postoperatively as well. Prior to restarting oral intake, a barium swallow should be obtained to ensure the integrity of the repair. If small esophageal leaks are identified in the postoperative period, covered esophageal stents may be placed under endoscopic guidance with reasonable success rate. Gastric leaks may require surgical exploration to repair and drain. Fluid collections may be identified by CT imaging and should be addressed via percutaneous drain placement. Larger fluid collections may require reoperation for drainage and repair.

Pneumothorax

Pneumothorax may occur during the mediastinal dissection in the surgical repair of a giant paraesophageal hernia when the pleural lining attached to the hernia sac is entered. Avoidance of this complication may be challenging as a large hernia sac may be fused or contiguous with either pleura. Pneumothorax may occur relatively quickly after violation of the pleura as the CO_2 insufflation used for proper exposure will easily enter the chest cavity. If small, and no significant hemodynamic compromise occurs, these pneumothoraces may be left alone. If the defect is large, or there is hemodynamic compromise, most pneumothoraces can be managed with a pigtail catheter placed under direct vision. While a tension pneumothorax can be a serious complication, it is important to note that the associated "floppy diaphragm" can facilitate tension-free crural approximation. We frequently and intentionally create a controlled left pneumothorax to facilitate re-approximation of the crura in the setting of a largely dilated hiatus. On the surgical side of the diaphragm, the degree of pneumothorax can be directly visualized by the surgeon, and with good communication with the anesthesia team, this "floppy diaphragm" can be beneficial to the repair with minimal negative consequences. The anesthesia team should be informed of the surgical plan, as they may see an increase in peak airway pressures as excessive CO2 enters the pleural cavity. This communication is important as tension pneumothorax can be associated with compromised oxygenation and blood pressure swings. Thus, if a pneumothorax is induced, the amount of air entering the pleural cavity should be monitored and controlled by the surgical team. As noted, this is generally easily treated by the pigtail being placed to suction, and temporarily stopping the insufflation of CO2 into the abdomen until the situation has stabilized. This pigtail is left in place to allow complete lung expansion and removal of CO2. During the procedure, the pigtail catheter can be used to direct more CO2 into the hemithorax to facilitate hiatal closure, owing to relaxation of the left hemidiaphragm.

Reherniation

Symptomatic control is maintained in the majority of patients who undergo laparoscopic hiatal hernia repair.[72, 83] Over time, there is a significant rate of hiatal hernia recurrence. In some reports utilizing radiographic evaluation, rate of reherniation may occur from 15.7 percent to upwards of 50 percent patients at long-term follow-up.[73, 84, 85] Acute large reherniations, however, are rare, occurring in less than one percent of cases. This complication may be avoided by a applying a careful approach to both the index operation and postoperative care. Redefining normal anatomy in a tension-free environment is a key component to long-term success of hiatal hernia repair. To that end, esophageal mobilization and dissection should occur circumferentially from the hiatus up into the mediastinum to the level of the inferior pulmonary veins and the right and left pleura. Care must be taken to identify and preserve the vagus nerves. Mobilization of the gastroesophageal fat pad can help to identify the true angle of his. Upon completion of this dissection, at least 2 to 3cm of distal esophagus should lie comfortably in the abdomen without any tension. A Collis gastroplasty may be employed if after circumferential mobilization there is inadequate intraabdominal distal esophageal length. Crural re-approximation should be performed with durable, non-

absorbable suture. We generally place at least two posterior and often one anterior crural stich, as closing the hiatus using only posteriorly placed sutures can create a false angulation at the GE junction. Late recurrence of hiatal hernia occurs preferentially at the anterior portion of the hiatus, thought likely due to stress at the hiatus and weakening of the central tendon,[86, 87] making this an important area to focus on in the index operation. In contrast, acute reherniation after hernia repair is often due to disruption of posterior crural sutures. Important postoperative care measures to prevent vomiting or retching should be undertaken to prevent this.

Acute reherniation may be suspected with acute onset abdominal pain (possibly provoked by increased intraabdominal pressure), or recurrence or worsening of hernia symptoms such as nausea, regurgitation, reflux, or early satiety. We recommend all patients receive a chest radiograph on postoperative day one to evaluate for a gastric bubble and placement of nasogastric tube. In our practice, all patients who undergo Nissen fundoplication or Collis gastroplasty undergo a barium swallow prior to initiation of diet. In addition to evaluation for a leak or perforation, herniation of a portion of the stomach or wrap may also be noted at this time.

All patients in our practice who undergo Nissen fundoplication and/or Collis gastroplasty as a component of laparoscopic paraesophageal hernia repair will leave the operating room with a nasogastric tube in place. This will remain for at least 24 hours (or longer in the setting of nausea or delayed gastric emptying). IV antiemetics are employed q4 hours to further avoid the tension placed on the repair by vomiting or dry heaving. Surgical repair is generally indicated for acute reherniation.

In the absence of acute instability, perioperative hiatal hernia recurrence may be repaired laparoscopically in the same manner of the index operation. Steep Trendelenburg can be utilized to reduce the hiatal hernia. At this point, the Nissen or Dor wrap may be taken down to facilitate exposure and to ensure that fundoplication is properly placed. The same principles for establishing intraabdominal GE junction in the absence of tension apply. Crural sutures are removed and may be replaced with pledgeted sutures to reinforce the repair. A left pneumothorax may be induced to aid in crural re-approximation. Rarely, crural relaxing incisions may be employed to further reduce tension. We do not routinely use a biologic mesh in our practice, but when crural integrity is in question this may be secured in place over the hiatus after the repair has been performed.

Conclusion

Postoperative complications following esophageal surgery are associated with increased morbidity and mortality. While sound surgical technique at the time of the primary operation provides the best results, timely diagnosis and proper implementation of interventions (both medical and surgical) will ultimately improve the outcomes following major esophageal surgery.

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CHAPTER 7

Bariatric Surgery: Management of Postoperative Emergencies

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Introduction

The prevalence of obesity continues to rise worldwide with reports evaluating body mass index (BMI) trends from 200 countries showing that it has increased in every country between 1975 and 2016.[1] Laparoscopic bariatric surgery is established as the most effective long-term treatment of morbid obesity.[2] The number of bariatric surgeries performed continues to increase worldwide. Since 2011, more than 1.5 million bariatric surgeries were performed in the United states alone.[3] Roux-en-Y gastric bypass is still considered to be the gold standard of bariatric surgery; however, sleeve gastrectomy has gained worldwide popularity and is currently the most commonly performed procedure.[4,5] Together, they are the most-performed procedures worldwide.[3,6] Other bariatric surgeries include adjustable gastric banding, single anastomosis gastric bypass (Mini-Bypass), biliopancreatic diversion, and duodenal switch.

Studies have shown consistently that bariatric surgery has an excellent safety profile.[7,8] However, the rising number of procedures performed will inevitably result in an increasing number of patients who will present with postoperative complications. This chapter aims to review the most common postoperative bariatric emergencies and offer insight on the best approach to their management. The chapter will focus on the three most performed procedures: Roux-en-Y gastric bypass, sleeve gastrectomy, and adjustable gastric banding.

Roux-en-Y Gastric Bypass

Laparoscopic Roux-en-Y gastric bypass (LRYGB) is the most popular form of gastric bypass. Several variations are reported; however, it usually involves creating a gastric pouch (≤30 cm^3), a Roux limb, and a biliary limb. The length of the Roux limb is usually between 100 cm to 150 cm. It can be constructed in an ante-colic or retro-colic approach. The length of the biliary limb can vary between 40 cm and 75 cm. A gastrojejunostomy (stapled or hand-sewn) and a jejunojejunostomy (usually stapled) restores gastrointestinal continuity. Food passes first through the pouch and then enters the Roux limb or alimentary limb. Food then passes through the "common channel"—the length of jejunum and ileum between the distal anastomosis and the ileocecal valve to join secretions from the biliary limb. The bypassed stomach is no longer part of the alimentary path but continues to secrete mucus and gastric acid. These gastric secretions join with bile and pancreatic secretion in the duodenum before passing though the ligament of Treitz into the biliopancreatic limb.

Thirty-day mortality following LRYGB is less than 0.5 percent.[8,9] Complications occurring following LRYGB can be divided into early complications (within 30 days) and late complications (after 30 days) **(Table 1)**.

Table 1. Complications following LRYGB

Early (<30 days postoperatively)	Late (>30 days postoperatively)
• Bleeding* • Leak* • Staple-line dehiscence* • Surgical site infection • Trocar site hernia • Venous thromboembolism • Acute nutritional deficiencies (for example, Wernicke encephalopathy)	• Internal hernia* • Intussusception • Anastomotic strictures* • Marginal ulceration/ perforation* • Gastro-gastric fistula • Incisional hernia • Cholelithiasis/ choledocholithiasis • Postgastric bypass hypoglycaemia (dumping syndrome)

Some complications can present as emergencies while others may be diagnosed in a clinic setting. We will focus on gastric bypass complications that may be encountered in emergencies and may require surgical management. These complications include bleeding, bowel obstruction, leak, staple-line dehiscence, and perforation.

Bleeding

Overall incidence of gastrointestinal (GI) hemorrhage following laparoscopic gastric bypass is 9.4 percent. Early bleeding (<30 days) in gastric bypass usually occurs postoperatively (12–48 hours) with an incidence of 1.5 percent.[10,11] Around 71 percent are related to inadequate haemostasis at an anastomotic staple or suture line or from the excluded gastric remnant.[12] The rest present late (>30 days postop) and are often due to bleeding ulcers (marginal or stomal), gastro-gastric fistula, and less commonly, neoplasm.

Clinical presentation and diagnosis

In early bleeding, the clinical presentation can mimic a leak or pulmonary embolism. In late bleeding, bleeding marginal ulcers are usually the cause, and the presentation is similar to patients presenting with upper GI bleed. Patients may present with tachycardia initially and progress to experience hypotension and oliguria as the haemoglobin levels drops. Cyclical tachycardia, corresponding to the bleeding episodes, as opposed to persistent tachycardia seen in cases of sepsis can be suggestive.[13] Patients may also experience hematemesis, haematochezia, or melena. History of abdominal pain may be present in some patients, particularly epigastric in cases of underlying ulcers (marginal or NSAID-induced).[14]

Management

Up to 80 percent of early postoperative bleeding in gastric bypass are self-limited. These are usually associated with the staple lines. There are four potential sites of staple line haemorrhage: gastric pouch, the gastrojejunostomy, the jejunojejunostomy, and the bypassed stomach.[10] In late GI bleed, marginal ulcers are the most common cause, and only 5 percent may present with upper GI bleed. Acute massive bleed is uncommon.[15] Stable patients should receive serial haemoglobin and vital signs monitoring. Transfusion may be required if patients develop early stages of haemorrhagic shock. Anticoagulation should be withheld, and care taken to carefully re-instate once bleeding stops to avoid thromboembolic complications, especially in the early postoperative period. In cases of severe bleeding or unstable patients, intervention may be required.

The bleeding in gastric bypass can be intraluminal or intra-abdominal. Hematemesis or blood per rectum, if present, suggests an intraluminal cause. Computerized tomography (CT) angiography may be necessary to identify the source of bleed and guide in the management.

Intervention consists of either endoscopic or surgical therapy. If the source is intraluminal and accessible, endoscopic therapy is advised. Clipping, epinephrine injection, or, less commonly, thermal coagulation is used to control the bleeding.

Endoscopy is often successful in cases of bleeding ulcers. Initiation of proton pump inhibitor and cessation of NSAID and work-up for Helicobacter pylori is recommended. Contrast study should be performed following endoscopic intervention to check for anastomotic integrity, particularly in the immediate postoperative period.

In cases of intra-abdominal bleeding and unstable patients, surgical intervention is warranted. Diagnostic laparoscopy is advised if local surgical expertise is available. Once the source is identified, clipping or over-sewing provides adequate control. Often, the site cannot be identified; however, evacuation of the hematoma will reduce fibrinolysis and reverse coagulopathy. Angioembolization has been described but should be kept as a last resort.[16]

Intestinal obstruction

Overall intestinal obstruction following laparoscopic Roux-En-Y gastric bypass (RYGB) ranges between 3.6 and 7 percent.[17,18] It can present early or late in the postoperative period. Early obstruction is usually the result of a technical problem, mostly at the level of the jejunojejunostomy. Late obstruction is most often the result of internal hernia or adhesions.[19] Other causes of obstruction include Roux limb constriction as it passes through the mesocolic window, kinking or stricture at the gastrojejunostomy or jejunojejunostomy, incarceration at an incisional or ventral hernia, and volvulus. A proper understanding of the anatomy of gastric bypass is key in establishing the diagnosis.

Clinical presentation and diagnosis

Obstruction affecting the alimentary limb can present with abdominal pain, nausea, and vomiting. Obstruction affecting the biliopancreatic limb, however, may be more challenging to diagnose since the alimentary limb may not be distended. With increasing distention of the gastric remnant, symptoms of fullness, bloating, pain, and hiccup may develop without any episodes of vomiting.

Abdominal films can only identify up 35 percent of intestinal obstruction and often miss distention affecting the biliopancreatic limb. Consequently, CT scans are crucial in diagnosing suspected obstruction in gastric bypass patients.[20] Patients should be kept nil by mouth and adequately resuscitated. Emergency obstructions in RYGB almost always require surgical treatment, and early intervention is crucial to prevent bowel ischemia or gastric perforation. Obstruction related to adhesion and incisional hernia should be addressed, as they would in general require surgical management. We will discuss in this section early obstruction following RYGB and late obstructions mainly secondary to internal hernia.

Management of early obstruction

Early bowel obstruction incidence varies between 0.5 and 5.2 percent with 60 percent occurring at the level of the jejunojejunostomy.[19,21] Patients will present with common symptoms of abdominal pain, nausea, and vomiting. A CT scan is often needed to differentiate from other abdominal pathologies. Common causes of obstruction include JJ kinking or narrowing and intraluminal blood clot. A patient showing signs of partial obstruction may be managed conservatively; however, up to 80 percent of patients will require surgical intervention. A laparoscopic approach is preferred in stable patients. Surgical management includes revision of the jejunojejunostomy or JJ bypass. For intraluminal hematoma, evacuation is often enough.

Management of obstruction from internal hernia

Internal hernias (IH) are relatively common after gastric bypass, and over time, the reported incidence can range between 0.5 and 11 percent.[22] The site of hernia can vary depending on the approach used to create the roux limb and whether mesenteric defects are routinely closed. Potential sites of hernias include the space between the mesentery of the jejunojejunostomy, the space between the transverse mesocolon and the mesentery of the roux limb (Petersen defect), and in a retrocolic approach, the mesocolic defect. A meta-analysis showed that routine closure of defects is associated with the lowest incidence of IH.[23] The antecolic as

opposed to the retrocolic approach in creating the roux limb is associated with the lowest overall incidence (1 percent), provided that both mesenteric defects are routinely closed using nonabsorbable sutures.[24]

In patients presenting with abdominal pain, a high index of suspicion should be present, as physical examination can be misleading. As the small bowel becomes entrapped, venous outflow is partially or completely occluded resulting in bowel ischemia. The patient may exhibit pain out of proportion to physical examination. Pain can be relieved by leaning forward or "getting down on all fours.". Laboratory tests may be unhelpful, and normal lactate levels can be misleading. CT scans are reported to be 76 percent sensitive and 60 percent specific in detecting IH, with a high degree of variation in reported literature.[25] The "swirl sign" of the spiralling mesentery is useful in diagnosis, with a sensitivity ranging between 68 and 89 percent and specificity between 63 and 86 percent.[26] Consequently, a negative CT does not rule out internal hernia, and surgical exploration remains the gold standard in patients with high clinical suspicion.

A laparoscopic approach should be attempted if experience is available. However, open exploration is an option in an unstable patient. Intestinal anatomy can be challenging to identify, especially if a significant length of bowel is trapped. Identifying the ileocecal and proceeding with a retrograde bowel run is often successful in identifying the distal anastomosis and reducing the bowels. Bowel viability should be assessed, and ischemic bowels resected. The defect should be closed with nonabsorbable running sutures. The other defects should be checked and closed if necessary.

Anastomotic leak and perforation

Overall incidence of leak following gastric bypass ranges between 0.3 and 5.6 percent.[27-29] Early leaks (<30 days) are usually due to technical failure, with 50 percent occurring within five days.[29] Causes include staple malfunction or anastomotic tension. The most common site of leak is the gastrojejunostomy (67 percent).[28,29] Other sites include the gastric pouch, remnant stomach, and jejunojejunostomy. Mortality following leaks at the jejunojejunostomy can be as high as 50 percent but tends to be much lower in leaks at the gastrojejunostomy (3 percent).[30,31] Late leaks are rare and can occur secondary to perforated marginal ulcer. It may occur in patients known to have marginal ulcers; however, it can also present acutely in previously asymptomatic patients.
Risk factors for leaks include elevated BMI, male gender, history of diabetes mellitus, sleep apnea, hypertension, cirrhosis, renal failure, history of prior abdominal surgery or revisional surgery, and smoking.[28,32,33]

Clinical presentation and diagnosis

Clinical presentation of leaks following gastric bypass tend to vary. The most sensitive indicator is persistent tachycardia.[34] Other symptoms include abdominal pain, tachypnoea, fever, and oliguria.[35] Laboratory findings of leucocytosis and a C-reactive protein (CRP) greater than 229 mg/dL[36] are highly suggestive of leaks. While upper GI series with water-soluble contrast are sensitive in detecting leaks, a CT scan allows for detection of abdominal collections and abscesses or other causes of the presentation and should be the modality of choice for diagnosing leaks. Nevertheless, sensitivity of both modalities varies greatly in reported literature with up to one-third of studies reported as false negatives.[33] Surgical exploration remains the most sensitive approach when clinical suspicion is high despite negative radiological findings.[37]

Management

Patient should be kept nil by mouth and adequately resuscitated. Unstable patients should receive surgical treatment. Conservative management can be attempted in stable patients with small, contained leaks. Broad-spectrum antibiotics and total parenteral nutrition should be started at the time of diagnosis. Contained leaks are drained percutaneously if accessible, with cultures and sensitivity sent, and antibiotics adjusted accordingly. The clinical condition should be continuously re-assessed with vital signs, white cell count, CRP, and serial physical exams. Nonoperative treatment can be successful in up to 80 percent of patients,[34,38] and upper GI series with water-soluble contrast is recommended to document healing before attempting oral intake. In persistent or worsening abdominal pain, clinical deterioration, or persistent leak, patients should proceed to operative treatment.

The principles of operative treatment are the same in early and chronic leak: sepsis control, washout and drainage of enteral contents, and establishing enteral feeding route for postoperative nutrition.

Primary repair can be attempted in leaks from the jejunojejunostomy or the gastric remnant where success is more likely than leaks from the gastrojejunostomy.[34] Alternatively, a T-tube can be placed into the leak site to establish a controlled entero-cutaneous fistula. Revision of the anastomosis is also an option if the patient is stable intraoperatively and surgical experience is available.

Endoscopic management of leaks following gastric bypass is also reported with variable results. Covered self-expanding stents are used to bypass the leak site and employed more commonly in leaks at the gastrojejunostomy. They are left in for four to six weeks, and oral intake can be resumed within days. They are generally well tolerated by patients; however, stent migration and associated complications (bleeding,

stricture, perforation) remain problematic.[39-41] For small wall defects, endoscopic clipping is also reported; however, literature is limited to case series and consensus is lacking.[42,43]

Sleeve Gastrectomy

Laparoscopic sleeve gastrectomy (LSG) first emerged as a standalone procedure in 2000 after an incomplete attempted laparoscopic duodenal switch in a patient with high BMI (>60 Kg/m^2).[44] Being technically easier and praised as being more "physiologic," as it does not involve any intestinal re-routing or anastomosis, it is no surprise that this procedure has gained popularity among both surgeons and patients. With comparable weight loss results as the gastric bypass,[45,46] LSG is today the most commonly performed bariatric/metabolic surgery in the U.S. and worldwide.[3-5]

In summary, the stomach is divided vertically along the lesser curvature using linear staplers and a calibration tube (usually 36F or 40F) 2 to 5 cm from the pylorus up to the angle of His. Depending on surgical technique, the staple line may be reinforced with buttress material or continuous serosal sutures. Some studies have reported decreased bleeding risk with staple-line reinforcement, while some reported increased risk of leak.[47-49] Other studies have reported decreased risk of leak with no significant reduction in bleeding rate.[50,51] To date, literature does not support one approach over another, and the decision to reinforce is left to the discretion of the surgeon.

The overall reported mortality in LSG is 0.242 percent.[52] Despite its perceived simplicity, complications from LSG can be challenging. The most feared complication is a staple line leak, with an incidence ranging between 0.9 and 2.2 percent.[53-55] Bleeding is also reported at 2 percent[56] with range varying between 1 to 6 percent. Porto-mesenteric and splenic vein thrombosis (PMSVT) is a rare but serious complication that also can present with symptoms mimicking a leak or bleed.[57] Other complications include stenosis and gastroesophageal reflux.

Staple Line Leak

Staple line leak (SLL) is a serious complication following LSG. Although rare in primary surgery, the incidence increases to more than 5 percent in revisional surgery.[55,58] The cause of leaks can be grouped into two categories: mechanical or ischemic.[59] SLLs are also classified based on their time of presentation, location, clinical presentation, and radiological appearance.[60] The clinical presentation can vary from asymptomatic to septic shock.

Clinical presentation and diagnosis

More than half of leaks will occur within 10 days postoperatively. Leaks occurring within 48 hours postoperatively are usually the result of technical failure. The proximal third of the stomach, namely the GE junction, is the site of 86 percent of leaks. Fever and tachycardia are the most common clinical signs in patients.[53,61] Abdominal pain, nausea, vomiting, left shoulder pain, and tachypnoea are also frequently reported. A high index of suspicion should be present, as acute leaks (<7 days) can present with severe symptoms while late leaks might present with more subtle signs such as vague abdominal pain and low-grade fever.

Patients suspected to have SLL should undergo a CT scan with intravenous and oral water-soluble contrast. The scan can provide information about leak site, collections, and degree of contamination in addition to other complications such as pulmonary embolism and PMSVT that would be otherwise missed on upper GI contrast study.[53] However, CT scans are only 56 percent sensitive, and if suspicion remains, surgical exploration is warranted.[34] The treatment of leaks can be challenging, but like leaks following gastric bypass, the principles of treatment remain the same: sepsis control, adequate nutrition, and restoring gastrointestinal continuity.

Management

To date, there is no adopted algorithm for the management of SLL, and the approach depends on the patient's clinical condition and available expertise. In unstable patients, laparoscopic drainage and washout is the recommended approach.[53] Inspection of the stomach is important to identify structural causes of staple line leaks such as stenosis or twisting that will later prevent healing. Primary closure of the leak site is not advised as it often fails. Nutrition access should be secured early on, ideally during the operation. This is best achieved via the enteral route by a feeding jejunostomy tube. Parenteral nutrition is another option if an enteral route cannot be secured.[62] Broad-spectrum antibiotics should be started early in the diagnosis and adjusted according to sensitivity.

In stable patients, the management of leaks becomes even more controversial and varies according to surgeon experience and preferences. In patients with well-defined collections, image-guided percutaneous drainage followed by appropriate antibiotic therapy and nutritional support is a valid approach. Early surgical drainage even in stable patients is also well advocated. Endoscopic internal drainage (EID) is also described and has the advantage of reducing risks of external fistula formation, with a reported success rate of 74.6 percent.[63]

Other endoscopic approaches include stent placement, over-the-scope clipping (OTSC), and EVAC and can be used as an adjunct treatment or as definitive treatment. Out of these modalities, stenting is the gold standard. Used initially to treat stenosis as it decreases intraluminal pressure, Serra et al. first described the use of covered stents in 2007, with a reported success rate of 83 percent.[64] Currently, there are different types of partially covered (Wallstent™) and

fully covered stents (Megastent™, Hanarostent™) designed specifically to manage SLL, with success rates ranging between 50 and 88 percent.[65,66] Complications associated with stenting include: migration (11.1–83 percent), difficulties in stent removal, and poor patient tolerance due to symptoms of retching, regurgitation, or epigastric and chest tightness.[67]

The safety and efficacy of OTSC for the management of SLL is showing promise; several studies are reporting good results with success rates as high as 80 percent.[68,69] This approach involves applying clips (OTSC®) to close the leak site. This approach is, however, technically challenging since most leaks are proximal at the gastroesophageal junction (GEJ), and the degree of inflammation can hinder proper grasping of the clips.

Finally, EVAC or endoscopic vacuum therapy is showing encouraging results. The process involves endoscopic placement of a vacuum drainage system (Endo-SPONGE®) with changes made every three to five days until the leak site is closed. Investigators have reported success rates up to 100 percent.[70,71] Larger studies are needed to validate these findings, and concerns about the need to change the system every three to five days under general anaesthesia have been raised.

Acute, early, and late fistula following sleeve gastrectomy can become chronic fistula despite all efforts to manage conservatively, and reoperation becomes the only solution. Conversion to a bypass procedure via Roux-en-Y gastric bypass or a fistuo-jejunostomy (Baltasar procedure) are often described.[72-74]

In conclusion, despite being a rare complication, management of SLL can pose significant challenges. Transfer to a bariatric center should be considered early in the treatment. Management often requires a multidisciplinary approach with surgical, nutritional, radiological, and infectious disease input. Patients may be subject to prolonged or repeated hospital admissions, with some requiring multiple corrective surgeries.

Bleeding

The incidence of postoperative bleeding in LSG is around 2 percent.[56] Bleeding can be endoluminal or intra-abdominal. The most common sites of bleeding are the staple line and the short gastric vessels. Patient factors (coagulopathy, fatty liver, high BMI) and technical factors (proper use of energy devices, proper size of staplers) can increase risk of bleeding.[75,76] Bleeding postoperatively can lead to prolonged hospital stay, reoperation, and even increased risk of leaks.[77]

Clinical presentation and diagnosis

Bleeding usually occurs within 48 hours postoperatively. In endoluminal bleeding, patients can experience hematemesis or melena. Bleeding is usually limited, and patients may not exhibit significant hemodynamic changes. In intra-abdominal bleeding, patient may complain of nonspecific abdominal pain or discomfort. As bleeding progresses, the patient may show signs of tachycardia, hypotension, and even shock. A serial blood test may show a drop in haemoglobin or increase in urea.

Management

In stable patients, conservative management is often effective.[78] Serial haemoglobin and vital signs monitoring are needed for close observation. Anticoagulation should be discontinued and re-assessed daily to avoid thromboembolic complications. A CT scan may be required to establish the diagnosis and assess ongoing bleeding and the size of a haematoma. Small haematoma can be left untreated, while large haematoma are better evacuated by surgical exploration to reduce risk of leaks.[75,77] In unstable patients, intervention is recommended. In patients with intraluminal bleeding, gastroscopy for control of bleeding can be achieved with adrenaline injection, clips, or bipolar probe. For intra-abdominal bleeding, early laparoscopic exploration is recommended. The bleeding is often at the staple line, and control can be achieved by clipping or suturing.

Porto-Mesenteric and Splenic Vein Thrombosis (PMSVT)

PMSVT is an uncommon but potentially fatal complication after bariatric surgery. It is more common after sleeve gastrectomy, with an incidence of 0.3 percent. Oral contraceptive pills, active smoking, previous surgery, and coagulopathy are identified as risk factors. Patients may present with abdominal pain (82.7 percent), leucocytosis (38 percent), and fever (12.7 percent).[57] Eighty-nine percent of patients present within the first month of surgery; however, this condition can present years after the surgery.5[7,79] The portal vein, superior mesenteric vein, and splenic vein are the most affected vessels.[57] The vague abdominal symptoms and similarities with other postoperative complications can be misleading, and clinicians should have a high index of suspicion.

CT scan with IV contrast is often the modality of choice for diagnosis. Therapeutic anticoagulation should be started as soon as possible. Though this complication is managed medically, delay in diagnosis can lead to serious consequences such a bowel ischemia, liver failure, and even death.[57]

Adjustable Gastric Band

Laparoscopic adjustable gastric band (LAGB) was once the leading bariatric surgery performed due to the ease of placement, quick recovery, low cost, and reversibility. With evidence showing suboptimal long-term weight loss and high incidence of complications reaching 40 percent at 10 years,[80] LAGB's popularity declined. In the U.S., the number

of LAGB performed in 2018 was 1.1 percent of total bariatric procedures compared with 35.4 percent back in 2011.[3] Worldwide, from 2014 to 2018, only 5 percent of bariatric procedures were gastric bands.[6]

LAGB involves the placement of an inflatable silicone band around the proximal stomach. The band is attached to a reservoir system that allows adjustment of the tightness of the band. A port is connected to the reservoir and placed subcutaneously. Major complications following gastric band are mainly band slippage and band erosion.

Band slippage

Band slippage or gastric prolapse occurs when part of the gastric wall herniates cephalad under the band. This is one of the most common band complications, with an incidence of 8 percent.[81] When placed, the band is usually fixed at an angle from the one o'clock to three o'clock position to the seven o'clock to nine o'clock position. The "phi" angle, the angle measured between a vertical line oriented to the vertebral column and another through the long axis of the gastric band, is normally between four and 58 degrees. The migrated gastric wall can cause tilting of the band angle and lead to obstruction.

Clinical presentation and diagnosis

Band slippage can be classified as acute or chronic, early, or late, or even anterior or posterior. Early or acute slippages are typically diagnosed prior to postoperative day three. Late or chronic slippages may present anywhere between four months and two years after the initial surgery.[82] Patients can present with epigastric pain, dysphagia, vomiting, food regurgitation, or food intolerance. The same symptoms can indicate having a tight band, so a high index of suspicion is required.[83] The diagnosis of band slippage can be made with an abdominal X ray or an upper gastrointestinal (UGI) series. Any variation to the orientation of the phi angle is suggestive of a slippage.

Management

If the work-up confirms band slippage, the band should be immediately deflated to avoid gastric incarceration or strangulation. If patient symptoms improve and the patient can tolerate fluid, an UGI series can be repeated in a week to see if the stomach has reduced below the band. If the symptoms persist or the patient cannot tolerate fluids, admission for monitoring and hydration is advised. Band deflation may allow the prolapsed stomach to be reduced; however, surgical management is often required if this fails. Previously, the band was unbuckled laparoscopically, the stomach reduced, and the band buckled again. Although shown to be safe, the risk of recurrence was high.[84,85] Most centers now recommend band removal. In rare cases when diagnosis is missed or delayed, band slippage may cause ischemia or necrosis of the prolapsed stomach. In such cases, immediate surgical exploration with band removal and possible gastric resection is necessary.

Band erosion

Band erosion is a serious yet uncommon complication of LAGB. It occurs when the band itself migrates into the lumen of the stomach. The overall incidence is 1.46 percent. The cause of band erosion can be underlying gastric damage during initial placement, cautery injury, or tension placed on the stomach by gastro-gastric sutures.[86] Though it appears to have significant consequences, band erosion usually follows a benign course.

Clinical presentation and diagnosis

The most common symptoms associated with band erosion include sudden loss of satiety, vague epigastric pain, dysphagia, heartburn, and low-grade fever. A late port site infection presenting months or years after band placement should raise suspicion of erosion.[87] Rarely, patient may present with peritonitis, haemorrhage, or obstruction.[87-89] Upper GI endoscopy is the modality of choice to diagnose band erosion since neither a upper GI series nor CT scan are specific enough. The presence of otherwise unexplained free air on a CT scan should alert the clinician to the diagnosis.[90]

Management

Laparoscopic removal of the band is the first line of management, although endoscopic retrieval of eroded bands is reported.[86,91] Often the perforation is already sealed by an inflammatory process and only band removal is needed. In case of persistent and identifiable gastric defect, primary closure can be attempted. Reinsertion of an adjustable gastric band or conversion to another bariatric procedure is described; however, this should be done in bariatric centers following a careful discussion with the patient.[86]

Conclusion

With the increasing number of bariatric surgeries performed worldwide, short- and long-term complications are more frequently encountered in the emergency setting. A good understanding of the anatomical and technical aspect of each procedure is key to properly diagnosing and managing each complication. With nonspecific signs and symptoms, the liberal use of CT scans and upper GI series to investigate these emergencies should be coupled with a high index of suspicion and a low threshold for surgical exploration in order to avoid serious and life-threatening complications.

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CHAPTER 8

Management of Gastric and Duodenal Perforation

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Abstract

In the last decade, the number of patients presenting with this gastric and duodenal perforation has declined due to improved medical management of peptic ulcer disease, which is the most common cause. However, gastric and duodenal perforation still remains a common cause of peritonitis. Gastroduodenal perforation is a common surgical emergency and may have life-threatening sequelae. At the present time, there is no general consensus about management of this complication. Certain important points are still debated such as the role of nonoperative management, the choice of laparoscopic versus open laparotomy approach, and the type of procedure to be used in emergency situations.

Introduction

Gastrointestinal perforation, with leakage of alimentary contents into the peritoneal cavity, is a common surgical emergency and may have life-threatening sequelae.

The most clinically significant and leading cause of these perforations is peptic ulcer disease**.** The incidence of peptic ulcer disease has decreased in recent years.[1] This is mainly due to a major revolution of medical management, with the development of antisecretory medications, including histamine 2 receptor blockers (H2RBs) and proton pump inhibitors (PPIs). The additional recognition that peptic ulceration is an infectious disease and treatment for Helicobacter pylori infection has further improved outcomes.[2] However, peptic ulcer complications, including perforation, still remain a substantial health care problem. This may be related to increased use of non-steroidal anti-inflammatory drugs (NSAIDs) and to the aging population.[3] Other less common causes include trauma, malignancy, chronic steroid use, and iatrogenic injury during endoscopic procedures. In particular, iatrogenic duodenal perforations are becoming more common following the widespread use of endoscopic procedures such as endoscopic retrograde cholangiopancreatography (ERCP).[4]

Optimal methods for the management of gastroduodenal perforations remain controversial. The gold standard for the management of gastroduodenal perforation has traditionally been open exploration with surgical repair in association with an acid-reducing procedure. However, the use of minimal access techniques has become increasingly frequent, resulting in similar outcomes to open surgery, with decreased perioperative pain. Additionally, nonoperative management has become more frequent in hemodynamically normal patients with minimal abdominal and systemic symptoms.[5] Emergency operations for perforated peptic ulcer disease result in a mortality rate of 6 to 30 percent.[6,7] Perioperative shock, renal failure, delayed operative intervention >12 hours, significant comorbidities, advanced age, cirrhosis, and immunocompromise have all been identified as risk factors for adverse outcome.[8,9] Therefore, an acute care surgeon must take into account many important factors when treating a critically ill patient needing an emergent surgical intervention.

Etiology

Causes of gastroduodenal perforations are shown in **Table 1**.

Peptic ulcer

Ulcer disease remains the most common cause of gastroduodenal perforation, with an incidence between 2 and 10 percent in patients with ulcers.[10]

Malignancy-related perforation

Neoplasms can perforate by direct penetration and necrosis, or by producing obstruction. Perforations related to tumors can also occur spontaneously, following chemotherapy or as a result of radiation treatments. It can also be related to interventions like stent placement for malignant obstruction.[11]

Strangulated hiatus hernia and gastric volvulus

Acute manifestations of hiatal hernia include gastric perforation by strangulated hiatal hernia and acute gastric volvulus.[12,13] Currently, the morbidity and mortality rates are up to 20 percent, and for this reason prompt surgical management is required. They can lead to perforation by gastric necrosis.

Iatrogenic

The stomach and duodenum may be injured in the course of a number of procedures.

Endoscopic perforation

Upper endoscopy is the main cause of iatrogenic perforations. The overall perforation rate is 0.11 percent for rigid endoscopy compared with 0.03 percent for flexible endoscopy. Iatrogenic perforations are more frequent in patients with preexisting gastric pathology. Rupture of the stomach due to excessive insufflation of the stomach can occur in the course of endoscopy or even unrelated procedures, such as cardiopulmonary resuscitation, and is typically located on the lesser curve where the organ is least distensible.[14] Gastroduodenal perforation has also been reported as a complication of a variety of abdominal procedures, including polypectomy, dilation of anastomotic strictures, endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD),1[5,16] ERCP,[17] and biliary stents.[18]

Operative injury

Marginal or stomal ulceration after bariatric procedures (RYGB and biliopancreatic diversion and biliopancreatic procedures with duodenal switch) have been reported in 0 to 16 percent of cases.[19]

Spontaneous idiopathic gastric perforation

Spontaneous perforation of the stomach is an uncommon event mainly seen in the neonatal period, the first few days of life, as a cause of pneumoperitoneum.[20]

Trauma

The stomach and duodenum are relatively protected by their anatomical location and are the third most frequently injured hollow intra-abdominal organs after small bowel and colon. Traumatic injury to the stomach and duodenum causing perforation is rare, comprising only 5.3 percent of all blunt hollow organ injuries, but it is associated with a complication

rate of 27 to 28 percent . It can occur in association with any penetrating trauma of the abdomen, such as gunshot and stab wounds.[21]

Ingested substances and foreign bodies
Medications or other ingested substances (caustic injury) and foreign bodies such as sharp objects (toothpicks), food with sharp surfaces (for example, chicken bones or fish), or gastric bezoar can cause gastroduodenal perforation.[22]

Other causes
Other causes of gastroduodenal perforation include autoimmune conditions (in other words, Crohn's disease, scleroderma, and vasculitis), infectious diseases, impacted gallstones, and ischaemic disorders.[23,24]

Table 1. Causes of gastroduodenal perforations

Underlying gastroduodenal pathology	• Peptic ulceration • Perforated carcinoma • Gastric volvulus • Strangulated hiatal hernia • Neoplastic obstruction • Ischaemic disorders • Autoimmune conditions • infectious disease • Impacted gallstones
Iatrogenic	• Endoscopic perforations • Operative injury
Spontaneous	• Spontaneous idiopathic gastric perforation
Trauma	• Stab wound • Blunt abdominal trauma
Ingested substances and foreign bodies	• Sharp foreign bodies • Implanted foreign bodies (endoprosthesis or vascular grafts) • Caustic injury

Outcomes

When diagnosed promptly and treated expediently, outcomes are excellent. Mortality rates range from 6 to 14 percent.[25-27] Increasing age, severe comorbidities, and delays in diagnosis and management greater than 24 hours have been related to poor outcomes.[28] In particular, advanced age (greater than 70 years) is associated with a higher mortality with rates of approximately 41 percent.[29,30]

Several scoring systems have been used to risk stratify patients and predict outcomes of patients with perforated ulcers. The Boey score[31] **(Tables 2a and 2b)** is the most commonly and easily implemented of these scoring systems, and it accurately predicts perioperative morbidity and mortality.[32]

Table 2a. Boey score

Concomitant severe medical illness
Preoperative shock
Duration of perforation >24 hours
Score: 0–3 (Each factor scores 1 point if positive)

Table 2b. Boey score and outcomes

Risk score	Mortality (OR)	Morbidity (OR)
1	8 percent (2.4)	47 percent (2.9)
2	33 percent (3.5)	75 percent (4.3)
3	38 percent (7.7)	77 percent (4.9)

Diagnosis

Prompt diagnosis of gastroduodenal perforation requires a high index of suspicion based on history and clinical examination. A history of intermittent abdominal pain or gastroesophageal reflux is common. Additionally, known peptic ulcer disease that has been inadequately treated or with ongoing symptoms and sudden exacerbation of pain can be an indication of perforation. A history of recent trauma or instrumentation followed by pain and tenderness should alert the clinician to the potential for injury. Patients with gastroduodenal perforation usually present with abdominal pain and peritoneal irritation from leakage of acidic gastric contents. However, physical examination findings may be equivocal, and peritonitis may be minimal or absent, particularly in patients with contained leaks.[33] Laboratory studies are not useful in the acute setting as they tend to be nonspecific, but leukocytosis, metabolic acidosis, and elevated serum amylase may be associated with perforation.

Free air under the diaphragm found on an upright chest X ray is indicative of hollow organ perforation and mandates further work-up and/or exploration. In the setting of an appropriate history and peritonitis on examination, free air on an X ray is sufficient to justify exploration. In patients without pneumoperitoneum on an admission chest radiograph should be evaluated with computed tomography (CT) scanning. The increased use of CT scans has greatly improved our ability to detect perforation. Suspicious findings on CT scan include unexplained intraperitoneal fluid, pneumoperitoneum, bowel wall thickening, mesenteric

fat streaking, mesenteric hematoma, and extravasation of contrast.[34,35] However, up to 12 percent of patients with traumatic perforations may have a normal CT scan. In the setting of trauma, diagnostic peritoneal lavage (DPL) has essentially been replaced by the focused assessment by sonography for trauma (FAST), which lacks specificity for hollow-organ perforation.[36,37] Victims of penetrating trauma with signs of peritonitis merit surgical exploration without further diagnostic workup. In blunt trauma patients, and in penetrating trauma patients without peritonitis, in whom the trajectory of the missile may be unclear, CT scanning of the abdomen and pelvis with oral and intravenous contrast remains the standard of care.

Management

Nonoperative management may be reasonable in selected cases with a perforated peptic ulcer. This subset includes those who are young, healthy, and hemodynamically stable and have no signs of diffuse peritonitis. The decision to pursue nonoperative management must be weighed against the risk of increased morbidity and mortality associated with surgical delay. The onset of symptoms of less than 24 hours, mild abdominal pain with minimal peritoneal irritation, hemodynamic stability, and an absence of systemic signs of sepsis in a patient under the age of 70 are all indications for a trial of nonoperative management.[38,39] Nasogastric tube decompression, fluid resuscitation, administration of a proton pump inhibitor, thromboembolic prophylaxis, and appropriate antimicrobial therapy should result in clinical improvement in a patient's symptomatology within 12 hours. However, it has been demonstrated that observation periods longer than 12 hours without clinical improvement worsen the outcomes from perforated peptic ulcers, and therefore should be avoided.[40,41] Patients with hemodynamic instability, onset of symptoms longer than 24 hours in duration, those with peritonitis on physical examination, and those with systemic signs of sepsis should be surgically explored. Additionally, patients who are age 70 or older are less likely to respond to nonoperative management and should be considered for early operative intervention.[42] Failure of nonoperative management, defined as increasing abdominal symptoms, fever, or worsening leukocytosis, should prompt urgent surgical intervention.

The site of perforation dictates the operative approach. The primary goals of surgical management in gastroduodenal perforations are to repair the perforation and minimize the degree of contamination. Most perforated peptic ulcers are located in the first part of the duodenum (35 to 65 percent), with 25 to 45 percent located in the pylorus and 5 to 25 percent located in the stomach. In the era of H. pylori therapy and acid-reducing medications, up to 90 percent of perforations may be treated with a primary repair in addition to an omental buttress if there are viable edges at the site of perforation.[43-45] However, especially in case of peptic ulcer disease, the tissue surrounding a perforation can be friable and the size of perforation can be greater than 2 cm, making primary repair difficult. In these cases, a gastric resection is required. For perforated gastric ulcers located along the greater curvature, antrum, or body, a stapled wedge excision of the ulcer can be performed.[46] Ulcers located along the lesser curvature and are unable to be excised and closed should be treated with a distal or subtotal gastrectomy combined with a Billroth I or II gastrojejunostomy or Roux-en-Y gastrojejunostomy.[47,48] The initial management of iatrogenic injuries associated with endoscopic procedures, specifically ERCP, should include, as aforementioned for gastric perforations, fluid resuscitation, antibiotic therapy, and possible nasogastric decompression. Stapfer is a commonly used classification system dividing duodenal perforations into four types.[49] It utilizes the anatomic location of injury as well as the mechanism and severity of injury **(Table 3)**.

Table 3. Stapfer classification

Type I	Lateral or medial wall duodenal perforation
Type II	Periampullary injuries
Type III	Bile duct or pancreatic duct injuries
Type IV	Retroperitoneal air alone

Medical management can be attempted in patients with retroperitoneal perforations who are hemodynamically stable and who exhibit no evidence of peritonitis.[50] Surgery should be reserved for patients with hemodynamic instability, exam findings consistent with peritonitis, a large free perforation, and a biliary obstruction, or for those who do not improve after a trial of nonoperative management.

Patients presenting with complicated duodenal ulcers in close proximity to the pancreatico-biliary system pose a technically difficult situation for the surgeon, as these ulcers are unable to be resected and can be difficult to close primarily or patch. In this setting, surgeons should consider adjunctive diversion and decompression of enteric contents to assist with healing. The use of "triple tube therapy" or pyloric exclusion accomplishes these goals. Triple tube ostomy approach includes placement of a tube gastrostomy, retrograde tube duodenostomy, and feeding jejunostomy.[51] In recent years, minimally invasive surgical techniques have gained in popularity. Several studies have demonstrated equivalent outcomes to open surgery.[52-55] In fact, the laparoscopic approach appears feasible in most cases, with a conversion rate to open surgery of less than 25 percent . Although operative times are generally longer, there appears to be no difference in the open versus laparoscopic approaches, except potentially in decreased postoperative pain. Patients with large perforations, perforations in the posterior

location, or patients with significant medical comorbidities are considered to have relative contraindications to the laparoscopic approach and should be considered for open surgery.

Summary

Although the improvement of medical management has led to a decrease of gastroduodenal perforations, they remain a surgical problem. The goal in all patients with gastroduodenal perforations is early diagnosis, and hemodynamic stabilization followed by antibiotic therapy and most often surgical intervention. Surgical techniques for the management of gastroduodenal perforation are varied. Laparotomy and omental patch repair remains the gold standard, while laparoscopic surgery should only be considered when expertise is available.

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CHAPTER 9

Endoscopic Approach in Gastrointestinal Postsurgical Complications

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Introduction

Gastrointestinal surgery (GIS) is becoming increasingly safer, which is mainly attributable to the introduction of minimally invasive techniques (for example, laparoscopy and robot-assisted surgery) and the integration of artificial intelligence into daily practice. Artificial intelligence has significant beneficial effects on safety and surgical outcomes.[1] However, complications in GIS cannot be totally avoided, and their occurrence often compromises the postoperative course, affects overall costs, and can lead to death. Complications in GIS depend on patient characteristics, the surgeon's expertise, and the surgical procedure type. The management of postoperative complications is often conservative, requiring more intense medical assistance. When this approach fails, more aggressive methods may be used. Gastrointestinal endoscopy (GIE), as a minimally invasive technique, is frequently chosen as the first-line treatment in several postsurgical complications. The advantages of GIE are the minimally invasiveness, repeatability, and cross-integration with other interventional techniques such as radiology and surgery.

The aim of this chapter is to describe the endoscopic techniques available to manage the most common postsurgical GI complications: postoperative ulcerations and bleedings, anastomotic dehiscence, GI fistulas, pancreatic and biliary fistula, biliary strictures, and leakages.

Anastomotic and Stress Ulcers

Gastrointestinal bleedings can occur after major surgeries and can compromise the patient's postsurgical course. Marginal ulceration (MU) and stress ulcers (SU) are possible sources of bleeding, which may require endoscopic examination and treatment. MUs generally occur at the gastro-jejunal anastomosis after partial gastrectomy (for example, distal gastrectomy, gastric bypass, pancreaticoduodenectomy), and their course is asymptomatic in up to 60 percent of patients.[2,3] Heartburn, nausea, and vomiting are possible clinical presentations and, rarely, bleedings and perforations can occur.[4,5] The incidence of MU, which is estimated between 0.6 and 16 percent after gastric bypass and between 0 and 18 percent after pancreatoduodenectomy, depends on surgery type and patient characteristics.[3, 6, 7] SU are gastric and duodenal mucosal injuries associated with psychological or physical stress. Major surgery, such as cardiothoracic and abdominal surgery, can lead to SU occurrence, particularly in elderly and fragile patients.[8, 9] SU are relatively rare, especially after the advent of proton pump inhibitors, but when occurring they can dramatically compromise the postoperative course.[10] GIE is the gold standard for diagnosis and treatment of gastrointestinal bleedings. After hemodynamic stabilization and a proper medical management (for example, blood transfusions, high-dose proton pump inhibitor), urgent endoscopy should be considered.[1] Early endoscopy (within 24 hours) is generally adequate, except for patients with high-risk features requiring a very early endoscopy (within 12 hours).[12] Endoscopic treatments available for hemostasis include epinephrine injection, mechanical therapy (through-the-scope clips [TTS] and over-the-scope clips [OTSC]), thermal therapy, and glues (for example, fibrin glue and hemostatic powders).[11] The choice between these treatments depends on the site, size, and type of the ulcer identified with endoscopy. Thermal therapy, mechanical therapy, and sclerosing agent injection are considered equal treatments to obtain endoscopic hemostasis and to reduce the risk of rebleeding.[13] Differently, epinephrine injection is comparable with other endoscopic treatments to achieve primary hemostasis, but it is inferior to reduce the risk of rebleeding. Baracat et al., in a meta-analysis involving 2,988 patients, concluded that epinephrine injection should not be used in monotherapy; thus, its combination with other endoscopic techniques significantly reduces the rebleeding rate and the need for surgery.[14] In active bleeding ulcers (FIa and FIb of Forrest classification, respectively active spurting **[Figure 1]** and active oozing), a combination therapy is required using epinephrine injection plus sclerosing agents, thermal, or mechanical therapy.[12]

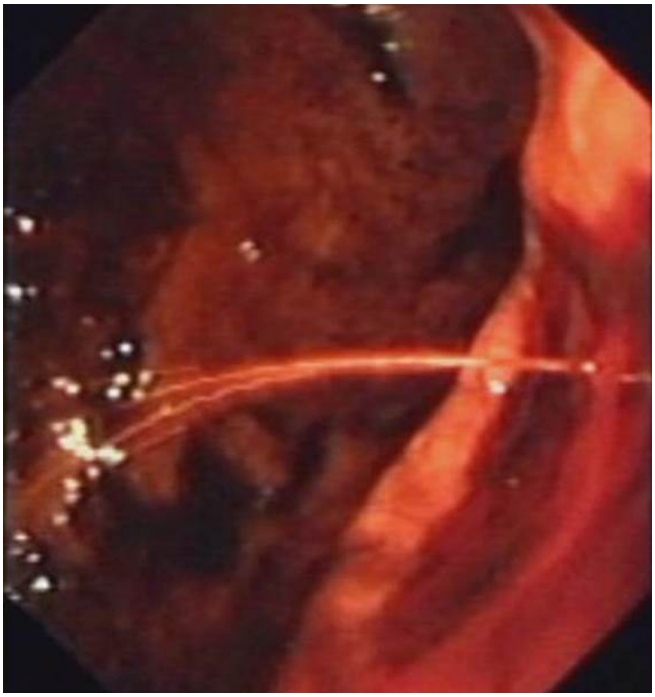

Figure 1. Forrest Ia active bleeding vessel in the stomach, close to a gastro-jejunal anastomosis

For nonactive bleeding ulcers with a visible vessel (FIIa of Foster classification), sclerosing agents, thermal, or mechanical therapy can be used as a monotherapy or in combination with epinephrine injection.[12] In selected patients, the local application of hemostatic powders has been described.[15] The advantages of hemostatic sprays are

the easy application without the need of direct contact with the bleeding site, the possibility to achieve difficult locations, and the applicability in wide areas. In FIIc (flat pigmented spot) and FIII (clean base) ulcers, no endoscopic treatment is required **(Figure 2)**. In case of persistent active bleeding despite a proper endoscopic treatment, transcatheter arterial embolization or surgery should be considered.[16] Differently, in case of bleeding recurrence after a prior successful endoscopic treatment, a second upper endoscopy should be performed, and only if this second attempt fails to achieve the hemostasis should the patients be referred to other treatment modalities.[17]

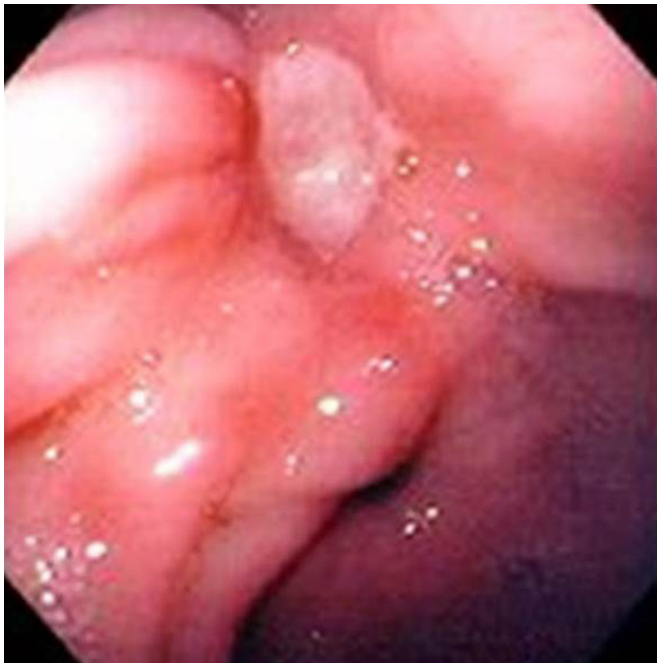

Figure 2. Forrest III, clean base ulcer in the stomach

Anastomotic Dehiscence and Fistulas

Anastomotic dehiscence (AD) is a serious complication that can occur after GIS. Foregut, midgut, and hindgut GIS are equally burdened by this life-threatening adverse event. For instance, the estimated incidence of AD is 0.5 to 11.5 percent after total gastrectomy with esophagojejunal anastomosis, 1 to 7 percent after sleeve gastrectomy, 2 to 5 percent after Roux-an-Y gastric bypass, and 11.4 to 21.2 percent after esophagectomy.[18,19,20] As it concerns hindgut surgery, the incidence is between 6 and 22 percent and is associated with a significant increase in 30-day mortality and long-term morbidity.[21] GI fistulas are another postsurgical complication defined as abnormal communication between two epithelized surfaces. Gastro-bronchial, gastro-pleural, gastro-colic, recto-bladder, and enterocutaneous fistulas are only few examples of this complication burdening both gastro-esophageal and colorectal surgery.[22-24] A prompt diagnosis and management of both AD and fistulas is mandatory to reduce the risk of septic complications (for example, abscesses, mediastinitis, peritonitis). Digestive endoscopy plays a crucial role both in the diagnostic and in the therapeutic algorithm. When an endoscopic procedure is performed in a patient with suspicion of GI defect, the use of CO_2 insufflation is mandatory.[25] Up-to-date endoscopic treatment options are TTSCs, OTSCs, plastic and metal stents, endoscopic suturing techniques, endoluminal vacuum therapy (EVT), and, most recently, fat grafting with mesenchymal cell injection.[26]

Endoscopic clipping

Endoscopy should be considered to treat all cases of AD or fistulas where repeated surgery is excluded. One of the endoscopic approaches to treat ADs or fistulas is to approximate the edges of the defect with the application of clips. Two types of endoscopic clips are currently available: TTSCs and OTSCs. TTSCs were formally introduced for hemostasis; however, their new design allows their applications also in GI perforations.[27] The reduced jaw opening capacity (11–16 mm) limits the use of TTSCs to small defects (less than 1 cm).[28] The technical procedure provides the placement of the first TTSCs at the distal edge of the defect (to reduce the risk of accidental clip displacement), and the subsequent clips are placed with a "zipper technique."[26] Few reports documented the use of TTSCs in the management of anastomotic leakage after both esophagogastric and colorectal surgery.[29,30] Conversely, the role of OTSCs in AD and fistulas has been more strongly defined. OTSCs are nitinol clips pre-loaded in a cap that is then mounted at the tip of the endoscope.[31] When compared with TTSCs, OTSCs have bigger arms and can grasp more tissue, allowing the treatment of larger defects.[32] The technical procedure foresees the suction of the defect into the cap, the advancement of additional instruments (for example, grasping forceps) to pull the edges inside the cap, and finally clip deployment.[31] An international multicentric study reported the use of OTSCs in 188 patients with GI perforations (108), ADs (48), and fistulas (32).[33] The defect closure rate was 90 percent in patients with perforations, 73.3 percent in patients with AD, and 42.9 percent in patients with fistula. They documented a higher success rate when OTSCs were used as the primary therapy and a longer success rate in patients with perforations and ADs if compared with fistulas. In case of very large defects (more than 20–30 mm), chronic leakage, fistulas, and presence of fibrotic tissue around the defect, the application of endoscopic clips is challenging, and other techniques are generally preferred.[29]

Stents

Self-expandable metal stents (SEMS) were formally introduced for the palliation of GI malignant stenosis. Three types of SEMS are available: fully covered SEMS (FC-SEMS), partially covered SEMS (PC-SEMS), and uncovered SEMS (U-SEMS).[34] The major complaint with U-SEMS is the ingrowth of tissue inside the metallic meshes, which makes their removal challenging; therefore, their use should be

strongly discouraged in benign strictures.[35] FC-SEMS are designed for removal but are burdened with increased risk of migration.[36] SEMS can be chosen in different diameters and length depending on patient characteristics.[37] SEMS deployment is performed under fluoroscopic and endoscopic guidance to ensure correct positioning and to reduce intraprocedural adverse events. When SEMS are deployed in colonic anastomosis, they can be placed only in end-to-end anastomosis with the distal end of the stent at least 5 cm proximal to the anal verge.[38] If SEMS are deployed too distally, they may cause fecal incontinence and tenesmus.[39]

To reduce the risk of migration, FC-SEMS can be fixed with endoscopic clips or with an endoscopic suturing device **(Figure 3)**.[40,41] FC-SEMS can be left in place for a maximum of four to six weeks. Longer periods can lead to stenosis occurrence at the end of the stent, perforation, major bleeding, or loss of the stent cover, which can lead to ingrowth through the meshes of the stents.[37]

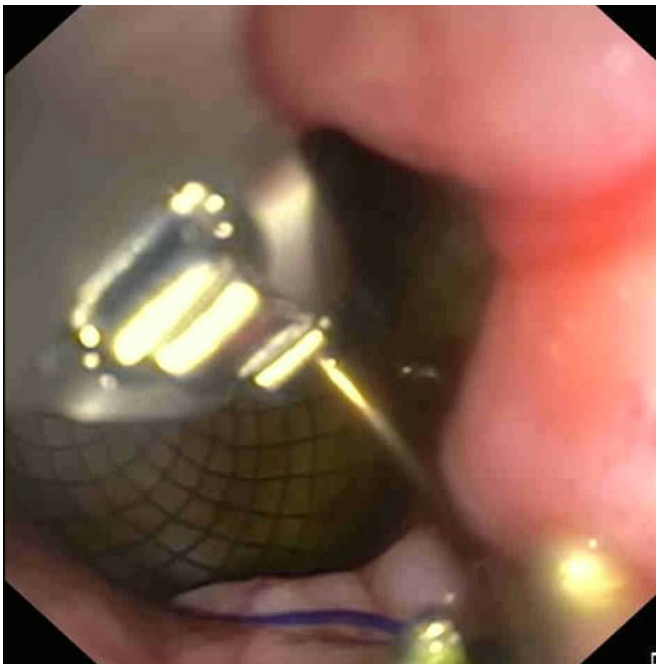

Figure 3. Endoscopic fixation with Apollo Overstitch of an esophageal fully covered stent

Feith et al. reported the use of FC-SEMS in 115 patients with AD after esophagectomy or gastrectomy.[42] A complete AD healing was achieved in 70 percent of patients. Major adverse events were stent migration (53 percent of cases) and symptomatic anastomotic strictures after stent removal (12 percent of patients). Debourdeau et al. described the endoscopic management of iatrogenic tracheoesophageal and bronchoesophageal fistulas in 22 patients.[43] Ninety-three endoscopic procedures were performed on 22 patients, and FC-SEMS placement was the main therapeutic procedure. The overall success rate reported was 45.5 percent. Lamazza et al. documented the use of SEMS in 22 patients with symptomatic anastomotic leakage after colorectal resection.[44] The AD healed in 86 percent of patients without stricture occurrence or major fecal incontinence. SEMS migration occurred in only one patient. Similarly, Arezzo et al., in a systematic review of 17 studies involving 68 patients treated with SEMS for AD and fistulas after colorectal surgery, reported a success rate of 75 percent.[45]

Double pigtail plastic stents are another available endoscopic alternative to manage anastomotic leaks and fistulas. When the lumen defect causes the occurrence of a fluid collection, the placement of a double pigtail allows the drainage of the collection into the GI tube with a consequent control of the local sepsis.[46] Furthermore, the presence of the stent stimulates granulation tissue growth promoting the closure of the defect. Donatelli et al. reported the use of double pigtails to treat AD in 33 patients after RYGB with a long-term success rate of 97 percent.[46] The same group described the transmural drainage of postoperative collections with double pigtails and EUS-guided drainage.[47] They reported an overall technical success rate of 100 percent and clinical success rate of 93.4 percent after a mean follow-up of 13.5 months.

The use of SEMS and double pigtail to manage AD is not well established. On the one hand, SEMS allow bypass of the leak, which promotes defect healing. On the other hand, double pigtails ensure a complete internal drainage of fluid collections. The use of double pigtails to drain collections occurring after bariatric surgery has been reported.[48] In this setting, double pigtails seem to enable a more physiological drainage of pathological fluids with concomitant progressive healing of the defect.

Endoluminal vacuum therapy (EVT)

The use of negative pressure for the treatment of chronic wounds is a well-established technique. The continuous suction provides the constant removal of a wound's secretion, induces granulation tissue growth, and increases angiogenesis.[37] The endoscopic technique involves the use of an open-pored, polyurethane sponge that is inserted into the cavity of the leakage **(Figure 4)**.[49] The sponge presents an evacuation tube that is connected to a vacuum system that creates a continuous negative pressure.[49]]A negative pressure of 125 mm Hg is generally required.[50] The sponge should be changed every three to four days until the defect has healed.[51]

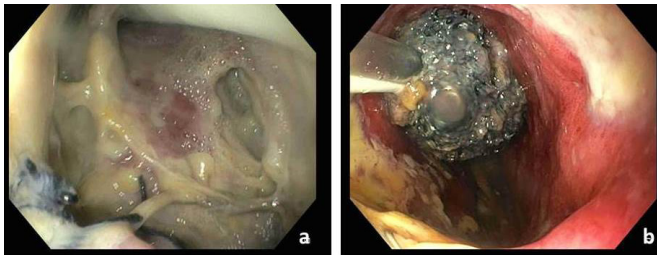

Figure 4. a. Large esophageal perforation in Boerhaave syndrome; b. After multiple treatments with EsoSPONGE® (B. Braun Melsungen AG, Melsungen, Hessen, Germany)

The presence of fluid collection around the GI defect is the main indication for EVT. The purulent collections must be drained to reduce the risk of septic complications, and the standard techniques are surgery and percutaneous drainage. However, EVT represents an effective and less-invasive alternative to obtain a continuous peri-perforation cleaning reducing the risk of infection and promoting defect healing.[52]

In a recent meta-analysis, Tavares et al. evaluated 23 studies with a total of 559 patients treated with EVT for AD occurring after esophagectomy or gastrectomy.[53] The overall success rate was 81.6 percent. When compared with SEMS, EVT showed a higher rate of defect closure and a lower risk for mortality. Similar results were reported in a meta-analysis involving 334 patients with AD after colorectal surgery.[54] The reported success rate ranged between 60 and 100 percent. The defect closure rate was only reported in 60 percent of studies and ranged between 31 and 100 percent. The adverse events associated with EVT are discomfort from the drainage tube, sponge displacement, bleedings, and anastomotic strictures.[55]

Endoscopic suturing techniques

Novel endoscopic suturing devices allow a full-thickness suture of the GI walls. These techniques are gaining popularity for their application in several settings, such as bariatric endoscopy and the endoscopic repair of wall defects.[56,57] OverStitch™ (Apollo Endosurgery, Austin, TX) and OverStitch Sx™ (Apollo Endosurgery, Austin, TX), which are compatible for their double-channel endoscope and a single-channel endoscope, are the most commonly used suturing devices. The endoscopic procedure involves the introduction of the device until the defect, the advancement of the Helix device (Apollo Endosurgery, Austin, TX) to grasp the tissue, if necessary, the placement of the full-thickness suture, and finally the performance of a knot **(Figure 5)**.[55] With this technique, continuous or intermittent sutures can be treated without the need for endoscope removal. In the management of AD and fistulas, endoscopic suturing can be used as the primary endoscopic treatment to obtain the approximation of the defect's edges, and it can also be used in combination with other endoscopic techniques (for example, endoscopic suturing is often used for the anchorage of SEMS).[58] Granata et al. reported 20 cases of AD divided in groups depending on the endoscopic procedure performed: endoscopic direct suture, combined endoscopic direct suture with FC-SEMS placement, anchoring, and FC-SEMS placement plus anchoring. The reported success rate was 77 percent, 85 percent, and 75 percent, respectively.[59] In a multicentric retrospective study, Sharaiha et al. analyzed the technical and clinical outcomes of endoscopic suturing in 122 patients (38.5 percent for stent anchorage, 32.7 percent for fistulas, 12.3 percent for AD, 16.4 percent for perforations).[57] The technical success rate was 97.5 percent, the immediate clinical success was achieved in 79.5 percent of patients, and the long-term clinical success rate was 78.8 percent. The success rates for anchorage, perforation, fistulas, and AD were 91.4 percent, 93 percent, 80 percent, and 27 percent, respectively. In GI fistulas, before attempting the endoscopic suture, a de-epithelization of fistula's edges should be performed to ensure a proper closure.[60] Coagulation and mechanical abrasion, all around the fistula, are the most-used techniques. Mukewar et al. reported the use of endoscopic suturing in 56 patients with various type of fistulas (51.8 percent gastro-gastric fistula). The immediate success rate was 100 percent. However, a persistent closure was obtained in 53.6 percent of patients.[61]

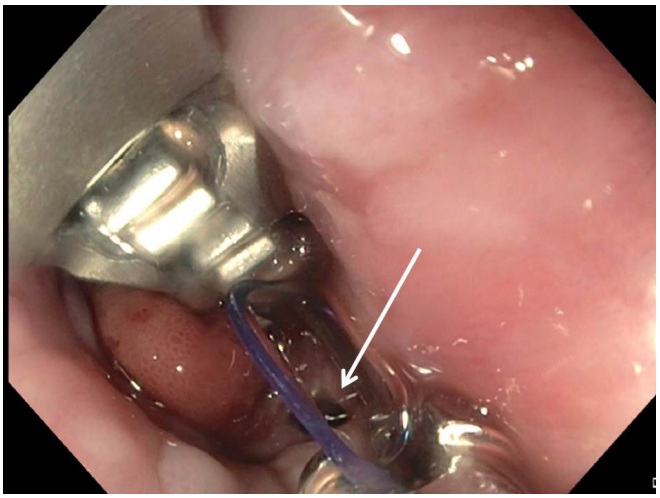

Figure 5. Endoscopic suture of a dehiscence in esophago-jejunostomy; the 5 mm dehiscence was successfully sutured with Apollo Overstitch

Fat grafting

Fat grafting (or lipotransfer) involves the harvesting of adipose tissue from a patient, the processing of the selected fat, and finally the re-injection of the graft in the same patient.[62] Formerly, fat grafting was introduced as a reconstructive method to manage soft-tissue volume loss. However, this technique is now gaining popularity in the field of regenerative medicine.[63] The mechanical emulsification of the harvested fat allows collecting mesenchymal stem cells and stromal vascular fraction, which have a pro-healing function promoting cellular regeneration, neo-angiogenesis, and inflammatory and immune system modulation.[64]

Recently, fat grafting has been described as an alternative option in the management of GI injuries.[65,66] Nachira et al. reported a case series of five patients with esophageal fistulas, not responding to standard techniques, who were successfully treated with endoscopic delivery of stromal vascular fraction obtained from autologous adipose tissue. All patients presented a complete healing of the fistula within seven days and a complete reepithelization without luminal stricture at the long-term follow-up (mean eight months).

Tan et al. reported the use of fat grafting in 11 patients with AD after low anterior rectal resection.[67] They documented a complete AD healing in almost 50 percent of cases. Importantly, one patient developed fat embolism, which was conservatively treated.

Pancreatic fistula

A pancreatic fistula (PF) is an abnormal connection of the pancreatic dust system with another structure **(Figure 6)**.[68] PFs are anatomically classified as internal pancreatic fistula (IPF) when a pancreatic duct is disrupted inside the abdomen and external pancreatic fistula (EPF) when the fistula communicates with the skin surface.[69,70]

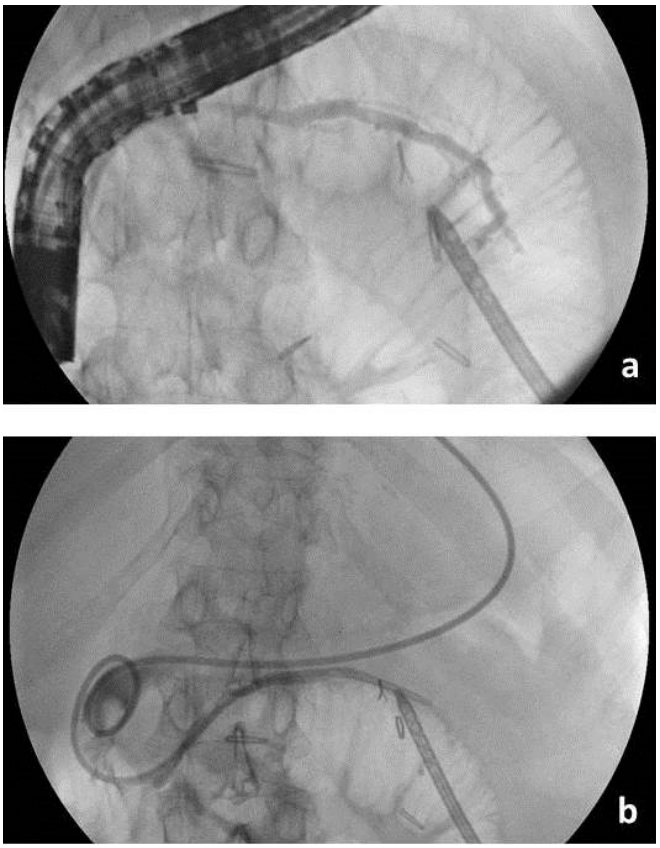

Figure 6. a. Pancreatography showing pancreatic fistula of the tail after splenectomy; b. After pancreatic sphincterotomy to depressurize the main pancreatic duct, a naso-pancreatic drain was placed

Any type of surgery in the peripancreatic region can cause a pancreatic injury with consequent pancreatic leaks. However, pancreatectomy is the surgical procedure that more commonly leads to PF (incidence varies between 5 and 29 percent).[71] PFs significantly affect morbidity and mortality rate of the postsurgical course. In PFs refractory to conservative treatments (total parental nutrition, fluid drainage, electrolytes supplementation, and pancreatic secretion inhibitors), an invasive approach is generally necessary.[72] Although surgery is considered the first-line treatment, endoscopy is emerging as an effective and minimally invasive alterative. The endoscopic treatments available can be divided in two groups: transpapillary drainage (ERCP-guided pancreatic duct stenting, naso-pancreatic drainage, and sealant injection) and transmural drainage (EUS-cystogastrostomy, cystoduodenostomy, pancreaticoduodenostomy, and pancreaticogastrostomy).[72] The choice among these different techniques depends on the specific type of PF and its clinical presentation.

Side-branch pancreatic fistula

Any type of surgery in the peripancreatic region can cause a parenchymal injury and leakage from side branches of the pancreatic duct system.[73] These PFs are generally low-volume leaks and respond well to endoscopic treatments. When this type of PF occurs on the head or the body of the pancreas, the endoscopic treatment consists of ERCP with pancreatic sphincterotomy and the insertion of a pancreatic stent or a naso-pancreatic drainage.[74] Sphincterotomy alone is generally not enough to resolve PF, necessitating insertion of a pancreatic stent to reduce the pressure inside the pancreatic duct system and to bypass duct disruption.[75] PFs occurring at the tail of the pancreas are more challenging because the small caliber of the pancreatic duct makes the insertion of stents more difficult. In this setting, the injection of a sealant solution has been described.[76, 77] Mutignani et al. reported a case series of four patients with EPF at the tail of the pancreas, refractory to conservative treatment and endoscopic drainage, who were successfully managed by the injection of Glubran 2 into the fistulous tract.[75]

Main pancreatic duct fistula

Main pancreatic duct (MPD) injuries can be partial, causing a pancreatic leak but maintain a continuity between the proximal and distal portion of the duct, or can transect completely (disconnected duct syndrome) with the upstream portion of the pancreas not communicating with the papilla and secreting the pancreatic juice directly in the abdominal cavity **(Figure 7)**.[72,78] Both of these conditions are associated with pseudocysts and peripancreatic fluid collections.

When the MPD is only partially disrupted, the standard endoscopic treatment consists of the insertion of a pancreatic stent or a noso-pancreatic drainage.[79] In a retrospective study, Das et al. described the endoscopic transpapillary drainage of PF in 107 patients with a success rate of 75 percent with a more favorable course in partially disrupted MPD.[80]

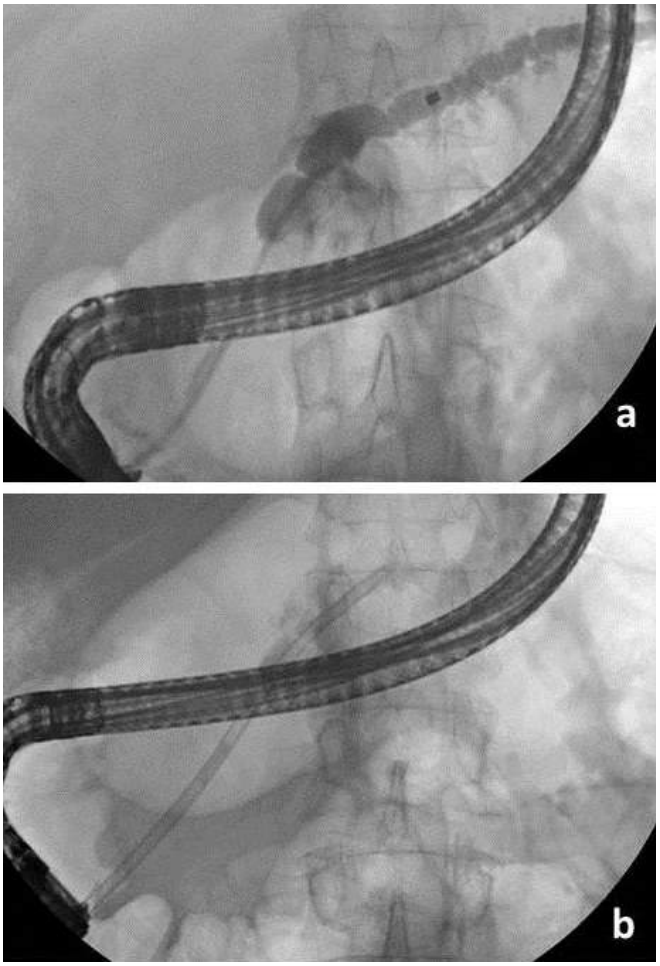

Figure 7. a. Endoscopic retrograde cholangio-pancreatography with pancreatic sphincterotomy b. Successful endoscopic bridging of a disconnected ruptured main pancreatic duct

When the MPD is completely transected, the transpapillary drainage is generally not feasible, and an echoendoscopic (EUS) transmural drainage is preferred.[81] EUS allows the identification of the peripancreatic collection and placement of a plastic stent to connect the collection with the gastric or the duodenal lumen (cystogastrostomy and cystoduodenostomy) to reduce duct system pressure and to evacuate peripancreatic collections.[82] The plastic stents should be maintained in place indefinitely to reduce the risk for pancreatic collection recurrence. Arvanitakis et al. randomized 28 patients with pancreatic collections undergoing EUS drainage with the stent left indefinitely in place (first group) and with stent removal after collections resolution (second group).[83] The recurrence of the pancreatic collection occurred in 0 and 38 percent of patients, respectively.

EUS-pancreaticoduodenostomy and EUS-pancreaticogastrostomy are other available techniques implying the connection of the pancreatic duct system with the stomach or the duodenal lumen.[84] These procedures are used mainly for duct decompression in chronic pancreatitis. However, their application in pancreatic duct disruption has been described.[85]

Postoperative pancreatic fistula (POPF)

POPF is a serious complication that significantly affects mortality and morbidity after pancreatic surgery. A relevant POPF is defined as a drain output of a fluid containing an amylase level three times the upper limit of normal serum amylase associated with a clinically relevant condition.[86] The standard treatment to manage POPF, which is not responsive to conservative therapy, consists in the placement of percutaneous drainage or a relaparotomy.[87] Few reports described the role of endoscopy in the management of POPF.[88,89,90,91] The endoscopic procedures available are trans-anastomotic intraductal pancreatic stent insertion, EUS-guided transmural drainage, EUS-pancreaticogastrostomy, and nose-to-collection drain insertion.

Mutignani et al. reported a case series of 13 patients who underwent endoscopic treatment for POPF.[92] In particular, five patients underwent trans-anastomotic intraductal pancreatic stent insertion, three patients underwent nose-to-collection drain placement, and four patients were managed with triple stent placement (in the jejunal stump, in the Wirsung, and in the bilio-digestive anastomosis). Technical and clinical success were achieved respectively in 100 and 83 percent of cases respectively.

Postoperative Biliary Strictures and Fistula

Postoperative biliary strictures (POBS) and fistulas may occur after any surgical procedure on the biliary tree. Laparoscopic cholecystectomy is the most common procedure associated with postoperative biliary strictures (POBS), with an incidence significantly higher when compared with laparotomic cholecystectomy (0.23–0.42 percent versus 0.1 percent).[93,94] The main mechanisms of POBS are the partial or complete clipping of the biliary duct, thermal injury during tissues dissection, and vascular damage with consequent ischemic injury.[95] Anatomical variants, local inflammation, and surgeon's expertise are well-known risk factors for postoperative biliary injury.[95] Several classifications have been reported to describe biliary injury. The most used are the Bismuth classification (distinguishing five different types of biliary strictures depending on the available healthy biliary

mucosa) and the Strasberg classification (including both biliary stricture and leakage).[96,97] Endoscopy represents the first-line treatment for patients with postoperative biliary injuries, reserving the use of percutaneous and surgical therapies only to selected cases.

The first endoscopic treatments reported for POBS were balloon dilatation and single stent placement. However, these procedures were associated with high risk for stricture recurrence. Nowadays, the multi-stenting progressive dilatation and FC-SEMS placement are available alternatives to regain the biliary duct patency.[98,99] The multi-stenting technique implies a progressive dilatation of the biliary stricture with the insertion of an increasing number of stents placed side by side every three months **(Figure 8)**.[98] Costamagna et al. reported a long-term evaluation of the multi-stenting therapy performed in 154 patients with POBS.[100] A mean number of 4.3 stents were placed and a mean of 4.2 ERCP were performed for each patient **(Figure 9)**. The resolution rate of the stricture was obtained in 96.7 percent of patients. After a mean of 11 years the recurrence rate was 9.4 percent.

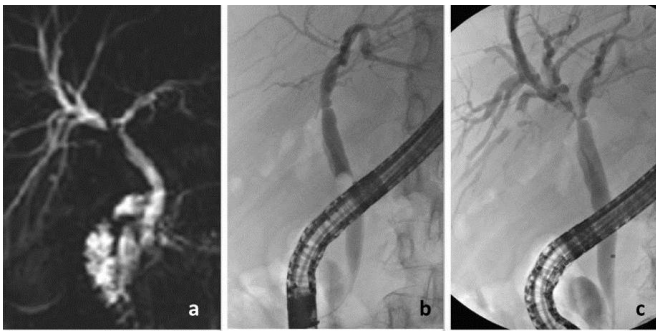

Figure 8. a. Magnetic resonance cholangio-pancreatography showing Bismuth and Lazorthes type V biliary stricture that occurred after laparoscopic cholecystectomy; b. and c. Endoscopic retrograde cholangio-pancreatography with negotiation of the stricture

Figure 9. Endoscopic appearance of multiple plastic biliary stents; in this case, eight 10 French biliary plastic stents were placed during endoscopic retrograde cholangio-pancreatography for a postoperative biliary stricture

The use of FC-SEMS for POBS has been described as a valid alternative to multi-stenting treatment **(Figure 10)**.[101] FC-SEMS have a significantly larger diameter when compared with plastic stents (the diameter of a SEMS corresponds to seven 10Fr plastic stents), and their temporary placement may reduce the need for multiple endoscopic procedures with a consequent increase of the patient's compliance.[99] Tringali et al. reported a multicentric prospective study involving 187 patients with benign biliary stricture treated with FC-SEMS.[99] FC-SEMS were removed in 83.3 percent of patients after an average of 10.9 months (in three cases the stent migrated spontaneously). The stricture resolution was obtained in 72 percent of cases, and at five-year follow-up 84.6 percent of patients remained stent-free.

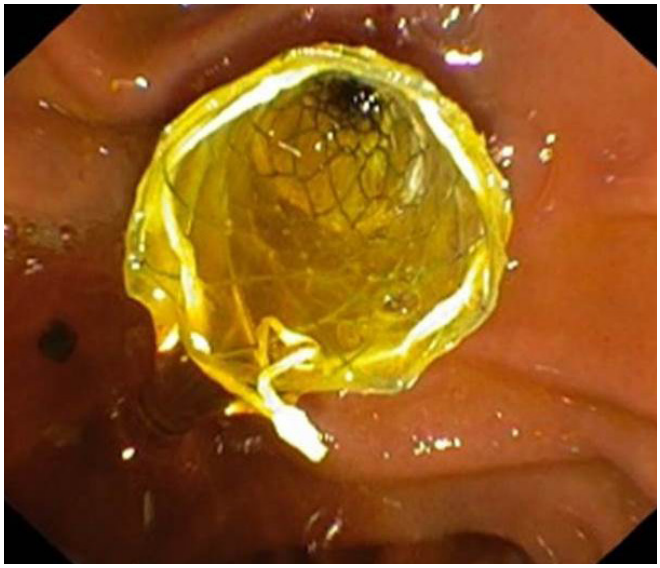

Figure 10. Endoscopic appearance of a biliary fully covered self-expandable metal stent

The presence of anatomical variants of the intrahepatic biliary tree is reported in 45 percent of the general population and represents a risk factor for surgical biliary injury.[102] In 12.3 to 24.1 percent of patients the right posterior or the right anterior sectorial ducts can join the common bile duct close to the cystic duct (also known as "aberrant duct").[103] This variant can lead to a wrong interpretation of the biliary tree anatomy during surgical dissection with consequent increase of biliary injuries. Tringali et al. performed a retrospective study involving 32 patients with postsurgical aberrant duct injury treated with endoscopic stents placement.[104] A mean of 3.7 biliary plastic stents were used for each patient with a mean treatment duration of 6.3 months. The reported success rate depended on the specific type of aberrant duct injury: patients with Strasberg type C injury, patients with Strasberg type E5 injury, and patients with isolated aberrant duct stenosis achieved duct patency 91 percent, 100 percent, and 100 percent of the time, respectively. Only one out of six patients with Strasberg type B injury achieved duct patency; however, no complications were reported (for example, cholangitis or cirrhosis), and atrophy of the liver parenchyma drained by the transected duct was documented.

In the presence of biliary leaks alone without strictures, biliary sphincterotomy and temporary stent insertion are the endoscopic treatments available. Dolay et al. compared biliary sphincterotomy with biliary stenting in 27 patients with biliary leak after cholecystectomy.[105] Biliary stenting was more effective and more rapid in achieving fistula closure when compared with biliary sphincterotomy alone. Mavrogiannis et al. compared the efficacy and safety of biliary stenting alone with biliary stenting plus sphincterotomy to treat postcholecystectomy biliary leaks.[106] No difference in efficacy was found between the two groups, while the incidence of adverse events was higher in the sphincterotomy group (10.71 versus 4.16 percent).

Biliary leaks can cause the development of a biloma, which is defined as a bile collection within the abdomen.[107] Percutaneous drainage is the standard technique to manage bilomas; however, EUS drainage has been reported.[108,109,110]

Conclusion

GIE represents a minimally invasive technique that allows the management of several postsurgical GI complications. Although GI surgery is becoming safer, the risk for the occurrence of postoperative complications is still present. A prompt diagnosis and treatment of this condition is crucial to reduce postoperative mortality and morbidity. The conservative approach is the first-line treatment in several postoperative complications. However, in patients refractory to medical therapy, an invasive approach is often required. Interventional radiology and surgery were formally considered gold standard methods for several GI complications. However, GIE offers an effective, safe, and less invasive approach.

GIE allows the use of mechanical therapies (for example, clips and stents), thermal therapies (for example, thermal coagulation), application of hemostatic substances (for example, fibrin glue and hemostatic powder), and transmural drainage of collections (for example, EUS-guided drainages). Nowadays, innovative endoscopic treatments are emerging in the field of regenerative medicine. The use of mesenchymal stem cells is gaining importance in the management of GI complications. In contrast to other endoscopic techniques, the injection of mesenchymal stem cells allows a paracrine activation of the patients' regeneration pathways, leading to a progressive and more physiologic healing of GI damages.

The introduction of artificial intelligence in surgery could significantly affect daily practice. New software has been introduced to allow automatic and real-time recognition of objects, actions, and surgical workflows. The rapid growth of artificial intelligence can represent an important tool for surgeons to reduce the risk of surgical complications, achieve an early detection of AEs in the postoperative course, and even treat postoperative complications with the best method at the right time.

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CHAPTER 10

Difficult Cholecystectomy: How to Prevent Biliary Injuries

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Difficulty, laparoscopic cholecystectomy, biliary duct injury, prevention, subtotal cholecystectomy

Abstract

The gold standard for the treatment of symptomatic cholelithiasis is laparoscopic cholecystectomy (LC) via the traditional 4-trocars approach. Other options include the open access (via a right subcostal or paramedian incision) and usually a consequence of conversion or contraindication to a laparoscopic cholecystectomy, single-trocar, robotic, and even NOTES (Natural Orifice TransEndoscopic Surgery) approaches, although this last one has been mostly abandoned.

Nonetheless, there are a number of conditions, situations, and circumstances that can increase the difficulty of the procedure and, hence, the risks associated with its performance. Among the latter, bile duct injury (BDI) is a huge concern of laparoscopic cholecystectomy, resulting in significant morbidity and mortality. Prevention of BDI should be systematically performed when confronted with a difficult cholecystectomy.

Introduction

The gold standard for the surgical treatment of symptomatic cholelithiasis is conventional laparoscopic cholecystectomy (LC). Although it has been associated with a slightly higher incidence of bile duct injury (BDI) in comparison with open cholecystectomy (OC), LC is considered a very safe operation.

Laparoscopic cholecystectomy is one of the most commonly performed operations worldwide with over 750,000 cases done in the United States annually. While the most common indication for the operation is uncomplicated biliary colic, there are a number of conditions that can increase the difficulty and risk of this procedure.[1]

The **"difficult gallbladder"** is a scenario in which a cholecystectomy turns into an increased surgical risk compared with standard cholecystectomy. The procedure may be difficult due to processes that either obscure normal biliary anatomy (such as acute or chronic inflammation) or operative exposure (obesity or adhesions caused by prior upper abdominal surgery).[2]

So, when confronted with a difficult cholecystectomy, the surgeon has a must: to turn the operation into a safe cholecystectomy, which can mean conversion (to an open procedure), cholecystostomy, or partial/ subtotal cholecystectomy. The surgeon should understand that he/ she needs to rely on damage control, to prevent more serious complications if choosing to advance and progress to a complete cholecystectomy.

In this chapter, we will not address the technical aspects of performing a laparoscopic cholecystectomy, but instead focus on how to manage a difficult case with the goal of prevention of biliary duct injuries in mind.

In this topic, we discuss risk factors that could predispose to a difficult gallbladder. Recognition of a potentially difficult gallbladder by the surgeon is the first step toward mitigating the high risks of operating on such patients. Pre- and intraoperative strategies of managing a difficult gallbladder are also presented.

It is of the utmost importance that the surgeon understands that conversion to an open procedure is not a failure and it should be done to complete the operation in a safe fashion; quite different is the situation when conversion is forced to treat and solve intraoperative complications.

Framing the Issue

The difficulty in performing a laparoscopic cholecystectomy may be linked to the following factors:

- **The procedure in itself.** We include in this point the characteristics of the procedure, patient factors (such as obesity, coronary artery disease, pulmonary restrictions), instrumentation and technical resources, and backup and the surgeon, who may be more or less experienced and more or less capable when confronting a difficult situation.
- **The anatomy.** Refers to potential aberrant ductal and arterial anatomy, a prominent liver, an intrahepatic or left-sided gallbladder, all factors very difficult to acknowledge in the preoperative stage.
- **The disease affecting the gallbladder.** Lastly, there are chances to find the following conditions: a fibrosed and contracted gallbladder, acute or relapsed cholecystitits, a xantogranulatomatous cholecystitis, or even an unexpected gallbladder carcinoma.

The management of a patient undergoing a laparoscopic cholecystectomy (LC) may be exposed to the occurrence of errors.[3] These errors may happen in three different stages, which allow a better understanding and problem-solving approach:

- **Errors in the preoperative stage.** They are usually linked with errors of knowledge and rules. This fact highlights the importance of a grounded diagnosis based on evidence, as well as following the adequate guidelines. In that sense, for example, operating on a patient with a 3 mm gallbladder polyp represents an incorrect surgical indication and frames the case of an unnecessary surgical procedure.
- **Errors in the intraoperative stage.** In this time frame, the errors are mostly related with the level of manual skills and dexterity as well as cognitive perception. However other errors, undetected in the previous stage, may become evident. For example, coagulation disorders or the presence of liver cirrhosis.
- **Errors in the postoperative stage.** Errors present at this moment are linked to the three levels of rules, skills, and knowledge, and in a practical sense to intraoperative errors whose consequences become evident later, during the postoperative course or undue management of postoperative complications.

When to Predict a Difficult Laparoscopic Cholecystectomy

A difficult cholecystectomy may be predicted preoperatively based on patient characteristics and ultrasound and laboratory findings. This is probably a very important step in mitigating the high risk associated with a difficult procedure and may serve either to reschedule the procedure or design intraoperative strategies of management to guarantee a safe performance of the surgical procedure.

The following situations are associated with a higher chance of a difficult cholecystectomy:[4]

- Acute cholecystitis (more than 5 days of onset)[5]
- Previous cholecystitis episode[6]
- Male sex
- Obesity[7]
- Cirrhosis[8]
- Sclero-atrophic gallbladder
- Thick walls (>5 mm)
- Previous signs of canalicular dwelling (clinical and laboratory)

Through multivariate analysis, Bourgoin identified these elements of predictive help to identify difficult LC: male sex, previous cholecystitis attack, fibrinogen, neutrophil, and alkaline phosphatase levels.[9]

Another important point is the fact of conversion from a laparoscopic procedure to an open and traditional cholecystectomy, usually through a right subcostal incision. Conversion should not be considered as a personal failure, and the surgeon needs to understand the concept of "safety first," considering that conversion is performed in order to complete the procedure without additional risks and preventing complications and not solving intraoperative complications.[10]

It is also useful to define a time threshold to aid in the decision to convert. It is not worth taking an hour and a half and still dissecting adhesions, preventing the correct visualization of the cystic pedicle. This time limit represents a method to prevent inefficiencies in the operating room (OR) schedule as well as additional expenditures.

A smart surgeon should rely to conversion in the following situations:

- Lack of progress in the procedure
- Unclear anatomy/any grade of uncertainty
- CVS not achieved
- Bleeding/vascular injury
- BD injury
- Lack of infrastructure, expertise, and support

Some of the Difficulties a Surgeon May Encounter and How to Deal with Them

In **Table 1**, the five steps of a laparoscopic cholecystectomy are described. In each of these steps the participating surgeon may encounter different situations, which will be tackled in a summarized way.

Table 1. The steps during laparoscopic cholecystectomy

1. Access to the abdomen
2. Gallbladder exposure
3. Dissection of the cystic artery and duct
4. Gallbladder ectomy
5. Gallbladder extraction

1. Access to the abdomen

- **Obesity.** Patients with higher BMI (body mass index) certainly pose an additional difficulty for access.
- **Previous surgery/ies.** The hostile abdomen represents an additional challenge for entrance in the abdominal cavity and the achievement of a safe pneumoperitoneum with CO_2 insufflation. Same precautions as previously explained should be taken, and the major concern should be preventing a viscus perforation due to adhesions to the anterior abdominal wall.
- **Risks.** Hollow viscus perforation/vascular injury/solid organ injury (liver, spleen, and so on). Surgeons should be aware of the proximity of the abdominal wall to the great vessels (aorta artery and inferior vena cava) as well as the iliac bifurcation and keep in mind these hazards. The first gesture when entering the abdominal cavity with the optic is a close exploration to rule out any injury.
- **Veress versus Hasson (closed versus open)/optic trocar.** Although the use of the Veress needle technique is not associated with an increased risk of viscus perforation or vascular injury, some prefer to use an open technique and a Hassan trocar. Another option when confronted with patients with high BMI or previous surgeries, is the use of an optical trocar with close monitoring of the entrance step to the abdominal cavity.[11]

2. Gallbladder (GB) exposure

- **A full exposure of the gallbladder** allowing and adequate retraction of the fundus and the neck is mandatory for a safe operation and is a precondition for its achievement. The exposure of the gallbladder may be compromised by its own condition or anatomy or by external factors.
- **Adhesions.** Should be safely taken down in order to allow a full retraction of the neighboring organs and a full exposure of the gallbladder, in particular the outlet of the gallbladder neck into the cystic duct.
- **Large liver/or fallen down.** A large liver or a liver that can not be adequately retracted may compromiso the full exposure of the gallbladder and the Calot triangle. If needed, an additional retractor via a fifth-5 mm trocar may be a useful trick.

- **Biliary fistulas.** The presence of abnormal connection between the gallbladder and other digestive portions (mainly the right colonic explosure, the duodenum, or small bowel) request a meticulous dissection and taking down the trajectory of the communication as well as the repair in the digestive segment by means of a mechanical suture or either stitches.
- **Mirizzi síndrome.** Represents a condition linked to the prolonged evolution of the gallbladder calculous disease.

This condition bears the name of Pablo Mirizzi, professor of surgery at the University of Córdoba School of Medicine (Argentina). He is credited with the performance of the first intraoperative cholangiography in 1931.

Mirizzi syndrome is defined as the obstruction of the common hepatic duct by an extrinsic compression due to an impacted stone in the gallbladder infundibulum or in the cystic duct. Usually patients present with jaundice, sometimes fever, and right upper quadrant pain. But most times they present asymptomatic and the condition is recognized intraoperatively, leading to a significant morbidity and increased risk of biliary duct injury if the surgeon is not aware, particularly during a laparoscopic procedure.

Nonetheless it should be acknowledged that Mirizzi did not describe the condition known today as Mirizzi syndrome.[12-13] The first published paper describing the condition known as Mirizzi syndrome belongs to Puestow[14] and some years later Behrend contributed with a similar report.[15]

It was McSherry who coined the term Mirizzi syndrome for this condition, and based on ERCP findings he described two types: type I, external compression of the bile duct by a large stone or stones impacted in the cystic duct or in the Hartmann pouch; and type II, cholecystobiliary fistula, caused by a gallstone or gallstones that have eroded into the bile duct.[16] Although Csendes et al. proposed a five type classification,[17] the one described by McSherry is still the most applicable and used.

The Mirizzi syndrome is relatively uncommon and frequently related to a long-standing calculous disease that has not received surgical treatment. It is found predominantly in the older population with no gender preference. It carries a higher risk of gallbladder cancer, probably due to persistent and recurrent irritation of the compromised area and chronic biliary stasis.[18] The treatment for this condition is laparoscopic cholecystectomy and if difficult, conversion with an incidence higher than 70 percent is recommended. Care to prevent injury to the porta hepatis and bile ducts is strictly recommended. When a fistula traject is present, a common bile duct repair is mandated or even a bilioenteric anastomosis with Roux-in-Y is recommended. Otherwise repair of the bile duct and placement of a T tube is recommended.[19]

3. Dissection of cystic artery and duct:

- In order to assure the safe dissection of both the cystic artery and duct, achievement and documentation of the critical view of safety (CVS) is of paramount importance.[20-21]

The CVS includes:

1. Clearance of the cystohepatic triangle (commonly referred to as the triangle of Calot), with the following boundaries: liver edge superiorly, cystic duct inferiorly and laterally, hepatic duct medially
2. Cystic plate exposure by removal of the lower one-third of the gallbladder from the gallbladder fossa
3. Confirmation that two, and only two, structures are entering the gallbladder (the cystic duct and cystic artery)

In Figure 1, the anatomy of the CVS is depicted.

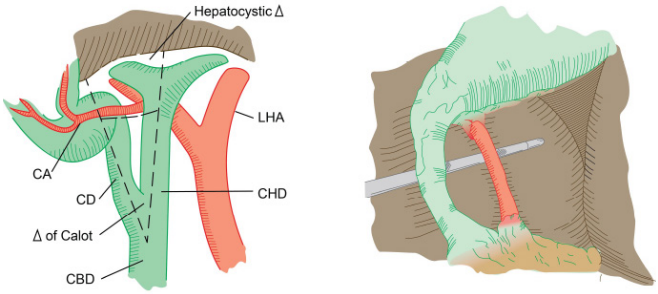

Figure 1. The critical view of safety

In Figures 2 through 6, images of the complete dissection of the CVs may be appreciated.

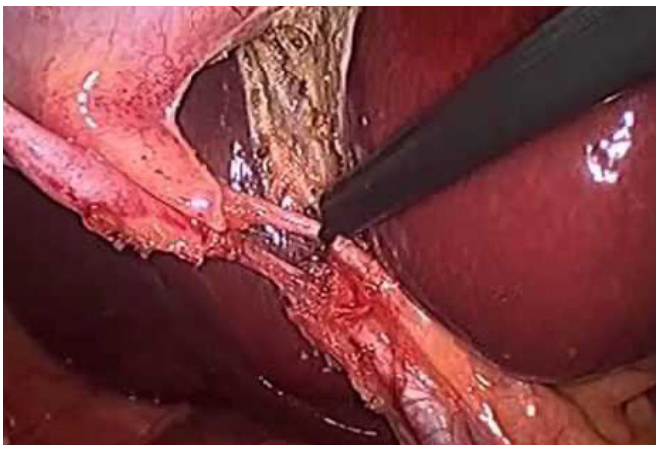

Figure 2.

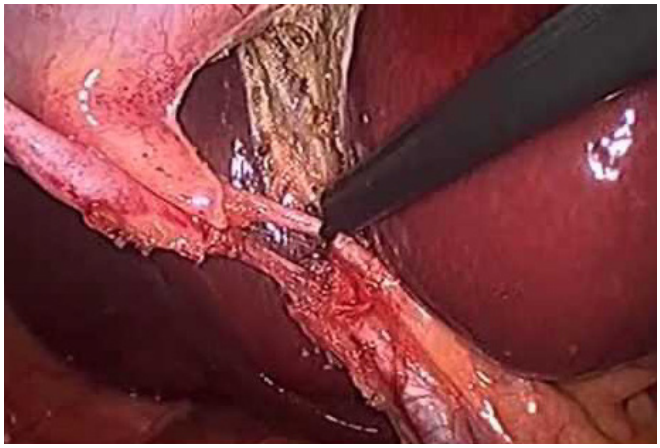

Figure 3.

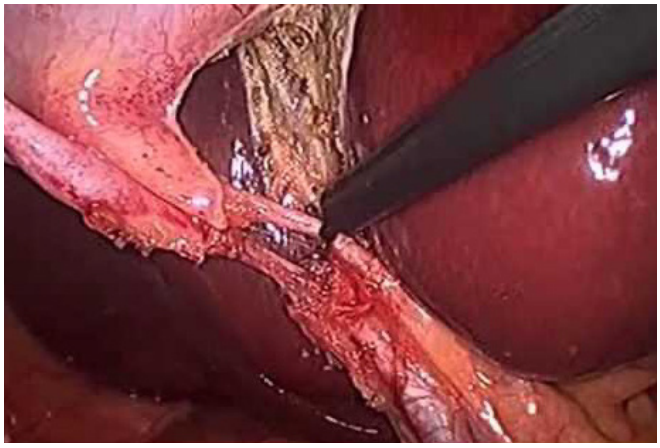

Figure 4.

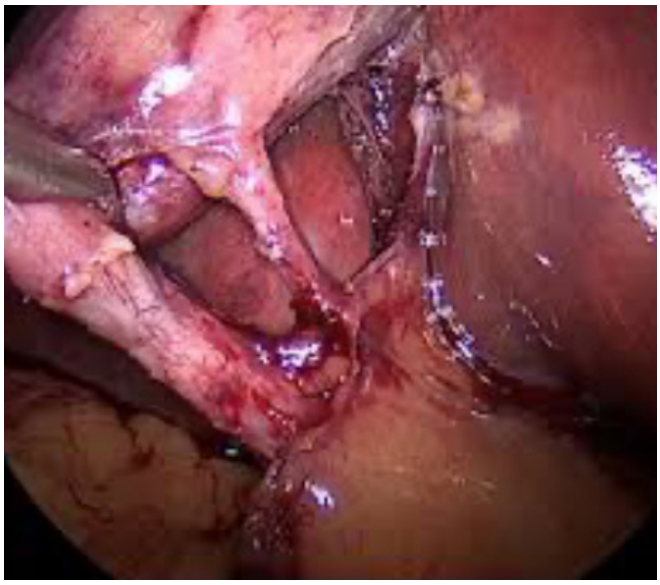

Figure 5.

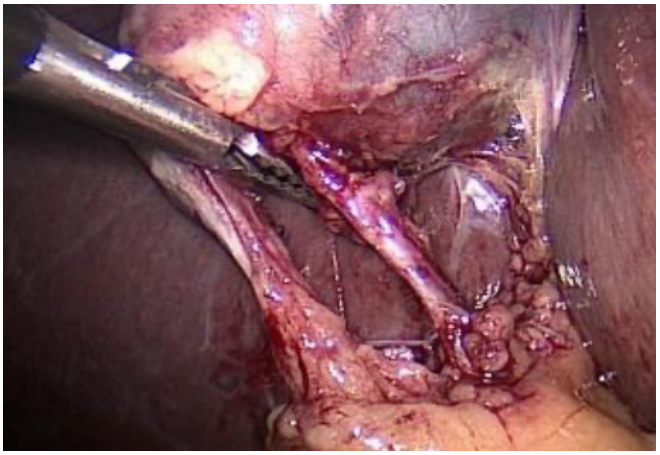

Figure 6.

- **Difficult Hartmann pouch.** Can prevent a good exposure of the gallbladder neck and the communication between it and the cystic duct. Many times it is secondary to the impaction of a stone, which makes it difficult to place a grasping forceps on it.
- **Anatomic variations.** Every surgeon should be aware of the chance of anatomic both of the biliary anatomy and the arterial supply to the gallbladder and the liver (cystic and hepatic artery).
- **Intraoperative cholangiography.** May be performed either by a transcystic approach or by puncture of the gallbladder.
- The issue of whether or not an **intraoperative cholangiogram (IOC)** prevents the occurrence of a bile duct injury is controversial, but there is no doubt the intraoperative cholangiogram is very useful in the intraoperative recognition of a bile duct injury.[22]
- An IOC is usually performed in the following situations:
    1. The biliary anatomy is unclear
    2. Choledocholithiasis should be ruled out
    3. There is concern for bile duct injury
    4. Other conditions request to be ruled out

There are three requirements for a normal IOC:

- The contrast is visualized in both the right hepatic duct (including the right anterior and right posterior sectoral ducts) and the left intrahepatic duct above their confluence
- Lack of filling defects in the common bile duct
- Free flow of contrast into the duodenum
- Thermal injuries: the use of energy sources (mostly electrocautery and sometimes, ultrasonic devices) requests care and delicacy in the management of tissues as well as to prevent using the electrocautery close to the titanium clips, since these last may expand the current and thus injure the bile duct

4. GB ectomy

The ectomy of the GB from its liver bed is an important step after placing clips and cutting both the cystic artery and the cystic duct. When facing difficulties the surgeon may rely on some tricks in order to complete the operation.

- **The puncture and aspiration of the gallbladder fluid** may aid in the ease of traction, exposure, and dissection.
- **Aperture.** Partial aperture of the gallbladder and extraction of stones, in particular those performing a mass effect on the neck and compressing other structures may aid in the recognition of other structures and the dissection of the gallbladder.
- **Traction.** Should be adequate, cephalad for the fórceps placed in the fundus and caudal for the fórceps placed in the neck área, thus allowing a good visualization.
- **Partial or subtotal cholecystectomy/cholecystostomy** (Delajenniere, Pribram). These techniques may aid in the prevention of biliary duct injuries by staying away from the cystic duct and the bile duct. The Delajenniere technique consists in leaving a remnant of the gallbladder, usually the neck and placing a tube for draining the bile. Other option is leaving the galllbladder attached to the liver bed and cauterizing it with the electrocautery. The subtotal cholecystectomy has turned into a widely accepted resource to avoid conversion, in particular with those surgeons not widely trained in open surgery.[23,24,25]
- **Fistulae.** The abnormal communication of the gallbladder with other structures (hepatic colonic flexure, duodenum or small bowel) speaks of a long disease evolution. The trajectory should be taken down, and a safe suture needs to be placed on the intestinal segment, very few times a resection is performed.

5. Extraction

The extraction of the gallbladder may be performed either by the umbilical or the subcostal trocar entrance and the use of a pouch is always recommended to avoid spillage and/or loss of stones in the abdominal cavity. When the subcostal trocar opening is enlarged to allow the "delivery" of the specimen, there may be an increased risk of injuring the epigastric artery. This condition may be solved just with the use of compression of the abdominal wall with an inflated Folley catheter placed through the opening. Some prefer to use the umbilical port, using a 2-cm dilator with the risk of a postoperative umbilical hernia.

The rupture or the gallbladder may result in spillage of its content, including stones and thus contribute to postoperative wound infection. The presence of retained stones in the abdominal cavity or in the subcutaneous tissue may generate collections and represent a medicolegal risk, since they may be considered as retained foreign bodies.

It is also important to examine the gallbladder specimen to verify that there is only one conduit (the cystic duct) entering into the gallbladder neck and thus confirm the avoidance of a biliary tract injury.

The Tokyo Guidelines 2018 recommend the following steps to achieve a safe cholecystectomy:[26]

- If the gallbladder is distended and interferes with view, it should be decompressed by needle aspiration.
- Effective retraction of the gallbladder to develop a plane in the Calot triangle area and identify its boundaries (countertraction).
- Starting dissection from the posterior leaf of the peritoneum covering the neck of the gallbladder and exposing the gallbladder surface above the Rouviere sulcus.
- Maintaining the plane of dissection on the gallbladder surface throughout LC.
- Dissecting the lower part of the gallbladder bed (at least one-third) to obtain the CVS.
- Creating the CVS.

For persistent hemorrhage, achieve hemostasis primarily by compression and avoiding excessive use of electrocautery or clipping.

Prevention of Biliary Duct Injuries (BDI)

BDI still remains a relatively infrequent event (<1 every 200 to 400 cases), although it represents a leading source of medical malpractice litigation claims against surgeons. Between 34 to 49 percent of all surgeons are expected to cause such an injury during their professional career activity. The repair of such injuries is often complex and usually requires several endoscopic and interventional radiology procedures and surgeries. Major CBD injury has a substantial and definitive impact of quality of life, functional status, and survival.

The incidence of BDI in laparoscopic cholecystectomy is reported between 0.4 and 0.6 percent.[27,28,29] Besides, biliary duct injuries account for repeated interventions, increased expenditure, with personal losses and impact as well as impairment on the quality of life of the affected patients.[30]

Although acute cholecystitis doubles the risk of BDI, the straightforward and "simple" and/or "piece of cake" gallbladder should be given due attention. Due to inappropriate and/or excessive traction (both cephalad and lateral), the cystic end into the common bile duct is usually unrecognized and the misinterpretation leads the consideration of the CBD for the cystic duct. A clip or two is applied and the CBD is cut; since most times an IOC is not performed the injury goes unrecognized and the surgeon ends with a total transection of the CBD in between clips.

The first symptom is usually represented by postoperative jaundice, leading to additional imaging studies and the postoperative diagnosis of the bile duct injury.[31,32]

There is discussion among the authors and researchers regarding the status of bile duct injuries. For many they represent a surgical complication, inherent to the procedure and most it not all surgeons will be confronted with a case in their surgical life. However, there is a growing trend to consider them as an example of a surgical technical error, many times as a consequence of misinterpretation, with the cognitive analysis of intraoperative decisions playing a major role in their production.[33]

The production of a biliary duct injury generates a devastating impact on the surgeon responsible for the production of one. However most of surveyed surgeons consider these injuries as unavoidable, less than half feel that its occurrence always represent a surgical error and less than 15 percent think these injuries may be avoided by the performance of intraoperative cholangiography.[34] Surgeon colleagues should be educated to remove the stigm of failures associated with conversion to an open procedure.

From the perspective of human factors and systems safety the accident analysis of BDI offers the following findings:

- BDI usually follow a definitive sequence
- The severity of injury depends upon the step in which the error is identified and when the surgeon stops the procedure
- In severe injuries, the CBD is cut and divided twice, with the site of injury close to the liver hilum
- In all situations, the root cause is the misidentification of the distal CBD as the cystic duct. Visual perception during the operation should be considered as a form of heuristics rules of thumb that assist in performing complex tasks and in making the mental construction represented by the vision of the surgeon and the whole team[35]
- However, many times the procedure is performed as smoothly as in a routine LC and the surgeon does not notice the BDI

So, it is recommended to be beware of the following conditions:

- Simple gallbladder, with very easy retraction
- Status of acute inflammation
- Sclero-atrophic gallbladder
- Suspicion of Mirizzi syndrome
- Bleeding of unsuspected origin
- Appearance of unpredicted vessels or ducts
- Deviation of the operating target
- Shifting of dissecting target

There are some warning signs of alert which may include the following: surgeon's feelings of hesitation or that something unusual has happened, or that a thorough reevaluation of the situation is mandatory. Encountering any of the above-mentioned circumstances typically means that the surgeon's proficency and ability to deal with the operative conditions have been surpassed.

The factors leading to injury may be grouped in the following:[36-37]

1. Patient and disease
2. Environment
3. Procedure
4. Human factors

In accordance, the prevention of BDI should be founded on the development of strategies for building a safe working system, including the described steps:[38]

1. Patient selection

As mentioned previously the identification of patients with high-risk factors which could increase the risk of injury may be a very strong help in the prevention of BDI; it may also aid in the assignment of more experienced surgeons to assist in the procedure or scheduling the case at an earlier time or make the arrangements for availability and disposal of intraoperative cholangiography.

These high-risk factors include:

- Current acute cholecystitis or previous episodes of acute cholecystitis
- Simple **laparoscopic cholecystectomy**
- Severe adhesions due to previous surgery/ies
- Scarring and inflammation, sclero-atrophic gallbladder, suspicion of xantogranulomatous cholecystitis
- Concomitant CBD stones, which may be cleared preoperatively by means of ERCP or simultaneously with transcystic management

2. Control of environment

The operating room environment (personnel, supplies, devices, infrastructure) should provide an appropriate response so that problems encountered during the course of the surgical procedure can be dealt with adequately before they compromise patient safety and the surgeon wellness.

3. Design error-proof procedures

The systematic implementation of such procedures, in particular in academic institutions, where surgical residents and young faculty are involved is of paramount importance. Some of the important steps to take into account in the performance of a safe laparoscopic cholecystectomy include these:

a. Identification of the important structures, in particular, the cystic artery, the cystic duct, and the common bile duct. This process of identification is not a dynamic action, but a state of close inspection. It is important for surgeons to develop an instinct of permanent awareness where the identification and overcoming of difficulties is always present.[39]
b. Recognition of ***landmarks,*** such as:
   – Confluence of the Hartmann pouch into cystic duct, as a way of staying away from the common bile duct
   – Cystic lymph node, noting that the cystic artery is usually located behind it
   – Cystic artery (parallel with cystic duct)
   – Common bile duct
   – Duodenum
c. Maintenance of proper and adequate traction, in both cephalad and caudal direction to expand and allow a correct visualization of the gallbladder fundus and neck.
d. Adequate dissection of Hartmann pouch from anterior, medial, and posterior lateral sides to expose the cystic duct and artery gradually and safely.
e. Proper ***check points***, which represent steps to be overcome in a safe fashion and which add precision to the procedure:
   – Gallbladder fundus pushed cephalic and Hartmann pouch pushed laterally right
   – Cystic duct before it is clipped and cut
   – Liver bed after gallbladder-ectomy
   – Inspection of the removed specimen with the visible orifice of cystic duct

4. Detailed training program for young surgeons under supervisión

This approach is mandatory in academic institutions and thus, will provide trainees with a set of adequate abilities and a tool box and training to surpass difficulties when no longer under strict supervision. Each institution should develop its own program fitted to the type of patients taken care in that facility or system. The content should be related to the following topics:

- An in-depth knowledge of the basics and fundamentals of anatomy and surgical techniques, as well as surgical alternatives when confronting intraoperative difficulties
- Technique-related skills, which should be honed in virtual or ex vivo simulation models
- The full development and steps included in a standard error-proof procedure
- Nontechnique-related skills, which include the ability to control the environment, the practical and effectiveness of leadership of a surgical team, proper personal behavior, the calm and appropriate response to difficult situations and intraoperative inconvenient, the avoidance of dangerous situations, the attention to warning signs, and the willingness to call for help so as not to compromise the patient's safety.

Final Remarks

The primary goal of a laparoscopic cholecystectomy in the treatment of symptomatic cholelithiasis is the safe remotion of the gallbladder and the absence of common bile duct injury.[40-41]

- Some tips to take into account:
  – Never perform a laparoscopic cholecystectomy without a skilled surgeon close by.
  – Beware of the easy gallbladder.
  – Slow down, take your time.
  – Knowledge is power, conversión can be the salvation!
  – Do not repair a bile duct injury (unless you have performed at least 25 hepaticojejunostomies).
  – Do not ignore postoperative complaints (pain, jaundice, major abdominal discomfort, fever)
- Other options when confronted with a difficult laparoscopic cholecystectomy are:[42]
  – A percutaneous cholecystostomy, if the risk was identified preoperatively or the patient is a poor surgical candidate
  – An intraoperative cholangiography, which may aid in identifying an injury to the bile duct and solve it, if you are an experienced surgeon
  – A subtotal or partial cholecystectomy
  – Ask for help
  – Conversion to an open procedure

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CHAPTER 11

Management of Acute Pancreatitis Complications and Pancreatic Necrosis

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Acute pancreatitis, necrosis, severe acute pancreatitis, endoscopic treatment, step-up approach, surgical treatment, management

Abstract

Acute pancreatitis represents one of the main causes of hospitalization for gastrointestinal (GI) diseases in the United States with an esteemed economic burden of approximately 2.6 billion dollars per year. Around 20 percent of patients develop a moderate-severe disease which is complicated by the occurrence of a systemic inflammatory response syndrome, multi-organ failure, and locoregional complications. The management of complications is crucial to determine a patient's outcome and requires a multidisciplinary approach that is the mainstay for the achievement of better outcomes. In the last decades, the paradigm for the treatment of acute pancreatitis has progressively shifted from a pure surgical emergency towards a medical emergency, often deserving endoscopic-percutaneous and surgical interventions. The step-up approach has represented a cornerstone of treatment and has progressively improved prognosis. In the current chapter we overview the current evidence on the management of acute pancreatitis and attempt to provide guidance on prevention, as well as early and delayed treatment of its complications.

Definition and Epidemiology

Acute pancreatitis is an acute inflammatory disease, caused by the inappropriate and early activation of the digestive enzymes into the parenchyma and resulting in the proteolytic and lipolytic digestion of the pancreas and of the surrounding tissues. The main triggers for inflammation are gallstone disease in 40 percent of cases, alcohol in 30 percent, and miscellaneous causes (drugs, direct toxicity, genetic mutation, metabolic, postendoscopic retrograde cholangiopancreatography (ERCP) in 20 percent. In about 10 percent of cases, the clear cause cannot be identified (idiopathic acute pancreatitis).

Acute pancreatitis accounts for 275,000 annual hospitalizations in the United States, representing one of the main causes of hospitalization for GI diseases. Its economic burden is estimated around 2.6 billion dollars per year.[1,2] The incidence of acute pancreatitis is increasing. However, its mortality rate is decreasing over the decades and is estimated to be less than 2 percent. Most of the death cases (>50 percent) occurs within 14 days from the outbreak of symptoms.[3,4] From a nosography point of view, we can discriminate between interstitial or necrotizing pancreatitis. The latter is characterized by the presence of nonenhanced parenchyma on contrast-enhanced computer tomography (CECT). The necrosis can exclusively involve the parenchymal (less common), the surrounding tissue (less common), or both (more common). Necrotic areas are visible on CECT no earlier than 48 hours, and they are present in up to 10 percent of acute pancreatitis. Infection of the necrosis is associated with higher morbidity.

Acute pancreatitis is responsible for the development of a systemic inflammatory response syndrome (SIRS). The median hospital stay is 72 hours, reflecting the fact that more than 80 percent of patients have mild and uneventful pancreatitis. Approximately 20 percent of patients develop a moderate-severe disease.[5] A patient from such a last group might develop locoregional or systemic complications. Particularly the development of transient or persistent multi-organ failure impacts the prognosis and is associated with increased rates of morbidity and mortality.[6] In acute pancreatitis, we can identify two phases. The first phase is characterized by the SIRS and the possible presence of organ failure. It spans up to two weeks after the onset of symptoms. The second is characterized by the development of locoregional complications such as necrosis. Typical of the second phase, which spans over the second week, are also infections. We can identify them at a very early stage, within the 72 hours from the onset of symptoms.[7] Currently, no drug is available to lessen the inflammatory process and to avoid the possible development of complications.[8]

In the early phase, the cornerstone of management is to identify the cause, predict the development of the possible severe course, and to support the organ's function. Further endpoints of treatment, which can be delayed after the first 72 hours, are nutritional support, prevention of locoregional and systemic complications, and control of pain. It is also essential to identify patients that might benefit from ERCP or early cholecystectomy. It is noteworthy that most evidence is focused on the management of complications that often occur in the late phase, while a considerably less body of evidence is focusing on the control of the early stage, which probably plays a significant role in the overall outcome of patients.

Diagnosis and Classifications

For the diagnosis, at least two of the following criteria must be present: (1) typical abdominal pain, (2) the increase of serum amylase/lipase more than three times the upper limit, and/or (3) typical imaging with contrast-enhanced computer tomography (CECT). The first two criteria are often sufficient for establishing the diagnosis, but the third might be necessary if the patient does not improve after the first seven days.[5] The Revised Atlanta Classification and the Determinant-Based Classification are the criteria most used in clinical practice for the assessment of severity.

The former classification divides acute pancreatitis into mild, moderate, and severe. Mild acute pancreatitis is characterized by the absence of organ failure and locoregional or systemic complications. Moderate acute pancreatitis is characterized by the presence of transient (<48 hours) organ failure or by the development of locoregional or systemic complications in the absence of organ failure. Severe acute pancreatitis is characterized by the presence of persistent (>48 hours) organ failure.[7]

The determinant-based classification divides acute pancreatitis into mild, moderate, severe, and critical. Mild acute pancreatitis implies the absence of (peri)pancreatic necrosis and the absence of organ failure. Moderate acute pancreatitis is characterized by the presence of a sterile (peri) pancreatic necrosis and/or transient (<48 hours) organ failure. Severe acute pancreatitis is characterized by the presence of infected (peri)pancreatic necrosis or the presence of (>48 hours) organ failure. Critical acute pancreatitis is characterized by the presence of infected (peri)pancreatic necrosis AND the presence of (>48 hours) organ failure. [9]

Such classifications display the same accuracy in identifying the severity and finding extensive application in the clinical practice.[6]

Different clinical scoring methods used as predictors of severity and based either on multiple and complicated clinical or radiological assessments (such as the APACHE II, SIRS, the Computer Tomography Severity Index, the Baltazar Score, The RANSON Criteria, and the Modified Glasgow Score) display low feasibility and therefore find scarce application in the clinical practice. Moreover, a prediction of severity seldom can lead to preventive intensive-care unit hospitalization.[10]

The Management of Acute Pancreatitis Complications

In acute pancreatitis, the management of complications must consider two distinct stages that are in the timeline, respectively, early and late:

- Early phase in which treatment should be focused on the prevention of complications through the application of early aggressive medical treatments
- Late phase in which treatment should be focused on the management of complications through endoscopic, percutaneous, and/or surgical approaches

Treatment in the Early Phase

Fluid resuscitation

Especially in the early phase and, ideally in the first 24 hours, fluid resuscitation remains the cornerstone of treatment. Aggressive fluid resuscitation maintains the good functioning of microcirculation. Microcirculation is often impaired by fluids extravasation due to cytokine cascades and local inflammation. Microvascular ischemic damage is the leading risk factor for the development of necrosis and for the dysfunction of the gut barrier that is also associated with a worse outcome.[11] Therefore, most guidelines encourage the administration of aggressive hydration. Evidence about the best type of fluid, the optimal amount, and the infusion rate is missing. The interpretation of results coming from relatively small and heterogeneous trials is hampered by an overall low consistency and results biased by the wide confidence intervals.[8]

When referring to outcomes, a goal-directed strategy that keeps in mind the maintenance of a proper organ function based on clinical assessment is generally recommended. Even here the evidence is impaired by the heterogeneity of metrics used to evaluate organ disfunction among different studies (heart rate, urinary output, creatinine, urea nitrogen, the partial pressures of oxygen and carbon dioxide in the blood gas analysis, hematocrit, stroke volume variation, blood central venous pressure, and intrathoracic blood volume).

The infusion of Ringer lactate has been suggested to decrease the rate of SIRS when compared to normal saline and is, therefore, the fluid of choice for the management of acute pancreatitis. The theoretical advantage of Ringer lactate is the decrease of acidosis and, thus, also the reduction of the trypsin activity. Unfortunately, further evidence is needed, as treatment arms and choices of outcomes impaired the interpretation of results in regard to critical outcomes.[8] The exact amount of fluid resuscitation has been compared in two randomized controlled trials. The first trial compares two different rates of infusion (10-15 mL/kg per hour versus 5-10 mL/kg per hour), showing the latter to be associated with a less degree of need for mechanical ventilation.[12] The second trial investigates whether a rapid hemodilution, aimed at decreasing the hematocrit <35 percent within the first 48 hours after the outbreak of symptoms, resulted in better outcomes when compared with patients having hematocrit >35 percent after 48 hours. Sepsis within 28 days and inhospital mortality was shown to be higher in the first group.[13]

Pain control

To reach a level of adequate analgesia is crucial. Evidence suggests a possible effect of pain on the impairment of arterial microcirculation, which is a risk factor for the development of necrosis. Several randomized controlled trials (RCTs) have investigated the use of analgesic in the setting of acute pancreatitis but a few percentages in a double-blind setting. The conclusions reveal that there is not a specific type of analgesia which is preferred over another. Thus, clinicians should follow the World Health Organization (WHO) pain treatment flowchart.

There is no evidence contraindicating the use of morphine. Parenteral analgesia is often required to achieve a reasonable control of pain, and some trials have also suggested the possible application of epidural analgesia. Epidural analgesia might improve arterial perfusion and the overall outcome of patients when compared to parenteral analgesia, and such a strategy might be considered in patients requiring high doses of opioids for a long duration. Further evidence is needed for epidural analgesia, which cannot be recommended routinely in clinical practice.[14,15]

Nutrition

Several RCTs and meta-analyses agree on the superiority of enteral nutrition over parenteral ones in terms of adverse events such as the development of complications, the need for surgical intervention, and overall mortality.[16] Meta-analyses of RCTs have shown the safety of enteral nutrition over the parenteral ones, with a twofold reduction in the risk of infections and a 2.5-fold less risk of death in the enteral nutrition group. A RCT has also shown that early refeeding (within 24 hours) displayed similar results as delayed and on-demand ones (>72 hours).[17] The use of nasogastric (NG) tubes appears as effective as nasojejunal (NJ) tubes and does not increase the risk of mortality, tracheal aspiration, and exacerbation of pain.[18–20] Polymeric feeding formulas seemed to reduce the risk of infections and mortality when compared

with the elemental feeding formula. Therefore, there is no convincing evidence of the superiority of semi-elemental and elemental formulas over polymeric ones, which are less costly.[19]

ERCP in acute biliary pancreatitis

Previous RCTs suggested a possible role of ERCP in decreasing the incidence of complications in gallstone-induced acute pancreatitis.[21,22] The main limitation of such studies was the inclusion of patients with ongoing cholangitis that might benefit more from ERCP. Other RCTs excluding patients with acute cholangitis failed to show any benefit of early ERCP, and a meta-analysis confirmed no difference in outcomes independently of severity and timing, except for patients with cholangitis.[23–25] More recently, the Dutch Study Group performed another randomized controlled superiority trial on the issue. Schepers NJ et al. randomized patients with predictive severe acute biliary pancreatitis to receive either urgent ERCP with sphincterotomy (<24 hours from the presentation of symptoms) or conservative treatment. The primary endpoint was a composite outcome that included mortality and the occurrence of significant complications. No differences were found for the primary endpoint in the two groups (38 versus 44 percent), except for acute cholangitis (2 versus 10 percent; RR 0.18, 95 percent confidence interval (CI) 0.04–0.78; p=0.010). Urgent ERCP in biliary pancreatitis is required only in cases of cholangitis/persistent cholestasis. In all other cases, the management can be conservative, and the ERCP can be delayed. [26]

Prevention of infections of the necrosis

Infected necrosis increases morbidity and mortality rates. The presence of infected necrosis can be documented with a positive culture or is highly suspected in the presence of gas bubbles in the cavity with CECT. It can also be presumed in the presence of clinical deterioration/fever and the synchronous absence of other possible causes (such as pneumonia or infection of the urinary tract). Infected necrosis often displays monomicrobial flora (60 to 87 percent). Polymicrobial flora can occur in a minority of cases (13 to 40 percent). The infecting microorganism is generally a Gram-negative aerobic bacterium. A positive Gram stain/culture does not represent a mandatory indication to intervention in the absence of other signs, because it can be the result of contamination or the result of other microbial infections. In noninfected collections, in the last decades, clinicians have tried to shed light on two possible preventive strategies: antibiotic prophylaxis and probiotic administration. The first has the rationale of preventing bacteria translocation from the gut into the necrotic cavity through the administration of systemic antibiotic therapy. Most studies investigated the possible role of fluoroquinolones, carbapenems, metronidazole, and cephalosporins.[8] Several RCT and meta-analyses have shown contradictory results; therefore, current guidelines do not recommend the use of preventive antibiotic therapy.[27,28]

Treatment in the Late Phase

In the late phase of acute pancreatitis, major complications might occur. The most severe ones include vascular complications (splanchnic vein thrombosis or pseudoaneurysm), the occurrence of fistulas (enteric perforation, development of cyst-enteric or enterocutaneous fistulas, and disconnected pancreatic duct syndrome) and the development of (peri) pancreatic collections.

Vascular complications

Splanchnic vein thrombosis occurs in up to 18 percent of acute necrotizing pancreatitis. The splenic vein is the most involved, but portal and superior mesenteric vein involvement can also occur. Butler et al. performed a meta-analysis reporting an incidence as high as 22.6 percent with a 6.7 percent risk of bleeding, 77.3 percent risk of gastric varices, and 53.0 percent of esophageal varices.[29] Although the gold standard for the diagnosis is gastroscopy, Perri et al. reported that a CECT scan displays a good sensitivity for the screening of both esophageal and gastric varices (90 and 87 percent, respectively).[30]

The etiology of thrombosis is likely related to local inflammation. Generally, the course is indolent and asymptomatic but can occasionally become complicated by the development of portal hypertension, variceal bleeding, and/or ascites. Splenic vein thrombosis is more often asymptomatic and generally does not require treatment with anticoagulants. There is no convincing evidence regarding a possible benefit of anticoagulants. Their effect on recanalization remains contradictory.[31] Harris S et al., in a study on 2,454 patients admitted for acute pancreatitis, reported a 1.8 percent rate of splanchnic vein thrombosis. The rates of thrombosis resolution were similar between patients treated with or without anticoagulants (12 versus 11 percent, p>0.05).[32] Possible benefits of thrombosis need to be carefully balanced with potential risks for bleeding (such as the ones occurring into the necrotic cavity).[10] Pseudoaneurysms are potentially life-threatening complications resulting from arterial wall erosion from pancreatic enzymes. It accounts for 60 percent of all acute hemorrhages in the presence of necrotizing pancreatitis. Pseudocysts or small vessels are rarer sources of hemorrhages in the absence of a pseudoaneurysm and accounts for 20 percent of bleedings. The mortality for arterial bleeding during acute pancreatitis has been historically reported between 34 and 52 percent.[33] More recently, Maatman et al. reported in a large series on 647 patients with acute necrotizing pancreatitis a 4.3 percent occurrence of pseudoaneurysm. The median time between onset of pancreatitis and the diagnosis of the pseudoaneurysm was 63.5 days (range 1–957 days) and 89 percent were successfully treated with percutaneous intervention, with 11 percent requiring surgery and an overall mortality of 14 percent.[34]

Fistulas and disconnected pancreatic duct

Pancreatic fistula is defined as the outflow of a persistent volume of fluid harboring amylase concentration at least three times greater than the upper serum value. It can flow out through a surgical wound or percutaneous catheter drainage after surgical endoscopic or percutaneous intervention for necrotizing pancreatitis.[10] Pancreatic fistula in the context of acute pancreatitis with drained necrosis displays an incidence between 17 and 76 percent. Morbidity is high, because pancreatic fistulas are complicated with the occurrence of metabolic and nutritional impairments, eventually resulting in a prolonged length of hospital stay. Conservative management is applied in most cases, although it can take more than three months for the fistula to heal. In cases of conservative treatment failure, pancreaticojejunostomy is the rescue treatment. Bakker et al. reported no difference in the fistula resolution comparing patients who had undergone endoscopic transpapillary drainage with conservative treatment (84 versus 75 percent; p=0.175), showing in the first group no statistically significant shorter time to resolution (71 days versus 120 days). The authors concluded that endoscopic transpapillary downstream control might be a safe and feasible alternative.[35]

Entero-cystic fistulas might also occur. Colonic fistula is a potentially fatal complication of necrotizing pancreatitis. In a large retrospective study of 1,750 patients with acute necrotizing pancreatitis, Gao et al. have reported that 41 percent developed an infection of the necrosis, and 19 percent developed a fistula to the colon. The authors treated all patients with a step-up approach, managing to avoid surgery by 47 percent. Overall mortality was 29 percent.[36]

The rupture of the main pancreatic duct reflects a lack of continuity between the GI tract and the left side body/tail of the pancreas, resulting in the development of pancreatic fistulas and peripancreatic fluid collections.[37] Early identification is crucial and a mainstay in the therapeutic decision-making process. Timmerhuis et al. recently compared the diagnostic accuracy of five diagnostic modalities in diagnosing a disconnected pancreatic duct in a systematic review of eight studies, including 142 patients with acute pancreatitis. Both endoscopic ultrasound (EUS) and ERCP displayed high sensitivity (100 percent), while magnetic resonance cholangiopancreatography (MRCP) with or without secretin showed lower sensitivity (83 percent). The addition of secretin to MRCP increased the sensitivity to 92 percent. The drain amylase measurements showed a sensitivity of 100 percent with a specificity of 50 percent. The number of included patients in the various studies varied between six and 31.[38] Studies comparing the diagnostic yield of MRCP versus EUS in the diagnosis of the disconnected pancreatic duct during acute pancreatitis is lacking. Bang et al. reported a 100 percent sensitivity of EUS. However, the study had some selection biases (such as the inclusion of patients with walled-off necrosis [WON] ≥6 cm, and exclusion of patients with suboptimal visualization parenchyma). The conclusions were that probably EUS might add diagnostic yield only in a selected group of patients. Considering feasibility and safety, it is reasonable to affirm that MRCP with secretin is a valuable second step after CT scan for the evaluation of patients with suspected disconnected pancreatic duct in the context of necrotizing pancreatitis.[39] The standard treatment implies the surgical resection of the excluded part of parenchyma. Roux-en-Y pancreatojejunostomy might be a valid alternative. Islet auto-transplantation might help to preserve the endocrine function.[10] A distinction has to be made between early and delayed surgery. Within the first 30 to 60 days, it is possible to perform distal pancreatectomy and debridement. Such an approach and timing harbors high morbidity (needs for transfusions, the development of fistula, and longer hospital stay) but has the advantage of providing a short cut for the overall course of the disease. If the patient does not require acute or subacute surgery, bridging therapy might allow for a planned elective surgery, often several months after the onset of symptoms. The residual local inflammation/fibrosis requires laparotomic approaches and splenectomy. Such an indication is particularly valid in cases of splenic thrombosis with the development of collaterals circles. Fischer et al. reported higher rates of grade B/C fistulas in patients treated early. Patients operated within 60 days versus 440 days displayed a fistula rate of 36 percent versus 7 percent rate, respectively.[40] Less invasive strategies, such as endoscopic or percutaneous drainages, should be considered either as a bridge therapy or as a possible definitive solution in patients unfit for surgery. For such a purpose, EUS-guided stenting gained increasing popularity in the last years, although further evidence is required to confirm its safety and efficacy in the long run. Minimally invasive approaches (laparoscopic or open transgastric) allow the creation of large cystogastrostomy that will bypass the need for further intervention, by creating a stable internal diversion of the pancreatic secretion. [41]

(Peri)pancreatic collections

The Revised Atlanta Classification recognized four possible peri(pancreatic) collections.[7] In the first four weeks after the outbreak of acute pancreatitis, it is possible to identify two possible collections. The first consists of acute (peri) pancreatic fluid collections, which are characteristics of interstitial edematous pancreatitis and are characterized by the presence of homogeneous fluid adjacent to the pancreas without a recognizable wall. The second consists of acute necrotic collections which are characteristics of necrotizing pancreatitis. In such a group, it is possible to recognize intra- and/or extrapancreatic necrotic collection without a well-defined wall.[10] Following four weeks after the outbreak of acute pancreatitis, it is possible to identify two other groups of potential collections. The first group consists of pancreatic pseudocysts, characterized by the presence of

an encapsulated well-defined collection with minimal solid component, which is usually lying outside of the parenchyma. Pseudocysts are typical of interstitial edematous pancreatitis and, if asymptomatic, do not require treatment. The second group consists of walled-off necrosis and is characterized by the presence of intra- or extrapancreatic collection with a well-defined wall. Such collections are typical of necrotizing pancreatitis. Since necrotic collections harbor a higher risk for morbidity compared to pseudocysts, such a classification also implies an important clinical message for risk stratification and subsequent management.

CECT, MRI, and EUS can all provide an excellent evaluation of the pancreas parenchyma and of eventual surrounding collections.[42,43] CECT remains the gold standard for the assessment of the presence and extension of necrosis, although MRI can also provide information about the existence of necrotic tissue through T1-weighted sequences with the main advantage of avoiding radiation exposure and providing a good quality imaging even in the presence of renal failure. Moreover, magnetic resonance cholangiopancreatography (MRCP) offers additional information on the presence of stone disease and the integrity of the main pancreatic duct. EUS can be performed bedside in critically ill patients and allows for the possible use of fine-needle aspiration (FNA) for the confirmation of the presence of infected necrosis and targeted antibiotic therapy. Nevertheless, routine FNA is not currently recommended because of the high risk of false negatives. Moreover, an isolated Gram-positive stain or culture does not represent a mandatory indication for the drainage. Further studies are needed to confirm the feasibility and clinical impact of FNA in daily practice.

In the management of acute necrotizing pancreatitis, it is crucial to understand whether the possible clinical deterioration is due to the SIRS in the coexistence of a sterile necrosis or if it is the result of the infection of the necrosis.

Indications for intervention are:

- The presence of infected necrosis
- Persistent organ failure, despite the absence of necrosis
- Pain or obstructive symptoms in sterile necrosis (after the development of a capsule)
- Ongoing symptoms in the presence of a disconnected main pancreatic duct

There are four possible approaches for the drainage of pancreatic necrosis:

1. Endoscopic
2. Percutaneous
3. Surgical minimally invasive
4. Surgical open

Timing

No specific indication is provided about timing for intervention, but it seems that differences exist between surgical and nonsurgical approaches. For instance, the mainstay of an open surgery approach is to postpone surgical intervention for at least 3-4 weeks, a period in which the capsule was considered mature and the intern contain had stated to liquefy. After the outbreak of mini-invasive approaches and endoscopic/percutaneous approaches, such a paradigm has been reversed. New evidence suggests an early mini-invasive approach in patients with infected necrosis might result in improved rates of organ failure without impacting the rate of complications such as perforation.

Trikudanathan et al. have investigated clinical outcomes and complications in early versus delayed interventions for endoscopic necrosectomy. The authors have shown similar rates of hemorrhages (11 versus 10 percent, $p>0.05$), but higher rates of mortality and rescue open necrosectomy in early interventions, (13 versus 4 percent, $p=0.02$) and (7 versus 1 percent, $p=0.03$), respectively. The first intervention group included sicker patients displaying higher rates of infection (91 versus 39 percent, $p<0.05$), and shock (13 versus 4 percent, $p<0.05$), but also higher rates of respiratory failure (41 versus 22 percent, $p=0.005$) and acute kidney injury (43 versus 32 percent, $p=0.09$). In both groups, the authors assisted in an improvement of organ failure after necrosectomy.[44]

Endoscopic approach

Indication to endoscopic drainage in patients with infected necrotizing pancreatitis comes from two RCTs. The transluminal endoscopic step-up approach versus minimally invasive surgical step-up approach in patients with infected necrotising pancreatitis (TENSION trial) compared video-assisted retroperitoneal debridement (VARD) (n=47) with the endoscopic approach (n=51). The endoscopic step-up approach was not superior to the surgical step-up in a composite endpoint, including major morbidity and mortality (43 versus 45 percent, $p=0.88$). Still, it displayed increased rates of complications such as pancreatic fistulae, with an overall longer hospital stay (53 versus 69 days, $p=0.014$). [45] The Minimally Invasive Surgery vs. Endoscopy Randomized (MISER) Trial for Necrotizing Pancreatitis also resulted in similar outcomes, with Bang et al. comparing endoscopy to the minimally invasive approach (laparoscopic/VARD). Again, there was no statistically significant difference in mortality rates (respectively, 8.8 versus 6.3 percent, $p=0.999$); however, there was a less degree of fistulae (0 versus 28.1 percent; $p=0.001$).

In general, the mean of major complications per patient was less for endoscopy (0.15 ± 0.44) than for surgery (0.69 ± 1.03), p=0.007. The three months' scores for quality of life were also better with endoscopy (*p*=0.039), which harbored lower costs when compared to surgery ($75,830 versus $117,492, p=0.039). Both studies have shown overall lower costs for endoscopy.[46] Depending on the localization of pancreatic necrosis (head, body, or tail) and its relationship with the visceral wall, it is possible to have either transgastric or transduodenal approaches. Collections in the proximity of the head are generally drained through a transduodenal approach. In contrast, collections in the proximity of the body-tail, are usually drained through a transgastric approach.[41] Both approaches seem to be safe and feasible. Despite the absence of high-quality RCTs comparing EUS-guided approach with the non-EUS transmural approach, the former is regarded as the safest. EUS allows for the possibility to perform color doppler imaging and, therefore, to avoid puncturing big vessels.[10]

Transmural drainages are performed by puncturing the necrotic cavity and deploying double-pigtails plastic stents, self-expandable metal stents (SEMS), or lumen-apposing metal stents (LAMS).[47] LAMS are shorter than traditional SEMS (1 cm versus 6-7 cm) and easier to deploy because of their peculiar electrocautery delivery systems. Despite the popularity that LAMS have gained in the last years, convincing evidence about their superiority over the traditional double-pigtail plastic stents is negligible. On the contrary, a recent RCT has shown similar efficacy when compared to the use of classical double-pigtails plastic stents which are also less costly.[48,49] An evident advantage of LAMS is the larger diameter that allows easier access to the necrotic cavity and the possibility to perform a repeated session of endoscopic necrosectomies. As an alternative is also possible to deploy a nasal-cystic tube for continuous irrigation with saline. The larger diameter might also avoid stent occlusion with debris, and the double flange is designed to avoid stent migration specifically. Further evidence is needed to establish whether endoscopic necrosectomy can be safely performed simultaneously with LAMS insertion or if it should be delayed. Moreover, it remains unclear whether patients should be scheduled with certain intervals or should be treated on-demand, according to their clinical conditions. Although not free from possible complications (such as bleeding, embolism, and perforation), endoscopic necrosectomy seems to provide better results when compared to the simple irrigation with saline.[50] Endoscopic necrosectomy is probably possible within four weeks from the onset, when clinically indicated. Nevertheless, to wait ≥ four weeks before endoscopic necrosectomy most likely decreases mortality. Trikudanathan et al. have shown that early drainage is associated with higher rates of mortality and higher rates of rescue surgery. A drainage performed <four weeks versus ≥four weeks resulted in 13 versus 4 percent, mortality rates (p = 0.02); and 7 versus 1 percent, rescue surgery (p = 0.03), respectively.[44] No definitive evidence can support neither the use of a specific adjunctive chemical therapy (such as antibiotics or hydrogen peroxide irrigation) nor the use of a specific tool during the sessions of necrosectomy. The use of proton-pump inhibitors should probably be avoided to facilitate the auto-debridement resulting from the effect of gastric acid. While pigtail plastic stents can be left in place for a long time, LAMS should be removed within several weeks. Long-standing LAMS might cause the occurrence of delayed bleeding when the cyst collapses. [49]

Percutaneous approach

Percutaneous catheter drainage involves the placement of single or multiple catheters, which can be progressively upgraded, according to the patient's clinical conditions. Catheters are inserted under ultrasound or CECT guidance and allow the drainage of collections unreachable with the endoscopic approach. The best candidates for such an approach are patients harboring flank or pelvic collections that are extended to the deep retroperitoneum. The percutaneous catheter might also provide guided access for further endoscopic or VARD interventions. Van Baal et al. performed a systematic review of 11 studies on a total of 384 patients. The authors included patients with necrotizing pancreatitis who had undergone a percutaneous approach for suspected peripancreatic infected necrosis or for symptomatic sterile necrosis. Percutaneous catheter drainage alone is effective in between 55.7 percent, with a 17.4 percent reported mortality rate.[51] Percutaneous catheter drainage is probably more useful as a bridge therapy to minimally invasive approaches rather than as an exclusive treatment. Ross AS reported a series of 117 patients who had undergone multimodality treatment combining percutaneous and endoscopic approaches for the treatment of symptomatic and infected walled-off necrosis. Disease-related mortality was 3.4 percent, with no patients needing additional surgical necrosectomy.[52] Noteworthy, both percutaneous catheters and VARD are hampered by higher risks of fistulas (up to 35 percent). Mallick et al. have compared 375 patients who have undergone percutaneous catheter drainages for acute necrotic collections and walled-off necrosis reporting similar efficacy and safety. The need for an additional surgical necrosectomy approach was 14 percent in patients with acute necrotic collections and 12 percent in the group with walled-off necrosis (p = 0.364). Mortality was also similar (19 versus 13.7 percent; p = 0.132). [53]

Surgical minimally invasive approach

In the last decades, the number of minimally invasive procedures to drain infected necrosis has increased. A surgical approach to pancreatic necrosis should be considered in cases of persistent organ dysfunction or failure despite mini-endoscopic or percutaneous approaches. It is

paramount to choose correct timing, as surgical subacute interventions (two to four weeks) are associated with higher mortality. Possible approaches include VARD, open transgastric debridement, and laparoscopic debridement.[10] VARD allows for the removal of larger pieces of solid debris by making a subcostal incision of 5 cm, by placing an irrigation catheter, and by removing debris through open surgical forceps. Between 23 and 47 percent of patients will improve with VARD alone. VARD should be considered when the necrosis is extended into the paracolic gutter and can be difficult to reach because of the vicinity of mesenteric vessels. The PANTER trial (Minimally Invasive Step-Up Approach versus Maximal Necrosectomy in Patients with Acute Necrotising Pancreatitis) compared the minimally invasive step-up approach with open necrosectomy, showing better outcomes in the first group in terms of new-onset multiple-organ failure (12 versus 40 percent), hernias (7 versus 24 percent), and new-onset diabetes (16 versus 38 percent). The mortality rate was similar in both groups (19 versus 16 percent, p=0.70) [54] The surgical transgastric approach is similar to the endoscopic one and consists of the creation of a surgical cystogastrostomy. It can be achieved both with a laparoscopic or open procedure. An anterior gastrotomy is performed to access the posterior wall and to deliver transmural access. A nasal-cystic tube is deployed to allow postoperative lavages. The surgical transgastric approach is a relatively easy debridement procedure, harboring low morbidity and allowing the establishment of a large-size connection between the stomach and the necrotic cavity, which is durable. Such an aspect might be relevant when disconnected pancreatic duct syndrome occurs. The best candidates are patients with a necrosis that is located centrally.

Surgical open approach

When patients display a large burden of necrosis diffuse in the abdomen after the failure of endoscopic, percutaneous, or minimally invasive approaches, it is possible to consider open surgical debridement. The need for open rescue surgery is greater in patients who were treated with early (<4 weeks) intervention when compared to the standard (>4 weeks) step-up approach (7 versus 1 percent, p = 0.03).[44] The open approach consists of laparotomy and debridement of necrosis in addition to an eventual cholecystectomy. Postoperative lavages are ensured by large-caliber drains that are left in place. Van Santvoort et al. compared the outcomes of open necrosectomy and the step-up approach in a multicenter RCT of 88 patients with acute necrotizing pancreatitis. The authors investigated a composite primary endpoint, including major complications or death. The primary endpoint was more frequent in open necrosectomy (69 versus 40 percent, p=0.006). Relative risk for the step-up approach was 0.57; 95 percent CI 0.38-0.87; p=0.006. Mortality rate was similar (17 versus 19 percent; p=0.70). [54]

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CHAPTER 12

Management of Acute Complications in Hepatic and Biliary Surgery

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Key words:

Bile duct injury, bile leakage, hepatectomy, hepatectomy complications, hepaticojejunostomy, liver abscess, percutaneous drainage

Abstract

Despite advances in surgical and perioperative management, the complication rate following hepatic and biliary surgical procedures remains high. Herein we discuss the management of the most commonly occurring complications that may necessitate surgical intervention, namely iatrogenic bile duct injury, post-hepatectomy bile leakage, and hepatic abscess. Biliary injuries occurring during laparoscopic cholecystectomies are recognized intraoperatively only in one-third of cases. In that scenario, injury repair should be attempted only if an experienced biliary surgeon is present. For postoperatively identified injuries, evaluation includes determination of the anatomy and extent of the injury using the appropriate imaging and endoscopic modalities. For minor injuries, percutaneous drainage and endoscopic stent placement can be effective. For transections and occlusions, surgical intervention with a Roux-en-Y hepaticojejunostomy may be needed. Post-hepatectomy bile leakage complicates approximately 10 percent of hepatic resections. Most patients may be managed with percutaneous drainage and endoscopic decompression. Pyogenic hepatic abscesses may develop following hepatic and biliary surgical procedures. Small abscesses can be managed with percutaneous aspiration, while for larger or multiloculated abscesses surgical debridement may be needed.

Introduction

Despite advances in surgical technique and perioperative management, complications in hepatic and biliary surgery remain frequent. Based on data from the American College of Surgeons–National Surgical Quality Improvement Program (ACS–NSQIP®), complications occur in 21 and 28 percent of patients undergoing hepatic and biliary procedures, respectively, while specifically for extended hepatic resection, complications occur in one-third of cases.[1] Therefore, recognizing and properly managing postoperative complications following hepatic and biliary procedures is of great importance. This chapter will focus on some of the most frequent complications that may necessitate surgical intervention, namely iatrogenic bile duct injury, post-hepatectomy bile leakage, and hepatic abscess.

Iatrogenic Biliary Injuries

Bile duct injury is one of the most feared complications of laparoscopic cholecystectomy and it occurs in approximately 0.7 percent of cases.[2] Surgeon inexperience, male gender, older age, obesity, complicated gallstone disease including acute on chronic cholecystitis, and bleeding obscuring the operative field have been associated with increased risk of biliary injury.[2-5] Intraoperatively, excessive cephalad traction of the gallbladder, liberal use of electrocautery, and deep dissection into the liver parenchyma have been implicated in biliary injuries as well. Aberrant anatomy such as an aberrant right hepatic duct may also increase the bile duct injury risk. Obtaining the "critical view of safety" is essential when performing a cholecystectomy in order to minimize the risk of a bile duct injury.[6,7]

Biliary injuries are anatomically classified using the Strasberg-Bismuth classification. The classification is based on both the most distal and proximal levels at which healthy biliary mucosa is available for anastomosis (**Table 1**).[2,8] Type A injuries involve a leak into the gallbladder bed from minor ducts or the cystic duct. Type B (occlusion) and C (transection) injuries involve injury to aberrant right hepatic ducts. Type D injuries represent lateral injuries to the major bile ducts. Type E injuries involve the hepatic duct and are further subclassified into E1-E5 according to the level of injury. This classification not only correlates with clinical presentation and outcomes, but may also assist in selecting the appropriate repair technique.

Diagnosis of biliary injuries occurs intraoperatively, or in the early or late postoperative period. Unfortunately, fewer than one-third of injuries are recognized intraoperatively due to late recognition of the anatomy or by continuous bile drainage into the field from the common bile duct. Depending on the type of injury, an intraoperative cholangiogram should be performed to evaluate the anatomy and confirm the presence of an injury. Upon confirmation of the injury, a hepatobiliary surgeon should be involved to repair it. If no hepatobiliary surgeon is available, one or two large closed suction surgical drains should be placed in the operative bed and the patient should be transferred to a center specialized in biliary surgery.[9] If an experienced biliary surgeon is available, repair can be attempted. Small Type D injuries can be repaired with placement of a T tube, while larger defects can be closed primarily with placement of a T tube through a proximal or distal choledochotomy. Injured isolated hepatic ducts smaller than 3 mm draining a single hepatic segment can be ligated. In case of more extensive thermal injury involving larger ducts, reimplantation with a Roux-en-Y hepaticojejunostomy should be performed. Primary choledochocholedochostomy should be avoided given the poor outcomes due to loss of length and devascularization due to thermal injury.

Table 1. Strasberg-Bismuth classification of iatrogenic bile duct injury[2,8]

Type	Definition
A	Injury to the cystic duct or small ducts in the liver bed
B	Occlusion of aberrant right hepatic duct(s)
C	Transection of aberrant right hepatic duct(s)
D	Lateral injury to major bile ducts
E	Injury to the hepatic ducts; classified by level of injury
E1	Injury more than 2 cm from bifurcation
E2	Injury less than 2 cm from bifurcation
E3	Injury at the bifurcation
E4	Separation of right and left hepatic ducts in the hilum
E5	Type C injury with concomitant injury in the hilum

The majority of biliary injuries are recognized postoperatively. Patients with biliary and cystic duct leaks (Types A, C, and D) typically present within two weeks postoperatively with fever, abdominal pain, and biloma or bilious ascites. Mild jaundice may be present. Laboratory findings are notable for leukocytosis and elevated alkaline phosphatase, γ-glutamyl transferase, and bilirubin. Patients with a Type B injury, which usually is an occult injury potentially leading to segmental cholestasis and right liver atrophy, may present late with cholangitis or right liver stone disease. Patients with Type E injuries typically present weeks to years after the procedure with jaundice.

Patients presenting with a suspected leak should be evaluated preferably with magnetic resonance cholangiopancreatography (MRCP) rather than computed tomography (CT) or ultrasound, due to its improved ability to delineate the biliary anatomy.[10–12] Once a collection has been identified, an imaging-guided catheter should be placed. The diagnosis of active bile leak is established with evidence of ongoing bile drainage. Injuries of the common bile duct can be delineated with a subsequent endoscopic retrograde cholangiopancreatography (ERCP), during which, an injury can be managed with stent placement and/or or sphincterotomy.[13–21] Stent placement can occlude the injury and reduce the pressure gradient over the lesion leading to decreased leakage and symptom resolution.[21] The stent is subsequently removed after six weeks.[20,21] Of note, ERCP with dilation and stent placement can also be used for the management of strictures.[22] Rarely, bile peritonitis or intra-abdominal sepsis does not resolve with percutaneous and endoscopic interventions, at which time surgical exploration is warranted.

For patients presenting predominantly with jaundice suggestive of an occlusion, an MRCP should be obtained. It can provide information on the location of injury, dilation of intrahepatic and proximal-to-lesion extrahepatic ducts, and presence of collections.[10–12] Once the occlusion is confirmed, percutaneous transhepatic cholangiogram should be performed in order to better evaluate the proximal extent of the injury, and a catheter should remain in place to decompress the biliary tree.[23] For proximal lesions, multiple catheters may be required to visualize and drain all sectors. Of note, for all patients with biliary injury, magnetic resonance or CT angiography can be considered to evaluate the presence of a concomitant vascular injury. Indeed, a right hepatic artery injury can occur as a result of misidentification as the cystic artery.[24]

Transections or occlusions necessitate surgical intervention. Prior to any procedure, the patient's biliary tree needs to be adequately decompressed and the injury needs to be anatomically well defined.[25,26] Patients presenting within days from the index operation may benefit from surgical intervention. However, patients presenting weeks later may benefit from a few weeks of decompression in order for the initial inflammation to subside. In patients with E1-E2 lesions where the confluence is intact, a tension-free end-to-side Roux-en-Y hepaticojejunostomy can be performed. In patients with an E3 lesion where the confluence is partially intact, a wide hepaticojejunostomy including both right and left ducts can be performed. For more proximal lesions, separate right and left hepaticojejunostomies are required. Transhepatic catheter(s) can be used to stent the anastomosis(es). Recurrent strictures develop in approximately 10 percent of cases, with the majority occurring within the first two years after the repair.[25,27,28] These strictures can be managed with stenting and dilation.

Post-Hepatectomy Bile Leakage

Postoperative bile leakage is a common complication occurring in up to 12.8 percent of hepatectomies[29] and increases the risk of serious complications such as hepatic failure and sepsis. Bile leak was formally defined by the International Study Group of Liver Surgery (ISGLS) and was further categorized in Grades A to C, with Grade C indicating the need for laparotomy[30] (**Table 2**). Male gender, larger lesions, major resection, repeat hepatectomy, longer operative time, higher blood loss, and longer vascular inflow occlusion time have been suggested as risk factors for post-hepatectomy bile leak.[29,31] Patients typically present with worsening abdominal pain and jaundice, and bile-stained fluid from their abdominal drains. Most post-hepatectomy bile leaks are managed with percutaneous drainage or endoscopic biliary decompression with ERCP and stent placement. Severe nonresponding cases (Grade C by definition) may require surgical exploration.

Table 2. Definition and grading of bile leakage after hepatectomy by the International Study Group of Liver Surgery[30]

Definition	Fluid with an increased bilirubin concentration in the abdominal drain or in the intra-abdominal fluid on or after postoperative day 3, or as the need for radiologic intervention because of biliary collections or relaparotomy resulting from bile peritonitis. Increased bilirubin concentration in the drain or intra-abdominal fluid is defined as a bilirubin concentration at least 3 times greater than the serum bilirubin concentration measured at the same time.
Grade	
A	Bile leakage requiring no or little change in patients' clinical management
B	Bile leakage requiring a change in patients' clinical management but manageable without relaparotomy, or a Grade A bile leakage lasting for >one week
C	Bile leakage requiring relaparotomy

Pyogenic Liver Abscess

Pyogenic liver abscess formation is another potential complication of hepatic and biliary surgery, but can also arise as a consequence of another infectious etiology. Pyogenic hepatic abscesses represent the most common type of visceral abscesses (within an abdominal organ) accounting for almost half of visceral and more than

10 percent of all intra-abdominal abscesses.[32] Men, diabetics, as well as patients with underlying hepatobiliary diseases, liver transplant recipients, immunosuppressed patients, users of proton pump inhibitors, and patients with chronic granulomatous disease are at increased risk of developing a pyogenic liver abscess.[33-35] Biliary and hepatic surgery, as well as prior biliary instrumentation are also risk factors, with abscesses complicating up to 25 percent of hepatectomies and 0.3 percent of laparoscopic cholecystectomies.[11,36] Specifically among patients undergoing major hepatectomies, larger hepatic tissue removed, Pringle maneuver longer than 20 minutes, longer operation duration, and higher blood loss volume have been associated with abscess formation,[36,37] while among patients developing a pyogenic abscess following hilar cholangiocarcinoma resection, vascular reconstruction and positive margins have been shown to be risk factors.[38]

Pyogenic abscesses also develop secondary to other sources of infection, such as biliary infection via direct spread in approximately half of the cases, or intra-abdominal infections via hematogenous spread (**Figures 1–3**).[35,39] Sources of systemic hematogenous seeding include, but are not limited to, appendicitis, diverticulitis, cholecystitis, and dental infections. Other sources of infection include penetrating wounds or ingested foreign bodies.[40] Most are polymicrobial with one-third containing anaerobes. *Escherichia coli*, *Klebsiella pneumoniae,* and streptococcal species appear to be the most common implicated pathogens depending on the geographic location.[41,42] In cases of hematogenous spread, a single organism such as *Staphylococcus aureus* or *Streptococcus milleri* is most likely to be responsible, while fungal abscesses have been reported in patients recovering from chemotherapy. Of note, liver abscesses caused by *Klebsiella pneumoniae* have been associated with colorectal cancer.[43]

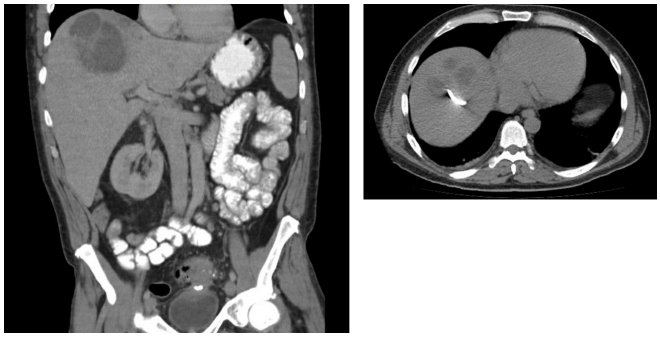

Figure 1. Computed tomography images of a 54-year-old male with prior diverticulitis and liver abscess 2 years ago (treated with percutaneous drainage and antibiotics for 3 months), who presented with a new liver abscess and recurrent diverticulitis. The abscess was drained for 7 days with no change in size. Blood cultures were positive for *E. Coli* and the patient experienced daily intermittent fevers to 103°F (39.4°C). The patient underwent laparoscopic debridement with subsequent resolution of fever. The drain was removed on postoperative day 7, antibiotics were administered for 2 weeks, and the patient returned to work on postoperative day 14.

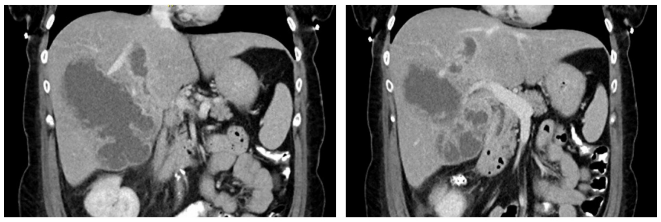

Figure 2. Computed tomography images of a 64-year-old type II diabetic male with symptoms of biliary colic and intermittent fevers who returned from travel in South America 8 weeks earlier. Stool and serum studies were negative for *E. histolytica.* He underwent laparoscopic drainage of the abscess and cholecystectomy, and was discharged home on postoperative day 3. He received antibiotics for 2 weeks and the drain was removed on postoperative day 7.

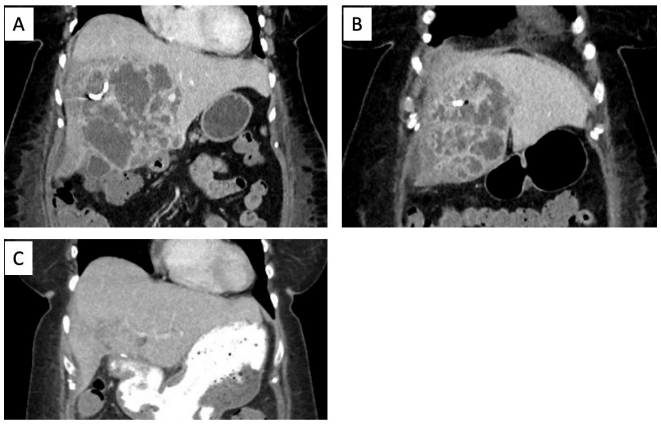

Figure 3. Computed tomography images of a 65-year-old female who developed intermittent fevers to 103°F (39.4°C) approximately 2 weeks after dental work. She presented in septic shock and a percutaneous drain was placed by interventional radiology. Two weeks later she continued to have a fever, at which point images A and B were obtained. Abscess fluid microbiology and blood cultures revealed *Streptococcus milleri*. The patient underwent surgical debridement. Image C was obtained 3 weeks postoperatively.

Patients typically present with fever and abdominal pain, while nonspecific symptoms such as anorexia, nausea, and weight loss may also be present. Abdominal signs including tenderness and guarding are most frequently localized to the right upper quadrant.[44] Laboratory findings are usually notable for leukocytosis, while serum alkaline phosphatase, bilirubin, and aspartate aminotransferase are elevated in more than half of patients.[39] Chest imaging may reveal elevation of the right hemidiaphragm, right lung base infiltrate, or a right-sided pleural effusion.

Abdominal CT with intravenous contrast is the diagnostic imaging modality of choice. Alternatively, ultrasound can be used, but is less sensitive than CT.[45] Most commonly, CT reveals a well-defined round lesion with central hypoattenuation. Peripheral rim enhancement and surrounding edema, although not common, are highly specific. In the post-hepatectomy setting, gas bubbles

or a gas-fluid level may be present at the resection site.[46] Most lesions are located in the right hepatic lobe due to its increased size and higher blood supply. Blood cultures should be obtained as part of the diagnostic evaluation, while serology/stool testing for *Entamoeba histolytica* should be performed in patients with no clear risk factors for pyogenic abscess but with risk factors for amebic abscess. Image-guided aspiration of the abscess and microbiologic evaluation confirm the diagnosis and help guide further management.

The mainstay of treatment is intravenous antibiotics and drainage, which can be performed percutaneously, laparoscopically, or with an open surgical procedure. Small unilocular abscesses up to 5 cm in diameter can be managed with either needle aspiration or drainage with catheter placement, since both have been shown to be effective in clinical trials.[47–50] In the former case, a repeat aspiration may be required in up to 50 percent of patients, while in the latter, the drain usually remains in place for up to 7 days. For unilocular abscesses greater than 5 cm in size, drainage with catheter placement is recommended, given that a recent meta-analysis of clinical trials found this modality to have a higher success rate.[51] Surgical drainage can also be considered. In fact, a large retrospective study comparing percutaneous to surgical drainage demonstrated a lower failure rate for the latter (28 versus 7 percent).[51] Multiple or multiloculated abscesses are typically managed with surgical drainage or resection, however in some cases percutaneous drainage has been shown to be successful.[52] Aggressive hepatic resection has also been suggested for patients with an acute physiology and chronic health evaluation (APACHE) score of 15 or higher.[53] Antibiotic therapy is guided by microbiologic evaluation. Empiric coverage should include enteric Gram-negative bacilli, streptococci, and anaerobes, and it is not unreasonable to cover *Entamoeba histolytica* if involvement of this organism cannot be excluded.

In terms of prognosis, mortality ranges from 2 to 12 percent, with the presence of an anaerobic organism, malignancy, and need for open drainage being associated with higher mortality rates.[54] Abscess manipulation can result in transient septic physiology. Abscess rupture has been reported in 3.8 percent of patients and can lead to overwhelming sepsis.[55]

Conclusion

In conclusion, patients with acute biliary and hepatic complications are at high risk of short- and long-term adverse outcomes. Iatrogenic biliary injuries can result in long-term consequences due to strictures, recurrent cholangitis, and hepatic/biliary atrophy. Post-hepatectomy bile leaks are most often managed with surgical or percutaneous drainage. Hepatic abscesses are managed with source control and systemic antibiotics. Correct management of these pathologies results in good short- and long-term patient outcomes.

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CHAPTER 13

Management of Acute Complications in Pancreatic Surgery

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Key words:

Pancreatectomy, pancreaticoduodenectomy, delayed gastric emptying, pancreatic fistula, post-pancreatectomy, hemorrhage, complications

Abstract

Major pancreatic resection is associated with significant postoperative morbidity. Common complications include postoperative pancreatic fistula (POPF), delayed gastric emptying (DGE), and post-pancreatectomy hemorrhage (PPH). The International Study Group of Pancreatic Surgery (ISGPS) has defined standardized criteria for the diagnosis of these complications following pancreatectomy which has significantly improved the universal reporting of these outcomes. Here we outline the definition, epidemiology, risk factors, clinical presentation, and management of these common complications. Goals for managing acute complications in pancreatic surgery include early risk stratification, preventative measures, precise operative technique, early recognition, and prompt multidisciplinary management of postoperative complications.

Introduction

Major pancreatic resection, including pancreaticoduodenectomy and distal pancreatectomy are associated with significant morbidity and mortality. While the operative mortality for pancreaticoduodenectomy has decreased dramatically over the last several decades and is now consistently reported to be less than 3 percent at high-volume facilities, morbidity remains high. Postoperative morbidity can occur in more than 50 percent of patients following pancreaticoduodenectomy and in more than 30 percent of patients following distal pancreatectomy.[1, 2] The most common complications include postoperative pancreatic fistula (POPF), delayed gastric emptying (DGE), and post-pancreatectomy hemorrhage (PPH). Prompt diagnosis of these complications with early and effective rescue are imperative to performing major pancreatectomy with good outcomes.

Pancreatic Fistula

Definition and epidemiology

Pancreatic fistula results from leakage of pancreatic fluid rich in amylase from a pancreatic-enteric anastomosis or directly from traumatized pancreatic parenchyma and is the most common complication after major pancreatic resection resulting in significant morbidity. The incidence of POPF after major pancreatic resection ranges greatly in the literature from 10 to 30 percent depending on the historical definition used.[3]

In 2005, the International Study Group of Pancreatic Surgery (ISGPS) developed a standardized definition and grading system for POPF.[4] POPF was defined as fluid output of any volume from an operatively placed drain with amylase >3 times the upper limit of normal serum amylase on or after postoperative day 3 and was further graded as A, B, or C based on clinical severity.[4] This grading system was subsequently refined in 2016 to better classify clinically insignificant from clinically relevant POPF.[5] The previous category of grade A POPF, defined as an elevated drain amylase without an associated clinically relevant condition or change in management was reclassified as a "biochemical leak." Patients with biochemical leaks have been shown to have no difference in morbidity or mortality when compared to patients with normal drain amylase values.[6] Clinically relevant postoperative pancreatic fistulas are now classified as grade B versus grade C, with grade C fistulas resulting in organ failure, the need for reoperation, or death (**Table 1**).

Risk factors and prevention

Several risk factors for the development of POPF have been identified in the literature. Commonly reported risk factors include a soft pancreatic gland texture, small pancreatic duct size, increased intraoperative blood loss and operative time, and high patient body mass index.[7-9] POPF is also more common following distal pancreatectomy than pancreaticoduodenectomy. Given the high prevalence of POPF following major pancreatic resection, numerous

Table 1. Updated International Study Group (ISGPS) definition and grading of postoperative pancreatic fistula (POPF).

	Biochemical Leak	**Grade B POPF**	**Grade C POPF**
Amylase >3 times the upper limit of serum amylase	Yes	Yes	Yes
Drainage > 3 weeks	No	Yes	Yes
Clinically relevant change in management* **(Prolongation of hospital/ICU stay, use of therapy for fistula management- somatostatin analogs, total parenteral nutrition [TPN], blood product transfusion)**	No	Yes	Yes
Percutaneous or endoscopic interventions	No	Yes	Yes
Angiographic intervention for POPF-related bleeding	No	Yes	Yes
Infection related to POPF	No	Yes	Yes
Reoperation for POPF	No	No	Yes
POPF-related organ failure	No	No	Yes
POPF-related death	No	No	Yes

* Prolongation of hospital/ICU stay, use of therapy for fistula management-somatostatin analogs, TPN, blood product transfusion

Adapted from Bassi et al., 2017

studies have evaluated the efficacy of strategies to prevent the development of POPF including surgical technique, internal or external pancreatic drainage, and the use of somatostatin analogues prophylactically.

Surgical technique

Pancreaticojejunostomy (PJ) has been compared to pancreaticogastrostomy (PG) in numerous randomized trials to determine which anastomosis is superior in reducing the rate of POPF following pancreaticoduodenectomy. A Cochrane review on this topic identified 10 randomized controlled trials comparing PJ versus PG following pancreaticoduodenectomy. From these 10 trials which enrolled a total of 1629 patients, there was no high-quality evidence supporting the superiority of PJ or PG.[10]

When creating the PJ, two techniques that are commonly used include a duct-to-mucosa anastomosis and invagination of the pancreatic remnant into the jejunum. Berger et al. performed a randomized trial comparing duct-to-mucosa PJ to invagination and stratified patients based on pancreatic gland texture. This trial demonstrated a lower rate of POPF in the invagination cohort (12 percent) versus the duct-to-mucosa cohort (24 percent) as well as a significant reduction in clinically significant POPFs.[11] This technique can be considered in patients at high risk for POPF.

As the rate of POPF is highest following distal pancreatectomy, different techniques have also been evaluated to help reduce the risk of POPF in this setting. The DISPACT trial was a multicenter European randomized trial designed to evaluate the efficacy of stapled versus hand-sewn closure of the pancreatic stump after distal pancreatectomy. After randomization of 450 patients, there was no significant difference in POPF rate, serious adverse events, or mortality between the two groups.[12]

Internal and external pancreatic stents

Stenting of the PJ anastomosis has been evaluated as an additional technical modification to reduce the risk of POPF following pancreaticoduodenectomy. Internal stenting consists of placing an internal stent that traverses the PJ anastomosis. External stenting requires the stent to traverse the anastomosis and be externalized by being brought out through the jejunal or gastric wall.

In a randomized trial evaluating the efficacy of internal pancreatic duct stenting in reducing the development of POPF following pancreaticoduodenectomy, internal stenting did not decrease the frequency or severity of POPF.[13] External stenting has also been compared to no stenting in a randomized trial that included patients at high risk for POPF (patients with a soft pancreas and a pancreatic duct of <3 mm). The externally stented group had a significantly lower overall rate of POPF compared to the no-stent group (26 versus 42 percent). However, there was no statistically significant difference in rates of clinically significant POPF (Grade B/C).[14] Lastly, a multicenter randomized trial compared external and internal pancreatic duct stenting and found clinically significant (Grade B/C) POPF occurred in 24.4 percent of patients with an external stent and 18.9 percent of patients with an internal stent, concluding there was a trend toward a higher rate of clinically relevant POPF with external stenting.[15]

Somatostatin analogues

Somatostatin analogues are additional adjuncts that have received great attention for their possible role of reducing the risk of POPF based on their mechanism of inhibiting pancreatic exocrine and endocrine function. A Cochrane review was performed to analyze the evidence of prophylactic somatostatin, or one of its analogues, to no drug or placebo and the rate of POPF. From 21 trials involving 2348 patients, prophylactic somatostatin, or one of its analogues, resulted in a lower incidence of pancreatic fistula. However, analysis of only trials that distinguished clinically significant fistulas demonstrated there was no statistically significant difference between the groups.[16]

The strongest evidence for the efficacy of a somatostatin analogue in reducing the incidence of POPF comes from a single-center, randomized, double-blind trial which compared perioperative subcutaneous pasireotide versus placebo in patients undergoing pancreaticoduodenectomy or distal pancreatectomy. In this trial, patients received 900 ug of subcutaneous pasireotide or placebo twice daily beginning preoperatively on the morning of surgery and continuing for 7 days. The pasireotide group demonstrated significantly fewer clinically significant (Grade B/C) POPFs (7.9 versus 16.9 percent).[17]

Clinical presentation and management

The first manifestation of a POPF is often a change in drain character. To diagnose a pancreatic leak, amylase levels should be obtained from the drain fluid once a patient is tolerating a diet or upon a change in drain character. Routine monitoring of drain amylase levels can promote early detection of a pancreatic leak. Drain management following pancreatectomy remains an active subject of debate. While some have proposed either early drain removal in the first several days postoperatively or foregoing prophylactic drains altogether, we continue to favor the routine placement and monitoring of drains given the high incidence of POPF following major pancreatectomy.

The primary strategy for managing POPF is wide local drainage and we advocate for the placement of intraoperative drains in all major pancreatic resections. Patients with a pancreatic leak who have no other clinical symptoms can be observed and operatively placed drains should remain until the leak resolves. We recommend continued oral enteral nutrition in patients with POPF. Enteral nutrition has been shown to result in faster fistula closure and overall higher rates of fistula closure when compared to total parenteral

nutrition in a randomized trial of patients with Grade B POPF.[18] Additionally, oral feeding does not negatively impact POPF healing or severity when compared to post-pancreatic enteral nutrition, and is associated with shorter hospital length of stay.[19]

Intraoperatively placed drains may be sufficient for the management of POPF but retained intra-abdominal fluid collections in patients with clinically significant POPF may require additional percutaneous drainage procedures. We recommend computed tomography (CT) imaging to evaluate for retained collections in patients with systemic signs of infection, high output leaks, or other evidence of clinical deterioration. Antibiotics are only used for POPF when patients also demonstrate signs of infections such as fevers and leukocytosis. Treatment duration can vary but typically antibiotics will be continued for at least four to seven days after adequate drainage and improvement in clinical symptoms. When a POPF is high output and also bilious due to biliary reflux and leakage from the PJ, percutaneous transhepatic biliary drainage can be employed to reduce fistula output.

Return to the operating room due to POPF is rare but may be necessary when abdominal collections are not accessible by percutaneous drainage and a patient is clinically deteriorating. When reoperating in this setting, the goal should be wide local drainage of the involved area. In extreme situations, total pancreatectomy has been reported as this prevents further leakage of pancreatic fluid but is associated with high mortality and the long-term sequela of brittle diabetes.[20]

Delayed Gastric Emptying

Definition and epidemiology

Delayed gastric emptying (DGE) after pancreatic surgery, while usually not life-threatening, can lead to significant patient discomfort, additional interventions, prolonged hospital stay, increased readmissions, and increased hospital costs.[21-24]

The pathophysiology behind DGE remains unresolved. Most of the research on this topic has been focused on DGE following pancreaticoduodenectomy and often classifies DGE as either primary or secondary in nature. The traditional explanations for primary DGE are a loss of motilin as a consequence of duodenal resection or operative devascularization and/or disruption of neural connections between the stomach and intestine from vagal denervation.[25] Secondary DGE is attributed to increased intraperitoneal inflammation from another postoperative complication, and has been associated with POPF, intra-abdominal abscesses, and postoperative sepsis.[24,26-29]

The reported incidence of DGE following pancreaticoduodenectomy ranges widely, from less than 5 to more than 50 percent, in large part due to heterogeneity in the definition of DGE.[21-23,26] This has made it difficult to properly study the causes, risk factors, and management of this complication. In 2007, the ISPGS released a consensus definition to address this issue. The ISPGS defines DGE as an inability to return to a standard diet by the end of the first postoperative week and a need for a nasogastric tube (NGT) after postoperative day 3, and established criteria for mild, moderate, and severe DGE (grades A, B, and C).[25] Grade A DGE is present if the patient requires NGT on postoperative days 4-7, needs NGT reinsertion after postoperative day (POD) 3, or is unable to tolerate a solid diet by day 7 but resumes a solid diet by day 14. In grade B DGE, NGT is required on POD 8-14, NGT reinsertion was needed after POD 7, or a solid diet is not tolerated by day 14 but is resumed by day 21. Grade C DGE is present when NGT cannot be discontinued or has to be reinserted after POD 14, or if normal solid oral intake is not resumed by day 21 (**Table 2**).[25]

Using this classification, one recent review reported that the average incidence of DGE after PD is 27.7 percent, and among studies that specify overall incidence as well as individual grades of DGE, the overall incidence is 31.9 percent, with grade A in 18.5 percent, grade B in 7.3 percent, and grade C in 6.2 percent of patients.[30]

Table 2. International Study Group (ISGPS) definition and grading delayed gastric emptying after pancreatic surgery

DGE grade	NGT requirement	Inability to tolerate solid oral intake by POD	Vomiting or gastric distension	Use of prokinetics
A	4-7 days or reinsertion >POD 3	7	Yes/No	Yes/No
B	8-14 days or reinsertion >POD 7	14	Yes	Yes
C	>14 days or reinsertion after POD 14	21	Yes	Yes

DGE: Delayed gastric emptying; POD: postoperative day; NGT: nasogastric tube.

To exclude mechanical causes of abnormal gastric emptying, the patency of either the gastrojejunostomy or duodenojejunostomy should be confirmed with endoscopy or upper- gastrointestinal Gastrografin series.

Adapted from Wente et al., 2007

Risk factors and prevention

The biggest risk factors for the development of DGE after pancreatic surgery include pancreatic fistula, postoperative sepsis, and repeat operation.[29] Other risk factors associated with DGE include diabetes mellitus, extent of surgical dissection, and degree of pancreatic parenchymal fibrosis.[23,24,31] Multiple surgical modifications have been attempted in an effort to reduce the incidence of DGE.

Pylorus and DGE

Early reports suggested that pylorus-preserving pancreaticoduodenectomy (PPPD) might have an increased risk of DGE when compared to standard pancreaticoduodenectomy, and numerous studies have since attempted to address this issue. While several retrospective studies and two small randomized controlled trials (RCTs) found an increased risk of DGE with PPPD, the majority of studies including a Cochrane systematic review have found no difference.[28,32-41]

Since pylorospasm was proposed as the reason for increased rates of DGE after PPPD, modifications targeting the pylorus have been introduced such as pyloric dilation and pyloric ring resection.[30,42] Pyloric dilation has been found in several retrospective studies, as well as one RCT, to significantly reduce the incidence of DGE compared with PPPD alone.[43-46] Pyloric ring resection offers an alternative way to address the issue of pylorospasm while maintaining the reservoir function of the stomach. Whereas the first part of the duodenum is divided in PPPD, preserving the entire stomach and pylorus, in pylorus-resecting pancreatoduodenectomy (PRPD), also known as subtotal stomach-preserving pancreatoduodenectomy (SSPPD), the division is made 2 to 3 cm proximal to the pylorus. Three meta-analyses found that PRPD or SSPPD had a lower incidence of DGE compared with PPPD.[47-49] While PRPD has not been evaluated against classic PD, it has been theorized that by preserving the motor innervation to the body of the stomach while eliminating the pylorus, pyloric-ring resection may accelerate gastric emptying.[30]

Antecolic versus retrocolic gastrojejunal anastomosis

An antecolic GJ anastomosis has been proposed to be superior to a retrocolic route due primarily to the theoretical advantage of having the colon positioned between the pancreato-enteric and GJ anastomoses. This may mitigate the effect of minor pancreatic leaks on gastric emptying. It may also lessen the chance of kinking the GJ anastomosis and may decrease venous congestion stemming from compression of the mesocolon on the jejunal loop. While several retrospective studies and two RCTs have found lower incidence of DGE with antecolic versus retrocolic gastrojejunal anastomosis, the majority of RCTs to date have not found any significant difference between the two routes.[21,37,50-58]

Reconstruction: Billroth I versus Billroth II versus Roux-en-Y

While Billroth I reconstruction offers the most physiological end arrangement, it places the GJ anastomosis in close proximity to the pancreatoenteric and biliary anastomoses, which may increase the risk of DGE secondary to leaks. Alternatively, Billroth II and Roux-en-Y mitigate this risk by placing the GJ anastomosis further away from the pancreatic and biliary anastomoses. Additionally, in the event of a PJ leak, food enters the intestines distally in a Billroth II or Roux-en-Y configuration. The available literature has shown Billroth II reconstruction to be superior to Billroth I in two retrospective studies and to be superior to Roux-en-Y in one RCT.[59-62]

Braun enteroenterostomy

Bile reflux has been implicated in the development of DGE. Braun enteroenterostomy involves an additional jejunojejunal anastomosis between the afferent and efferent loop of the gastrojejunostomy thereby diverting alkaline bile away from the GJ, which may prevent bile reflux-induced DGE. While data from RCTs are lacking, the vast majority of retrospective studies on this topic as well as a meta-analysis of these studies have found that Braun enteroenterostomy is associated with significantly lower rates of clinically relevant DGE.[36,63-68] Additionally, a Braun allows two routes of egress from the stomach and may also theoretically lower the pressure in the afferent limb decreasing leakage from either the PJ or HJ.

Other modifications

Other modifications have been attempted to decrease the rate of DGE after pancreatic surgery. These include double Roux-en-Y reconstruction, stapled gastrojejunostomy, omental flaps, preservation of the left gastric vein (to prevent venous congestion), and preservation of the right gastric artery and innervation along the lesser curvature of the stomach to prevent ischemia of the pyloroduodenal complex.[41,69-74] While shown to have favorable results in isolated retrospective studies, more evidence is needed to support routine use.

Clinical evaluation and management

Initial signs and symptoms of DGE include oral intolerance, nausea, and vomiting. At the authors' institution, initial diagnosis is empirically based on oral intolerance and a large gastric bubble on abdominal X ray. In cases where symptoms persist beyond 1 week, an upper-gastrointestinal series radiographic contrast study is considered. A positive test will demonstrate the stomach emptying at a slower rate than normal in the absence of a mechanical obstruction.[42] An abdominal CT scan is also utilized to evaluate for the presence of concomitant complications, such as POPF or fluid collection, which may be contributing to a functional gastroparesis. Esophagogastroduodenoscopy can be used to evaluate the intestinal anastomosis (in the case of PD) and

ulcers, as well as facilitate the placement of a feeding tube if needed. Dilation of the anastomosis can also be performed under endoscopic guidance.

In the absence of a clear understanding of the pathophysiology of DGE, treatment is mainly symptomatic and consists of nasogastric decompression, prokinetic agents, and supplemental nutrition. Erythromycin at lower dosages has been proposed to augment gastric motility by binding to motilin receptors and triggering phase III of the gastric migratory motor complex. Studies in patients who underwent pancreaticoduodenectomy have shown a 37 to 75 percent decrease in DGE and increased gastric motility when erythromycin was administered prophylactically.[75,76] Metoclopramide, a dopamine D2 receptor antagonist that stimulates the secretion of acetylcholine, is another popular prokinetic agent often used in this setting, however thus far evidence for its efficacy is limited. The prophylactic use of octreotide, a somatostatin analog, was found in a placebo-controlled RCT to have no beneficial effect on DGE.[77]

Whereas the benefits of enteral nutrition (EN) over total parenteral nutrition (TPN) after major abdominal surgery are well defined, the impact of EN in the treatment of DGE remains less clear. Some studies have shown an advantage with EN compared with TPN while others have not found a significant advantage.[78-82] Perhaps more important than the route of supplemental nutrition is the timing of administration, as early recognition of DGE and initiation of supplemental nutrition before POD 10 has been associated with faster resumption of regular diet, less weight loss, and fewer readmissions than those who had delayed intervention.[26]

In the case of DGE secondary to a complication such as POPF, intra-abdominal infection, or sepsis, the underlying complication must also be addressed. Indeed, given the strong association between DGE and other complications, especially POPF, some surgeons stress that prevention of POPF and other complications may be the key to mitigating DGE.[83,84]

Post Pancreatectomy Hemorrhage

Definition and epidemiology

Post-pancreatectomy hemorrhage (PPH) is one of the most severe complications following pancreatic resection and has an incidence of 4 to 16 percent following pancreaticoduodenectomy and 2 to 3 percent following distal pancreatectomy.[9] The ISGPS has defined post-pancreatectomy hemorrhage based on the timing of onset, location, and severity.[85] The timing of onset is classified as early if it occurs less than or equal to 24 hours after the end of the index operation or late if it occurs after 24 hours. Location is classified as intraluminal or extraluminal. Severity is classified as mild if blood loss is of small or medium volume (drop in hemoglobin of < 3g/dL) and requires only noninvasive treatment (such as a transfusion of less than or equal to 3 units of packed red blood cells) versus severe if there is a large volume of blood loss (drop in hemoglobin ≥ 3 g/dL), if there is a clinically significant deterioration in the patient's condition (tachycardia, hypotension), or if there is need for invasive treatment. Based on the above criteria, PPH is graded as A, B, or C (**Table 3**). Patients with Grade A PPH are clinically well appearing and exhibit early, mild bleeding. Grade B PPH can manifest as an early and severe bleed or as a late and mild bleed. Lastly Grade C PPH is late and severe.

Table 3. International Study Group (ISGPS) grading of post-pancreatectomy hemorrhage (PPH).

Grade	Timing	Location	Severity
A	Early	Intra- or extraluminal	Mild
B	Early	Intra- or extraluminal	Severe
	Late	Intra- or extraluminal	Mild
C	Late	Intra- or extraluminal	Severe

Adapted from Wente et al., 2007

Possible sources of PPH following pancreaticoduodenectomy include the stump of the gastroduodenal artery, tributaries of the superior mesenteric vein and portal vein, branches of the hepatic artery and superior mesenteric artery, suture lines, and the gallbladder fossa. Sources of PPH following distal pancreatectomy include the pancreatic stump, branches of the splenic artery, the splenic vein stump, and the splenic hilum if the spleen is preserved.[85]

Risk factors and prevention

Early PPH is usually the result of a technical failure, inadequate intraoperative hemostasis, or an underlying coagulopathy. In contrast, late PPH is often secondary to erosion of a peripancreatic vessel or ulceration at the gastroenteric anastomosis (marginal ulcer). Pathophysiological explanations for late PPH include enzymatic digestion of blood vessels by pancreatic exocrine enzymes in the setting of a pancreatic leak, erosions of vessels adjacent to an intra-abdominal infection, and vascular injury during the index operation leading to the late development of pseudoaneurysms.[85]

Commonly reported risk factors for the development of PPH include Grade B/C POPF, biliary leakage, and intra-abdominal abscesses.[86,87] More than 50 percent of patients who develop PPH have a concurrent diagnosis of a POPF.[87] Given these risk factors, prevention and prompt management of the forementioned complications are essential for mitigating the increased risk of PPH.

The placement of tissue flaps over the stump of the gastroduodenal artery or skeletonized vessels may protect against the exposure of the vessel wall to pancreatic fluid or infection and reduce the risk of erosion of the vessels in the setting of a POPF or infection. While this has not been proven in a systematic fashion, we routinely employ this technique with omental or round ligament flaps.

Clinical evaluation and management

Early PPH typically manifests as a drop in hemoglobin in the immediate postoperative period (<24 hours from the index operation) in conjunction with increased sanguineous output from an intra-abdominal drain or nasogastric tube. Early PPH can usually be managed conservatively with observation, serial complete blood counts, correction of underlying coagulopathy, and transfusions. In the setting of severe intraluminal bleeding, endoscopic evaluation can be employed to diagnosis the source of bleeding and obtain hemostasis. In the setting of severe extraluminal bleeding or a patient that is hemodynamically unstable, return to the operating room is necessary to obtain adequate hemostasis.

Late PPH can occur at a median of 12 to 27 days postoperatively. Additionally, the most frequent site of late PPH is extraluminal into the abdominal cavity in about 60 percent of cases and intraluminal in approximately 40 percent of cases. Less than 10 percent of cases present with both extraluminal and intraluminal bleeding.[87] Postoperatively, prompt attention should be given to a patient with sanguineous drain output, hematemesis, melena, or an unexplained drop in hemoglobin. There are institutional differences in how these patients are worked up, but interventional angiography should be considered up front. In a hemodynamically stable patient, the interventional radiologists will often ask for a CT angiography as they are coming in and setting up and this can sometimes be useful to demonstrate a pseudoaneurysm or even extravasation. For a suspected intraluminal source of bleeding in the setting of hematemesis or melena, endoscopy is often used in a hemodynamically stable patient as it may localize the source of bleeding and allow for endoscopic hemostasis. However, CT angiography may be more sensitive than endoscopy in detecting an acute gastrointestinal bleed.[88] The clinician must remain suspicious of a potentially life-threatening concurrent extraluminal source of bleeding even when endoscopy identifies an intraluminal source.

CT angiography has a low sensitivity in identifying the source of hemorrhage in patients with Grade B or C PPH, with a reported sensitivity of 26 percent in one retrospective series.[89] However, sensitivity may be improved if the CT angiography is obtained urgently while bleeding may still be ongoing. Alternatively, angiography can localize the source of bleeding in up to 90 percent of patients and arterial bleeding can be successfully treated with coil embolization or covered stenting in more than 80 percent of cases.[87] The most frequent source of arterial bleeding after pancreaticoduodenectomy is the gastroduodenal artery (~50 percent of all arterial hemorrhages), followed by the common hepatic artery (21 percent) and proper hepatic artery (11 percent).[87] Radiological approaches for managing delayed PPH include coil embolization in the setting of a gastroduodenal artery stump bleed and implantation of a covered stent in the setting of bleeding from the hepatic artery, superior mesenteric artery, or gastroduodenal artery when there is insufficient room to place coils.

Traditionally, patients who are hemodynamically unstable and unresponsive to immediate resuscitation require emergent operative exploration or a hybrid approach with the option for immediate conversion to open surgery if endovascular techniques fail. The mortality of PPH requiring relaparotomy approaches 50 percent due to the challenging nature of obtaining adequate hemostasis in the reoperative field.[87]

Summary

Major pancreatectomy is associated with major morbidity including POPF, DGE, and PPH. However, prompt recognition and precise multidisciplinary management of these complications can still result in good outcomes and early rescue of these patients. Universal reporting of these complications based on the ISGPS definitions will continue to help improve our understanding of the risk factors for these complications, strategies to mitigate their incidence, and best practices in management.

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CHAPTER 14

Management of Acute Complications in Liver Transplantation

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Abstract

Liver transplantation is the only cure for end-stage liver disease, acute liver failure, unresectable malignancies, and a wide variety of metabolic disorders. While perioperative morbidity and mortality have significantly decreased in the half-century since the first successful liver transplant performed by Thomas E. Starzl in 1967,[1] there remains significant potential postoperative complications of the procedure. The donor allograft quality, recipient comorbidities, and medication side effects may derive liver transplant complications, besides surgical, technical, and infectious concerns related to the liver disease progression and immunosuppression requirements, respectively.

Any subtle change in patient status or laboratory values should prompt early and persistent investigation, as even the subtlest of signs may signal catastrophic events. Management varies from surgical, retransplant or reoperation; to ancillary team involvement in interventional radiology and gastroenterology, to medical management. The goal of this chapter is to explore—both the common and rare—potential complications acutely following liver transplant, and guide timely intervention.

Abbreviations

AA = arterial anastomosis
ACS = abdominal compartment syndrome
AMS = altered mental status
AR = arterial reconstruction
AOHC = aortohepatic conduit
BPM = beats per minute
CNI = calcineurin inhibitor
CT = computed tomography
CTA = computed tomography with angiography
DBD = donation after brain death
DCD = donation after circulatory death
EAD = early allograft dysfunction
ECD = extended criteria donor
ECMO = extracorporeal membrane oxygenation
ESLD = end-stage liver disease
FFP = fresh frozen plasma
HAPA = hepatic artery pseudoanseurysm
HAT = hepatic artery thrombus
ICU = intensive care unit
INR = internal normalized ratio
LFT = liver function test
MRA = magnetic resonance with angiography
MRI = magnetic resonance imaging
MELD = Model for End-Stage Liver Disease
NAF = normal allograft function
OLT = orthotopic liver transplant
OR = operating room
PNF = primary nonfunction
PRES = posterior reversible encephalopathy syndrome
PTA = percutaneous transluminal angioplasty
TEE = transesophageal echocardiography
TPA = tissue plasminogen activator
TRALI = transfusion-related acute lung injury
VA = veno-arterial
VV = veno-venous

Allograft Dysfunction

Initial poor function of the liver allograft manifested by continued hemodynamic instability or laboratory abnormalities has wide-ranging potential causes, from emergent complications that may require reoperation or retransplant to common challenges that may simply require time and support.

Primary nonfunction

Ischemia and reperfusion injury of the liver allograft is an increasing area of concern and research specifically as extended criteria donor (ECD) organs are utilized to lessen the organ shortage. ECD livers may be categorized as such secondary to increased donor age, presence of hepatic steatosis (macrosteatosis in particular), donation after circulatory death status, and hepatitis B, C, or other infectious donor exposures, in addition to other events associated with donor deaths affecting their liver function. While ECD options expand the donor pool, they are not the standard or ideal allograft option and associated with significant potential complications.

Marginal graft function early in the postoperative period, or early allograft dysfunction (EAD), is variable in the extremes of its presentation but well recognized in the transplant community. EAD will demonstrate one of the three following laboratory findings: elevated bilirubin or internal normalized ratio (INR) on postoperative day (POD) 7 (total bilirubin >10 or INR >1.6), elevated liver enzymes, aspartate transaminase (AST), or alanine aminotransferase (ALT) >2000 once by POD 7.[2] EAD is associated with increased graft loss and increased patient mortality. In the Olthoff et al. study, EAD was associated with 18.8 percent patient mortality and 26.1 percent graft loss at 6 months posttransplant compared to 1.8 percent mortality and 3.5 percent graft loss in the non-EAD comparison group. Primary nonfunction (PNF), is the most severe form of EAD where the graft never functions. It is irreversible and not attributable to vascular or immunological factors and is reported in 2 to 5 percent of liver transplants.[2,3,4]

PNF requires emergent recognition for relisting and retransplant. The Organ Procurement and Transplantation Network (OPTN) designates liver relisting as status 1A for PNF patients who meet specific criteria (**Table 1**) as described in the OPTN policies.[6] These patients have hemodynamic instability, hypothermia and other typical manifestations of acute liver failure, hypoglycemia, coagulopathy, and acidosis. Reversible causes of graft failure must be excluded using imaging studies to demonstrate patent inflow and outflow of the vasculature and tissue diagnosis (either surgical or transjugular biopsy given coagulopathy risk) to exclude hyperacute rejection. In the absence of these factors PNF is assumed and lethal if retransplant is not performed.[5]

These patients often return to the operating room (OR) early after transplant to exclude technical or mechanical causes for graft dysfunction, hepatic artery thrombus (HAT) or portal vein thrombus (PVT), or to evacuate hematoma/bloody ascites and obtain biopsy. Grossly the liver appears enlarged, a light shade of pink and firm. While awaiting retransplant, resuscitation is attempted to control coagulopathy, but as a hallmark of PNF, these patients are resistant and remain coagulopathic. As the allograft necroses, metabolic disarray worsens and necessitates explant and creation of a portocaval shunt, rendering the patient anhepatic. Anhepatic patients are also registered as status 1A for emergent retransplant.[6]

Rejection

Accelerated or hyperacute rejection of the transplanted liver is a rare event, particularly without ABO mismatch. It occurs minutes to hours after reperfusion and results from the recipient having preformed anti-HLA and/or anti-ABO

Table 1. OPTN liver re-listing criteria for status 1a

Classification	Type of liver transplant	Time from primary transplant	AST*	Requires one of the following lab values*
Primary Non-Function (PNF)	Whole liver	7 days	3000	• INR greater than or equal to 2.5 • Arterial pH less than or equal to 7.30 • Venous pH less than or equal to 7.25 • Lactate greater than or equal to 4 mmol/L
Primary Non-Function (PNF)	Liver segment, deceased or living donor	7 days	No requirement	
Hepatic Artery Thrombosis (HAT)	Any	7 days	3000	

*All laboratory results reported for the tests required above must be from the same blood draw taken 24 hours to 7 days after the transplant.

antibodies against the donor.[7] The transplanted liver is not functional, and the recipient will reflect that as described in PNF patients. Tissue diagnosis is the gold standard to make the diagnosis, by open or transjugular biopsy given the coagulopathy of the recipient. The gross appearance is characteristic and often seen intraoperatively given the rapid onset. In contrast to PNF, the liver with hyperacute rejection appears mottled, cyanotic, and exceptionally soft with a loss of turgor or structure.

A biopsy demonstrates edema, enlarged and damaged endothelial cells, dilated capillaries, hemorrhage, and necrosis. Additionally, antibody and complement depositions in arterioles are demonstrated on special staining of the biopsy tissue.[8] Imaging, again, is important to distinguish from other reversible causes but also to find any thrombosed vessels as hyperacute rejection is associated with increased risk of portal vein thrombosis.

Attempt at medical management of hyperacute rejection is similar to other severe antibody mediated rejection (AMR) events. The recipient requires emergent plasmapheresis to remove the preformed antibodies and additional treatment may include pulse steroids, intravenous immunoglobulin (IVIg) to add helpful antibodies (lowering the level of HLA antibodies blocks their ability to attack the allograft), and infusion of monoclonal CD20-directed antibody (rituximab) to remove peripheral circulating B cells.[9]

Acute rejection is typically T-cell mediated (acute cellular rejection) and rarely occurs before POD 4; most cases occur prior to 90 days posttransplant. Management includes reaching a therapeutic range of tacrolimus (typically 6-8 ng/mL for liver transplant; at our center we aim closer to 8 ng/mL if evidence or concern for rejection) and a short course of pulse steroids.

Compartment syndrome

Abdominal compartment syndrome (ACS) is a well-described critical illness defined as intra-abdominal hypertension greater than 20 mg Hg combined with new organ failure or dysfunction. While the abdominal cavity can extend particularly the compliance of the anterior abdominal wall is ultimately limited. In the more common causes of ACS, intraperitoneal or retroperitoneal bleeding in trauma, aggressive resuscitation in sepsis or pancreatitis, and so forth. Physical exam in ACS is reliably taught as the abdominal compliance is exceeded.

The liver can develop its own hepatic compartment syndrome distinct from ACS. While not widely reported in the literature outside of case reports primarily related to trauma, hepatic compartment syndrome is well recognized in the transplant community.[10] The liver housed in the right upper quadrant surrounded by the rib cage has less compliance than the rest of the abdomen, especially in the anterior-posterior axis. Events that affect the liver space and do not necessarily affect the rest of the abdomen such as hematoma accumulation, intrinsic hepatic edema from ischemia-reperfusion injury, and hepatic outflow obstruction/congestion from heart failure all can put pressure on the liver and cause hepatic dysfunction without affecting the rest of the abdomen. The abdominal exam may not be characteristically taught as the high intra-abdominal pressure is confined to the space behind the rib cage. The physical exam is less reliable than in ACS and a soft abdomen does not rule out hepatic compartment syndrome.

Allograft dysfunction coupled with rising trends in central venous pressure (CVP), lactic acid levels, hemodynamic instability, and rising liver function test (LFT) patterns are concerning for hepatic ischemia from hepatic compartment syndrome. Initial management is the same as in traditional ACS; the fixed space must be opened to allow for improved perfusion of the organ. If the source is surgical and can be managed operatively, hematoma evacuation and control of surgical bleeding, then the abdomen may be closed. If the compartment syndrome is secondary to intrinsic edema of the allograft, in the case of ischemia-reperfusion, pulmonary hypertension or heart failure, the abdomen should remain open with a temporary closure device (ABThera or Gortex interposition) and delayed closure once the liver has decompressed. Final closure will likely require mesh as the abdominal wall retracts over time; in those cases, biologic mesh closure is recommended.

An unusual source of congestive hepatopathy in the posttransplant patient is that of venous outflow obstruction. Rarely a small allograft, or a liver segment, placed in a large space, may rotate across the cranio-caudal axis resulting in outflow obstruction. When returning to the OR the liver is untwisted and the graft's falciform is sutured to the overlying diaphragm or the remnant of the recipient's falciform. This is also a good preventive measure at the time of transplant when size discrepancy is noted. Outflow obstruction may also occur from hepatic vein or caval thrombus, which is later addressed.

Vascular Complications – Arterial

Hepatic artery

The liver has a dual vascular supply from the hepatic artery and the portal vein. The hepatic artery supplies approximately half of the oxygenated blood supply to the liver but only 25 percent of the total blood flow, with the remaining supplied by the partially deoxygenated portal vein. Complications involving the arterial supply to the liver is associated with significant morbidity and mortality[11] and most identified events arise early. Importantly, the biliary system depends largely on the arterial system for oxygenated

blood, as opposed to the hepatic parenchyma which derives its supply from both sources, making arterial complications particularly devastating to the biliary tract.

The identification of vascular complications is often detected by ultrasonography, whether routine or for concerning patient symptoms or laboratory values. One of the more common arterial complications is hepatic artery stenosis (HAS). Understanding ultrasound patterns following liver transplant can help differentiate normal changes from true complications. Arterial stenosis is suggested on ultrasound when parvus tardus waveforms are seen. Parvus tardus refers to a slow systolic upstroke with a small, rounded amplitude. The resistive index (RI) is often low (<0.5) secondary to the small difference between the systolic and diastolic pressures. In contrast early after transplant a resistive index (RI) may be transiently high (RI >0.8) particularly in older donor allografts or those with a prolonged cold ischemia time. The RI typically falls within the normal range of 0.55-0.8 in a couple of days. The waveform in a normal posttransplant artery has a sharp upstroke and peak amplitude. A normal arterial anastomosis often has swelling immediately postop and a waveform with features reminiscent of parvus tardus; it is important to evaluate the clinical picture and assess the perfusion of the graft with laboratory trends and stability of the patient. The ultrasound can be repeated and trended if the clinical picture is reassuring.

HAS with parvus tardus waveforms and low RI immediately after transplant necessitates a return to the OR for revision. Often the diagnosis is less obvious on ultrasound and requires computed tomography with angiography (CTA) for confirmation. Once out of the immediate postoperative period endovascular therapy is a less invasive and useful tool in improving flow in experienced hands. At our center we use endovascular balloon angioplasty and stenting as early as POD 3 in patients with clinically significant HAS.

HAS puts the allograft at risk for hepatic artery thrombosis (HAT). HAT is the most-feared vascular complication and most common complication necessitating retransplant. It is particularly concerning in the early period (this period is not clearly defined, but generally referred to as 1 to 4 weeks posttransplant). Recipients with early HAT may be relisted for transplant in two scenarios. United Network for Organ Sharing (UNOS) policy guidelines allow for a patient with HAT diagnosed within 14 days of transplant but does not meet criteria for status 1A to be given an exception model for end-stage liver disease (MELD) score of 40 (**Table**).[6]

In addition to ischemia and necrosis necessitating early retransplant, HAT at any point may result in significant ischemic cholangiopathy, a vicious cycle of biliary strictures, bilomas with superimposed infection, infectious cholangitis eventually requiring retransplant as endoscopic stenting, percutaneous drains, and other measures very rarely control the process. Secondary biliary cirrhosis is another sequela of this complication.

Lack of arterial flow identified early on requires emergent return to the operating room, particularly if identified on the immediate postoperative ultrasound. Etiologies of hepatic artery thrombus may be dissection, stenosis, angulation or redundancy, small caliber, use of conduit, or vascular reconstruction.[11] Upon return to the operating room the artery is evaluated intraoperatively and thrombectomy is attempted either via balloon catheter or surgical. If adequate flow is achieved and the artery is intact (no evidence of dissection), the anastomosis is revised. Any poor positioning or angulation may be addressed at this time.

If flow is not adequately restored or if there is dissection in the artery an interposition graft may be needed to provide inflow as direct anastomosis of the donor artery to alternative recipient inflow is likely limited by donor artery length. Ideally the donor iliac artery is used for a conduit; if unavailable, stored iliac artery from prior donors may be used and lastly synthetic graft, polytetrafluoroethylene (PTFE). Long-term success is related to the conduit choice.[19] Source of inflow depends on recipient anatomy. The supraceliac aorta has a lower occurrence of HAT presumed secondary to shorter length[17] but may be technically challenging with significant collateral vessels and varices overlying the aorta. Infrarenal aorta and right iliac artery are more commonly used but given the length of conduit required, there is an increased risk of HAT. Following the restoration of flow, serial planned ultrasound imaging should be obtained to detect any subsequent issues. There is likely no effect on posttransplant renal function whether using a suprarenal or an infrarenal site of inflow when performing aorto-hepatic arterial reconstruction and it should not impact site choice.[18] Following reconstruction and stabilization postoperative antiplatelet therapy with aspirin is recommended; however, strong literature on the benefits of anticoagulation and type of therapy, vitamin K antagonists versus antiplatelet therapy, and so forth is found to be lacking.

Depending on patient stability and the time that has passed since the transplant, additional contrast CT imaging may help with operative planning or the use of interventional radiology-guided procedures to restore flow. However acute events (within the first week after transplant) generally result in a return to the operating room.

Dissection without occlusion or an intimal flap is more difficult to detect on ultrasound imaging unless it is significantly affecting flow; it is better seen on computed tomography angiography (CTA). The decision to intervene

is based on the degree of the allograft dysfunction. If the dissection is flow limiting some intervention must be considered, whether that be operative, endovascular, or anticoagulation. An endovascular approach may further propagate the dissection and should be approached after careful consultation with interventional radiology. An operative approach would be as described for arterial occlusion with new inflow and would likely require a conduit.

If, however, the dissection does not appear flow limiting and occurs only in the recipient vasculature, this may represent a chronic issue to be monitored. If the allograft does not appear to be affected by dissection, it may be addressed conservatively with anticoagulation and anti-impulse control, as would be done in the setting of an aortic dissection, pain control, and the maintenance of both a heart rate between 60-90 beats per minutes (BPM) and a systolic blood pressure (SBP) between 90-120.

Celiac artery

Thrombosis or dissection of the celiac artery is detected and treated in a similar fashion to that of the hepatic artery. In the early period, operative intervention is warranted. If unable to perform a satisfactory thrombectomy or if dissection is present, a conduit, as described above, will be necessary.

Median arcuate ligament syndrome (MALS) is compression of the celiac artery by the median arcuate ligament. If this is present in the recipient, it may result in poor perfusion of the allograft or even thrombosis of the celiac or hepatic artery. Often this can be seen preoperatively on cross-sectional imaging, particularly in the sagittal cuts. Intraoperative evaluation of the hepatic artery with Doppler during ventilation will demonstrate the presence of any celiac compression effecting arterial flow. The signal in the hepatic artery will be stronger during inhalation than exhalation; this should also be evident on palpation of the pulse in the vessel since the pulse is stronger during inhalation. When identified pre- or intraoperatively the median arcuate ligament release should be performed during the transplant procedure.

If MALS anatomy is not noted and intervened upon at the time of transplant postoperative ultrasound will show respiratory variation in the signal quality in the hepatic artery and there will often be laboratory abnormalities including rising liver function test (LFT) levels and acidosis. If ultrasound imaging is not confirmatory, cross-sectional imaging with intravenous (IV) contrast should demonstrate compression of the celiac access; sagittal images are the most helpful. If suspected or confirmed the recipient should return to the OR for a median arcuate release. If this does not restore adequate flow, celiac reimplantation may be performed if the vessel is intact (no evidence of dissection). Alternatively, if damage to the celiac is suspected, a conduit may be used as described above.

Pseudoaneurysm and rupture

Hepatic artery pseudoaneurysm, (HAPA) reported to occur 0.3 to 2.6 percent in liver transplants, is a potentially fatal complication.[16] Pseudoaneurysms may be detected on routine imaging, usually Doppler ultrasound, but more effectively with contrast-enhanced CT, with angiography. HAPA takes time to develop and is uncommon in the early posttransplant period but like all vascular pseudoaneurysms, it is strongly associated with intra-abdominal infection; measures should be taken to prevent its development in early posttransplant. In the setting of a known intra-abdominal infection or biloma/bile leak early after liver transplant, operative washout is warranted particularly in the setting of operative repair of the source of infection. If interventional radiology or endoscopic treatments are used instead, collections or bilomas should be drained percutaneously to prevent intra-abdominal infection and HAPA development.

Vascular Complications – Vous

Portal vein

Knowledge of preoperative portal vein thrombus (PVT), particularly the extent of PVT, is helpful in operative planning and in donor selection. The ideal donor for a recipient with known PVT would allow for a long donor portal vein (important should pancreas recovery be considered) and open iliac vessels for use as conduit. It is also helpful knowledge for anesthesia colleagues when planning for potential increased blood loss.

Risk factors for postoperative PVT include preoperative PVT, pediatric transplant, prior splenectomy, size discrepancies in donor and recipient portal vein, technical issues (redundancy in portal vessel length, stenosis in anastomosis, or kinking), prior venous shunt procedures, and use of portal vein conduit during the transplant.[11]

Diagnosis of early postoperative PVT is often found on routine Doppler ultrasonography from lack of flow. Partial occlusion on the portal or tributary may be managed with therapeutic anticoagulation based on patient stability and allograft function. However, total occlusion should be intervened upon. During the transplant procedure, eversion thrombectomy is performed for preoperative PVT, especially for chronic thrombus and/or one that extends toward the confluence of the splenic and superior mesenteric veins. Limited extent, acute, or recently developed PVT may be managed with a Fogarty catheter thrombectomy. If unable to restore flow through the native recipient portal vein, alternative inflow from the left renal vein or a left splenorenal shunt via conduit is used. The conduit is ideally a donor iliac vessel. Operative management of postoperative PVT (**Figure 1**) is operative with take down of the portal vein anastomosis partially or completely, and direct or Fogarty catheter-assisted thrombectomy. Attention should be paid to the hepatic artery

and biliary anastomoses to avoid their disruption during the thrombectomy. Narrowing of the anastomosis is a risk factor for the thrombosis as are large porto-systemic collaterals that shunt the portal flow away from the portal vein. These large collaterals are usually identified on pretransplant imaging and cause decreased portal flow during the transplant procedure. Both portal vein narrowing and large porto-systemic collaterals should be addressed at the time of return to the operating room for thrombectomy, and preferably at the time of the initial transplant procedure to prevent this complication. Postoperative PVT should not be managed with shunting as the newly transplanted liver is heavily dependent on portal inflow for perfusion.

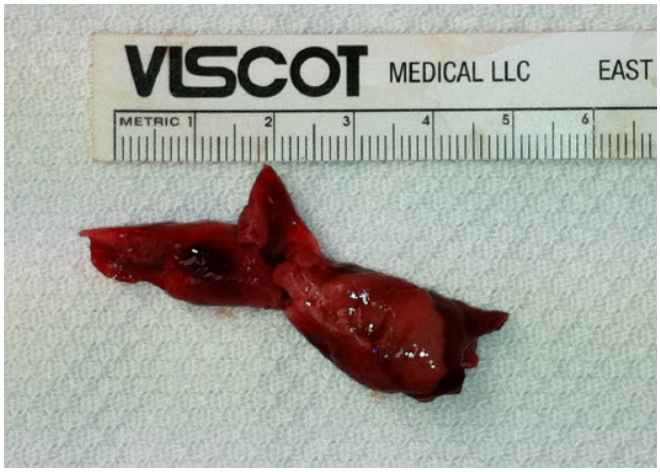

Figure 1. Portal vein thrombus

As there are no randomized trials regarding post-liver transplant, anticoagulation treatment of postoperative anticoagulation is center specific and largely based on case reports, observation studies, and experience. Given the frequent coagulopathy of posttransplant, a patient's initial therapy, at our institution, is often via an infusion with a short half-life (for instance, a low molecular weight dextran or heparin drip) and transitioned to oral vitamin K antagonist (coumadin) once stabilized. We consider a posttransplant PVT a provoked thrombus and continue therapy for at least 3-6 months but not life-long.[12] After therapy is stopped the allograft is monitored with serial ultrasound imaging.

Vena cava and hepatic veins

Potential complications arising from the inferior vena cava (IVC) or hepatic veins often depends on the method of caval anastomosis at transplant, piggyback or bicaval. In the case of piggyback approach to a liver transplant, outflow is from the left and the middle hepatic veins as the right is taken in the native hepatectomy. With the bicaval approach the donor liver IVC is placed as an interposition to the recipient IVC with suprahepatic and infrahepatic caval anastomoses. In either case, should there be suprahepatic outflow, stenosis hepatic congestion results, as discussed in the allograft dysfunction section. The patient may show persistently elevated LFT patterns and persistent ascites. Normal ultrasound of the hepatic veins should show bidirectional flow with respiratory variation; the absence of bidirectional flow is concerning for outflow obstruction. Suprahepatic narrowing is best addressed by interventional radiology with angioplasty and stenting.

In a bicaval approach, the narrowing at the infrahepatic anastomosis is another potential complication. While this does not present with liver dysfunction these patients may demonstrate bilateral lower-extremity edema. Infrahepatic stenosis is best approached operatively with anastomotic revision, as stenting at the area is close to the renal veins. Renal dysfunction may also result from outflow issues of the IVC with either suprahepatic or infrahepatic stenosis but often is not typically a herald of the condition given how common AKI is found in liver transplant recipients.

Cardiopulomonary Complications

Preoperative cardiac assessment of the liver transplant candidate is perhaps the most important assessment for transplant candidacy. Portal hypertension leads to splanchnic vasodilation and hyperdynamic circulatory syndrome[13] that complicates cardiac evaluation of patients with cirrhosis.[14] But even with excellent cardiac evaluation and screening the liver transplant operation itself is fraught with potential cardiopulmonary complications including cardiogenic shock, pulmonary embolism, and transfusion-related acute lung injury (TRALI). Extracorporeal membrane oxygenation (ECMO), either veno-arterial or veno-venous depending on the support required, has been trialed successfully in select recipients and published in center-specific reports.[15] Portal reperfusion of the graft is the most likely intraoperative time for pulmonary embolism and cardiac events in general, secondary to a bolus of potassium and acid accumulated in the vasculature of the allograft during the ischemic time and decreases in body temperature as cold fluid is flushed into the recipient's systemic circulation. Cardiogenic shock, specifically of the right heart, impacts liver function by hindering hepatic outflow and leading to congestive hepatopathy. If severe, ECMO may be warranted to offload the return to the heart and allow time for cardiac recovery and improve hepatic congestion.

Pulmonary embolism is most often seen after the release of the suprahepatic venous clamp and results in dramatic cardiac instability. The wide use of intraoperative transesophageal echocardiography (TEE) by anesthesia colleagues will quickly show the embolism in conjunction with arrythmia. Full anticoagulation with tissue plasminogen activator (tPA) or heparin for resolution of the clot will make the remainder of the liver transplant difficult from a hemostatic standpoint and may require open abdomen and packing with a plan for return to the OR once anticoagulation has worn off.

Hemorrhage and Resuicitation

Patients with end-stage liver disease (ESLD) present for transplant with complex coagulopathy, resembling disseminated intravascular coagulation (DIC). ESLD patients are often coagulopathic from reduced liver-derived procoagulant factors and thrombocytopenia and at the same time, hypercoagulable with reduced anticoagulation factors and elevated von Willebrand factor. Much of the patient's coagulopathy is addressed with resuscitation by the anesthesia team during the recipient hepatectomy but posttransplant can be quite variable as the liver allograft quality and recovery time following the ischemia and reperfusion insults.

Many ESLD posttransplant recipients need blood product resuscitation following their operation. There is significant raw surface area following the native hepatectomy as the site for nonsurgical blood loss. At our institution, we do not transfuse fresh frozen plasma (FFP) for elevated INR, cryoprecipitate for low fibrinogen, or platelets for thrombocytopenia at face value. Alternatively, we prefer to use trends to gauge new liver allograft function unless there is evidence or suspicion for bleeding (increasing pressor requirements, increasing tachycardia, falling hemoglobin) in which case correcting coagulopathy is paramount. We believe this re-balance of the natural physiologic liver state is crucial during resuscitation period.

Unless active surgical bleeding is suspected, return to the OR for washouts is avoided until 24 hours after transplant to give the new allograft time to produce procoagulant factors. If a patient receives >6-8 units of PRBC transfusion they are typically washed out 48-72 hours after transplant. We suspect that the hematoma continues to use the transfused procoagulant products as most patients cease to need further resuscitation after washout.

While the liver allograft should produce thrombopoietin, recipients' platelet counts are slow to recover and are typically low for several days to weeks following the transplant. Rarely is a splenectomy performed at the same time as the liver transplant and may contribute to platelet sequestration in those patients who had portal hypertension preoperatively, resulting splenomegaly. Unless levels are concerning for spontaneous bleeding (platelets < 20,000 ccm) transfusion is avoided.

Neurologic Complications

Altered mental status (AMS) is common pre- and post-liver transplant. It is most common postoperatively in those who already have encephalopathy going into their liver transplant and those with alcoholic cirrhosis, MELD >15, metabolic disorders, or who are critically ill requiring ventilatory support.[20] Postoperative AMS is often multifactorial, and very common, but for a transplant recipient to make no strides in mental status recovery, or not wake up from the procedure, urgent investigation and concern for cerebrovascular accident (CVA), or in the case of intraoperative cardiac event, a cerebral ischemia work-up should be initiated with help from neurology colleagues.

Plasma sodium levels are also a potential contributor to AMS. ELSD patients are typically chronically hyponatremic entering the OR and correction should be gradual postoperatively to avoid osmotic demyelination syndrome. Infection causing AMS is common further out from the procedure but in the acute perioperative phase it is unlikely if appropriate preoperative screening has been performed. Finally, immunosuppressant medications, specifically calcineurin inhibitors (CNI: cyclosporine and tacrolimus), may lead to varying degree of neurotoxicity, from mild tremor to posterior reversible encephalopathy syndrome (PRES). PRES is usually associated with high blood levels of CNI but can present at any level. MRI is diagnostic but often presenting symptoms of tremor, AMS and in its extreme seizure may diagnose before an MRI is obtained. In the absence of other etiology with persistent AMS, a change from tacrolimus to another agent (even another CNI such as cyclosporine) may help. Corticosteroids may also contribute to AMS and a quick wean may also benefit the patient.

Conclusion

Acute complications following liver transplant are often vascular in nature and close postoperative monitoring with bedside ultrasound is the least invasive and is easy to perform. In the absence of vascular issues extremely rare issues including allograft dysfunction of PNF or hyperacute rejection are possible and should be ruled out, but most often the allograft needs time to warm up and "wake up" with aggressive resuscitation and support before hemodynamic and laboratory values begin to normalize.

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CHAPTER 15

Management of Lower GI Bleeding

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Lower gastrointestinal bleeding, hematochezia, diverticular bleeding, colonoscopy, bowel preparation, endoscopic treatment, angiography, embolization, surgery

Abstract

Acute lower gastrointestinal bleeding (LGIB) accounts for up to 30 percent of all major episodes of gastrointestinal (GI) bleeding. The annual incidence of hospitalization in the United States is approximately 36/100,000 population. LGIB has been recently redefined as bleeding originating beyond the ileocecal valve and which can be evaluated by colonoscopy. The clinical presentation varies greatly depending on the underlying bleeding cause. The majority of patients have self-limited bleeding that can be managed with conservative measures. Diverticulosis, ischemic colitis, colorectal neoplasia, and angiodysplasia are the most common causes of LGIB. Colonoscopy, after appropriate bowel preparation, is the preferred strategy for managing patients with active colonic bleeding. Colonoscopy should be performed within 8 to 24 hours of admission; however, the optimal time threshold has not been determined. Colonoscopy is both diagnostic and therapeutic and several endoscopic hemostatic techniques have been described. In the emergency setting, patients with active bleeding in whom colonoscopy has failed to identify a bleeding source should proceed with angiographic evaluation. Transcatheter arterial embolization (TAE) is the treatment of choice following a positive computed tomography (CT) angiogram. Several embolic agents can be used for TAE. The choice of material for embolization depends on the location of the bleeding site and the experience and preference of the interventional radiologist. Surgical management is considered the final therapeutic option, when all minimally invasive attempts have failed.

Introduction

Acute lower gastrointestinal bleeding (LGIB) is a clinical emergency, accounting for up to 30 percent of all major episodes of all gastrointestinal (GI) bleeding. The annual incidence of hospitalization in the United States is approximately 36/100,000 population, significantly lower compared with upper GI bleeding (61/100,000).[1] The mortality rate is low (less than 5 percent) even in elderly patients and usually results from comorbid conditions and nosocomial infections rather than uncontrolled hemorrhage[2]; however increasing age, multiple comorbidities, intestinal ischemia, bleeding after admission for another condition, and hypovolemia are strong predictors of inhospital mortality.[2,3] Conversely, data from Spain reported a 50 percent increase in hospitalizations for LGIB over the past decade (from 20/100,000 in 1996 to 33/100,000 population in 2005), a higher mortality rate, and a longer length of stay compared with upper GI bleeding events.[4]

LGIB refers to the acute onset of GI bleeding originating from a site distal to the ligament of Treitz. However, because of the modern advances in endoscopic examination of the small intestine, the traditional definition of the site of bleeding (upper or lower GI bleeding) has been recently revised and classified as follows: upper, mid- and lower GI bleeding. A new definition of LGIB has been proposed as hemorrhage distal to the ileocecal valve which can be evaluated by colonoscopy.[5] A lower GI bleeding source is usually suspected when patients present with hematochezia, defined as the passage of bright red blood per rectum, with or without abdominal pain, conversely, hematemesis and/or melena are the most common signs of acute upper GI bleeding. The underlying disorder can vary widely from life-threatening variceal bleeding to intermittent hemorrhoidal bleeding. Diverticulosis, ischemic colitis, colorectal neoplasia, and angiodysplasia are the most common causes of LGIB. Hematochezia more frequently occurs when bleeding originates from the large intestine, although it can also result from massive and very rapid bleeding coming from the upper digestive tract. Approximately 15 percent of patients with suspected LGIB have an upper GI bleeding (UGIB) source despite the absence of common signs of upper hemorrhage and despite a negative nasogastric aspirate.[6] The majority of patients have self-limited bleeding that can be managed electively in the outpatient setting. In case of massive or severe hematochezia, patients require urgent admission with intensive medical monitoring, and active intervention to control the bleeding.

In case of massive ongoing bleeding, immediate diagnostic and therapeutic interventions are needed. The emergency setting may result in more inpatient resource utilization (blood or platelet transfusions, diagnostic and endoscopic procedures, utilization of intensive care services) and long hospitalization leading to increase in health care costs. A comparative study of resource utilization between upper versus lower GI bleeding has shown no significant differences in terms of length of stay, mean number of endoscopic procedures, and mean costs.[7]

In this chapter, the initial evaluation and algorithm for the management of patients with LGIB will be reviewed, analyzing the several underlying etiologies and main diagnostic and treatment strategies, including endoscopic or nonendoscopic interventions.

Etiology of LGIB

The clinical presentation varies greatly, depending on the underlying bleeding cause **(Table 1a).** A summary of the main causes of LGIB is described as follows.

Table 1a. Common causes of lower gastrointestinal bleeding[8]

Etiologies	n%
Diverticulosis	20-65%
Ischemic colitis	1-19%
Colorectal neoplasia	5-17%
Angiodysplasia	3-15%
Hemorrhoids	2-10%
Postpolypectomy	2-8%
Solitary rectal ulcer	0-8%
Crohn disease	1.2-6%
Ulcerative colitis	0.1-4.2%

Diverticular bleeding

Although the incidence of hospitalization declined from 30.4/100,000 to 23.9/100,000 population between 2001 and 2009, colonic diverticular bleeding remains the most common cause of LGIB, accounting for about 30 to 65 percent of LGIB cases.[1-2,8] Approximately 3 to 15 percent of patients with diverticulosis may develop diverticular hemorrhage.[9] Rectal bleeding usually occurs as a result of vasa rectum rupture into the intestinal lumen. The use of anti-inflammatory drugs increases the risk for diverticular bleeding, moreover, comorbid conditions and the use of antithrombotic drugs may contribute to severe bleeding. The prevalence of diverticular bleeding increases in elderly patients. Clinical presentation can range from painless minor bleeding to life-threatening hematochezia. In most patients, bleeding ceases spontaneously but may recur in up to 40 percent of patients within 4 years.[10-11] However, early rebleeding (within 30 days) after endoscopic treatment is uncommon. Two recent studies reported no early rebleeding in 32 patients successfully treated with endoscopic clips for diverticular hemorrhage; long-term follow-up demonstrated

late rebleeding in 18 and 22 percent of patients after 15 and 22 months, respectively.[12-13] Of note, late rebleeding may occur from diverticula in a different location. Diagnosis is confirmed by the presence of diverticular hemorrhage at colonoscopy and the absence of other bleeding sources or pathologic findings. Gayer et al. enrolled more than one thousand patients with acute LGIB.[14] Two groups, from two time periods (1988-1997 versus 1998-2006), were compared. Diverticulosis, hemorrhoids, and cancer were found to be the most common etiologies of severe GI bleeding, additionally, colonic diverticular hemorrhage caused the highest rates of rebleeding. Diverticulosis was more frequent in the later time period with an increase in the rate of endoscopic procedures from 1 to 4 percent with a corresponding decrease in the need of operative intervention to control the bleeding. Specific therapeutic interventions for diverticular bleeding are described as follows.

Ischemic colitis

Ischemic colitis (IC) is the second-most common cause of colonic hematochezia accounting for up to 19 percent of patients with LGIB, and mainly affects elderly patients.[8,15-18] It results from a sudden, often transient reduction in mesenteric blood flow secondary to hypoperfusion, vasospasm, or occlusion of the mesenteric vasculature. Any part of the colon may be affected, although the left colon is the most frequently involved in approximately 75 to 85 percent of patients. In particular, the "watershed areas" including the Griffith point (splenic flexure) and the Sudeck point (rectosigmoid junction), are the most sensitive to ischemic damage mediated by decreased blood flow.[19-21]

Although isolated right colon ischemia is less frequent, it tends to be more severe[22]. Cosme et al. prospectively analyzed 135 consecutive patients with IC, the authors reported that the right side significantly increased the risk of severe disease and that more than 50 percent of patients with right colon involved (6/10) required surgery.[23] In the Cosme study the global mortality rate in patients with IC ranged from 8 to 10 percent.

Several clinical conditions, including congestive heart failure or other underlying cardiovascular diseases, trauma, shock from hypovolemia or sepsis, diuretics, vasoactive drugs, and NSAIDs, may lead to a decrease in mesenteric arterial blood flow and vasoconstriction. Mesenteric occlusion related to cardiac thromboembolism has been reported in up to one-third of patients with IC.[24] The consequent reduction of colonic perfusion leads to mucosal injury, erythema, ulcers, or even transmural erosions.

Clinical presentation varies depending on the severity and extent of the disease. Usually, patients present with acute abdominal pain, followed by hematochezia or bloody diarrhea within one day from pain onset. Characteristic endoscopic findings are submucosal hemorrhage and ulcerations in the colon. IC typically presents a segmental distribution with an abrupt transition between abnormal and normal mucosa. The rectum is usually spared because of its dual blood supply. However, these findings are not pathognomonic of ischemic colitis and inflammatory or infectious colitis should remain in differential diagnosis. Computed tomography angiography (CTA) is helpful in case of severe IC or when there is a suspicion for underlying thromboembolism.

Most patients have transient, self-limited ischemia and can be managed conservatively. However, when the right colon or entire colon are involved, or in the presence of concomitant small bowel ischemia or transmural infarction, surgery may be required.

Cosme at al. reported that the estimated cumulative recurrence rates of ischemic colitis at 1, 2, 3, and 5 years were 2.9 percent, 5.1 percent, 8.1 percent, and 9.7 percent, respectively.[23] Thus, it is important to identify individual factors (arrhythmia, cardiovascular disease, hypercoagulable state, or intake of vasoactive drugs) that may increase the likelihood of recurrence. Additionally, patients with mesenteric thrombosis and an episode of IC or a recurrence may benefit from prophylactic anticoagulant therapy.

Colorectal neoplasia

Colorectal neoplasia accounts for approximately 17 percent of LGIB cases.[8] Changes in bowel habits, weight loss, rectal bleeding, low hemoglobin level, and abdominal pain should raise suspicion for neoplasia and a colonoscopy should be performed for diagnostic and localization purposes. Right-sided tumors usually present with occult blood loss and anemia whereas cancers of the left colon typically present with hematochezia. Severe hemorrhage in combination with colorectal neoplasia, more likely results from ulcerated and locally advanced tumors.

In a series of 604 patients referred for flexible sigmoidoscopy for evaluation of rectal bleeding from 1996 to 1999, age (<50 years: OR = 1, 50–69 years: OR = 5.09, 95 percent confidence interval (CI) = 1.4 to 18.6; ≥70 years: OR = 8.19, 95 percent CI = 2.11 to 31.82) and the presence of blood mixed with stool (OR = 3.78, 95 percent CI = 1.36 to 10.47) were the most significant predictors of CRC.[25] The finding of hemorrhoids, even in the presence of bright red bleeding as an isolated symptom, did not significantly lower the risk of finding CRC.

Additionally, among 563 patients with positive fecal occult blood test, 439 had one or more lower GI symptoms, rectal bleeding, abdominal pain, weight loss, tenesmus, and change in bowel habits were common but were not predictive of colorectal neoplasia.[26] This could be explained by the high prevalence of benign conditions associated with rectal bleeding and higher adherence to screening programs in symptomatic compared with asymptomatic patients.

Patients presenting in the emergency setting with life-threatening bleeding from rectal cancer may be amenable to endoscopic intervention or selective transcatheter arterial embolization, or palliative radiotherapy, with emergency surgery limited to performing fecal diversion.

Angiodysplasia of the colon

Angiodysplasia is among the most common causes of chronic or recurrent lower GI bleeding, accounting for 3 to 15 percent of LGIB cases.[8] Additionally, it is the most frequent etiology of small bowel bleeding, formerly called obscure GI bleeding (OGIB), in patients >60 years old.[27] Hospitalization for LGIB angiodysplasia has decreased from 5.54/100,000 to 4.30/100,000 population from 2001 to 2009.[1] Angiodysplasia is an acquired vascular malformation characterized by the presence of dilated and tortuous vessels in the mucosal and submucosal of the lower GI tract. It mainly occurs in elderly patients. Although the exact etiology remains unknown, data suggest that it may be related to age-related vessel degeneration and is associated with cardiovascular and pulmonary diseases as well as aortic stenosis.[27-28]

Angiodysplastic lesions are more frequently located in the cecum and ascending colon.[29] At colonoscopy, flat, red ectatic blood vessels, radiating from a central feeding vessel and ranging from a few millimeters to several centimeters may be observed. Patients can be asymptomatic with occult anemia or may present with melena, hematochezia, or even severe bleeding, especially in patients on an anticoagulant or antiplatelet therapy.[30-31] Bleeding from angiodysplasia is usually painless and distinguishing it from diverticular bleeding is challenging. Risk factors associated with poor outcome include advanced age, liver disease, and hypovolemic shock at presentation. The diagnosis is based upon endoscopic findings, iron deficiency anemia, or association with systematic diseases. The Heyde syndrome is characterized by angiodysplasia with lower GI bleeding in patients with aortic stenosis.

The majority of patients present with self-limiting bleeding that resolves spontaneously. In case of severe or persistent bleeding, when the source of bleeding is identified, therapeutic interventions, via endoscopic (coagulation) or radiological (superselective embolization) approaches are usually performed. Surgical resection is rarely needed in cases of uncontrolled bleeding. Specific therapeutic interventions for angiodysplasia are later described.

Hemorrhoids

Hemorrhoids are the most frequent anorectal disorders, affecting around 10 million Americans per year.[32] Hemorrhoids arise from abnormal dilation and distortion of vascular submucosal cushions in the anal canal leading to inflammation and prolapse. They are classified into internal or external hemorrhoids based on their relationship to the dentate line. In most cases they are a common incidental finding. Hemorrhoidal bleeding accounts for up to 10 percent of LGIB cases.[8]

In a retrospective review of 1,112 patients admitted to an urban emergency medical center from 1988 to 2006, hemorrhoids (22.5 percent) were among the most common causes of severe acute LGIB.[14] Additionally, in a large population-based study, among 76,186 patients undergoing colonoscopy for hematochezia from 2002 to 2008, internal hemorrhoids were reported in 64.4 percent.[33]
Patients usually present with intermittent bright rectal bleeding, pruritus, or prolapse. Differential diagnosis includes anal fissure, abscess, fistulas, and solitary rectal ulcer. Because of these nonspecific symptoms, rectal evaluation should be performed, consisting of digital rectal examination and anoscopy or rigid/flexible sigmoidoscopy to confirm the diagnosis. Flexible sigmoidoscopy provides a high yield of positive findings in patients with LGIB (58 percent).[34]
The initial management of these patients usually involves conservative measures to minimize constipation and straining, including dietary and lifestyle changes in addition to topical treatments for symptom relief. In case of bleeding refractory to conservative measures, office-based procedures routinely performed include rubber band ligation (RBL), sclerotherapy, electrocoagulation, and laser or infrared coagulation. However, RBL has been shown to be superior to sclerotherapy in the treatment for both grade I, II, or grade III hemorrhoids with no significant difference in the complication rate.[35] Sclerotherapy and infrared coagulation have shown a greater need to require additional therapy than RBL, although RBL is more painful.
Surgical interventions including hemorrhoidectomy, hemorrhoidopexy, or Doppler-guided hemorrhoid artery ligation (DG-HAL) may be considered only for those patients with severe bleeding resulting from grade III-IV hemorrhoids with prolapse who fail or cannot tolerate office-based procedures.

Post-polypectomy bleeding

Post-polypectomy bleeding accounts for 2 to 8 percent of acute LGIB[8]; it's one of the most common complications of endoscopic polypectomy and has been observed in 0.2 to 1.8 percent of cases.[36] A recent large study using Medicare data reported that patients undergoing polypectomy had a 4 times higher risk of lower GI bleeding than the screening group (8.7/1000 procedures versus 2.1/1000 procedures).[37]

Post-polypectomy bleeding can occur immediately or can be delayed by up to 3-4 weeks.[18,38] Post-polypectomy bleeding depends upon several variables partially attributable to either patient characteristics or endoscopic procedures. Immediate bleeding (within 12 hours of endoscopic resection) is typically arterial and results from inadequate hemostasis of the blood vessel in the polyp stalk, whereas

delayed bleeding (after 12 hours of endoscopic resection) is more frequently related to the inappropriate management of anticoagulant and/or antiplatelet therapy. Kim et al. identified nine risk factors significantly associated with immediate post-polypectomy bleeding: age (>65 years), polyp size greater than 1 cm, pedunculated or laterally spreading tumor morphology of polyp, cutting mode of the electrosurgical current, incidence of inadvertent cutting of a polyp before current application, cardiovascular or chronic renal disease, anticoagulant use, and poor bowel preparation.[39]

Additionally, right-sided colonic polyp, hypertension, associated extra-intestinal diseases, and tubular adenoma were identified as additional risk factors for post-polypectomy bleeding.[40-42] Sawhney et al. confirmed the results of Kim and colleagues, however in this study, hypertension and aspirin use did not increase the risk of post-polypectomy bleeding.[43]

The management of anticoagulant drugs in the setting of acute GI bleeding and in patients undergoing endoscopic procedures is challenging. Polypectomy is considered a high-risk procedure for bleeding.[44] Therefore, in the case of a planned procedure and in a patient at low risk of thromboembolic event, discontinuing anticoagulant therapy in the periprocedural period is recommended. In the case of patients at high risk of thromboembolic event, bridge therapy may be suggested. Additionally, in patients with severe LGIB undergoing urgent endoscopic procedures, anticoagulants agents should be held to facilitate hemostasis. The 2016 American Society for Gastrointestinal Endoscopy (ASGE) guidelines, recommend that endoscopic therapy should not be delayed in patients with severe GI bleeding and INR <2.5.[44] A pre-endoscopy INR level has not been found to predict rebleeding, but in patients with INR >2.5 at onset, the use of reversal agents or anticoagulant interruption were a strong predictor of thromboembolism.[45] Because of the low evidence regarding bleeding risk associated with new oral anticoagulants (NOACs) in combination with ASA, recommendations to guide the management of these drugs prior to polypectomy is not possible. Specific therapeutic interventions for post-polypectomy bleeding are later described.

Solitary rectal ulcer

First described by Cruveihier in 1829, solitary rectal ulcer syndrome (SRUS) is a rare chronic benign disorder with unclear etiology and different strategies of treatment.[46] The incidence of SURS is equally distributed among men and women, and is more frequent in young patients, although some cases were observed in elderly patients and children.[47-49] Endoscopy ulcers are usually located along the anterior rectal wall. Clinical features include rectal bleeding, mucorrhea, mucosal prolapse, fecal evacuation disorder, and perineal pain. Rectal bleeding varies from minimal to severe hemorrhage requiring transfusion.[50-51] However, up to 26 percent of patients are asymptomatic.[52] Biopsy of the involved area is crucial for the diagnosis; key histological features have been described as sensitive markers to differentiate solitary ulcer of the rectum from other disorders.[53-54]

The underlying cause is chronic local ischemia of the rectal wall and many causes can play an important role. Rectal prolapse and intussusception, puborectalis syndrome, localized rectal trauma, chronic constipation, and radiotherapy are frequently associated with SRUS. Therefore, different treatment modalities for the management of SRUS have been reported, ranging from biofeedback, lifestyle changes, dietary management, steroid enema, topical treatments, and surgery; the choice of treatment depends on the severity of symptoms.[55-59] Argon plasma coagulation (APC) has shown to be more effective in controlling bleeding in patients with SRUS compared with conservative therapies. In a trial of 24 patients with SRUS, one group (n=12) was treated with multiple sessions of APC plus conservative therapy, whereas the control group (n=12) received conservative therapy only (fiber supplement, laxatives, biofeedback, and so forth).[60] Bleeding control was achieved in 100 versus 41.6 percent in each group, respectively ($p=0.0046$). Additionally, complete healing of rectal ulcers was observed in 75 percent of patients in the APC group with a reduction in ulcer size in the remaining 25 percent. In another randomized controlled trial, APC has shown to be effective in treating SRUS.[61] Patients receiving APC (n=41) showed a better response to treatment in controlling the bleeding than traditional therapies (n=59) ($p<0.001$), moreover, APC was found to improve the healing of rectal ulcers.

In the case of refractory bleeding, rectal prolapse surgery may be necessary. In 64 patients with SRUS who failed medical treatments, 49 underwent rectopexy, 9 Delorme procedure, 2 anterior resection (AR), and 4 required primary colostomy as initial operation. In approximately 60 percent of patients, rectopexy and Delorme operation showed comparable and satisfactory long-term results after a median of 90 and 38 months, respectively.[62]

Other etiologies of LGIB

Other uncommon causes of LGIB may be responsible for severe hemorrhage and should be considered in the differential diagnosis.

Rectal bleeding is reported in approximately 13 percent of patients after radiation therapy.[36] Radiation causes a direct rectal inflammation, inducing endarteritis obliterans and neovascularization with telangiectasias in the rectum. Bleeding may occur due to the oozing from the friable inflamed mucosa and the rupture of these radiation-induced telangiectasias. Diagnosis is confirmed by endoscopy.

Several medical therapies (hyperbaric oxygen therapy, short chain fatty acid therapy, sucralfate enema therapy, 5-aminoisalicylic acid, sulfasalazine, and rectal steroids) and endoscopic hemostatic therapies (APC, bipolar electrocoagulation, cryotherapy, and laser therapy) have been described.[63-64]

Rectal application of 4 percent formalin is safe, effective, easy to apply, inexpensive, and the treatment can be carried out in outpatient clinic. In the largest prospective randomized controlled trial, the use of formalin was found to be superior to a sucralfate-steroid enema for chronic hemorrhagic radiation proctitis[65]; 102 patients with rectal bleeding following radiation therapy, were randomly allocated to either topical formalin (n=51) or sucralfate-steroid enema (n=51). Patients showed a significant decrease in symptom score and better results with respect to sigmoidoscopy grade after treatment with 4 percent formalin. In another randomized controlled trial, APC had comparable efficacy for controlling hemorrhagic radiation proctitis relative to topical formalin.[66] After a median of follow-up of 111 months, one patient for each group required further treatment for rectal bleeding.

Acute LGIB in inflammatory bowel disease (IBD) is uncommon, accounting for only 1.2 to 6 percent of all hospital admissions in patients with Crohn's disease and 0.1 to 4.2 percent in patients with ulcerative colitis. More commonly, patients with Crohn's disease present with significant rectal bleeding when the inflammation involves the colon rather than the small bowel.[67-68] Spontaneous bleeding cessation occurs in up to 50 percent of patients, however, recurrence is not uncommon and may be observed in up to 35 percent of patients.[69] The initial management of these patients consists in blood transfusions and supportive measures. Medical management with biologics can be effective as well. Surgery is generally preferred in case of recurrent bleeding in the setting of severe colitis refractory to medical treatment.

Colonic Dieulafoy lesions are an uncommon cause of massive colonic bleeding accounting for 1 to 2 percent of acute GI bleeding. The incidence of hospitalization has slightly increased from 0.09/100,000 to 0.17/100,000 between 2003 and 2009.[1] Colonic Dieulafoy lesions can result in life-threatening gastrointestinal hemorrhage.[70] They are caused by a vascular abnormality consisting in a protruding tortuous arterial vessel emerging from a small mucosal defect. More commonly, Dieulafoy lesions are present in the elderly population with multiple comorbidity conditions, often hospitalized, on NSAIDs, aspirin or anticoagulants, presenting with massive hemorrhage, and with no previous history of GI pathology. To date, the management of these lesions has become primarily endoscopic.

Acute hemorrhagic rectal ulcer syndrome (AHRUS) is characterized by sudden massive rectal bleeding from solitary or multiple rectal ulcers, is usually painless, and is more frequently observed in elderly patients with underlying comorbidities. The syndrome has been described as the most common cause of acute lower GI bleeding in hospitalized patients with comorbidities.[71-72] A case control study of 38 patients with AHRUS and 123 patients without AHRUS was conducted by Komai et al. to determine risk factors for, and prognosis of AHRUS.[73] Endoscopic hemostasis therapy using clipping or band ligation was performed in 21 percent of the AHRUS group. Rebleeding occurred in two patients and was treated successfully with reclipping. Sixteen of the 38 patients (42 percent, 95 percent CI 28 to 58 percent) required blood transfusions. Hospitalization, antithrombotic drug use, and hypoalbuminemia were significant risk factors for AHRUS. Mortality rate was reported in 17 percent of patients within one year after the episode of rectal bleeding from AHRUS-unrelated causes.

Small bowel bleeding

Bleeding from the small intestine is a rare condition, accounting for 5 to 10 percent of all patients presenting with GI blood loss.[74] Small bowel angioectasias is one of the most common causes of small bowel bleeding, followed by Crohn's disease, Meckel diverticulum, neoplasms, Dieulafoy lesions, and ulcers or erosions secondary to NSAIDs[74] **(Table 1b).** The 2015 American College of Gastroenterology (ACG) clinical guideline reclassified the term obscure GI bleeding (OGIB) as small bowel bleeding. The term OGIB is only reserved for patients with recurrent or persistent bleeding and negative colonoscopy and upper endoscopy and in whom either video capsule endoscopy (VCE), deep enteroscopy, and CT enterography fail to identify a source of bleeding. Indeed, up to 25 percent of patients remain without a diagnosis.[75]

Table 1b. Common causes of small bowel bleeding[74]

Etiologies
Angioectasia
Inflammatory bowel disease
Meckel diverticulum
Small bowel neoplasia
Dieulafoy lesions
NSAID ulcers

Meckel diverticulum should be considered in all patients with GI bleeding under age 30.[1] The incidence of hospitalization has decreased from 0.29/100,000 to 0.24/100,000 population over the decade of 2001-2009.[1] The diagnosis is challenging, and symptoms can mimic other medical conditions. Technetium-99m pertechnetate radioisotope scintigraphy,

enteroscopy, or VCE help confirm the diagnosis and localize bleeding. In few data published, endoscopic resection of Meckel diverticulum using double-balloon enteroscopy was successful described[76-78]; iatrogenic bowel perforation was reported in one case and the patient received urgent laparotomy with segmental resection of the ileum.[79] Segmental small bowel resection is the choice of treatment when bleeding is massive and/or recurs.[80]

Management of LGIB

Initial assessment

Thorough review of the patient's medical history is of paramount importance including a history of bleeding internal hemorrhoids, IBD, aortic aneurysm, previous bleeding episodes, current medications (such as NSAIDS, anticoagulants, and antiplatelet agents), recent endoscopic surgery, gastrointestinal surgery or anorectal procedure, and a history of radiation therapy. A history of alcohol abuse, cirrhosis, or chronic liver failure may suggest portal hypertension and potential origin from gastroesophageal or rectal varices. Careful review of the clinical presentation may also suggest the most likely source of LGIB. Bright red blood triggered by defecation most suggests an anorectal source, however, massive and brisk bleeding from the upper intestinal tract can manifest in the same way. Abdominal pain, bloody diarrhea, and weight loss are usually associated with ulcerative colitis, ischemic colitis, or colorectal cancer. Painless and massive rectal hemorrhage is common in diverticular bleeding.

Careful physical examination including vital signs and laboratory tests are required. Initial tests should include a complete blood count, electrolytes, coagulation studies, blood typing, and screening. Abdominal, digital rectal examination, and anoscopy should be performed to allow rapid evaluation and exclude an anorectal source.

If there is concern for a potential upper GI bleeding source, nasogastric aspirate/lavage should be performed.[7,81-82] A positive or nondiagnostic aspirate necessitates upper endoscopy prior to proceeding with colonoscopy. Patients with massive hematochezia and hemodynamic instability should be transferred to an intensive care setting, with prompt esophagogastroduodenoscopy (EGD) followed by a colonoscopy once an upper GI source has been excluded[83] **(Figure 1)**. In hemodynamically stable patients with severe hematochezia, urgent colonoscopy should be performed first, followed by an EGD, in case of a negative finding at colonoscopy.[84] The primary purpose of an early colonoscopy is to improve the chance of localizing and treating the source of bleeding.

Initial management—resuscitation

Although the majority of patients present with self-limited bleeding that does not require close monitoring, acute LGIB may result in hemodynamic instability, hemorrhagic shock requiring aggressive fluid resuscitation, and blood transfusion.[85] Unstable patients should be monitored in an intensive care unit. Early and aggressive resuscitation

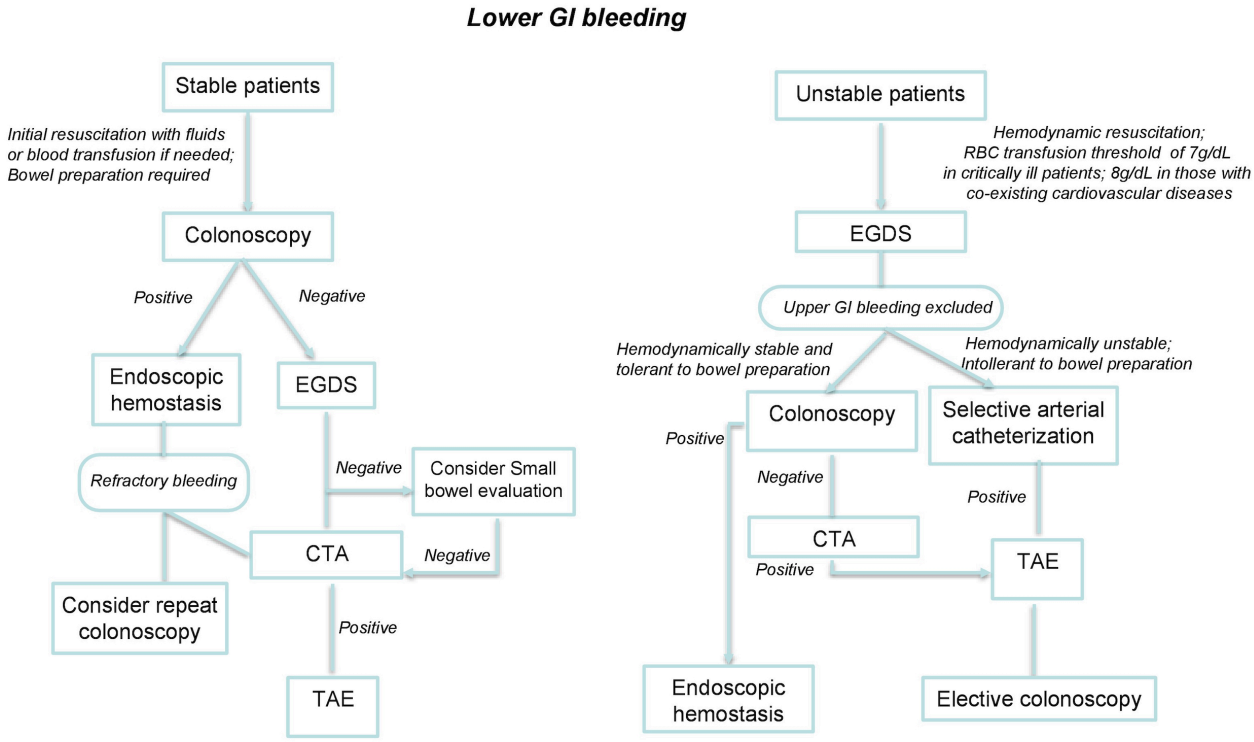

Figure 1. Algorithm for the management of patients with lower GI bleeding. *CTA*, Computed tomography angiography, *EGD,* esophagogastroduodenoscopy, *TAE,* transcatheter arterial embolization.

plays a fundamental role in the management and outcomes of patients with LGIB. Precautions against the risk of aspiration, IV access with two large-bore intravenous catheters, strict monitoring of I&Os, and serial blood counts are recommended.[85] Achieving an adequate fluid balance in the early resuscitation phase is often challenging. Concerns arise about which type of fluids to use as first line (colloid versus crystalloids) and the risk of excessive fluid administration. Unstable patients should receive 1-2 liters of clear fluids, ringer lactate solution is generally preferred.[86] In the CRISTAL trial, the use of colloids versus crystalloids did not result in significant differences in the 28-day mortality rates in patients presenting with hypovolemic shock, however a trend toward higher mortality at 90 days was observed in the crystalloids group (493 versus 434 deaths, p=0.19).[87] Laboratory tests should be used to assess baseline hemoglobin and platelet levels, the arterial blood gases and acid-base balance, and to monitor the effectiveness of resuscitation.

Hemodynamic instability, active bleeding, age, and comorbid conditions have been associated with poor outcomes in patients with LGIB.[18] Several scoring systems have been described to help predict the risk and severity of bleeding and facilitate decision-making regarding management. Strate et al. identified 7 independent risk factors for severe LGIB (tachycardia, hypotension, syncope, a nontender abdomen, rectal bleeding with 4 hours of hospital admission, aspirin use, and two or more comorbidities).[88] Moreover, the number of risk factors predicted the risk of rebleeding as well as the need for blood transfusions, surgery, and death. Additionally, Velayos et al. identified hematocrit less than 35 percent, abnormal vital signs after 1 hour, and gross blood on initial rectal examination as independent predictors of severe GI bleeding.[89] Severe GI bleeding occurred in 79 percent, 54 percent, 17 percent, and 0 percent of patients having 3, 2, 1, and no risk factors, respectively. Patients with 2 or 3 risk factors (52 percent) were reasonable candidates for urgent interventions.

Blood transfusion

The decision to transfuse red blood cell (RBC) units depends on several factors including age, underlying cardiovascular diseases, hemodynamic parameters, and whether ongoing bleeding is suspected. In upper GI bleeding, a restrictive approach to RBC transfusions has been associated with reduction in rebleeding and mortality rates.[90-91] A large trial randomly assigned 461 patients with acute upper GI bleeding to a restrictive transfusion strategy (the hemoglobin threshold was 7g/dL) and 460 patients to a liberal transfusion strategy (the hemoglobin threshold was 9 g/dL).[92] Patients with massive bleeding and with a recent history of an ischemic event, trauma surgery, or transfusion were excluded. Liberal transfusion policy was associated with higher mortality and complications rates, recurrent bleeding, and adverse events (transfusion reactions and cardiac events) and the results were found statistically significant. Moreover, in a meta-analysis of 5 randomized controlled trials comparing restrictive and liberal transfusion strategies among 1,965 patients with severe upper GI bleeding, a restrictive approach reduced mortality and lowered the risk or recurrent bleeding.[90]

With respect to LGIB, there is no evidence to support a restrictive or liberal blood transfusion strategy in these patients. In the post-hoc analysis of a large prospective observational study conducted by Kherad et al., no significant differences in rebleeding rates following restrictive (<8 g/dL, n=388 patients) versus liberal transfusion strategies (>9 g/dL, n=220 patients) were observed in patients with LGIB.[93] Moreover, no statistically significant differences in readmission and inhospital mortality were found in this study. Although there was a trend toward lower mortality in the restrictive group, this did not reach statistical significance. Independent risk factors for rebleeding were age, melena, and active bleeding on admission. However, further studies to guide the appropriate use of RBC transfusions in patients with LGIB are warranted.

Concerns about blood transfusions arise with respect to patients with coexisting cardiovascular diseases. An increased risk of adverse outcomes may derive from anemia. Guidelines from the British Society of Gastroenterology recommend a hemoglobin threshold level of 8 g/dL in patients with cardiovascular comorbidities and a target hemoglobin of 10 g/dL after transfusion.[94] Conversely, critically ill patients without underlying cardiovascular diseases, should not receive RBC transfusions until the hemoglobin level is <7 g/dL.[94] These findings are supported by the current AABB (American Association of Blood Banks) guidelines.[95]

Whether the liberal transfusion policy is more effective than restrictive strategy in the setting of cardiovascular comorbidities remains unclear. In a randomized controlled trial of 110 patients with symptomatic coronary artery disease, the restrictive transfusion strategy (threshold Hb<8 g/dL) was associated with an increase in death and cardiovascular complications.[96] These findings were not supported by a smaller trial of 45 patients with acute myocardial infarction in which the liberal strategy (threshold hematocrit <30 percent) was instead associated with an increased risk of congestive heart failure, recurrent myocardial infarction, and death.[97] The conflicting data reported to date highlight the need of further larger trials.

Impact and management of anticoagulation therapies

Antithrombotic therapy, including anticoagulants and antiplatelet medications, significantly reduces the risk of cardiovascular events. However, management of these

medications in the setting of acute GIB requires careful consideration, taking into account individual patient risk factors such as recent acute coronary syndrome (ACS), recent percutaneous coronary intervention (PCI) and mechanical heart valves, cardiac arrhythmias, and other risk factors for cardiovascular accidents.[44] Furthermore, other significant factors to be taken into consideration include the presence of the new-generation drug-eluting stents (DES) which are associated with a lower risk of stent thrombosis compared with bare-metal stents (BMS).

There is very little evidence to guide the timing of resumption of antiplatelet therapy (APT), however, early resumption of APT, once hemostasis is achieved, is recommended.[44,98-99] The management of patients under dual-antiplatelet therapy (DAPT) is crucial, especially in patients with ACS and PCI; premature discontinuation of APT after LGIB, is associated with a progressively increased risk of stent thrombosis and death. In such cases, stratification of thrombotic risk is of paramount importance.

Low-dose aspirin should not be discontinued in patients with a high thrombotic risk (such as ACS/PCI less than 30 days prior to bleeding event) and resumption of the second antiplatelet agent should be effective as soon as hemostasis is achieved.[44,100] In a randomized trial of 156 patients with peptic ulcer bleeding successfully treated endoscopically and with a history of aspirin use, 156 patients were randomly assigned to receive aspirin (n=78) or placebo (n=78) for 8 weeks after endoscopic treatment. All patients received infusion or oral pantoprazole. Continuation of low-dose aspirin therapy was associated with lower mortality rates compared with patients in the placebo group.[101] However, a higher risk for recurrent ulcer bleeding within 1 month has been observed (from 5.4 percent in the placebo group to 10.3 percent in the aspirin group).

If thrombotic risk is moderate (such as PCI one-12 months before bleeding), aspirin should be resumed as soon as bleeding is stabilized (preferably within 3 days).[100] The choice of restarting the second antiplatelet agent depends on the timing of the PCI as well as the estimated risk of recurrent bleeding.

Patients with medically treated ACS, who therefore do not undergo PCI and stenting, can be managed with a single antiplatelet agent after the bleeding event (rather than DAPT).

Of note, antiplatelet therapy should not be discontinued if the source of bleeding is identified as low-risk stigmata or endoscopic therapy has been successful in stopping the bleeding. In addition, the choice of an alternative antiplatelet agent may be considered after bleeding.[100]

Target-specific oral anticoagulants including dabigatran, rivaroxaban, and apixaban are associated with an increased risk of GI bleeding.[102] Careful evaluation of patient thrombotic risk is required and should be individualized. Interruption of anticoagulants, even for a short period of time, is associated with an increased risk of stroke in patients with atrial fibrillation.

If GI bleeding occurs, anticoagulation should be restarted as soon as the thrombotic risk is thought to outweigh the risk of bleeding.[100] An antidote (monoclonal antibody) may be available for the new oral anticoagulants (NOACs) if massive bleeding occurs and should be considered as an option in clinical management. The American College of Chest Physicians (ACCP) recommends that patients on warfarin receive 4-factor prothrombin complex (PCC) and vitamin K, or fresh frozen in case of serious GI bleeding.[103] Additionally, several patients have conditions that require both antiplatelet and anticoagulant therapy (such as patients with atrial fibrillation undergoing PCI). Management of these patients in the case of bleeding includes using the lowest dose of NOAC effective for stroke prevention and a target of INR toward the lower limits (2-2.5). Discontinuation of antiplatelet agents may be considered based on overall thrombotic/bleeding risk and timing of PCI.

Moreover, platelet transfusions should also be considered in patients who have a normal platelet count but receive massive RBC transfusions. The use of platelet transfusion in patients with GI bleeding under APT without thrombocytopenia has not been found to reduce rebleeding but has been associated with higher mortality.[104]

In conclusion, the management of antithrombotic medications in the setting of active GI bleeding is challenging. For elective procedures, a washout period based on the drug half-life is recommended but may not be possible in patients with ongoing, acute bleeding or at high risk of thromboembolic events.[102] A multidisciplinary team approach in managing antithrombotic medications is recommended to assess the benefit/risk balance of bleeding versus thromboembolic events.

Diagnosis

Colonoscopy

Stable patients presenting with acute LGIB should undergo colonoscopy because of its dual diagnostic and therapeutic role.[34,105] A careful examination of the colonic mucosa and terminal ileum should be performed. Endoscopes of different sizes can be used to facilitate the introduction of hemostatic tools for bleeding control. Because in most cases bleeding ceases spontaneously, colonoscopy is often delayed allowing for adequate bowel preparation.

The diagnostic yield of colonoscopy in LGIB varies considerably, from 45 to 100 percent. However, it is higher than scintigraphy, or angiography which both require active bleeding at the time of examination, and flexible sigmoidoscopy which only assesses the left colon.[9,81-82,105-108] The timing of colonoscopy, the quality of bowel preparation, and expertise of the endoscopist are important factors that affect the diagnostic yield of colonoscopy.

Adequate colon preparation is required for successful colonoscopy. It allows better visualization, facilitates localization of the bleeding source, and may also decrease the risk of bowel perforation.[7,9,18] Ideally, colonoscopy is performed within 6-8 hours of the last fluid intake. The role of enemas prior to colonoscopy in the setting of LGIB is poorly reported in the literature.[109] Enemas have been described as part of mechanical bowel preparation (MBP) prior to elective rectal surgery to facilitate the manipulation for the mechanical anastomosis and prevent infectious complications.

Studies reporting large and rapid volume purge protocols with polyethylene glycol-based solutions followed by urgent colonoscopy showed accurate diagnosis and that endoscopic interventions were successful in achieving hemostastasis.[9,81-82] Although polyethylene glycol is a balanced electrolyte solution, fluid overload leading to pulmonary edema has been observed particularly in patients with congestive heart, liver, or renal failure.[82,110] Additionally, aspiration pneumonia is a potential risk, particularly in patients with altered mental status. Magnesium-based preparations should be avoided in patients with chronic kidney disease.[110] Therefore, careful selection of the most appropriate bowel preparation regimen is needed.

The ASGE guidelines recommend early colonoscopy (within 8 to 24 hours) in stable patients with severe GI bleeding.[8] However, the utility and optimal timing of colonoscopy in the evaluation of LGIB is unclear with limited data to guide clinical practice.

Colacchio et al. reported an 85 percent rate of positive findings when colonoscopy was performed during active hemorrhage. They encouraged aggressive diagnostic evaluation to increase the accuracy of the diagnosis, guide treatment, and improve survival.[111] Strate and Syngal described a cohort of 144 patients with lower intestinal bleeding who underwent an inpatient colonoscopy, successful hemostasis was achieved in 29 percent of colonoscopies performed within 12 hours of admission, 13 percent between 12 and 24 hours, 4 percent between 24 and 48 hours, and 0 percent in colonoscopies performed after 48 hours.[106] Moreover, other studies have shown that a prompt repeat colonoscopy for recurrent lower GI hemorrhage had a higher diagnostic yield.[13,81]

However, two studies showed no improvement in outcomes with respect to rebleeding or need for salvage surgery when colonoscopy was performed within 8-12 hours of presentation.[6,81] In a prospective randomized trial, 50 patients with severe lower intestinal hemorrhage received urgent colonoscopy within 8 hours of admission and 50 received standard care, where the standard of care consisted of a technetium scan, followed by angiography which, if positive for active bleeding, was followed by embolization.[81] Moreover, all patients with positive or negative angiography underwent elective colonoscopy (within 4 days of admission and after adequate bowel preparation). Among patients randomized to urgent colonoscopies, 17 underwent endoscopic intervention compared with 10 patients who underwent embolization in the standard care group. Urgent colonoscopy was associated with improved definitive diagnoses (42 versus 22 percent, odds ratio, 2.6, p=.03) with no significant differences between interventions with respect to mortality (2 versus 4 percent), rebleeding rate (22 versus 30 percent), blood transfusions (4.2 units versus 5.0 units), interval need for surgery (14 versus 12 percent) and length of stay (5.8 versus 6.6 days). It is important to note that the quality of bowel preparation was deemed as insufficient in most patients undergoing urgent colonoscopy.

In another randomized controlled trial conducted in patients with severe hematochezia and no clinical evidence of an upper GI source of bleeding, 72 patients were randomly assigned to urgent (within 12 hours of admission) or elective colonoscopy (36-60 hours following admission).[6] Higher rate of identification of the bleeding source was found in the urgent colonoscopy group (78 versus 67 percent). However, urgent colonoscopy was not associated with significant decrease in rebleeding rates, need for transfusion, length of stay, or need for subsequent diagnostic or therapeutic interventions compared with elective colonoscopy. Underlying medical comorbidities, concurrent use of antiplatelet or anticoagulant agents, and the type of endoscopic intervention used may contribute to the incidence of rebleeding.[112]

Once hemodynamic stability of the patient is achieved, a second-look colonoscopy should be considered.[74] Colon lesions missed at initial endoscopy and responsible for the bleeding may be detected on a second examination performed within the same hospital admission. Alternate imaging studies (scintigraphy, CTA, VCE, and so forth), should be reserved for those patients with ongoing or recurrent bleeding from an unknown source. The available imaging techniques are described as follows.

Scintigraphy

Scintigraphy of GI bleeding or tagged red blood cell (RBC) scanning is generally performed with technetium -99m (^{99m}-Tc) to mark red blood cells and help localize bleeding sites. It is a noninvasive localizing test with high sensitivity which allows for the detection of active bleeding as low as 0.1-0.35 mL/min.[113] ^{99m}-Tc is injected after 15-20 minutes from the intravenous administration of pyrophosphate (a nonradioactive drug), dynamic images are obtained for 60-90 minutes with time intervals of approximately two hours in the case of a negative CT finding. Due to the persistence of labeled RBCs in the body, it has the capability to acquire imaging over a prolonged period (up to 24 hours) with the advantage of continuous monitoring, making it useful to detect intermittent or obscure GI bleeding. However, the diagnostic accuracy of scintigraphy for detecting the sources of bleeding is 66 percent, a false positive rate is reported in up to 25 percent of cases. The rapid blood migration in the bowel lumen doesn't allow focal accumulation of the minimum blood volume required for detection and may increase the number of false positive results.[18,114]

A positive finding with immediate radionuclide blush on ^{99m}Tc-labeled RBC scintigraphy should prompt urgent angiography. Patients with delayed blush however have a low yield of positive angiographic findings, in the latter cases, patients may be observed and/or be evaluated with colonoscopy.[115]

Tagged red blood cell (RBC) scintigraphy is not routinely used as first line to localize the source of LGIB, but it can be used to triage patients for subsequent selective angiography. In a retrospective review, patients with suspected active bleeding were first evaluated with RBC scintigraphy (n=249), arteriography was performed in case of a positive result. The protocol implementation with scintigraphy screening increased the diagnostic yield of arteriography by a factor of 2.4.[116]

Scintigraphy using ^{99m}-Tc pertechnetate, has been shown to be highly predictive in the evaluation of patients with GI hemorrhage and suspicious for a Meckel bleeding diverticulum, ^{99m}-Tc pertechnetate is taken up by the gastrin mucin-producing cells and is extremely effective for the detection of ectopic gastric mucosa.[117] The reported sensitivity is 97 percent, while the specificity is 94 percent.[119] In a pediatric population, scintigraphy using ^{99m}-Tc pertechnetate is reported to have both a sensitivity and specificity of 100 percent for the diagnosis of hemorrhagic Meckel diverticulum. Among 144 pediatric patients undergoing scintigraphy with ^{99m}-Tc pertechnetate for clinical suspicion of bleeding Meckel diverticulum, 22 had a positive scan and all of them were found to have a bleeding Meckel diverticulum at surgery.[118]

Computed tomography angiography (CTA)

CTA is a noninvasive imaging modality that is fast and readily available. It can detect active bleeding at rate ≥0.3 mL/min with a sensitivity and specificity of 86 and 95 percent, respectively. [119-121] It is the imaging modality of choice when evaluating a hemodynamically patient with active or severe hemorrhage, when colonoscopy is not feasible or cannot be performed in a timely fashion. CTA is also preferred over colonoscopy in hemodynamically unstable patients and in whom bowel preparation cannot be safely performed.[94] CTA can localize lesions or possible causes of bleeding and provides additional information regarding vascular anatomy and anatomical variants, particularly relevant when planning surgical or endovascular intervention. Major drawbacks include significant radiation exposure and intravenous contrast related side effects.

Both scintigraphy and CTA can localize the bleeding source and/or confirm active hemorrhage thereby increasing the therapeutic yield of subsequent angiography, and both rely on active bleeding at the time of imaging in order to identify extravasation. Unlike colonoscopy, scintigraphy and CTA are diagnostic but not therapeutic, thus, in case of severe hemorrhage, careful consideration should be given to endovascular versus surgical intervention based on hemodynamic status and specific etiology of the bleeding.

Selective arterial catheterization

Patients with ongoing bleeding and a positive CTA should undergo selective angiography. Angiography can detect bleeding rates of 0.5 to 1 mL/min.[17,122] Overall sensitivity, specificity, and positive and negative predictive values for digital subtraction angiography in investigating acute LGIB are 60 percent, 100 percent, 100 percent, and 24 percent, respectively.[123] In addition to its diagnostic capability, selective catheterization of the leaking vessels can be achieved with subsequent embolization. Angiography can be performed in the emergency setting in hemodynamically unstable patients without the need for bowel preparation. It is an attractive minimally invasive alternative to emergency surgery in high-risk patients.

EGD, enteroscopy, and video capsule endoscopy (VCE)

Patients with LGIB and a negative EGD and colonoscopy, may have an occult bleeding source originating in the small bowel. In these cases, consideration should be given for push enteroscopy and colonoscopy with cannulation of the terminal ileum.[74] If negative, VCE is a noninvasive test that allows examination of the entire small bowel that should be performed prior to push enteroscopy. The diagnostic yield of VCE for detection of bleeding small bowel lesions ranges from 38 to 83 percent and with the greatest yield when performed within 48 to 72 hours of the bleeding event.[74,124]

Major drawbacks include potential capsule retention, the lack of therapeutic capability, and the difficulty to control its movement in the GI tract and precisely localizing bleeding lesions.

Double-balloon enteroscopy and CT enterography (CTE) should be performed if a small bowel source of bleeding is suspected despite negative VCE. Double-balloon enteroscopy is both diagnostic and therapeutic. Additionally, magnetic resonance enterography (MRE) is a noninvasive diagnostic modality in evaluating small bowel pathologies and should be considered prior to planned small bowel resection to rule out enteric and extraenteric manifestations such as strictures, abscess, and fistula in the setting of IBD.

Provocative mesenteric angiography

Provocative mesenteric angiography stimulates bleeding with vasodilator, thrombolytic, and anticoagulant medications in order to define the source of bleeding in patients with recurrent occult LGIB. Success in identifying the bleeding site ranges from 33 to 37 percent.[125-128]

Kim et al. reported the largest series of patients undergoing provocative mesenteric angiography for lower GI hemorrhage.[128] Angiographically visible active extravasation was detected in 11 of 36 procedures (31 percent), no procedure-related complications were observed. The administration of intravenous heparin (5,000– 7,000 U) and vasodilator (nitroglycerin 200 µm) in conjunction with thrombolytic therapy (tissue plasminogen activator 4-25 mg) was shown to maximize the chances to provoke and visualize the site of active bleeding. Superselective embolization was then successfully performed in 10 patients (92 percent).

Endoscopic Therapeutic Interventions

The most common causes of LGIB amenable to endoscopic therapeutic interventions include diverticular bleeding, angiodysplasia, and post-polypectomy bleeding. Referral to expert endoscopists, lesions characteristics, and the anatomic location are key elements to guide the choice and success of endoscopic treatment. Endoscopic interventions to control LGIB have been shown to be effective and safe. Adverse events have been reported in 0.3 to 1.3 percent across more than 2,400 colonoscopies performed for acute LGIB.[18,129] However, conversely to upper GI bleeding, current data on the use of endoscopic interventions are predominantly based on retrospective and observational nonrandomized studies.

Endoscopic treatment of diverticular bleeding

Endoscopic management for colonic diverticular bleeding has shown excellent results. Endoscopic treatments include injection therapy (most commonly epinephrine), contact thermal therapies (bipolar/multipolar electrocoagulation, heat probe), noncontact thermal therapies (argon plasma coagulation), endoscopic clipping devices, and band ligation. Thermal contact therapies can be used alone or in combination with epinephrine injection. When active diverticular bleeding is present, dilute epinephrine submucosal injection into four quadrants around the bleeding site is recommended to obtain initial hemostasis. Then, thermal devices or endoscopic clipping devices can be used for definitive control of the bleeding vessel(s). The choice between the two latter treatments is based on the anatomic location of the bleeding source, the patient's comorbidities, and the endoscopist's experience. A nonbleeding adherent clot should be injected with epinephrine around the pedicle of the clot and guillotined by using a polypectomy snare. Subsequently, the underlying stigma should be treated with a thermal probe or hemoclips. Ink tattooing should be made adjacent to the diverticulum, to allow for later identification in case of recurrent bleeding or subsequent need for surgical intervention.

In a prospective study of 121 consecutive patients with severe hematochezia, 27 had diverticular hemorrhage and 10 patients received urgent endoscopic treatment.[9] Endoscopic therapies consisted of epinephrine injection (n=5) for patients with active bleeding and bipolar thermal coagulation (n=2) for those with a nonbleeding visible vessel, for patients with an adherent clot (n=3), dilute epinephrine was injected around the site of bleeding, the clot was removed, and any underlying stigmata was treated with bipolar thermal coagulation. At a median follow-up of 30 months, none of the patients endoscopically treated had recurrent rebleeding, emergency surgery, or required further blood transfusions. No complications were reported. However, this was not a randomized study and only a few patients were analyzed.

Endoscopic clipping of diverticular bleeding by experienced endoscopists has been shown to be safe and a valid alternative treatment to thermal coagulation. When a vessel within the thin dome of a diverticulum is observed at colonoscopy, hemoclips are usually preferred than thermal therapies, (bipolar/multipolar electrocoagulation, heat probe), to prevent the risk of transmural injury or mini perforation.[130-131] Hemoclips can be placed directly over a bleeding vessel at the neck of a diverticulum or by closing the diverticular orifice in a zipper fashion, thereby tamponading a vessel within the dome.[13] Kaltenbach et al. reported the short- and long-term outcomes of 24 patients with acute diverticular bleeding treated with endoscopic clips.[12] Successful hemostasis was achieved in 88 percent of patients. No complications or early rebleeding was observed. Recurrent diverticular bleeding occurred in 22 percent of patients. Of these, 4 patients were treated again with hemoclips and 2 required embolization. Additionally, Strate and Naumann reviewed 137 cases of diverticular bleeding treated endoscopically.[18] Endoscopic therapy included endoclip (n=71), epinephrine (n=20), thermal contact (n=17), thermal contact plus injection (n=25), and band

ligation (n=4). Hemostasis was achieved in 92 percent and no complications were reported. Early and late rebleeding occurred in 8 and 12 percent of patients, respectively.

Recently, emerging endoscopic treatments including topical hemostatic powder-based or spray agents have been described.[132-134] Topical hemostatic agents used at the bleeding site have shown to achieve very rapid hemostasis. TC-325 with the brand name Hemospray® (Cook Medical Inc, Bloomington, IN) has the property to absorb water it concentrates blood cells and clotting factors producing a quick mechanical barrier to stop bleeding. However, only few data evaluating the Hemospray effectiveness are reported in the literature and are predominantly related to upper GI events.[135-137] No adverse events have been reported so far.

Endoscopic band ligation (EBL) has been described in some small series showing effectiveness and safety for the treatment of diverticular bleeding.[138-140] However, EBL may be more challenging in active bleeding. In a retrospective study, Shimamura et al. identified 95 patients with diverticular bleeding that successfully achieved initial hemostasis with EBL.[141] No adverse events were observed. Early rebleeding (<30 days), occurred in 15 patients and in 4 cases more than one EBL attempt was required to achieve hemostasis control.

The use of Doppler probe to detect the arterial blood flow underlying stigmata before and after hemostasis has been reported to be a safe and useful tool for the endoscopic treatment.[142] However, no studies comparing patients undergoing endoscopic treatment with or without Doppler probe monitoring have been reported. Further data are warranted.

Endoscopic treatment of angiodysplasia of the colon

Endoscopic hemostasis is recommended in patients with acute or chronic bleeding. Both contact and noncontact thermal endoscopic therapies are effective for the treatment of colonic angiodysplasia. However, the noncontact thermal method of hemostasis, such as APC is more frequently used.

In a large case series of 100 patients with colonic angiodysplasia in whom APC was used to control bleeding,[143] 85 percent of patients remained free of recurrent bleeding at a median follow-up of 20 months. Complications occurred in 2 patients and were treated conservatively. Among the 15 patients with recurrent bleeding, APC was repeated with 2 patients requiring blood transfusions after treatment and one patient required surgery for refractory bleeding.

APC was shown to be safe even in patients with substantial comorbidities.[144] Additionally, successful application of hemoclips combined with APC has been reported for bleeding from colonic angiodysplasia with underlying arteriovenous malformation.[145]

Post-polypectomy bleeding

More than 90 percent of post-polypectomy bleeding can be managed conservatively if adequate endoscopic expertise is available.[146] Endoscopic interventions include clipping, contact thermal coagulation with or without the combined use of dilute epinephrine injection, band ligation, and hemostatic topical powders/sprays. However, endoscopic clipping, with or without epinephrine injection, may be preferred to avoid tissue injury that occurs with contact thermal coagulation therapy.

Recently, an over-the-scope clip system (OTSC®, Ovesco Endoscopy, Tubingen, Germany) consisting of nitinol alloy has shown to be safe and effective in managing GI bleeding.[147] In a large case series of 100 patients with GI bleeding managed endoscopically, the clinical success rate was significantly higher when OTSC was used as a first-line rather than a second-line treatment (8.2 versus 28.2 percent, p=0.009).[148]

Additionally, rebleeding rates were reduced with the use of OTSC placement as first-line rather than second-line therapy (4.9 versus 23 percent, p=0.008). However, further data to confirm the safety and effectiveness of OTSC are needed.

Colonic Dieulafoy lesions

Colonic Dieulafoy lesions are effectively managed endoscopically in the majority of patients using epinephrine injection, endoscopic clipping, or thermocoagulation.[70] However, only few cases and no randomized trial have been published in the literature. Angiographic embolization or surgery may be required when bleeding lesions are refractory to endoscopic interventions.

Rectal tumors

Palliative treatment for locally advanced and unresectable bleeding rectal tumors includes ablation with neodymium yttrium argon garnet (Nd: YAG) laser. Control of bleeding is usually achieved after 2 to 5 laser sessions with durable response.[149] However, it is less effective in the case of circumferential and long tumors. Side effects are reported in up to 15 percent, mainly due to perforation, rebleeding, fistulas, and stenosis. APC has been recently proposed as an alternative to laser therapies because of its lower cost, feasibility, and efficacy for bleeding control. Due to its minor depth of penetration through colonic tissues, it provides an effective superficial coagulation and lowers the risk of perforation than the available laser therapies. However, no studies comparing APC versus laser therapy have been reported. Further endoscopic techniques including electrocoagulation, photodynamic therapy, cryotherapy, and injection of alcohol and sclerosing agents have been described, however, due to the higher adverse effects and complications reported, these treatment modalities are not recommended.[149] Finally, palliative radiotherapy has been

shown to be effective in achieving bleeding control without major toxicity in patients with limited life expectancy, data report bleeding control in up to 100 percent.[150] However, the lack of both prospective studies and the great variability of the prescribed radiotherapy dose among studies, make standardization of palliative radiation protocols difficult.

Non-endoscopic treatment of acute LGIB

Novel and sophisticated endovascular diagnostic and therapeutic options have become widely available in the management of lower GI hemorrhage. Patients with LGIB in whom endoscopic attempts have failed to identify and/or treat the source of bleeding, and patients with massive bleeding with positive CTA are candidates for endovascular intervention. Accurate localization of the bleeding source is key for successful endovascular therapies.

Transcatheter arterial embolization (TAE)

TAE is the treatment of choice following positive CTA and in hemodynamically unstable patients with active hemorrhage in whom colonoscopy has failed to localize and/or treat the source of bleeding. Depending on the suspected anatomical localization of the bleeding vessels, an angiographic catheter is positioned in the superior mesenteric artery (SMA), or inferior mesenteric artery (IMA) main branch and further advanced to the bleeding tributary. The angiographic catheter should be placed as close as possible to the bleeding point during the procedure.[151] Embolization as distal as possible is recommended to reduce the risk of postembolic infarction. The target artery of embolization for LGIB in several studies is the vasa recta or the marginal artery in some difficult cases.[152-154]

Several materials can be used for TAE and include coils, glue, onyx, Gelfoam® Compressed Sponge, polyvinyl alcohol particles (PVA), and Amplatzer™ Vascular Plug. The choice of material for embolization depends on the location of the bleeding site, and the experience and preference of the interventional radiologist. However, coils and PVA particles larger than 250 μm are most commonly used for LGIB. [155-157]

Coils are available in different sizes and shapes allowing for adaptation in almost any vessel. After placement, coils are easy to visualize under fluoroscopy and newer types can be removed after they are deployed. Moreover, they are radiopaque and may therefore be more accurately placed in target vessels. Superselective embolization using coils has shown to be effective and safe with satisfactory long-term results.[158-159] A technical success rate was achieved in 67 percent (26/39) of patients presenting with colonic hemorrhage undergoing transcatheter coil embolization. Early rebleeding was detected in 3 out of 26 patients. Long-term follow-up (mean 33 months) revealed an additional 4 patients (4/26) with late rebleeding and two of these patients were managed surgically. No adverse events were reported.[160]

Additionally, Ahmed et al. reported a technical success in 16 out of 20 patients (80 percent) undergoing embolization with coils for colonic hemorrhage; the remaining three patients were surgically treated while one patient remained stable and did not require further intervention. The long-term follow-up (mean 72 months) revealed rebleeding in 4 patients, and ischemic complications in 3 patients. Thirteen patients died from causes unrelated to procedure and to the bleeding event, most patients had multiple comorbidities and poor physiological reserve.[159]

Severe complications such as rebleeding or coils migration are rarely reported. In a large cohort of patients undergoing TAE for GI bleeding, 11 of 1415 patients had an extravascular coil found on endoscopic examination during the follow-up period. However, rebleeding following extravascular coil migration or major complications were not observed.[161]

TRUFILL®N-butyl cyanoacrylate (n-BCA) (Cordis, Miami, Florida) is an alternative to microcoils, is a permanent liquid embolic agent approved by the U.S. Food and Drug Administration in 2000, and recently used for the treatment of GI bleeding. n-BCA can be inserted through a smaller catheter than typically used for standard microcoils or gelatin sponge, thus more peripheral delivery is possible. It typically requires a single injection to achieve permanent vessel closure regardless underlying coagulopathy. Additionally, the reported rebleeding rates are lower compared with coils or particles (4 to 15 versus 0 to 26 percent).[162-163]

However, n-BCA has some major drawbacks: high costs, steep learning curve, fast gluing, reflux, possible adherence of catheters, and the inability to direct the flow of the embolic agent to the bleeding point.

In a recent metanalysis of 440 patients including 179 with LGIB and 259 with UGIB, TAE with n-BCA was shown to be safe and effective with a high clinical success rate and low risk of major complications.[164] In the LGIB group, diverticulosis was the most common cause of bleeding. Superselective embolization was performed with n-BCA alone in 92.6 percent of patients (162 of 175) and in combination with other agents (such as coils or gelatin sponge particles) in 7.4 percent (13 of 175). Four patients (2.2 percent) experienced technical failure as a result of an inability to select the target vessels with the microcatheter. The pooled clinical success for the 259 patients with UGIB and for the 175 with LGIB in whom technical success was achieved were 82.1 percent (95 percent CI, 73.0 to 88.6 percent) and 86.1 percent (95 percent CI, 79.9 to 90.6 percent), respectively. Major complication rates in the 259 patients with UGIB and in the 175 with LGIB were 5.4 percent (95 percent CI, 2.8 to 10.0 percent) and 6.1 percent (95 percent CI, 3.1 to 11.6 percent), respectively. Coagulopathy, the site of bleeding, and clinical failure were independent predictors of 30-day mortality.

Another potential agent, the ethylene-vinyl alcohol (EVOH) copolymer, (Onyx™, Medtronic, Minneapolis, MN) is a nonadhesive liquid embolic agent that has become increasingly used. It is a plastic polymer dissolvable in a potent organic solvent (dimethyl sulfoxide). Lenhart et al. described a 100-percent technical success rate with the use of ethylene-vinyl alcohol copolymer in the setting of acute UGIB.[165] No procedure-related complication was recorded.

The main advantages of Onyx™ include the controlled release, high radiopacity and excellent visibility, progressive solidification from the periphery to the center, nonadhesive properties, and high vascular penetration. The embolic agent is not carried by blood flow, but it is directly deployed by the operator with the pressure inside the syringe and acts independently of any underlying coagulopathy Therefore, the interventional radiologist may decide to stop the procedure at any time leaving the angiographic catheter in situ.[166] Moreover, no evidence of bowel ischemic damage requiring surgery has been reported.[167] However, the cost of the embolic agent might be prohibitively high.

Overall, success rates of TAE in patients with LGIB range from 88 to 96.4 percent.[152,155,162,168] Studies have found TAE to be safer than surgery in high-risk patients with a decrease in 30-day mortality rate.[168-169] Additionally, in a recent meta-analysis, diverticular bleeding was shown to be more amenable to embolization than other sources of bleeding, regardless of patient's age or the embolization technique used.[170] Superselective embolization, as first-line therapy, controlled diverticular hemorrhage in 85 percent of patients versus 50 percent of those in nondiverticular bleeding. Moreover, pooled analysis of the 6 studies demonstrated a significantly lower rebleeding rates within 30 days following superselective embolization for diverticular versus nondiverticular disease (15 versus 45 percent). However, the meta-analysis only included small retrospective case series and no randomized trial.

TAE is also associated with low rebleeding and ischemic complication rates.[18,160] The early rebleeding rate within the first 30 days following TAE ranges from 10 to 30 percent, likely due to a new site of hemorrhage or recanalization of the embolized vessel.[152,155,162,171-173] In a review of 20 studies reporting the use of angiographic superselective embolization for colonic bleeding, immediate hemostasis was achieved in 96 percent and early rebleeding occurred in 22 percent. Major complications, among which bowel ischemia was the most frequent, occurred in 17 percent.[18]

An institutional review over 7 years reported 32 patients undergoing superselective embolization for LGIB.[173] The embolic materials used consisted in microcoils (n=23), coils combined with particles (n=3) or gelfoam (n=1), particles alone (n=2), and gelfoam (n=1) and vasopressin (n=2). Clinical success was achieved in 97 percent (n=31) with only 1 patient (3 percent) developing ischemic complications. Early rebleeding was observed in 7 (22 percent). Of note, a preprocedure Hct level ≤20 and a lowered platelet level ≤140x109/L was associated with a significantly higher risk of rebleeding and was more likely to occur if the site of bleeding was located in the small bowel compared with the colon. Additionally, superselective embolization using a 1.7-Fr catheter and soft bare coils has shown to be particularly useful in 5 consecutive patients with acute small intestinal bleeding. Technical success rate was achieved in all patients (100 percent). No rebleeding or embolization-related complications were reported.[174]

Minor complications following TAE include arterial injury such as dissection, perforation, pseudoaneurysm, vasospasm, contrast dye reactions and nephrotoxicity, hematoma formation, thrombosis, and transient ischemic attacks.[175] Because of possible side effects or potential complications by the use of angiography and TAE, their use is limited in high-risk categories, particularly in the elderly patients and with comorbid conditions.

TAE for rectal tumors

TAE is considered a valid alternative for rectal bleeding tumor control when endoscopic attempts to manage hemorrhage have failed. The procedure is performed to minimize the vascular supply to the tumor by selectively embolizing tributaries. Selective embolization for bleeding rectal tumors is rarely been described in the literature. In a 20-year retrospective study, 34 patients underwent rectal artery embolization for treatment of massive rectal hemorrhage.[176] Etiologies included benign rectal ulcer (47.1 percent), rectal tumors (20.6 percent), postoperative bleeding (14.7 percent), radiation proctitis (5.9 percent), post-polypectomy bleeding (2.9 percent), and bleeding of unknown etiology (8.8 percent) In most patients (24/34) a single type of embolic agent was used (microcoils, gelatin sponge, or n-BCA). Technical success was achieved in almost all patients (33/34), one patient with a benign rectal ulcer rebled one day after embolization and the procedure was repeated with no further bleeding reported. Twenty-two patients achieved bleeding control (64.7 percent) and 11 patients (32.4 percent) experienced recurrent bleeding, among 11 patients who rebled, 2 underwent repeat endoscopic interventions with no further bleeding, 3 underwent repeat embolization of the rectal artery with control of the bleeding achieved, 3 underwent surgery, and 3 died from hypovolemic shock. One serious adverse event occurred in one patient who developed thrombosis of the right femoral artery.

Surgery

Surgical management for lower GI bleeding is considered the final therapeutic option, when all minimally invasive procedures, both radiological and endoscopic, have failed. Surgical intervention is usually required for patients whose underlying cause of bleeding is colorectal neoplasia, ischemic or ulcerative colitis refractory to medical therapy, or persistent bleeding from unknown source. Blind colorectal resection is not recommended. However, in the case of a massive ongoing bleeding from unknown etiology, subtotal colectomy with or without ileostomy may be necessary. Current data reported low rebleeding rates after surgical intervention.[177-180]

All patients undergoing colorectal resection for LGIB were identified in the American College of Surgeons National Surgery Quality Improvement Program (ACS NSQIP ®) Database, from 2012 to 2013, patients who underwent partial colectomy (n=364) were compared with the patients who underwent total colectomy (n=63).[181] Patients who underwent total colectomy were more likely to have received more than 4 units of RBCs prior to surgery than those with partial colectomies. Additionally, on univariate analysis, total colectomy was associated with a high risk of postoperative complications (ileus, cardiac, and renal complications) and mortality ($p<0.05$). An increased number of partial colectomies could reflect the high accuracy of modern diagnostic techniques in localizing bleeding sites and thus guiding resection.

There are no data comparing TAE versus surgery in the treatment of recurrent LGIB following endoscopic therapy. Further studies are warranted.

Conclusions

The management of patients with acute LGIB is challenging. Urgent colonoscopy (within 8 to 24 hours of admission) is the diagnostic test of choice in hemodynamically stable patients, as it has both diagnostic and therapeutic capabilities. CTA is the imaging modality of choice when evaluating a hemodynamically patient with active or severe hemorrhage, when colonoscopy is not feasible or cannot be performed in a timely fashion, and it is also preferred over colonoscopy in hemodynamically unstable patients and in whom bowel preparation cannot be safely performed. Following a positive CTA, TAE is the preferred treatment with choice of material for embolization based on the location of the bleeding site, and the experience and preference of the interventional radiologist. In the current era of increased access to advanced endoscopists, CT angiography, and advances in techniques and materials for selective and superselective TAE, surgery serves a limited role in the treatment of acute lower GI hemorrhage.

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CHAPTER 16

Management of Small Bowel Obstruction

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Small bowel obstruction, bowel ischemia, nasogastric tube decompression, gastrografin, diagnostic laparoscopy, adhesiolysis, bowel resection

Abstract

Small bowel obstruction (SBO) is a common surgical problem, comprising 15 percent of acute surgical gastrointestinal admissions.[1] The annual incidence of SBO in the United States is reportedly between 300,000 and 350,000.[1] SBO is largely a clinical diagnosis, although computed tomography (CT) is valuable for confirming the diagnosis, assessing bowel perfusion, and guiding operative planning. The decision to proceed with nonoperative versus operative management hinges on the clinical suspicion for ischemic bowel, which increases the mortality of SBO from 3 to 30 percent.[2] In addition to bowel rest and nasogastric tube (NGT) decompression, the administration of gastrografin, a water-soluble contrast agent, can be both diagnostic and therapeutic in the nonoperative management of SBO. Indications for surgical exploration, either laparoscopic or open, include failure to progress with nonoperative management and the development of bowel ischemia, either initially or later in the hospitalization. Ultimately, despite the feasibility of nonoperative management in many patients, SBO remains a surgical disease with attendant morbidity and mortality that should be managed primarily by surgeons.

Etiology and Differential Diagnosis

The **pathophysiology** of small bowel obstruction (SBO) fundamentally involves mechanical obstruction of the small bowel lumen. This leads to proximal small bowel dilation both from swallowed air and from the accumulation of intestinal contents and fluid secretions. Intestinal stasis promotes bacterial proliferation and fermentation, which further exacerbates small bowel dilation while increasing intestinal wall pressure.[1] Eventually, the wall pressure exceeds the capillary pressure, causing bowel ischemia. Alternatively, bowel strangulation occurs when the underlying etiology of mechanical obstruction itself (such as a single adhesion or intestinal volvulus) results in the physical compression of the bowel vasculature, leading to congestion and ischemia. Bowel ischemia, in turn, promotes intramural bacterial invasion, which leads to pneumatosis, portal venous gas, and finally, frank perforation as the final stage of irreversible bowel ischemia, also described as bowel infarction.[3]

Table 1. Causes of small bowel obstruction

Etiology	Percentage*
Adhesions Postsurgical Congenital Post-inflammatory/Post-infectious (peritonitis, diverticulitis, pelvic inflammatory disorder, and others)	67–74%
Hernia External hernia (femoral, inguinal, umbilical, ventral) Internal hernia (obturator, paraesophageal, transmesenteric/omental)	2–8%
Neoplasm Extrinsic compression Primary small bowel neoplasm Metastatic lesion to small bowel	5–13%
Inflammatory Bowel Disease (Crohn's disease)	4–7%
Other Radiation enteritis Gallstone ileus Foreign body Volvulus Intussusception Sclerosing mesenteritis	4–12%

*Data come from Miller G, Boman J, Shrier I, Gordon PH. Etiology of small bowel obstruction. *Am J Surg*. 2000;180(1):33-36.

The differential diagnosis of abdominal pain in the setting of acute bowel dilation and obstipation includes several possible etiologies. Mechanical small bowel obstruction is an important consideration, particularly in the setting of isolated small bowel dilation with a possible transition point and absence of distal air (**Figures 1A, 1B**).[1] The etiology of SBO itself is variable (**Table 1**). Adhesions are the most common culprit, even in patients who have not undergone abdominal surgery. Within the differential of SBO, the possibility of a closed-loop obstruction or a Richter hernia (incarceration or strangulation of only part of the bowel wall) should be considered.

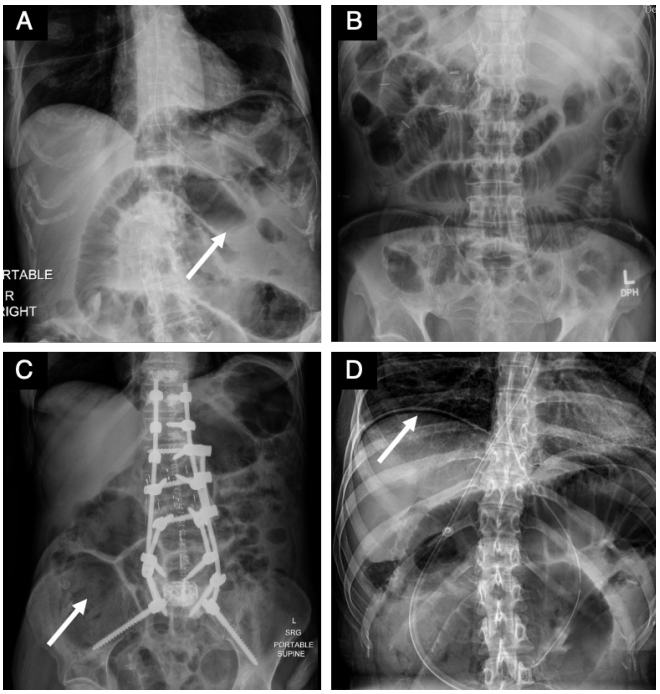

Figure 1. The abdominal radiograph is an important tool in the diagnosis of SBO

(A) Upright abdominal radiograph shows dilated loops of small bowel with air-fluid levels (*arrow*), most consistent with small bowel obstruction. (B) Abdominal radiograph shows dilated loops of small bowel without air-fluid levels, consistent with small bowel obstruction versus ileus. (C) Severe cecal (*arrow*) and colonic dilation without significant small bowel dilation after spine surgery, consistent with colonic pseudo-obstruction. (D) Dilated small bowel with free air under the right diaphragm (*arrow*), consistent with perforation.

Functional obstruction due to ileus is often confused with mechanical obstruction. Most commonly, postoperative ileus is due to intestinal hypoperistalsis or aperistalsis resulting in secondary bowel dilation and the inability to pass flatus.[1] Opioids and anticholinergic medications can interfere with intestinal muscle contraction while increasing

anal sphincter tone, leading to small bowel ileus or colonic pseudo-obstruction (Ogilvie syndrome).[1] As both conditions are due to decreased or uncoordinated peristalsis throughout the small bowel or colon, respectively, there is no transition point, distinguishing these from a mechanical SBO. Both ileus and colonic pseudo-obstruction can be exacerbated by electrolyte disturbances, neurologic disorders, and transabdominal surgery. In particular, spine surgery via an anterior approach is commonly associated with postoperative colonic pseudo-obstruction or ileus (**Figure 1C**).[4]

Colonic obstruction is distinguished from isolated SBO by the presence of a colonic mass or transition point. If the patient has an incompetent ileocecal valve, which allows air and fluid to flow retrograde into the small bowel, then functionally both their small bowel and colon will be obstructed. Finally, acute mesenteric ischemia can lead to bowel dilation and should be considered in the differential diagnosis. However, ischemia is the primary event as opposed to mechanical obstruction.[1]

Clinical presentation

The clinical presentation of SBO is variable. Patients commonly present with a combination of abdominal pain, nausea, emesis, obstipation, and constipation.[1] Bowel wall distension can be quite painful, and reported abdominal pain ranges from colicky or cramping to acute or sharp. Peristalsis persists despite mechanical obstruction, leading to a sensation of crampy, intermittent pain, as each peristaltic wave exacerbates bowel distension.[3] Eventually, bowel dilation becomes so severe that peristalsis ceases, and the pain becomes constant.[3]

Many patients present with nausea or emesis**.** The character of the emesis can provide clues to the level and chronicity of obstruction. Nonbilious emesis suggests a gastric outlet obstruction or obstruction in the first portion of the duodenum. Alternatively, bilious emesis results from obstruction distal to the Ampulla of Vater. Feculent emesis is an indication of long-standing or distal obstruction, while bloody emesis suggests gastrointestinal bleeding and requires a different treatment pathway .[1]

On physical exam, patients may be tachycardic or hypotensive secondary to hypovolemia from ongoing emesis, lack of oral intake due to pain, or sepsis from bowel ischemia. Fever may be due to bowel ischemia or underlying infection such as gastroenteritis that may ultimately prove to be the primary diagnosis. The abdominal examination is primarily focused on identifying peritonitis and incarcerated hernias. Guarding, rebound tenderness, abdominal rigidity, and abdominal wall skin changes are all concerning. Abdominal distension and tympany may be mild or moderate in proximal obstruction. Although bowel sounds are often described as "high-pitched and tinkling" in the early phases of SBO before becoming absent once peristalsis has ceased, they are neither sensitive nor specific in the diagnosis of SBO.[1,3] Immunosuppressed and obese patients may have none of the previous exam findings. Therefore, the provider should maintain a high level of suspicion for bowel ischemia when treating these patients.

Diagnostic work-up

SBO is fundamentally a clinical diagnosis. Although numerous studies dating back to the 1960s have demonstrated that identifying bowel ischemia based simply on physical exam or laboratory findings is unreliable, labs can still be useful.[5,6] On presentation, patients with suspected SBO should undergo standard laboratory evaluation. All patients should receive a complete blood count, basic chemistry panel, venous blood gas, and plasma lactate level. Leukocytosis with neutrophil predominance and lactic acidosis are concerning for bowel ischemia and possible sepsis. Lactate levels in the setting of bowel strangulation may be falsely normal in a closed-loop obstruction, as the venous return is excluded from the portal, and therefore systemic, circulation.[3] Prolonged emesis will result in a hypokalemic, hypochloremic metabolic alkalosis as well as a prerenal azotemia evidenced by elevated blood urea nitrogen and creatinine levels.[1] These laboratory findings are nonspecific. However, monitoring these laboratory values during resuscitation can be helpful in guiding continued resuscitation and making treatment decisions.[6]

Imaging is very helpful in guiding the clinical management of SBO. If the patient's condition is unstable, it should be stabilized with goal-directed fluid resuscitation, intravenous (IV) antibiotics, and vasopressors as needed prior to imaging. If the clinical suspicion for SBO is high, patients should be treated with bowel rest and NGT decompression pending imaging.

The abdominal radiograph is an important tool in the diagnosis of SBO. Small bowel dilation greater than 3 cm, decompressed distal bowel loops, and air-fluid levels are all indicative of SBO and can all be visualized on an abdominal radiograph (**Figure 1**).[3] Free air secondary to a perforation will also be evident (**Figure 1D**). Ideally, the abdominal radiograph is obtained with two views: dependent (supine or prone) and nondependent (upright or lateral decubitus). The sensitivity of a two-view abdominal radiograph for SBO ranges from 60 to 93 percent.[7] Free air on an abdominal radiograph is sufficient evidence for the surgeon to proceed with operative exploration to treat perforated viscous.

Abdominal CT is the most useful tool in identifying SBO, with a sensitivity of 94 percent, specificity of 96 percent, and accuracy of 95 percent in detecting SBO.[8] The negative predictive value of CT for SBO is nearly 100 percent; therefore, a negative CT can effectively rule out SBO.[3] IV contrast is helpful in assessing bowel perfusion

and is recommended unless the patient has a strong contraindication for its use. Even in the setting of allergy, it is recommended to treat the allergy, and, if possible, proceed with administration of IV contrast. Water-soluble oral contrast (such as gastrografin) instilled via the NGT can be helpful in identifying the level of obstruction. However, it is not well tolerated, can obscure IV contrast, and can lead to aspiration when the patient is supine in the CT scanner.[1] Therefore, it is contraindicated in the emergent setting.

CT, when available, is critical in diagnosing mechanical obstruction as well as bowel ischemia. With regard to mechanical obstruction, small bowel dilation greater than 3 cm and identification of a transition point without colonic dilation is diagnostic of SBO (**Figure 2**). Additional radiographic evidence of SBO includes mesenteric swirling (**Figure 3**) due to twisting of the bowel and mesentery and fecalized small bowel due to water absorption of stagnant small bowel content. CT demonstrating dilated small bowel in between two transition points is diagnostic of a closed-loop SBO if both transition points are intra-abdominal.[1] Alternatively, two small bowel transition points within a hernia sac suggest closed-loop obstruction within a culprit hernia.

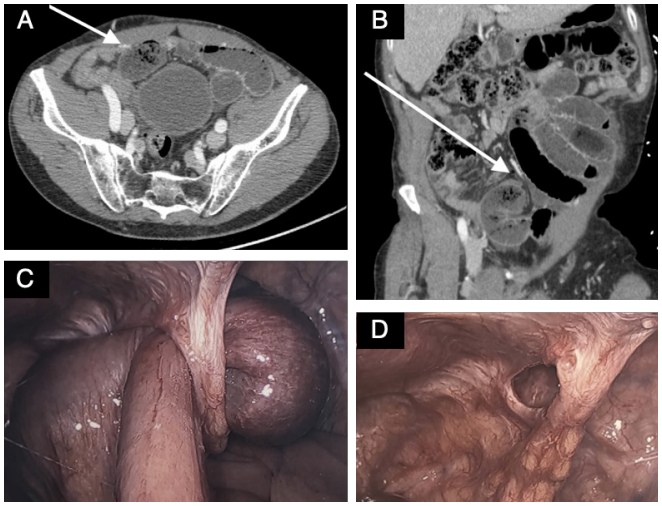

Figure 2. Small bowel obstruction caused by a single adhesion without evidence of bowel ischemia

Axial (A) and coronal (B) CT show transition point (*arrows*) in the right lower quadrant with proximal small bowel fecalization. (C) After failure of gastrografin to reach the colon by 24 hours, diagnostic laparoscopy revealed a single adhesion causing obstruction of a segment of small bowel. (D) The bowel was reduced, and the adhesion was lysed. Postoperatively, the patient had prompt return of bowel function.

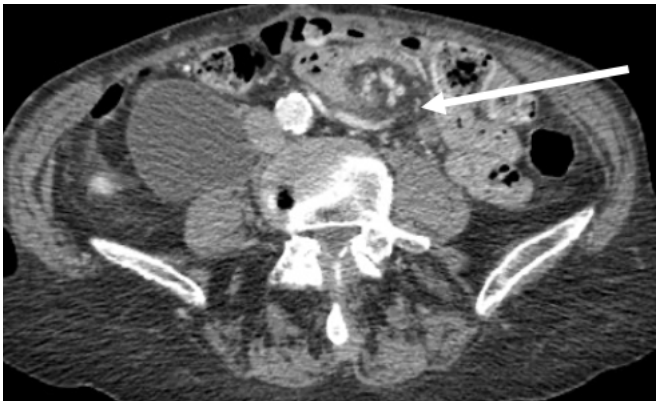

Figure 3. Midgut volvulus of the entire small bowel with mesenteric swirling (*arrow*)

On exploration, the volvulus was due to a fibrous band extending from the antimesenteric border of the proximal jejunum to the base of the mesentery of the descending colon.

CT can identify bowel ischemia with a sensitivity of 56 percent and specificity of 94 percent.[6] The following signs are concerning for bowel ischemia: decreased bowel wall enhancement, bowel wall thickening, pneumatosis, mesenteric venous congestion, mesenteric edema or hemorrhage, mesenteric venous gas, portal venous gas, free fluid in the abdomen or hernia sac, and free air (**Figure 4**). A retrospective review of 192 adult patients who underwent surgery for SBO over an 11-year period concluded that reduced bowel wall enhancement on computed tomography (CT) scan, peritoneal signs on physical exam, and leukocytosis were independently predictive of bowel ischemia.[6] Ultimately, the diagnosis of ischemia in the setting of SBO requires careful interpretation of all available data.

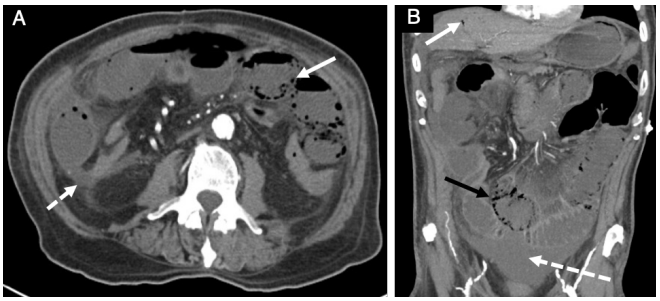

Figure 4. Small bowel obstruction with evidence of bowel ischemia (A) Axial CT shows small bowel pneumatosis (*solid arrow*) and mesenteric edema (*dashed arrow*). (B) Coronal CT shows portal venous gas (*solid white arrow*), small bowel pneumatosis (*solid black arrow*), and intra-abdominal free fluid (*dashed arrow*). The patient underwent exploratory laparotomy which revealed a closed-loop obstruction due to an adhesive band. The patient required small bowel resection at both the index operation and second-look laparotomy. The patient was left with approximately 70 cm of small bowel and went on to develop short bowel syndrome.

Management of Small Bowel Obstruction: Nonoperative

Nonoperative management of SBO is successful in up to 85 percent of patients with obstruction due to adhesive disease.[9,10] The crux of the clinical decision therefore becomes the determination of which patients are candidates for nonoperative management. Patients must be hemodynamically stable and have resolved their leukocytosis and acidosis after appropriate resuscitation to be appropriate for nonoperative management.[3] Nonoperative management is inappropriate for patients whom the surgeon suspects may have an internal hernia, neoplasm, peritonitis, closed-loop obstruction, or ischemic bowel.[11] The surgeon should understand that although nonoperative management is associated with shorter hospital length of stay, these patients have slightly higher recurrence and shorter time to readmission than patients who undergo surgery for SBO.[11]

All patients with SBO, regardless of whether they have an indication for surgery, should have appropriate resuscitation as part of their initial management. Crystalloid is recommended over colloid.[12] A balanced electrolyte solution, such as Lactated Ringer, is indicated. Normal saline should be avoided because it can lead to acidemia.[13] After initial resuscitation, it is our practice to continue maintenance fluids in addition to replacing high fluid losses (for instance, NGT output) at a rate of 0.5 mL crystalloid for every 1.0 mL of output above 1000 mL. Placement of a urinary catheter for accurate measurement of intake and output can be helpful to guide resuscitation in these patients. During resuscitation and bowel decompression, electrolytes should be monitored daily and replaced because hypokalemia, hypomagnesemia, and hypophosphatemia may contribute to hypoperistalsis.[1] The following electrolyte goals are recommended: magnesium ≥2.0 mg/dL, phosphorous ≥3.0 mg/dL, and potassium ≥4.0 mmol/L.

No pharmacologic agents have been shown to hasten the resolution of SBO. However, opiates and anticholinergic medications may contribute to hypoperistalsis and therefore should be used judiciously. Oral naloxone may be considered in patients with high opiate requirements. However, there are no randomized controlled trial data showing benefit to its use in SBO.[14] IV antiemetics are important for symptom management and to decrease the likelihood of emesis and potentially life-threatening aspiration.

Bowel rest and decompression with an NGT are fundamental in the management of SBO. Oral intake increases the intestinal intraluminal pressure, thereby worsening pain and increasing aspiration risk. It also increases the metabolic demand of the small bowel, which may worsen ischemia. An NGT should be placed during the initial resuscitation efforts. We recommend a double-lumen tube with a minimum tubing caliber of 16 French. These tubes require frequent flushing to maintain patency. A nonfunctioning NGT in an obstructed patient can be dangerous. It acts to stent open both the epiglottis and the lower esophageal sphincter, putting the patient at high risk for aspiration. The dual-lumen NGT is designed such that the clear port suctions out the gastric contents, while the blue sump port is open to the atmosphere. The blue port allows air into the stomach to prevent the tip of the tube from suctioning against the stomach wall and rendering the tube nonfunctional (**Figure 5**). A properly functioning dual-lumen NGT with a sump port can be placed to low continuous suction, while a single-lumen NGT requires low intermittent suction to allow for the intermittent separation of the tube from the stomach wall.

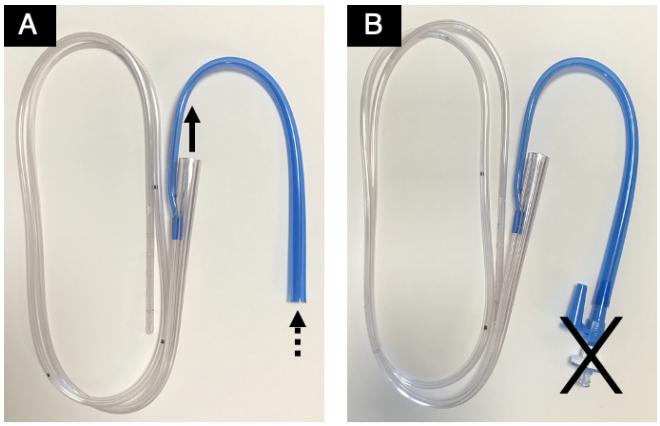

Figure 5. Nasogastric sump tube

(A) The clear port (*solid arrow*) is connected to low continuous wall suction and functions to suction out gastric contents. The blue sump port (*dashed arrow*) is open to the atmosphere to allow air into the stomach to prevent the tip of the tube from suctioning against the stomach wall. When troubleshooting a nasogastric tube, saline or water should be instilled through the clear port and air through the blue sump port. (B) It is the authors' preference to avoid use of anti-reflux filters (marked with X) given these will clog and prevent air passage through the blue port, rendering the tube nonfunctional.

A useful tool in the nonoperative management of SBO is the gastrografin challenge, which has diagnostic and therapeutic utility. Gastrografin is a water-soluble, radiopaque solution containing diatrizoate meglumine and diatrizoate sodium. Gastrografin is preferred to other contrast agents such as barium, which can cause a chemical peritonitis in the setting of perforation. Gastrografin is given orally or via NGT 24 to 48 hours after decompression depending on the patient's resuscitation requirements and ability to tolerate the contrast.[11] At our institution, the protocol is to administer 100 mL of gastrografin via the NGT prior to a 2-hour NGT clamp trial. If the patient develops nausea or emesis during that time period, the NGT is immediately placed back to suction. Abdominal radiographs are then obtained at 0, 4, 8, 12, and 24 hours after gastrografin administration. These radiographs can demonstrate the location of the contrast in the bowel over time, thus serving a diagnostic purpose (**Figure 6**). The hyperosmolar contrast can increase pressure across the obstruction while also promoting fluid shift from the edematous bowel wall to the bowel lumen, thereby serving a therapeutic role in promoting SBO resolution.[1,15] Studies have shown that the presence of contrast in the colon within 24 hours predicts resolution of SBO with a sensitivity of 92 percent and specificity of 93 percent.[15] If the contrast reaches the colon prior to 24 hours, no further radiographs are necessary. Conversely, failure of the gastrografin to reach the colon by 24 hours is an indication that nonoperative management has failed.

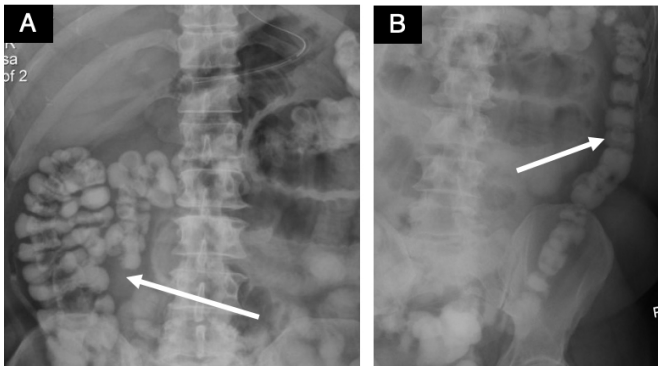

Figure 6. Gastrografin trial

Four hours after administration of 100 mL of gastrografin via an NGT, abdominal radiographs show gastrografin in the (A) right colon (*arrow*) and (B) descending colon (*arrow*) and rectum. The patient subsequently had return of bowel function and successful nonoperative resolution of the SBO.

Despite the success of nonoperative management for many patients presenting with SBO, SBO is fundamentally a surgical condition and should be managed primarily by surgeons on a surgical service when possible. A review of approximately 100,000 admissions for SBO revealed primary management on the medical service was an independent risk factor for longer hospitalization, greater inpatient costs, higher 30-day readmission rates following nonoperative management, and delay in necessary surgery.[16] Patients with SBO often have comorbidities, and it is appropriate to involve medical services in a supporting role. Ultimately, the nonoperative management of SBO demands serial reevaluation and requires the treating physician to have a nuanced appreciation for subtle changes concerning for strangulation which might necessitate urgent operative intervention.

Management of Small Bowel Obstruction: Operative

Indications for operative management

The indications for the operative management of SBO can be linked to the likelihood of bowel ischemia and failure of nonoperative management (**Figure 7**). If physical exam, imaging, and laboratory work-up are concerning for bowel strangulation, nonoperative management is inappropriate. In a series of 405 patients with mechanical SBO, the prevalence of bowel strangulation was 10.1 percent, with the likelihood of strangulation varying depending on the underlying etiology of the obstruction.[17] Although patients with SBO due to hernia had a strangulation rate of 33.3 percent, patients with adhesive SBO had a strangulation rate of only 9.0 percent.[17] Not only is mechanical obstruction due to suspected or known neoplasm, irreducible hernia, or closed-loop obstruction unlikely to resolve without surgical intervention, but suspicion for strangulation is higher in these groups, warranting urgent surgical intervention.[11]

Ultimately, the decision to proceed to the operating room with a patient with SBO requires careful weighing of all clinical factors. For example, patients with prior Roux-en-Y gastric bypass are at high risk for closed-loop obstruction due to an internal hernia at Petersen defect (mesenteric defect at the gastrojejunostomy) and often do not present with peritonitis or any of the other classic signs and symptoms of SBO. Therefore, clinicians should have a higher suspicion for strangulation and ischemia in patients with prior gastric bypass, even in the absence of concerning laboratory or imaging findings, and these patients warrant immediate surgical intervention. A retrospective review of patients with SBO demonstrated that greater than 500 mL of NGT output after 72 hours of decompression or persistent abdominal pain at four days were predictive of nonoperative management failure.[3,18] An exception to this is SBO secondary to Crohn's disease. Patients with Crohn's disease may require NGT decompression for up to several weeks during which time they can receive medical therapy that often leads to SBO resolution.[3]

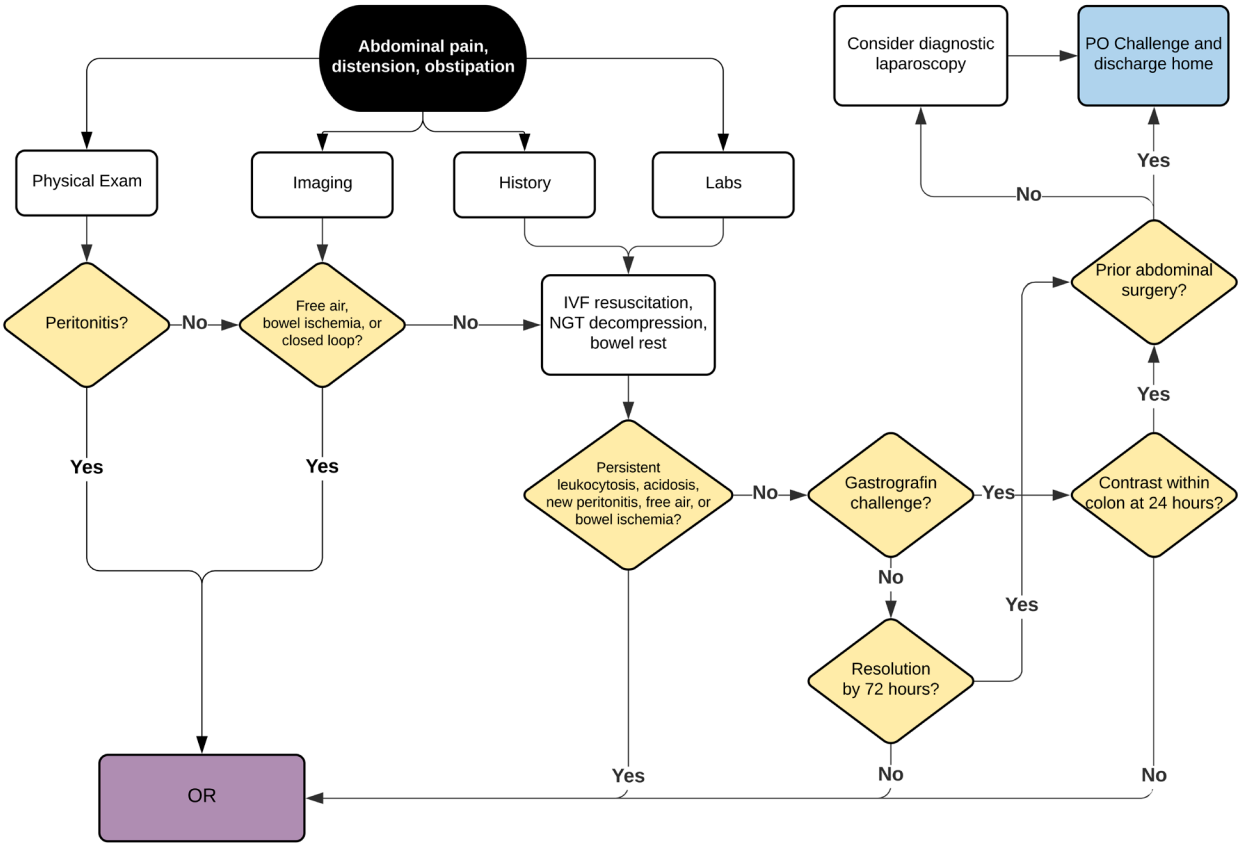

Figure 7. Overview of the management of small bowel obstruction

Although patients without prior abdominal surgery may have adhesions due to congenital abnormality or prior inflammatory or infectious processes, there is concern that SBO in this population is due to an undiagnosed neoplasm causing mechanical obstruction. As such, these patients should be explored with either diagnostic laparoscopy or exploratory laparotomy when they present with SBO unless there is a strong contraindication to surgery. A recently published systematic review and meta-analysis of six studies including a total of 442 patients aimed to assess the safety of foregoing surgery in patients presenting with SBO in the setting of no prior abdominopelvic surgery.[19] While de novo adhesions were the most common etiology of SBO in these patients (54 percent), 7.7 to 13.4 percent of patients without prior abdominal surgery had SBO due to malignancy. Thus, the authors of this study conclude that operative management should be pursued in these patients, supporting common practice.

Another group that deserves careful consideration are patients that present in the early postoperative period (defined as less than 6 weeks after abdominopelvic surgery) with SBO. Early postoperative SBO is commonly due to adhesions, although external or internal hernia, volvulus, anastomotic stenosis, or malignant obstruction should be considered (**Figures 8,9**).[20] It can be particularly difficult to distinguish early postoperative SBO from postoperative ileus. Although some patients may be managed nonoperatively, some may require operative intervention for resolution. In a prospective cohort study of 242 patients undergoing abdominopelvic surgery, 9.5 percent developed SBO within 30 days of surgery.[21] In this group, SBO was defined as the development of abdominal pain, vomiting, and radiographic findings consistent with intestinal obstruction after the initial return of intestinal function. SBO resolved with nasogastric decompression alone in 87 percent of these patients and 13 percent underwent reoperation.

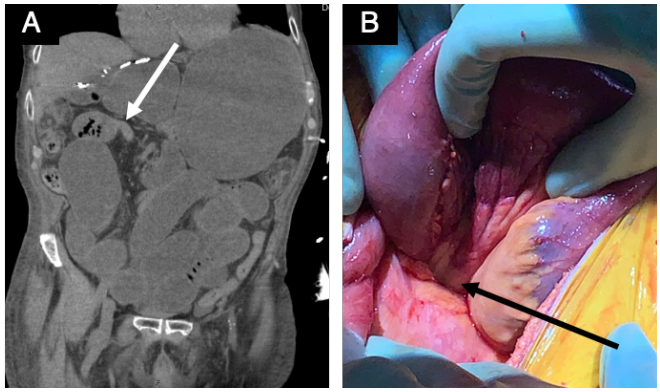

Figure 8. Small bowel obstruction caused by internal hernia due to mesenteric defect from prior bowel anastomosis

(A) Coronal CT (without contrast given the patient's renal function) shows a massively dilated stomach and small bowel with a transition point in the right upper quadrant (*arrow*). (B) The patient underwent exploratory laparotomy which revealed an internal hernia through the mesenteric defect (*arrow*) from the patient's prior jejuno-jejunostomy.

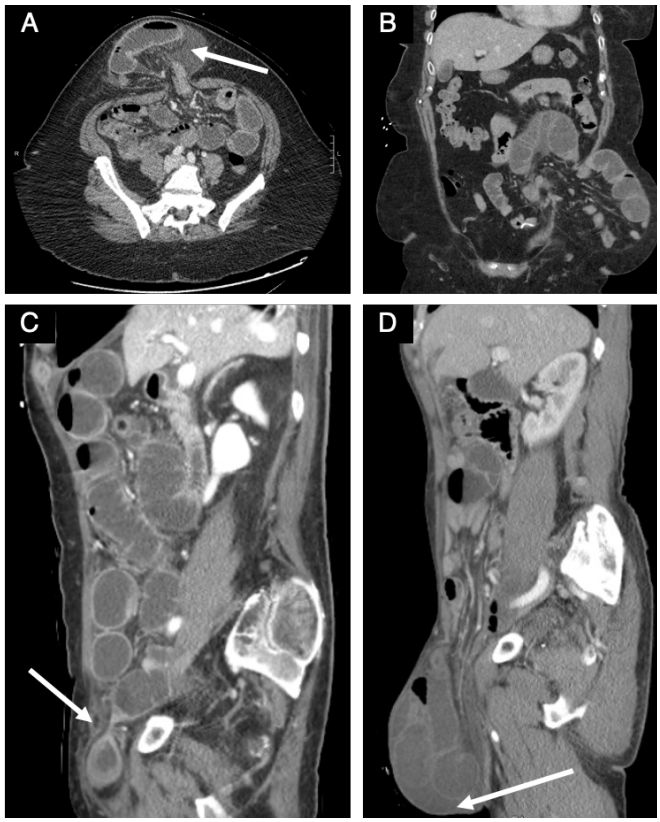

Figure 9. Small bowel obstruction due to incarcerated hernia

Various abdominal CTs show (A) SBO with transition point in an incarcerated ventral hernia with evidence of bowel wall edema and free fluid in the hernia sac (*arrow*) concerning for ischemia. (B) SBO due to an incarcerated parastomal hernia. (C) SBO due to an incarcerated inguinal hernia (*arrow*). (D) SBO due to a large inguinal hernia with free fluid in the hernia sac (*arrow*).

In the early postoperative period, the timing of return to the operating room is a delicate one, as the risk of iatrogenic injury in a postoperative, potentially hostile abdomen has to be weighed against the risk of developing bowel ischemia. In the immediate postoperative period, the risk of iatrogenic bowel injury is high because of dense, inflammatory adhesions that develop by postoperative days (POD) 10-14.[20] A retrospective review of 189 patients who underwent re-exploration for early SBO demonstrated a higher incidence of enterotomy in patients who had re-exploration between POD 14-42 as compared to POD 1-13.[20] This result suggests that the risks of reoperation after two weeks may outweigh the benefits in many patients.

Surgical approach

SBO can be managed via laparoscopic or open approaches, and the proportion of cases started laparoscopically has almost doubled from 17.2 percent in 2006 to 28.7 percent in 2013.[22] Laparoscopy may be attractive for hemodynamically stable patients with SBO in whom conservative management failed due to a single adhesive band (**Figure 2, page 164**). These cases are successfully managed laparoscopically 74 to 95 percent of the time.[3] However, it is often difficult to predict preoperatively which patients will have a single adhesive band. Successful laparoscopic approaches are associated with reduced length of hospital stay, rate of postoperative complications, and postoperative mortality.[1] However, laparoscopy in SBO is not without disadvantages. The rate of enterotomy during laparoscopic management of SBO has been reported to be 4.7 percent, with 1.3 percent of obstructive causes missed at the time of laparoscopy.[23] Significant bowel dilation can make laparoscopy challenging given poor visualization, as the dilated small bowel takes up any potential space in the abdominal cavity. There is a higher risk of iatrogenic injury when significantly dilated and edematous bowel is grasped with laparoscopic instruments. Indeed, it is recommended that only the mesentery or distal, collapsed bowel be handled with laparoscopic graspers. This makes it challenging to "run the bowel" to ensure that all culprit adhesions have been addressed. Regardless of approach, a complete lysis of adhesions may not be advised due to the risk of damage to otherwise normal, uninvolved bowel.[3]

Beginning an operation laparoscopically does not commit the surgeon to completing the operation minimally invasively. Published conversion rates from laparoscopy to laparotomy for SBO management range from 0 to 50 percent.[24] Several factors predictive of successful laparoscopic management have been identified.[24] Patients with fewer than two prior laparotomies, nonmidline prior laparotomies, adhesions secondary to prior appendectomy, single band adhesions, less than 24 hours of symptoms, no evidence of peritonitis, and increased surgeon experience are more likely to undergo successful laparoscopy. In a prospective, multicenter database

study of 537 patients from 1995-2006 who underwent laparoscopic management of SBO, 32 percent of patients required conversion.[23] More than half of these conversions were due to the inability to visualize the site of obstruction because of dense adhesions, whereas intraoperative complications and small target incisions for bowel resection together made up the remaining half. Although emergency operations (defined as surgery performed within 24 hours of hospital admission) had higher conversion rates, this did not result in significantly increased complication rates. Instead, conversion prompted by intraoperative complication was associated with higher postoperative complication rates as compared to preemptive conversion due to impaired visualization. In fact, multivariate regression showed that the only independent risk factor for postoperative morbidity was conversion to laparotomy in response to intraoperative complication.[23] Thus, the surgeon should not only proceed with great caution when beginning an operation for SBO laparoscopically, but also have a low threshold for conversion to laparotomy.

In both laparoscopic and open approaches, incision placement should be based on the site and reason for obstruction, as well as prior abdominal surgeries and scars. Generally, laparotomy for SBO is approached through a midline incision. This is also true in SBO due to hernia. However, the incision should be placed to allow for optimal access to the hernia sac and fascial defect while avoiding bowel adhered to the prior incision, which may require beginning the incision superior or inferior to the hernia itself. In the laparoscopic approach, abdominal entry with the open Hasson technique is recommended in order to have direct visualization upon entry into the abdomen so as to avoid injury to the distended bowel. A 10-12 mm vertical incision directly above or below the umbilicus is recommended for the Hasson trocar, as this allows for extension to a midline incision if conversion to laparotomy is required. We recommend starting the diagnostic laparoscopy with two additional 5-mm ports that are triangulated to the suspected transition point. Careful review of the preoperative CT scan is useful to determine the most likely location of the transition point and guide port placement. Additional laparoscopic ports can be added as needed depending on operative findings.

The goal in the management of SBO is to identify patients who need an operation and to perform that operation before the development of irreversible bowel ischemia that would necessitate a bowel resection. However, the surgeon should be prepared to perform a bowel resection if the patient is found to have frankly necrotic bowel or a perforation. A retrospective review of nearly 900 patients with SBO between 2003 and 2007 showed that increased time to the operating room was associated with a higher incidence of small bowel resection.[25] Therefore, if there is any concern for bowel ischemia, it is appropriate to proceed urgently to the operating room to avoid progression to infarction requiring resection. Although iatrogenic enterotomy can potentially be repaired primarily, perforation due to ischemia necessitates resection to ensure the healthy edges needed for appropriate healing. In the setting of injury, a defect greater than 50 percent of the small bowel circumference requires resection and anastomosis as primary repair may narrow the bowel. However, if the injury is less than 50 percent of the bowel circumference, then primary repair in two layers may be appropriate depending on the appearance of the tissue.[3]

The goal in any operation for SBO should be to preserve as much bowel as possible. The normal length of small bowel ranges from 300 – 800 cm, and adults with less than 180 cm of small bowel are at risk for developing short bowel syndrome.[26] An intact ileocecal valve is equivalent to an additional 50 cm of small bowel, as it functions to increase intestinal transit time.[26] Patients with less than 120 cm of intestine without colon or less than 60 cm of intestine with colonic continuity are likely to need permanent parenteral nutrition.[26] Short bowel syndrome has been reported to occur in up to 15 percent of patients who undergo intestinal resection.[27] While 75 percent of these cases are due to massive small bowel resection during one operation, the remaining 25 percent of patients develop short bowel syndrome after repeated resections.[27] As such, the authors recommend a consistent practice of measuring the entirety of the patient's small bowel as well as the amount resected during every operation and documenting this clearly in the operative report.

Special consideration should be given to bowel that appears to be marginally viable with potentially reversible ischemia, especially in patients for whom bowel preservation may be critical. Visual inspection alone is deceptive, as the serosa may appear dark due to transient venous insufficiency. A mesenteric pulse may be absent due to hypotension or vasospasm.[28] Consequently, additional methods are needed to assess bowel perfusion. Among these is perfusion fluorometry, an excellent tool that continues to evolve. Traditional perfusion fluorometry involves the IV administration of fluorescein followed by illumination of the bowel with an ultraviolet light (such as a Wood's Lamp).[28] However, fluorescein cannot be used for repeated measurements because it stays in the tissues for over 24 hours. Laser fluorescence angiography (LFA) with indocyanine green (ICG), a fluorescent dye, is being used more frequently, but may not be available at every institution.[28] ICG remains within the vasculature and is rapidly cleared by the liver and excreted in the biliary tract. Thus, ICG allows for repeated measurements. In a retrospective study of 638 patients undergoing oncologic colorectal resection, use of LFA added only an average of seven minutes to the operative time. Inadequate perfusion at

resection margins necessitating wider resection was found in 13.9 percent of patients in whom LFA was used. Ultimately, anastomotic leak was lower in the LFA group (3.5 percent) compared to the control, non-LFA group (7.5 percent),[29] highlighting its use as an important tool in the assessment of bowel perfusion.

In the setting of marginal-appearing bowel, a second-look laparotomy in 24 to 36 hours should be considered. When a second-look laparotomy is planned, the abdomen may be left open or closed at the conclusion of the index operation. If the bowel appears ischemic but potentially viable, the decision to proceed with a second look can be made before bowel resection. Alternatively, if there is a clear area of necrotic bowel flanked by marginal bowel, the second look can proceed after resection to assess whether additional bowel needs to be resected. Supportive measures such as fluid resuscitation and hemodynamic normalization between the index operation and second-look laparotomy may lead to recovery of marginal bowel.[30] In a retrospective review of 96 patients undergoing emergency general surgery and second-look laparotomy, more than half (n=55/96) required bowel resection exclusively in the index operation, while a third (n=18/96) required bowel resection at both operations, and only 4.2 percent (n=4/96) required resection exclusively in the second-look operation.[30] Thus, as the plan for second-look laparotomy is made due to surgeon concerns about intraoperative bowel viability, the second-look laparotomy should not be abandoned simply because the patient has improved clinically at the time when reoperation would take place.[31]

Postoperative management

The hallmark of postoperative management of small bowel obstruction is bowel rest and decompression until bowel function returns. If not done preoperatively, an NGT should be placed intraoperatively. The NGT should be kept in place until the output is <500 mL daily and the patient has return of flatus. The patient's intravascular volume status and electrolyte levels should be carefully monitored during this period. Special attention must be given to the patient's nutritional status, as this is critical for wound healing. Total parenteral nutrition should be considered if the total time without oral nutrition (pre- and postoperative) will exceed seven days. Particularly in patients with chronic SBO and prolonged periods of inadequate nutrition, it is important to be aware of possible refeeding syndrome and monitor plasma electrolytes.

Special Considerations in Small Bowel Obstruction

Malignant SBO warrants special consideration. Malignant SBO is diagnosed when there is narrowing of the small bowel with clinical evidence of obstruction in the setting of diffusely metastatic intra-abdominal cancer with peritoneal involvement and no reasonable expectation for a cure (**Figure 10**).[32] This differs from SBO caused by an underlying neoplasm, such as a solid tumor causing mechanical obstruction of the small bowel lumen, which is often treated surgically.

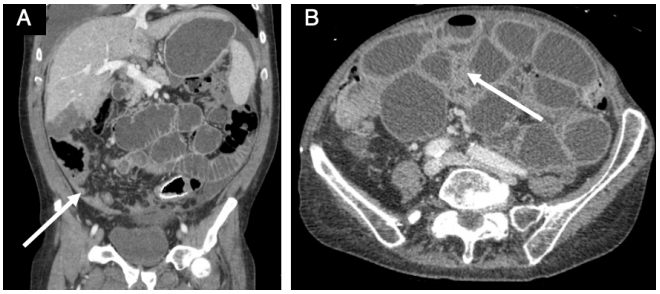

Figure 10. Malignant small bowel obstruction

(A) Coronal CT demonstrates malignant SBO in a patient with sigmoid colon cancer with peritoneal carcinomatosis (*arrow*). (B) Axial CT shows malignant SBO in a patient with metastatic ovarian cancer with thickened bowel due to diffuse peritoneal carcinomatosis (*arrow*).

A primary small bowel tumor or primary tumor external to the small bowel, abutting and compressing it, may be successfully resected, possibly curing the patient of their cancer and resolving their SBO. In contrast, symptom management remains the mainstay of treatment for malignant SBO, as this signifies a terminal phase of cancer for most patients and a palliative care team should be involved.[33] Goals of care discussions are paramount, especially before any invasive measures are considered. Medical management with NGT decompression and antimotility, antisecretory, and antiemetic drugs can provide patient comfort. Total parenteral nutrition can be considered based on shared decision-making with the patient, caregivers, and providers, although its benefit in patients with malignant SBO may be limited. If within the patient's goals of care, there are surgical options that can be discussed. Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy are not generally indicated in the setting of malignant SBO, though there may be some benefit in patients with peritoneal carcinomatosis and good functional status. Venting gastrostomy, proximal diversion, bowel resection with anastomosis, and intestinal bypass may provide some symptom relief, although it is difficult to predict the duration of relief. Ultimately, even for patients with malignant SBO presenting with a surgical emergency such as free air or clear bowel ischemia, a nonoperative approach may be considered if the overall disease prognosis and the patient's goals of care are not consistent with surgical intervention.

Another unique cause of SBO that deserves discussion is gallstone ileus. In gallstone ileus, the SBO is due to a gallstone that has become impacted in the small bowel after traversing a cholecystoenteric fistula (**Figure 11**). These cholecystoenteric fistulae generally result from pressure necrosis secondary to large gallstones pressing on the wall of the duodenum over time. Generally, if the gallstone is large enough to cause intestinal obstruction, then the obstruction will not resolve without surgical intervention. The primary goal of the operation is to remove the stone, thereby relieving the obstruction. The cholecystoenteric fistula should not be addressed at the index operation. Not only do the majority of cholecystoenteric fistulae close without treatment, but higher mortality and longer hospital stays have been reported for one-stage procedures.[34] Thus, surgical closure of the cholecystoenteric fistula should be performed at a second-stage operation only in those patients whose fistulae remain symptomatic.

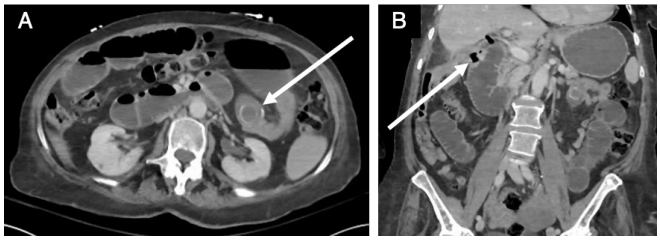

Figure 11. Gallstone ileus

CT shows SBO due to an impacted gallstone in the small bowel (A, *arrow*) which traversed a cholecystoenteric fistula (B, *arrow*).

In contrast to gallstone ileus, SBO due to Crohn's disease should be managed medically if at all possible. Patients with Crohn's disease are at high risk for SBO recurrence. With multiple lifetime operations, these patients are at high risk for developing short bowel syndrome. Depending on the etiology of the SBO in these patients, medical management may be successful. For example, SBO due to inflammatory strictures may be reversible with medical therapy, whereas SBO due to chronic or fibrotic strictures will likely require surgical intervention.[1] Imaging and a careful review of the patient's Crohn's treatment and surgical history can be helpful in delineating the etiology and informing appropriate management. Colorectal surgical specialists should be involved in these patients' care.

Outcomes

Overall, outcomes in SBO are favorable, although for most patients, intermittent obstruction can be a lifelong issue. Mortality is variable in SBO, ranging from 3 percent in simple obstruction to as high as 30 percent in patients with bowel necrosis or perforation.[2] The natural history of SBO varies, but many patients are at risk for recurrence.[35] With adhesive disease as the most common etiology, any surgical intervention to address SBO could lead to new adhesion formation which may contribute to another SBO in the future. Successful nonoperative management does not remove the culprit adhesions, which may become problematic again. Methods to reduce adhesion formation intraoperatively have been widely investigated, including anti-inflammatory agents, fibrinolytic agents, and liquid or solid barriers.[36] Hyaluronate-carboxymethylcellulose membrane (Seprafilm®) is a bioresorbable material that transforms into a hydrophilic gel, coating tissues during remesothelialization with the goal of preventing adhesion formation.[36] A prospective, randomized, double-blind, multicenter trial of 175 patients undergoing colectomy and ileal pouch-anal anastomosis with diverting-loop ileostomy showed dense adhesions in only 15 percent of patients who received Seprafilm compared to 58 percent of controls at the time of diverting-loop ileostomy takedown.[37] However, a systematic review and meta-analysis of 4,203 patients undergoing abdominal operations concluded that although Seprafilm does decrease adhesion formation after abdominal surgery, it does not reduce the incidence of SBO and is associated with increased risk of abdominal abscess and anastomotic leak.[36]

Regardless of whether patients undergo surgery to treat SBO, they are at risk of recurrence. A retrospective study of 410 patients admitted with SBO over a 10-year period showed 34 percent of patients treated nonoperatively and 32 percent of patients treated surgically were readmitted at a later date with recurrent SBO.[35] Although the overall readmission rates are similar, patients treated nonoperatively had earlier recurrence than those treated surgically, with a mean time to readmission of 2.0 years compared to 4.3 years.[35] Of those treated surgically, recurrence risk was variable based on operative findings. Lysis of a single adhesive band was associated with a 25 percent recurrence rate whereas complex lysis of matted adhesions led to a 49 percent recurrence rate.[35] SBO requiring small bowel resection was associated with a 22 percent recurrence risk.[35] Risk of recurrence increases as the number of prior admissions increases.

Comprising 15 percent of acute surgical gastrointestinal admissions, SBO remains one of the most common acute surgical presentations of patients to the emergency department.[1] Both general and acute care surgeons should be aware of the differential diagnoses and treatment options for these patients (**Table 2**). Many patients will require operative intervention. However, with the lifetime risks of short bowel syndrome and formation of new adhesions, a patient's candidacy for nonoperative management should be carefully considered. Wise surgical decision-making is paramount in the management of SBO in order to reduce its morbidity and mortality.

Table 2. Classic patient presentations with possible management

Clinical Presentation	**Imaging** **KUB** – SB diameter 4 cm, air-fluid levels	Laboratory Findings	Diagnosis	**Management**
63F with prior C-section with 1 day of nausea, distension, obstipation. AF, HDS. Abdomen soft, distended, tender without peritonitis.	**CT** – SB diameter 4 cm with TP in the RLQ, trace free fluid.	**WBC** – 8.3 **Lactate** – 2.0 **Cr** – 0.94 **Hct** – 43	SBO due to postoperative adhesion(s) (unable to confirm non-operatively)	Admission to surgical service, NPO, NGT decompression, IVF resuscitation, serial exams, gastrografin challenge
34M with remote Roux-en-Y gastric bypass with 2 days of nausea, distension, abdominal pain. AF, HDS. Abdomen soft, distended, tender without peritonitis.	**CT** – SB diameter 4 cm with TP in mid-abdomen, trace free fluid.	**WBC** – 8.3 **Lactate** – 2.0 **Cr** – 0.94 **Hct** – 43	Closed-loop SBO due to internal hernia	Admission to surgical service, NPO, NGT decompression, IVF resuscitation, urgent (within 6 hours) diagnostic laparoscopy
58M with ventral hernia after multiple prior exploratory laparotomies with 1 day of bilious emesis, severe abdominal pain. T38.7, HR115, BP 134/78. Large, firm, irreducible ventral hernia with overlying erythema, exquisitely tender, and with guarding.	**CT** – SB diameter 4 cm with TP in bowel-containing ventral hernia. Bowel within hernia has decreased wall enhancement, surrounding free fluid and mesenteric edema.	**WBC** – 14.7 **Lactate** – 4.6 **Cr –** 1.36 **Hct** – 49	Strangulated ventral hernia	Admission to surgical service, NPO, NGT decompression, IVF resuscitation, emergent exploratory laparotomy
67F without prior abdominal surgery with 3 days of nausea, distension, obstipation. AF, HDS. Abdomen soft, distended, tender without peritonitis.	**CT** – SB diameter 4 cm with TP in the RLQ, trace free fluid.	**WBC** – 8.3 **Lactate** – 2.0 **Cr** – 0.94 **Hct** – 43	SBO due to external tumor compression	Admission to surgical service, NPO, NGT decompression, IVF resuscitation, serial exams, diagnostic laparoscopy this hospitalization (consider even if resolution of SBO with nonoperative management)
27M with stricturing Crohn's disease and multiple prior admissions for SBO with 4 days of worsening abdominal pain, nausea, vomiting, and obstipation. AF, HR 110, BP 126/69. Abdomen soft, distended, diffusely tender without peritonitis. Multiple well-healed surgical scars.	**CT** – SB diameter 4 cm with TP in the terminal ileum. Small bowel wall hyper-enhanced and thickened. Trace free fluid.	**WBC** – 8.3 **Lactate** – 2.0 **Cr** – 0.94 **Hct** – 35	SBO due to stricturing Crohn's disease	Admission to medical service with gastroenterology and surgical consults, NPO, NGT decompression, IVF resuscitation, medical therapy (steroids, biologics), serial abdominal exams

Abbreviations: *AF*, afebrile; *BP*, blood pressure; *Cr,* creatinine; *CT,* computed tomography scan; *Hct,* hematocrit; *HDS*, hemodynamically stable; *HR,* heart rate; *KUB,* kidney, ureter, bladder (abdominal) radiograph; *NGT,* nasogastric tube; *NPO,* nil per os; *RLQ,* right lower quadrant; *SB,* small bowel; *TP,* transition point; *WBC*, white blood cell count.

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CHAPTER 17

Management of Acute Complications in Patients with Crohn's Disease

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Crohn's disease, acute bowel obstruction, intra-abdominal sepsis, intra-abdominal abscess, bowel perforation, intestinal hemorrhage, appendicitis, perineal sepsis

Abstract

Crohn's disease is a chronic and evolving inflammatory disease that causes acute complications requiring emergency multidisciplinary treatment. The most common complication, acute bowel obstruction, is frequently due to worsening inflammation of a diseased loop of bowel and usually resolves with anti-inflammatory medical therapy; however, in the long term, the intestinal wall becomes indurated with deposition of connectival tissue and surgical or endoscopic treatment of strictures may become necessary. Intra-abdominal sepsis can be due to abscesses, free bowel perforation, or severe colitis. Contained perforation with abscess formation can be managed with antibiotic therapy and percutaneous drainage, followed by elective resection of the underlying disease, if indicated, once the acute flare has resolved. Prompt resuscitation and surgical exploration is necessary for free perforations. Rescue therapy can be initiated in the management of severe colitis, but failure to improve or concern for free bowel perforation must be addressed with emergent surgical resection. Massive hemorrhage in Crohn's disease is rare and requires prompt resuscitation, localization, as well as definitive control through surgical, endoscopic, or angiographic means. Appendicitis in the setting of Crohn's disease requires resection that includes the extent of the ileocecal disease. Perineal sepsis due to fistulae and abscesses must be controlled with adequate drainage. In each situation, management is individualized based on the patient's clinical presentation and the location and type of disease.

Acute Complications

Crohn's disease (CD) is a chronic inflammatory bowel disease that can affect any part of the gastrointestinal tract from mouth to anus. It is characterized by transmural granulomatous inflammation, and it may affect discontinuous segments in the gastrointestinal tract. The disease location usually remains stable over the patient's lifetime, but the behavior varies in severity. Phenotypes include nonstricturing, nonpenetrating (for example, inflammatory), fibrostenotic, or penetrating disease. Symptoms evolve in a relapsing and remitting manner, but, ultimately, both disease severity and behavior may progress over the course of the disease, with 19 to 38 percent of patients showing stricturing or penetrating complications at the time of diagnosis, and 61 to 88 percent of patients developing these manifestations after 20 years of disease.[1]

The incidence of CD continues to increase worldwide. The incidence and prevalence of CD is greater in developed countries and is rising in developing countries. Incidence and prevalence are greater in urban areas than rural areas. Incidence is highest in Canada, Northern Europe, New Zealand, and Australia (10.6 to 29.3 per 100,000). Due to the chronic and incurable nature of the disease, as well as the improvements in maintenance therapy, prevalence is much higher than incidence, with the highest rates in Europe, Canada, and the United States (214 to 322 per 100,000).[2] The annual rate of hospital admissions is approximately 20 percent, with up to 80 percent of patients hospitalized at some point during the course of their disease.[2,3] Overall the need for surgery has decreased in the last six decades, but for the individual, the risk increases with duration of disease, with a risk of surgery of 16 percent, 33 percent, and 47 percent at 1, 5, and 10 years, respectively, after initial diagnosis.[4] Nearly one-third of patients who undergo surgery require multiple operations.[5]

Despite the trends towards reduced hospitalizations and surgical procedures in the era of biologic therapy, the incidence of surgical emergencies in CD has remained stable.[6] Acute surgical emergencies in patients with CD are associated with a high morbidity and mortality. Postoperative mortality rates for nonelective surgeries in CD have decreased, but remain significantly higher than the mortality rate following elective surgery (3.6 versus 0.6 percent).[6,7] Although the majority of acute complications of CD are managed nonoperatively, it is important to recognize those that require surgical management. The indications for emergency surgery include acute bowel obstruction, intra-abdominal sepsis due to abscess or free intestinal perforation, severe colitis, profound intestinal hemorrhage, appendicitis, and perineal sepsis.

Abdominal Complications

Acute bowel obstruction

Small bowel obstruction is the most common complication in CD requiring surgery, affecting 35 to 59 percent of patients with CD.[8,9] Most patients present with recurrent episodes of partial obstruction, rather than complete bowel obstruction. Inflammation and bowel wall edema result in obstruction. Over time, repeated inflammation leads to stricture formation secondary to fibrosis and scarring, and obstruction may occur due to acute inflammation in a stenotic bowel segment or, less frequently, due to intestinal angulations secondary to inflammatory adhesions of a normal loop of bowel to an adjacent phlegmon or abscess. Most obstructions occur in the small bowel. Gastroduodenal obstruction is rare, occurring in 0.5 to 13 percent of patients. Strictures also rarely occur in the colon, with an incidence of 5 to 17 percent, and should prompt suspicion of malignancy. Patients with gastroduodenal strictures present with postprandial fullness, early satiety, vomiting, and upper abdominal pain. Patients with obstruction of the small intestine present with nausea, vomiting, dehydration, crampy abdominal pain, bloating, obstipation, and constipation.

Patients with colonic obstruction may present without nausea and vomiting, but with bloating, distension, and abdominal pain, in addition to obstipation and constipation.

Initial management of bowel obstruction includes bowel rest, IV hydration, and nasogastric decompression in the presence of vomiting. Once an abscess has been ruled out or percutaneously drained, most patients improve with steroid therapy and initiation or modification of biologic therapy. Most obstructions resolve with this treatment over the course of 24 to 72 hours. If there is no resolution, the possibility of a fixed obstruction (such as a malignant obstruction) rather than an inflammatory obstruction must be considered. If there is a concern for malignancy, surgery should be performed following oncologic principles. Resection can be performed with or without reconstruction of intestinal continuity depending on the location, the clinical setting, the underlying pathology, and the findings at surgery.

Following resolution of the acute obstruction, up to 75 percent of patients require further endoscopic or surgical treatment of underlying stricturing disease. Endoscopic approaches are limited to areas that are endoscopically accessible - gastroduodenal, colonic, and terminal or neo-terminal ileal.[10] Endoscopic balloon dilation can be performed on short-segment (<5 cm) fibrotic strictures with little inflammation.[11–14] Technical success is achieved in 90 percent of cases, but fewer (70 to 80 percent) report short-term improvement in symptoms, 73.5 percent require repeated dilations, and 43 percent require surgery within

2 years.[15] Endoscopic stricturotomy using an endoscopic needle knife is a promising new development in the endoscopic treatment of strictures, reporting lower rates of progression to surgery on short-term follow-up, but longer-term data are still required.[16,17]

Surgical options include resection and strictureplasty. Patients with a single inflammatory, fibrotic, or mixed stricture with limited bowel involvement do well with resection and primary anastomosis. Strictureplasty in the small bowel is an option for fibrotic strictures in the setting of inactive disease without inflammation, particularly if multiple strictures are present with intervening normal intestine or when recurrent strictures develop in a patient with previous bowel resections at risk for short bowel syndrome.[18–22] Prior to performing a strictureplasty, careful examination of the stricture with biopsies of suspicious areas must be performed to rule out malignancy.[23]

Intra-abdominal sepsis

Intra-abdominal abscesses

Overall, 10 to 28 percent of patients undergoing surgery for CD present with an intra-abdominal abscess, and up to 40 percent have an associated fistula.[24–26] The majority of abscesses are caused by perforation of transmural bowel inflammation that creates secondary adhesions to adjacent structures, leading to walled-off collections. Depending on the location of the intestinal inflammation and the location of the perforation, the abscess may develop in an intraperitoneal, interloop, retroperitoneal, or intramesenteric location. Given that the most common location of active CD is in the ileocecum, most abscesses occur in the right lower quadrant.[25] Hematologic seeding of bacteria from diseased bowel may also lead to more remote abscesses, such as liver abscesses.

Presentation may appear similar to a flare of CD and depends on the location of the abscess. Patients may present with fevers and localized abdominal pain or symptoms related to the affected surrounding organs, such as urinary symptoms or vaginal symptoms. Retroperitoneal and iliopsoas abscesses may cause low back pain or pain radiating down the leg that worsens on flexion of the hip. Imaging with computed tomography (CT) or magnetic resonance imaging (MRI) is useful to diagnose the abscess and assess its size and accessibility for percutaneous drainage. CT or MR enterography provide additional information about the degree of associated luminal disease and possible associated fistulae or strictures. Ultrasound (US) is an option, but is operator dependent and is less effective at imaging deep pelvic or retroperitoneal collections.

For abscesses less than 3 to 4 cm in size, treatment with antibiotics is usually sufficient. Antibiotics should be chosen to cover enteric Gram-negative and facultative bacilli, enteric Gram-positive streptococci, and obligate anaerobic bacilli. Length of treatment is planned based on the severity of the disease and the patient's response to treatment, with more mild cases treated with 1 week and more severe cases treated with 2 to 3 weeks of antibiotics. While 60 percent of patients may show resolution with antibiotics alone, 50 percent of those patients will eventually require surgery due to the severity of the underlying disease.[27–30] Small abscesses without an associated fistula in patients who are naïve to immunomodulators or biologic therapy are the most likely to respond to antibiotic therapy alone.[28,31]

For larger abscesses greater than 4 cm in size, drainage of the abscess is indicated whenever feasible. Improved interventional radiologic techniques have increased the frequency and the success rate of percutaneous drainage. Percutaneous drainage is successful in 50 to 100 percent of cases depending on the indication for drainage, the technique, and the definition of failure.[29,30,32,33] However, 8 to 20 percent require more than one drainage procedure. Steroid use, Crohn's colitis, and multiple or multilocular abscesses have been shown to be associated with failure of percutaneous drainage.[32] Percutaneous drainage followed by anti-**tumor necrosis factor** (TNF) therapy has been shown to decrease the risk of abscess recurrence.[34,35]

Surgery may be avoided in a selected group of patients after percutaneous abscess drainage, but the majority will need definitive surgical treatment. Surgery should be planned at least 6 to 8 weeks after successful antibiotic treatment and/or percutaneous drainage. This time interval is necessary in order to decrease the degree of local sepsis and to optimize the patient's clinical and nutritional statuses, leading to a reduction in postoperative complications and stoma creation at the time of surgery.[36] Preoperative endoscopic and imaging workup is recommended to understand the extent of the disease and to evaluate for the possibility of underlying malignancy.

Free bowel perforation

Perforation may occur in the setting of a Crohn's flare, severe colitis, obstruction, or malignancy. Free perforation is rare, occurring in only 1 to 3 percent of cases.[37–41] More commonly, transmural inflammation leads to adhesions between the affected segment of bowel and neighboring structures, resulting in sealed perforations and focal abscesses (discussed in the previous section). Perforation may occur anywhere along the gastrointestinal tract; they most commonly occur in the colon, with colonic perforations accounting for 20 to 50 percent of cases.

The presentation of free perforation depends on the location of the segment that perforates and the degree of contamination. Patients may complain of diffuse abdominal pain or referred shoulder pain associated with fever and tachycardia. A high index of suspicion is required in patients on high doses of steroids that may mask the signs of peritonitis.

All patients who present with suspected perforation should be resuscitated and started on broad-spectrum antibiotics in anticipation of surgery. Bloodwork will usually reveal leukocytosis. Upright X rays of the chest may show free intraperitoneal air, but will not provide information about the site of perforation. Although CT scan may offer additional information, an unstable patient should not await additional imaging and should proceed to the operating room emergently. The history of the disease location and the inciting events prior to the perforation may provide additional clues as to the location of the perforation.

The surgical treatment of perforation depends on the degree of contamination, the etiology of the perforation, and, to a lesser degree, the location of the perforation. Additional factors influencing the operative strategy include nutritional status and chronic steroid use. In general, the loop of intestine harboring the perforation is resected. Primary anastomosis may be considered when the patient is hemodynamically stable, the degree of contamination is limited, and the location of the perforation is in the small bowel.[42,43] Perforation in the setting of a small bowel obstruction occurs immediately proximal to the stricture, and the resection should include both the perforation and the stricture unless doing so would sacrifice a large amount of intestine. If there is a significant amount of bowel involved, formation of a proximal stoma and distal mucous fistula allows for immediate control of the acute perforation and safely defers the treatment of the strictured bowel to a later time. Perforated segmental colitis at the site of active disease can also be resected with fecal diversion or, rarely, primary anastomosis. Pancolitis with colonic perforation requires a subtotal colectomy with diversion. Perforation in the setting of a distal large bowel obstruction usually occurs in the cecum; options include an ileocolectomy with ileostomy and mucous fistula (with plans for subsequent resection of the distal-obstructing intestinal segment and reestablishment of the intestinal continuity at a later date) or, alternatively, a subtotal colectomy to include both the area of perforation and the area of stricture. In the setting of extensive inflammation, proximal diversion and drainage may be performed with plans for subsequent resection and restoration of gastrointestinal continuity after the inflammatory reaction has receded.[39] Perforation in the setting of malignancy requires an oncologic resection.

There are two additional situations in which patients with CD may experience perforations but for which Crohn's is not the immediate cause: anastomotic dehiscence after surgical resection and free perforation after endoscopic manipulations. Depending on the clinical picture, an anastomotic dehiscence can be treated with (1) antibiotics and bowel rest, (2) resection of the anastomosis with stoma creation or, rarely, primary anastomosis, (3) resection and redo of the anastomosis with proximal diversion, or (4) proximal diversion alone.[44] Perforation that occurs during endoscopy depends not only on the area of perforation, but also on the underlying disease, the indication for endoscopy, and the degree of bowel preparation. Perforation that occurs during surveillance endoscopy with a complete bowel prep and a small tear allows for the option of suture repair or resection with primary anastomosis. However, if endoscopy was performed for a known or endoscopically discovered underlying surgical pathology, the perforation and the pathology should both be addressed at the time of operation when possible.

Severe colitis

Severe colitis, as originally described by Truelove and Witts in 1955[45] and more recently widely agreed upon by the American College of Gastroenterology,[46] the Association of Coloproctology of Great Britain and Ireland,[47] and the European Crohn's and Colitis Organization,[48] is defined as >6 bloody bowel movements per day with one additional sign of systemic toxicity, such as fever, tachycardia, anemia, or elevated erythrocyte sedimentation rate (ESR). This definition, with well-defined diagnostic criteria, allows for evidence-based practice standards and reported outcomes. The more inexact term "toxic colitis" or "fulminant colitis" is occasionally used to convey a more critical scenario with systemic toxicity, defined as >10 bloody bowel movements per day, associated with one or more of the following: hematochezia requiring blood transfusion, fever, tachycardia, abdominal tenderness and distension, and elevated ESR.

Severe colitis may occur as the initial presentation of the disease or at any time during the course of the disease. Although its incidence has decreased recently with better medical management, CD accounts for roughly half of all cases of severe colitis. Pathologically, the colon develops transmural vascular congestion and muscle atony, leading to dilation. The bowel wall thins, and deep ulcerations are often seen. Disease progression can lead to perforation. Narcotics, anticholinergics, hypokalemia, recent instrumentation with colonoscopy, or abrupt weaning of steroids or anti-inflammatory medications may trigger or exacerbate severe colitis and toxic megacolon.[49]

The diagnosis of toxic megacolon includes the clinical diagnosis of severe colitis and the radiographic evidence of colonic dilation greater than 6 cm.[50,51] The rate of colonic expansion and the clinical condition of the patient is more important than the absolute dimensions of the colon. Dilation may be segmental or diffuse. Segmental dilation is most commonly seen in the transverse colon, possibly due to its elevated location in the abdomen in a supine patient. Haustra may appear thickened early in the disease, and later the imaging may show loss of normal-appearing haustra and presence of "thumb printing" due to wall edema. Upright X rays may show air-fluid levels, as well as linear air parallel to the colon wall suggestive of submucosal ulceration and wall dissection. CT scans are important to rule out distal obstruction and evaluate for pneumatosis or pneumoperitoneum.

Expeditious evaluation and close monitoring with simultaneous initiation of supportive resuscitation and intensive medical therapy is important. Physical exam is typically notable for fever, tachycardia, abdominal tenderness and distension, signs of dehydration, hypovolemia, and hypotention, and mental status changes. Steroid use may mask signs of peritonitis. Laboratory testing includes complete blood cell counts to assess for anemia and leukocytosis, and metabolic panel to assess for electrolyte disturbances, notably hypokalemia and hypomagnesemia, and acute kidney injury. Nutritional status can be assessed with albumin and prealbumin, although albumin, as an acute phase reactant, may be falsely low in the setting of acute inflammation. Inflammatory markers, such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR), can be used to trend the response to therapy.

Concomitant infection with bacterial agents, such as *Clostridium difficile, Salmonella, Shigella, Campylobacter, or Yersinia*, viral agents, such as cytomegalovirus (CMV), or parasitic agents, such as cryptosporidium, must be evaluated. Colonoscopy is nearly always contraindicated due to the risk of perforation, but limited endoscopy will show pseudomembranes in *C. difficile* colitis, and biopsies will show inclusion bodies in CMV infections. *C. difficile* is associated with increased morbidity and mortality and is treated with oral vancomycin and intravenous flagyl.[52] CMV infection is present in more than 25 percent of patients with steroid refractory colitis and is treated with intravenous ganciclovir followed by oral valgancyclovir.[53–55]

Severe colitis is an emergent life-threatening complication of inflammatory bowel disease. Immediate and aggressive medical therapy should be initiated, while also preparing for the possibility of surgery. Fluid and electrolyte resuscitation should be initiated promptly. Blood transfusions should be given if needed. Broad-spectrum antibiotics are warranted because a thin and ulcerated bowel wall may allow for enteric organism translocation into the blood stream. Additionally, antibiotics may reduce the septic complications from impending perforation and peritonitis. Narcotics must be used with caution as they can worsen the dysmotility of the bowel and may mask worsening of the disease or the development of peritonitis. Anti-diarrheals are contraindicated, and nasogastric decompression is indicated for associated ileus.

Medical therapy with parenteral glucocorticoids or biologic agents may be initiated. Intravenous methylprednisolone 60 mg per day in divided doses or hydrocortisone 300 mg per day in divided doses can be used as the initial steroid dosing. Patients who improve can then be transitioned to maintenance therapy. Patients receiving glucocorticoids should start to show improvement within 2 to 3 days.[56] In patients who are stable, but not improving, the addition of rescue therapy with cyclosporine or infliximab has been shown to increase the number of patients who were able to avoid surgery.[57] Although no direct comparison trials have been published, infliximab is generally preferred due to the reduced toxicity, ease of administration, and the ability to be continued for maintenance therapy.[58] A favorable response to a biologic agent should be noted within 5 to 7 days.[56] The overall reported success of medical management varies widely from 6 to 75 percent.[49] Close monitoring for any signs of deterioration is necessary if nonoperative management is pursued, as toxic megacolon complicated by perforation that is managed conservatively carries a mortality rate of greater than 80 percent.[49]

Prompt surgery is indicated for patients with severe colitis and any sign of free perforation, peritonitis, or massive hemorrhage. Surgery is also indicated if there is no clinical improvement within 48 to 72 hours despite aggressive medical therapy in order to avoid progression of disease. Surgery done prior to perforation carries a mortality rate of 2 to 8 percent, whereas surgery done following perforation carries a mortality rate of greater than 40 percent.[49] Severe colitis is best managed with resection and diversion, taking into account the condition of the patient and the condition of the bowel.[51,59,60] Subtotal colectomy with end ileostomy allows for removal of the majority of the diseased intestine, avoids an anastomosis in a critically ill patient, and avoids the increased morbidity and mortality associated with pelvic dissection for a proctectomy. The distal rectosigmoid stump may be left at the pelvic brim, brought through the fascial closure and implanted into the subcutaneous space, or matured as a mucus fistula.[61] Data are limited supporting the placement of a transrectal or intraperitoneal drain to prevent dehiscence of the rectal stump or limit intraperitoneal contamination.[61] A more aggressive proctocolectomy unnecessarily increases the risk of pelvic dissection and denies the patient an ileorectal anastomosis at a later date. Alternatively, diverting-loop ileostomy has been advocated

as a less-invasive treatment in acutely ill patients followed by subsequent colectomy in a more stable situation;[62] however, because the colon remains in situ, it can result in ongoing bleeding and serve as a potential source of ongoing infection.[49]

Profound bleeding/hemorrhage

Mild gastrointestinal bleeding is common in CD; however, severe bleeding is a rare phenomenon, with an incidence of <1 to 6 percent.[49,60,63,64] Massive bleeding is often localized, caused by erosion into blood vessels within deep ulcerations in the bowel wall. Bleeding can occur at any age or disease duration. The average age at presentation is 30 years, suggesting that patients have had CD for a number of years prior to presenting with bleeding.[64]

As CD is almost always located distal to the ligament of Treitz, the presentation of massive hemorrhage is usually gross bleeding per rectum and hemodynamic instability. The patient must first be resuscitated and stabilized. Despite an unlikely gastroduodenal source, a nasogastric tube should be placed, and upper endoscopy should be performed if there is blood present in the nasogastric output. Similarly a colonoscopy should also be performed in order to visualize and possibly control lower gastrointestinal bleeding. Overall, the majority of cases the bleeding originates from the small bowel.

As CD is a segmental and potentially multisite disease, localization of the site of bleeding should be pursued with CT angiography (in the presence of ongoing hemorrhage) or with push enteroscopy or capsule endoscopy. The use of capsule endoscopy is limited due to concerns for capsule retention in the presence of strictures, but it can be useful in diagnosing obscure gastrointestinal bleeds. A nuclear medicine Technetium-99m-labeled red blood cell scan can localize slower bleeding. However, in most cases a definitive bleeding site is not identified and the bleeding is presumptively attributed to diffuse oozing from active inflammation.

Initial management includes supportive measures with hydration, transfusions as needed, and medications used to treat the inflammation of CD including mesalamine, 6-Mercaptopurine (6-MP), or infliximab. Endoscopy may be not only diagnostic but also therapeutic through the use of thermocoagulation, epinephrine injection, or placement of hemostatic clips. Superselective embolization is also an option for angiogram-positive gastrointestinal bleeding.

Surgery is indicated in patients who have ongoing massive bleeding. Preoperative localization of the hemorrhage is crucial as intraoperative localization is quite challenging and ultimately frustrating, even with intraoperative endoscopy. If bleeding is localized to an area in the small bowel, resection and primary anastomosis can be performed in a stable patient. If the bleeding is due to diffuse Crohn's colitis, a total abdominal colectomy may be necessary. If the rectum is healthy and the patient is stable, an ileorectal anastomosis may be performed. If the rectum is diseased or the patient is not stable, an end ileostomy can be created to leave the rectum to be addressed later. Ongoing bleeding from the residual rectum is rare and may be addressed with rectal packing, topical enemas, or endoscopic ablation.

The most challenging situation is represented by patients who require multiple blood transfusions in the absence of overt intestinal bleeding or who have a primary or recurrent hemorrhage without an identifiable source of bleeding. In these cases, the likelihood of successfully eradicating the source of hemorrhage through a "blind" intestinal resection must be weighed against the risk of recurrent bleeding and of creating short bowel syndrome in patients with extensive disease or multiple previous resections.

Appendicitis in Crohn's disease

Crohn's terminal ileitis is difficult to distinguish from acute appendicitis based on the similar history and physical exam findings of pain, tenderness, and fullness in the right lower quadrant. Localization of inflammation to the appendix or more diffusely to the terminal ileum and ascending colon with a CT scan can be extremely helpful. Overall, less than 1 percent (0.2 to 0.5 percent) of patients who present with a clinical picture consistent with appendicitis are diagnosed with CD.[65] A preexisting history of chronic gastrointestinal symptoms such as recurrent abdominal pain or diarrhea, coupled with a lack of fevers and with signs of chronic disease—such as weight loss, microcytic anemia, hypoalbuminemia, and hypoproteinemia—should raise the suspicion of CD rather than acute appendicitis.[66] Approximately 25 percent of patients with ileal CD and 50 percent of patients with colonic CD have appendiceal involvement.[67] CD isolated to the appendix is a debated condition that may be a milder variant of CD or a distinct entity of granulomatous appendicitis.[65,68,69]

In CD isolated to the appendix, without ileal or cecal involvement, appendectomy can safely be performed. [65] In patients with appendiceal CD, the risk of CD recurrence elsewhere in the bowel is 3 to 10 percent, occurring at an average of 4 years postoperatively.[70] These patients should be followed postoperatively with radiologic and endoscopic surveillance.

Medical management is advocated for an acute flare of ileocecal CD. Similarly, a trial of medical management is also indicated in patients with appendicitis and ileocolonic CD in an attempt to avoid an ileocecectomy. If surgery is required, an ileocecectomy should be performed in the presence of cecal inflammation given the higher risk of

dehiscence from the appendiceal stump and the higher risk of requiring further surgery following appendectomy. The risk of enterocutaneous fistula following appendectomy in patients with CD is 3.5 percent, but the risk is 34 to 58 percent in Crohn's patients with cecal involvement who undergo appendectomy. [65,70,71] In patients with appendicitis, a normal cecum and acute Crohn's terminal ileitis, the decision of performing an appendectomy or an ileocectomy is based on the severity of symptoms the patient has experienced related to the terminal ileitis. In the presence of mild or no symptoms, an appendectomy followed by medical treatment for the Crohn's terminal ileitis may be all the patient requires; in the presence of severe symptoms, limiting the surgical intervention to just an appendectomy will cause the patient to continue to have symptoms from their Crohn's disease, with 38 percent requiring resection within 1 year, 65 percent within 3 years, and 85 percent within 5 years even with appropriate medical management, In contrast, following ileocolic resection, symptoms related to Crohn's are abated and the majority of patients go on to prophylactic treatment with biologic therapy.

If a patient is taken to the operating room for suspected acute appendicitis and is found to have findings suspicious for CD, the entire small and large bowel should be carefully examined to determine the extent of the disease and active inflammation and rule out additional pathology. Intestinal resection(s) should not be performed if the intestinal segments appear inflamed without any septic complications of perforation or abscess. If the appendix looks normal, an appendectomy can be performed to avoid future diagnostic dilemmas as long as the ileocecum is not involved by CD. A formal inflammatory bowel disease (IBD) work-up should be performed and appropriate medical treatment should be initiated.

Perineal sepsis

Perianal abscesses and fistulae are common in individuals with CD. Perianal disease is present in 17 to 43 percent of all cases of CD.[72] It is usually associated with left-sided colon and rectal involvement, but isolated perianal involvement without luminal disease may be present in 5 percent of cases.[73,74] The etiology of perianal septic complications in CD may be infection in an anal gland that leads to microperforation at the dentate line and local sepsis, similar to that which occurs from cryptoglandular abscesses and fistulae-in-ano; alternatively, it may develop from extension of a deep ulceration in the distal rectum. Perianal septic complications are associated with frequent relapses requiring multiple surgical interventions.

Superficial perianal abscesses form in the subcutaneous space near the skin surface or in the intersphincteric space without cephalad extension above the dentate line. Deep abscesses form in the ischiorectal space or in the supralevator space. A fistula is an underlying tract communicating between the two epithelialized surfaces, such as the anus or rectum and the skin. More complicated fistulae may have multiple external openings, may communicate to adjacent organs, or may be associated with the presence of an anorectal stricture and/or active proctitis.

The most common presenting complaint of a perineal infection is perianal pain. Patients frequently complain of the acute onset of pain that is worsened by defecation or sitting, with or without spontaneous or elicited discharge of purulent fluid. Patients may or may not complain of systemic symptoms or fever. Complaints of fevers, worsening pain, or urinary retention are concerning for pelvic sepsis. Evaluation of the patient should include obtaining a history of their CD, any previous perianal disease or procedures, and any symptoms of incontinence.

Patients who present with systemic signs of sepsis – fevers, tachycardia, or hypotension – require immediate resuscitation and broad-spectrum antibiotics. Physical examination may be sufficient to visualize perianal swelling and erythema, and to palpate warmth and fluctuance. Perianal pain without obvious fluctuance or drainage suggests an occult deeper-underlying abscess. Imaging may be pursued to further evaluate deeper or more complex abscesses and fistulae. Endorectal ultrasound (EUS) has a sensitivity of 87 percent and specificity of 43 percent, but it is limited by operator dependence and by the patient's discomfort during the examination. It can serve as an adjunct at the time of surgery and has been shown to change surgical management in 10 to 15 percent of cases.[75,76] Pelvic MRI has an overall sensitivity of 87 percent and specificity of 59 percent, and is considered the noninvasive gold standard.[75,77] Gadolinium-enhanced T1-weighted imaging can differentiate between fluid, pus, or granulation tissue. However, in the acute setting, MRI is not always immediately available. Although CT only has a sensitivity of 77 percent, less than EUS or MRI, it is effective, noninvasive, readily available, and less expensive.[75,78–80] CT has poorer resolution of soft tissue, but is able to identify a fluid/air collection indicative of an abscess, a fluid-/air-filled soft tissue tract indicative of a fistula, and the surrounding inflammation present in the setting of infection and acute anorectal sepsis.[81]

If the abscess is clinically obvious and superficial, drainage may be performed with local anesthesia. For patients who do not tolerate examination and drainage or for occult, deeper, extensive, or complex fistulae, examination under anesthesia (EUA) provides an opportunity for both diagnosis and treatment. EUA involves external inspection, palpation of the perineum externally and the anal canal internally, and anoscopy. Intraoperative ultrasound can also enhance diagnostic accuracy, ensure drainage of loculated collections, and delineate complex fistula tracts.

In the acute setting, adequate drainage is key. Delays in drainage or inadequate drainage may lead to progressive perianal sepsis with necrotizing infections. Incisions made for drainage should be made over the most fluctuant and tender area, as close to the anal verge as possible, radially from the anus, and must be large enough to allow for ongoing drainage. Drainage of deep ischiorectal or supralevator abscesses can be enhanced by placement of a mushroom tip catheter or Malecot drain within the abscess cavity. Drainage of large subcutaneous abscesses can be facilitated by placing a wide seton, such as a Penrose drain, through an incision and a counter-incision at each end of the cavity to avoid creating a large wound. If a fistula is suspected, a probe can be passed through it to delineate the tract(s). Injection of the tracts with hydrogen peroxide and methylene blue can help to identify complex tracts. A loose, draining, noncutting seton, such as a silastic vessel loop, can be placed through fistula tracts to maintain patency and allow for ongoing, controlled drainage. Fistulotomies are contraindicated in the setting of perianal sepsis due to the increased risk of anal sphincter injuries.

Severe refractory septic complications, especially in the setting of proctitis, may require fecal diversion with a loop ileostomy or colostomy. Fecal diversion may allow the perineal sepsis and the underlying anorectal disease to heal, and intestinal continuity may be reestablished when healing is achieved. However, the majority of patients who undergo diversion never have intestinal continuity restored, and those that do have a high risk of recurrent perineal sepsis.

Rectal disease and multiple recurrences of perianal disease increase the need for proctectomy in patients with perianal CD. The rate of proctectomy is 77.6 percent in patients with active rectal CD compared to only 13.6 percent in patients with rectal-sparing disease.[82] The rate of proctectomy is 23 percent in patients with multiple complications compared to only 10 percent in patients with a single complication.[82] Diversion prior to proctectomy allows for perineal sepsis and active proctitis to subside, potentially allowing for a smaller area of perineal resection and improving the rate of successful wound closure at the time of proctectomy. For large perineal defects or for perinea scarred by multiple previous abscesses, fistulae, and drainage procedures, musculocutaneous flaps may be necessary for wound closure.

Medical management is not sufficient in the treatment of abscesses. However, after the acute sepsis has been eliminated, medical management is important, especially in the setting of active proctitis. The main goal of medical management is to achieve and maintain disease remission. Antibiotics, oral metronidazole and ciprofloxacin, have been used in mild to moderate disease.[83] It is unclear whether their efficacy is due to their antimicrobial or immunosuppressive properties. Both have been shown to lead to improvement in symptoms; however, recurrence is common after cessation of antibiotics.[74]

Anti-TNF medications can be started following control of perianal sepsis to promote healing of perianal fistulae. Patients who do not demonstrate improvement after the first two treatments of infliximab are unlikely to respond.[84] For those that respond, setons may be removed after two treatments and after the fistula has stopped draining. Infliximab, adalimumab, and certolizumab have all been shown to promote fistula closure, without head-to-head comparison trials. Local injection of infliximab adjacent to fistula tracts has been investigated as a topical treatment to reduce systemic side effects.[82,85,86] Azathioprine (AZA) and 6-mercaptopurine (6-MP), are associated with fistula healing in 54 percent of patients (versus 21 percent of patients who received placebo).[87,88] Combining infliximab with immunomodulator agents, AZA and 6-MP, may result in longer remission. Due to the prolonged onset of action, these medications are often started in conjunction with other medications, such as antibiotics or infliximab.[74] Successful healing of perianal septic complications and their sequelae is more common in patients 40 years or older, with recent onset of perianal complications and without underlying fistulae.[89]

Cyclosporine and tacrolimus are calcineurin inhibitors with potent immunomodulating properties. Cyclosporine has demonstrated a high fistula closure rate of approximately 90 percent; however, recurrence rates are high following discontinuation of treatment.[90] Tacrolimus has been shown to elicit improvement in fistula drainage in 43 percent of patients (versus 8 percent control), but not in fistula remission (10 versus 8 percent).[91,92] Both medications require frequent monitoring of drug levels and are associated with significant side effects, such as renal impairment. Due to the limited evidence of their use and the significant toxicity, these agents are limited to second-line treatment.[93]

A mature fistula may persist following resolution of acute perianal sepsis and remission of active distal luminal disease. Surgical closure of a fistula cannot be considered until both infection and active disease have been controlled. Primary fistulotomy results in the highest rate of successful healing (72 to 100 percent),[94,95] but must be weighed against the higher risk of incontinence (40 to 60 percent).[95,96] Even small alterations in continence are particularly problematic in patients with CD in light of the risk of recurrent disease and accompanying loose stools/diarrhea. Therefore, the role for fistulotomy is limited to fully continent patients with simple, very low fistulas in the setting of well-controlled CD.

Various sphincter-sparing strategies have been advocated for the treatment of more complex fistulae with widely variable, but mostly disappointing, success rates.[82,97] Fibrin glue and fistula plugs have mostly fallen out of favor. Fibrin glue consists of fibrinogen and thrombin to promote healing, hemostasis, and angiogenesis. Without altering the anatomy, the glue can be injected to fill and seal the fistula tract and has been shown to be safe, tolerated with a minimal risk profile, and more effective than no therapy in patients with CD (31 to 67 percent reported success).[98,99] The fistula plug can also be placed into the fistula tract, acting as a scaffold for endogenous growth of the patient's cells, but studies show no benefit of the fistula plug over removal of the seton alone in CD (15 to 86 percent reported success).[85,88,100–102]

The endorectal mucosal advancement flap is the most commonly performed procedure for closure of fistulae-in-ano and rectovaginal fistulae in Crohn's disease. The procedure aims to close the internal opening of the fistula with healthy endogenous tissue. Advancement flaps are technically more difficult and less likely to heal in the setting of active proctitis, or with chronically fibrotic tissues or a "woody" rectum. Careful selection of patients without rectal Crohn's disease or with rectal Crohn's disease under good control is key to success (50 to 85 percent reported success).[94,103] Another promising procedure is the ligation of the intersphincteric fistula tract (LIFT) procedure. This procedure can be performed in fistulae-in-ano but not in rectovaginal fistulae. It divides the fistula tract in the intersphincteric groove, closing the internal portion, and leaving the external component open to drain and granulate in by secondary intention. Although data regarding the utilization of this procedure in patients with CD are sparse, the reported healing rates are on par with other methods of repair (48. percent reported success).[104,105] For patients who are refractory to medical and surgical treatments, mesenchymal and hematopoietic stem cells offer a novel therapeutic approach. Currently, the use of stem cells remains investigational, but clinical trials have shown that the injections are well tolerated with promising early results.[86,106–108]

Conclusions

Crohn's disease is a chronic, panintestinal, recurrent inflammatory disease that can present with acute complications. The patient's clinical status and assessment of the background disease location and severity must be considered in order to guide diagnosis and treatment of the acute complications. CD is unremitting and incurable, and, therefore, treatment aims to induce a deep and prolonged remission, prevent and address complications of the disease, avoid extensive bowel resections, and improve quality of life.

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CHAPTER 18

Management of Difficult Acute Appendicitis

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Complicated appendicitis, appendectomy, abscess

Abstract

Acute appendicitis is one of the most common causes of acute abdomen, and the most common surgical disease among adult and pediatric patients presenting to the emergency department both in the United States and Europe. The pathogenesis of acute appendicitis is multifactorial, and a major role is played by environmental exposures. Incidence peaks in the early teens and the male-to-female ratio is 2:1. Around 25 percent of the appendicitis cases are defined as complicated. In cases of complicated appendicitis with generalized peritonitis due to the rupture of the inflamed appendix into the peritoneal cavity, surgical intervention is the gold standard. Conservative management is a feasible strategy, however approximately 14 percent of patients will have recurrent appendicitis usually within 12 weeks; some can further be managed nonoperatively although approximately 50 percent will require percutaneous drainage. Treatment strategies in pediatric patients resemble those of the adults, while in cases of pregnant women appendectomy is advised when the diagnosis is relatively certain.

Introduction

Acute appendicitis is one of the most common causes of acute abdomen, and is certainly the most common surgical disease among adult and pediatric patients presenting to the emergency department both in the United States and Europe.[1] Nowadays, acute appendicitis affects 9.4 per 10,000 people annually, resulting in about 300,000 cases per year;[2] its lifetime risk is about 1 in 15, and one-third present with a perforated appendix.[3] The incidence has currently stabilized for both perforated and nonperforated appendicitis, while the incidence of appendectomy has steadily decreased as a result of advances in diagnostic modalities, medical management, and surgical techniques.[4, 5] As a matter of fact, cases of appendicitis may be managed with antibiotics and medical treatment depending on their presentation and severity.[6, 7] Acute appendicitis and appendectomy are associated with morbidity, mortality, and significant costs to the health care system.[1] However, from the early 1990s to the current practice, outcomes have significantly improved due to the capability of health care systems to quickly diagnose and treat acute presentations, distinguishing the uncomplicated from the progressive and complicated cases. Indeed, prompt differentiation directly influences management and therefore outcomes of patients.

Pathogenesis, Clinical Presentation, Diagnosis, and Management

The pathogenesis of acute appendicitis is multifactorial, and a major role is played by environmental exposures. Incidence peaks in the early teens and the male-to-female ratio is 2:1. Young males with a reduced fiber intake are at higher risk.[8] Winter season and smoking have also been reported as risk factors, while air pollution seems to be related to an increased risk of perforation.[9, 10] Acute appendicitis occurs when the lumen of the appendix becomes inflamed following an obstruction caused by a fecalith (35 percent), hypertrophied lymphoid tissue (55 to 65 percent, most commonly in the young), foreign body, parasitic infections, or a tumor (such as carcinoids).[11] Rising intraluminal pressure leads to vascular suffering, ischemia, necrosis, and possible perforation.

The initial presentation of acute appendicitis includes right lower quadrant (RLQ) pain, followed by loss of appetite, nausea, and vomiting. However, in more than half of the cases, the pain typically starts in the periumbilical region and later migrates in the RLQ. As the location of the appendix varies in each individual (retrocecal or pelvic), pain could sometimes be atypical, mimicking different diseases (especially in females). Indeed, the inflammation may spread to another organ and produce the clinical picture of a totally different disease (enteritis, salpingitis, diverticulitis, cystitis, cholecystitis). In case of perforation, partial pain relief is possible but peritoneal signs such as guarding and rebound will ultimately develop. Patients with acute appendicitis may also present with fever and elevated white blood cells (WBC) count. The higher WBC count the greater is the risk of a gangrenous or perforated appendix.[12, 13] Although clinical presentation and blood work might be enough to diagnose a patient with acute appendicitis, imaging modalities are normally required to enhance specificity. A nonionizing radiation-based imaging modality such as ultrasound (US) and magnetic resonance imaging (MRI) should be preferred; however computed tomography (CT) is most commonly used as it is able to precisely identify the inflammation, locate the appendix, and help to rule out a possible differential diagnosis. An appendiceal diameter >6 mm, wall thickness >2 mm, the presence of a fecalith, and periappendiceal inflammation are all signs of acute appendicitis.

Using clinical presentation, physical examination and imaging modalities, the caregiver could distinguish acute appendicitis into uncomplicated and complicated forms. The former is a clinical syndrome with no signs of perforation, abscess, or phlegmon. It typically presents in children and young adults and it is equally distributed among males and females. The duration of symptoms is short (24 hours or less), with elevated WBC count (>10,000 cells/mm^3) and c-reactive protein (CRP) greater than 40 mg/L. Conversely, complicated appendicitis results from the appendiceal rupture into the peritoneal cavity, with subsequent abscess or phlegmon formation. About 30 percent of acute appendicitis cases in the United States are defined as complicated.[2] The very young and very old are most likely the patients presenting with complicated appendicitis as they are often unable to refer their symptoms effectively, leading to a delayed evaluation, diagnosis, and treatment. Symptoms have a longer duration (>48 hours), WBC count is significantly elevated (>16,000 cells/mm^3) , as well as CRP (>140 mg/L). Finally, while right lower quadrant pain, nausea, vomiting, diarrhea, anorexia, and fever are symptoms related to both complicated and uncomplicated appendicitis, dysuria is more frequent in patients with a complicated presentation (**Table 1**).[13]

The Alvarado score is a validated tool that combines patient symptoms, physical signs, and laboratory values to help diagnose and manage acute appendicitis. [14] A score of 7 or more is predictive of the need for appendectomy while patients with lower scores should be observed closely; more specifically, scores of 4 to 6 should undergo an additional CT scan to confirm the diagnosis while scores of 3 or lower do not need further investigations as their likelihood of acute appendicitis is sufficiently low. The use of the Alvarado score in women is much more limited due to the presence of gynecologic diseases that may mimic acute appendicitis. In these cases, a pelvic examination might be useful to rule out gynecologic sources.[15, 16] Imaoka and colleagues performed an interesting study to evaluate the predictors of complicated appendicitis. Of 116 adult patients included, 55 percent had complicated appendicitis. The authors specifically tested body

Table 1. Characteristics of complicated and uncomplicated appendicitis

	Complicated	Uncomplicated
Age	<3 years and >65 years	Children and young adults
Gender	Slightly increased risk in men	No differences between men and women
Symptom duration	48 hours or more	24 hours or less
WBC count	greater 16,000 cells/mm3	greater than 10,000 cells/mm3
CRP	greater than 140 mg/L	greater than 40 mg/L
RLQ pain	59%	49%

WBC: White blood cells; CRP: c-reactive protein; RLQ: right lower quadrant.

temperature >37.4°C, CRP >4.7 mg/dL, and fluid collection surrounding the appendix on CT scan. Patients with none of these 3 signs had all uncomplicated appendicitis at surgical exploration while patients with 1, 2, or 3 predictors had complicated appendicitis in 37 percent, 81 percent, and 100 percent of cases, respectively.[17]

The management of acute appendicitis depends on several factors and could be divided in nonoperative and operative treatment. Generally speaking, nonoperative treatment includes bowel rest, intravenous fluids, and antibiotics, with close monitoring for possible evolutions of symptoms or signs. Drainage of any abscess by interventional radiology also falls into the "nonoperative management" definition; this is sometimes indicated in complicated conditions (see later). Operative management with surgery is the definitive treatment for acute appendicitis. Appendectomy can be performed both in open and in laparoscopic surgery. Before the introduction of laparoscopy, open appendectomy was the only surgical option. Incision was placed at the point of maximal tenderness or at the McBurney point (one-third the distance from the anterior superior iliac spine to the umbilicus) and this still represents an important landmark for open appendectomy cases. Laparoscopic appendectomy has been widely described in the past years and has nowadays become the favored approach for noncomplicated appendicitis.[18] Port placement can vary depending on the surgeon's preference but the key is to respect triangulation of the instruments to improve ergonomics and easily and safely remove the appendix. Generally speaking, three trocars are placed at the umbilicus, in the left lower quadrant, and suprapubic.

Patients presenting with acute and noncomplicated appendicitis are normally scheduled to receive appendectomy ideally within 24 hours.[19] However, randomized studies have showed that nonoperative management with antibiotics can be successful in patients with noncomplicated appendicitis who wish to avoid surgery and accept the risk of recurrence.[7, 20] Conversely, the treatment of acute appendicitis in the complicated setting is still controversial.

Management of Complicated Appendicitis

About 300,000 appendectomies are performed each year worldwide and 25 percent of these are defined as complicated. [21, 22] In these cases, a perforation of the appendix happens and sometimes evolves into a phlegmon or abscess; 20 percent of these patients in fact, will develop an abscess.[23] Treatment allocation of patients with complicated appendicitis is controversial and far from easy. Patients could be approached by either immediate surgery, or nonoperative management including antibiotic treatment or abscess drainage, followed or not by interval appendectomy. A nonoperative strategy would typically involve intravenous antibiotics and possible drainage of the abscess.[24] Later, an interval appendectomy is considered around 8 to 12 weeks after the acute presentation has resolved, allowing for the inflammation to subside.[25] An immediate operative intervention is usually curative but surgery is made technically difficult because of the severe inflammation and distortion of the anatomy. While successful nonoperative management offers favorable outcome in patients with complicated appendicitis, when this fails to resolve clinical presentation, morbidity of patients is high.[26, 27]

Operative management: surgery

An argument favoring immediate surgical exploration and appendectomy in complicated cases is that illness is dealt with one single admission at a time when the benefit is most apparent to the patient and therefore the risk of recurrence is resolved. Furthermore, as already mentioned, if conservative management fails, there might be a substantial increase in morbidity. In cases of complicated appendicitis with generalized peritonitis due to the rupture of the inflamed appendix into the peritoneal cavity, surgical intervention is the gold standard. Contained perforations and abscess may also be considered for immediate appendectomy; however, careful considerations of possible complications should be made. Indeed, a contained perforation may become a free perforation during exposure maneuvers, requiring significant irrigation to minimize abscess formation.[28, 29]

Additionally, a severely inflamed surgical field may hamper physiologic closure of the appendiceal stump, leading to the consideration of an ileocecal resection. Most of the times, a laparoscopic approach is feasible, however an open appendectomy should be considered to ensure adequate visualization and irrigation of the peritoneal cavity. Despite many having speculated that laparoscopic approach is still safe in this setting, the University Health System Consortium has disclosed that open appendectomies are performed more than laparoscopy in the case of complicated appendectomies and that conversion rates are about 10 percent only in experienced hands. Notwithstanding, a meta-analysis has demonstrated that laparoscopic technique results in reduction in surgical site infections, length of hospital stay, and a reduced time to oral intake even in the setting of complicated appendicitis.[30]

Appendectomy is frequently considered as the first step in a surgical training; however, unanticipated difficulties can occur and should therefore be considered. Good exposure is fundamental, and a difficult operation can be made easy by good exposure. Once the exposure is guaranteed, localization of the appendix is pursued. Sometimes this step is difficult and identification of the caecum and its taenia coli guarantees access to the appendix. When a diffuse peritonitis is encountered, the appendix should be removed and the peritoneal cavity irrigated when a localized abscess is present and dissection maneuvers are dangerous, appendectomy might be contraindicated, and a lavage and drainage approach preferred. If the appendectomy is carried out, dissection maneuvers are aimed to identify the base of the appendix. During these maneuvers there is generally oozing due to the local inflammation and the production of thrombokinase by the inflamed tissue. Dissection should be carefully performed to avoid injury to surrounding structures (such as the iliac vessels, bowel loops, and testicular or ovary vessels). Meso-appendix and its vasculature should be securely sealed and cut; sometimes this is not even identifiable due to the inflammation process that might have led to vascular thrombosis. When it comes to the appendiceal base, sometimes this can be enlarged, inflamed, and difficult to dissect. Stapler firing could be indicated to secure the appendiceal stump. Drainage should always be considered.

Nonoperative management

Conservative management with antibiotics has been well established for abdominal infection of other sources (such as an uncomplicated acute diverticulitis), while nonoperative management of acute appendicitis has been largely investigated and questioned over time. Randomized and nonrandomized studies have promoted antibiotic treatment for noncomplicated appendicitis with a success rate as high as 90 percent at 30 days and 75 percent within 1 year of treatment.[7, 20, 31, 32] Furthermore, results of nonoperative management with antibiotics in children have confirmed that conservative treatment is a safe and effective strategy with 64 to 86 percent success rates, lower incidence of complications, and no differences in the rate of complicated appendicitis compared to appendectomy.[33, 34] Despite this, the evidence concerning nonoperative management of acute appendicitis in the complicated setting is much more complex.

The rationale to delay appendectomy at a later stage is to let the inflammation subside, allowing for the inflammatory process to localize and for the edematous inflamed bowel to recover. Nonoperative treatment for complicated appendicitis showed symptom resolution in about 90 percent of patients.[35] However, a 5 to 15 percent recurrence rate has been demonstrated.[21, 22, 28] A close monitoring of patients to promptly identify any evolution of the clinical presentation is mandatory and CT scans are repeated for patients with symptoms suggesting that the inflammatory process is still active or progressing. Finally, it should be considered that other conditions (such as inflammatory bowel diseases and colorectal cancer) could mimic complicated appendicitis and should therefore be investigated appropriately.[36]

The evidence that acute appendicitis can be managed conservatively was first published in 1910.[37] This was later validated in a series of 137 patients with acute appendicitis successfully treated by conservative management.[38] Currently, despite the World Society of Emergency Surgery advocating for nonoperative management as the appropriate initial treatment in cases of complicated appendicitis, surgeons worldwide still use both approaches depending on clinical judgment, imaging, clinical conditions, and experience.

In a study on 36 patients with complicated appendicitis undergoing a trial of nonoperative management, the success rate was 86.1 percent. Five patients (16.1 percent) were managed with percutaneous drainage of abscess and five patients (16.1 percent) failed conservative treatment and were operated within 48 hours from admission with a significantly longer hospital stay. Causes of failure were persistent abdominal pain, tachycardia, and fever despite antibiotic treatment.[39] Three of these patients required an open appendectomy. Importantly, no patients developed generalized peritonitis or septic shock while on conservative treatment.

A meta-analysis of 44 studies reported that failure of nonoperative management in patients with appendiceal abscess or phlegmon was 7.2 percent.[35] This high success rate is most likely due to the use of percutaneous drainage through radiological intervention. However, failing conservative treatment had a significantly longer hospital stay and higher rates of complications requiring percutaneous or surgical interventions. Furthermore, Young and colleagues showed that patients failing nonoperative management more frequently required open surgery, and more than

half required bowel resection.[27] Patients undergoing conservative management for complicated appendicitis should be informed about the risk of prolonged hospital stay, complications, postoperative infections, and open appendectomy. Factors predicting failure of conservative management have been studied; Nadler and colleagues suggested that phlegmons on imaging as opposed to abscess are more likely to respond to conservative management.[40] Furthermore, the need for abscess drainage increases the failure rate, perhaps because of inadequate source control. Finally, an initial increased band count of more than 15 percent is associated with failure and more complications.[41]

A recent meta-analysis favored nonoperative management because of fewer overall complications (odds ratio [OR] 0.24; 95 percent confidence interval [CI] 0.13-0.44), wound infections (OR 0.28; 95 percent CI 0.13-0.60), abscess (OR 0.19; 95 percent CI 0.07-0.58), bowel obstruction (OR 0.35; 95 percent CI 0.17-0.71), and reoperation (OR 0.17; 95 percent CI 0.04-0.75).[42] However, 14 percent of patients will have recurrent appendicitis usually within 12 weeks; some can further be managed nonoperatively although about 50 percent require percutaneous drainage.[28]

Interval appendectomy

The need for interval appendectomy after successful conservative treatment is controversial. The risk of recurrent appendicitis and missed pathological findings (Meckel diverticulitis, Crohn's disease, and malignancy) is still an issue. However, some authors have questioned the necessity for interval appendectomy because of the low risk of recurrent appendicitis and the potential complications of surgery.[41, 43-45]

Delayed appendectomy could reveal uncovered medical conditions requiring further treatment. In a study involving 46 patients undergoing interval appendectomy, 16 percent had a normal appendix while 84 percent of patients had different pathology results including acute inflammation (44 percent), mucinous cystadenoma (4 percent), or inflammatory bowel disease (IBD) (4 percent).[46] Another retrospective study by Rosen et al. confirmed the forementioned findings demonstrating that only three out of 34 patients had a pathologically normal appendix.[47] Further support comes from a review of 6038 patients with acute appendicitis.[22] One hundred eighty-eight patients were treated conservatively and of these, 89 patients underwent an interval appendectomy. Looking specifically at the rates of neoplasms in the removed appendix, the authors found that 12 percent of patients had a pathological diagnosis of neoplasm (55 percent mucinous neoplasm). Furthermore, 16 percent of patients over 40 years had a neoplasm.[35, 48] Finally, in a study from Furman and colleagues 17 out of 376 patients underwent interval appendectomy and 29.4 percent of these were found to have an appendiceal tumor. Furthermore, they disclose that during the study period, two patients who did not undergo interval appendectomies later returned to the hospital with stage IV appendiceal cancer.[25]

Although the evidence seems to support interval appendectomy for the forementioned reasons, there is still controversy. In a study conducted on 94 patients with complicated appendicitis treated conservatively, the recurrence rate was 14.6 percent with 53 percent occurring within 3 months. The authors speculate that it is possible to place a hold on interval appendectomy and treat the recurrences. No cases of malignancies were identified on subsequent appendectomies.[28] Adding more controversy to the topic, Senekjian and colleagues determined cost-effectiveness of interval appendectomy;[49] based on the results, patients with more than 34 years without atypical symptoms or a family history of cancer should not undergo interval appendectomy from a cost-benefit perspective. Patients with a family history of cancer or symptoms concerning for IBD should be considered for more aggressive management.

Patients should be treated with antibiotics for a period of time and those whose symptoms fail to resolve should have operative intervention. If this is not pursued, patients should be counseled about the possibility of a recurrence of appendicitis and encouraged to seek medical attention. Younger patients who are those more frequently affected by acute appendicitis, seem to be at lower risk of neoplasm and complications. Perforations, complications, and cancers increase with age.

Management of Complicated Appendicitis in Pediatric Patients

Appendectomy for acute appendicitis in children is the most common abdominal surgical procedure that pediatric surgeons face anually.[50] It has been estimated that approximately 7,000 children are operated on each year for acute appendicitis in the United States, with an overall lifetime risk of 23 percent for females and 12 percent for males. The incidence of acute appendicitis peaks at 10-14 years for males and 15-19 years for females.[51] As in adults, acute appendicitis can present as uncomplicated and complicated clinical scenarios in pediatric patients. Approximately 30 to 74 percent of children present with complicated appendicitis, with rates ranging between 69 to 93 percent in children 2 to 5 years of age, reaching 100 percent in children aged 1.[52-54] Treatment in pediatric patients resembles that in adults and can be approached by immediate surgery, nonoperative management including antibiotic treatment, or abscess drainage, followed or not by interval appendectomy. Despite that operative management has been considered as the mainstay of treatment in children with acute appendicitis, the presence of distorted anatomy due to the severe inflammation may lead to iatrogenic injuries to surrounding tissues and bowels, dissemination of the

infection, increased blood loss and operative time, abscess and fistula formation in the postoperative period, as well as wound complications.[55,56] Although the literature is quite limited on the topic, evidence suggests that nonoperative management in complicated clinical scenarios may be effective and safe.[57,58] The standard of care for complicated appendicitis in children endorses the prompt administration of antibiotics. A recent survey showed that 96 percent of surgeons use antibiotics comprising an aminoglycoside, a beta-lactam, and an anaerobic coverage.[59] However the American Pediatric Surgical Association (APSA) recommends that a broad-spectrum single or double agent is equally effective as a three-drug regimen.[60] Several authors has reported good results with percutaneous drainage, reducing complication rates, acceptable hospital stay, and rapid recovery.[61-63] Gasior and colleagues suggested that only abscesses greater than 20 cm^2 should be drained.[64] Despite further evidence being needed, abscess drainage has been reported to be associated with lower recurrence rates and lower possibilities of requiring an interval appendectomy as compared to patients treated only with antibiotics and not drained.[63]

Although many studies have recommended immediate operation in children presenting with acute complicated appendicitis, only 2 randomized controlled trials are reported to date favoring this approach.[65,66] Both studies randomized children in two groups comparing immediate surgery versus conservative management with delayed appendectomy. Blakel and colleagues found that patients in the nonoperative management group had higher complication rates, higher hospital stay, and charges than those treated with surgery immediately. As a further support, a recent meta-analysis disclosed fewer complications and fewer readmissions in patients with perforated appendicitis and early appendectomy.[67]

Management of Complicated Appendicitis During Pregnancy

In the first six months of pregnancy, the incidence of appendicitis is the same as in nonpregnant women and abortion following treatment is rare. However, it has been reported that pregnant mothers with acute appendicitis are at higher risk to suffer fetal loss and have a five-fold increased risk for maternal death compared to those without acute appendicitis. [68] As a matter of fact, in the last three months of pregnancy, appendicitis is rare, but abortion following treatment is more common. Diagnosis can be challenging, in cases of pregnancy the appendix is displaced upwards and laterally, so that local signs tend to be in the flank. Differential diagnosis includes ectopic pregnancy, round ligament syndrome, indigestion, pyelonephritis, HELLP (hemolysis, elevated liver enzymes, and low platelets) syndrome, abruptio placenta, and uterine rupture. MRI showed high sensitivity and specificity for the diagnosis of acute appendicitis in pregnant women, with the advantage of not exposing patient and fetus to ionizing radiations.[69] It represents the imaging modality of choice when US examination is inconclusive. The administration of gadolinium has some theoretical concerns regarding fetal safety and should be carefully evaluated. Regarding the surgical technique, both laparoscopic and open appendectomy are considered safe in pregnancy, however there are no consistent data in literature to demonstrate which is more accurate. [70] Pregnant women are also more likely to suffer from a complicated appendicitis compared to nonpregnant controls, either perforated or gangrenous, but are managed more often with a conservative approach. [71] Long-term outcomes and prognosis are generally good although few reports are available.

Conclusions

Acute appendicitis is a common disease. The clinical scenario of complicated appendicitis is difficult to manage, and treatment allocation remain controversial. Although appendectomy is widely performed and considered safe, surgery carries the risk of complications. Conversely, the rate of recurrences and the chance of hidden malignancy should be considered if nonoperative management is chosen. Complicated appendicitis with persistent symptoms or risk signs (such as fecalith on CT scan) is at a higher risk for complications and failure of nonoperative treatment and should therefore be strongly considered for interval appendectomy.

Complicated appendicitis with perforation and disseminated peritonitis should be managed by immediate surgery. On the other side, abscess or phlegmon formation seems to prefer nonoperative management with or without drainage depending on the patient's condition, clinical presentation, and the surgeon's preference.

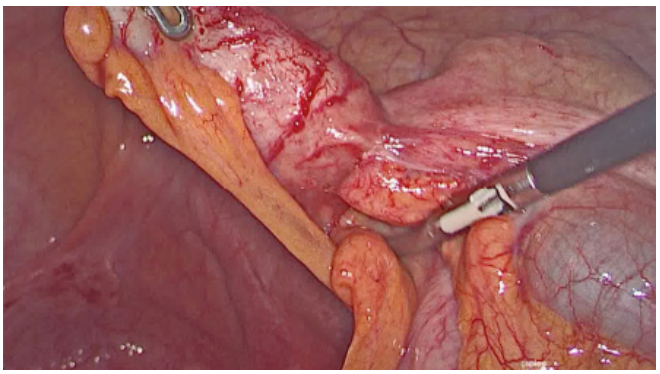

Figure. After exposure and dissection manuevers, the appendix is identified following the teniae of the cecum

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CHAPTER 19

Management of Large Bowel Obstruction

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Key words:

Large bowel obstruction, colonic obstruction, cancer volvulus, diverticulitis, pseudo-obstruction, emergency, management, colectomy, stent

Abstract

The management of acute large bowel obstruction (LBO) is complex in the emergency setting. LBO describes any obstruction to the flow of the intraluminal contents of the colon or rectum. Timely diagnosis and management are crucial because of the potential life-threatening complications. Acute LBO often results in the need for laparotomy. However, the surgeon must not only treat the obstruction but also investigate the underlying etiology. It is recognized that not all obstructions are mechanical; some can be nonmechanical pseudo-obstructions and should be included in the differential diagnosis, as their treatment is quite different. The majority of LBOs are caused by cancer, volvulus, and diverticulitis, while causes can be benign or malignant, intrinsic or extrinsic to the bowel wall. Due to this diverse etiology and symptoms, surgeons must diagnose the LBO and its cause, formulate a differential diagnosis, and initiate the appropriate treatment. Experience and technology have advanced; thus, several treatment options are now available for the acute care surgeon.

Abbreviations

ACPO: Acute colonic pseudo-obstruction
CD: Crohn's disease
IBD: Inflammatory bowel disease
LBO: Large bowel obstruction
UC: Ulcerative colitis

Introduction

Bowel obstruction is defined as the interruption of the passage of the intestinal contents. It is the cause of 15 percent of all emergency admissions for acute abdominal pain, 300,000 hospitalizations/year, 30,000 deaths/year, and 3 billion dollars of medical care expenses/year in the United States .[1] Although on most occasions it is located in the small bowel, 25 to 36 percent of the cases are located in the large bowel.[2–4] The accumulation of gas and fluid proximal to the obstruction essentially leads to bowel distension and to an increase in intraluminal pressure, both of which circumstances lead to increased peristalsis in the beginning and decreased peristalsis later.[5] This sequence of events leads to intraluminal bacterial overgrowth and to an increased translocation of bacteria and endotoxins to both mesenteric lymph nodes and to the systemic circulation, which could be the reason for a portion of the systemic septic sequelae of bowel obstruction.[1,5,6] Additionally, the continuously increasing intraluminal pressure impairs bowel wall perfusion – initially venous drainage and later arterial supply – and can lead to ischemia, necrosis, and even perforation, particularly in the case of a closed bowel loop.[1,5,6] Based on the Laplace law (wall tension = radius * intraluminal pressure), the wall of the cecum develops the highest tension in the gastrointestinal system due to the cecum's large diameter. This increased tension can lead to muscle fiber separation, dissection of air into the wall (pneumatosis), or even perforation, particularly if the diameter of the cecum exceeds 9 cm.[5]

The vast majority of large bowel obstructions (LBOs) occur distal to the transverse colon (**Figure 1**)[7] and can be attributed to various causes (**Table 1**).[8] The most common cause of LBO is colorectal cancer, with LBO being the first clinical manifestation in nearly 30 percent of the colon cancer cases, especially for those of the distal colon and rectum, which due to their limited luminal size commonly obstruct earlier.[7,9] Volvulus is the most frequent benign cause of LBO (15 percent) in the United States,[10] while in the developing world sigmoid volvulus can be the most common cause of LBO in total (60 to 72 percent).[3,4,11] The aim of the present chapter is to describe the management of LBO according to the cause of the disease.

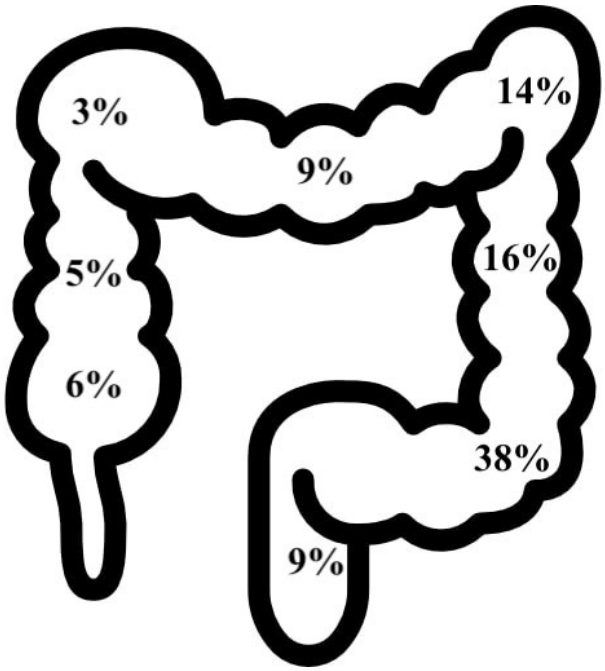

Figure 1. Sites of large bowel obstruction, according to Buechter et al.[7]

Table 1. Causes of large bowel obstruction[8]

Common (>95%)
Primary colon cancer (60–80%)
Volvulus (11–15%)
Diverticulitis (4–10%)
Uncommon (<5%)
Intussusception
Hernia
Inflammatory bowel disease
Extrinsic compression from abscess or masses
Fecal impaction
Foreign body
Acute colonic pseudo-obstruction

Initial Management

Acute LBO is a challenging emergency and should be managed in a hospital setting (**Figure 2**). It requires early identification and timely intervention to reduce postoperative complications and mortality.[12] Regardless of the cause, the initial management principle of LBO is often referred to as "suck and drip".[12] It consists of supportive care, including gastrointestinal decompression with nothing by mouth and a nasogastric tube ("suck"), intravenous fluid therapy,

monitoring of urine output usually with a urinary catheter, correction of electrolyte abnormalities ("drip"), and empirical broad-spectrum antibiotics .[12,13] After resuscitation, the definitive treatment of LBO depends on the etiology of the obstruction and the clinical status of the patient.[12] Unlike small bowel obstructions, about 75 percent of LBOs require surgical intervention during the same hospital admission.[2] In general, patients with anastomotic strictures can be treated with transanal stricturoplasty, stenting, dilation, and surgical resection.[14] Other initial management options are decompression for sigmoid volvulus,[15] and palliative stenting for malignant obstruction or as a bridge to surgery.[16]

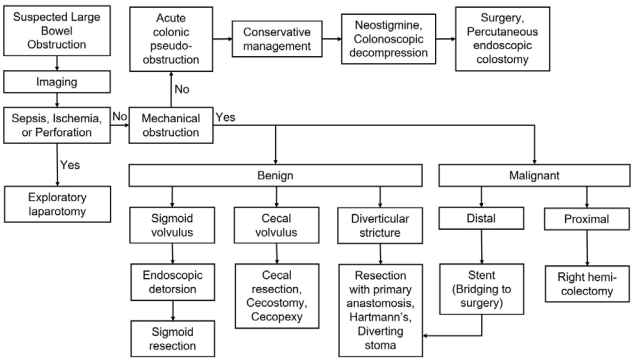

Figure 2. Algorithm for the management of acute large bowel obstructions

Cancer

Colorectal cancer is the most common cause of LBO. Management of LBO due to cancer requires a complex and multimodal approach, depending on tumor location and stage, patient's condition, and surgeon's experience.[17] Patients who are acutely unwell, with peritonitis, or are septic, need emergency surgery[13] without intraoperative colonic lavage.[18] However, many patients may not be fit for emergency surgery; thus, nonsurgical options should be considered.[12] These can be appropriate for patients without peritonism or with advanced disease.[12] Alternatives options are endoscopic tumor ablation, self-expanding metallic stents, and endoscopic colonic decompression with decompression tubes.[12] Laparoscopy in the management of acute LBO is not well studied. However, it has been found to be safe with low complication rates and short hospital length of stay.[19]

Right colon obstruction

For cancers obstructing the right or transverse colon, right hemicolectomy with immediate primary ileocolic anastomosis is considered safe, as long as the oncologic resection rules are followed.[17] It offers a definitive procedure with no stoma formation or need for further surgery.[12] Colectomy can be performed with or without prior endoscopic stent decompression.[18] The incidence rate of anastomotic leak after primary anastomosis is similar between patients with (10 percent) and without obstruction (6 percent).[20] Segmental resection should include the tumor's lymphatic and vascular drainage, and minimum margins of 5 to 7 cm proximal and distal to the mass must be obtained.[18] Preoperative bowel preparation is not beneficial for mechanical obstruction,[21] while intraoperative colonic irrigation is not recommended.[18] Also, primary resection and anastomosis should only be performed in the absence of hemodynamic failure or fecal peritonitis.[17] In this situation, and in the absence of intestinal perforation, a loop-stomal diversion can be performed with second-stage colectomy.[17]

Complete or hand-assisted laparoscopic colectomy is considered safe and effective when performed by experienced surgeons. One must have a low threshold to open conversion, and a sound oncologic operation must be performed.[22,23] In the elective setting, minimally invasive colectomies for transverse colon cancer have been shown to decrease the risk of postoperative adverse events and hospital length of stay.[24] Due to the better outcomes of elective minimally invasive versus emergent open colectomy, stenting can be suggested as a bridge to elective surgery in right LBO. Indeed, there is evidence, although limited, that in experienced centers, stenting can be effective and safe.[16,25]

Left colon obstruction

Left-sided lesions (**Figure 3**) are treated differently than the right ones because the anastomoses are regarded as more susceptible to leakage.[26] There are various surgical options. In general, for patients with curable disease and left-sided colon-obstructing cancer, initial colectomy or initial endoscopic stent decompression and interval colectomy can be performed.[18] In cases of synchronous tumors or proximal bowel damage, subtotal colectomy is performed.[27] This allows for a single-stage resection and anastomosis, with the disadvantage of increased daily frequency of stools.[17] For high-risk patients, the Hartmann operation (primary resection with end colostomy) is preferred.[27] It is frequently performed in the emergency setting because it is quick, technically less complex, and avoids the complications from an anastomosis.[27] However, a second operation to reverse the colostomy is only performed in less than 50 percent of cases and is associated with high morbidity.[27,28] The one-stage primary resection and anastomosis is now considered feasible for left-sided malignant obstructions and is preferred for low-risk patients[27,29] as it attempts to treat the disease and restore the intestinal continuity in a single operation, avoiding the complications of colostomy and its reversal. Intraoperative irrigation has no benefit.[27] Lastly, simple colostomy is only used for very ill patients who are not fit for other procedures.[27]

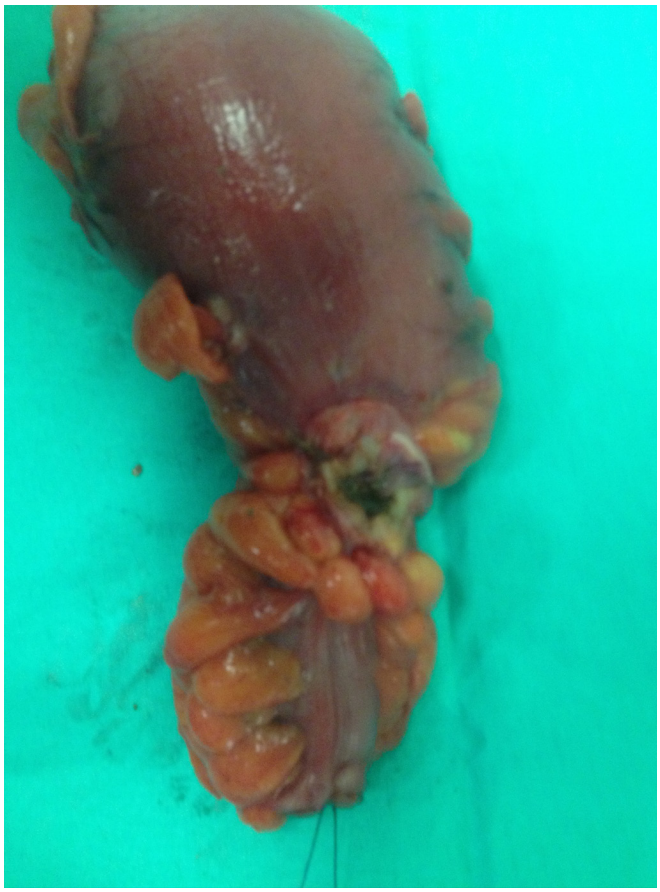

Figure 3. Specimen of colonic obstruction due to sigmoid cancer

Colonic stenting is a recent option for palliation or as a bridge to surgery for left colon obstruction.[30] It is successful in up to 90 percent of cases in specialized groups[17] and reduces complications, mortality, and the need for colostomy.[27] However, if stenting is not possible, loop colostomy can be chosen for patients with high surgical risk.[17]

Rectal obstruction

Obstruction due to rectal cancer is a clear sign of locally advanced malignancy. For obstructions of the middle or lower rectum, the creation of a stoma prior to the start of neoadjuvant treatment is indicated.[31] Patients with endoscopically obstructed rectal cancers should undergo immediate neoadjuvant chemoradiotherapy.[32] These patients can safely be managed without diversion or stenting, as only 4.3 percent without them progress to a complete obstruction.[32] An alternative to surgical decompression is self-expanding metal stenting. They are as effective and safe for malignant rectal obstruction as they are for left colonic obstruction; however, total obstruction is associated with higher complication rates.[33] Also, the prolonged interval until curative surgery, due to the need for neoadjuvant treatment, increases the risk of stent failure.[31]

Colonic Volvulus

Acute colonic volvulus (**Figure 4**) results from the torsion of a segment of the colon along the mesenteric axis, typically arising in the sigmoid colon or cecum.[34] Prompt surgery is required for patients with signs of perforation, peritonitis, and unsuccessful or recurrent nonoperative decompression.[35]

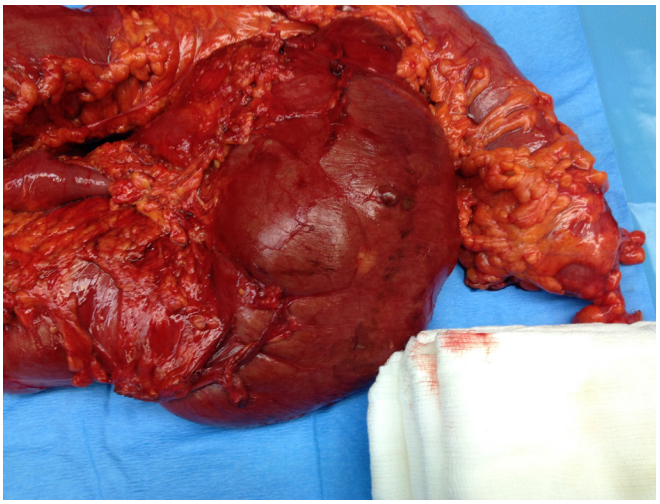

Figure 4. Specimen of large bowel ischemia due to colonic volvulus

When endoscopic detorsion is not possible, or the colon is nonviable or perforated, urgent sigmoid resection is indicated for sigmoid volvulus.[36] Otherwise, the first-line treatment for stable patients with sigmoid volvulus includes nonoperative detorsion with flexible sigmoidoscopy.[36] Endoscopic decompression, both a diagnostic and therapeutic procedure, is successful in up to 95 percent of patients .[37] Patients should be observed for recurrence (present in up to 86 percent of patients),[37] which may be prevented with a rectal tube,[12] and sigmoid colectomy is performed during the same hospital admission.[36] In general, nonresective procedures, such as detorsion, sigmoidoplasty, and mesosigmoidoplasty, are inferior to sigmoid colectomy to prevent recurrence.[36] However, when operative interventions are contraindicated, endoscopic fixation of the sigmoid colon may also be considered.[36]

For cecal volvulus, however, surgery is preferred over colonoscopy as endoscopic reduction is not commonly effective and is associated with an increased risk of perforation.[36,38] Resection, the recommended management method, is required in good operative candidates or in patients with perforated or nonviable bowel.[10,36] Nonresective methods are not widely used due to the high recurrence rates, often reported up to 75 percent for detorsion and up to 40 percent for additional cecopexy.[39]

Diverticulitis and diverticular strictures

Diverticulitis can rarely cause severe LBO. However, partial obstruction due to bowel wall edema and inflammation or abscess may occur.[40] In the chronic phase, intramuscular fibrosis can also cause obstruction in 10 to 20 percent of patients.[40] Surgical management of diverticulitis should maintain intestinal continuity by using a laparoscopic approach and controlling infection to bridge patients to single-stage procedures.[41] Patients who present with LBO due to acute diverticulitis are treated with surgical resection of the involved segment.[42] It is important to directly visualize the large bowel lumen even in CT-confirmed diverticular disease,[43] as 2.2 percent of patients with diverticulosis can have colonic cancer.[12] Thus, surgery can rule out cancer and also relieve the obstruction. Colonic obstruction secondary to diverticular disease is rarely complete, allowing for bowel preparation before surgery.[42] Obstruction that does not respond to medical management requires laparotomy, and colectomy with end colostomy is the safest procedure. However, colectomy with primary anastomosis, with or without on-table lavage, and proximal diversion can be appropriate for stable patients.[42]

Endoluminal stenting is rarely required,[42] and may not be beneficial for colonic obstruction due to diverticulitis compared to malignant obstruction, as it more often results in perforation, stent migration, and recurrent obstruction.[44] When stenting is used as a bridge to surgery, only 43 percent of patients successfully avoid a stoma.[44] However, diverticular strictures can be treated with self-expanding metal stenting before elective surgery.[12]

Inflammatory bowel disease

Crohn's disease (CD) and ulcerative colitis (UC) are referred to as inflammatory bowel diseases (IBDs). The causes of LBO related to UC are usually strictures or pseudopolyps.[12] Management options for UC strictures include surgery or endoscopic balloon dilatation.[12] Large bowel strictures, especially in UC, right-sided, and appearing after 20 years of known UC, should raise concern for malignancy,[12,45] and when an emergent colectomy is needed, oncologic principles must be followed.[45]

Although in CD the most common location for bowel obstruction is the terminal ileum, obstruction may also occur in the colon or rectum, with an incidence of 5 percent of patients.[45] If the obstruction is due to an inflammatory stricture, patients may improve with steroids or biologic therapy. However, 75 percent of patients with an intestinal stricture from CD require endoscopic dilation or surgical resection.[46] A stent as bridge to surgery can be considered.[45] Surgeries performed include two- or three-stage proctocolectomy with ileal pouch anal anastomosis, permanent ileostomy, or ileorectal anastomosis.[45] Segmental resection is possible in CD colitis.[45]

Treatment of toxic megacolon, which is usually a complication of IBD, should aim to reduce the severity of colitis, restore normal motility, and prevent perforation.[47] Patients should be resuscitated and given appropriate antibiotics, and the initial medical therapy can prevent surgery in up to 50 percent of patients.[47] Absolute indications for surgery include general clinical deterioration, perforation, massive hemorrhage, and increasing transfusion requirements.[47,48] Colectomy is recommended if there is persistent colonic distention after 48 to 72 hours, although some recommend medical therapy for up to seven days if the patient is clinically improving despite a persistent megacolon without perforation.[47] The procedure of choice for emergency surgery is subtotal colectomy with an end ileostomy.[49] This technique has lower complication rates and mortality than the single-stage proctocolectomy and allows for subsequent re-anastomosis. Early surgery in patients without perforation results in much lower mortality.[47] Additionally, blowhole colostomy has been used to treat toxic megacolon due to C. difficile infection.[50]

Acute Colonic Pseudo-Obstruction

Acute colonic pseudo-obstruction (ACPO), or Ogilvie syndrome, is an acute massive dilation of the large bowel without mechanical obstruction.[51] It is usually associated with various factors, such as surgery, trauma, sepsis, medications, and metabolic imbalances.[51] Conservative management is the first-line treatment for patients with uncomplicated ACPO (such as no significant abdominal pain, peritonitis, ischemia, or a cecum greater than 12 cm in diameter).[37] It includes discontinuation of predisposing factors such as narcotics, a nasogastric tube, nothing by mouth, correction of electrolyte disorders, mobilization, and treatment of any infection.[52] The overall success ranges from 77 percent to more than 85 percent.[53] However, if symptoms are present for more than 48 to 72 hours, pharmacotherapy or endoscopic decompression should be considered.[37] Although several other pharmacologic agents have been studied, such as metoclopramide and erythromycin,[51] neostigmine is the drug of choice for ACPO and is effective in up to 94 percent of cases.[54]

In patients whom conservative measures have failed or neostigmine therapy is contraindicated,[36] colonoscopic decompression can be performed, with initial successful decompression in up to 95 percent of patients.[55] While some studies have found that colonoscopic decompression may be superior to neostigmine, others state that the two options are equivalent.[37] An alternative but invasive method is percutaneous endoscopic colostomy of the cecum.[56] Although surgical intervention for patients with ACPO is associated with high mortality rates, this is the next step for those with failure of the aforementioned treatment options. Also, patients who present with a cecal diameter greater than 12 cm, ischemia, perforation, peritonitis, or clinical

deterioration should be referred for surgery.[37] Options include percutaneous cecostomy, subtotal colectomy, or surgically placed cecostomy tube; the latter is associated with higher morbidity and mortality.[37]

Intussusception

Intussusception is responsible for 1 percent of all cases of adult bowel obstructions, although only about 20 percent of them occur in the large bowel.[57] About 90 percent of adult intussusception cases are due to an underlying pathological condition,[57] with about 79 percent of the cases caused by primary adenocarcinoma.[57] Compared to children, adults with LBO due to intussusception often present with relatively nonspecific symptoms,[12] and preoperative reduction with air or barium is not suggested.[59] That is because an initial reduction may result in the dissemination of malignant cells.[60] Instead, intussusception causing LBO needs prompt laparotomy.[60] Colonic intussusception must be resected en bloc because of the high rates of adenocarcinoma.[57] Therefore, for old patients with large bowel intussusceptions, which is usually caused by bowel cancer, formal oncologic resection with a primary anastomosis is recommended.[61] In contrast, when the preoperative diagnosis is benign, the intussusception can be reduced, allowing for a limited resection.[61] The laparoscopic approach has also been used for adult intussusception due to benign and malignant lesions of the large bowel.[62,63] Experienced surgeons can establish the diagnosis and find underlying disease on selected patients, and perform reduction and en bloc resection with the same method.[61]

Iatrogenic Bowel Disease

Both surgery and investigations can potentially cause LBO. Although adhesions are relatively common in small bowel obstruction, they are a rare cause of LBO, with only a few reported cases.[12] Adhesions are the most common postoperative complication of abdominal and pelvic surgery,[64] but only a minority of the reported LBO due to adhesions can be considered iatrogenic.[65] Obstruction commonly occurs at the caecum, hepatic and splenic flexures, and recto-sigmoid colon.[65] Another rare potential cause of LBO is inspissated barium following imaging. It can be managed with enema, gastrografin, manual evacuation, lactulose, endoscopy, or laparotomy with colectomy or colostomy.[12] Chronic radiation colitis, which is often precancerous, can also lead to LBO, typically partial, that can be treated conservatively with parenteral support and nasogastric suction.[66] Surgical management can be challenging due to diffuse fibrosis and alterations in the intestinal structure, with a significant risk of anastomotic leakage.[66]

Conclusion

LBO is a condition frequently encountered by acute care surgeons. Despite advances in management, the treatment of LBO remains a complex decision-making process. Surgeons must rapidly evaluate the patient and apply the appropriate algorithm to limit complications and mortality. Multiple treatment options exist to treat LBO, both surgical and endoscopic, giving the flexibility to the surgeon to achieve the best possible outcomes and quality of life for patients. Thus, each case should be individualized, and the patient should be well informed prior to interventions.

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CHAPTER 20

Management of Volvulus

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Abstract

Colonic volvulus is a closed-loop obstruction that occurs when a mobile and lax segment of colon twists around its mesentery. Volvulus accounts for less than 5 percent of large bowel obstructions. Volvulus can occur in several anatomic locations but the most common type in the United States is sigmoid volvulus, usually occurring in an elderly patient with multiple comorbid conditions. Initial work-up of sigmoid volvulus should focus on excluding the presence of threatened bowel or a perforation. Endoscopic decompression of the volvulus followed by elective sigmoid colectomy remains the mainstay of treatment for most patients with sigmoid volvulus. Emergent laparotomy is reserved for endoscopic failure or evidence of colonic necrosis. Resection is preferred for cecal volvulus, bascule, and other rare volvulus variants and endoscopic decompression should be avoided. Nonresective procedures can be considered for either cecal or sigmoid volvulus and viable colon. However, data on the risk of recurrence and procedural complications are limited.

Epidemiology

The most common causes of large bowel obstruction are colorectal cancer, diverticular disease, and colonic volvulus.[1] Volvulus occurs when a mobile portion of the colon twists around its mesentery. This twisting can progress to obstruction and compromise the blood supply to the affected segment, leading to ischemia and perforation. Anatomically, the sigmoid colon is most susceptible to volvulus owing to its redundant length, as well as its tall mesentery on a narrow root base.[2]

There are several disparate patterns of volvulus incidence.[3] In parts of South America, Africa, the Middle East, and South Asia volvulus is a relatively common cause of large bowel obstruction, accounting for as many as a third of all such obstructions.[4] In these regions volvulus tends to be of the sigmoid colon, has a strong male predominance, and occurs in younger patients.[3]

In Western countries volvulus is comparatively rare, accounting for less than 5 percent of cases of large bowel obstruction. In the United States, the sigmoid location accounts for approximately two-thirds of cases. There is a peak incidence around 80 years of age, with a two-to-one male-to-female predominance.[5] Many patients have multiple comorbid diseases and neuropsychiatric conditions are especially common.[6,7]

Volvulus occurring elsewhere in the colon most typically affects the cecum and transverse colon.[8,9] This tends to occur in younger patients without comorbid conditions. Cecal volvulus has approximately a three-to-one, female-to-male predominance, and in women it tends to occur around 50 years of age.[5]

Clinical Features

Patients with volvulus present with a constellation of clinical signs and symptoms generally consistent with large bowel obstruction.[10] A careful history should be taken, noting any predisposing history such as longstanding constipation or the presence of a neuropsychiatric condition. Patients will typically report a sudden onset of abdominal pain, severe distention, and complete obstipation. The onset of symptoms is typically rapid, in distinction to other causes of large bowel obstruction. For example, large bowel obstruction from colorectal malignancy usually has a more gradual, progressive course. If the ileocecal valve is competent there may be little or no associated nausea and vomiting, in contrast to small bowel obstruction.

On exam the abdomen will be distended, tympanitic, and tender. These findings are again relatively nonspecific, as they are shared with other causes of large bowel obstruction. The anatomic location of the involved segment of colon will not greatly affect the symptoms or physical findings. If the volvulus is not addressed quickly, ischemia of the colon will result. Ischemia can progress to necrosis, perforation, peritonitis, and septic shock. The physical exam should therefore be attentive to any signs of generalized peritonitis, which would suggest the need for emergent operation.

Evaluation

After evaluation with a focused history and physical exam, a standard laboratory evaluation should be sent, including a complete blood count, metabolic panel, coagulation profile, and lactate. Elevated lactate or a leukocytosis should alert the clinician to a more advanced state of the disease, with the possibility of bowel ischemia.[11]

Radiologic investigation is essential to determine the diagnosis as well as appropriate management.[12] The sequence and type of imaging to be obtained is dependent on the available resources, acuity of the patient, and physical findings. Regardless of the imaging modality chosen, it is essential to confirm the diagnosis of colonic volvulus, determine the anatomic region involved, and identify pneumoperitoneum if present. Each of these findings will dictate subsequent steps in management.

An upright chest X ray is typically the most expeditious means of identifying pneumoperitoneum, but it will not elucidate the etiology of obstruction. Plain abdominal films are frequently the initial diagnostic imaging obtained. Radiographs will show a large, dilated lucency containing the involved colonic segment filling much of the abdomen. This finding has been referred to variously as a "coffee bean," "kidney bean," or "bent inner-tube" sign. A radio-opaque stripe at the center of the volvulus will point toward the area where the volvulus arose. For example, in the case of sigmoid volvulus the central stripe or notch will point toward the left lower quadrant.[13] In cecal volvulus the distal colon will be decompressed and haustra will be present. There may be one air-fluid level. In sigmoid volvulus the proximal colon and small bowel may be distended, and haustra will be absent. Multiple air-fluid levels are more likely to be seen.[14] The dilated segment of colon extending cephalad to the transverse colon is also highly suggestive of volvulus, with a sensitivity of 86 percent in a small series of sigmoid volvulus cases.[15]

Water-soluble contrast enema or CT imaging can also be used to establish the diagnosis of volvulus. Contrast enema will demonstrate a bird's beak-shaped narrowing of the colon at the level of the volvulus. In a small series of patients presenting with volvulus in Australia, sigmoid volvulus was correctly identified by plain radiography or contrast enema in 90 percent of cases, whereas plain film and contrast enema established the diagnosis in only 42 percent of cases of cecal volvulus.[16] When performing contrast enema the use of barium should be avoided. CT imaging is quick, highly accurate, and readily available in most settings. A

major advantage of CT over plain radiographs with or without contrast is the ability to identify any associated bowel compromise as evidenced by pneumatosis or lack of contrast enhancement. CT can also distinguish volvulus from more common causes of large bowel obstruction such as malignancy, benign stricture, or colonic pseudo-obstruction. CT is also less invasive than contrast enema. There are no robust case series with sufficient follow-up to define the accuracy of CT in the diagnosis of volvulus. However, in a small series of 43 patients undergoing imaging for suspected cecal volvulus, CT was 100 percent sensitive in identifying the volvulus, with a specificity that ranged from 57 to 76 percent. Swirling of the mesentery was the most predictive feature for volvulus.[17]

Management of Sigmoid Volvulus

After identifying a sigmoid volvulus, the presence or absence of perforation or peritonitis should be assessed. Patients with evidence of compromised bowel should be taken for emergent laparotomy. Attempting endoscopic decompression in these cases can lead to worsening peritonitis and clinical deterioration. Additionally, detorsion of ischemic bowel either endoscopically or in the operating room can release endotoxins and cellular products of colonic necrosis, worsening the physiologic insult to the patient.

The choice of operation in the emergent setting is dictated mostly by the health of the remaining colon, degree of abdominal contamination, and the fitness of the patient. The three most common options for reconstruction after sigmoidectomy include primary colorectal anastomosis, primary anastomosis with proximal diversion, or resection with end colostomy and oversewing of the rectal stump (Hartmann procedure). Interpretation of the data in this area is hampered by selection bias for Hartmann procedure in the setting of higher disease severity. There are no prospective studies in volvulus patients available to guide decision-making. In retrospective case series the selection of Hartmann procedure is associated with the presence of colonic ischemia, as well as both preoperative and postoperative morbidity.[18] The most useful data may come indirectly from the diverticulitis literature. The LADIES trial randomized patients with purulent or feculent peritonitis due to diverticulitis to either the Hartmann procedure or primary anastomosis. In the primary anastomosis group the need for proximal diversion was determined by the operating surgeon. Stoma-free survival at one year was superior in the primary anastomosis group, 95 versus 72 percent, and there were no differences in short-term postoperative morbidity and mortality.[19] These data should be applied to the care of volvulus patients cautiously. Many patients presenting with sigmoid volvulus are considerably older and have more comorbid conditions than the patients enrolled in the LADIES trial, who averaged 62 years old, and were mostly American Society of Anesthesiologists class I or class II.

For patients without peritonitis or perforation, endoscopic decompression should be performed initially for both diagnostic and therapeutic purposes. This can be accomplished by rigid proctoscopy, but flexible sigmoidoscopy affords greater visualization. At the point of volvulus the mucosa will appear twisted and folded onto itself in a spiral pattern.[20] The mucosa should be examined and confirmed to be viable. After successful detorsion a rectal tube should be placed to prevent immediate recurrence of the volvulus. The technical success of endoscopic decompression is high. A very large Turkish series of 827 patients reported successful endoscopic detorsion in 70 percent of patients, but included patients over a 38-year period and may not reflect current practice.[21] Bruzzi et al.[22] reported a more recent series of patients with sigmoid volvulus presenting to a single French center from 2003 to 2013. Endoscopic decompression was successful in 95 percent of cases in which it was attempted. Laparotomy is required in the rare instance where endoscopic decompression is unsuccessful.

Approximately two-thirds of patients will experience recurrent volvulus if they are treated by decompression alone without any further intervention. One series of patients medically unfit for surgery reported that 67 percent recurred by follow-up at 5 years.[22] Another single-center series of 57 patients noted that of the 31 treated conservatively, 61 percent had recurrent volvulus at just one month of follow-up.[23] Such a high frequency of recurrence emphasizes the importance of additional intervention whenever possible.

After successful endoscopic decompression, several options are available for preventing recurrence of sigmoid volvulus in the elective setting. These approaches can be broadly classified as resective or nonresective in nature.

In the elective setting, sigmoid colectomy with primary colorectal anastomosis affords a risk of recurrence which approaches zero. Bruzzi et al.[22] reported one recurrence at 130 months out of 65 patients treated with sigmoidectomy, and Yassaie et al.[23] reported no recurrences in 57 patients undergoing surgery. A large Turkish series of elective sigmoidectomy in 104 patients also reported no recurrences.[24] Sigmoidectomy can generally be performed without proximal diversion. Our practice is to allow several days for the colon to decompress after detorsion. Once the patient's physiology has recovered from the volvulus and the colon has had time to completely evacuate, we proceed with colectomy. This should generally be undertaken during the index admission.

Morbidity from sigmoidectomy in these medically frail patients can be considerable. In a cohort of patients in the Nationwide Inpatient Sample from 2002-2010, Halabi et al.[5] reported a perioperative mortality of 9.4 percent for the 19,220 patients undergoing sigmoid colectomy. 15.8 percent

of the cohort had an anastomotic complication, and median length of stay was 15 days. Unsurprisingly, peritonitis and coagulopathy were independently associated with worse outcomes. There are several small, single-center case series available which generally report lower complication rates. For example Bruzzi et al.,[22] reported a major complication rate of 6 percent in their small series of patients. Yassaie et al.[23] reported one anastomotic leak and no deaths among 29 patients undergoing sigmoidectomy for volvulus. However, the outcomes from case series are likely heavily influenced by reporting and selection biases and incomplete follow-up.

A laparoscopic approach in the acute setting has been reported in a small number of patients.[25] However, laparoscopy is often precluded by severe abdominal distention, the fragile state of the distended colon, and the need to extract a large specimen. The mesenteric hypermobility which predisposes the sigmoid to volvulus also usually allows for relatively easy medialization of the specimen through a small midline incision.

Nonresective techniques have been used to reduce the likelihood of volvulus recurrence without incurring the morbidity of colectomy and the potential for anastomotic failure. Nonresective options include fixation or extraperitonealization of the sigmoid colon (sigmoidopexy) or broadening and fixation of the sigmoid mesentery (mesosigmoidoplasty). In contrast to the low risk of recurrence after resection, these nonresective approaches have a higher risk of recurrence. However, the overall quality of evidence in regard to recurrence after a nonresective procedure is low. In a series of 84 patients undergoing detorsion and sigmoid extraperitonealization in the abdominal wall, there were no observed recurrences.[26] In contrast to these optimistic results, the large series of patients reported from Turkish centers with long-term follow-up reported volvulus recurrence after mesosigmoidoplasty in 16 to 21 percent of patients.[21,24]

Rather than attempting fixation via a transabdominal approach, several endoscopic procedures for sigmoid fixation have been described. After endoscopic reduction of the volvulus either percutaneous T-fasteners or percutaneous tube colostomy can be used to fix the colon to the anterior abdominal wall. A variable number, type, and spacing of these fixation points has been described in a small case series of patients unfit for surgery.[27,28] Major complications can result from these procedures however. A 2020 systematic review of case series reporting percutaneous procedures for volvulus noted 10 recurrences in 81 patients, though most of these occurred after device removal.[29] In one retrospective case series of 27 patients undergoing percutaneous endoscopic colostomy, there were no volvulus recurrences while the tube was in place, but 77 percent of the group developed infectious complications and two of the 27 (7 percent) developed feculent peritonitis due to dislodgement of the fixation device.[30] Endoscopic and real-time image guidance can also be used to place fixating transabdominal seromuscular sutures, avoiding the need to create a transmural defect in the colon.[31] The most recent ASCRS practice guidelines recommend percutaneous fixation only in highly select patients with prohibitive operative risk.[32] In summary, endoscopic decompression of the volvulus followed by elective sigmoid colectomy remains the mainstay of treatment for the majority of patients with sigmoid volvulus. Emergent laparotomy is reserved for endoscopic failure or evidence of colonic necrosis. For patients with prohibitive risk, nonresective procedures can be considered as an adjunct to endoscopic decompression.

Management of Cecal Volvulus and Bascule

Obstruction can occur in two main anatomic variants in the right colon. Twisting of the colon around its mesentery in a mesentero-axial manner represents true cecal volvulus. Folding or reflection of a hypermobile cecum cephalad results in cecal bascule. Bascule is relatively rare and accounts for approximately 20 percent of cases of right-sided volvulus.[33] In either instance, the functional outcome of a closed-loop colonic obstruction is the same. The predisposing factors for cecal volvulus or bascule and sigmoid volvulus are also the same. These factors include hypermobility, redundancy, and lack of peritoneal attachments to the retroperitoneum or abdominal sidewall. The initial work-up, imaging, and fluid resuscitation should follow a similar approach. However, in distinction to sigmoid volvulus, cecal volvulus is generally not amenable to endoscopic decompression as a temporizing measure. In two small case series of endoscopic decompression, a total of 2 out of 16 cases of cecal volvulus were successfully endoscopically reduced.[6,34] While there are individual case reports of success with an endoscopic approach, it is discouraged by the American Society Colon and Rectal Surgeons (ASCRS) practice guidelines given the high failure rate, delay to definitive therapy, and risk of perforation.[32,35]

Once a cecal volvulus is identified, either a resective or nonresective approach must be taken. There are very little recent data to guide management of cecal volvulus, with no large case series in the last twenty years, and the majority of studies having been performed in the 1980s or earlier.[36,37] Extrapolating data from left-sided volvulus, several principles can be cautiously applied. Resective techniques can be presumed to have the lowest recurrence rate, at the cost of operative morbidity.[8] Patients presenting with necrotic colon or perforation should clearly receive an ileocolic resection. Our preference is to perform ileocolic resection and primary anastomosis whenever it is safe to do so. In cases where the patient has a high risk of anastomotic failure, a resection and end ileostomy, with or without mucous fistula, can be performed.

Nonresective techniques for cecal volvulus include cecopexy, cecostomy, and appendicocecostomy. Cecopexy can be performed with simple seromuscular sutures, or with the creation of a peritoneal flap. In a case series from 1986, Anderson et al.[38] noted a recurrence rate of 20 percent with cecopexy, similar to the recurrence rate they observed with resection. In a systematic review of the available literature, cecostomy tube placement tends to be associated with the most postoperative complications, particularly infectious complications.[39] Our preference is to employ a nonresective approach only in select patients with viable bowels who are very poor operative risks, and for whom an end ileostomy would be difficult to manage.

Rare Volvulus Locations: Transverse Colon and Ileosigmoid Knotting

Although the sigmoid and cecum are the predominant anatomic locations for colonic volvulus to occur, there are other configurations of volvulus that arise in rare situations.

The transverse colon is a rare site of volvulus. In the Nationwide Inpatient Sample there were 587 resections for transverse colon volvulus between 2002 and 2010, compared to more than 22,000 resections for cecal volvulus.[5] Of all possible anatomic locations of colonic volvulus, transverse volvulus had the highest risk of perioperative mortality. The reasons for this risk are unclear, but potentially related to diagnostic delay or the need for a more extended resection. As with cecal volvulus, endoscopic decompression should be avoided, and prompt operative intervention is prudent, with the extent of resection dependent on the operative findings.

Ileosigmoid knotting is a rare entity, most prevalent in Africa and the Eastern Mediterranean. This volvulus variant occurs when a loop of ileum wraps around the base of the sigmoid colon mesentery. The resulting "knot" creates closed-loop obstructions of both the small and large bowel. It has been hypothesized that eating one large meal per day, as is common in some cultures that observe daytime fasting, predisposes to ileosigmoid knotting. Eating a sudden large food bolus is theorized to produce a lead point for the wrapping.[40] Ileosigmoid knotting is very rare, with fewer than 500 cases reported worldwide as of 2018.[41] Surgical intervention is usually required to undo the wrapping and resect any infarcted bowel. Diagnostic delay is common due to the lack of distinct plain radiographic findings. The sigmoid colon will typically appear distended and can be mistaken for a straightforward sigmoid volvulus. Endoscopic reduction should be avoided as it will be unable to undo the "knot" and risks perforating the colon.[42]

Conclusion

Colonic volvulus is an uncommon cause of large bowel obstruction that a surgeon will nonetheless occasionally encounter. Management is dependent on the anatomic location of the volvulus and the presence of bowel ischemia or perforation. When possible, resection should be performed to afford the lowest risk of recurrence. Other, non-esective approaches are possible, but safety and efficacy data are limited.

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CHAPTER 21

Management of Acute Diverticulitis

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Introduction and Epidemiology

Diverticular disease occurs more frequently in Western countries but its incidence continues to increase worldwide. Why diverticular disease is less common in underdeveloped countries is unclear, but it is presumably secondary to dietary factors and lifestyle.

Acute diverticulitis, the most frequent clinical manifestation of diverticular disease, is the third-most common inpatient gastrointestinal diagnosis in the United States. The prevalence of diverticulitis has been rising over the past several decades, affecting an estimated 180/100,000 persons per year in the country.

The economic burden is relevant: in a study of data from the National Inpatient Sample, 216,000 hospital admission for acute diverticulitis in 2012 were found to cost 2.2 billion dollars. The main cost driver is the use of hospital facilities, which accounts for 65 percent to 70 percent of the total health care costs associated with diverticulitis. Another major impact on health care costs associated with acute diverticulitis is the routine nonselective use of antibiotics.[1]

While diverticulosis and its complications have historically been considered prerogative of the elderly, the increasing prevalence of symptomatic diverticular disease in younger individuals has significantly altered the profile of the disease and its clinical management.

Etzioni et al. examined admission rates for acute diverticulitis in California between 1995 and 2006 and found significant increases in rates of hospitalization and elective surgical management for diverticulitis. The changes in these rates over the study period were most pronounced in patients between 20 and 34 years old (estimated percent annual change 8.6 percent) and those between 35 and 40 years old (estimated percent annual change 5.7 percent).[2]

Similar trends have been noted by other groups in North America, New Zealand, Europe, and Asia, where the Western diet and lifestyle have become a new normal in the era of globalization. Previously, it was believed the lifetime risk of acute diverticulitis in patients with diverticulosis ranges from 4 percent to 25 percent. However, more recent findings have shown the numbers to be closer to 1 percent to 4 percent. Of patients with incident disease, approximately 20 percent have one or more recurrent episodes within 10 years.[3]

In Italy, between 2008 and 2015, an increasing rate of hospitalization for acute diverticulitis from 39 to 48 per 100,000 inhabitants has been reported. The increased rate of hospitalization was accounted for patients less than 60 years old. The hospitalization rate for patients aged ≥70 years was higher, but the trend remained unchanged during the study period. An increasing rate of hospitalization for complicated acute diverticulitis and admissions associated with surgery especially for younger patients was also demonstrated in the study by Binda et al. The rate of emergency surgery for perforated diverticulitis showed a significant mean annual increase (+3.9 percent per year), whereas elective admissions for surgery remained stable.[4]

The pathophysiology of acute diverticulitis remains poorly understood, but is thought to be secondary to high baseline levels of circulating inflammatory mediators.[5]

Risk factors for diverticulitis include smoking, the use of nonsteroidal anti-inflammatory drugs (NSAIDs), and physical inactivity. Diets rich in refined carbohydrates, red meat, and low in fiber have also been associated with an increased risk of diverticulosis and diverticulitis.

Multiple studies have shown an association between increased body mass index (BMI) and visceral fat ratio to the development of acute diverticulitis in patients with diverticulosis compared to healthy controls.[6, 7]

Several retrospective cohort studies have also shown a strong association between the use of NSAIDs, corticosteroids, and opioids and the risk of perforation. It is hypothesized that opioids slow the colonic transit time and may therefore cause fecal stasis and thus raise intraluminal pressure, which may increase the risk on inflammation and perforation.[8-10]

Case-control studies have investigated the hypothesized protective effect of calcium-channel blocker therapy and statin therapy on the development of colonic perforation in acute diverticulitis. Calcium-channel blockers have been reported to decrease the frequency of high-pressure colonic contractions and improve mucosal blood flow. This potential mechanism was thought responsible for the prior finding of a reduced association between users of these drugs and diverticular perforation.[8,11]

Perforation may result from a combination of increased intraluminal sigmoid pressure and impairment of the colonic mucosal barrier.

If a diverticulum perforates freely into the abdominal cavity, diffuse peritonitis results, whereas diverticula covered by mesentery are contained, creating a phlegmon or abscess, and resulting in a localized peritonitis. Adjacent organs, such as the bladder, small bowel, and vagina may be involved in the inflammatory process, resulting in fistula formation.

Although more than 70 percent of cases of acute uncomplicated diverticulitis are mild and respond well to conservative management, further complications including pericolic abscess, pelvic abscess, and perforation with purulent or fecal peritonitis may potentially ensue.

Current evidence suggests that the natural history of sigmoid diverticulitis is more benign than thought in the past. Most perforations do not occur after recurrences, but after the first attack of acute diverticulitis.

The overall recurrence rate of diverticulitis is reported in literature as 13 percent to 19 percent, and only less than 5 percent of patients with recurrent diverticulitis develop complications. Moreover, current evidence suggests that multiple recurrences are currently not associated with a higher chance of mortality.

Over the past decades, four major innovations have changed the management of acute diverticulitis:

1. Complicated diverticulitis is now reliably distinguished from uncomplicated disease by the use of contrast-enhanced CT scan;
2. The implementation of large clinical databases have facilitated more complete follow-up of large populations, resulting in advancements in the understanding of the natural history of diverticulitis, clinical and behavioral risk factors for the disease, and what the indications and outcomes of its treatments are;
3. Two randomized controlled trials have demonstrated that adding broad-spectrum antibiotics does not decrease treatment failure, recurrence, complications, hospital readmission, and need for surgery compared to nonantibiotic treatment, thus questioning the necessity of the use of antibiotics for uncomplicated diverticulitis; and
4. Surgeons are pursuing less-invasive interventions, increasing the use of percutaneous drainage and laparoscopic surgical techniques.

Table 1. Five key clinical points on epidemiology of acute diverticulitis

In industrialized countries, the rate of diverticulitis-related emergency department attendance and hospital admissions has risen steadily over the past few decades.
The highest rates of increase are occurring in patients under 40 years of age.
Increased BMI and the visceral-to-subcutaneous fat ratio are associated with an increased risk for acute diverticulitis.
Current evidence does not support the hypothesis that nuts, seeds, and popcorn cause acute diverticulitis. Conversely, long-term NSAID, corticosteroid, and opiate use have been associated with increased risk of perforation in the setting of acute diverticulitis.
Immunosuppressed patients, such as those with HIV, those undergoing chemotherapy, and patients who received a solid organ transplant, are at increased risk for developing acute diverticulitis.

Diagnosis and Classification

Physical examination and laboratory markers

A physical exam is recommended for all patients with suspected acute diverticulitis.[3] The symptoms depend on the severity of the inflammatory process and its complications. Abdominal pain is the most common complaint, with fever, abdominal tenderness, and/or constipation. Diagnosis of acute diverticulitis based on just clinical examination has a very low accuracy, with a positive and negative predictive value of 65 percent and 98 percent, respectively.[12]

C-reactive protein (CRP) has a diagnostic and prognostic value and it should be included in the laboratory evaluation.[3] Imaging is highly recommended for those patients with CRP >50 mg/L, pain in the left lower abdomen, and absence of vomiting. A recent study has shown that a CRP value >150 mg/L can significantly discriminate uncomplicated from complicated acute diverticulitis.[13] However, due to the 48-hour delay of the CRP in reaching its peak, a low CRP value should never exclude acute diverticulitis.

Ultrasound (US)

US is recommended when a CT scan cannot be performed and only at centers with experience in abdominal US.[14] It can miss complicated diverticulitis, mainly due to the dependency of the operator, the difficulties in patients with free gas and deeply located abscess, and the poor assessment in obese patients. Its accuracy has been investigated, with reported rates of sensitivity and specificity around 90 percent.[15]

A step-up approach with a CT scan performed after an inconclusive or negative US has demonstrated to be a safe approach for patients with suspected acute diverticulitis.[16]

CT scan

The gold standard for the diagnosis of acute diverticulitis is the CT scan.[17] It has a sensitivity ranging from 95 percent to 97 percent and it is very accurate at identifying colonic perforation, which can have a direct impact on the management of the patient.

There are multiple classification systems based on CT imaging and on preoperative findings.[18-23]

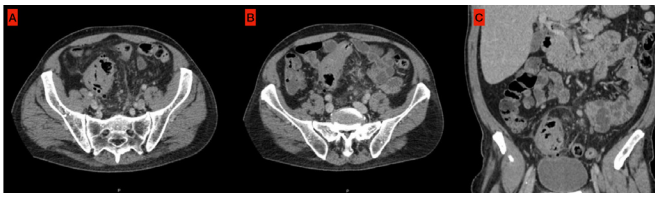
It goes beyond the diagnosis, providing with the grade of severity and tailoring the treatment options. They all range in severity from uncomplicated diverticulitis to perforation, but several modifications have been included, according to more advanced and detailed CT imaging. However, none of them have proved to be superior in predicting patient outcomes.

The traditional Hinchey classification was introduced by E.J. Hinchey in 1978, and it was based on macroscopic intraoperative findings alone, developed before the advent of the CT scan. It classified the anatomic findings into four levels:

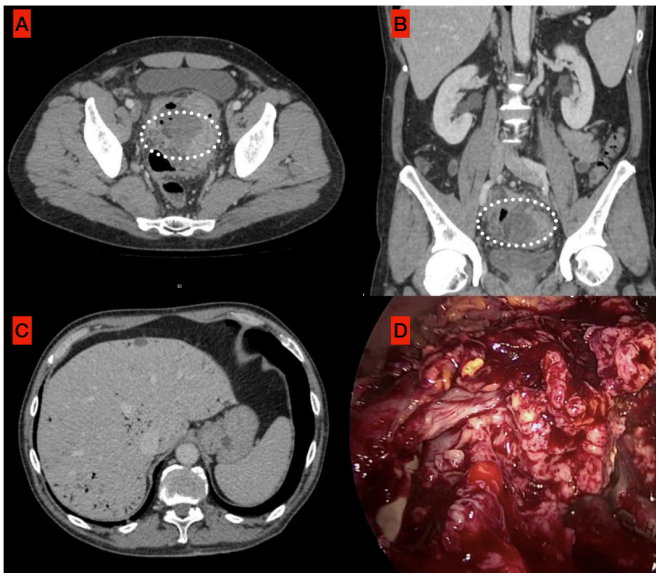
1. Pericolic abscess
2. Pelvic, intra-abdominal, or retroperitoneal abscess
3. Generalized purulent peritonitis
4. Generalized fecal peritonitis

CT accuracy is poor for differentiating Hinchey grades[24,25] and this is the main limitation of its clinical usefulness. Another drawback of the Hinchey's classification is that some patients cannot be classified, such as patients with distant retroperitoneal air or pericolic air. Due to the advancements in imaging modalities, several modifications have been proposed over the years. New subcategories have been added that take radiological findings into consideration. Currently, the most common classification used is the Wasvary Hinchey modification, which distinguishes four stages of complicated acute diverticulitis regarding its severity:[26]

- Stage 0: Mild clinical diverticulitis
- Stage 1a: Confined pericolic inflammation or phlegmon (**Figure 1**)
- Stage 1b: Confined pericolic or mesocolic abscess
- Stage 2: Pelvic or distant intra-abdominal abscess (**Figure 2**)
- Stage 3: Generalized purulent peritonitis
- Stage 4: Faecal peritonitis at presentation (**Figure 3**)



Figures 1A–C. CT scan images showing uncomplicated Hinchey stage Ia acute diverticulitis (Wasvary Hinchey-modified classification)



Figures 2A–B. Abdominal CT scan showing a large pelvic abscess (Hinchey stage IIb)

(C) Pneumobilia caused by a contained perforation involving the root of the sigmoid mesentery (D) Intraoperative image showing a Hinchey stage II diverticular abscess (Wasvary Hinchey-modified classification)

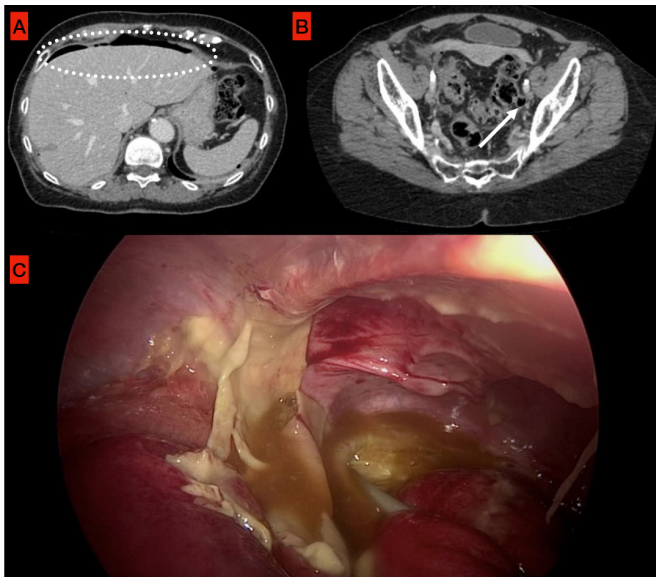


Figure 3.

(A) Preoperative CT scan showing pneumoperitoneum, caused by (B) perforated acute diverticulitis (*white arrow*) (C) Intraoperative image showing Hinchey stage IV perforated diverticulitis (Wasvary Hinchey modified-classification). Hartmann procedure was carried out due to patient's hemodynamic instability.

The World Society of Emergency Surgery (WSES) developed a simple classification with the aim to guide surgeons in the management of acute diverticulitis, by dividing the findings into two subcategories, uncomplicated and complicated diverticulitis [17]:

- Uncomplicated: The infection only involves the colon.
  - Stage 0. Diverticula, thickening of the wall, increased density of the pericolic fat
- Complicated: The infection also involves the peritoneum.
  - Stage 1a. Pericolic air bubbles or small amount of pericolic fluid without abscess (within 5 cm from inflamed bowel segment)
  - Stage 1b. Abscess <4 cm
  - Stage 2a. Abscess >4 cm
  - Stage 2b. Distant gas (>5 cm from the inflamed bowel segment)
  - Stage 3. Diffuse fluid without distant free gas
  - Stage 4. Diffuse fluid with distant free gas

The guidelines have been recently updated, incorporating the latest changes in the management of this disease, according to their CT classification system.

Table 2. Historical review of acute diverticulitis classifications

Author	Hinchey	Neff	Wasvary (Modification of Hinchey classification)	*Ambrosetti*
Year	1978	1989	1999	2002
Categories	Pericolic abscess Pelvic, intra-abdominal, or retroperitoneal abscess Generalized purulent peritonitis Generalized faecal peritonitis	Uncomplicated diverticulitis; thickening of the wall, increased density of the pericolic fat Locally complicated with local abscess Complicated with pelvic abscess Complicated with distant abscess Complicated with other distant complications	Stage 0: Mild clinical diverticulitis Stage 1a: Confined pericolic inflammation or phlegmon Stage 1b: Confined pericolic or mesocolic abscess Stage 2: Pelvic or distant intra-abdominal abscess Stage 3: Generalized purulent peritonitis Stage 4: Faecal peritonitis at presentation	Moderate diverticulitis Localized sigmoid wall thickening (>5 mm) Pericolic fat stranding Severe diverticulitis Abscess Extraluminal gas Extraluminal contrast
Name	*Mora Lopez*	*Kaiser (modified Hinchey)*	*Sallinen*	*WSES*
Year	2013	2005	2014	2015
Categories	Uncomplicated diverticulitis; thickening of the wall, increased density of the pericolic fat Locally complicated Localized pneumoperitoneum in the form of gas bubbles Abscess <4 cm Complicated with pelvic abscess Complicated with distant abscess Complicated with other distant complications	Stage 0: Mild clinical diverticulitis Stage 1a: Confined pericolic inflammation Stage 1b: Confined pericolic abscess Stage 2: Pelvic or distant intra-abdominal abscess Stage 3: Generalized purulent peritonitis Stage 4: Faecal peritonitis at presentation	Uncomplicated diverticulitis Complicated diverticulitis with small abscess (<6 cm) Complicated with large abscess (>6 cm) or distant intraperitoneal or retroperitoneal gas Generalized peritonitis without organ dysfunction Generalized peritonitis with organ dysfunction	Uncomplicated: Stage 0. Diverticula, thickening of the wall, increased density of the pericolic fat Complicated Stage 1a. Pericolic air bubbles or small amount of pericolic fluid without abscess (within 5 cm from inflamed bowel segment) Stage 1b. Abscess <4 cm Stage 2a. Abscess >4 cm Stage 2b. Distant gas (>5 cm from the inflamed bowel segment) Stage 3. Diffuse fluid without distant free gas Stage 4. Diffuse fluid with distant free gas

Table 3. Five key clinical points on diagnosis and classification of acute diverticulitis

None of the multiple classification systems for acute diverticulitis has been conclusively demonstrated to be superior to another in predicting patient outcomes. The modified Hinchey classification is the most commonly used in the day clinical practice.
Patients with left-lower quadrant abdominal pain and tenderness in the absence of vomiting, and a CRP >50 mg/L are highly likely to have acute diverticulitis. Selective imaging is recommended in these patients.
Contrast-enhanced CT scan of the abdomen is the imaging technique of first choice in patients suspected of having acute diverticulitis.
US can be used in the initial evaluation of patients with suspected acute diverticulitis where it is performed by an expert operator.
A step-up approach with CT performed after an inconclusive or negative US may be a safe approach for patients suspected of acute diverticulitis.

Conservative Treatment

Uncomplicated diverticulitis

Uncomplicated diverticulitis accounts for approximately 75 percent of cases of acute diverticulitis. Patients with uncomplicated diverticulitis can be managed on an outpatient basis in the absence of high fever, clinically significant laboratory derangement, abscess at CT scan, or immunological disorders.

Data show that rates of admission to the hospital after emergency department evaluation for diverticulitis dropped from 58 percent in 2006 to 47 percent in 2013.[27]

In the presence of strong evidence against the routine use of antibiotics, and in light of the rise of antibiotic resistance, currently the conservative treatment of uncomplicated acute diverticulitis with no antibiotics should be the standard of care in immunocompetent patients.

A recent meta-analysis of more than 2,000 patients has shown that there is no significant difference in major clinical outcomes when antibiotics are not used in patients with uncomplicated acute diverticulitis compared with those who receive antibiotics. Readmission rates and emergency sigmoid resection are also not statistically different.[28]

Two randomized controlled trials have investigated the use of antibiotic therapy in the treatment of uncomplicated acute diverticulitis. The randomized clinical trial of antibiotics in acute uncomplicated diverticulitis (AVOD trial) included more than 600 patients with CT-confirmed uncomplicated acute diverticulitis to either antibiotic or nonantibiotic therapy, and demonstrated equivalent rates of abscess and free perforation in both groups (<2 percent).[29,30] The Long-Term Effects of Omitting Antibiotics in Uncomplicated Acute Diverticulitis (DIABOLO) trial, published in 2017, similarly randomized more than 500 patients, and reported an equivalent time to full recovery with and without antibiotics (12 days versus 14 days).[31]

Similarly to the AVOD trial, also in the DIABOLO trial there were no observed differences in complicated diverticulitis (2.6 versus 3.8 percent), ongoing diverticulitis (4.1 versus 7.3 percent), or recurrence and surgery at one year. Conversely, the duration of initial admission was longer, and the rate of antibiotic-related adverse events was higher in the antibiotic group.

Cases of uncomplicated diverticulitis with microperforation were not included in either trial, and while DIABOLO included few patients (<10 percent) with modified Hinchey 1B disease, the authors caution against using nonantibiotic therapy in such patients until larger cohorts are studied.

In accordance with the results coming from a systematic review including nine studies and more than 2,500 patients, the only variables that have been found to be significantly related to the failure of the nonantibiotic treatment strategy were associated comorbidities. Failure of nonantibiotic strategy was observed in 5 percent of patients versus 3 percent of patients who received antibiotics. Around 75 percent of the patients were treated conservatively without antibiotics and about half of them were treated on an outpatient basis.[32] Immunocompetent patients presenting with uncomplicated acute diverticulitis and mild symptoms may be managed in the outpatient setting.

The "Outpatient versus hospitalization management for uncomplicated diverticulitis: a prospective, multicenter randomized clinical trial" (DIVER) is the only randomized controlled trial evaluating the safety of outpatient management for patients with uncomplicated acute diverticulitis published to date. One hundred and thirty-two patients were randomized to admission or outpatient therapy, and all received antibiotic therapy. There was no difference in readmission due to failure of medical treatment between the two groups (4.5 versus 6.1 percent).[33]

Other prospective cohort studies also found no difference in readmission rate in the outpatient group versus the inpatient group, and no need for emergency surgery or percutaneous abscess drainage in either group. However, most of these studies only included patients with uncomplicated acute diverticulitis without serious comorbidity or an immunocompromised state that were able to tolerate oral intake and had an adequate social or family support. For these types of patients, outpatient treatment seems to be safe without significant short-term and mid-term adverse outcomes.

Inpatient management is indicated in cases of high fever (>38.5 °C), leukocytosis, complicated disease on CT (abscess, free fluid), immunosuppression, serious comorbidity, inability to receive oral intake, need for pain control, and lack of home support. During hospitalization, standard management includes bowel rest, pain control, and antibiotics, usually administered intravenously because of the patient's inability to receive oral intake.

For patients who are able to receive oral intake, randomized controlled trials have shown no significant benefit of intravenous over oral antibiotics in these patients.[34]

Antibiotic therapy should cover Gram-negative and anaerobic bacteria. Typical antibiotic regimens include cephalosporins plus metronidazole, or single-agent therapy with a β-lactam or β-lactam/β-lactamase inhibitor combination, or meropenem. However, carbapenem-sparing treatments should be recommended particularly in the settings where there is a high incidence of carbapenem-resistant K. pneumoniae. When a conservative treatment has been established, symptoms typically improve within three days after the initiation of treatment, at which time the diet is commonly advanced to a semisolid and then to a low-residue diet.

A lack of improvement, or deterioration, should prompt repeat CT scan.

Pericolic extraluminal air

Nowadays, along with an increasing usage and quality of CT in diagnosing acute diverticulitis, pericolic extraluminal air is encountered more frequently. Although in approximately 15 percent of all patients with acute diverticulitis pericolic extraluminal air is found, little is known about the natural course and whether these patients should be treated following strategies usually applied to uncomplicated cases, or more aggressively as for complicated diverticulitis.

Published studies demonstrated that no more than 11 percent of patients with contained perforation or localized pericolic free air within the mesentery actually need emergency surgery during the initial acute diverticulitis episode. These rates are higher than those reported in uncomplicated diverticulitis in the literature (1 percent to 2 percent).

Where pericolic air alone is seen, 99 percent of patients avoided further intervention, decreasing to 66 percent to 93 percent for distal air.[35,36]

Only the presence of an associated abscess seems to predict the need for further treatment.

Based upon the scarce evidence to date, the majority of stable patients with radiological evidence of extraluminal air and no extravasation of contrast on CT scan can be successfully managed conservatively.

Table 4. Five key clinical points on diagnosis and classification of acute diverticulitis

In immunocompetent patients presenting with uncomplicated acute diverticulitis, symptomatic treatment without antibiotics provides similar outcomes to treatment with antibiotics. Conversely, immunocompromised patients with uncomplicated acute diverticulitis should be considered at high risk for failure of nonantibiotic treatment.
Immunocompetent patients presenting with uncomplicated acute diverticulitis and mild symptoms may be managed in an outpatient setting.
In the absence of high-risk features, the detection rate for malignant lesions during a colonoscopy after an episode of uncomplicated acute diverticulitis is very low. Routine colonoscopy after successfully treated uncomplicated acute diverticulitis is not recommended, unless high-risk features on CT scan are present.
In patients requiring antibiotic therapy, oral administration should be preferred whenever possible. Alternatively, an early switch from intravenous to oral therapy may facilitate a shorter inpatient length of stay.
The majority of stable patients with CT evidence of extraluminal air and no extravasation of contrast can be successfully managed nonoperatively. The presence of an associated abscess or distant air are predictors of failure of nonoperative management. A close follow-up must be performed in these patients.

Diverticular abscess

The majority of Hinchey Ib-II abscesses can successfully be managed nonoperatively, leaving the option of acute surgery to those who have exhausted nonoperative management strategies without improvement of symptoms.

Antibiotics should be first-line therapy for acute diverticular abscesses.

Abscesses smaller than 3 to 4 cm in diameter are not amenable to percutaneous drainage and are usually treated with antibiotics alone.

Larger abscesses are less common, and may be managed by percutaneous drainage on initial presentation or if antibiotic treatment fails. Failure of antibiotic-based conservative strategy is more likely in patients with abscesses larger than 5 cm.

Up to 70 percent of patients with large abscesses ultimately undergo surgery in a semi-elective or elective setting. However, fewer than half the patients have recurrent diverticulitis and the recurrences are effectively managed conservatively.[3]

A systematic review of 8,766 patients from 42 observational studies found that antibiotic therapy alone is successful in 81 percent of abscesses. An inverse size relationship was observed (antibiotic success 100 percent ≤3 cm, 82 percent 3-10 cm, 66 percent 3-18.5 cm). For smaller abscesses, antibiotic therapy alone and percutaneous drainage have similar success rates, morbidity, and mortality. However, no firm evidence exists to define when to recommend percutaneous drainage over antibiotic therapy.[37]

Drain placement has a reported 2.5 percent complication rate, consisting primarily of small bowel injury and fistulation.[38] A 15 percent recurrence rate has been reported following drainage, with abscesses >5 cm presenting an increased risk.[39,40]

A step-wise management strategy where drainage is added for accessible abscesses that fail to, or are not expected to, resolve with antibiotic therapy is the suggested pathway by several clinical guidelines to date.[3,17]

Risk of recurrence

The risk of recurrence after an episode of acute diverticulitis varies widely among published series. Systematic reviews show a recurrence rate of 10 percent to 35 percent after the first episode of uncomplicated diverticulitis, and the risk of future emergency surgery is approximately 4 percent to 7 percent. Therefore, available evidence does not support a routine policy of prophylactic sigmoidectomy.[3,17] After the second episode, the risk of recurrence is higher. However, the severity of the recurrent episodes is similar to that of earlier episodes.

Two large multicenter studies showed that recurrence is rare and is a relatively benign process for the majority of patients.[41,42] In the study by Broderick-Villa et al., 86 percent of patients hospitalized with acute diverticulitis and treated conservatively required no further admissions for diverticular disease over the 9 years of follow-up. Recurrence occurred in only 13 percent of patients and only 4 percent had a second recurrence. Notably, no patient with a second recurrence required an operation. Similarly, Binda et al. found that, over a mean period of 10.7 years, 61 percent of patients did not require further hospitalization for diverticular disease. Only

Table 5. Five key clinical points on non-resectional management of complicated acute diverticulitis

Antibiotics should be considered first-line treatment for all diverticular abscesses. Antibiotic therapy alone is associated with a very high treatment success rate for abscesses <4 cm.
Percutaneous drainage successfully resolves abscesses >4 cm in 80 percent of patients, with a low complication and re-intervention rate.
When a drainage procedure is indicated, there is no evidence to support a prolonged course of antibiotics after source control is achieved. Antibiotics must cover Gram-negative and anaerobic bacteria based on antibiotic stewardship principles.
In Hinchey Ib-II abscesses, or presence of pericolonic air on CT scan, acute surgery should be reserved to patients who have exhausted nonoperative options without improvement of symptoms.
In patients with diverticular abscesses treated conservatively, a colonoscopy should be planned at 4 to 6 weeks.
A laparoscopic peritoneal lavage and drainage should be performed only in very selected patients with Hinchey III peritonitis by surgeons with appropriate expertise. The lower stoma rate should be weighed against the higher risk of complications and re-intervention. Elderly patients and those with immunosuppression or severe systemic comorbidity are at risk of reoperation after laparoscopic lavage.

17 percent had a recurrent episode resulting in an emergency surgical operation. The risk of recurrence is higher among patients younger than 50 years and among those with at least three previous episodes.

According to the study by Gaertner et al., after percutaneous drainage, nearly 60 percent of patients had no further diverticular episode in the following seven years.[39] When initial management is compared, 16 percent of percutaneously drained abscesses recur in the short term compared with 25 percent of those managed with antibiotics alone.[38]

The use of 5-Aminosalicylic Acid (ASA) agents to prevent recurrent diverticulitis has been studied in multiple placebo-controlled, double-blind, randomized controlled trials. The DIVA trial, PREVENT-1, and PREVENT-2 trials failed to show a reduction in recurrence at 52 weeks and 104 weeks, respectively, with mesalamine.[43,44] There were also no differences in health-related quality of life outcomes over the follow-up period, including global symptom scores. A 2017 Cochrane Review summarized the available data, and concluded that 5-ASA agents were not superior to control interventions for the prevention of recurrent diverticulitis.[45]

With regard to other medical therapies or dietetic measures to prevent diverticulitis recurrence, such as rifaximin, probiotics, or a diet rich in fibers, the evidence is far inferior for or against their use.

Several important considerations have recently challenged routine elective surgical management for recurrent or chronic diverticulitis. First, complicated recurrence after recovery from an uncomplicated episode occurs in fewer than 5 percent of patients whose care was managed nonoperatively.[46] Second, the occurrence of multiple subsequent episodes did not increase the risk of major complications of diverticulitis. Third, complicated diverticulitis most commonly occurs during the first episode, rather than during the recurrent episodes. Last, but not least, 5 percent to 25 percent of patients who underwent an operation for chronic diverticulitis report no sustained symptom relief.

For these reasons, following a single episode of successfully treated Hinchey I/II acute diverticulitis, surgery should not be routinely offered solely to avoid future episodes.

Risk of colonic cancer

Several international guidelines recommend routine colonoscopy after an episode of acute diverticulitis to rule out malignancy.[47,48]

The American Gastroenterological Association suggests that previous colonoscopy, comorbidity, and persistent symptoms may influence the decision. Conversely, the World Society of Emergency Surgery (WSES) recommends omitting colonoscopy only in patients with uncomplicated acute diverticulitis.[17]

The risk of having colorectal adenocarcinoma seems to be comparable in patients with uncomplicated acute diverticulitis and asymptomatic controls.[49]

The AVOD trial, which evaluated the use of antibiotics in the treatment of uncomplicated diverticulitis, reported a 0 percent detection rate for cancer among 545 patients who received a follow-up colonoscopy 6 to 8 weeks after their disease presentation.[29]

A systematic review and meta-analysis aggregated all of the available data, and reported a pooled estimate of 0.7 percent for cancer detection among 1,497 patients with uncomplicated diverticulitis, comparable to the reported cancer rate of 0.78 percent among 68,324 asymptomatic patients undergoing screening colonoscopy. On the other hand, among patients with perforation and an abscess, the cancer detection rate is estimated at 10.8 percent.[50]

So, based on these data, among patients treated successfully for uncomplicated acute diverticulitis, routine colonic evaluation is not indicated, unless high-risk features are present.

Colonoscopy is still recommended in patients with an associated perforation and/or abscess, suspicious findings on CT scan, or ongoing symptoms.

Emergency Surgery

Patients with perforated diverticulitis and peritonitis should be evaluated early for operative intervention with the aim of sepsis control.

Emergency surgery is indicated for diffuse peritonitis, whereas urgent surgery is indicated if the patient's condition fails to improve despite medical management or percutaneous drainage. There is little data to inform the timing of operative intervention, but the clinical status of the patient should guide urgency of surgical intervention.

A CT scan should be obtained preoperatively in hemodynamically stable patients with sepsis and peritonitis, in order to localize perforation and rule out other diagnoses.

Extracolonic air on abdominal CT scan, when found at a distance from the site of perforation, has a sensitivity of 76 percent to 100 percent and a specificity of 83 percent to 91 percent in detecting colonic perforation. It is a radiological sign predictive of diffuse peritonitis and commonly considered, together with the presence of intra-abdominal free fluid, an indication for urgent operation in septic patients.[51]

A standardized therapeutic approach is still lacking, as the type of surgery for Hinchey III and IV are yet to be universally agreed; Hartmann procedure (HP), laparoscopic lavage (LL), or resection and primary anastomosis (PA) represent the most common therapeutic choices in these patients.

Seventy-one articles were included in the recently published systematic review about emergency surgery in acute diverticulitis by Beyer-Berjot et al. High-quality studies showed that LL was associated with an increased morbidity and that HP was associated with poorer long-term outcomes than PA with diverting ileostomy, but Hartmann procedure is still acceptable, especially in high-risk patients.[52]

Resection with colostomy creation: The Hartmann procedure

Hartmann procedure is the preferred operation for hemodynamically unstable patients with diffuse peritonitis from perforated diverticulitis; it has been advocated in the case of fecal peritonitis, septic shock, chronic steroid therapy, and a patient's poor baseline clinical condition[53] (**Figure 4**).

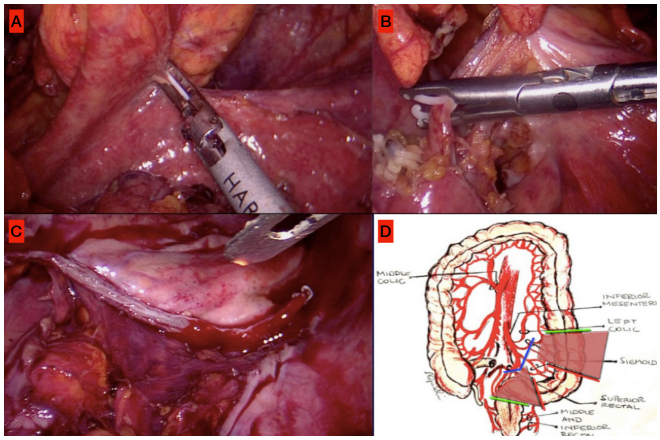


Figure 4. Step-by-step laparoscopic Hartmann procedure

(A) Sigmoid mesentery dissection close to the bowel. (B) Sigmoid arteries dissection and ligation with clips. (C) Rectal stump transection with the endostapler at the level of the sacral promontory. (D) Anatomic landmarks for the Hartmann procedure.

In patients who are hemodynamically unstable, damage control surgery, defined as resection without anastomosis, temporary closure and second-look, is an option. A recent series, including only patients with severe peritonitis, reported a mortality rate of 11 percent and a stoma rate of 45 percent.[54] Temporary abdominal closures may be underutilized in perforated diverticulitis and although limited by relevant selection bias, some evidence suggests that damage-control surgery decreases the need for HP and increases primary anastomosis rate.[55]

Although there are no studies evaluating the extent of sigmoid resection in the emergency setting, limiting the resection to the segment that is acutely affected without compromising blood supply of the remnant bowel is recommended. A dissection performed close to the bowel wall will decrease the risk of injury to surrounding structures and organs especially in the context of peritonitis and a phlegmon (**Figure 4**).

Hartmann reversal is a challenging operation, with a higher morbidity and mortality compared to the reversal of a diverting ileostomy, with an overall reversal morbidity of 44 percent. More than 30 percent of Hartmann reversal result in permanent colostomy.

Laparoscopic lavage

Laparoscopic lavage has been shown to decrease stoma formation rate without impacting one-year mortality, although short-term morbidity may be increased.[56]

Laparoscopic lavage may be considered in selected Hinchey III patients by surgeons with appropriate expertise and the ability to perform full lavage, including all intra-loop spaces.

Surgeons who decide to perform a LL should ensure careful patient monitoring is in place, including the ability to engage in emergency sigmoidectomy, when indicated. Given the lack of reports and concerns aforementioned, visualized perforations or Hinchey IV disease should not be managed with LL outside of research settings and conversion to resection appears indicated when fecal peritonitis is unexpectedly identified during the surgical procedure.

In 2013, a multicentric study of the Dutch Diverticular Disease Collaborative Study Group reported on the early results of LL for perforated diverticulitis.

Out of 38 included patients, 18.4 percent developed uncontrolled sepsis, 13.1 percent needed reoperations, and 5.2 percent died due to multiorgan failure.[57]

The SCANDIV trial enrolled 162 patients with Hinchey II to IV diverticulitis: 89 patients underwent LL and 83 had a colectomy (62 HP and 21 PA). Within 1 year after surgery, results demonstrated a significant trend towards more reoperations after LL than after resection (27 versus 10 percent), although the rate of severe complications and disease-related mortality were similar.[58]

The LOLA group of the LADIES trial compared LL with sigmoidectomy for patients with Hinchey III perforated diverticulitis (excluding patients with faecal peritonitis, aged older than 85 years, with high-dose steroid use, and hemodynamic instability). The primary endpoint was a composite endpoint of major morbidity and mortality within 12 months. Ninety patients were randomly assigned in the LOLA section of the LADIES trial, when the study was terminated by the data and safety monitoring board because of an increased event rate in the LL group. The primary endpoint occurred in 30 (67 percent) of 45 patients in the LL group and 25 (60 percent) of 42 patients in the sigmoidectomy group, thus concluding that LL is not superior to sigmoidectomy for the treatment of purulent perforated diverticulitis.[59]

Recently, the two-year results of the DILALA randomized trial comparing LL with colonic resection have shown that patients with Hinchey III disease in the LL group had a 45 percent reduced risk of undergoing one or more surgical operations within 24 months and had fewer operations compared with patients in the HP group. No difference was found in readmissions rate, as well as in mortality between the two treatment arms.[60]

The recent systematic review and meta-analysis by Penna et al. found no significant differences for mortality, 30-day reoperations, and unplanned readmissions when comparing LL and colonic resection. Laparoscopic lavage had higher rates of intra-abdominal abscesses, peritonitis, and increased long-term emergency reoperations. Conversely, benefits of LL included shorter operative time, fewer cardiac complications, fewer wound infections, and shorter hospital stay.[56,61]

Further meta-analyses of all three randomized controlled trials published to date showed no differences in 12-month mortality, quality of life, or readmission. LL was associated with a higher rate of postoperative abscess formation and reoperation. The risk of reoperation was quantified as 10 percent higher, but LL was also associated with decreased stoma formation (15 versus 90 percent), fewer wound infections, and shorter hospital length of stay.

Table 6. Summary of main outcomes reported in the RCTs comparing laparoscopic lavage (LL) and sigmoid resection (SR) for Hinchey III-IV perforated diverticulitis

Study (year)	N. of patients randomized		Primary outcome	Mortality	Morbidity	Reoperations	Stoma rate at 1 year	Recurrent diverticulitis	Final comment
	LL	SR							
Vennix S (2015)	46	42	Major morbidity and mortality within 12 months	Equivalent	Favor SR	Equivalent	Not reported	Favor SR	LL is not superior to SR for the treatment of purulent perforated diverticulitis
Thornell A (2016)	43	40	% of patients having one or more reoperations within 12 months	Equivalent	Equivalent	Favor LL	Favor LL	Not reported	LL reduces the need for reoperations, has a similar safety profile to HP, and may be an appropriate treatment of choice for Hinchey III diverticulitis
Shultz JK (2017)	89	83	Severe complications (Clavien-Dindo grade IIIa or more) at 1 year	Equivalent	Equivalent	Favor SR	Favor LL	Favor SR	The advantage of LL should be weighed against the risk of secondary intervention (if sepsis is unresolved)
Kohl A (2018)	43	40	% of patients with ≥1 secondary operation from 0 to 24 months after the index procedure	Equivalent	Equivalent	Favor LL	Favor LL	Equivalent	LL is a better option for Hinchey III perforated diverticulitis than HP

Resection with primary anastomosis

Although HP currently still represents the treatment of choice for patients presenting with purulent or fecal-perforated diverticulitis with diffuse peritonitis in many surgical departments worldwide, evidence is growing that in hemodynamically stable, immunocompetent patients, colectomy with primary anastomosis should be preferred over HP.

A prospective study with 591 patients who underwent emergency left-sided colonic resections in several countries was promoted by the European Society of Coloproctology (ESCP). Primary anastomosis (PA) was associated with a similar major complication rate to HP in multivariable models. A diverting ileostomy (DI) was used only in 24 percent of patients. Even if not limited to perforated diverticular disease, the study confirmed the safety of PA in an emergency setting.[62]

Recent randomized controlled trials (RCTs), as well as the guidelines of the European Association for Endoscopic Surgery (EAES) and of the World Society of Emergency Surgery (WSES), suggested that resection with PA is a safe alternative to nonrestorative colon resection in selected patients with Hinchey III-IV.[3,17,63,64]

An additional diverting ileostomy is routinely performed following PA. However, sub-group analyses from the aforementioned trials questioned this strategy, and seemed to highlight favorable results even without ileostomy, especially in patients with Hinchey III diverticulitis.

The RCT published in 2012 by Binda et al. investigated the hypothesis that the adverse events rate following PA was not superior to those following HP for Hinchey III-IV diverticulitis but was prematurely stopped due to recruitment difficulties. During the 3-year study period, 90 patients were randomized to undergo PA with diverting ileostomy or HP in 14 centers throughout eight countries. Results showed that there were no differences in mortality (2.9 versus 10.7 percent) and morbidity (35.3 versus 46.4 percent) rates following PA with diverting ileostomy and HP. 64.7 percent of patients with diverting ileostomy and 60 percent of HP patients underwent stoma reversal, but complications following stoma reversal were significantly higher after HP (4.5 versus 23.5 percent).[65]

Primary anastomosis with diverting ileostomy and HP for patients presenting with Hinchey III-IV diverticulitis peritonitis were also investigated in comparison by Oberkofler et al. in a RCT enrolling 62 consecutive patients published in 2012.[66] Even this trial was stopped, because the interim safety analysis reported significantly more serious complications with stoma reversal after HP than after PA (20 versus 0 percent). Thirty patients randomized to HP and 32 to PA with diverting ileostomy showed equivalent rates of overall complications (Clavien-Dindo grades I-V) and hospital mortality. The total number of complications was significantly higher in the HP group. Only 58 percent of end colostomies were eventually reversed, whereas the stoma reversal rate after diverting ileostomy was significantly higher (90 percent). The incidence of overall complications and serious adverse events was significantly higher in the HP group.

The DIVA arm of the LADIES RCT aimed to assess outcomes after HP versus PA (with or without diverting ileostomy) for perforated Hinchey stages III/IV diverticulitis.[64] Twelve-month stoma-free survival and secondary endpoints (morbidity, mortality, and quality of life during 12-month follow-up) were investigated in a cohort of 130 patients with exclusion criteria consisting of age >85 years, patients under high dose of steroids (≥20 mg/day), and hemodynamic instability. Sixty-six patients underwent HP and 64 patients PA. Stoma-free survival at 12 months was significantly better for PA (6.25 versus 24.2 percent), without differences in short-term morbidity (43.9 percent in the HP group versus 39.1 percent in the PA group) and mortality (3 percent in the HP group versus 6.2 percent in the PA group) after index resection. Overall morbidity was not significantly different for HP and PA in both Hinchey III (37 percent in both treatment arms) and Hinchey IV patients (60 versus 44.4 percent). In 27 percent of patients who underwent PA without diverting ileostomy, the morbidity rate was similar to that in the HP group, whereas no mortality occurred. Stoma reversal rates were 66.2 percent and 87 percent in the HP and PA groups, respectively. Overall morbidity after stoma reversal was lower in PA than in HP (8.1 versus 30.2 percent), therefore confirming the findings of previously published trials that PA is superior to HP as a treatment for Hinchey III-IV perforated diverticulitis.

Table 7. Summary of main outcomes reported in the RCTs comparing sigmoid resection with primary anastomosis (PA) with/without diverting ileostomy and Hartmann procedure (HP) for Hinchey III-IV perforated diverticulitis

Study (year)	N. of patients randomized		% of diverting ileostomy in PA	Primary outcome	Mortality (1st operation)	Morbidity (1st operation)	Complications after stoma reversal	Stoma rate at follow-up	Final comment
	PA	HP							
Binda GA (2012)	34	56	100%	Adverse events (mortality/ morbidity)	Equivalent	Equivalent	Equivalent	Equivalent	No conclusions may be drawn on preference of one treatment over another
Oberkofler CE (2012)	32	30	100%	Overall complication rate	Equivalent	Favor PA	Favor PA	Favor PA	This trial provides evidence in favor of PA with diverting ileostomy over HP
Bridoux V (2017)	50	52	60%	Mortality rate at 18 months	Equivalent	Equivalent	Equivalent	Favor PA	This trial provides additional evidence in favor of PA with diverting ileostomy over HP
Lambrichts DPV (2019)	64	66	63%	12-month stoma-free survival	Equivalent	Equivalent	Favor PA	Favor PA	In hemodynamically stable, immunocompetent patients, PA should be preferred over HP

Advantages of emergency laparoscopic surgery in sigmoidectomy for Hinchey III-IV diverticulitis

Laparoscopy is widely recognized as the best approach to most colorectal procedures in elective setting. The benefits of minimally invasive surgery are justified by a reduced injury response caused by surgery, and subsequent enhanced recovery. This could be even more relevant in emergency interventions (**Figures 5 and 6**).

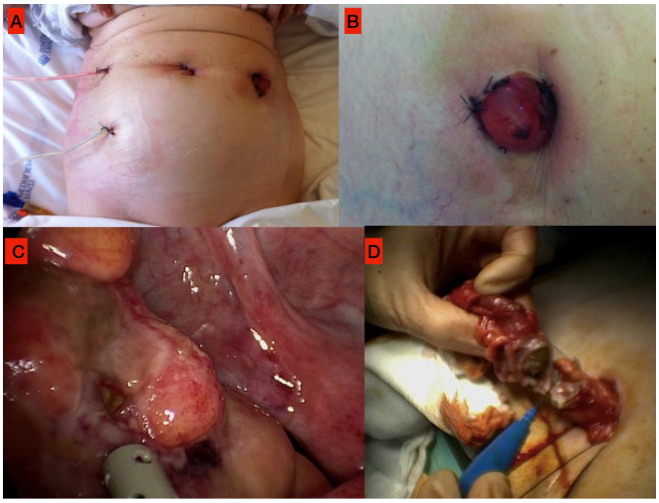


Figure 5.

(A) Final view of the abdominal wall in a patient who underwent laparoscopic Hartmann procedure for perforated diverticulitis. (B) The end colostomy. (C) Intraoperative view of the diverticular perforation. (D) The end-colostomy construction.

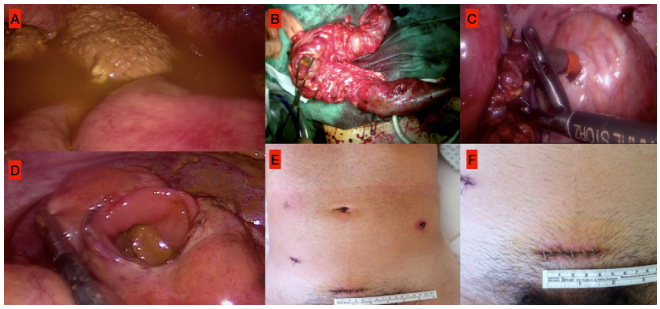


Figure 6.

(A) Intraoperative view of fecal Hinchey IV perforated diverticulitis (Wasvary Hinchey-modified classification) treated with laparoscopic sigmoid resection and primary anastomosis. (B) The sigmoid loop is exteriorized through a mini-Pfannenstiel incision and resected. (C) Knight-Griffen end-to-end colorectal anastomosis. (D) Intraoperative image showing an overt sigmoid perforation. (E–F) Final view of the abdominal wall after laparoscopic sigmoidectomy and primary anastomosis.

Potential contraindications to a laparoscopic approach include hemodynamic instability, distended bowel loops, and known extensive adhesions, as well as a lack of surgeon's laparoscopic experience.

Recent studies showed that laparoscopic sigmoidectomy in the treatment of Hinchey III-IV diverticulitis is safe and feasible in hemodynamically stable patients, if performed by experienced laparoscopic colorectal surgeons. Laparoscopic HP is still the preferred approach, followed by PA with or without diverting ileostomy. The conversion rate varies from 0 percent to 19 percent, with very low reintervention and anastomotic leakage rates.[67]

A recent systematic review and meta-analysis by Cirocchi et al.[68] investigating the role of emergency laparoscopic colectomy for complicated sigmoid diverticulitis including four nonrandomized controlled studies showed significant advantages associated with laparoscopy in terms of complication rates.

Similarly, a propensity score-matched analysis comparing acute laparoscopic and open sigmoidectomy for perforated diverticulitis found no differences in inhospital mortality and reinterventions between groups. Laparoscopy was associated with lower morbidity rate and shorter length of stay. When the HP was performed laparoscopically, the likelihood of reconstruction was significantly higher than in open (88 versus 62 percent).[69]

Laparoscopic surgery may be perhaps technically easier in Hinchey IV than in Hinchey II and III, for several reasons: mesenteric dissection could be less challenging and safe as less thick and less edematous tissues are encountered in Hinchey IV (whereas in case of Hinchey II and III the mesentery is usually friable, easily bleeding, retracted, and stuck to the retroperitoneum and surrounding structures, due to a more long-standing and slowly evolved local inflammation). Anatomical planes are less inflamed in Hinchey IV than in stages II-III of the disease since the free perforation usually develop suddenly and cause immediately diffuse peritonitis. Furthermore, small bowel loops in Hinchey II-III cases are often stuck to a long-standing inflamed area, and this could lead to a higher risk of iatrogenic tears during laparoscopic colectomy.

However, several factors are limiting the generalizability of the laparoscopic technique for Hinchey IV patients: being strongly influenced by the variability of practice patterns and of expertise, the relatively small number of cases encountered in the daily clinical practice until now and, last but not least, the challenges of conducting randomized studies in an emergency situation.

Table 8. Five key clinical points on emergency resective surgery in acute diverticulitis

Patients with perforated diverticulitis with Hinchey III-IV peritonitis and sepsis signs should undergo emergent surgical intervention.
For hemodynamically stable patients, laparoscopic sigmoid resection with or without stoma in the emergency setting has been shown to decrease overall complications compared to open resections.
In Hinchey III diverticulitis, sigmoid resection with primary anastomosis with proximal diversion has similar mortality, lower morbidity, and lower stoma rate at 12 months compared to Hartmann procedure with reversal.
Hartmann procedure remains the preferred operation for hemodynamically unstable patients with perforated diverticulitis.
In hemodynamically unstable patients with perforated diverticulitis, damage-control strategies (resection without anastomosis, temporary abdominal closure and second look) show acceptable mortality and morbidity and lower stoma rates.

Acute Diverticulitis in Specific Patients' Groups

Immunosuppressed patients, such as those who received a solid organ transplant, patients with collagen vascular diseases, malnutrition and chronic renal failure, or patients under steroid therapy, had 5-fold the increased risk of complicated recurrence and perforation compared with immunocompetent patients (36 versus 7 percent).[70,71]

The reason for which, the threshold for these patients to proceed with elective sigmoid resection after one or more episodes of acute diverticulitis is lower.

A systematic review including a total of 11,866 posttransplant patients demonstrated that a pooled 40 percent of immunocompromised patients with acute diverticulitis have a complicated stage of the disease. This finding has been recently confirmed by two observational studies reporting even higher proportions of complicated diverticulitis in this subgroup of patients (56 to 57 percent).[72]

Similarly, a systematic review of five studies comparing patients with and without steroids use has shown significantly higher rates of diverticular perforation in patients on steroid.[73] Conversely, the association between diabetes mellitus and complicated diverticulitis is less obvious to date.

Diabetic patients were seen to have a small but significantly higher rate of complicated diverticulitis than nondiabetics (Hinchey III+IV: 12 versus 9 percent) although the success of nonoperative management is not different and remains appropriate.[74]

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CHAPTER 22

Management of Acute Complications in Colorectal Surgery

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Abscess, anastomotic leak, stoma, ureteral injury, gastrointestinal bleeding

Abstract

Complications after colorectal surgery are inevitable. A majority of problems will occur during the immediate postoperative period, often while the patient is still recovering in the hospital. A few other complications, particularly related to stomas, may present later in the first 3 to 4 weeks after surgery. The morbidity of these complications is variable ranging from mild with minimal impact on the patient, to severe and potentially fatal (in cases of anastomotic leak). This chapter will review the problems caregivers may encounter strictly in the immediate postoperative period (<30 days) and discuss diagnosis, evaluation, and treatment options. Indications for return to the operating room and considerations during such an event will also be reviewed.

Introduction

Many parameters are monitored during the postoperative care of the surgical patient. While return of bowel function is an encouraging sign that recovery is likely to be successful, many other indices can be useful in early detection of complications. Vital signs, specifically temperature and heart rate, should be frequently examined to establish a trend as by postoperative day (POD) 5 to 7; an abscess or anastomotic leak may be detected. Strict monitoring of intake and output in conjunction with laboratory monitoring may help identify patients at risk of dehydration upon discharge with high stoma output. A daily bedside abdominal exam is paramount when assessing the postoperative patient, although at times the exam may be unremarkable and should not always be relied upon in the presence of tachycardia and/or leukocytosis. There should be a low threshold for cross-sectional imaging to exclude surgical site infection or anastomotic leak, as early detection and treatment before the patient exhibits severe sepsis markedly reduces morbidity and mortality.

Postoperative Intra-Abdominal Abscess

Given the inherent nature of colorectal surgery and bowel manipulation, patients remain at high risk for infectious complications. The Centers for Disease Control and Prevention (CDC) defines three categories of surgical site infection (SSI): superficial, deep, and organ/space (1–3). Superficial SSI involves only skin or subcutaneous tissue of the incision. Deep SSI involves the deep soft tissue of the incision such as fascial and muscle layers. Organ/space SSI includes any part of the body, excluding the skin incision, fascia, or muscle layers that are opened or manipulated during the operative procedure. Superficial SSI must have occurred within 30 days after any colon resection procedure, while deep incisional SSI or organ/space SSI may occur up to 90 days following the index operation.[1,2] Multiple definitions for diagnosing SSI exist as set forth by the CDC.[3]

The consequences of SSI may be significant and add to patient morbidity, mortality, hospital length of stay, cost, and readmissions.[4] Substantial effort has been placed in reducing the incidence of postoperative SSI through preoperative risk factor modification. Patient-specific risk factors for infection include body mass index (BMI) 30kg/m^2, American Society of Anesthesiologists (ASA) score 3, male gender, smoking, and diabetes mellitus, among several others. Perioperative risk factors include transfusion length of operation, intraoperative hypothermia, creation, revision, or reversal of an stoma, and spillage of enteric contents.[1,5–8]

Several tools are now utilized, primarily within a bundle of measures in the perioperative period.[2,9,10] A care bundle is a set of evidence-based practices that have been proven to improve patient outcomes.[9] Preoperatively, all infections should be identified and treated, patients should be nutritionally optimized, and patients undergoing elective surgery should bathe in antiseptic soap the night before.[11] The advent of laparoscopy to colon and rectal surgery has further reduced postoperative infection risk by more than 50 percent relative to open surgery.[12] While the process of reducing SSI in colon and rectal surgery has evolved over the last few decades, several practices are routinely in place to reduce infection. Preoperative mechanical and antimicrobial bowel preparation remains a point of controversy. Some studies failed to confirm decreased rates of anastomotic leak or infectious complications.[13,14] Proponents of mechanical bowel preparation cite ease of manipulation of the colon.[15] Conversely, multiple studies have highlighted the importance of preoperative oral antibiotics in reducing colorectal SSI rates.[16,17] The role of intravenous antibiotics prior to skin incision in reducing SSI is well documented, and most studies favor the use of a second-generation cephalosporin with or without metronidazole.[5,18,19] Routine use of postoperative antibiotics is not supported. Mechanical bowel preparation along with two doses of neomycin and metronidazole the day prior to surgery for major abdominal and perineal operations is routinely used. Maintenance of normothermia appears to be important in preventing SSI in colorectal surgery, although there is controversy in its universal acceptance as conflicting data exist.[20–22] Studies generally favor the use of supplemental oxygen during surgery and in the postoperative recovery area.[23] Hyperglycemia has been associated with increased SSI, thus perioperative glycemic monitoring and insulin administration should be instituted.[1,24,25] Wound protection devices should be used to cover wound edges as a protective barrier.[26,27] Gloves and gowns should be changed and a dedicated clean closing tray should be used prior to incisional closure.[28] Fluid administration during and following surgery should be directed at maintaining euvolemia. While under-resuscitation may decrease end-organ perfusion and increase the risk of acute kidney injury, hypervolemia is associated with postoperative ileus and delayed return of bowel function.[29–31] Routine use of drains for infection prevention has also been extensively studied without conclusive evidence demonstrating a benefit for this reason.[32] Wound irrigation at the completion of the operation is commonly employed as a means to potentially reduce SSI by removing clot and loose debris. However, it is unlikely to alter the bacterial burden bound to the wound surface.[1] Wound management in the highest risk population with obvious contamination and spillage of enteric contents remains a challenge. Many surgeons prefer to close the fascia, opting to leave the skin open allowing healing by secondary intention or delaying primary closure 3 to 5 days following surgery if the wound is clean. Another intervention that has gained support is the use of closed-incision negative-pressure therapy, which has been associated with decreased SSI.[33] For procedures involving stoma reversal, the purse-string closure has a lower risk of SSI than conventional primary closure, and its use is advocated.[34]

Once an SSI is diagnosed, prompt intervention is required. Treatment may include empiric broad-spectrum antibiotics and anatomic source control. Specific options include opening and debriding the wound to allow appropriate drainage of infected fluid or pus, local wound care, resuscitation, and drainage either by means of surgical intervention or image-guided percutaneous abscess drainage in the case of organ/space SSI. Aspirate from the wound should be sampled for microbiology analysis. A superficial incisional SSI that is opened and drained does not require antibiotics. Antibiotics should be initiated in patients who meet criteria for systemic inflammatory response syndrome, sepsis, or who are immunocompromised.[35] Antibiotics should be narrowed down according to the resultant microbial cultures of the aspirate and antibiogram, and duration of treatment should be guided by the patient's clinical response. While the average duration of antibiotic therapy has been 10 to 14 days, recent well-designed trials are refuting this recommendation.[36] Once source control is achieved, the beneficial effect of continuing systemic antibiotics diminishes, thus a short course of as few as three days may be utilized, limiting patient exposure to further risk of complications from antibiotics, notably from *Clostridioides difficile* colitis.

Anastomotic Leak

Anastomotic leak is one of the most dreaded complications after colorectal resection. Reported incidences vary widely, between 1.5 to 19 percent[37–41] with a 30-day mortality rate of 0.7 to 8.4 percent.[42–45] The fatality rate is dependent on many patient factors that are beyond the practitioner's control including age, gender, comorbid conditions, diabetes, obesity, and immune status. Other considerations that predispose to anastomotic leak are hemodynamic instability, tension on the anastomosis, history of radiation to the area, and quality of the tissue, and presence of inflammation or fibrosis. Colonic location of the anastomosis is a factor, with low anastomoses exhibiting higher leak rates than right-sided resections (19 percent for coloanal versus 0.5 percent for ileocolic).[41,46]

Postoperative leak can range from subclinical (undetected) to feculent or purulent peritonitis resulting in septic shock. Grades of leak are classified according to clinical management; grade A – no change in management, B – active intervention not requiring reoperation, and C – reoperation.[47] Grade A leaks may be an incidental radiographic finding or found months later on preoperative workup at the time of diverting ostomy closure and have no impact on the clinical course. Grade B leaks may manifest as mild distress with pain, ileus, or other indicators but are manageable by CT-guided or transanal drainage or other endoscopic interventions. Grade C patients are overtly septic or have leaks that require diversion or washout, and thus require a return to the operating room. The timing of anastomotic leaks may help identify the etiology, whether from technical factors (<6 days) or due to ischemia-related factors (5 to 7 days).[48] Several studies have shown that leaks occur later than this time period, between 8 to 12 days, and that suspicion of a leak should remain high if the patient represents to the emergency department or is readmitted.[42,49]

Tachycardia, fever, leukocytosis, ileus, renal failure, and abdominal pain can all be indicators of an anastomotic leak. On physical exam, aside from attention to peritoneal signs, a gentle digital rectal exam palpating for defects in low anastomoses or even careful bedside anoscopy may be performed. CT scan should be obtained with oral, intravenous, and rectal contrast. The rectal contrast should be diluted (2 to 3 percent) so that artifact will not obscure the leak.[50] Although not 100 percent sensitive for detecting a leak, CT can provide valuable information to guide management. Small locules of air in a collection around the anastomosis should be considered a leak, and the extent of contrast extravasation into the peritoneal cavity can indicate whether or not the leak is contained. It is important to consider the timing of the scan, as inflammatory stranding, locules of air, and pelvic fluid may all be common in the early postoperative period (3-4 days). While it is common to feel "reassured" if the patient has a diverting-loop ileostomy, the presence of a stoma is not protective of a leak. A large study of 1078 patients showed a leak rate of 4 versus 3.8 percent in nondiverted versus diverted patients, respectively.[51]

Endoscopic techniques

Endoscopic salvage techniques may be considered if the patient is stable with CT evidence of fluid around the anastomosis, and a contained extraperitoneal leak is suspected in low pelvic anastomoses. Endoscopically placed covered stents have shown success, although they need to be placed at least 5 cm above the anal verge and are often associated with symptoms of tenesmus and fecal incontinence. The most frequent complication is stent migration in up to 41.5 percent, and often needs to be replaced.[52] The reported rates of anastomotic salvage are 73 to 86 percent, and more than half of these patients are diverted.[53] Endoscopic clip placement has been described for small defects and acute leaks with a 58 percent success rate in 7 out of 12 patients and a 75 percent success rate if combined with stent placement.[54] There has been increasing interest in the use of the Endo-sponge (B. Braun Medical Ltd., Bethlehem, PA, USA), which is a form of vacuum-assisted closure (VAC) therapy. Similar to its wide use in wound closure, this device reduces edema and bacterial colonization, promoting granulation tissue formation. While not approved for use in the U.S., it is increasingly utilized in Europe and carries a 66 to 100 percent rate of anastomotic salvage.[53] Indications for the Endo-sponge® are low extraperitoneal leaks that are difficult to drain. The sponge is inserted transanally through the anastomosis into the abscess cavity, which becomes gradually smaller over time until only a sinus

tract remains. At that point, fibrin glue can be injected or spontaneous healing may occur. The disadvantage is that the sponge must be frequently changed in the endoscopy suite, typically 8 to 10 changes over 4 weeks although sometimes longer. These patients are usually diverted, although it is not absolutely necessary. Complications are anastomotic necrosis and stricture. One study illustrated an advantage of using this modality in the early postoperative period (<6 weeks) rather than later, with success rates of 75 before 6 weeks versus 38 percent after 6 weeks.[55]

Radiographic/local drainage

Small-(<3 cm) contained leaks not communicating with the anastomosis can be managed by antibiotics alone, with or without CT-guided aspiration. Larger abscesses or the presence of loculations typically require CT-guided drain placement in the absence of a surgical drain or in cases of drain malfunction. The potential complication associated with CT-guided drains is fistula development. If the leak is contained and low enough, transrectal drainage under anesthesia can be advantageous if the abscess is in continuity with the anastomosis. If this method is employed, a Malecot or mushroom catheter is placed through the anastomosis into the cavity and is subsequently downsized or removed after 7 to 10 days to allow spontaneous healing. Diversion may help divert the fecal stream and prevent drain dislodgement. A study of 37 patients comparing medical management, reoperation, or transanal drainage showed that transanal drainage was associated with a trend toward better stoma closure rates and anastomotic salvage.[56] The cited complications regarding transanal management of these leaks were that 36 percent needed a second transanal drainage, 33 percent developed an anastomotic stricture, 40 percent had some degree of fecal incontinence, and 13 percent required a stoma due to poor function. While the sample size in this arm of the study was small (n=16), these potential complications should be considered when deciding on management options.

Reoperation

Patients exhibiting signs of sepsis or abdominal distress require reoperation. Edden et al. appropriately summarized the principles of reoperation: minimizing the extent of operative intervention, shortening the procedure as much as possible, providing adequate abdominal washout, and proximal fecal diversion.[57] The intraoperative findings dictate the strategy. Feculent or purulent peritonitis with a clearly disrupted anastomosis will require takedown/resection of the anastomosis similar to a Hartmann procedure in cases of left-sided leaks. In other less ominous findings of contained or walled-off collections in the pelvis, abdominal washout with drain placement and creation of diverting loop ileostomy (if not already present) is typically the procedure of choice. In cases where the index operation was laparoscopic and the plan is to divert/drain, the second operation can also be safely laparoscopically attempted. A threefold increase in the likelihood of stoma reversal was demonstrated with procedures leaving the anastomosis in place in a salvage attempt versus takedown and colostomy creation.[58] In cases of minimal contamination or a minor anastomotic defect, local repair of the anastomosis may be attempted, although the tissues may be too inflamed to hold stitches. Placement of an omental pedical flap over the anastomosis may be another option. The success rate of diversion and drainage alone is upward of 76 percent for extraperitoneal leaks (37). Colostomy is typically not advised for diversion, as reversal is more complicated and may result in much more colon resected at the time of reversal.

Lastly, preoperative resuscitation is of paramount importance in patients with generalized peritonitis and high-grade sepsis. Source control should occur within the first 12 hours of severe sepsis or septic shock.[59] Intraperitoneal leaks almost always require resection and diversion; in rare cases of early technical failure, right-sided anastomoses may be recreated. Otherwise, if the patient is acutely ill, on vasopressors, and the etiology is a nonmodifiable patient factor, stoma creation with or without mucus fistula is necessary. Drains should be placed due to contamination and a high risk of abscess. For low rectal anastomoses, the rectal stump may be stapled or sutured; however if the tissue is too friable, a transrectal drain should be placed.

It is important to note that none of these treatment recommendations change if the diverted patient has a leak. A sick patient requires source control and reoperation for washout or takedown of the anastomosis. If the colon was not prepped at the time of the first operation, irrigation through the distal limb of the ileostomy may be attempted to limit further contamination.

Early Postoperative Small Bowel Obstruction

Delayed return of bowel function in the early postoperative period is common, usually attributed to ileus or generalized bowel dysmotility. Contributing factors include anesthesia, operative time, intraoperative bowel manipulation, narcotics, decreased ambulation, and the stress response of surgery or the presence of infection. Nausea, vomiting, bloating, absence of flatus or bowel movement, abdominal distention, and tympany all may be observed on exam. These findings, however, are also hallmarks of adhesive bowel obstruction rather than ileus and it is the responsibility of the clinician to consider the patient's progress (or lack thereof), and findings on serial examinations when deciding clinical management.

Early postoperative small bowel obstruction (within 30 days of operation) has an incidence of 0.7 to 9.5 percent and an average time of symptom onset of 4.3 days.[60–62] While adhesions are the most common cause of bowel obstruction, other etiologies must be considered including internal hernia, small bowel volvulus, technical failures in anastomotic creation contributing to obstruction or narrowing, and abdominal wall hernia. While fascial dehiscence after an open operation can cause hernia, this process should not be ruled out in laparoscopic procedures. Case reports exist of port site hernias despite closure of the fascial defect and even occurring at 5 mm port sites that are not routinely closed.[63,64] Unlike the gastric bypass literature that has well-defined complications associated with open mesenteric defects, there are variable data in the colorectal literature proving this maneuver to be useful. The rate of internal hernia through an open mesenteric defect in colon resection is very low (<1 percent) and there was no difference when comparing laparoscopic and open operations.[65,66]

Inflammatory cytokines and macrophages are present in the first several days of adhesion formation; 72 hours after surgery, the adhesions are formed but are typically soft and easily disrupted.[67] As organization and reabsorption of the adhesions take place over the next 10 to 14 days, fibroblasts become the predominant cell type resulting in dense vascular adhesions.[68] The complex clinical decision on when to operate and if the patient can safely return to the operating room without elevated risk typically must be made within the first 14 days. After this time period, the traditional surgical dictum is that enterotomies, seromyotomies, and the risk of enterocutaneous fistula is too great to warrant a return to the operating room. The rate of inadvertent enterotomy was found to be 19 percent during adhesiolysis at abdominal reoperation.[69]

Clinical management of patients with signs and symptoms of ileus or obstruction should first be managed with nasogastric (NG) decompression. Appropriate intravenous fluid resuscitation should be guided by output from the NG tube as well as urine output, as many patients become intravascularly volume depleted as a result of third spacing into the gut lumen. Attention should be paid to the patient's abdominal exam, as internal hernia or volvulus can result in ischemic bowel and urgent return to the operating room is indicated. Most patients will be stable and only mildly uncomfortable from the distention, and an abdominal X ray may be performed to get a general idea of the degree of stomach/bowel distention and assess for the presence of air in the colon. If abdominal distention continues for a few days and NG output continues to be significant or any sign of clinical deterioration occurs, further imaging should be performed.

The decision to initiate parenteral nutrition (PN) in the postoperative patient who cannot tolerate oral intake is dependent on the patient's baseline nutritional status as well as the expected duration of protein calorie deprivation. During the first 24 to 48 hours, alongside the fluid resuscitation guided by vital signs and urine output, dextrose should be added to maintenance fluids to avoid ketosis. The 2017 consensus recommendations from the American Society for Parenteral and Enteral Nutrition (ASPEN) for the initiation of PN are centered around the nutritional assessment of the individual patient as the key determining factor.[70] In short, they recommend that peripheral PN can be used during transition periods or if the duration of nil per os is expected to be <1 week. Nourished, stable adults should be supplemented with PN after seven days of no oral intake, after 3 to 5 days if nutritionally at risk, or as soon as possible if the patient has baseline moderate-to-severe malnutrition.[70]

Imaging to differentiate ileus versus obstruction may include water-soluble contrast transit studies or cross-sectional imaging. It has been popular practice to instill Gastrografin (Bayer AG, Germany) down the NG tube, as the osmotic gradient from the contrast reduces bowel wall edema and it is theorized that the intraluminal volume then becomes large enough to "push past" the area of obstruction. A meta-analysis concluded that Gastrografin small bowel follow-through (SBFT) had a 96 percent sensitivity and 98 percent specificity for predicting successful nonoperative management of small bowel obstructions.[71] It should be noted, however, that the studies included were not limited to the early postoperative period. Khaswneh et al. specifically evaluated early (<6 weeks) obstructions, finding only 69 percent reliability in predicting nonoperative management.[72] They also found no difference in reoperation rates with versus without the use of Gastrografin SBFT in an effort to resolve the obstruction. The group that had SBFT also had a significantly longer length of stay.[72] It is our practice to combine any possible therapeutic benefits of Gastrografin with modalities that may be more helpful in discerning the problem and prefer CT of the abdomen/pelvis using Gastrografin as the oral contrast agent. This will reveal any abscess/fluid collections that may be a cause of ileus as well as rule out internal or abdominal wall hernias and identify transition points that may impact the decision to return to the operating room.

Cases of early small bowel obstruction that persist over several days to weeks cause a great deal of angst for both the patient and the surgeon. There are no clear guidelines directing the decision to operate versus continue expectant management, and strategies have evolved over time. A large study reviewing 10 years of management of 101 patients with early bowel obstruction was reported in 1987.[62] Of the cohort, 78 were managed nonoperatively with an average of

6.3 days (range of 1 to 17 days, only 3 patients in 14 to 17 days) of NG decompression. Ellozy et al. reported similar findings in which 20/23 patients had resolution with NG decompression alone within 6 days.[61] If the decision is made to continue expectant management, one must have a low suspicion for ischemia from the obstruction due to an internal hernia. None of the remaining 23 patients that were operated on in the cohort of 1010 patients had ischemic bowel.[62]

In an era in which laparoscopic surgery is increasingly performed, the threshold for returning to the operating room may be lower. When comparing early reoperations after laparoscopic versus open surgery, laparoscopic surgeries had more focal adhesive bands or stenosis than diffuse, widespread adhesions found after open surgery.[73] Other relevant findings from this study were earlier diagnosis and time to reoperation in the laparoscopic group, much longer recovery in the open group, and 25 percent of the laparoscopic group were able to have successful laparoscopic reoperations. This option is generally preferred, especially if the index operation was laparoscopic. The surgeon must assess the degree of bowel distention and assure that abdominal access can be safely performed and exercise extreme caution during manipulation of dilated bowel. Additionally, because open operations are often given more time for conservative management due to diffuse adhesions, the authors examined patients operated on between 2 to 6 weeks (late) from the index operation. There was a higher rate of serosal tears and severe complications in patients operated on in this time frame compared to the early group.[73]

Acute Stoma Complications, Management, and Timing of Reversal

Stoma creation is commonplace in colorectal surgery and may be required in a variety of benign and malignant conditions including inflammatory bowel disease, cancer, obstruction, and perforation, among others.[74] Loop ileostomy, in particular, serves to defunction an anastomosis thereby limiting the clinical impact of an anastomotic leak, a feared complication with grave potential consequences.[75] The morbidity from stomal complications can be significant and may range from 21 to 70 percent.[76] End ileostomy and colostomy tend to have lower complication rates than loop configurations, with loop colostomy having the highest complication rate.[76] Early complications occurring within 30 days of surgery are generally technical in nature or associated with suboptimal stoma site selection. The most frequent complication is peristomal skin irritation. Other early complications include ischemia/necrosis and retraction, while chronic complications include stenosis, prolapse, parastomal varices, and parastomal hernias.[74,77] The most common cause of readmission with stoma creation is dehydration from high-volume ileostomy output.[78]

Skin irritation

Preoperative and postoperative stoma education, along with preoperative site marking by an enterostomal therapist, should be performed whenever possible as this reduces postoperative stoma complication rates and improves long-term outcomes.[74,79,80] Peristomal complications often arise secondary to leakage of stoma content, mucocutaneous separation, and mechanical injury from stoma appliance and adhesives. An enterostomal therapist can be critical in managing these complications, which may often resolve with conservative measures including skin barrier rings to improve appliance seal, topical therapy to protect the surrounding skin, and the use of convex appliances to enhance stomal protrusion further improving appliance sealing.[74] The opening of the appliance should match the outer diameter of the stoma. Exposed skin visible between the mucocutaneous junction and cut edge of the appliance may serve as a nidus for irritation from enteric contents. Stomal adhesive paste can be used to facilitate proper seating. Superficial mucocutaneous separation can occur, and a pectin-based stoma powder can help with adherence.[81] In an effort to minimize these complications, it is important to create a protuberant ileostomy of 2 to 3 cm, and a colostomy of at least 1 cm.[82,83] A stoma of <10 mm is a predisposing factor to complications.[63] If technically feasible, skin-level stomas should be avoided. If there is difficulty in getting the intestine to reach several centimeters above the abdominal wall, there are several maneuvers available to increased intestinal reach. These include selective mesenteric vessel ligation, creation of an "end-loop" stoma, and selecting an upper-abdominal site for the stoma trephine, as the subcutaneous fat is often thinner above the umbilicus.[80] Ultimately, if conservative measures are unable to improve patient quality of life due to persistent peristomal skin complications or an ill-fitting pouch, then operative intervention in the form of relocation, revision, or reversal must be considered.[74,83]

Stoma necrosis

Vascular compromise of stomas varies in clinical severity, with the incidence of early stomal necrosis occurring in up to 17 percent of cases.[79] Risk factors for necrosis include obesity due to thickened and foreshortened mesentery, emergent operation, and colostomy creation, and is less likely to occur in loop stomas due to their dual blood supply.[74] The primary reasons for the development of ischemia and potentially necrosis include either venous congestion or arterial insufficiency. Outflow obstruction resulting in venous congestion can occur if the fascial defect is too small and may result in mucosal sloughing, but this is generally transient and tolerated. However, ischemia secondary to arterial insufficiency often results in full-thickness necrosis. Stomas should always be evaluated prior to leaving the operating room with any concerns for viability appropriately

addressed. Postoperatively, if a concern for necrosis arises, it is important to distinguish depth. Necrosis above the fascia may be managed expectantly, but extension below the fascia requires operative intervention for a thorough evaluation. Assessment may be performed by bedside evaluation using a flashlight and glass tube inserted into the stoma as well as by flexible endoscopy.

Stoma retraction

Stoma retraction occurs in up to 14 percent of new stomas and is often the result of tension from inadequate mobilization and a thickened and foreshortened mesentery in the setting of obesity, inflammatory bowel disease, malnourishment, or immunosuppression.[63,74,77] Complications as a result of retraction include a poorly fitting stoma appliance and leakage of enteric contents often leading to peristomal skin complications, as previously noted. If an intact mucocutaneous junction is present, then conservative measures can be applied in the form of a convex stoma appliance to manage stoma effluent. Should local stoma care prove insufficient, then operative management may be indicated, optimally several weeks following the index operation to allow resolution of the postoperative inflammatory process. A typical surgical approach involves local revision with disconnection of the mucocutaneous junction and subsequent mobilization of the bowel to facilitate creation of a tension-free stoma. If this is challenging or prohibitive due to adhesive burden or a foreshortened mesentery, then a laparoscopy or laparotomy should be employed to allow for more complete bowel mobilization.

High stoma output

The most common reason for readmission following stoma creation is dehydration secondary to high ileostomy output. Patients with new stomas are at highest risk for dehydration in the first three to eight days postoperatively at a time when oral intake may be insufficient.[76] Rates of readmission may be as high as 17 percent and are associated with acute kidney injury and chronic kidney disease.[84] Thus, meaningful effort has been placed in creating pathways to decrease readmission risk. Nagle et al. were the first to introduce such a pathway with components including preoperative education and standardized teaching, patient engagement during the postoperative hospital stay, observation of patient stoma management, and postdischarge tracking of intake and output with a goal of <1,200 mL per day. The introduction of this pathway resulted in a significant reduction in 30-day readmission rates.[85] If ileostomy output remains high, then it is important to closely monitor fluid balance and serum electrolytes, particularly monitoring urine output for dehydration. Dietary modifications may initially be attempted and include increasing the intake of complex carbohydrates, avoiding simple sugars and hypotonic drinks (tea or coffee), and increasing salt intake. Psyllium fiber will thicken the effluent but may decrease electrolyte and mineral absorption. A series of medications may be added to decrease motility. First-line agents include loperamide (up to 4 mg four times daily before meals and at bedtime) and atropine/diphenoxylate (at the same doses). Second-line antidiarrheal alternatives include tincture of opium and codeine, while antisecretory agents include octreotide, proton pump inhibitors, and histamine receptor blockers. The bile acid sequestrant cholestyramine may be an alternative in patients with colons to protect from the caustic effects of bile acids that may incite colonic inflammation which reduces absorption and exacerbates diarrhea.

The timing of stoma closure requires careful evaluation on a case-by-case basis. Prior to closure, evaluation of the distal anastomosis is critical, though there is no consensus on the best evaluation method. Modalities include contrast enema as well as clinical examination with digital rectal examination and endoscopy.[86] In general, ileostomy closure should occur no sooner than 60 days and optimally prior to 90 days if performed in conjunction with a sphincter-preserving proctectomy. This range represents a time when patients have recovered from the primary surgery, intra-abdominal adhesions may be more manageable, and stoma inflammation and edema have resolved.[86] Delaying surgery will continue to expose patients to many of the ostomy-associated complications mentioned previously as well as chronic complications such as parastomal hernia. Conversely, some institutions have advocated early ileostomy closure within 10 days of the index operation and have shown feasibility with this approach being safe in a small pilot series of a selected population.[87] However, this approach is in the midst of being evaluated in randomized controlled trials.[86] Timing of Hartmann reversal remains more controversial. In general, it is advocated to wait at least three to six months to allow for a reduction in pelvic inflammation and adhesion density.[86,88]

Postoperative Anastomotic Bleeding

Postoperative anastomotic bleeding is a rare but serious complication that requires prompt diagnosis and evaluation. Most cases of postoperative bleeding are minor and self-limited, often ceasing early in the postoperative period. Major bleeding, as evidenced by hemodynamic instability can become life threatening requiring intervention. With the advent of circular staplers, the reported incidence ranges from 0.5 to 1.8 percent with transfusions required in less than 5 percent of cases.[89,90] Identified risk factors include cardiac disease, age >75 years, and tumors of the rectum, and likely include others not yet identified.[91,92]

Upon completion of the anastomosis, it is prudent to follow important steps to prevent postoperative bleeding. Each created staple line is carefully inspected, particularly side-to-side anastomoses and, as needed, may even evert the side-to-side staple line prior to closure of the common enterotomy. Any identified sites of bleeding are suture ligated with absorbable suture rather than being treated with electrocautery. The antimesenteric borders of each bowel limb are used and prior to creation of the anastomosis; the mesenteric border of the bowel is dissected and cleaned to limit inclusion of any mesentery in the staple lines, which can serve as sources for bleeding.

There are no set criteria as to when and to what extent one should intervene, but guidance generally follows similar principles as those precepts for lower gastrointestinal bleeding. Initial management is supportive; patients should be closely monitored for hemodynamic changes and resuscitated with intravenous fluids and serial laboratory values are obtained and monitored as indicated. Underlying coagulopathy should be diagnosed and corrected, with transfusions administered, if appropriate. Nonoperative therapy is successful in up to 82 percent of cases thus obviating the need for laparotomy.[90,93] Early endoscopic evaluation should be considered; possible interventions to achieve hemostasis include saline washout, mucosal sclerosis, electrocoagulation, epinephrine injection, and application of hemostatic clips. These endoscopic interventions are not mutually exclusive, and different interventions can be attempted simultaneously in order to achieve hemostasis, with no one particular intervention identified as more efficacious than the others in this setting. Ultimately, if endoscopic intervention fails, surgical exploration is required and may entail suture ligation of identified areas of hemorrhage, or even the need to reconstruct the anastomosis (94).

Ureteral Injury

Aside from anastomotic leak, ureteral injury after pelvic surgery is another major complication. The current incidence of ureteral injury is 0.2 to 2 percent,[95] with a decline from 7.1 percent over 15 years ago, likely due to increased vigilance.[96] Some surgeons prefer to routinely place ureteral stents just prior to the start of surgery, while others reserve stents for selected patients such as severe abscess, inflammation, cancer, prior radiation, or history of prior pelvic surgery. While most of the literature indicates that stent insertion can help with early/intraoperative detection leading to better outcomes, few studies conclude that the procedure decreases the incidence of injury.[97–99]

Reflux anuria

Stent placement carries well-described procedural risks including ureteral perforation, damage to the mucosa, hematuria, and urinary tract infection. Specifically, in colorectal surgery, there has been a higher associated rate of acute kidney injury (AKI). A large study of 2910 patients in the ACS National Surgical Quality Improvement Program (**ACS NSQIP®**) database found that 4.4 percent of patients had stents placed at the time of surgery, and had a 32.6 percent rate of AKI compared to 10.5 percent in patients who did not have stents.[100] When considering the etiology of AKI in postoperative patients, the clinician should be aware of the rare but well-described complication of reflux anuria. Occurring at an incidence of 0 to 7.6 percent, catheter-induced obstructive anuria (a more appropriate descriptor for "reflux anuria") is characterized by the absence of urine output after ureteral manipulation because of edema and obstruction.(101) AKI occurs from a postrenal or obstructive etiology, and rising creatinine with intrarenal values for the fractional excretion of sodium (>1 percent) may be found.[101] Imaging may not immediately show significant hydronephrosis as this is an acute process. The mainstay of treatment is supportive, although with any of these ureteral complications, expert consultation from a urologist is advised. It is recommended to place a bladder catheter, if not already present. Although support with dialysis until edema resolution has been described, most studies advocate for replacement of ureteral stents to relieve the obstruction.[98,99,101] This problem can be bilateral; Bothwell et al. suggest 24-hour staged removal of stents postoperatively to reduce the incidence of reflux anuria.[102] We have found ureteric stents helpful and safe and routinely use them.[103] Other methods of ureteral identification include dissection and fluorescence imaging.

Ureteral injury

Intraoperative detection and repair of ureteral injury has consistently shown better results than delayed detection.[104,105] The astute clinician will serve their patients well to have a high index of suspicion postoperatively to diagnose and treat these injuries as quickly as possible. Presenting symptoms can include nausea and vomiting if an ileus is present due to a fluid collection or urinoma, and if infected may progress to peritonitis and sepsis. Fever and leukocytosis are common, and if a surgical drain is present, the effluent should be sent for creatinine and urea nitrogen. Values at levels 20 times the serum values indicate ureteral injury.[106] The diagnosis is typically made 5 to 6 days after surgery.[96,107] Imaging is often guided by presenting symptoms. Renal ultrasound may be performed as an initial study in cases of low urine output (developing urinoma) or rising creatinine, and CT imaging may be done to investigate fever and ileus

with an unexpected finding of fluid consistent with urine in the abdominal cavity. Intravenous pyelogram (IVP) and retrograde ureteropyelography are the standards to identify location and extent of injury.[108] If these cannot be performed, CT intravenous pyelography (CT-IVP) with delayed images may be an appropriate alternative.[109]

Injury to the ureter can occur via inadvertent suture ligation, ischemia or devitalization from extensive dissection, crush injury, or transection – either sharply or with the use of energy devices. Al-Awadi et al. performed a comprehensive review and found that 31 percent of injuries were diagnosed after surgery and 64 percent of these injuries were in the lower third of the ureter.[96] Although there was more associated morbidity when the diagnosis was delayed, overall they reported 93.9 percent successful resolution in the management of these injuries. It was noted that 2/75 patients required nephrectomy due to extensive ureteral injury or ongoing renal failure. There are fewer complications with immediate repair (<1 week), with success rates of 78 versus 61 percent (immediate versus delayed repair, respectively).[105] Despite inflamed tissues, a definitive procedure can be performed with less morbidity, nephrostomy tube management, need for further visits, and subsequent procedures as would occur with delayed treatment.[110] Initial management with a double "J" stent placed either in a retro- or antero-grade fashion can be attempted to allow an incomplete injury to heal. Further surgery may or may not be indicated, depending on the outcome. However, if this intervention cannot be performed due to complete transection or if the defect cannot be traversed, operative repair is indicated. The options for repair at the time of re-exploration depend on the type of injury – if the ureter is ligated, remove the suture and assess for viability and peristalsis.[107] Partial transections may be primarily repaired over a stent, while complete transections require either ureteroureterostomy or ureterneocystostomy, depending on location.[107] If the injury is too severe or in the presence of an infected field, percutaneous nephrostomy as a bridge to delayed reconstruction may be utilized with appropriate management of intra-abdominal abscess, as described earlier.[111]

Conclusion

Complications after colorectal surgery occur with enough frequency that a high index of suspicion is indicated in the care of the postoperative patient. Given the inherent nature of procedures performed on the gastrointestinal tract, and the colon in particular due to its high bacterial count, the risk of infection is significant. Abscess, anastomotic leak, and surgical site infections should not go undetected otherwise peritonitis and sepsis may result. As always, the patient's clinical condition will guide the management of these complications. In the stable patient with an anastomotic leak, attempts should be made for anastomotic salvage as this leads to less morbidity, better outcomes, and higher rates of stoma reversal as opposed to takedown of the anastomosis and end colostomy. When feasible, if the index operation was laparoscopic, reoperative complications may also safely be laparoscopically managed. Stoma-related complications are usually minor but are the leading cause of early readmission rates and attention must be given to the amount of effluent as well as patient education at the time of discharge. High ileostomy output with the potential to cause acute kidney injury from dehydration is a frequent and potentially avoidable problem with timely discharge occurring only when an acceptable quantity (<1200 cc/day) of stoma output is recorded. Early detection of any of the complications discussed is vital to successful management and clinical outcomes.

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CHAPTER 23

Management of Incarcerated and Strangulated Abdominal Wall Hernias

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Introduction

"Always explore in cases of persistent vomiting if a lump, however small, is found occupying one of the abdominal rings and its nature is uncertain."
—Augustus Charles Bernays (1854–1907), St. Louis

"Do not let the sun rise upon a strangulated hernia if first seen at night; and do not let the sun set upon a strangulated hernia if first seen by day."
—Georg Friedrich Louis Stromeyer (1804–1876), Hanover

Incarcerated and strangulated abdominal hernia is a common surgical emergency and may be associated with significant morbidity and even mortality. Overall, abdominal wall hernia has haunted humanity from its very beginning through modern times, and is one of the most common clinical entities that general surgeons address on a daily basis.

The management of incarcerated and strangulated abdominal wall hernia is surgical, but the extent of the operation depends on clinical presentation, and location and the content of the hernia. However, all hernias should be treated early and in a timely fashion, as delayed diagnosis and treatment may significantly affect the morbidity and overall outcomes. No one should die because we did not address surgically and in a timely fashion small or large, even debilitating hernias of the abdominal wall (**Figure 1**). In this chapter, we aim to briefly summarize the definitions, epidemiology, clinical presentation, diagnosis, and treatment with focus on ventral hernia and their management.

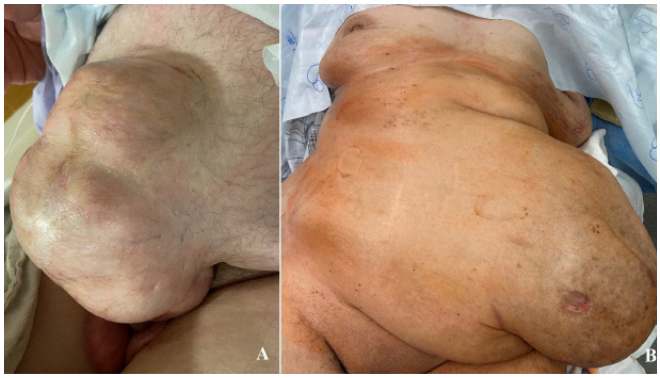

Figure 1. Examples of debilitating abdominal wall hernia

Epidemiology and Natural Progression of Hernia

The lifetime risk of developing a groin hernia is given in the literature as 27 to 42 percent for men and 3 to 5.8 percent for women.[1–4] The incidence of incisional hernia after abdominal surgery was estimated to be 11 percent in a prospective cohort study[5] and 12.8 percent in a meta-analysis of randomized trials involving 14,618 patients.[6] Fitzgibbons et al. evaluated the natural history of inguinal hernia in males by randomizing 720 men to either watchful waiting or surgical repair and found that the incidence of acute incarceration was 1.8 in 1,000 patient-years.[7] Nonetheless, in their report 32 percent of patients crossed over to the surgery arm due to symptoms and three additional patients experience acute incarceration.[8] Although these authors recommended watchful waiting as a reasonable and safe strategy, we do not agree with this approach, and we strongly support early surgical treatment of abdominal wall hernias, including groin hernias. Hernandez-Irizarry et al. found the incidence rate of emergency hernia repairs to be 7.6 in 100,000 in a population-based study.[9] Another population-based study utilizing National Center for Health Statistics data from 2001 to 2010 found that the incidence of emergency hernia repairs increased from 16.0 to 19.2 per 100,000 person-years in 2001 and 2010, respectively.[10] Emergency hernia repair rates were highest among adults 65 years and older, with 71.3 and 42.0 emergent hernia repairs per 100,000 person-years for men and women, respectively. Rates of emergent incisional hernia repair were high but relatively stable among older women, with 24.9 and 23.5 per 100,000 person-years in 2001 and 2010, respectively. However, rates of emergent incisional hernia repair among older men rose significantly, with 7.8 to 32.0 per 100,000 person-years from 2001 to 2010, respectively. A total of 3,970 out of the recorded 148,277 groin hernia repairs (2.7 percent) were primary femoral hernias in the Danish Hernia Database.[11] Femoral hernias accounted for 2.8 percent of initial groin hernias and 18.9 percent of all groin hernias in females in the American College of Surgeons National Surgical Quality Improvement Program database, as reported by Halgas et al.[12] Thanks to the diagnostic superiority of laparoscopy, the incidence of femoral hernia has been reported to be as high as 23.54 to 37 percent in women and 3 percent in men.[13–15] Robotic inguinal hernia repair that has become a very common procedure may prove that femoral hernias are much more common that we thought in the past.

In the United States, 105,000 incisional hernias and 255,000 other ventral hernias were repaired in 2003 alone and with an increasing trend over time.[16–18] The rates of incisional hernia following laparoscopic colectomy was found to be similar to that of its open approach (3.9 versus 4.1 percent).[19] A study of the Danish National Patient Register including 569 patients with incisional hernia and 789 patients with umbilical/epigastric hernia estimated that the probability for patients who underwent watchful waiting to receive later surgical repair was 19 percent for incisional hernias and 16 percent for umbilical/epigastric hernias after 5 years. The probability of requiring emergency repair in the watchful waiting group was 4 percent for both incisional and umbilical/epigastric hernias at 5-year follow-up.[20] Dissimilarly a Dutch study comparing watchful waiting to surgery in 104 and 151 patients, respectively, found the cross-over rate to be 33 percent (34 patients), of which 24 percent were due to incarceration.[21] Emergency umbilical/epigastric or incisional hernia repair was reported to be associated with a 15-fold

higher mortality, reoperation, and readmission rates as compared to those of elective repair.[22] This study found older age, female gender, and umbilical hernia defects between 2 and 7 cm or incisional hernia defects up to 7 cm to be important risk factors for emergency repair.

Most recently, hernia surgery has undergone major advances starting with tensionless hernia repair, and abdominal wall reconstruction and reinforcement. In addition, the general development in surgical science including modern approaches to nutrition, intensive care, devices, materials, evidence-based medicine, and guidelines led to a major improvement in the outcomes of hernia repairs in the emergency setting.

In summary of this section, the abdominal wall hernias have been a focus of surgeons and physicians since the dawn of anatomical and surgical history[23] and have gone through a number of phases from the ancient era (ancient times to 15th century) to the most current,[2-5] as well as being a subject of detailed description of surgical techniques.[6-15]

Definitions and Classifications

Abdominal wall hernia has three components: hernia gate, hernia sac, and the content of hernia sac. Knowing each of these elements can guide treatment modalities, as well as prognosis. Reducible hernia is a type of hernia, in which contents of the hernia sac may be easily reduced into the abdominal cavity. Incarcerated hernia is defined as a hernia in which the content has become irreducible.[26,27] However, in our opinion, reducibility of hernia, most of the time is temporary, if not a myth, because most of the hernia "reduced", comes back very soon after taxis, if not immediately, due to the adhesion of hernia content in the edges of the abdominal defect or the gate. Incarcerated hernias can be divided into acute and chronic by the time interval from the onset of incarceration to diagnosis. Acute incarcerated hernia is usually diagnosed within hours to days from the time point when a hernia became irreducible and painful, whereas chronic incarcerated hernia usually presents within weeks to months, if not years. Incarcerated hernias can also be divided by the presence of symptoms into asymptomatic and symptomatic incarcerated hernias. The former classes are not to be confused with the latter. More specifically, even acutely incarcerated hernia is not always very symptomatic, particularly in obese and super-obese patients. Similarly, chronic incarcerated hernia is not synonymous to asymptomatic (**Figure 2**).

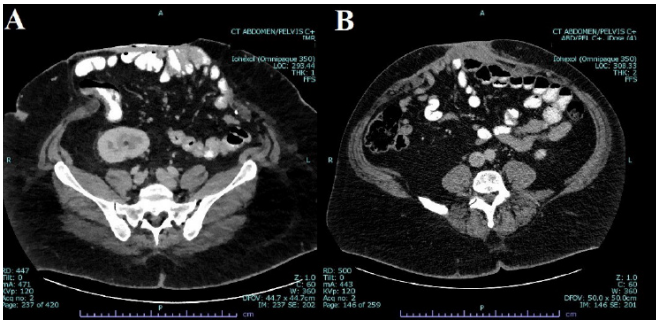

Figure 2. Examples of chronic incarcerated symptomatic hernia

(A) CT scan image of chronically incarcerated hernia with loss of abdominal wall domain. (B) Chronic low-output sinus tract from an infected synthetic mesh.

Obstruction is defined as the situation when compression on the distal aspect of the incarcerated bowel by the constriction ring of the hernia gate is larger than that on the proximal aspect.[28,29] This leads to the accumulation of the bowel content in the incarcerated bowel loop, albeit in the hernia sac, gradually rendering reduction of the bowel loop impossible (**Figure 3**). In obese patients, the bowel in the hernia sac can perforate, and advance into the gangrene of both bowel and or hernia sac, and have relatively minor symptoms, and be hemodynamically stable (**Figure 4**). This can be deceiving. The progression from incarcerated to strangulation is not rare and may be a life-threatening clinical challenge that requires immediate surgical intervention.[30] In this state, the blood supply to the contents of the hernia sac is compromised because of compression by the constriction ring of the hernia gate, or a twist of mesentery, or in case of an internal hernia, from an adhesion (**Figure 5**). While one would expect that if the intestinal segment is dead, the biochemical profile including lactate and base deficit should be elevated, however, in many of these cases, the profile may be totally normal, and may serve as a real distraction and delay immediate surgical treatment (**Figure 6**).

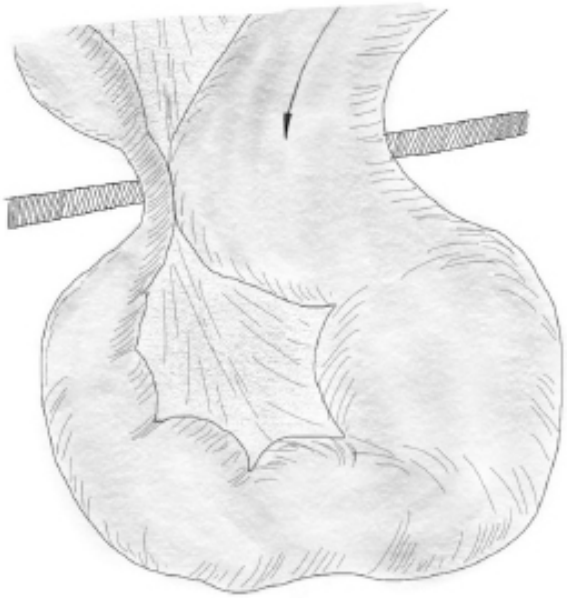

Figure 3. Schematic description of the mechanism of obstructed hernia

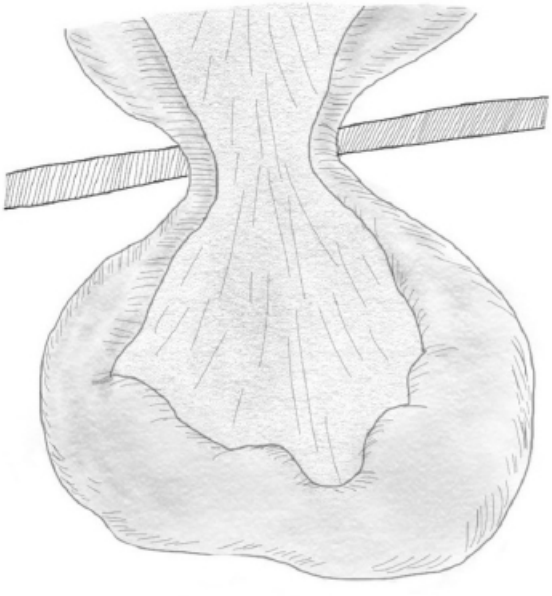

Figure 5. Schematic description of the mechanism of strangulated hernia

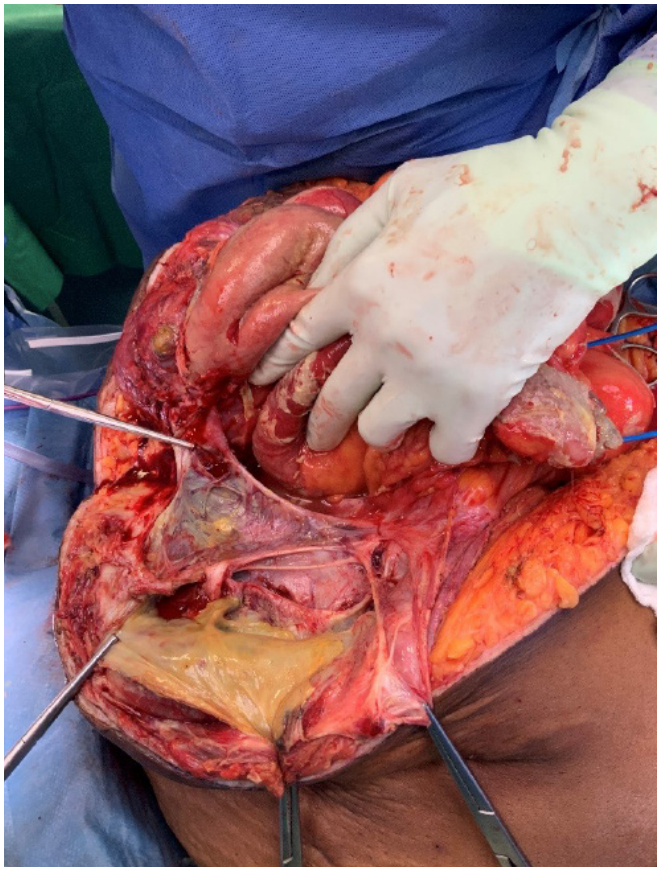

Figure 4. Acute incarcerated hernia with the necrosis of both the incarcerated bowel loop and the hernia sac

Detailed etiopathogenesis of incarcerated hernia is outside the scope of this chapter, but factors such as as connective tissue disorders, advanced age, poor nutrition, smoking, or abdominal surgery, ascites, increased intra-abdominal pressure (physiological or pathological), strenuous physical activities, pregnancy, chronic constipation, chronic coughing, chronic difficulty urinating, severe blunt trauma, or abdominal tumors have been described.[31,32] Most commonly, however, hernia is a result of previous surgeries. Figures 3 and 6 illustrate obstruction progression to strangulation.

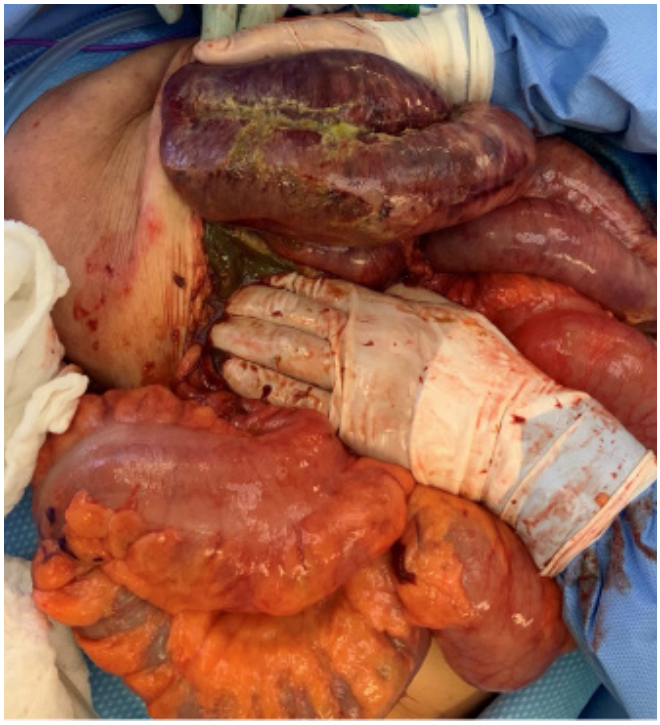

Figure 6. Obstructed hernia, which led to the strangulation of the efferent bowel loop

Another distinct type of strangulation is retrograde strangulation. In this case, a hernia sac contains and entraps two or more adjacent bowel loops, none of which gets involved in the closed-loop strangulation mechanism and hence, both manage to continue receiving some blood supply, whereas the bowel loop between these two gets strangulated in a closed-loop fashion inside the abdominal cavity (**Figure 7**).

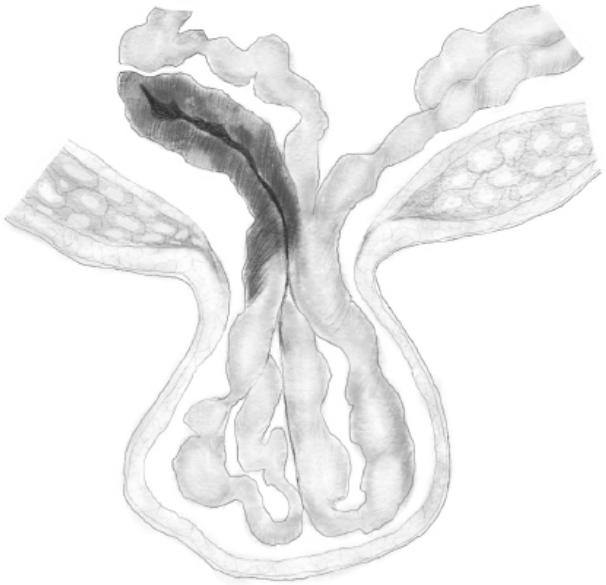

Figure 7. Schematic description of the mechanism of retrograde strangulation

Another type of strangulated hernia is Richter hernia, which is defined as a strangulation of a partial enterocele (**Figure 8**).[26-27]

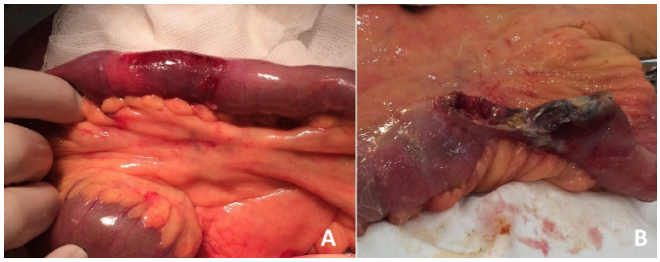

Figure 8. Richter hernia

(A) Ischemia with no perforation. (B) Necrosis with perforation.

In addition, surgeons and other clinicians should also be aware of the phenomenon called pseudo-strangulation, also alluded to as Broca strangulation[34] that occurs when inflammatory exudate associated with another abdominal emergency fills the hernia sac, and freely communicates with the peritoneal cavity and a previously reducible hernia becomes irreducible.[35] One common cause of pseudo-obstruction, tuberculous peritonitis, in which the intestinal loops adhere to the hernia sac and may present with pain mimicking strangulated hernia[36] is rarely seen in our practice. Such cases may be misdiagnosed as a strangulated hernia, which may lead to a delay in the diagnosis and treatment of the primary abdominal emergency.

Clinical Presentation

The clinical presentation of incarcerated hernia greatly depends on the location of hernia, mechanism of incarceration, hernia sac contents, time from the onset of incarceration to diagnosis, and comorbid conditions. The signs and symptoms of incarcerated hernia can be divided into local signs and systemic signs (**Table 1**).

Peritonitis or systemic inflammatory response symptoms are the last to occur in patients with late presentation or delayed diagnosis.[37]

As incarcerated hernia is associated with poor prognosis; it should be thus suspected with any of the following clinical manifestations: 1) severe abdominal pain, with persistent pain during the interim periods of paroxysmal pain; 2) gradually increased shock; 3) evident peritoneal irritation, and increased body temperature, heart rate, and white blood cell count; 4) bloody fluid in vomit or intestinal excreta, or from abdominal puncture; and 5) asymmetrical bloating, palpable and tender intestinal loops with rebound tenderness.[38]

Table 1. Clinical presentation of incarcerated hernia

Local Signs/Symptoms	Systemic Signs/Symptoms
Discomfort in hernia site Pain in hernia site Tenderness in hernia site Nonreducible tense mass Changes in the overlying skin (pain to palpation; hyperemia; laceration with serous, purulent, or fecal discharge; necrosis)	Intestinal obstruction symptoms: • Colicky abdominal pain • Abdominal distension • Nausea/Vomiting • Inability to pass flatus or stool Peritoneal irritation symptoms: • Severe abdominal pain, aggravating with movement Systemic inflammatory response symptoms: • Tachycardia • Hypotension • Tachypnea • Hyperthermia

Diagnostic modalities for incarcerated hernia include abdominal X ray, ultrasonography, and CT scan.[39–42] Incarcerated hernia is a clinical diagnosis in the majority of cases; however, most of the time, these patients are investigated using CT scan and on occasion a plain abdominal film. The most accurate diagnostic test is an abdominal CT scan, which may demonstrate bowel dilation, perforation, mesangial thickening, pneumatosis intestinalis, and other signs at hernia sites (**Figure 9**). Contrast-enhanced scans can allow to identify the presence of bowel strangulation. Moreover, CT scan allows for the diagnosis of incarcerated hernias with smaller hernia gates such as femoral or obturator hernias, which are difficult to diagnosis.

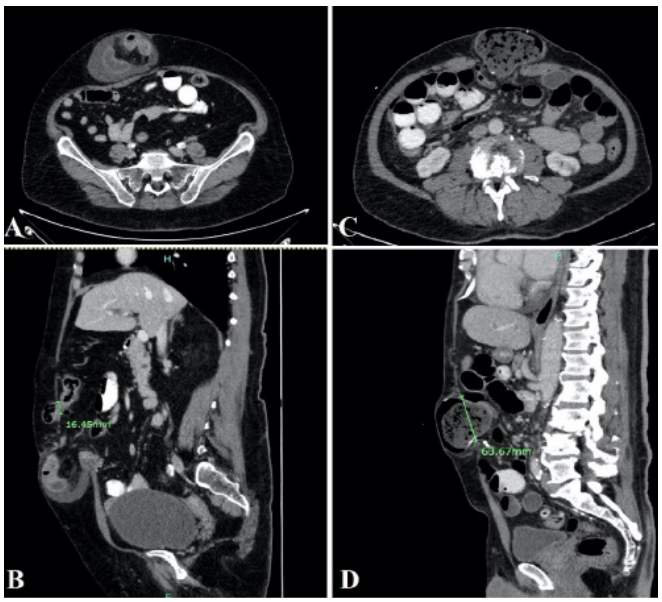

Figure 9. Examples of abdominal CT scans revealing incarcerated abdominal wall hernia

On the left: Incarcerated bowel loop with fluid in the hernia sac. (A) Axial plane. (B) Sagittal plane. On the right: Obstructed bowel loop. (C) Axial plane. (D) Sagittal plane.

Table 2. Risk factors for strangulation, bowel ischemia, and bowel resection

Risk factors
Female sex
Age >65 years
Severe comorbidities
Delayed hospitalization
Femoral hernia
Skin changes
Bowel obstruction symptoms
ASA class
Elevated WBC count
Neutrophil-to-lymphocyte ratio >6.5
Hyponatremia
Blood lactate ≥1.46 mg/dL

ASA, American Society of Anesthesiologists; *WBC*, white blood cell.

Table 2 summarizes previously reported risk factors for strangulated hernia with bowel ischemia. In a retrospective cohort study totaling 323 patients, Chen et al. found neutrophil-to-lymphocyte ratio >6.5 and bowel obstruction symptoms to be independent predictors of bowel resection.[43] Another retrospective cohort study totaling 163 patients found hyponatremia and skin changes to be predictive of bowel ischemia.[44] A retrospective study of 67 patients found blood lactate ≥1.46 mg/dL to be predictive of bowel resection.[45] Other previously reported and well-recognized predictors include female sex, older age, severe comorbidities, delayed hospitalization, femoral hernia, American Society of Anesthesiologists (ASA) class, and elevated white blood cell (WBC) count.[46–50]

Complex Abdominal Wall Reconstruction (CAWR) for Ventral/Incisional Hernia

Although historically many different treatment methods for incarcerated hernias from hernia trusses to watchful waiting were tested, surgery appears to be the only curative approach. The motto: "Any hernia that becomes painful, inflamed, tender, and is not readily reducible should be regarded as a surgical emergency!" Another golden rule is that surgery for acute incarcerated hernia repair should be carried out without undue delay. Prompt surgery frequently prevents bowel resection. Open surgery is still the gold standard for acute incarcerated hernia, although a number of authors have advocated for laparoscopic approach.[51–53] Another core principle is that if strangulation resolves spontaneously and strangulated contents of the hernia sac return to the abdominal cavity during the induction of anesthesia, the strangulated bowel should still be carefully assessed for possible ischemia. One of the best approaches in such cases is hernioscopy, which is defined as laparoscopy through the groin hernia sac.[54]

Abdominal wall hernias may similarly be approached either via open, laparoscopically, or robotically; most surgeons will proceed with open repair.

As most ventral hernias are postsurgical, redefining the anatomy may be difficult, and previous operative reports should be studied carefully, whenever available, and if possible, a direct conversation with the previous surgeon should be conducted. This is particularly important if the patient was operated on at a different hospital or by another surgeon.

Often times, strangulated hernias are in the presence of intestinal obstructions with a combination of fistulas and or stomas requiring emergency surgery. Our strategy for these patients is "more is less", and often the definitive surgery is the only optimal choice to be performed—that is both fistulas and/or stomas should be addressed at the index operation. Often, damage control surgery and return to the operating room for definitive reconstruction is practiced. The objective of the surgery in cases with strangulated hernia is to reduce the incarceration, resect and reestablish gastrointestinal (GI) tract continuity when required, and complete abdominal wall reconstruction.

How to execute definitive surgery on these patients depends on many factors, including the site of hernia, the complexity of findings (gangrene or ischemia requiring resection), the magnitude of abdominal wall loss of domain, and the physiology of the patients. A combination of different approaches is often required. Understanding the anatomy of the abdominal wall and surgical expertise is mandatory.

Getting in the Abdomen

Entering the abdominal cavity in most patients with strangulated hernias, particularly those with previous surgeries and or fistulas/stomas, presents a major challenge on itself. When possible, the surgeon should avoid going through the same incision(s) used in prior operations. Instead, they should enter from nonviolated areas of the abdominal wall such as the superior epigastric region or just over the pubic region, making way in under direct vision from the inferior or superior aspect of the wound using sharp dissection.

Once the abdominal cavity is entered, the surgeon often faces a large ball of intestines wrapped by adhesions. The surgeon should mobilize the entire segment of intestines, from the ligament of Treitz to the rectosigmoid. In patients with the presence of fistulas, multiple enterocutaneous fistulas (ECFs), or enteroatmospheric fistulas (EAFs), resecting all of the fistulas may be challenging, but fistulas must be taken down and the gastrointestinal (GI) tract must be reconstituted, using not staplers, but rather the hand-sewn, double-layer technique. In our practice, we use the Connell technique.

Once the continuity of the GI tract has been established or diverted, the timing of CAWR must be based on the physiology of the patient. Whichever approach one uses, the goal is to create functional and durable coverage of the abdominal cavity and to improve the patient's quality of life. Native abdominal wall should be used; if that is not possible, biologic or prosthetic mesh should be used instead. In most patients, some sort of combination of reconstruction techniques will be needed. However, if midline tissue cannot be easily approximated or if mesh reinforcement is needed (as it is in almost all abdominal wall defects larger than 6 cm), then other techniques such as component separation should be considered. Over the last five years, we have changed from anterior component separation (ACS) to posterior component separation (PCS) in most patients that require CAWR. While most surgeons do not do CAWR in the acute phase, recently we have reported CAWR in all patients undergoing damage control surgery both for trauma or emergency surgery; CAWR has become a common practice, mostly using PCS.[58] If ACS is used, separation of the anatomic components allows significant mobilization for tensionless approximation of muscles at the midline. The component separation technique provides the advantage of preserving the innervation to the muscle flaps, hence maintaining the dynamic support and integrity of the abdominal wall.

In the ACS (**Figure 10**), flaps containing skin and subcutaneous tissue are lifted off of the underlying anterior rectus sheath and the external oblique fascia. Based on the size of the defect these flaps should extend caudally to the inguinal ligament and cranially beyond the costal margin.

The blood supply of the skin comes from perforators arising from the deep epigastric and superficial inferior epigastric arteries. Extensive dissection of the skin flaps, however, can disrupt these perforators, predisposing the overlying skin flaps to surgical site infections, skin necrosis, and wound dehiscence. Component release should be performed bilaterally. It is important to avoid dissection deep to the internal oblique as the neurovascular plane exists between the internal oblique and the transversus abdominis muscles where blood vessels and nerves supplying the obliques and the rectus abdominis muscle traverse.

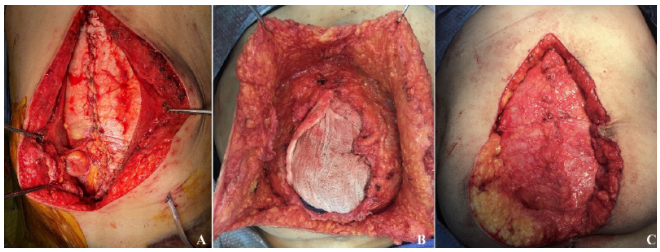

Figure 10. Complex abdominal wall reconstruction (CAWR) (A) Posterior component separation (PCS) with posterior rectus fascia closed around ileostomy. (B) Anterior component separation. (C) Closure of midline over the biologic mesh placed underlay.

Posterior Component Separation with Transversus Abdominus Release

Posterior component separation (PCS) with or without transversus abdominus release (TAR) has become popular. Detailed technical aspects of this procedure paying particular attention to the surgical anatomy have been reported.[59] The main principle of PCS is that the perforating vessels are spared, and the mesh is placed between rectus muscle in a sublay fashion, over the posterior rectus fascia and/or over the transverse abdominal muscle and posterior aspect of the recti muscles. Once all adhesions and other concomitant procedure have been dealt with, such as reconstitution of GI tract or other procedures as described above, the posterior approach to the retrorectus space is performed by incising the medial edge of the posterior rectus sheath at the medial edge of the rectus abdominis muscle. The edge of the transected posterior rectus sheath is grasped with clamps and retracted medially and posteriorly, allowing easy lateral dissection of the retrorectus space. During this stage of the operation one has to be cognizant not to injure intercostal nerves that perforate rectus muscle. The posterior lamina of the internal oblique aponeurosis is incised just medial to the entry of the intercostal nerves as they enter the rectus muscle posteriorly.[59]

This extraperitoneal space now can be extended laterally and caudally in order to make space for the prosthesis. I prefer that this space extends to the costal margin and joins the central tendon of the diaphragm in the midline. Once the space is created to satisfaction, the posterior rectus sheaths are approximated with running absorbable suture. Fixation of the mesh superiorly, inferiorly, and laterally with sutures will help with positioning the mesh appropriately. A number of techniques can be used to place the rest of the sutures. I prefer to use a Carter-Thomason suture passer, but other suture passers are just as acceptable to fix the mesh to the anterior abdominal wall (**Figure 11**).

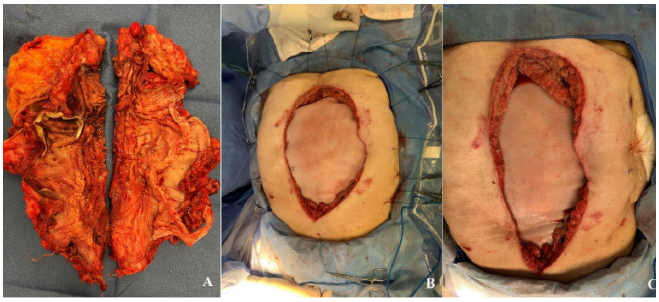

Figure 11. An example of CAWR in a patient requiring resection of abdominal wall (30 x 20 cm) and multiple layers of synthetic mesh (A) for a perforated colon entrapped into hernia, using a combination of underlay and bridge biologic mesh (B, C)

The superiority of PCS with TAR have been demonstrated when compared with ACS with a 50 percent decrease in wound morbidity with the posterior approach.[60] Moreover, this technique has been suggested for patients who previously had ACS but have recurrence of hernia.[61]

Mesh Graft Selection

By definition, patients with strangulation/obstruction or perforation, those with ECFs, EAFs, or stomas, or requiring bowel resection have contaminated wounds. Synthetic mesh has been used in the past, but it was associated with high rates of wound infection (often necessitating removal of infected mesh for source control of infection) and with other complications (such as newly created fistulas). Most recently, biologic mesh has become standard in high-risk patients with contaminated and dirty-infected wounds.[62] Level I evidence, however, is needed. Over last few years, we have studied intensely the use of biologic in these patients.[26,58,63–67]

The hernia grading system[68] is used to classify the risk for infectious complications to help surgeons decide on the technique and potentially the mesh to be used. Grade 1 refers to a low risk for infections or complications in patients who have no history of wound infections; grade 2 indicates comorbidities such as smoking, diabetes, obesity,

a suppressed immune system, and **chronic obstructive pulmonary disease** (**COPD**); grade 3 refers to those with previously contaminated wound infections, stomas, or intraoperative violations of the GI tract; and grade 4 indicates infected mesh and septic foci. Obviously, grades 3 and 4 present serious medical and surgical challenges for the patient and for the health care team, whether led by a general surgeon, trauma surgeon, or plastic surgeon. Even grade 2 can indicate patients that may harbor a significant risk and need to be thoroughly evaluated preoperatively; otherwise, a significant problem could arise. Our results suggest that biologic mesh implantation is a valid option for complex abdominal wall reconstruction in the high-risk trauma and acute care surgery population.

In our practice, we aim to complete the definitive procedure in a single operation. On occasion, we have used the principle of damage control, returning the next day or so to complete, if at all possible, the operation. Since 2005, in all of our patients with clean-contaminated or dirty-infected wounds, we have used biologic mesh, primarily AlloDerm® and Strattice™.[69] In case of a large loss of abdominal wall domain, a combined bridging and underlay mesh placement (**Figure 11**) is used with skin coverage, whenever possible. With sublay or underlay mesh placement, one large drain between the mesh and fascia is used, and then three to four drains over the fascia and under the skin and subcutaneous tissue. To avoid drain displacement, all of the drains to tissue with fine chromic sutures are fixed. The drains are kept in until each drain has <25 cc/24 hours.

Postoperative Care

All patients who have undergone acute incarcerated hernia repairs require prophylactic antibiotics, thromboprophylaxis, adequate analgesia, and hydration, postoperatively. Patients with systemic diseases such as diabetes or those after bowel resection may require an extension of the antibiotic prophylactic antibiotics beyond 3 to 5 days. Patients with large ventral hernias may require mechanical ventilation or other respiratory therapy. Treatment of concomitant systemic diseases should also be continued following surgery. Surgical incisions should be regularly checked for signs of infection in patients who had strangulation requiring bowel resection. Superficial incisional surgical site infections (SSI) may develop within the first days to weeks following surgery. In contrast, deep incisional SSIs may develop later and may be associated with mesh infection. Enhanced recovery protocols should be followed postoperatively.

Guidelines and Gray Areas in Evidence

Recently, two sets of guidelines were published, which attempted to synthesize the evidence and generate recommendations for surgeons. One of these guidelines, namely those by the World Society of Emergency Surgery (WSES), were specifically focused on complicated hernias and emergency surgery.[70] The second guidelines were published by the HerniaSurge Group in 2018.[71] These guidelines focused on the management of groin hernia and included evidence synthesis and recommendations on complicated groin hernia only.

The HerniaSurge guidelines evaluated the question of the optimal diagnostic modality for incarcerated groin hernias and stated that clinical diagnosis alone is sufficient in almost all cases. The guidelines recommended clinical examination of the groin in all patients presenting with bowel obstruction. Both HerniaSurge and WSES guidelines evaluated the evidence on the question of the timing of surgery and both guidelines concluded that incarcerated hernias with bowel obstruction symptoms should undergo surgery immediately as delay in diagnosis and treatment increases morbidity and mortality. Optimal surgical approach was discussed and evaluated in both HerniaSurge and WSES guidelines. The HerniaSurge acknowledged that the question of optimal approach remains open for further research. The WSES guidelines recommended that diagnostic laparoscopy is a helpful tool to assess bowel viability in cases when strangulated hernia is spontaneously reduced (grade 2B recommendation) and that repair of incarcerated hernias may be performed only in the absence of strangulation and risk of bowel resection. Both guidelines advocated for mesh repair only in clean surgical field or Centers for Disease Control and Prevention (CDC) wound class I (grade 1A recommendation). Both guidelines concluded that mesh can be used in clean contaminated surgical field (CDC wound class II), with the HerniaSurge guidelines recommending monofilament large-pore polypropylene mesh and the WSES guidelines recommending mesh only in the absence of gross enteric spillage (grade 1A recommendation). The role of biologic meshes is evaluated by the WSES guidelines, which recommended that biologic mesh can be used in a contaminated-dirty surgical field and the decision between cross-linked or non-cross-linked should be based on defect size and degree of contamination (grade 2C recommendation). Antibiotic prophylaxis was evaluated in both guidelines. The HerniaSurge guidelines recommended IV antibiotics during and following emergency hernia repair, the duration to be decided depending on the extent of contamination. The WSES guidelines recommended short-term antibiotic prophylaxis in CDC wound class I, 48-hour antibiotic prophylaxis in CDC wound classes II and III, and antimicrobial therapy in in CDC wound class IV (grade 2C recommendation). The WSES guidelines have also evaluated an optimal approach to unstable patients and recommended open abdomen to prevent abdominal compartment syndrome with early definitive closure upon stabilization of the patients.

Conclusion

Diagnosis and treatment of incarcerated abdominal wall hernias have improved in the recent years. Yet, there are still a number of gaps and controversies and paucity of high-quality data in the literature. Further experimental and prospective longitudinal studies as well as evidence synthesis initiatives are needed to improve our knowledge and ultimately benefit our patients with incarcerated abdominal wall hernias. As hernias will not get smaller, we suggest that abdominal wall hernias, should be repaired early and electively.

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CHAPTER 24

Management of Fulminant Clostridium Difficile Colitis

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Key words:

Clostridium difficile colitis, pseudomembranous colitis, vancomycin, fidaxomicin, total abdominal colectomy, diverting loop ileostomy, fecal microbiota transplantation, bezlotoxumab

Abstract

Clostridium difficile infection (CDI) is a major health problem and has become the leading cause of nosocomial infection in developed countries.[1] CDI may present as an asymptomatic infection, a more serious colitis, and sometimes evolve into fulminant disease and toxic megacolon.

The first line of treatment consists of antibiotics, fluids, and electrolytes replacement, and the elimination of previous antibiotic treatment when feasible. Escalation to surgical intervention is necessary only in cases of severe bowel compromise, causing systemic deterioration and evolution toward septic shock.[2] While the traditional surgical treatment consists of subtotal colectomy with end ileostomy, recently, a more conservative approach resulting in the formation of a loop ileostomy and antegrade colonic lavage has provided promising results with comparable cure rates and significant reduction in morbidity.[2]

New evolving strategies have also been tested with the aims to improve the cure rate and reduce recurrence rates.[3] Fecal microbiota transplantation and the monoclonal antibody bezlotoxumab have demonstrated to achieve good results in addition to traditional antibiotic treatments.

Introduction

Clostridium difficile infection (CDI) is the leading cause of hospital-acquired diarrhea with increased incidence worldwide over the last two decades. Clinical presentation can vary from an asymptomatic carrier to fulminant colitis.

Conversely CDI treatment ranges from systemic and topical antibiotics, to fecal microbiota transplantation (FMT) and life-saving surgical intervention. Treatment guidelines and protocols are well established for moderate colitis, while debates still persist for the more severe forms.[1,2] New treatment options are under investigation, with promising early results and will likely represent valid alternatives in the near future.[3] For all these reasons, the pathogenesis, natural history, diagnosis, and management of CDI are important topics for surgeons facing the multifaceted clinical presentations of the disease.

Epidemiology, Pathogenesis, and Risk Factors

Clostridium difficile is an anaerobic, spore-forming, Gram-positive bacteria, which is part of the normal intestinal microbiota in healthy babies and colonizes the gastrointestinal tract in adults when the normal gut flora is altered.[2] C. difficile produces two toxins which are responsible for its virulence: toxin A, an exotoxin that binds the brush border of the intestinal mucosa and causes its disruption; and toxin B, a cytotoxin that destroys cytoskeletal structure of the enterocytes, leading to the formation of pseudomembranes.[4]

C. difficile has an oro-fecal pathway of transmission and it is usually associated with hospital stay and use of antibiotics. Over time new strains of C. difficile have emerged, such as B1NAP1/027, a hyper-virulent strain causing hyper-production of toxins A and B.[5] It represents up to 28.1 percent of CDI in the United States.[6] It is known to be resistant to fluoroquinolones, and the excessive use of antibiotics in the general population might have created an advantage in its selection.

The two most common risk factors for CDI are exposure to antibiotics and hospital stay, due to the fact that C. difficile is one of the most commonly hospital-acquired infections. Antibiotics play a crucial role in the disruption of normal intestinal flora, allowing C. difficile to become the prominent bacteria in the colon. Broad-spectrum antibiotics, like clindamycin and fluoroquinolones are considered at high risk for CDI, but potentially any exposure to antibiotics may increase the risk of CDI. Patients have 7 to 10 times the increased risk of CDI at 1 month and two times at 3 months after the cessation of antibiotics.

Other known risk factors are age >65, presence of comorbidities, recent gastrointestinal surgery, recent exposure to anti-neoplastic agents, inflammatory bowel disease, longer length of stay in hospital, or health care facilities.[1,2] Additionally, other medications such as proton-pump inhibitors are also linked to CDI. The reduced gastric acid production allows the ingested bacteria to survive in the stomach and colonize the distal gastrointestinal tract.[7] Taking into consideration all the aforementioned risk factors, it is easy to understand why surgical patients are at a significantly increased risk of CDI having several risk factors concomitantly present during their hospital admission.

Clinical Manifestations and Diagnostic Work-Up

Clostridium difficile presentation ranges from an asymptomatic carrier and self-limiting diarrhea, mild-to-moderate self-limiting infection, to severe-to-fulminant colitis. The severity of the infection is due to the imbalance between the virulence of bacteria and the compromised host defense mechanisms. Clostridium difficile infection has been classified based on expert opinion in mild-to-moderate colitis and severe-to-fulminant colitis.[2] Disease classification and clinical features are summarized in **Figure 1**.

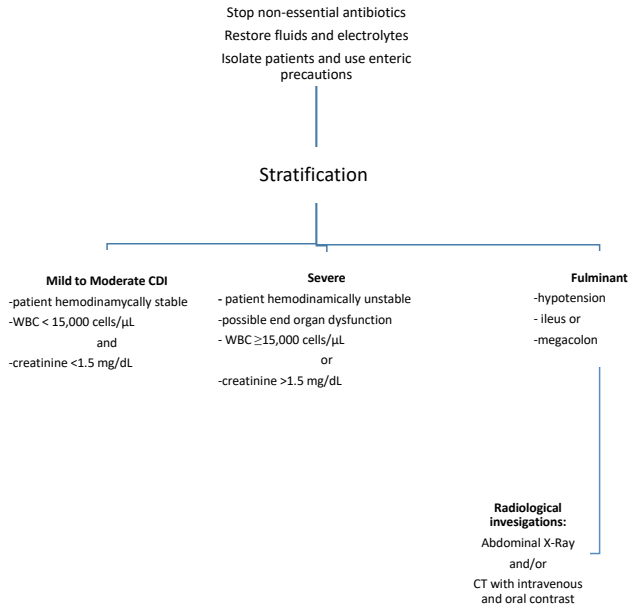
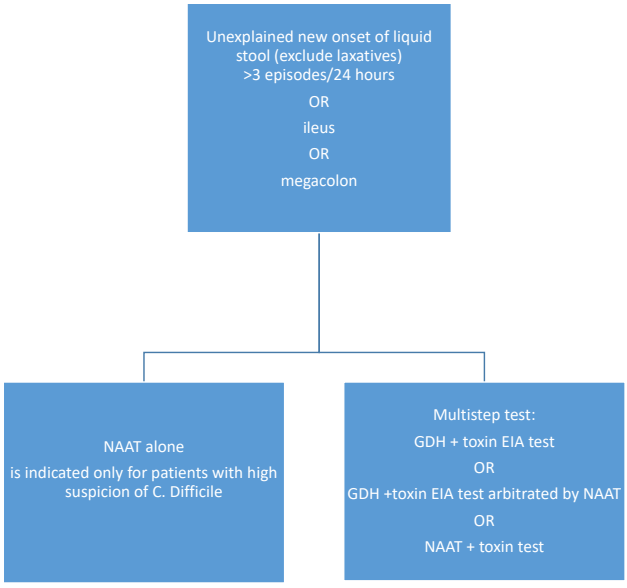


Figure 1. Clostridium difficile diagnostic algorithm and disease severity stratification

Mild-to-moderate colitis

Patients with mild-to-moderate colitis usually present with new-onset diarrhea (at least 3 episodes over the last 24 hours without the use of laxatives) after recent hospital admission or antibiotic administration for an unrelated source. On clinical examination, these patients appear to be hemodynamically stable, sometimes with low-grade fever and with mild abdominal discomfort. Laboratory results are usually mildly deranged with white blood cell count (WBC)<15,000 cells/μL and creatinine <1.5 mg/dL).

In case C. difficile infection is suspected, the next step is to obtain either a stool sample for patients with clinically significant diarrhea or to use a rectal swab for patients with a proximal diversion. There are several laboratory tests available for the diagnosis of CDI, and for a definitive diagnosis the recommendation is to combine two different tests (**Figure 2**).[2]



Abbreviations:

NAAT: nucleic acid amplification test

EIA: enzyme immunoassay test

GDH: glutamate dehydrogenase

Figure 2. Diagnostic tests for Clostridium difficile

A nucleic acid amplification test (NAAT) uses polymerase chain reaction to detect genes specific to toxic strains to C. difficile with high sensitivity and specificity.[10].However, NAAT detects toxic genes, but cannot test for production of active toxins and might lead to misdiagnosis and unnecessary treatment. As a consequence, NAAT should be performed only in patients with a high suspicion for CDI or it should be included in a two-step algorithm starting with toxin-enzyme immunoassay (EIA).

Enzyme immunoassay (EIA) tests are available for C. difficile glutamate dehydrogenase (GDH) and EIA for C. difficile toxins A and B. The GDH screening test has high sensitivity, but it detects an enzyme present in both virulent and nonvirulent strains and it should be used in association with toxins A/B EIAs in an algorithm, including screening for GHD followed by a toxin assay EIA.[1,2] EIA for toxins A and B is very specific to virulent strains, but it is not recommended alone, because it has scarce sensitivity, due to the fact that a large amount of toxin is needed for the test to show positive results.[11]

Severe and fulminant colitis

Patients who progress to severe colitis present with symptoms of systemic hemodynamic compromise, severe diarrhea or ileus, and end-organ failure. Patients with severe colitis and hemodynamic instability usually appear to be intravascularly depleted with abdominal distension, tenderness, and signs of peritoneal irritation. In this situation multiple episodes of diarrhea and evidence of systemic infection result in hypovolemia and septic shock. The clinical picture may progress to toxic megacolon, characterized by colonic distension and obstipation, rather than diarrhea in the most advanced cases.

Patients with severe and/or fulminant colitis have usually elevated WBC (>15,000 cells/mL) or leukopenia and evidence of one or multiple end-organ dysfunction with consequent electrolytes derangement, hypovolemia, lactic acidosis, and hypoalbuminemia.

These patients should initially be evaluated with plain abdominal X ray that typically will show dilated large bowel loops and small bowel if the ileocecal valve is incompetent (**Figure 3**). The definitive test is a contrast-enhanced computer tomography (CT)[12] with oral and IV contrast when possible, given the abdominal distension and renal dysfunction. CT might have nonspecific findings such as colonic wall thickening (**Figure 4**), which can be present in inflammatory bowel disease. Typical CT features for C. difficile colitis (CDC) are the "accordion sign" which describes the entrapment of oral contrast between edematous haustral folds, and the "double-halo sign, target sign", which is the attenuation of intravenous contrast at the level of submucosa, due to inflammation and hyperemia. Ascites might be present as well as free air due to colonic perforation (**Figure 5**).

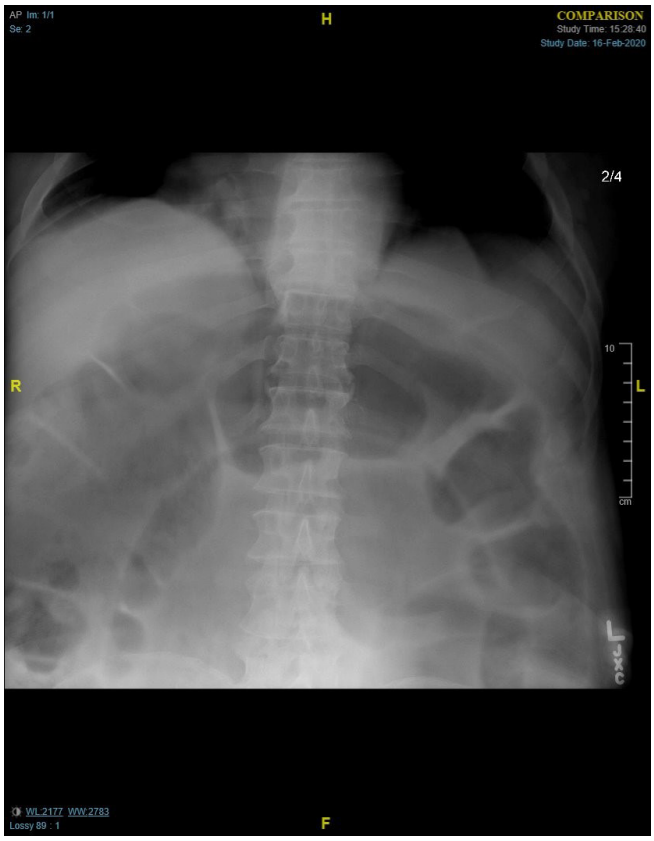


Figure 3. X ray showing typical dilated large bowel loops in a case of severe Clostridium difficile colitis

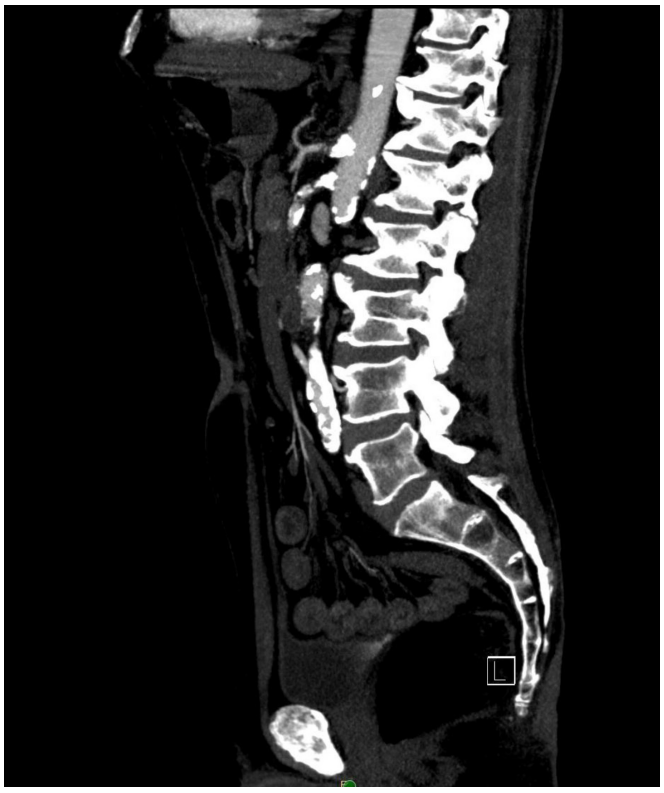


Figure 4. CT scan showing diffuse colonic wall thickening

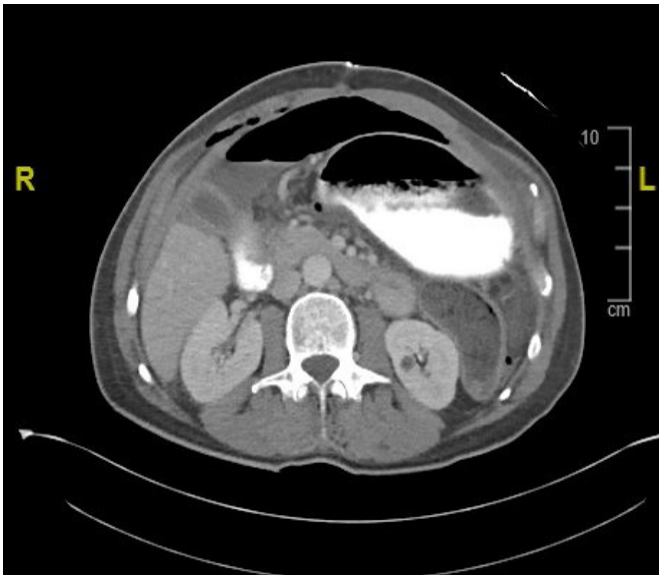


Figure 5. CT showing colonic perforation ad ascites

Endoscopic assessment might be used in patients with megacolon for decompression or to clarify the diagnosis when C. difficile is suspected in a patient with ileus or proximal diversion. The visualization of typical pseudomembranes will prove the diagnosis (**Figure 6**). Pseudomembranes are caused by the cytotoxic effect of C. difficile toxins causing mucosal ulceration, and are described as yellow/white plaques with continuous or patchy distribution. The benefit of endoscopic evaluation should be weighed against the risk of perforation.[1,9]

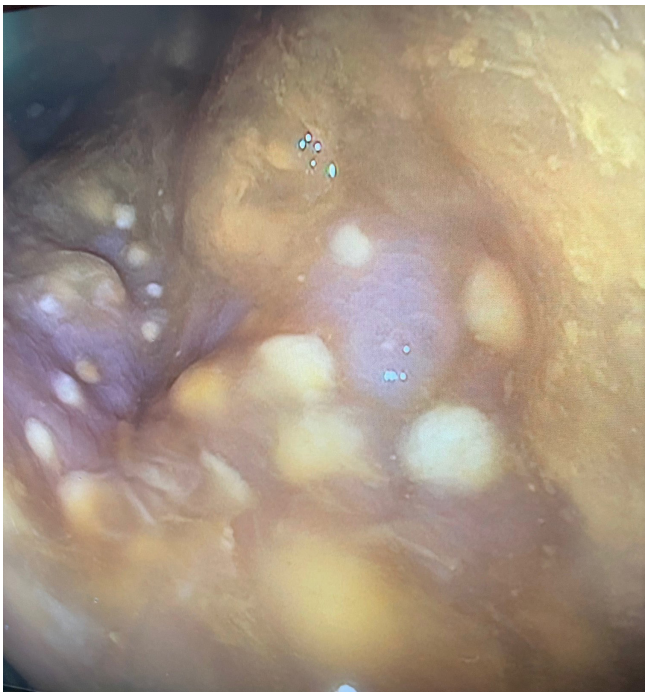


Figure 6. Endoscopic picture of pathognomonic Clostridium difficile pseudomembranes

Management

In case of suspected CDI, antibiotic agents and proton-pump inhibitors (PPIs) should be discontinued when possible[1,2], and empirical antibiotic therapy toward C. difficile should be avoided unless there is a strong suspicion for CDI. Bagdasariana et al.[13] in a recent meta-analysis showed that the prolonged use of antibiotics in patients with persistent symptoms and severe CDI is associated with an increased risk of recurrence. However, if antibiotic treatment cannot be discontinued for treatment of an unrelated primary infection, antimicrobial agents that are less likely to precipitate CDI should be considered, such as aminoglycoside, sulfonamides, macrolides, vancomycin, or tetracycline/tigecycline. Conservative and surgical treatment options are summarized in **Figure 7**.

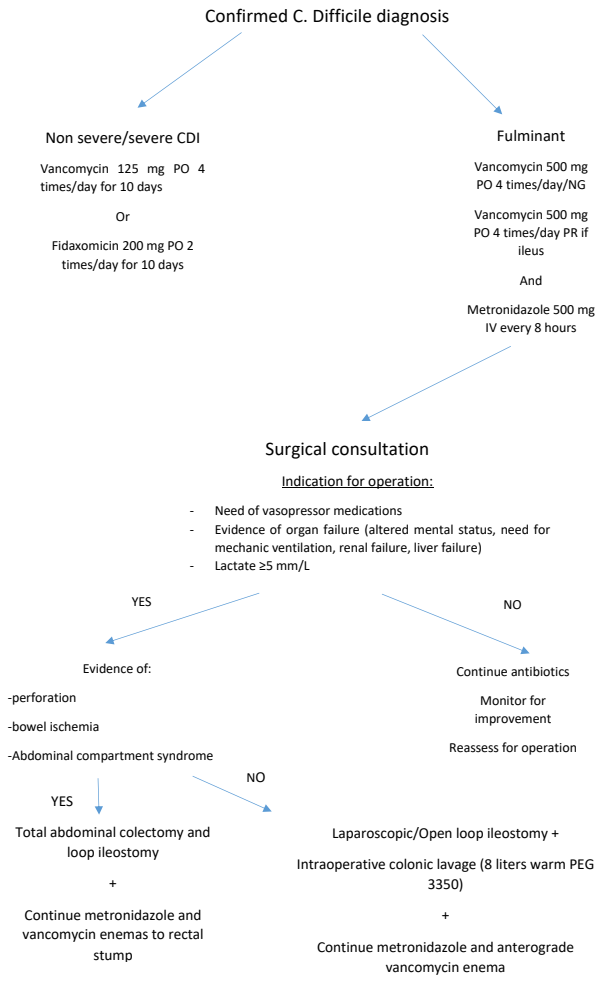


Figure 7. Clostridium difficile treatment (adapted by Bowman et al.[3])

Antibiotics therapy

According to the most recent guidelines[1,2] and a Cochrane review[14], either vancomycin or fidaxomicin are recommended over metronidazole for the first episode of CDI. The recommended dosage for vancomycin is 125 mg orally 4 times a day and for fidaxomicin 200 mg twice daily for 10 days. Metronidazole is recommended only for initial treatment of a mild episode of CDI if vancomycin and fidaxomicin are not available. The recommended dose for metronidazole is 500 mg orally 3 times a day for 10 days, with the suggestion to avoid repeated and prolonged courses of metronidazole to avoid the risk of cumulative effect and potential irreversible neurotoxicity.

Nelson et al.[14] in their Cochrane review included 22 studies for a total of 3215 participants with mild to moderate CDI. Vancomycin was found to be more effective than metronidazole for achieving symptomatic relief. Overall, 72 percent (318/444) of patients treated with metronidazole achieved symptomatic resolution compared with 79 percent (339/428) of patients treated with vancomycin (risk ratio [RR] 0.90, 95 percent confidence interval [CI] 0.84 to 0.97). Fidaxomicin was found to be more effective than vancomycin. In fact 71 percent (407/572) of patients on fidaxomicin achieved symptomatic relief compared with 61 percent (361/592) of patients on vancomycin (RR 1.17, 95 percent CI 1.04 to 1.31).

In side-by-side comparison, oral vancomycin has been shown to be superior to metronidazole in severe CDI.[15,16] Vancomycin has an effect on the gut lumen if administered orally, while if administered parenterally, it is not eliminated via the fecal route and it does not reach the same concentration. A vancomycin enema might be a valid alternative in patients with ileus, administered through the stoma for antegrade irrigation or by direct application during an endoscopic exam.[1]

Fidaxomicin has been proven to be noninferior to vancomycin in different trials[17,18] and also according to a recent systematic review.[19] The recent EXTEND trial[20,21] (Extended-pulsed fidaxomicin versus vancomycin for Clostridium difficile infection in patients 60 years and older) has enrolled 362 hospitalized patients with CDI older than 60 among 86 European hospitals and treated them with extended-pulsed fidaxomicin (200 mg oral tablets twice days 1 to 5, then once daily on alternate days on days 7 to 25) or vancomycin (125 mg oral capsules, 4 times every day on days 1 to 10). The entire length of follow-up was 90 days; they demonstrated that extended-pulse fidaxomicin was superior to vancomycin, with the lowest recurrence rate observed in trials for CDI (p=0.001). Fidaxomicin should be considered for treatment of patients with an increased risk of recurrence, such as elderly patients with associated comorbidities who cannot discontinue current antibiotics in use.

For fulminant CDI, the recommendation is to administer oral vancomycin 500 mg 4 times every day; if ileus is present 500 mg of vancomycin should be diluted in 100 mL normal saline and administered per rectum every 6 hours as a retention enema. Concomitant intravenous metronidazole 500 mg every 8 hours should be administered together with oral or rectal vancomycin.[2]

Timing for operative management and identification of surgical candidates

Patients who progress to severe or fulminant disease despite medical treatment should have an early surgical consultation. Guidelines found in the medical surgical literature are conflicting. According to the 2018 Infectious Disease Society of America (IDSA) guidelines[2], management of fulminant CDI is medical, and surgery should be reserved for "severely ill" patients, even if their characteristics are not further delineated. Even the 2015 American Society Colon and Rectal Surgeons (ASCRS)[22] guidelines and the 2013 American College Gastroenterologists (ACG) guidelines[23] recommend surgical consultation only in case of complicated disease such as perforation, peritonitis, abdominal syndrome, or hypotension requiring vasopressor. On the contrary, the 2014 Eastern Association for the Surgery of Trauma (EAST) guidelines[24] recommended that surgical consultation should be obtained before clinical signs of organ failures, which corresponds between 3 and 5 days after diagnosis in patients who are not improving with conservative management.

Prognostic markers for the development of fulminant colitis in patient with CDI have been analyzed by Girotra et al.[25] in a 10-year single-institution retrospective review of patients that underwent total abdominal colectomy. The markers include age over 70, recurrent CDI, profound leukocytosis (over 18,000/mm^3), hemodynamic instability, use of antiperistalsis medications, increasing abdominal pain, distention, and diarrhea. Based on current evidence, operative treatment should be performed prior to development of shock, vasopressor requirement, end-organ failure, and mental status change to reduce mortality rate.[26] In a systematic review by Stewart et al.[27] mortality rates between surgical and medical treatment for fulminant CDC were analyzed. In total, 510 patients from 6 different studies were included; the odds ratio of mortality of surgery compared with medical therapy was 0.70 (0.49-0.99), with the conclusion that emergency colectomy has a therapeutic role in patients with CDC nonresponsive to medical strategies.

Hall et al.[28] had retrospectively analyzed 1059 patients that had a primary diagnosis of CDI and underwent open total abdominal colectomy, excluding patients operated on the day of admission, with the aim to investigate the effects of delaying surgery in terms of morbidity and mortality. Days from admission to surgery (DATO) was associated with a higher risk of 30-day mortality ([odds ratio] 1.022, p=0.040), any complication (OR 1.040, p=0.001), and infection complications (OR 1.040, p=0.001). Total length of stay, intensive care unit length of stay, and direct-cost increase with longer DATO (p<0.001). Considering that patients with CDI have often a disease progression between days and weeks, this timeframe might be used as a "window of opportunity" for early surgical consultation. They concluded that an early surgical evaluation should be performed prior to patients' decompensation resulting in the use of vasopressors, end-organ dysfunction, altered mental status, and admission to the intensive care unit.

Similar results have been found by Ahmed et al.[29] who analyzed timing for surgery in 163 patients with toxic megacolon due to C. difficile, using the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP®) database from 2012 and 2016. They divided patients in two groups: those who underwent colectomy before the diagnosis of septic shock, the "early colectomy group"; and those who underwent colectomy in florid septic shock, the "late colectomy group". They found a significant decrease in 30-day mortality in patients who underwent colectomy before the onset of septic shock versus the late group (13) (21 percent) versus 28 (45.2 percent), (p=0.009). The early group also had a significant decrease in hospital stay compared with the late group (median 20 [14-34] versus 25 days [21-37], p=0.011). In addition, a higher proportion of patients in the late group continued to be in septic shock after colectomy, when compared with the early group (38.2 percent versus 8.25 percent, p=0.002). The take-home message is that when surgery is performed early, there is a significant reduction in mortality and hospital stay. These findings are in agreement with several previous studies, which showed an increased mortality when surgery was performed after hemodynamic compromise.[30,31] As a total abdominal colectomy is not a minor procedure, it is important to identify the "window of opportunity" to avoid a high postoperative mortality rate or unnecessary colectomy.

The University of Pittsburgh Medical Center (UPMC) developed a scoring system to predict the need for surgery[32] (**Table 1**).They assigned 1 point to chronic medical condition, abdominal pain and/or distension, hypoalbuminemia (<3 g/dL), fever (38.5 °C), and intensive care admission; 2 points to CT findings of pancolitis and bowel wall thickening, white blood cells ≥15,000, creatinine 1.5-fold>baseline; 3 points to abdominal peritoneal signs and 5 points to vasopressors requirement, mechanical ventilation, and disorientation and confusion. In total, 88 patients were included in the study, 2 percent of the total population (3,713) diagnosed with CDI from January 2007 to December 2012 at UPMC. Of those, 59 (67 percent) patients required surgery. The two groups had similar characteristics in regard to age, sex, body mass index (BMI), and comorbidities. A score ≥15 predicted the need for surgery 75 percent of the time, while patients scoring ≥22 had surgery in 100 percent of cases. In the surgical group, 42 percent of patients had respiratory failure

requiring mechanical ventilation compared with 0 percent in the nonsurgical group (p<0.0001); 49 percent required vasopressors for septic shock before operation in the surgical group compared with 0 percent in the nonsurgical group (p<0.0001); acute kidney injury was present in 92 percent of the surgical group versus 72 percent in the nonsurgical group (p=0.026). Overall, the mortality rate in the surgical group was 30 percent, while there was 0 percent mortality in the nonsurgical group. They concluded that early surgical consultation and the use of the UPMC scoring system might lead to better patient selection, earlier surgical intervention, and reduction in mortality rate.

Table 1. Proposed Clostridium difficile severity scoring system

Criteria	Points
Immunosuppression and or chronic medical conditions	1
Abdominal pain and/or distension	1
Hypoalbuminemia (<3 gr/dL)	1
Fever >38.5° C	1
Intensive care unit admission	1
CT scan with nonspecific findings or pancolitis, ascites and/or bowel thickening	2
White blood cells count >15,000 and/or band count >10%	2
Creatinine 1.5-fold >baseline	2
Abdominal peritoneal signs	2
Vasopressors required	5
Mechanical ventilation requires attributed to C. difficile	5
Disorientation, confusion, or decreased consciousness	5

Points:
1–3: Mild-moderate disease
4–6: Severe disease
7 or more: Severe, complicated disease

Predictors of mortality in patients undergoing emergency surgery for C. difficile have been described in retrospective reviews.[33-35] Sailher et al.[33] reviewed 4796 patients with CDI diagnosis, 199 (4.1 percent) with fulminant colitis, and a mortality rate of 34.7 percent. Independent predictors of mortality were age over 70, severe leukocytosis (>35,000/μL) or leucopenia (<4000), bandemia (neutrophil bands ≥10 percent), and cardiorespiratory failure. Lee et al.[34] analyzed the ACS-NSQIP database from 2005 to 2010 looking at emergency open colectomies for C. difficile, and noted a mortality rate of 33 percent (111/335). Higher mortality rate was associated with renal failure requiring hemodialysis, chronic obstructive pulmonary disease, age over 80, thrombocytopenia (platelets lower 150 x10^3/mm^3), coagulopathy (international normalized ratio >2.0), and acute kidney failure (blood urea nitrogen >40 mg/dL). Kulaylat et al.[35] analyzed 532 patients who underwent surgery for CDC, and noted a 32.7 percent 30-day postoperative mortality. Patient covariates associated with significantly increased mortality included age greater than 80 (OR 5.5, p = 0.003), need for preoperative mechanical ventilation (OR 3.1, p <0.001), chronic steroid use (OR 2.9, p <0.001), underlying cardiopulmonary disease (OR 2.0, p = 0.001), and acute renal failure (OR=1.7, p = 0.03).The aforementioned factors do not represent contraindication to surgery but should be taken into account to evaluate the pros and cons to surgical intervention and to stratify patients' risks.

Operative management

An early surgical consultation is recommended for all patients with severe, complicated CDI colitis. On average, 1 percent of patients with CDI will evolve to fulminant colitis and 30 percent of those will eventually require surgery.[36] Traditionally, the procedure most commonly performed is a total abdominal colectomy (TAC) with end ileostomy. The colitis is usually diffuse and the goal of surgery is to eliminate the source of sepsis, reduce the risk of perforation, and divert the fecal stream without the added morbidity of a pelvic dissection. However, TAC in the setting of severe C. difficile is associated with a mortality rate ranging from 32 to 36 percent.[33,37] Furthermore, patients are exposed to the long-term sequelae of an end ileostomy, such as dehydration, electrolytes abnormalities, parastomal hernia, and stoma retraction resulting in poor quality of life[38,39].

In 2011, Neal et al.[40] published a colonic-preserving approach for surgical management of fulminant CDI, which includes an assessment of colonic viability, abdominal washout, formation of diverting loop ileostomy (DLI) , and infusion of 8 liters of warm polyethylene glycol solution via a catheter in the efferent limb of the ileostomy. Postoperatively, boluses of 500 mg vancomycin are administered via the efferent limb every 8 hours, in addition to intravenous metronidazole. This prospective study was conducted among 42 consecutive patients at UPMC between June 2009 and January 2011. A significant reduction of 30-day mortality (19 versus 50 percent, p=0.006) was noted. Furthermore, preservation of the colon was achieved in 39 of the 42 patients (93 percent); the procedure was done laparoscopically in 35 patients (83 percent) and 79 percent of patients in the DLI group had their ileostomy reversed. Unfortunately, despite the initial enthusiasm, these excellent results have not been reproduced in subsequent studies.[41-44]

Two recent meta-analyses[45,46] have assessed the effects of diverting loop ileostomy (DLI) versus total abdominal colectomy (TAC) for CDC in terms of mortality and morbidity. They both included five nonrandomized studies[20-24], with a total of 3683 patients treated for CDI: 733 treated with DLI and 2950 with TAC. The overall mortality was equivalent among the two groups, with cumulative rates of 31.3 percent for patients undergoing TAC and 26.1 percent for patients undergoing DLI (P=0.22)[26]. There was no difference in terms of postoperative morbidity including DVT (P=0.18), acute renal failure (P=0.10), surgical site infection (P=0.97), respiratory (P=0.97), urinary tract infection (P=0.72), and reoperation (P=0.78). The ostomy reversal rate was significant higher in the DLI group, ranging between 76 and 100 percent (P=0.0002).

Surprisingly the two systematic reviews could not demonstrate a significant reduction in morbidity and mortality after DLI for medically refractory fulminant colitis. The main long-term advantage of DLI noted was the higher rate of colonic preservation, limiting the long-term sequelae of an end ileostomy. Because CDI is usually confined to the mucosa, in the absence of toxic megacolon, necrosis or perforation, DLI and colonic lavage might represent a valid alternative, with limited morbidities compared with TAC.

TAC for CDC has been compared with segmental colectomy, in a retrospective study using American College of Surgeons National Surgical Quality Improvement Project (ACS NSQIP).[47] Patients with primary diagnosis of CDC from 2007 and 2015, who underwent total or partial colectomy (PC) were included. A total of 733 patients were identified, 582 underwent TAC. There was no statistically significant difference in 30-day mortality between the two groups, (34.7 percent TAC and 37.1 percent PC, p=0.59). When controlling for patients' characteristics, there were no significant differences in any complication between the two groups. The main advantage of PC was the shorter postoperative hospital stay (18 days after TAC versus 15.1 days after PC, p=0.08). These findings suggested that a PC might be a safe surgical alternative for patients, but definitive conclusion cannot be drawn due to the relatively small sample size and the limited data available in the literature. Previous studies have demonstrated that PC should be considered an inferior choice as an additional 15.9 percent of patients will eventually need a completion colectomy.[48]

Another minimally invasive approach is gastrointestinal lavage (GIL).[49] Kidane et al. conducted a retrospective cohort study of hospitalized patients with severe, complicated CDI who failed conventional medical therapy and were referred for surgical consultation at two academic tertiary-care hospitals between January 2009 and January 2015. After surgical assessment, the attending surgeon decided to proceed either with bedside GIL or directly to colectomy. Bedside GIL involved nasojejunal tube insertion followed by flushing with 8 L of polyethylene glycol 3350/electrolyte solution over 48 hours. Both patient groups received standard medical treatment with vancomycin 500 mg every 6 hours enterally and metronidazole 500 mg intravenously three times daily for 14 days. In total, 19 and 17 patients with similar baseline characteristics underwent GIL and direct colectomy, respectively. The inhospital mortality rate was 26 percent (5/19) and 41 percent (7/17) for the GIL and colectomy groups, respectively (p = 0.35). Only one patient in the GIL group failed the protocol, requiring colectomy. There were no significant differences in complications in the two groups and the conclusion was that bedside GIL appeared to be safe for the treatment of patients with severe, complicated CDI who had failed conventional medical therapy. This protocol is under a more extensive investigation through a 1-year single-center, pilot randomized controlled trial.[50]

Evolving Treatment Options to Manage Clostridium Difficile Colitis

Fecal microbiota transplantation

Fecal microbiota transplantation (FMT) is the transfer of stool from a healthy donor to a patient to treat a disease related to the altered microbiome. It is considered an effective treatment option for patients with multiple recurrences of CDI who have failed antibiotics treatment.[1] The rationale is that CDI is the result of the disruption of normal colonic flora, and the reintroduction of normal flora via donor feces might correct the imbalance.[51]

A recent systematic review conducted by Quaraishi et al.[52] studied the efficacy of FMT in patients with recurrent and refractory CDI. The review included 37 studies, 7 randomized controlled trials and 30 case series. FMT was more effective than vancomycin (RR=0.23, 95 percent CI 0.07-0.08) for treatment of recurrent and refractory CDI. Significant efficacy differences were observed based on the FMT delivery. The efficacy was respectively 95 percent when FMT was delivered in the lower tract versus 88 percent in the upper tract (p=0.02). The administration of consecutive courses of FMT following the initial treatment resulted in increased efficacy.

Hvas et al.[53] conducted a randomized control trial between 2016 and 2018. They enrolled 64 patients assigned to three different groups: 24 received FMT, applied by colonoscopy or nasojejunal tube, after 10 days of vancomycin (125 mg, 4 times daily); 24 received 10 days of fidaxomicin (200 mg twice daily); and 16 received 10 days of vancomycin. Clinical resolution was observed in 22 patients given FMT and vancomycin (92 percent), 10 patients in the fidaxomicin group (42 percent), and 3 patients in the vancomycin group (19 percent, p=0.002, p<0.0001, p=0.13). They concluded that FMT combined with vancomycin is superior to fidaxomicin and vancomycin alone in treating patients with recurrent Clostridium difficile infection.

The route of administration for FMT and its consequent effect on FMT efficacy has been investigated in a recent systematic review[54] including 14 studies and 305 patients comparing FMT administered via upper and lower gastrointestinal route. At 30 and 90 days, the risk of clinical failure was 5.6 and 17.9 percent in the upper group compared with 4.9 and 8.5 percent in the lower group, respectively (p = 0.028). More recently, a randomized control trial has investigated the administration of FMT through capsules and compared it with colonoscopy administration.[55] Among 116 patients, 57 were assigned to the capsule group, with a noninferiority margin of 15 percent. They found that FMT via oral capsules was not inferior to delivery by colonoscopy with the end point of recurrence at 12 weeks. A greater proportion of participants receiving capsules rated their experience as "not at all unpleasant" (66 versus 44 percent, difference 22 percent [P=0.01]).

Monoclonal antibodies

The expression of toxins A and B are mandatory for development of CDI. Monoclonal antibodies against the toxins are designed to prevent cytotoxic effect and control the disease. In 2016, the FDA approved bezlotoxumab, which is a human monoclonal antibody that is able to prevent the binding of toxin B to host cells, which limits epithelial damage. Bezlotoxumab can be used in combination with antibiotics to reduce recurrence rates.[56]

Two randomized double-blind[57,58], placebo-controlled trials, MODIFY I and MODIFY II, have recruited 2655 patients receiving antibiotics according to guidelines, plus Bezlotoxumab or placebo, with the primary endpoint of recurrence of infection at 12 weeks. In both trials, the recurrence rate of CDI was significantly lower in the Bezlotoxumab group compared with the placebo group (MODIFY I: 17 versus 28 percent p<0.001; MODIFY II: 16 versus 26 percent <0.001).

A post-hoc analyses of (MODIFY) I/II data assessed bezlotoxumab efficacy in participants with increased risk for recurrent CDI such as age ≥65 years, history of CDI, compromised immunity, severe CDI, and ribotype 027/078/244. The majority of enrolled participants (75.6 percent) had ≥1 risk factor. Patients treated with bezlotoxumab experienced the following reductions in CDI recurrence for each of the risk categories: -20.1 percent (range -27.0,-13.2) for age ≥65 years, -17.9 percent (range -27.7,-7.6) for history of CDI, -17.0 percent (-28.0,-2.8) for immunocompromised patients, and -12.9 percent (range -28.0,-1.6) for infection with ribotypes 027/078/244. All of the groups demonstrated a statistically significant reduction in CDI recurrence, with the exception of infection from ribotypes 027/078/244. When patients were stratified for numbers of underlying risk factors, there was a greater impact on prevention of CDI recurrence as the number of risks factors increased, with patients having more than 3 risk factors experiencing the greatest reduction in CDI recurrence of -24.8 percent (range -39.1%, -9.3%). Based on these findings the World Society of Emergency Surgery recommends using bezlotoxumab with antibiotics to prevent recurrences of CDI, particularly in high-risk patients.

Conclusions

Clostridium difficile colitis remains a challenging disease, both from a medical and surgical point of view. Conservative medical management has been consolidated especially for mild to moderate disease, while an early surgical consultation is advised for cases not improving, before deterioration to septic shock requiring more intensive care. There are still open questions about timing for surgery and what surgical approach might guarantee radical treatment, limited morbidities, and reduced mortality. Long-term consequences and quality of life for different treatment options need to be established in order to ensure a reduced recurrence rate and good functional outcomes.

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CHAPTER 25

Abdominal Compartment Syndrome: Open Abdomen Strategies in Acute Care Surgery

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Key words:

Intra-abdominal hypertension, abdominal compartment syndrome, decompressive laparotomy, open abdomen management

Abstract

Intra-abdominal hypertension (IAH) and abdominal compartment syndrome (ACS) are well recognized entities among surgical patients and are well-established causes of morbidity and mortality in critically ill patients. Therefore, a high index of suspicion and early intervention in the setting of IAH and ACS is essential to improve outcomes. Nonoperative management options include volume reduction of intraluminal and extraluminal content within the abdominal cavity and optimizing abdominal wall compliance. Once IAH progresses to ACS, a decompressive laparotomy is the gold standard for treatment. The treatment phase of ACS not only includes this initial decompression but also includes care of the open abdomen (OA) and the subsequent temporary closure (TAC) and long-term abdominal wall reconstruction. TAC options include skin only, plastic closure, and vacuum-device closure. If definitive fascial closure cannot be achieved at the index hospitalization, absorbable and nonabsorbable mesh or skin closure techniques may be utilized to facilitate abdominal closure. In such situations, patients are left with large ventral hernia defects that require complex abdominal wall reconstruction after recovery. This chapter presents an overview of the definitions, etiology, consequences, and management of ACS and the current strategies available for management of the OA when a decompressive laparotomy is utilized for the management of ACS.

Abdominal Compartment Syndrome

Definitions

Given that the abdominal cavity is a closed anatomic space, abdominal wall compliance is dictated by the elastic recoil of the abdominal musculature and diaphragm elasticity. The intra-abdominal pressure (IAP) will vary with diaphragmatic excursion: it increases with diaphragmatic contraction during inspiration and decreases with expiration. When there is a decrease in abdominal wall compliance, any increase in intra-abdominal volume will lead to a significant elevation of IAP, the development of intra-abdominal hypertension (IAH), and in certain situations the development of abdominal compartment syndrome (ACS). Normal IAP is actually below 0 mmHg. In the setting of conditions such as morbid obesity, pregnancy, and liver disease with ascites, IAP may be chronically elevated to 10 to 15 mm Hg without evidence of altered physiology.[1]

While recognized for more than a century ACS was again highlighted in the 1980s, when Kron and colleagues described the course of its development following repair of a ruptured abdominal aortic aneurysm.[2] The term was then coined by Fietsam in 1989 in patients undergoing abdominal aortic surgery.[3] Since that time, much progress has been made in its management, including the diagnosis, treatment, and prevention of IAH and subsequent ACS.[4]

The World Society of the Abdominal Compartment Syndrome (WSACS) convened in 2004 to create a consensus statement on the definition, diagnosis, and treatment of IAP, IAH, and ACS. The most recent iteration published in 2013 lists the following definitions: IAP is a steady-state pressure and in critically ill patients is reported to be 5 to 7 mm Hg. IAH is a sustained or repeated physiological increase of IAP to ≥12 mm Hg. IAH follows a graded classification ranging from 12 mm Hg to 15 mm Hg (Grade I) to >25 mm Hg (Grade IV) (**Figure 1**). ACS is defined as sustained IAP>20 mm Hg and an associated new organ dysfunction or organ failure.[5]

Grade	IAP (mm Hg)
I	12-15
II	16-20
III	21-25
IV	>25

Figure 1. Grading of intra-abdominal hypertension (IAH)
IAP**:** Intra-abdominal pressure

IAH and ACS are classified into three categories: primary, secondary, and recurrent. Primary IAH or ACS is attributed to trauma or disease processes within the abdominopelvic region (bleeding, acute accumulation of ascites in cases of pancreatitis and decompensated cirrhosis, rapidly growing tumors, retroperitoneal edema, intra-abdominal infections) that may require intervention (surgical or catheter drainage). Secondary IAH or ACS is caused by conditions that do not originate in the abdominopelvic region (burns, massive fluid resuscitation for hemorrhage or sepsis, ischemia/reperfusion) but lead to the accumulation of ascites and/or bowel and retroperitoneal edema. Increasingly it is recognized that secondary ACS is partly iatrogenic due to excessive fluid resuscitation.[6]

Recurrent IAH or ACS develop after prior medical or surgical management of primary or secondary ACS has taken place.[7] For example, following abdominal packing and temporary abdominal closure in the setting of damage-control laparotomy for trauma or an acute abdomen. While primary IAH/ACS is due to a direct insult that cannot be avoided, secondary and recurrent IAH/ACS may be preventable by early intervention and goal-directed resuscitation.

IAH is reported in 32.1 percent of critically ill patients.[8] IAH is also a predictor for mortality and is seen in 30 to 50 percent of intensive care hospitalized patients.[9] Therefore it is important to have a high index of suspicion for elevated IAP in susceptible patients and minimize the development of IAH/ACS.

Etiology

Risk factors that increase IAP and lead to the development of IAH and ACS include:

- **Diminished abdominal wall compliance**: Body anthropomorphism and habitus (age and obesity)[10-12] , abdominal surgery,[10,11,13] trauma,[13-15] burns with abdominal eschar, prone positioning in acute respiratory distress syndrome patients [ARDS],[16,17] and mechanical ventilation with positive end-expiratory pressure (PEEP)>10.[10,16]
- **Increased intraluminal content**: Gastroparesis and gastric distension,[18] ileus, colonic pseudo-obstruction, Clostridium difficile colitis, and colonic volvulus.
- **Increased intra-abdominal content:** Acute pancreatitis, hemoperitoneum and pneumoperitoneum,[19] intra-abdominal infection/abscesses,[20] retroperitoneal edema or hematomas, intra-abdominal or retroperitoneal tumors, cirrhosis/massive ascites,[10] and peritoneal dialysis.
- **Bowel edema and increased capillary leak in the setting of massive transfusion or large-volume crystalloid resuscitation** and associated acidosis,[18] hypothermia,[20] sepsis, increased Acute Physiologic Assessment and Chronic Health Evaluation (APACHE-II) score or Sequential Organ Failure Assessment (SOFA) score,[19] shock, or hypotension.[10,14,18]

Starkopf et al. found that the risk of IAH in mechanically ventilated patients is very low especially if they have a PEEP <10 cm, H_2O, ratio of arterial oxygen partial pressure to fractional inspired oxygen (PaO2/FiO_2) >300, and body mass index <30 kg/m2 and without pancreatitis, hepatic failure/cirrhosis with ascites, gastrointestinal bleeding or laparotomy, and the use of vasopressor/inotropes at admission.[21]

Physiological Consequences of Increased IAP, IAH, and ACS

a. Cardiovascular system
Decreased cardiac output is a result of the direct effect of IAP on stroke volume through reduction of preload and contractility and an increase in afterload. With increased IAP, the diaphragm is pushed upward. This will lead to a direct cardiac compression and reduction of ventricular compliance and contractility. The increased intrathoracic pressure results in a decrease in venous return and end-diastolic filling and therefore a decrease in preload. Finally, the increased IAP compresses the aorta and pulmonary parenchyma leading to increased systemic and pulmonary vascular resistance and a result an increase in afterload.[22-25]

b. Pulmonary system
Increasing intrathoracic pressure leads to increased peak airway pressures, reduced pulmonary compliance, atelectasis, and decreased functional residual capacity (FRC).[7] Ventilated patients on volume-limited modes will experience an increase in peak inspiratory pressures, and those on pressure-limited modes will have lower tidal volumes and an overall inability to ventilate.[7] In the setting of aggressive resuscitation and capillary leak, pulmonary edema will develop leading to the development of ARDS. ARDS, itself carries a high morbidity and mortality.[26] Overall, lung protective strategies with lower tidal volumes and an increase in PEEP are required to maintain adequate oxygenation and ventilation and as a result will exacerbate the cardiovascular detrimental effects.

c. Gastrointestinal system
IAP reduces celiac and mesenteric artery blood flow, which is augmented in the setting of hypovolemia. Reduction in mesenteric flow can occur at IAP of only 10 mm Hg. IAP of 40 mm Hg can reduce the celiac artery blood flow by 43 percent and superior mesenteric artery flow by 69 percent.[22, 27] The increased pressures will also lead to compression of mesenteric veins and impede the lymphatic flow by direct compression and increased intrathoracic pressure. This results in bowel edema and the development of ascites which in turn worsens the IAP.[22,28] The overall worsening perfusion leads to decreased intraluminal pH, bowel ischemia, bacterial translocation, metabolic acidosis, and overall an increased mortality.

d. Renal system
Oliguria and renal failure were among the earliest effects of ACS described in the surgical literature.[7] Decreased cardiac function and subsequent hypoperfusion lead to reduction of renal blood flow, increased renal vein pressure, increased renal vascular resistance, and impaired glomerular filtration.[29] Additionally, extrinsic compression of the renal veins due to IAP, leading to an outflow obstruction, along with compression of the renal cortex, has also been reported as the cause of renal dysfunction in the setting of IAP and ACS.[7] Studies have shown that oliguria can develop at an IAP of 15 mm Hg and anuria at an IAP of 30 mm Hg.[30]

e. Central nervous system
Decreased lumbar venous flow, decreased cerebral venous outflow, and increased cerebral blood flow due to increased P_aCO_2 all lead to increased intracranial pressure in the setting of IAH and ACS.[31]

f. Hepatic function
Decreased hepatic perfusion leads to impairment of hepatic cell function, decreased lactate clearance, and mitochondrial dysfunction.[22]

The two most common and earliest presenting forms of organ dysfunction in the setting of ACS are the inability to ventilate due to increased intrathoracic pressure and acute kidney injury due to hypoperfusion and rapid progression from oliguria to anuria. Often multiple organ systems fail and lead to the development of multiple organ dysfunction syndrome (MODS). **Figure 2** summarizes all the pathophysiological implications of IAH and the development of ACS.

Measurement of Intra-Abdominal Pressure

IAP is fairly uniform throughout the abdomen and measurement anywhere within the cavity should accurately reflect IAP. Direct measurement of IAP is the gold standard for diagnosing IAH and ACS. Multiple techniques exist but the most used technique per WSACS recommendations, which was first described by Kron et al. in 1984, involves measurement of intravesical pressure, also known as bladder pressure.[2]

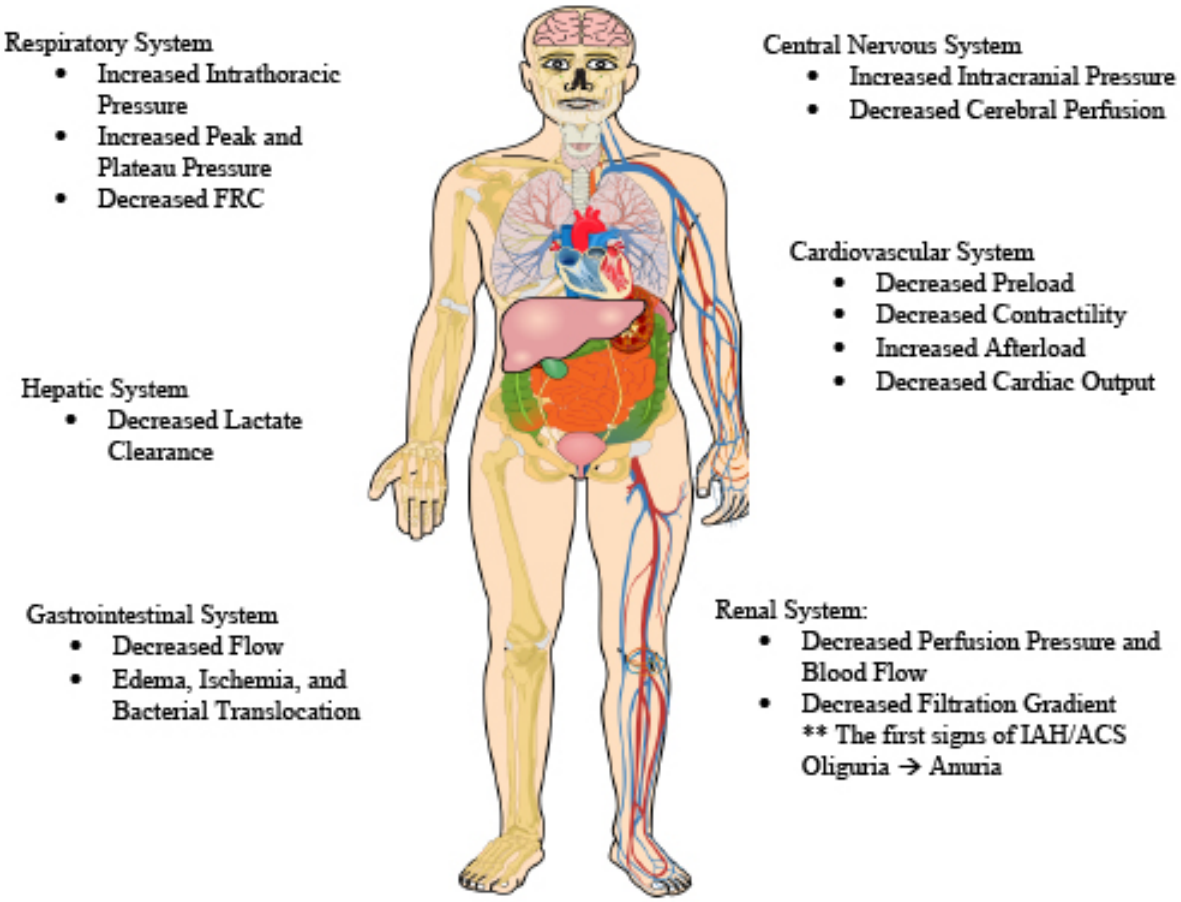

Figure 2. Pathophysiological implications of intra-abdominal hypertension

The bladder is filled with normal saline with the urinary catheter clamped at that time. The volume of saline recommended by the WSACS is not more than 25 mL.[5] The urinary bladder wall acts like a passive diaphragm and transduction of intravascular pressure is performed by attaching a pressure transducer to the catheter. This allows an estimated measurement of IAP. IAP should be measured at the end of expiration and the patient should be in supine position and the transducer zeroed in the midaxillary line at the level of the iliac crest.[5,32] (**Figure 3)**

If the patient is active or the abdomen is tense, the pressure may be interpreted as falsely elevated. In such situations, sedation or chemical paralysis should be considered to obtain an appropriate IAP.[7] Additionally, any pelvic space occupying material, such as packs, masses, or retroperitoneal hematomas will decrease bladder wall compliance and lead to a false increase in IAP.

Other methods to measure IAP include manometry from abdominal drains, intragastric pressure measurement though a nasogastric tube, measuring pressure from the central venous catheter placed via the femoral vein in to the pelvic veins or vena cava, abdominal wall thickness measurement, and measurements using point-of-care ultrasound.[22] Nonetheless, bladder pressure remains the standard of care at this time, given that it is the only method that has been validated by comparing bladder pressures to true intra-abdominal pressure during laparoscopy.[33]

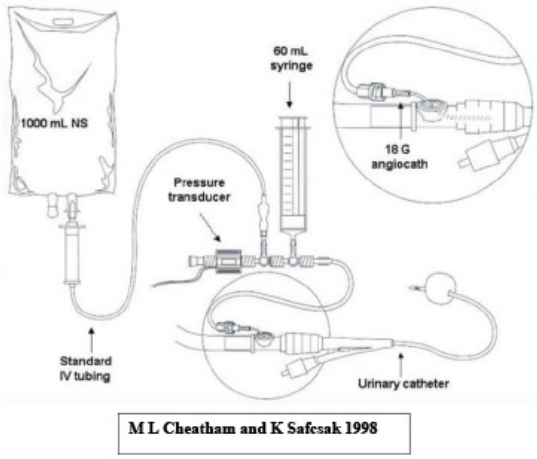

Figure 3. Bedside set-up for the measurement of bladder pressure

Management

It must be emphasized that prevention of the development of IAH and ACS is the best treatment. Nonetheless, if IAH has been suspected or diagnosed, the goal should be the optimization of systemic perfusion and organ function. To accomplish this, the main questions to be addressed are:

- What is the etiology of the elevated IAP?
- What is the best method for intervention to prevent progression to ACS?
- How urgent should the intervention be implemented?

When IAH is recognized with an IAP ≥12 mm Hg, the goal should be to promptly reduce the elevated IAP and prevent progression of ACS. The guidelines for the medical management of IAH have been reported by the WSACS.[5] Medical management should focus on improving abdominal wall compliance, evacuating any intra- or extraluminal content, and correcting fluid balance. IAP pressure should be measured every 4 hours in critically ill patients. A summary of the recommendations and grade of recommendations is listed below.

a. Nonoperative management

1. Reducing intraluminal volume
   Evacuation of intraluminal content can be accomplished through decompression and utilization of prokinetic agents and enemas. Decompression of the gastrointestinal tract can be achieved through the insertion of nasogastric tubes (GRADE 1D), rectal tubes, endoscopic colonic decompression, or utilization of neostigmine in the setting of colonic pseudo-obstruction (GRADE 1D).[5] This may achieve some reduction in the most proximal and distal aspects of the gastrointestinal system only and therefore limits their effectiveness.
2. Reducing extraluminal volume
   Minimally invasive strategies focused on percutaneous drainage (PCD) can be used as a definitive treatment option in some patients with cirrhosis and ascites, burn patients, and the evacuation of residual hemoperitoneum after vascular interventions.[34-36] Reports of PCD allowing for the avoidance of the morbidity associated with a laparotomy and the subsequent OA in the setting of blunt solid organ trauma hemoperitoneum and large-volume resuscitation in the setting of severe necrotizing pancreatitis have been described.[37-39] Cheatham and colleagues demonstrated 81 percent treatment efficacy of this modality. These authors suggested that drainage of less than 1000 mL and a decrease in IAP of less than 9 mm Hg in the first 4 hours are predictive of failure.[40] PCD can also be utilized as a temporizing measure while further investigation of the cause of IAH/ACS is underway but urgent decompression is needed. The current recommendations are for utilization of PCD catheters in an attempt to improve IAH/ACS when technically feasible.[5] (GRADE 2C)
3. Improving abdominal wall compliance
   In some conditions, impaired abdominal wall compliance can be easily corrected and enables a rapid improvement in increased IAP. Burn eschars can be treated with an escharotomy, tight bandages can be released, and body positioning can be adjusted.[34] In other cases, a decreased in IAP can be achieved through adequate sedation and analgesia (GRADE 2D),[5,41] neuromuscular blockade when indicated (GRADE 2D),[1,41] and avoiding elevation of the head of the bed >30 degrees (GRADE 2D).[5,42] Finally, optimizing fluid administration through goal-directed fluid resuscitation, utilization of hypertonic solutions, and aiming for negative fluid balance (diuresis and possible dialysis) may be utilized to prevent and treat elevated IAP and IAH.[5]

b. Surgical decompression

When medical management fails and IAH leads to ACS, the gold standard for treatment is emergent abdominal decompression via laparotomy. This is the most rapid and definitive method to decompress ACS. Decompression results in improved preload, pulmonary function, and visceral perfusion.[43] The treatment phase of ACS not only includes this initial decompression but also includes care of the open abdomen and the subsequent closure and abdominal wall reconstruction. Appropriate management of the open abdomen and the prevention of complications are essential.

Management of the Open Abdomen (OA)

Damage control laparotomy (DCL) and the OA

The earliest description of the management of catastrophic abdominal injuries with the use of the OA technique was by Ogilvie in 1940 during World War II.[44,45] "A dodge that has twice helped me in a difficulty is the use of light canvas or stout cotton cloth sterilized in Vaseline. A double sheet of this is cut rather smaller than the defect in the muscles and sutured into place with interrupted catgut sutures. This device is obviously temporary, but it prevents retraction of the edges of the gap, it keeps the intestinal contents from protruding during the early days when they are so difficult to retain, and it allows the abdominal wall to be used as a whole in respiration."

Since then, the concept of DCL and OA technique has gone through various evolutions, and many surgeons since have refined the technique. Stone and Lamb,[46] Stone,[47] Lucas and Ledgerwood,[48] and Rotondo et al.[49] helped usher in the modern era of DCL in trauma surgery.

In a seminal paper, Stone et al. wrote that abdominal tamponade with laparotomy sponges was a well-known technique at the time to control solid organ injury. They described several patients transferred to Grady Hospital from

referring physicians with "obvious packs protruding from the abdomen". Despite an improvement in survival from 7 to 65 percent in the original case series of Stone et al., historically, leaving the abdomen "open" was considered a surgical failure. Exiting the operative theater before completing all definitive repairs was thought to result in increased intra-abdominal abscess, intestinal fistulas, evisceration, multiorgan dysfunction, and mortality.[47,50]

In 1993, Rotondo et al. hypothesized that with new weaponry the injury patterns of trauma patients had changed and that although definitively addressing all injuries may have been preferable in the past it may no longer be possible in patients with multiorgan and severe vascular injuries.[49,50]

As our understanding of the vicious triad of coagulopathy, acidosis, and hypothermia grew, the need for abbreviated surgery and rapid return to the intensive care unit (ICU) for aggressive resuscitation was emphasized. Nowadays, damage-control laparotomy is defined by three stages: an index operation to control (hemorrhage, intra-abdominal sepsis, intra-abdominal hypertension/ACS) and an open abdomen where fascial edges are left not approximated, aggressive resuscitation to correct physiologic derangements, and finally a 'second-look' -planned relaparotomy and subsequent operations that lead to definitive fascial closure.

ACS has become one of the key life-saving indications for DCL and OA technique. Moreover, the use of the DCL and OA technique has been extended to the management of emergency general surgery (intra-abdominal sepsis/acute pancreatitis) and vascular surgery.[50]

Once the DCL and OA has been employed, the main aim should be to achieve fascial closure in an expedited manner. While DCL and OA are now viewed as a critical technique in the treatment of severely injured patients, a delay in the ability to achieve fascial closure is associated with an increased risk of complications. These include infections, complex abdominal wall hernias, prolonged hospitalization, enterocutaneous fistula formation, and recurrent ACS.[7]

OA in trauma

In areas where trauma and emergency surgery systems are not so advanced, IAH and ACS can occur in up to 40 percent of critically ill patients.[4] On the other hand, with the advancements in medical care, the incidence of ACS in acute care tertiary centers has fallen from 30 to almost 0 percent.[6] The main indications for OA in the trauma patient include (1) the need for a "second-look" operation following a DCL. DCL has been utilized for the packing of bleeding from remote areas not amenable to surgical correction to allow endovascular intervention, resected bowel with subsequent need for anastomosis or stoma, complex liver injury treated with packing, and the need for transfer to a higher-level facility; (2) avoiding the development of IAH/ACS; (3) intra-abdominal sepsis secondary to missed injury or anastomotic leaks and need for subsequent reoperation to control intra-abdominal sepsis; and (4) partial or complete loss of the abdominal wall due to extensive surgical debridement after necrotizing soft tissue infections of the abdominal wall following blast injuries and contamination.

Risk factors for IAH/ACS in trauma patients include an increased extraluminal volume due to increased intraperitoneal and/or retroperitoneal contents in the setting of solid organ hemorrhage or pelvic injury and emergency surgery with intra-abdominal or preperitoneal packing for hemorrhage control, and increased visceral edema following massive transfusion or resuscitation. Increased intraluminal contents secondary to postinjury gastroparesis and small bowel and colonic ileus also cause IAH/ACS. Decreased abdominal wall compliance in patients with high body mass index or in burn patients who experienced a third-degree burn of the abdominal wall and associated eschar can cause IAH/ACS.

Given that untreated postinjury ACS is an independent predictor of organ failure,[51] aggressive postoperative management to prevent the development of increased IAP is essential. This can be achieved with adequate sedation and analgesia, nasogastric tube placement, the use of prokinetic medication, colonic decompression, goal-directed resuscitation, and attempting to achieve negative fluid balance once the patient's hemodynamics allow and as early as postoperative day one.

OA in intra-abdominal sepsis and pancreatitis

The main aims of surgical intervention in the management of intra-abdominal sepsis and severe infected necrotizing pancreatitis is to facilitate the clearance of the infectious material, expediting subsequent surgical interventions and preventing the development of ACS.[6]

To achieve the above, the staged DCL/OA surgical approach can be utilized in situations where source control cannot be achieved at the time of the index operation, due to the patient's labile hemodynamics necessitating the use of inotropes to maintain perfusion, severe physiologic derangements, and poor tissue quality in the setting of severe inflammation. This is followed by planned, post-resuscitation, repeat laparotomy and subsequent operations where definitive bowel anastomosis and abdominal wall closure is achieved.

Similar to trauma patients, risk factors for the development of IAH/ACS in the emergency general surgery patient involve large-volume fluid resuscitation resulting in capillary leak; visceral edema and intra-abdominal free fluid; retroperitoneal, intra-abdominal and abdominal wall

bleeding, and postoperative bowel paresis. IAH/ACS can be avoided via goal-directed resuscitation, nasogastric tube decompression, and attempting to achieve negative fluid balance once the patient's hemodynamics allow.

Management in the intensive care unit (ICU)

The primary goal after DCL and OA is to achieve fascial closure in an expedited fashion to avoid the morbidity and mortality associated with prolonged OA. The management should also focus on reducing the risk of developing secondary and in some cases recurrent ACS and associated multiorgan system failure. In the ICU, a patient with OA requires specific management which includes: adequate sedation and analgesia, proper antibiotic coverage directed toward the underlying cause of intra-abdominal infection, and correction of hypothermia with the goal of achieving a temperature >37°C through passive rewarming, air warmers, and Bair Hugger ™ is essential.[52] Coagulopathy should be corrected via treatment with balanced transfusion in the setting of restrictive fluid management.[53] pH should be maintained >7.2 and checked with a frequent measurement of arterial lactate level.[6] Lung-protective ventilatory strategies, such as low tidal volumes, should be utilized to avoid acute lung injury and ARDS. Strategies to avoid ventilator-associated pneumonia, blood stream infections, and surgical site infections should be implemented, given that extra-abdominal infectious complications are associated with failed abdominal closure.[54]

One fundamental issue in critically ill patients with OA is fluid and electrolyte balance. Patients with OA have an increased insensible fluid loss, as a result volume status should be monitored closely, and goal-directed therapy for resuscitation to achieve adequate perfusion and clearance of lactic acidosis should be undertaken. Volume status can be monitored using parameters such as blood pressure, urine output, central venous pressure, and pulmonary capillary wedge pressure if a pulmonary artery catheter is in place. Devices for minimally or noninvasive cardiac output monitoring using arterial pressure tracings and pulse-contour analysis (such as FloTrac®, Edwards Lifesciences, Irvine, CA) or chest bioreactance (non-invasive cardiac output monitoring [NICOM], Cheetah Medical, Inc, Wilmington, DE) have been developed and used with mixed results.[55] Bedside critical care ultrasound use for diagnosis and management of shock has become commonplace and is emerging as the standard of care in emergency intensive-care settings. One of the most comprehensive and frequently cited protocols is the rapid ultrasound in shock (RUSH) examination. The RUSH protocol evaluates the heart, the lungs, inferior vena cava, the abdominal compartment, and the aorta and femoral veins. The goal of RUSH is to identify a source of shock or hypotension. Sources include cardiac dysfunction, pneumothorax, intra-abdominal hemorrhage, abdominal aortic aneurysm, hypovolemia, and pulmonary embolism. No studies have yet demonstrated that this practice actually changes patient outcomes.[56] Another emerging approach is the transthoracic-focused rapid echocardiographic evaluation known as FREE. This is a comprehensive assessment of stroke volume, stroke-volume variation, and volume status, including velocity time integral (VTI) measurements and an inferior vena cava examination.[57]

Finally, a critically ill patient in a hypercatabolic state is associated with muscle proteolysis, acute protein malnutrition, and impairment in immune function. OA is a source of nitrogen loss in the critically ill patient with an estimated loss of 2 g of nitrogen per liter of abdominal fluid output.[6] A patient with OA represents one of the sickest, most inflamed, and subsequently most hypermetabolic among surgical patients. Particular attention must be given to this critical aspect: once the resuscitation is near complete and the GI tract allows, enteral nutrition should be initiated as soon as possible as it is associated with a lower time to fascia closure and a lower pneumonia and fistula rate.[6]

Temporary abdominal closure

Several different TAC techniques that allow the abdomen to be left open exist. The ideal one should be easy to apply and remove, allow rapid access for a surgical second look, drain any excess intra-abdominal fluid, reduce lateral fascial retraction, facilitate closure, and reduce morbidity and mortality.[6] Throughout the years, the following options have existed (**Figure 4):**

- Simply reapproximating the skin with a simple running suture or towel clips.
- Placing a Bogota bag which consists of a sterile intravenous infusion bag that can be sutured between the fascial edges or to the skin.
- Barker vacuum packing: first described by Brock et al. in 1995, it involves the placement of a perforated plastic sheet or cassette drape, surgical drains to be connected to continuous negative pressure, a moistened towel on top, and a large adhesive sheet to allow for an airtight seal. (58) The dressing should be changed every 48 hours in the operating room or potentially at the bedside in the ICU. It has been reported to be associated with a 68 percent fascial closure rate and a complication rate of 15 percent.[59]
- Wittman patch: first described in 1993, it consists of two opposite Velcro sheets sutured to the fascia and connected in the middle.[60] This allows easy access to the abdominal cavity. Additionally, the patch can be serially tightened to assist with the stepwise reapproximation of the fascia to minimize fascial retraction, prevent loss of domain, and potentially lead to definitive fascial closure.

- ABThera™ device (KCI, San Antonio, TX): this helps reduce fluid losses by reducing evaporation, allows more accurate estimate of fluid losses through drainage into a dedicated canister,[6] actively removes fluids and reduces edema, and provides medial tension which minimizes fascial retraction and loss of abdominal domain. The ABThera provides separation between the abdominal viscera and the abdominal wall, protecting intra-abdominal content.[61,62] and is associated with higher primary fascial closure and lower 30-day all-cause mortality.[61]

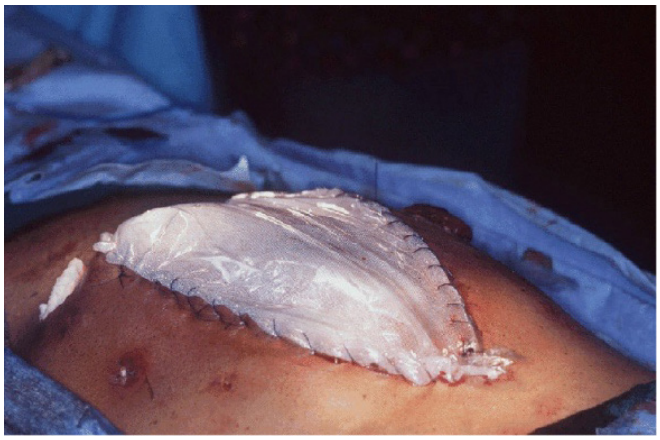

Figure 4a. Bogota bag

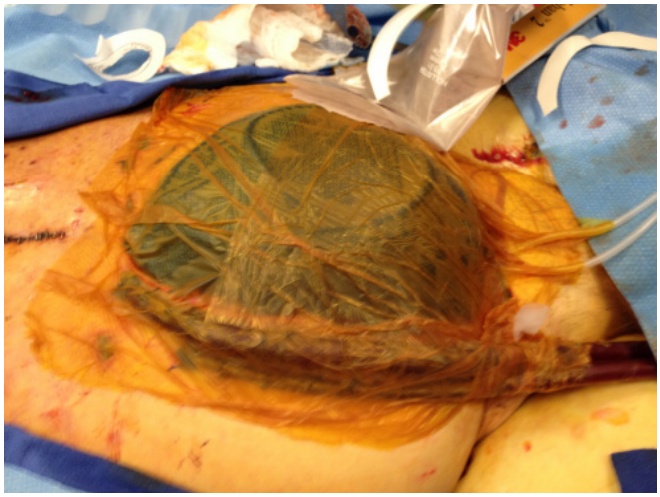

Figure 4b. Barker vacuum dressing

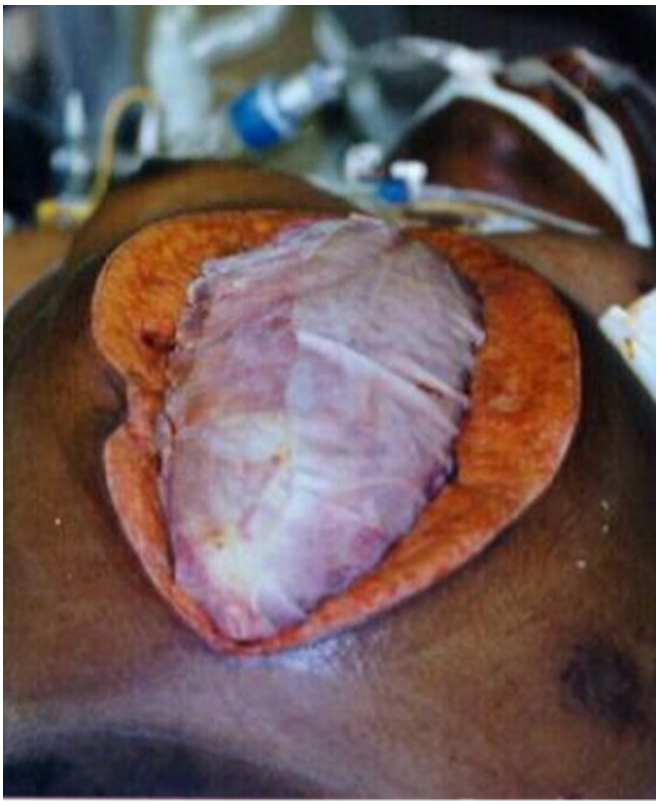

Figure 4c. Wittman Patch

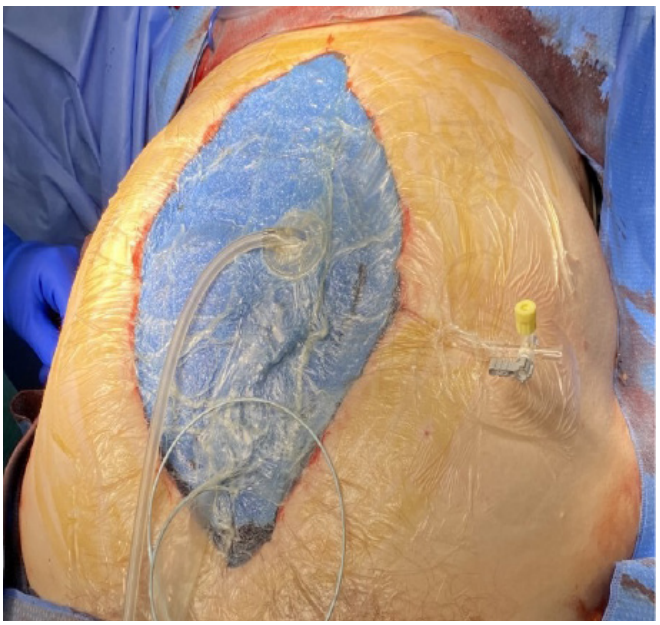

Figure 4d. ABThera device

In addition to the techniques just listed previously, additional combination techniques have been described in the literature. Burlew et al. reported a 100 percent fascial closure rate using a combination of the vacuum-assisted closure (VAC®) system (KCI, San Antonio, TX) which included placement of a white sponge over the bowel, polydioxanone (PDS) sutures placed along the fascial edges to maintain moderate tension, and subsequent sequential closure of the abdomen during the following change of dressing every 48 hours.(63) Pettersson described a combined technique using the VAC system with a polypropylene mesh applied on the fascia edge to keep it in traction and reported a fascia closure rate of 76.6 percent.[64] A small case series from Turkey utilized a technique that consisted of the use of the ABRA® wall closure system (Canica Design Inc, Almonte, Ontario, Canada), which consists of a dynamic fascial tension device with elastomers anchored to the abdominal wall with plastic "button anchors" with the VAC system and reported fascial apposition rate of 83 percent.[65]

The ideal management of the OA is still unclear; the technique is relatively new, and the data reported are variable. The 2018 World Society of Emergency Surgery (WSES)[66] published recommendations regarding techniques for temporary abdominal closure:

- Negative pressure wound therapy (NPWT) with continuous fascial traction should be suggested as the preferred technique for temporary abdominal closure (Grade 2B).
- Temporary abdominal closure without negative pressure (such as the Bogota bag) can be applied in low-resource settings, accepting a lower delayed fascial closure rate and higher intestinal fistula rate (Grade 2A).

Definitive closure during index hospitalization

Definitive fascial closure should be achieved within eight days from the index operation to minimize the mortality and complications associated with the OA.[66] If the abdomen is open for longer periods, the fascia will retract laterally with loss of domain and large abdominal wall defects will develop requiring future complex abdominal wall reconstruction. Miller et al. reported a progressive complication rate, and increased morbidity and mortality in patients with an OA that remains open >8 days.[67]

Primary fascial closure is the ideal option to restore the abdominal wall anatomy but is not always possible in the setting of fascial dehiscence, visceral edema that precludes a tension-free closure, frozen abdomen, loss of abdominal domain, or formation of enterocutaneous fistulas.

In certain situations, when fascial reapproximation cannot be achieved, a planned ventral hernia remains the main option for closure. This can be broadly divided into nonmesh-mediated techniques and mesh-mediated techniques.

Component separation, while an effective technique in restoring abdominal wall anatomy, should be reserved for long-term definitive closure once the patient has recovered from the index hospitalization.[66]

Nonmesh-mediated techniques include skin closure only, or utilization of a NPWT. If a NPWT device is used, coverage of the exposed bowel with omentum when possible is preferred. In addition, a layer of nonadhesive petroleum jelly impregnated sheets or a white sponge is placed over the bowel to prevent direct contact of the NPWT black sponge with the viscera and to minimize formation of enterocutaneous fistulas. The goal of the NPWT is wound-healing promotion, reduction of wound size, and formation of granulation tissue and subsequent possible split-thickness skin graft coverage of the abdominal wall defect **(Figure 5).**

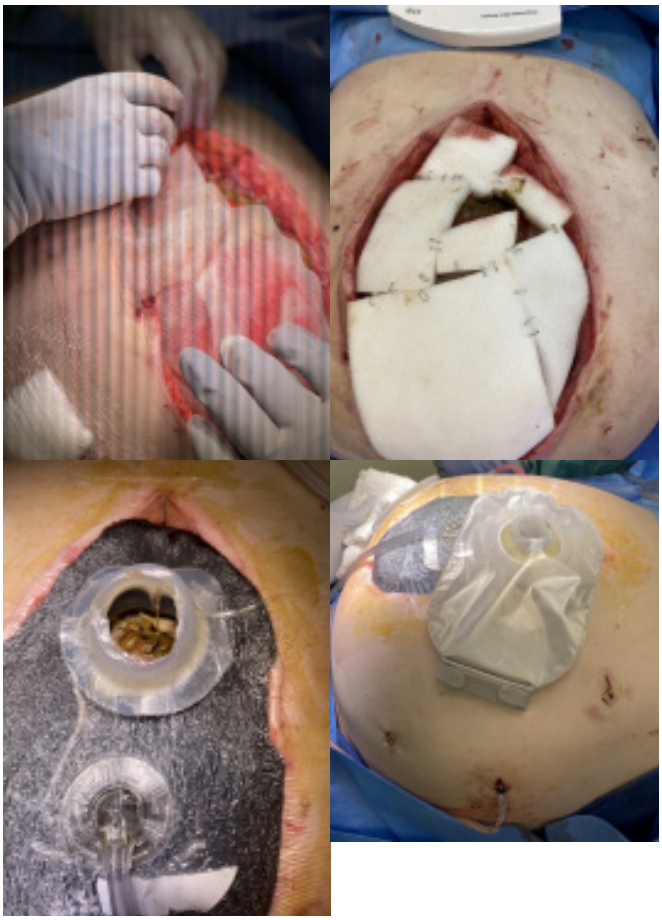

Figure 5. Placement of a negative pressure wound vacuum device

Mesh-mediated closures include the utilization of absorbable and nonabsorbable mesh. The absorbable meshes available include polyglycolic acid (Dexon) and polyglactin 910 (Vicryl) and can be sewn to the fascial edges. This form of mesh is durable and allows for acute coverage and formation of granulation tissue but can also be associated with an increased risk of enterocutaneous fistula formation in the absence of a layer of omentum covering the underlying small bowel **(Figure 6)**.

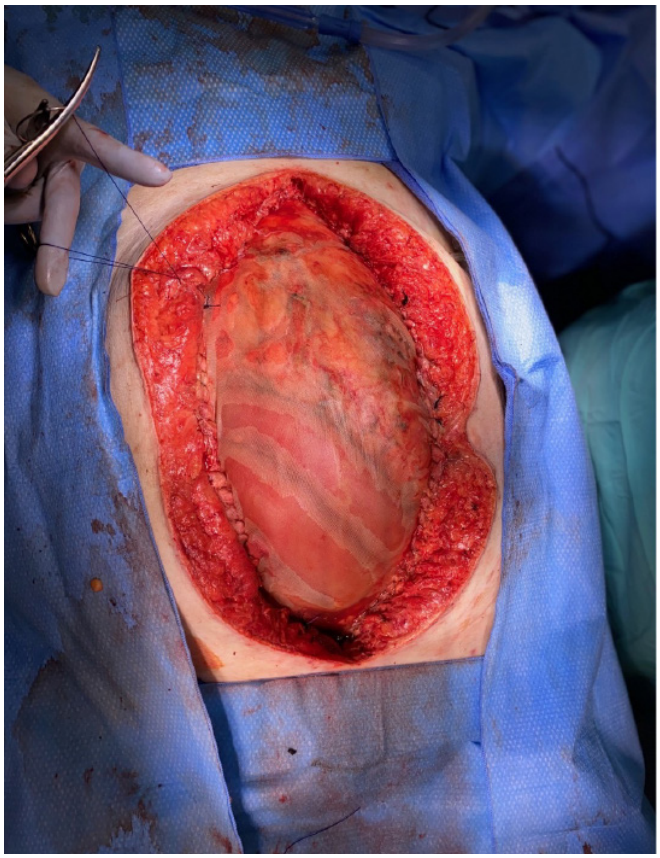

Figure 6. Placement of a Vicryl mesh for temporary closure

An alternative option is the use of biologic mesh which is derived from biologic (human, bovine, or porcine) sources or absorbable synthetic material that incorporate into the native tissue and have the ability to resist infection.[68] While initially designed to perform as a surgical prosthesis in complex abdominal wall hernia repairs, biologic mesh can be used to bridge large abdominal wall defects.[66] Non-cross-linked biologic mesh is easily integrated with reduced fibrotic reactions, infections, and removal rate when compared with the cross-linked biologic that is thought to decrease biocompatibility and the strength of incorporation into the host's tissues.[69] Current WSES guidelines recommend the use of non-cross-linked biologic mesh as an underlay and cross-linked in a fascial-bridge position when large abdominal wall defects necessitate the use of biologic mesh for OA coverage (GRADE 2B).[66]

Finally the use of nonabsorbable synthetic mesh (polypropylene polytetrafluoroethylene (PTFE) and other polyester products) as a bridge for fascial closure, is not recommended due to the risk of adhesion, erosions, and fistula formation.[66] Additionally nonsynthetic mesh placement in contaminated fields is not recommended.[70]

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CHAPTER 26

Vascular Emergencies in Gastrointestinal Surgery

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Acute mesenteric ischemia, endovascular, mortality, aortoenteric fistula, aortoenteric erosion

Abstract

Vascular emergencies cause significant morbidity and mortality in gastrointestinal surgery. In this chapter, two types of vascular emergencies are reviewed: acute mesenteric ischemia and aortoenteric fistulae/erosions. There are several different types of acute mesenteric ischemia based on their causative pathology that include embolic, thrombotic, nonocclusive, and venous acute mesenteric ischemia. The management of embolic and thrombotic acute mesenteric ischemia has traditionally been with open revascularization. However, endovascular therapy has become more prominent and is now commonly used for the treatment of acute mesenteric ischemia. Aortoenteric fistulae and aortoenteric erosions are rare but devastating complications of aneurysmal disease and infections of aortic bypass graft. Both processes derive from a combination of mechanical, infectious, and inflammatory etiologies. Management traditionally involves open surgical reconstruction; however, endovascular therapy has a role in select instances. Left untreated, both acute mesenteric ischemia and aortoenteric fistulae/erosions are likely to progress to life-threatening ischemia or hemorrhage, respectively, and ultimately to death. The cornerstones of management for both of these entities include prompt recognition, resuscitation, and immediate surgical intervention. With the advent of newer reconstruction techniques, patients have experienced improved short- and long-term outcomes compared to historic data.

Acute Mesenteric Ischemia

Introduction

Acute mesenteric ischemia (AMI) is an uncommon but devastating disease attributed to a lack of mesenteric blood flow resulting in bowel ischemia and necrosis. Patients with AMI will present with a variety of symptoms and in varying clinical states. There are two forms of mesenteric ischemia: AMI and chronic mesenteric ischemia (CMI). This chapter will describe the clinical presentation, diagnosis, management, and outcomes of AMI. AMI can be categorized into four subtypes based on the pathophysiology: embolic, thrombotic, nonocclusive mesenteric ischemia (NOMI), and mesenteric venous thrombosis (MVT). Prompt evaluation, diagnosis, and treatment is essential when AMI is suspected. Although AMI is an infrequent cause of abdominal pain, it carries a high mortality rate ranging from 60 to 80 percent.[1]

The incidence of AMI is less than 1 in 1000 hospital admissions.[1] There was a reduction in mortality in 2000-2012 from 12.9 to 5.3 deaths per million, likely due to improved disease recognition, improved imaging abilities, more frequent treatment, risk factor reduction, and the increased use of statins, and antiplatelet and anticoagulant therapy.[2] Acute mesenteric ischemia incidence increases with age and has an exponential increase with patients over the age of 75, as seen in a review performed in Finland (**Figure 1**).[3] Embolic causes of AMI are the most common resulting in 40 to 50 percent of cases.[1] Thrombotic AMI accounts for approximately 35 percent of cases, which can further be subcategorized to dissection, inflammation, or vasculitis. NOMI and MVT account for 5 to 15 percent of cases each. The diagnosis for each of the categories of AMI follows a similar pathway, but they do not always have the same clinical presentations and are managed differently.

Clinical evaluation

Presentation

The mesenteric vasculature is supplied by the celiac artery (CA), superior mesenteric artery (SMA), and the inferior mesenteric artery (IMA). The SMA provides the majority of the blood supply to the small bowel with a collateral network between the SMA and CA. Loss of the blood flow from the SMA can cause ischemia to a large amount of the small bowel and parts of the colon if there is not an adequate collateral circulation.[1] The resulting bowel ischemia can cause profound abdominal pain, electrolyte disorder, acid-base disequilibrium, organ failure, hemodynamic decline, and death if not recognized and treated promptly.

Embolism of the SMA causes acute onset of severe abdominal pain, with 50 percent of cases of embolic AMI presenting with atrial fibrillation.[4] Patients with an embolism of the SMA will often present with pain out of proportion to exam. A study examining the presenting symptoms of AMI found

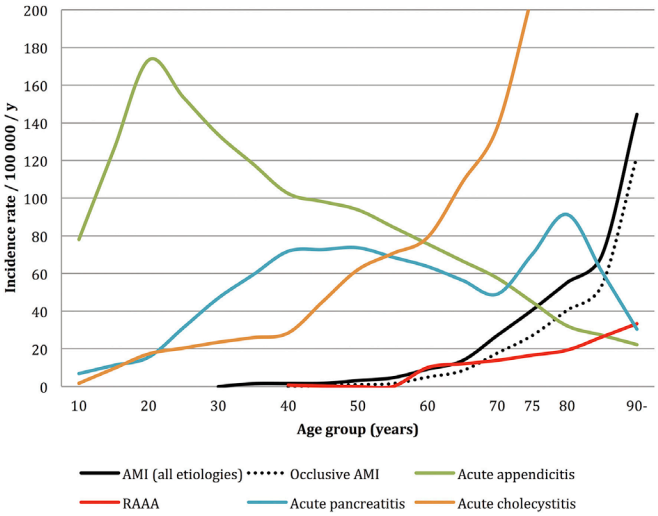

Figure 1. The age-related incidence rates of acute mesenteric ischemia (AMI), ruptured abdominal aortic aneurysm (RAAA), acute pancreatitis, acute appendicitis, and acute cholecystitis in Kupio/Finland between the years 2009 and 2013. Reproduced with permission from Best Practice & Research: Clinical Gastroenterology. Kärkkäinen JM, Acosta S. Acute mesenteric ischemia (part I): Incidence, etiologies, and how to improve early diagnosis. *Best Pract Res Clin Gastroenterol.* 2017;31(1):15-25. doi:10.1016/j.bpg.2016.10.018

that 95 percent of patients present with abdominal pain, 44 percent with nausea, 35 percent with vomiting, 35 percent with diarrhea, and 16 percent with blood per rectum.[4] Patients with thrombotic occlusions typically present after an acute thrombosis of a chronic narrowing of the SMA. These patients often have abdominal pain that is chronic and becomes worse after the acute thrombosis. The chronic narrowing of the SMA will result in a more robust collateral network between the SMA and CA. A thorough history taking will reveal that these patients likely have a history of chronic postprandial abdominal pain, weight loss, and food fear, and are likely to have had prior vascular procedures.[4]

Unlike embolic and thrombotic occlusions where patients present with abdominal pain, the clinical presentation of NOMI is quite different. NOMI occurs when there is hypoperfusion of the splanchnic circulation. This is most often seen in critically ill patients with systemic illnesses and diseases. Many of these patients are in the intensive care unit, intubated, and cannot report abdominal pain. New-onset abdominal distention, diarrhea, hemodynamic instability, bacteremia, acidosis, and electrolyte abnormality should raise the clinician's concern of ongoing bowel ischemia. In patients that are not intubated, abdominal pain is reported to be diffuse and episodic and can wax and wane with cardiac performance.[4]

MVT results from occlusion of the venous mesenteric vasculature. MVT can be seen in patients with a hypercoagulable disorder, cancer, cirrhosis, or an intra-abdominal inflammatory process.[1,3] Patients can present acutely and within 24 to 72 hours of clot formation with abdominal cramping, nausea, and vomiting. However, these symptoms may not present for several days to weeks for a subacute clot.[5]

Laboratory testing

Patients with bowel ischemia will often have abnormalities in laboratory testing, such as the development of leukocytosis, metabolic acidosis, and an elevated lactate. However, early in the disease process, some or all of these abnormalities may not be present.[3] There currently is no available biomarker test available to diagnose AMI. D-dimer can be used to assist in the diagnosis of AMI, but has not been shown to be an adequate biomarker of diagnosis. D-dimer was reported to be an independent risk factor of intestinal ischemia thought to be from the ongoing process of clot degradation in the mesenteric vasculature.[4] One study reported that patients without bowel ischemia had a normal D-dimer and those with ischemia had a D-dimer >0.9 mg/L with a sensitivity, specificity, and accuracy of 82 percent, 60 percent, and 79 percent, respectively.[4]

Imaging

Prompt imaging is critical for the diagnosis of AMI. There are various modalities used to diagnose AMI, such as abdominal X ray, duplex ultrasound, magnetic resonance imaging, multi-detector computed tomography angiography (CTA), and angiography.

Abdominal X ray has minimal use in the diagnosis of AMI and is generally ordered as an initial imaging screening modality, as it can be easily and quickly performed to evaluate for bowel obstruction, perforation, or pneumatosis intestinalis.[4]

Duplex ultrasound has a sensitivity and specificity of 85 and 90 percent, respectively, for the diagnosis of AMI; however, it is highly dependent on the skill of the technologist performing the exam.[1] Its use in the diagnosis of AMI can be difficult due to the length of the study and the amount of abdominal pressure that is applied to visualize the vasculature, which is not tolerated in patients with severe abdominal pain. Bowel gas can also severely limit the imaging of the aortic and mesenteric vessels. For these reasons, it is generally not used in cases of AMI and reserved for screening of CMI.[1,3]

Magnetic resonance imaging with gadolinium contrast allows visualization of mesenteric blood flow and avoids radiation and contrast exposure; however, it can overestimate the degree of stenosis and takes longer to perform compared to CTA. Due to the length of the exam it is not ideal to perform with an acute ischemic process and thus has a smaller role.[1]

CTA has replaced angiography as the gold standard for imaging acute mesenteric ischemia.[3] A CTA must be a biphasic scan with the following three requirements: 1) pre-contrast scans to detect vascular calcification, intravascular thrombus, and intramural hemorrhage; 2) an arterial and venous phase to demonstrate thrombus of the mesenteric arteries and veins, abnormal enhancement of the bowel wall, and infarction of other organs; and 3) multi-planar reconstruction to assess the origin of the mesenteric arteries.[4] CTA provides the benefit of being fast, widely available, and noninvasive.[6] A study of 79 patients presenting with concern for AMI underwent a CTA with 28 confirmed cases of AMI. CTA diagnosed 27 of these cases, resulting in a specificity of 98 percent and a sensitivity and specificity for visceral artery occlusion of 93 and 100 percent, respectively.[7] One concern regarding the use of CTA is the potential for contrast-induced nephropathy in patients with preexisting acute kidney injury or chronic kidney disease. However, when considering the greater risk of mortality resulting from delay in diagnosis, providers who suspect AMI should not hesitate to utilize CTA for further evaluation.[4]

Angiography was once the gold standard of diagnosis for AMI, but has been supplanted by CTA. Although angiography is no longer the modality of choice for diagnosis of AMI, it is used for therapeutic purposes.[1]

Pathogenesis

Anatomy and physiology

As described earlier, the mesenteric vasculature arises from three vessels: the CA, SMA, and IMA, with the majority of blood flow originating from the SMA with a small collateral network between the SMA and CA. If there is chronic stenosis of the CA or SMA, this collateral network can become more robust and clinical ischemia may not develop until both the CA and SMA become occluded.[1] The splanchnic circulation receives about 15 to 35 percent of the cardiac output, but oxygen extraction is relatively low and the small bowel is capable of compensating for a 75 percent reduction of splanchnic blood flow for up to 12 hours.[4] An occlusion and ischemia of the bowel will initially cause a vasodilatory response; however, after prolonged ischemia this will transition to vasoconstriction.[1]

Embolus

Embolism of the SMA is the most common cause of AMI. The majority of embolisms lodge 3 to 10 cm distal to the ostium of the SMA (**Figure 2**), creating a classic distribution of ischemia when compared to thrombosis.[4] Because the embolus typically lodges just past the jejunal arteries and middle colic artery, the ischemia of an embolus results in the sparing of the proximal jejunum and transverse colon with ischemia of the remaining small bowel and ascending colon (**Figure 3**). There are several risk factors for developing an embolus of the SMA including, but not limited to, atrial fibrillation, recent myocardial infarction, prior embolic events, and an atherosclerotic aorta.[3,4] With the increased use of endovascular surgery, there have been reports of the development of embolisms of the SMA after these procedures. A case series out of England reviewed 99 patients undergoing an endovascular aortic aneurysm repair and found a 5 percent incidence of embolism of the SMA.[3]

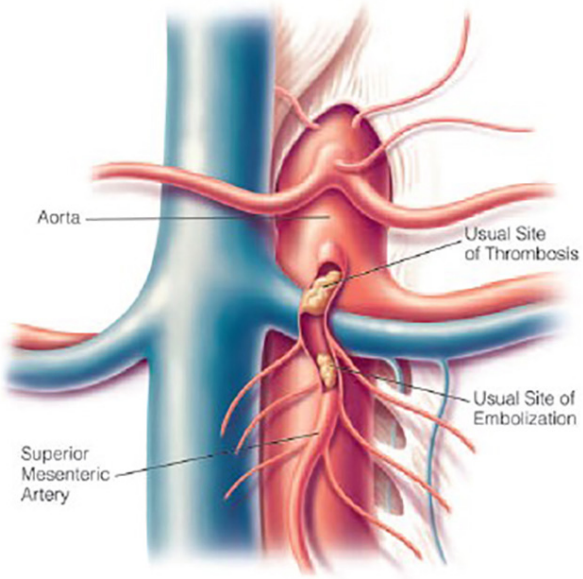

Figure 2. Schematic drawing demonstrates usual site for superior mesenteric artery thrombus versus embolus. Reproduced with permission from ACS Surgery: Principles and practice. Mohammad H. Eslami, MD, MPH; Acute Mesenteric Ischemia. In: *Surgery* [online]. Toronto ON: Decker Medicine; March 2016. Available at https://www.deckerip.com/products/surgery/

Thrombosis

Thrombosis of the SMA can be due to an acute thrombosis on chronic narrowing, chronic narrowing leading to critical stenosis, dissection, inflammation, or mycotic aneurysm.[3,4] Due to the chronic nature of this disease, a collateral network typically develops between the CA and SMA. Due to the increased collateral network, ischemia may not develop until there is an occlusion or narrowing of both the CA and SMA (**Figure 4**).[4] Unlike an embolism, thrombosis of the SMA occurs at the ostium, resulting in ischemia of the entire small bowel and can involve the colon up to the transverse colon, as the middle colic artery is usually involved (**Figure 3**).

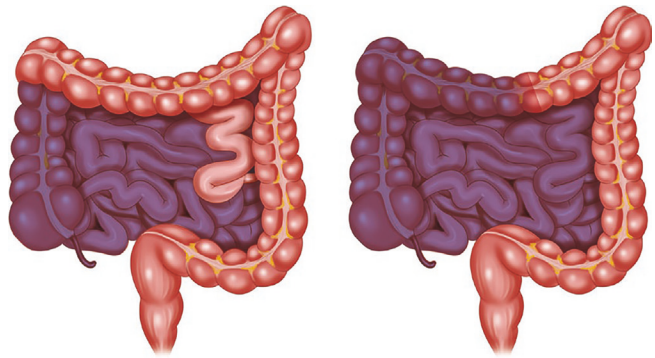

Figure 3. Pattern of bowel ischemia seen in embolic (left) versus thrombotic (right) acute mesenteric ischemia etiology. The left image shows sparing of the proximal jejunum and transverse colon. Reproduced with permission from Emergency General Surgery: A practical approach. Carlos V. R. Brown, Kenji Inaba, Matthew J. Martin, Ali Salim. Emergency General Surgery : A Practical Approach [Internet]. Cham, Switzerland: Springer; 2019 [cited 2020 Aug 16]. Available at: http://search.ebscohost.com.libproxy.lib.unc.edu/login.aspx?direct=true&db=nlebk&AN=1934440&site=ehost-live

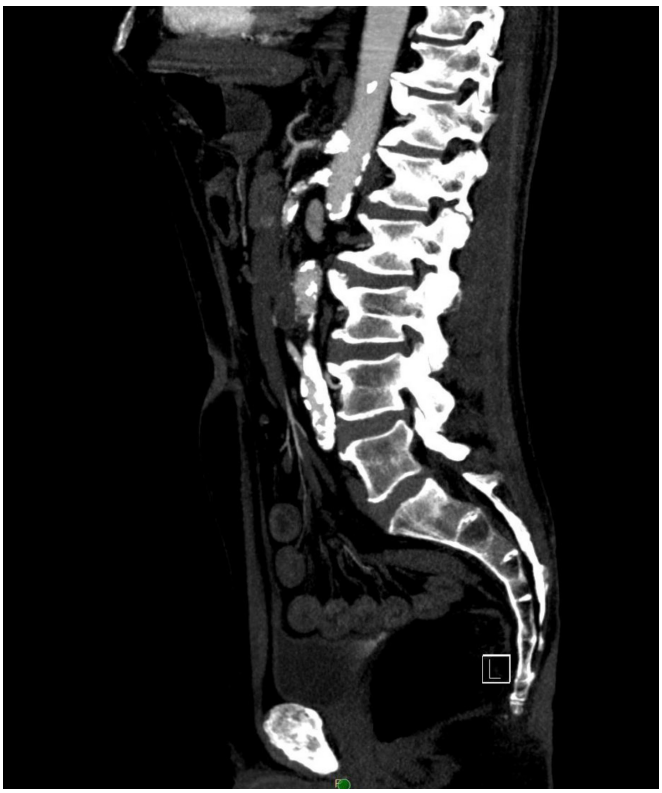

Figure 4. Computed tomography angiography demonstrating occlusion of the celiac artery with a high-grade severe stenosis of the calcified superior mesenteric artery

Nonocclusive mesenteric ischemia

Nonocclusive mesenteric ischemia occurs secondary to severe vasospasm of the splanchnic circulation resulting in profound hypoperfusion. It is often found in critically ill patients with conditions such as hypovolemia, sepsis, heart failure, vasopressor use, drug intoxication (such as cocaine and ergot derivatives) and intra-abdominal hypertension.[3,4] As blood flow is redirected from the splanchnic circulation to other vital organs, severe intestinal ischemia occurs.[3]

Mesenteric venous thrombosis

MVT results from a primary thrombus of the superior mesenteric vein (SMV) with or without extension to the portal vein in 95 percent of cases.[3,5] The inferior mesenteric vein (IMV) is primarily involved in 5 percent of cases. MVT is found in patients with a hypercoagulable disorder, cancer, cirrhosis, trauma, or it can be due to an inflammatory process such as pancreatitis, diverticulitis, cholecystitis, or cholangitis.[1,8] Ischemia from MVT is less common, but if there is a significant outflow obstruction, bowel edema can develop, resulting in arterial capillary spasm leading to infarction of the bowel.[3] Chronic MVT can lead to portal hypertension and splenomegaly.[5]

Management

Hemodynamics and electrolytes

AMI creates an intense inflammatory response and it is not uncommon to find these patients in septic shock. The inflammatory response creates extensive capillary leakage and results in a significant volume deficit requiring aggressive fluid resuscitation.[1] Due to the ongoing ischemia and cell death, many of these patients can develop electrolyte disturbances including hyperkalemia and acidosis requiring close monitoring and correction.[1] Hypotension creates a unique dilemma in these patients, as using vasopressors can worsen the ischemia. When patients present with hemodynamic instability, it is best to start with fluid resuscitation and reserve vasopressor use to avoid volume overload and abdominal compartment syndrome.[4]

Anticoagulation and antibiotics

AMI requires prompt anticoagulation, which is often administered as an unfractionated heparin drip, thus allowing the medication to be stopped relatively quickly if there is ongoing bleeding or the need for repeat operations.[4] Intestinal ischemia results in loss of the intestinal mucosal barrier leading to bacterial translocation.[4] It is recommended that patients be placed on broad-spectrum antibiotics as the benefits outweigh the risks of bacterial resistance.[4]

Embolus

The traditional technique for a SMA embolus is an open embolectomy. This is performed by exposing the SMA below the transverse mesocolon, making a transverse arteriotomy and performing an embolectomy with a size 2 or 3 French Fogarty balloon.[8] The SMA embolus may also be treated using endovascular techniques such as mechanical aspiration and catheter-directed thrombolysis. Mechanical aspiration for AMI was developed from its use in intracranial occlusions.[8] Mechanical aspiration can achieve reperfusion more quickly than thrombolysis, making it a better alternative than thrombolysis alone.[8] Catheter-directed thrombolysis is generally used as an adjunct to a primary treatment and has been used in cases of incomplete mechanical aspiration.[8,9] Small case series have evaluated mechanical aspiration and thrombolysis. Jia et al. looked at 21 patients presenting with AMI to a hospital in China from 2005 to 2012.[9] Fourteen patients had partial occlusion on CTA and 7 patients had complete occlusion on CTA, yet none had evidence of bowel ischemia. Using a combination of mechanical aspiration and/or thrombolysis, 6 patients had complete success with revascularization (28.6 percent) with 3 receiving only mechanical aspiration and 3 with a combination of mechanical aspiration and thrombolysis. Fifteen patients (71 percent) had partial success with revascularization with 4 receiving mechanical aspiration, 10 receiving a combination of mechanical aspiration and thrombolysis, and 1 receiving mechanical aspiration, thrombolysis, and stent placement. The 30-day mortality rate of 9.5 percent demonstrates that percutaneous revascularization for AMI can be a promising alternative to open revascularization.

Thrombosis

The open technique for SMA thrombosis is an open surgical bypass or thromboendarterectomy.[10] There are several inflow options for the bypass including supraceliac aorta, infrarenal aorta, and the iliac arteries. In the case of AMI, supraceliac access could prove problematic, as this can further worsen the ongoing mesenteric ischemia and cause renal ischemia due to the proximal inflow control. The ideal graft is a reversed autologous saphenous vein; in cases where there is no suitable vein graft a polytetrafluoroethylene graft can be used providing the benefit of withstanding kinking.[10] Endovascular options for thrombosis of the SMA include angioplasty and stenting and a hybrid approach called retrograde open mesenteric stenting (ROMS). Arterial access for stenting and angioplasty can be obtained via the brachial or femoral artery; however, brachial access provides a better angulation at accessing the SMA.[8] Benefits of angioplasty and stenting allow for quick revascularization, but this technique can prove troublesome with access of the SMA and complications including dissection, puncturing of a jejunal branch, and stent thrombosis.[3,11] ROMS provides the advantage of visualizing the bowel. This approach is

performed by exposing the SMA similar to performing an open embolectomy and the SMA is then accessed in a retrograde fashion allowing for angioplasty and stenting (**Figure 5**). If access to the aorta from the SMA proves difficult, an antegrade wire can be used in combination with access from the SMA. Oderich et al. examined 54 patients who underwent ROMS between 2001 and 2013 from 7 different institutions and found a 30-day mortality rate of 39 percent and a survival rate of 55 percent at 1 year and 43 percent at 2 years.[11]

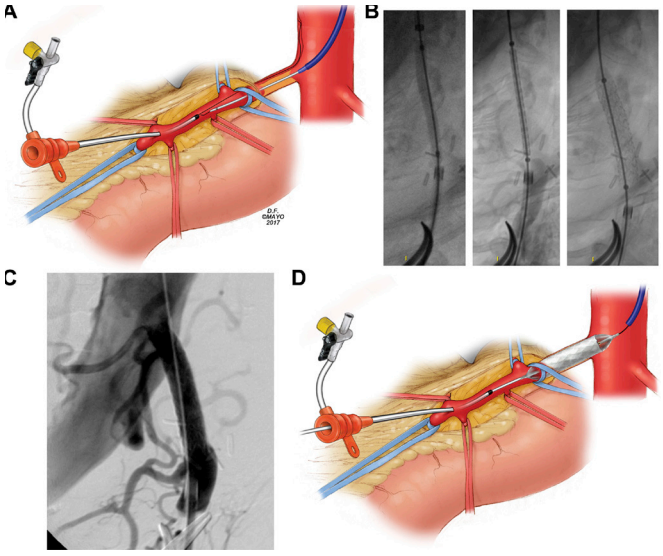

Figure 5. The modified retrograde open mesenteric stenting (ROMS) technique. (**A)** A guidewire from the ante-grade approach is exteriorized through the retrograde sheath, establishing through-and-through access between the brachial artery and superior mesenteric artery (SMA). (**B)** Predilation of the lesion, following deployment of the balloon-expandable covered stent. (**C)** Control angiography without residual stenosis or dissection. (**D)** During catheter manipulations, angioplasty, and stent placement, the distal SMA and its branches were controlled with Silastic vessel loops to avoid distal embolization. Reproduced with permission from Journal of Vascular Surgery. Oderich GS, Macedo R, Stone DH, et al. Multicenter study of retrograde open mesenteric artery stenting through laparotomy for treatment of acute and chronic mesenteric ischemia. *J Vasc Surg*. 2018;68(2):470-480.e1. doi:10.1016/j.jvs.2017.11.086

Nonocclusive mesenteric ischemia

NOMI is unique in that there is no clot present in the vasculature and therefore does not require a revascularization procedure. Cases of NOMI are secondary to an ongoing systemic illness causing hypoperfusion of the bowel. The management involves correcting the underlying cause with volume resuscitation, resolution of any ongoing anemia, correcting electrolytes, and initiation of antibiotics.[8] Selective catheterization of the SMA can be performed with infusion of a vasodilator such as papaverine, prostaglandin, or iloprost.[8]

Mesenteric venous thrombosis

Treatment for MVT is based on the clinical status and symptoms of the patient with the mainstay of treatment being anticoagulation.[8] Patients presenting with mild symptoms and no evidence of bowel thickening can be managed with low-molecular-weight heparin and transitioned to warfarin. However, if there is evidence of bowel wall edema, patients should be placed on a heparin drip so that it may be discontinued if surgery is necessary.[8] Approximately 5 percent of patients will deteriorate with bowel ischemia and require an operation.[1]

Endovascular management includes thrombolysis and mechanical aspiration with access options including transhepatic portovenous, transarterial through the SMA, and combined transarterial through the SMA and transvenous through the SMV.[5] Di Minno et al. examined 32 patients presenting with acute MVT. Fourteen patients received systemic anticoagulation and 18 patients underwent percutaneous transhepatic thrombolysis and thrombectomy.[12] The mortality was similar between the two groups. One patient required bowel resection in the endovascular treatment (6 percent) versus 5 with only anticoagulation (36 percent). A difference was also found in the long-term complication rate with two patients developing portal hypertension with endovascular treatment (11 percent) versus 7 with only anticoagulation (50 percent).

Bowel viability

The goal of AMI is to reestablish blood flow, resect necrotic bowl, and preserve viable bowel. All necrotic bowel should be resected in the initial operation, but bowel that appears borderline should not be resected, as this portion of bowel may improve after reestablishing blood flow. Unfortunately, many cases of AMI result in the resection of a large amount of small bowel leading to short bowel syndrome. Short bowel syndrome stems from a loss of enterocyte mass resulting in dehydration, diarrhea, and malabsorption that may require enteral supplementation and in severe cases, parenteral nutrition that may need to be lifelong.[13] There are multiple studies looking at the length of remaining bowel that will result in short bowel syndrome; however, multiple factors go into developing short bowel syndrome other than the length of remaining bowel, such as the preservation of the colon, preservation of the ileum, and if the remaining bowel is healthy or diseased.[14]

Operations for AMI and significant bowel ischemia and/or necrosis are usually managed as damage-control with resection of necrotic bowel, no bowel anastomosis, and the abdomen left open for a second operation to evaluate the viability of the remaining bowel. The second-look laparotomy should be performed within 48 hours as patients often need further resection of bowel.[4] When the patient has stabilized and no further bowel resection is needed, consideration

must go into performing an anastomosis or an ostomy, as the bowel is often edematous creating a higher risk of an anastomotic leak.

Outcomes

AMI has a historically high mortality rate with open revascularization procedures. However, with the increased use of endovascular techniques to treat AMI, increasing from 12 percent in 2005 to 30 percent in 2009, some argue that outcomes have improved.[1] As there are no prospective randomized controlled studies examining open versus endovascular revascularization for treating AMI, several retrospective case series have looked at the morbidity and mortality of endovascular compared to open revascularization.[5,15] A retrospective review of the Nationwide Inpatient Sample Database was performed on 679 patients presenting with AMI and undergoing vascular interventions.[16] One hundred and sixty-five patients (24 percent) received endovascular revascularization and 514 patients (76 percent) underwent open revascularization. Endovascular therapy was found to have an 87 percent success rate. A comparison of incidence of death showed a rate of 25 percent versus 49 percent in endovascular and open revascularization groups, respectively. Length of stay was 13 days versus 17 days in endovascular and open revascularization groups, respectively. A criticism of studies comparing endovascular versus open revascularization is their inherent section bias.[17] Critically ill AMI patients are more likely to undergo open revascularization and less critically ill patients are more likely to undergo endovascular revascularization, thus making endovascular therapy appear to be a better option.[17]

Long-term management

Patients with AMI resulting from an arterial embolus, MVT, or an inherited thrombophilia should be placed on anticoagulation indefinitely or until the cause of the embolism or thrombus has been resolved.[1] In cases of thrombosis, patients should be on lifelong aspirin and clopidogrel should be continued for a minimum of 1 to 3 weeks after an endovascular procedure, longer if tolerated.[1, 8] In addition to anticoagulant and antiplatelet therapy, patients should also undergo lifestyle modification, such as blood pressure control, smoking cessation, and the initiation of statin therapy.[1] Endovascular stents that are placed will need to be monitored for restenosis. Reports of restenosis range from 20 to 66 percent, with restenosis being more common in occlusions >30 mm and severely small, calcified vessels <6 mm.[18] Nutrition will need to be monitored in patients that required a significant bowel resection, as these patients are at high risk for acquiring short bowel syndrome.

Conclusion

Acute mesenteric ischemia is associated with significant morbidity and mortality. Endovascular therapy is being used with increased frequency; however, the mortality rate for AMI still remains high. It is imperative that if a clinician is concerned for AMI the patient must undergo prompt diagnosis for earlier revascularization and improved outcomes.

Aortoenteric Fistula and Aortoenteric Erosion

Introduction

First described in 1839, aortoenteric fistulae (AEF) represent catastrophic manifestations of mechanical, inflammatory, and infectious trauma either between native aorta and the gastrointestinal (GI) tract or between graft and the GI tract, which if left untreated can progress to sepsis, hemorrhage, and death.[19]

Primary AEF (PAEF) occur in the absence of prior vascular surgery, such as in the case of an atherosclerotic aortic aneurysm, mycotic aneurysm, or penetrating atherosclerotic ulcer.[20-22] PAEF are exceedingly rare, with about 250 cases reported to date. From studies of patients with PAEF, it has been noted that the mean age of presentation is 64 years; there is a male-to-female ratio of 3:1; and the mean aortic diameter is 6.2 cm.[23]

Secondary AEF (SAEF) occur when the proximal suture line between the aortic graft and native aorta erodes into the adjacent GI tract, with or without the presence of a pseudoaneurysm. Additionally, aortic grafts may erode but not fistulize into the nearby GI tract, with bleeding arising from the cut edges of mucosal surfaces and not from the aorta itself. This is referred to as an aortoenteric erosion (AEE) and is a subcategory of SAEF. SAEF are more common than PAEF, with an estimated incidence of 0.36 to 1.6 percent after open vascular repair and may occur anywhere from weeks to years following an operation.[24,25] With the increase in endovascular surgery for abdominal aortic aneurysm repair, the incidence of associated SAEF has remained within this range at 0.56 percent, although when utilized for aortic pseudoaneurysm, the incidence of SAEF has been reported as high as 3.9 percent.[26] The most common surgical procedures implicated in the development of SAEF are open aneurysm repair (36.5 percent) and bypass grafting for aortoiliac occlusive disease (30.6 percent) (**Figure 6**).[27]

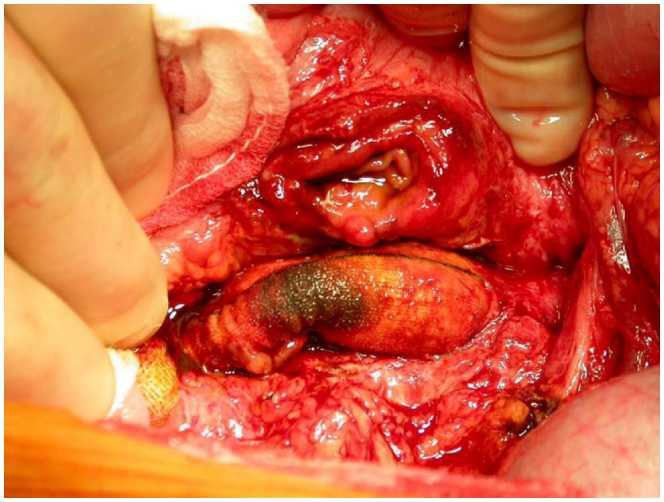

Figure 6. Intraoperative photograph of an aortoenteric fistula. Note the bile-stained aortic graft where it had been dissected free of the duodenum. Reproduced with permission from Seminars in Vascular Surgery. Chung J, Clagett GP. Neoaortoiliac System (NAIS) procedure for the treatment of the infected aortic graft. *Semin Vasc Surg*. 2011;24(4):220-226.

Clinical evaluation

Presentation

In general, if a patient presents with new-onset gastrointestinal bleeding and the history reveals prior aortic surgery or the presence of an aortic aneurysm, AEF/AEE must be included in the differential diagnosis. The classic triad for an AEF is described as abdominal pain, new-onset gastrointestinal bleeding, and a pulsatile abdominal mass. This complete triad has only been identified in 11 percent of cases, whereas the most common initial presentation involves new-onset melena, hematochezia, or hematemesis, otherwise referred to as a "herald bleed."[23] Herald bleeds are usually self-limited because of vasospasm and thrombus formation, and though they may lead to a hospital admission immediately, some patients experience multiple episodes before initial presentation. Regardless of the initial presentation, an untreated herald bleed commonly develops into a life-threatening hemorrhage within hours to months.[28] The work-up of any patient with new-onset gastrointestinal bleeding is first determined by hemodynamic stability. If the patient is unstable, most often resuscitation and source control will be best performed concurrently in the operating room either by diagnostic laparoscopy or exploratory laparotomy. If the patient is hemodynamically stable, however, the provider has more time to elucidate the cause of bleeding.

Laboratory testing

A complete blood count may reveal leukocytosis or decreased hematocrit. Gram stain and culture of the blood may reveal the presence of bacteremia. *Salmonella* species is frequently cultured from surgical specimens, but results are frequently polymicrobial and may also include *Staphylococcus aureus*, Group B *streptococcus*, Group D *streptococcus*, *Escherichia coli*, *Klebsiella* species, *Pseudomonas* species, *Citrobacter* species, and *Serratia* species.[29-31]

Imaging

Imaging is divided into noninvasive and invasive modalities including plain abdominal radiography, computed tomographic angiography (CTA), esophagogastroduodenoscopy (EGD), digital subtraction angiography (DSA), and tagged white blood cell scanning.

In the work-up of new-onset gastrointestinal bleeding, plain radiography is a simple noninvasive test that may reveal pneumoperitoneum. Almost always, this finding alone warrants further evaluation in the operating room with laparoscopy or laparotomy. If this is not the case, CTA is currently the diagnostic test of choice because it is also noninvasive, widely available, and rapid in data acquisition.[30]

Common CTA findings may include effacement of periaortic fat planes, soft tissue thickening, perigraft fluid, and ectopic gas (**Figure 7**). Rarely detected, a pathognomonic finding for AEF would be the visualized passage of contrast from aorta into bowel. CTA carries a widely variable sensitivity and specificity, ranging from 40 to 90 percent and 33 to 100 percent, respectively.[32] An advantage of CTA over endoscopic diagnostic approaches is that should the patient have an abatement of symptoms due to thrombus formation, this modality does not risk potential thrombus dislodgement and uncontrolled hemorrhage.[32]

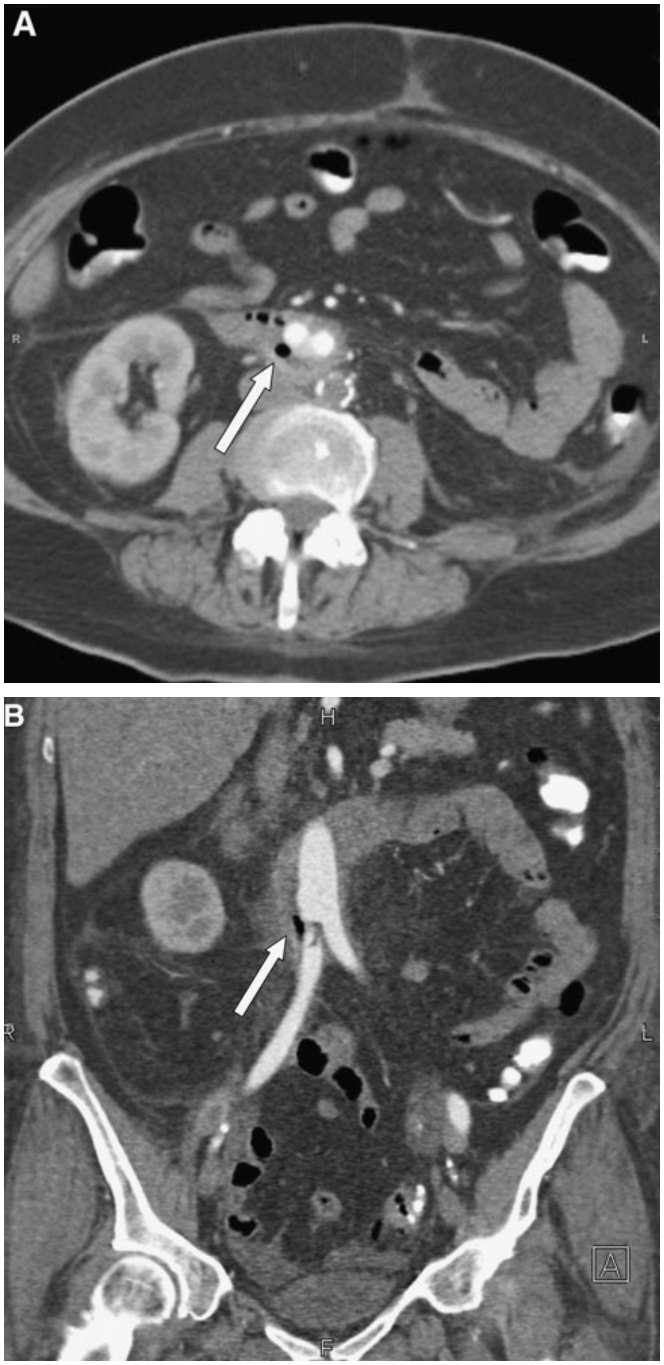

Figure 7. A patient presenting with an aortoenteric fistula with a history of multiple open abdominal aortic aneurysm repairs and revisions. (**A)** Axial CT imaging showing ectopic gas (*arrows*) in the periaortic space. (**B)** Coronal CT images demonstrate soft-tissue thickening and fluid surrounding the aorta, a tethered adjacent duodenum, and ectopic gas (*arrows*) in the periaortic space. Reproduced with permission from Abdominal Imaging. Raman, S.P., Kamaya, A., Federle, M. et al. Aortoenteric fistulas: spectrum of CT findings. *Abdom Imaging.* 2013; 38**,** 367–375. https://doi.org/10.1007/s00261-012-9873-7

EGD is an essential tool in the evaluation of new-onset gastrointestinal bleeding. As the most common cause of new lower GI bleeding is upper GI bleeding, the primary purpose of EGD is to exclude other pathological processes that may cause upper GI bleeding, such as peptic ulcer disease, Mallory-Weiss tears, gastritis, duodenitis, esophagitis, esophageal or gastric varices, arteriovenous malformations, tumors, or other causes. The third and fourth portions of the duodenum must be visualized for a complete study, as these areas are among the most common locations for AEE/AEF to develop (**Figure 8**). If these areas cannot be reached with a standard endoscope, a pediatric colonoscope or side-viewing endoscope may provide the necessary length.[30] Prognostic findings include active bleeding, ulcerations, petechiae, blood clot, extrinsic pulsating mass, or graft erosion into bowel. Of note, however, the detection rate for AEF by EGD is reported to be about 24 to 56 percent, so a negative endoscopy does not preclude diagnosis if pretest suspicion is high.[33,34] Furthermore, endoscopy carries the risk of thrombus dislodgement; as such, some authors advise performing EGD in the operating room if pretest suspicion is high.

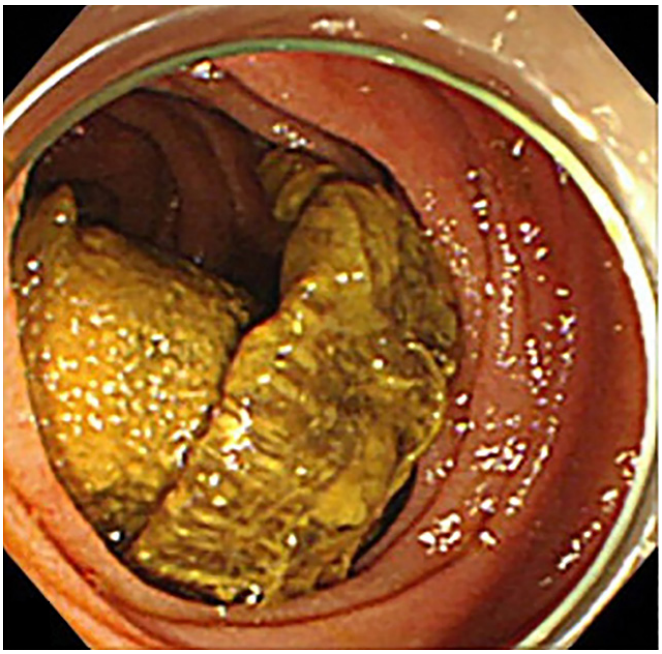

Figure 8. Endoscopy demonstrating polyester vascular prosthesis perforating the transverse portion of duodenum. Reproduced with permission from Radiology Case Reports. Iwaki T, Miyatani H, Yoshida Y, Okochi T, Tanaka O, Adachi H. Secondary aortoduodenal fistula without gastrointestinal bleeding directly detected by CT and endoscopy. *Radiol Case Rep*. 2012;7(4):774.

DSA assists with the visualization of the aortic anatomy, noting abnormal angulation or stenosis, and if brisk bleeding is identified, endovascular intervention may be useful for abatement of symptoms. However, it is otherwise considered an adjunctive diagnostic tool because of its invasive nature and potential for thrombus dislodgement with high-pressure contrast injection.

In patients who do not have overt signs of graft infection, but for whom AEE/AEF is suspected, radio-labeled indium-111 or technetium-99m hexametazime white blood cell scanning shows promising results, with 60 to 100 percent sensitivity and 94 percent specificity.[35,36] Radiolabeled technetium-99m red blood cell scans are also beneficial in localizing fistulas in patients with slow or indiscrete but active bleeding.[31,36]

Pathogenesis

The pathogeneses of PAEF and SAEF are not fully understood but are thought to derive from a combination of mechanical, infectious, and inflammatory etiologies. In the case of PAEF, the pulsatile pressure from an expanding aneurysmal aorta against a fixed area of bowel leads to local compression, ischemia, erosion, and fistula formation. In the case of SAEF, pressure from a noncompliant prosthesis against bowel may result in ischemia of the involved bowel wall and eventual fistulization. Another mechanism implicated in SAEF pathogenesis is suture line disruption, often from graft infection, leading to the formation of an expanding pseudoaneurysm, compressing adjacent bowel and fistulization. In both cases, prosthetic graft material plays a significant role in SAEF development. Infection may be introduced via bacteremia, foreign body, radiation enteritis, enteric infection with transmigration such as diverticulitis or peptic ulcer disease, or even inoculation of the prosthesis during the index operation. Inoculation of the prosthesis can be due to inadvertent bowel injury or intraoperative bowel ischemia leading to weakening of the bowel wall and subsequent inoculation of the nearby prosthesis.

The most common location for AEF is near the distal duodenum and proximal jejunum, occurring in >75 percent of cases. This is thought to occur because the ligament of Treitz fixes this portion of intestine in one place. However, any portion of the GI tract which lies near the aorta may be affected. There is even report of an aortoappendiceal fistula.[37] There have been approximately 20 cases reported of SAEF following endovascular abdominal aortic aneurysm repair and 20 cases of aortoesophageal or aortobronchial fistulae following thoracic endovascular aortic repair.[38]

Management

Facilitated by accurate and timely diagnosis, the principles of management for AEF/AEE include resuscitation, antibiotic therapy, surgical resection and debridement, and arterial and enteric reconstruction. As surgery may prove highly morbid, it is imperative to have a discussion with the patient and/or responsible medical parties regarding goals of care prior to an operation. Broad-spectrum antibiotic coverage for Gram-positive and enteric organisms, along with antifungal coverage for *Candida* species, should be initiated preoperatively. A nasogastric tube should be placed preoperatively for decompression and should remain in place until bowel function has returned postoperatively. Resuscitation must be the top priority from the first moment the patient presents to the postoperative course, and surgeons should not hesitate to pause intraoperatively where possible to allow for adequate rewarming, correction of any metabolic derangements, and restoration of intravascular volume.[39]

Surgical options range from damage control and palliation to full resection and reconstruction. As with work-up, if a patient presents with hemodynamically unstable GI bleeding, surgeons may not be afforded the opportunity to consider various options and exploratory laparotomy may be the only option available.

Extra-anatomic bypass

In stable patients with AEF/AEE, one option is to perform an extra-anatomic bypass as the first of a two-stage operation. This approach establishes viable limb perfusion to minimize the risk of limb ischemia during subsequent resection of the fistula/erosion. This may, however, establish competitive flow to the lower extremities between the new bypass and prior bypass or native circulation. If this approach is utilized, the interval between revascularization and resection of the infected aortic graft should be minimized to allow for adequate postoperative resuscitation and the patient should be systemically heparinized to minimize the risk of thrombosis in either pathway.[30] Extra-anatomic bypass conduits may include axillobifemoral, axillounifemoral with femorofemoral, bilateral axillounifemoral, or distal attachments of the above to popliteal artery.[40,41] As part of resection, the aorta is closed proximal to the site of affected tissue, with oversewing in two layers of monofilament sutures over an area of healthy, viable aortic tissue. This "aortic stump" should then be protected circumferentially from surrounding bowel using either parietal peritoneum, omentum, or bovine pericardium.[30,42]

In-situ reconstructions

It may sound controversial to replace one fistulized or eroded graft with another graft in the same infected field, but outcomes for in situ reconstruction have proven noninferior to extra-anatomic bypass in terms of perioperative mortality, early or late graft occlusion, or graft infection.[43] Furthermore, as a one-stage procedure, in-situ reconstruction is an attractive option for patients who may not have the physiologic reserve to tolerate a longer operation and avoids the potential complication of aortic stump rupture. For patients with active bleeding from AEF/AEE, this approach is favored. This first entails adequate resection and meticulous debridement of involved fistula/eroded tissues, and irrigation to reduce bacterial load. Common reconstructive conduits for in-situ repair include cryopreserved aortoiliac allograft (CAA), rifampin-soaked or silver-impregnated Dacron graft, or creation of a neo-aortoiliac system (NAIS) using femoropopliteal vein.[28]

Cryopreserved aortoiliac allograft (CAA) is one option for in-situ reconstruction because of its resistance to infection. Additionally, if an allograft contains branch vessels, these might also provide conduits for concomitant renal or mesenteric bypass procedures, which may limit morbidity and mortality associated with aortic clamping.[44]

Rifampin-soaked and silver-impregnated Dacron graft are two other options for in-situ reconstruction. Rifampin has excellent activity against most Gram-positive cocci (including methicillin-resistant *Staphylococcus aureus* [MRSA] and not including *Enterococci*), *Haemophilus influenzae*, *Neisseria* species, *Legionella*, and *Listeria monocytogenes*.[45] Rifampin also has an affinity for the collagen and gelatin coatings on grafts.[46] Silver-impregnated Dacron may be soaked in Rifampin as well.[46]

In the case of creating a neo-aortoiliac system (NAIS), autologous femoropopliteal vein is utilized to replace the existing segment of affected aorta/graft (**Figure 9**).[47] Because autologous tissue is utilized, the conduit is at minimal risk for bacterial seeding as compared with a prosthetic material construction.

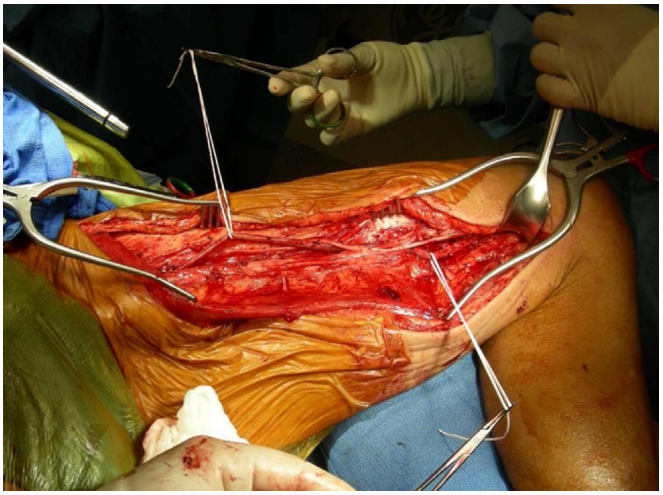

Figure 9. Dissection of the femoropopliteal vein, as utilized for the neo-aortoiliac system (NAIS) procedure. Reproduced with permission from Seminars in Vascular Surgery. Chung J, Clagett GP. Neoaortoiliac System (NAIS) procedure for the treatment of the infected aortic graft. *Semin Vasc Surg*. 2011;24(4):220-226.

Endovascular repair

Finally, as mentioned earlier, endovascular repair has become increasingly popular in select situations despite the infected nidus remaining. Placement of a covered aortic stent graft from within a fistulized graft may exclude the fistula from the normal circulation, effectively eliminating ongoing hemorrhage if present. Because of the endovascular technique, patients in extremis may tolerate this procedure better than open surgery and it may serve as either a temporizing procedure en route to definitive treatment, or as definitive treatment for patients with a limited life expectancy.[28] Of note, endovascular exclusion is not useful for erosions, as the bleeding originates from bowel edges instead of from the aorta or graft itself.

Outcomes and long-term management

In general, perioperative morbidity and mortality is influenced by preoperative American Society of Anesthesiologists Physical Status class ≥4, operative blood loss ≥3 L, and infection with *Candida glabrata*.[48] Parenteral antibiotics are continued for 5 to 7 days postoperatively, with the regimen tailored to culture sensitivities for approximately 4 to 6 weeks. In the case of extensive polymicrobial infections, growth of *Candida* species, or immunocompromised state, intravenous antibiotics, rather than oral antibiotics, should be utilized.[48]

Extra-anatomic bypass

When possible, a follow-up of 5 years is recommended in the outpatient clinic after axillobifemoral bypass repair, evaluating graft patency by clinical examination, ankle-brachial indices, and/or duplex scanning.[49] One-year survival is approximately 67 percent, and 5-year survival is approximately 56 percent.[49] Primary patency of grafts seems to increase with size, with 8-mm grafts having greater patency than 6-mm grafts, but graft size may not influence overall survival.[49] Following creation of an aortic stump, there is a rare (3 to 9 percent) but measurable risk of aortic stump disruption which is almost certainly fatal.[41,50] These studies, however, were published more than two decades ago, in 2000 and 1984, respectively, and may be lower with newer surgical techniques. Nevertheless, clinicians should remain ever vigilant of this devastating complication during follow-up.

In-situ reconstructions

In a study evaluating CAA in-situ reconstruction, 4 percent of patients had a recurrence of graft infection after a mean 30 months' follow-up.[44] The administration of lifelong anticoagulation for CAA is controversial. One analysis of patients with infected aortoiliac grafts who underwent in-situ CAA reconstruction reported that no patient was on anticoagulation beyond postoperative prophylaxis.[51] However, trials which featured more distal bypass procedures with CAA did utilize lifelong anticoagulation to maintain long-term patency.[52,53] Further investigation may be required to clarify the indications for lifelong anticoagulation after CAA aortic reconstructions.

Rifampin-soaked grafts reportedly feature a 5-year patency rate of 92 percent, with only a 4 percent graft infection rate over this same time interval.[54] In the study reporting these data, all patients who survived initially achieved limb salvage.

The NAIS procedure seems to have the lowest rates of recurrent infection (<2 percent), early graft occlusion, or late graft occlusion, with a 5-year patency rate ranging from 75 to 91 percent.[48] Of note, development of thrombosis in the popliteal vein stump after NAIS procedure is not uncommon, but subsequent pulmonary embolism is not possible given the harvested femoropopliteal vein. Thus, standard anticoagulant therapy is unnecessary.[48] Furthermore, the risk of limb edema after NAIS procedure has been surprisingly rare.[47]

Endovascular

Finally, given the usual patient population of critically ill, severely exsanguinated, and septic patients who may only tolerate endovascular repair, outcomes are predictably poor, with a high incidence of persistent or recurrent infection or recurrent bleeding.[55] Therefore, endovascular therapy should only be utilized as a bridge to more definitive therapy after resuscitation.

Conclusion

Aortoenteric fistula and aortoenteric erosion remain considerations in the diagnosis of any patient who presents with new-onset gastrointestinal bleeding in a context of prior vascular disease. There are newer strategies for resection and reconstruction with better long-term outcomes, but surgical decision making must be influenced by the patient's condition, wishes, and accessible options.

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CHAPTER 27—PART I

Bowel Perforation during Oncologic Treatment with Biological Agents

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Abstract

Bowel perforation is a rare, serious complication occurring in the oncologic patient as a possible direct consequence of chemotherapeutic administration, notoriously able to induce tumor necrosis and weakening of the bowel wall.[1]

Biologic agents, such the anti-VEGF (vascular endothelial growth factor) bevacizumab, alone or in combination with chemotherapy, has been related to an increased risk for bowel perforation.[2]

More recently, novel biologic agents called immune checkpoint inhibitors (ICIs), have received approval for several kind of malignancies, revolutionizing the therapeutic landscape of several cancer types, including those with dismal prognosis.[3] However, despite the outcome improvement and the safe toxicity profile, several cases of bowel perforation have been reported in the literature following the administration of ICIs.[4]

This chapter will provide surgeons with a brief report of bowel perforation induced by biologic agents adopted in cancer care, including the anti-VEGF (bevacizumab) and ICIs.

Intestinal Perforation in Patients Receiving Anti-VEGF Agents

Introduction

Cancer growth maintenance and metastasis development rely on an adequate blood supply through the formation of new blood vessels. Hence, the tumor vasculature represents one of many possible targets for tailored oncology treatment.

VEGF is a potent angiogenic factor, whose overexpression is observed in many human tumors and associated with tumor progression and poor prognosis.[5] Bevacizumab (Avastin) is a recombinant humanized monoclonal IgG1 antibody (rhu-Mab) directed against vascular endothelial growth factor A (VEGF-A) and belonging to the class of antiangiogenic drugs.[6]

In 2004, bevacizumab received approval for the treatment of metastatic colorectal cancer (mCRC), in addition to a fluorouracil (5-FU) chemotherapy backbone.

In this regard, this biologic agent was demonstrated to improve survival in the first-line setting.[7,8] To date, bevacizumab, alone or in combination with a chemotherapy regimen, has several indications for different advanced malignancies including glioblastoma,[9] non-squamous non-small cell lung cancer (NSCLC),[10] renal cell carcinoma,[11] and ovarian[12] and breast cancer.[13] Despite the relevant improvement in clinical outcomes, particularly in the setting of first-line unresectable CRC,[14] bevacizumab has been related to infrequent but potentially life-threatening complications, such as gastrointestinal (GI) perforations.[15]

Indeed, clinical trials reported a well-defined risk of GI perforation, including perforated gastric ulcer, bowel perforation, fistula formation in the gastrointestinal tract, intra-abdominal abscess, and free air under the diaphragm without identified sources.[16]

Colonic perforation is a serious iatrogenic complication with an incidence ranging from 1 to 4 percent and a reported fatality rate of up to 20 percent.[17]

Pathophysiology

Gastrointestinal perforation associated with bevacizumab has been defined as the finding of intraperitoneal air with or without gastrointestinal or enterocutaneous fistula. Although the exact mechanism of bevacizumab-associated GI perforation is not clear, one possible explanation lies in the limitation of blood flow to the gastrointestinal tract, eventually determining bowel infarction and perforation.[18]

Indeed, bevacizumab induces the regression of normal blood vessels in the GI tract resulting in lower vascular density and this mechanism may directly contribute to the mucosal injury responsible for GI perforation. Also, the presence of an intact GI tumor may provide some grade of stability to the intestinal wall and perforation occurrence may be exacerbated by bevacizumab-induced cancer cell's death at the tumor site.[19]

Epidemiology

According to the available set of evidence, gastrointestinal perforation is more likely to occur in the first 3 to 6 months of treatment with bevacizumab, while it is rarely described beyond 12 months of bevacizumab use.[15] Indeed, during the early phase of treatment, in addition to bevacizumab-induced and cytotoxic treatment-induced mucosal injury, the primary tumor might progress and cause perforation.[20]

History of diverticulitis, peptic ulcer disease, pelvic/abdominal radiation exposure, intestinal obstruction, tumor necrosis, recent sigmoidoscopy or colonoscopy, and multiple previous surgeries are among the most recognized risk factors.[21]

The use of concomitant cytotoxic chemotherapeutic agents[22] as well as the presence of peritoneal carcinomatosis, may also raise the risk of bowel perforation.[23]

Indeed, symptomatic peritoneal carcinomatosis, together with the presence of huge, ulcerated lesions or a colic stent, contraindicates the use of bevacizumab.

Furthermore, a slightly higher risk of colonic perforation has been described in the presence of an intact primary CRC tumor (3.3 versus 1.4 percent).[24,25] The risk of colonic perforation may also vary with the bevacizumab dose. In a large meta-analysis, patients receiving bevacizumab at a higher dose (5 mg/kg per week) had a significantly higher risk of developing GI perforation compared to those receiving 2.5 mg/kg per week. In addition, tumor type may affect the risk of bowel perforation, with higher risk observed in patients with colorectal carcinoma (relative risk 3.10, 95 CI 1.26-7.63) and, possibly, renal cell cancer (relative risk 5.67, 95 percent CI 0.66-48.42).[18]

A varying incidence of bevacizumab-associated GI perforation has also been described in patients with different cancer types, resulting higher in cancers that involve the GI tract such as advanced pancreatic cancer (8 percent) and gynecological malignancies including recurrent, refractory ovarian cancer (3 to 11 percent).[23,26,27,28]

Clinical presentation and management

The clinical findings of colonic perforation at the time of presentation include increasing abdominal distension, nausea, or emesis.[29] Localized abdominal pain may indicate a localized microscopic perforation, while generalized abdominal pain may suggest diffuse peritonitis. A physical

examination will demonstrate signs of peritonism or a rigid abdomen with rebound tenderness. Fever, tachycardia, hypotension, and signs of sepsis (such as pallor, sweating) may also be noted.

Careful assessment of the patient's history should include looking for evidence of past diverticulitis or ulcers, radiation exposure, recent sigmoidoscopy or colonoscopy, resection of the primary tumor, gastrointestinal obstruction, and previous surgeries. Additionally, an accurate assessment of the patient's disease state, including knowledge of the tumor mass involving the bowel wall and abdominal carcinomatosis, is highly suggested. Blood testing including a CBC; a basic metabolic panel; liver function tests; and lipase, amylase, and inflammatory markers (C-reactive protein, PCR) must be performed. Common findings such as leukocytosis, elevated amylase, or elevated CRP level are nonspecific for diagnostic purposes. A computed tomography (CT), demonstrating intraperitoneal free air, is the primary imaging modality for detection and localization of bowel perforation. Also, a CT scan may be helpful in determining if the area has spontaneously walled off or if there has been a progression to abscess formation, as well as to identify inflammatory involvement of surrounding structures.[29]

The U.S. Food and Drug Administration recommends that bevacizumab be permanently discontinued in patients with gastrointestinal perforation.[17]

The severity of symptoms at presentation will guide the work-up in each case. Prompt recognition of symptoms followed by surgical assessment is necessary along with bowel rest, fluid replacement, and intravenous broad-spectrum antibiotics. An exploratory laparotomy may provide the most important diagnostic measure in patients with severe abdominal pain and confirmed bowel perforation.[30] All patients undergoing emergency surgery should be advised of the possibility of a stoma creation. An anastomosis is not recommended, due to high rates of bevacizumab-associated wound-healing complications (4.4 to 13 percent).[24,31]

Some evidence suggests surgery is not always the best management for this iatrogenic condition and a single-center study of patients who developed perforation while on bevacizumab revealed that selected cases were successfully managed nonoperatively.[32]

Conclusions

Despite the growing knowledge of predisposing factors and possible mechanisms of bevacizumab-induced bowel perforation, little is known on the best method to predict this severe, potentially fatal complication.

For this reason, patients at higher risk for developing bowel perforation should be identified before the initiation of bevacizumab and carefully monitored for early clinical signs of colonic perforation.

The use of concomitant chemotherapeutic agents, which may cause bowel inflammation and inflammatory wound healing, raises concerns regarding the best treatment option in these fragile patients. Indeed, the increased likelihood of surgical complications in patients receiving this antiangiogenic targeted treatment, particularly the high rate of wound-healing complications, would suggest considering a conservatory approach as an alternative to early surgical management in selected cases.

For this reason, a multidisciplinary discussion with the radiotherapist and oncologist is always recommended before surgical intervention and will guide the best treatment option.

Immune-Related Gastrointestinal Toxicity and ICI-Induced Bowel Perforation

Introduction

Immune checkpoint inhibitors (ICIs) are a relatively new class of monoclonal antibodies against inhibitor receptors expressed on the surface of cytotoxic T cells (such as programmed cell death protein 1 [PD-1], and cytotoxic T-lymphocyte-associated protein 4 [CTLA-4]) or their ligands expressed on antigen-presenting cells (for instance, programmed cell death ligand 1 [PD-L1]).[33,34]

CTLA-4/B7 and PD-1/PD-L1 axis integrity has been shown to be crucial in regulating the immune response to self-antigens. Indeed, they both act in preventing the onset of autoimmune reactions; the first by inhibiting T-cell activation in central lymphoid organs; the second by limiting the effector function of activated T cells in the periphery.[35] In the last 10 years, ICIs have revolutionized the treatment of several malignancies, especially melanoma, non-small cell lung cancer (NSCLC), renal cell carcinoma, and urothelial carcinoma.[3]

Along with the remarkable benefit of improved overall survival (OS) and delay of disease progression, cancer patients may develop a specific pattern of side effects named immune-related adverse events (irAEs).[36]

IrAEs can involve almost all the tissue and body systems including the gastrointestinal (GI) tract, where this kind of toxicity may develop in the form of immune-mediated diarrhea (IMD) and colitis (IMC).[37]

The increasing use of ICI in daily medical cancer care makes it essential for the surgical oncologist to be familiar with severe-IMC management and its related fatal toxicities, including bowel perforation.

Pathophysiology

To date, the pathophysiology of IMD and IMC is not entirely understood. Several biological mechanisms could explain why an ICI-induced disruption of CTLA-4 and PD-1/PD-L1 axes may simultaneously lead to an effective antitumor response, alongside the emergence of GI-irAEs. CTLA-4 and PD-1/PD-L1 pathways play an essential role in regulating mucosal homeostasis at the GI level. PD-1/PD-L1 interaction has been shown to prevent CD8+ T cell-mediated autoimmunity against intestinal self-antigens.[38] In addition, CTLA-4 plays a key role in the accumulation and action of a regulatory subpopulation of T lymphocytes (Tregs) in the intestinal lamina propria, with clear suppressive function toward autoreactivity.[39, 40]

Among the most investigated factors potentially able to trigger GI-irAES there are tumoral (such as an underlying cancer histology), host (baseline gut microbiota composition, host-barrier integrity, autoimmune disorders), and immunologic factors (immune tolerance, cytokines role, ICI pharmacokinetics).[41, 42, 43, 44]

Epidemiology

GI-irAEs incidence varies with the class of agent adopted and the dose administered. GI-irAEs rates are higher in patients receiving the anti-CTLA-4 ipilimumab and tremelimumab compared to the anti-PD-1 nivolumab and pembrolizumab (IMD 31 to 49 percent versus 2.9 to 11.5 percent, IMC 7 to 11.6 percent versus 1.35 to 2.9 percent) [37,45] and the combination of anti-CTLA-4 and anti-PD-1 increases the frequency of both IMD (9.4 to 10.6 percent) and IMC (13.6 percent).[46,47]

GI-irAEs kinetics is variable and mainly related to the agent adopted; the median time to symptoms' onset ranges between 1 month and 3 months after anti-CTLA-4 and anti-PD-1 initiation, respectively.[48] A small proportion of patients may also develop delayed-onset symptoms.[48] IMC fatality rate is reported to be around 5 percent. Of note, fatal toxic events associated with ICIs tend to occur very early in treatment (median of 49 and 14.5 days for monotherapy and combination immunotherapy, respectively).[49]

Clinical Presentation and Management

Immune-mediated colitis (IMC) has been reported to occur in 0.3 to 7 percent of patients treated with ICIs and most commonly, but not exclusively, affects the rectum and sigmoid colon.[4] IMC may display diverse grades of severity, according to the Common Terminology Criteria for Adverse Events (CTCAE) version 5, developed by the National Cancer Institute (**Table 1**). IMC should be suspected in all patients while on ICI or in those having recently completed ICI treatment complaining about diarrhea, abdominal pain, distention, hematochezia, and/or mucus in the stools. The presence of abdominal pain, fever, and change in bowel habits with ileus or peritoneal signs suggests a grade 3 IMC. Early recognition of grade 3 IMC symptoms is essential and patient assessment should be handled rapidly as this condition can easily progress to life-threatening events, featuring grade 4 GI-irAEs.[50]

Patient assessment should include a thorough review of patient medications, baseline bowel patterns, number of bowel movements, urgency, gas, bloating, diet, and previous surgery. In addition, a work-up of blood (complete blood count [CBC], comprehensive metabolic panel, thyroid-stimulating hormone [TSH], erythrocyte sedimentation rate [ESR], C-reactive protein [CRP]) and stool (culture, Clostridium difficile, parasite, cytomegalovirus [CMV]) should be done to rule out potential bacterial and viral infectious causes.[51,50]

Colonoscopy with biopsy is recommended for patients with grade 3 colitis to evaluate the extent and severity of the disease.[50] Normal mucosal findings are not sufficient to exclude the presence of immune-mediated diarrhea and colitis (IMDC), as cases of isolated ileitis or enteritis without colitis have been described in the literature.[52]

Both ASCO® and the National Comprehensive Cancer Network (NCCN) guidelines recommend withholding immunotherapy in cases of grade 3 IMC and initiating high-dose intravenous methylprednisolone (2 mg/kg/day for 1-2 weeks) with tapering within 30 days. The tumor necrosis factor (TNF)-α antagonist infliximab (IFX) at a dose of 5 mg/kg is effective in managing steroid-refractory conditions.[53,23] Patient hospitalization is strongly recommended, as grade 3 IMC may potentially progress to life-threatening bowel perforation.[50]

Bowel perforation, with or without intra-abdominal abscess, is a rare but well-documented condition, requiring emergent surgical attention.[54] It occurs in 1 to 6 percent of patients treated with ICI (1.0 to 1.5 percent of melanoma patients treated with ipilimumab and up to 6 percent of ipilimumab-treated patients with renal cell carcinoma).[50] The National Cancer Institute (NCI) Surgery Branch reported that among 198 patients treated with the anti-CTLA-4 ipilimumab, 41 patients (21 percent) developed enterocolitis. Five patients (12 percent) required colectomy: four patients had colonic perforation and one patient had intractable bleeding. Two patients eventually died from sepsis after perforation.[55] The pathological mechanism of immune reaction resulting in intestinal perforation is similar to that of an inflammatory reaction.[56]

Patients with preexisting autoimmune GI disease, including inflammatory bowel disease (IBD), are at a higher risk of developing G3 IMC and colonic perforation.[57]

Bowel perforation should be suspected in all patients while on or having recently completed ICI, who present with severe abdominal pain, rectal bleeding, and fever. In these cases, hospitalization is mandatory and will allow close monitoring and prolonged administration of intravenous fluids for dehydration as well as surgical consultation. The clinical examination may reveal abdominal distension, tenderness, rebound tenderness, and muscle stiffness. Tachycardia and fever may also be noted.

In the case of suspected bowel perforation, abdominal and pelvic computed tomography (CT) with or without contrast should be performed if the patient is hemodynamically stable.[58] The presence of free air near the large intestine at CT scan will confirm the suspicion. In this case, early surgical consultation to evaluate indications for operative intervention is mandatory. Referral to a surgeon is also indicated in the case of intractable diarrhea, persistent rectal bleeding, or worsening abdominal pain despite bowel rest, IV corticosteroids, and infliximab.

In the case of the unstable patient with signs of shock surgical referral should not be delayed and exploratory laparotomy is indicated. Emergency subtotal colectomy with a colostomy is needed if bowel perforation is confirmed; the extent of the colectomy will depend on the amount of colon severely involved as seen intraoperatively.[59] A primary anastomosis is not recommended as patients will be receiving corticosteroid treatment after surgery. After surgery and once corticosteroids have been tapered and then held, in a patient without recurrence of GI symptoms, a surveillance colonoscopy should be performed. The endoscopic assessment with a confirmation of complete resolution of the inflammatory process in the pathology report will help the surgeon to determine the right time of the colostomy reversal.[60]

Currently, there are important unresolved questions regarding postsurgical care of patients that present with colonic perforation after treatment with immunotherapy. First, it has not been determined yet if re-starting of ICI treatment is advisable after surgical treatment, although NCCN guidelines recommend to permanently discontinue the immunotherapy agent responsible for grade 4 IMC.[53]

Furthermore, perioperative and postoperative use of steroids or infliximab maintenance therapy should be better evaluated, as some evidence suggests an increased risk of complications such as intra-abdominal and wound dehiscence.[61,62,63]

Conclusions

As an important option for cancer treatment, cancer immunotherapy has come of age. Despite ICIs' established efficacy in cancer treatment, new and generally mild immune-related adverse events have been observed, including IMC, of which surgeons must be aware. Early recognition and management of IMC may limit rare but severe life-threatening GI complications, such as bowel perforation.

The possibility of colonic perforation should be suspected either initially or during ICI administration in patients complaining of severe GI symptoms, whether no improvement over steroid treatment is observed. Early surgical consultation is strongly recommended, and surgery must be performed in all cases of documented bowel perforation at CT scan.

A subtotal colectomy with ileostomy or sigmoidostomy is recommended because colonic lesions are generally extensive and segmental colonic resection is generally followed by severe inflammation of the remaining colon in the postoperative phase.

Several issues should be explored in the near future, especially regarding the best pre- and postoperative management strategies for patients receiving ICIs.

Table 1. Grading of immune-mediated diarrhea (IMD) and immune-mediated colitis (IMC) in patients treated with Immune Checkpoint Inhibitor (ICI) therapy

	DIARRHEA	**COLITIS**
GRADE 1	Increase of <4 stools/day over baseline	Asymptomatic
GRADE 2	Increase of 4-6 stools/day	Abdominal pain, mucus, blood in the stool
GRADE 3	Increase of ≥7 stools/day	Severe pain, fever, peritoneal signs
GRADE 4	Life-threatening consequences such as hemodynamic collapse	Life-threatening consequences such as perforation, ischemia, necrosis, bleeding, toxic megacolon
GRADE 5	Death	Death

Adapted from the Cancer Therapy Evaluation Program, National Cancer Institute Common Terminology Criteria for Adverse Events v5.0 Program, Common Terminology Criteria for Adverse Events v5.0.

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CHAPTER 27—PART II

Colorectal Cancer Emergencies

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Introduction

Colorectal cancer (CRC) is the second-leading cause of cancer death in the U.S., with 50,000 deaths each year and an incidence of 150,000 new cases per year.[1] Despite robust screening efforts, more than 20 percent of patients with CRC will require urgent or emergent surgical intervention upon initial presentation.[2] Additionally, acute presentations can occur during initial diagnosis, while undergoing systemic treatment, or toward the end of life. The surgical emergencies related to CRC in order of incidence are obstruction, perforation, and hemorrhage.[3] Compared with patients who undergo elective surgery, patients who undergo emergency surgery for CRC have increased morbidity and mortality.[4] These rates are not only attributed to increased surgical risk, but also related to patient factors such as dehydration, electrolyte abnormalities, and poor nutrition. Additionally, cancers that are resected emergently are more likely due to have an advanced T stage with higher histologic grade, lymphovascular invasion, and even metastatic disease.[5] The principles of oncologic resection remain consistent even in the emergent setting, including adequate margins with high ligation of the lymphovascular pedicle. The goals of treatment of CRC-related surgical emergencies include alleviation of the complication while achieving an appropriate oncologic resection and ensuring timely recover to allow for initiation of adjuvant therapy.

Obstruction

Large bowel obstruction is the most common indication for emergency surgery among patients with CRC, comprising up to 75 percent of emergencies.[6] Relatedly, cancer is the most common cause of large bowel obstruction in adults. Malignant large bowel obstruction can be caused by intraluminal blockage, extraluminal compression, or even intussusception and carries a 5 percent mortality rate.[7] Patients with an obstructing colon cancer will report a gradual onset of symptoms as well as self-medication with over-the-counter stool softeners and laxatives. Associated abdominal distension, colicky abdominal pain, or obstipation are common. This insidious onset can lead to severe dehydration, electrolyte abnormalities, or malnutrition. Computed tomography (CT) is the imaging modality of choice for patients for whom you suspect an intestinal obstruction because of its high sensitivity of 96 percent as well its ability to visualize locoregional or distant spread.[8] CT may also show pneumatosis intestinalis or portal venous gas, which are signs of tissue ischemia with impending perforation. Colonoscopy offers the ability to localize the lesion and sample tissue while simultaneously reliving the obstruction should a stent be placed to traverse the lesion. However, this modality is often not available in the emergent setting and is not recommended if a patient presents with physiologic derangements requiring immediate surgical intervention.

Patients with colonic obstructions should undergo a standard oncologic operation even if a diagnosis of cancer has not yet been made. Essentially, patients with large bowel obstruction should undergo a curative operation in the absence of metastatic disease.[9] The location of obstruction impacts treatment options, using the splenic flexure as an anatomic landmark to define proximal or distal obstructions. Proximal obstructions are less common than distal obstructions due to the large diameter of the cecum, ascending colon, and transverse colon compared with the narrow luminal diameter and thicker stool of the left and sigmoid colon. The surgical management of proximal obstructions is relatively straightforward, requiring a right hemicolectomy or an extended right hemicolectomy with ileocolonic anastomosis. Primary anastomosis is considered safe in this setting with anastomotic leak rates ranging from 2.8 to 4.6 percent.[10]

Distal obstructions occur in 75 percent of patients presenting with an obstructing CRC.[3] The operative treatment distal obstructing CRC is still a matter of debate, centering on whether these tumors should be resected in staged procedures or resected with a primary anastomosis. There are several concerns surrounding performing a primary anastomosis in the distal colon in the emergency setting, particularly the patient's critical illness, increased operative time, difficult mobilization of distended bowel, and severe malnutrition, which poses a significant risk for anastomotic leak.[11] The most common operation performed for obstructing distal colon cancer is the segmental colectomy with end colostomy, which provides an oncologic resection without the risk of potential leak. This eliminates any subsequent delay in chemotherapy if a leak were to occur. However, stomas are not without their own complications, can negatively impact quality of life, and have only a 20 percent rate of reversal among patients with CRC.[8]

Recent large studies have established the safety of primary resection and anastomosis in the appropriately selected patient.[12] Retrospective data have shown the anastomotic leak rate similar to that of elective colon resection. Thus, in the carefully selected patient without risk factors associated with anastomotic leak, primary resection and anastomosis may be performed with or without a diverting loop ileostomy. In patients with hereditary CRC syndromes or in patients with ischemic proximal colon or concern for cecal perforation, a total abdominal colectomy may be performed. For patients in whom an appropriate oncologic resection cannot be performed, whether due to patient comorbidities, acute physiologic derangements, or locally advanced cancer, a staged approach should be considered. The obstruction is first managed with a creation of a loop colostomy, which alleviates the obstruction while allowing for completion staging and multidisciplinary treatment planning. This is also the preferred surgical approach for an obstructing middle or lower rectal cancer.[13]

Lastly, self-expandable metal stents (SEMS) present an endoscopic modality to address distal colonic obstructions. Proponents of SEMS argue that stenting can relieve the obstruction, examine the colon for synchronous lesions, and provide a "bridge to surgery" while clinicians stabilize the patient, improve nutritional status, and complete oncologic staging. In a large meta-analysis, the rate of clinical success was significantly less than surgery, with similar rates of stoma creation and anastomotic leakage.[14] SEMS should only be performed by experienced endoscopists and should truly be considered in patients with short life expectancy for whom a less morbid approach allows for quicker resumption of systemic chemotherapy.

Perforation

Colonic perforation is the second-most common CRC-related emergency. Perforations most commonly occur at the site of the primary tumor due to its invasiveness and necrosis.[3] However, perforations can also occur at remote proximal sites due to colonic wall ischemia as a sequela of increasing pressure and distension at the site of the malignant obstruction.

The management of perforated colon cancers depends on the clinical status of the patient as well as the nature of the perforation. Patients with frank contamination in the peritoneum will present with peritonitis and possibly sepsis. CT, with a sensitivity of 95 percent and specificity of 97 percent, will show free air and/or free fluid.[2] Free perforation is a surgical emergency with poor outcomes and a perioperative mortality rate of 9 percent.[7] Thus, patients and families should be thoroughly counseled. Surgery involves open exploration, washout, and oncologic resection of the perforated site as well as thorough examination of the entire bowel. In the event of cecal ischemia or perforation due to a distal obstruction, a subtotal colectomy is performed with either an end ileostomy or primary anastomosis.

In contrast to free perforations, colonic perforations may be contained. Patients may present with localized tenderness and CT will reveal fluid collection or abscess, which is more likely to be associated with a distal malignancy. This clinical presentation can be challenging because it can mimic complicated diverticulitis. The immediate goal is source control with prompt recovery so as not to delay therapy. Thus, percutaneous drainage and antibiotics are recommended prior to either systemic chemotherapy or surgery, depending on the cancer staging.

Bleeding

Although bleeding occurs in the majority of patients with CRC, it is usually self-limited and does not require intervention. Unlike perforation and obstruction, bleeding is often an early symptom of CRC.[2] Clinically significant GI bleeding requiring intervention is rare. The initial treatment is centered on resuscitation, by establishing large-bore IV access and hemodynamic stabilization with crystalloid, blood transfusions, and correction of underlying coagulopathy. Surgery is the definitive approach to GI hemorrhage due to CRC and should be considered before the site of bleeding is localized if the patient remains hemodynamically unstable despite continued transfusions or inability to stop hemorrhage with endoscopic or endovascular techniques.[15] In the case of unlocalized hemodynamically significant GI bleeding, a total abdominal colectomy should be performed. The decision to create a stoma or perform a primary anastomosis should be considered in the context of the patient's clinical presentation, hemodynamics, and comorbidities.

If possible, the source of bleeding should be localized in a clinically stable patient. Endoscopy is able to identify the source in approximately 80 percent of cases while also obtaining tissue diagnosis. However, this may be difficult in the unprepped colon. Furthermore, tagged red blood scans can localize the source in about 50 percent of cases and can detect bleeding rates as low as 0.1 mL/min.[16] Lastly, angiography with embolization can be diagnostic and therapeutic but carries a risk of intestinal ischemia.

Conclusion

Patients with colorectal cancer may present with a surgical emergency at any point during their work-up or treatment choice. The management of such emergencies is centered on the correction of the acute clinical problem while adhering to oncologic surgical principles. It is feasible to perform an oncologic resection in the emergency setting. Several studies have documented R0 resection of >90 percent and adequate lymphadenectomy in >70 percent of emergency colectomies.[6] However, outcomes for patients with CRC presenting with an emergency is significantly worse than patients who do not. Emergently resected tumors are more likely to be T4 or lymph-node positive, thus conferring a worse prognosis. Patients with a proximal malignant obstruction should undergo a right hemicolectomy with primary anastomosis, whereas the treatment of distal malignant obstruction should be individually tailored to fit each patient. Colonic perforation is a surgical emergency with prompt exploration, resection, and anastomosis as clinically allowed. Surgery for acute lower GI hemorrhage associated with CRC is rare and should be reserved for persistent unlocalized bleeding.

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CHAPTER 27—PART III

Emergencies in Gastric Cancer

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Introduction

Gastric cancer is the second-most common cause of cancer death worldwide and is responsible for 11,000 deaths in the U.S.[1] The vast majority of patients present with chronic symptoms such as weight loss, poor appetite, and vague abdominal discomfort. However, gastric cancers can initially present or progress to causing gastric outlet obstruction, hematemesis, or perforation in up to 15 percent of patients.[2,3] Recent advances in early diagnosis and treatments have improved overall survival in patients with gastric cancer, but emergent complications are associated with higher disease stage and worse prognosis.[4] Furthermore, several studies have shown that patients who present with alarm symptoms, such as weight loss, dysphagia, or iron deficiency anemia, are less likely to undergo an R0 gastrectomy and have shortened overall survival.[4,5]

Gastric Outlet Obstruction

Gastric outlet obstruction (GOO) is a common condition among patients with gastric cancer and is accompanied by nausea, vomiting, dehydration, and malnutrition. In the acute setting, prompt diagnosis and electrolyte correction with attention to refeeding syndrome is paramount. Nasogastric decompression may be warranted if there is clinical concern for aspiration. Two treatment modalities are commonly used: surgical gastrojejunostomy (GJ) and an endoscopic self-expendable metal stent (SEMS). There have been few direct comparisons between the two treatment modalities, with most investigators and clinicians recommending SEMS insertion for patients with limited survival.[6] Several retrospective studies have demonstrated no difference in technical success, resolution of symptoms, quality of life, or median survival. SEMS placement is consistently associated with shorter time to oral food intake, shorter hospital stay, and decreased cost. However, SEMS placement is associated with quicker and more frequent recurrent obstructive symptoms and requires re-intervention more often than GJ.[7-11] Small randomized trials have produced similar results.[6,12] In general, SEMS placement is preferable to GJ in patients with poor clinical condition and short life expectancy.

Perforation

Spontaneous perforation of gastric cancer is rare, occurring in 1 percent of patients with gastric cancer.[13] The hospital mortality rate ranges from 30 to 80 percent.[14,15] The main cause of gastric perforation is a gastric ulcer, but gastric cancer is responsible for about 10 percent of such cases.[16] Malignant gastric perforation is associated with advanced cancer and lymph node metastasis.[13] In most cases, gastric carcinoma is not suspected or known as the cause of perforation prior to emergency laparotomy and is known on postoperative histologic examination. It is difficult to distinguish a gastric ulcer from cancer at the time of surgery. Thus, an intraoperative frozen assessment is recommended, if available. The surgical management aims to address the emergency condition of peritonitis while adhering to oncologic principles. An R0 resection provides improved survival in patients with perforated gastric cancer. Thus, in the hemodynamically stable patient with a known malignancy, a gastrectomy with lymphadenectomy is appropriate. However, a two-stage gastrectomy achieves similar survival rate and has a higher rate of R0 resection, >75 percent compared with 50 percent in a single-stage approach.[17] Nonetheless, the clinical state of the patient should be the ultimate factor in surgical decision-making. An omental patch repair is suitable for unstable patients, regardless of known malignancy status at the time operation.

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CHAPTER 27—PART IV

Ruptured Hepatocellular Carcinoma

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Introduction

Hepatocellular carcinoma (HCC) is the third-leading cause of cancer mortality worldwide, with approximately 700,000 patients dying from cancer every year.[1] In more than 85 percent of cases, HCC will develop in the setting of cirrhosis of the liver.[2] Rupture is the third-most common cause of death from HCC following cancer progression and liver failure.[3] The initial goal of treatment for ruptured HCC is the stabilization of the patient by means of correcting the hypovolemic shock followed by multidisciplinary care at achieving hemostasis. Conservative management following resuscitation is associated with very poor outcomes, with reported mortality at more than 80 percent.[4] The two main options of management following resuscitation include trans-arterial embolization (TAE) and surgical resection. These therapeutic options are dictated by factors such as tumor stage, feasibility of resection, and underlying liver function.

Incidence and Risk Factors

The incidence of ruptured HCC exhibits strong global variation, with rates less than 3 percent in the Americas and Europe but more than 20 percent in Asia and Africa.[5,6] There is some evidence that there has been a recent decrease in the mortality from ruptured HCC, owing to earlier detection of HCC and improved interventional techniques. For example, a report out of Japan showed a decrease in mortality of ruptured HCC from 10 to 6.4 percent over time.[7] While the pathophysiology of HCC rupture has not been fully described, several hypotheses exist, including HCC growth into the liver capsule, venous congestion from tumor progression, and vascular injury. Translated into clinical factors, HCC is at increased risk of rupture if there is worse underlying cirrhosis, portal vein thrombosis, systemic hypertension, size greater than 5 cm, and an exophytic or sub-capsular location.[4,8] There is also some evidence that prior treatment with trans-arterial chemoembolization or Sorafenib, a protein kinase inhibitor used in advanced HCC, increases the incidence of rupture.[9,10]

Presentation and Diagnosis

The successful management and treatment of ruptured HCC requires prompt diagnosis as it has the potential to have life threatening consequences. This can be made even more complicated in a patient without a history of cirrhosis or HCC. The most common presenting symptom is acute abdominal pain and can be accompanied by shock depending on the severity and chronicity of the rupture.[12] Less likely, but possible, symptoms include abdominal distention and acute liver failure.[13,14]

The modality of choice in the diagnosis of ruptured HCC is computed tomography (CT). There are several CT findings that can suggest rupture of HCC. These include a peripherally located tumor with a contour bulge, a break/tear in the liver capsule, hemoperitoneum, subcapsular hematoma, and active extravasation.[15] The most specific CT finding for ruptured HCC is the "enucleation sign" associated with surrounding hematoma and/or contrast extravasation.[16] The "enucleation sign" is seen as a hypervascular peripheral liver mass showing central necrosis discontinuous with hepatic parenchyma on arterial phase imaging.[17] The use of hepatic artery angiography for diagnosis of ruptured HCC is limited because active extravasation, the important diagnostic feature of HCC rupture, can be seen in less than half of all cases.[18] CT has been shown to be more reliable than angiography in detecting the site of active extravasation.[19]

Management

The initial phase of management of ruptured HCC involves the correction of the underlying hypovolemic shock from intraperitoneal hemorrhage as well as the preservation of liver function. Because the overall treatment strategies can differ, a careful initial evaluation is critical. Important factors to take note of are hemodynamic status, underlying liver function, HCC stage, and tumor characteristics.[3] Only patients who are hemodynamically stable without active bleeding should be managed conservatively, followed by definitive treatment. Conservative treatment consists of immediate vascular access and volume resuscitation, including blood products and the correction of coagulopathies. Prompt cardiovascular monitoring is also important for continual monitoring of hemodynamic status. At the same time, an assessment and review of the patient's current liver function and tumor stage should be undertaken to determine the most appropriate definitive treatment. Historical outcomes of conservative management alone have proven to be quite poor, with inhospital mortality rates between 85 and 100 percent.[20] In a large, multicenter study in China, 91 percent of all patients with ruptured HCC who only received conservative management died within 30 days, with cause of death in most of these patients being rebleeding (66 percent) or liver failure (28 percent).[21] Therefore, conservative management alone should be offered to those patients proceeding with palliative care options where both surgery and TAE are not feasible.

In the hemodynamically unstable patient, control of the bleeding immediately following or during resuscitation is paramount. The method of achieving hemostasis is achieved through an interventional radiological approach with TAE or directly through a surgical approach. TAE, as the less invasive approach, has a high success rate of 50 to 100 percent. It also has a significantly lower complication profile than emergent open surgery. Because emergent surgery may be difficult due to hemodynamic instability and acute liver failure,

TAE followed by definitive staged liver resection provides an optimal solution. The main and feared complication of TAE is the development of liver failure, which occurs at a rate of 12 to 34 percent.[14] This can be potentially mitigated by selective embolization of the bleeding artery, particularly in those patients with multifocal HCC. The main predictor of survival after TAE is underlying liver function. Lau et al. showed a mean survival time of 218, 83, and 11 days in Child-Pugh A, B, and C patients, respectively, who underwent TAE for ruptured HCC.[22] As with surgical resections of the liver, bilirubin levels have been shown to be a reliable predictor of liver function in patients with HCC rupture.[19] Multiple studies have shown that a bilirubin level of 2.9 mg/dL or lower was predictive of improved survival in patients with ruptured HCC and is used as a reasonable cut-off for predicting successful TAE outcomes.[23-25] Less frequent complications of TAE include post-embolization syndrome, abscess, and re-bleeding.[14] Re-bleeding occurs between seven and 25 percent of patients undergoing TAE and confers a significantly worse prognosis.[24]

Surgical resection can occur in either a staged fashion as definitive treatment following conservative management or TAE, or as an initial treatment to achieve hemostasis of a ruptured HCC. As expected, emergency resection is complicated by higher inhospital mortality and lower rates of an R0 resection when compared with a staged resection.[14] About half of the hospital mortality associated with emergency liver resection for ruptured HCC is postoperative liver failure.[11] While TAE is still preferred as first-line therapy for hemostasis, emergency resection can potentially provide both hemostatic control and curative resection in a single intervention while reducing the occurrence of peritoneal dissemination of the cancer as seen in a staged resection.[26] Additional surgical interventions include hepatic artery ligation and perihepatic packing, though these are seldom used today. Additionally, intraoperative hemostatic techniques such as hepatic artery clamping or the Pringle maneuver may aid in resuscitative efforts during surgery. Emergency liver resection should be considered a good treatment modality in select stable patients with preserved liver function and an easily accessible tumor.[14]

With regards to transplantation, HCC rupture is not currently an absolute contraindication to transplantation by the Milan criteria. However, the current American Joint Committee on Cancer (AJCC) TNM classification classifies ruptured HCC as a T4 tumor, which would preclude transplantation as a viable treatment option.[27] However, it is not uncommon for small, solitary tumors that have no vascular or biliary involvement to rupture. In fact, a retrospective analysis of patients with T4 HCC lesions showed that patients with ruptured HCC without shock had improved survival compared with patients with nonruptured T4 lesions, indicating that these patients are potentially understaged and may be helped by liver transplantation.[28] On the other hand, the rate of intraperitoneal spread of ruptured HCC has been reported to be as high as 20 percent. Select centers may offer liver transplant in unique cases, but transplant is otherwise not a typical treatment option for these patients.

Prognosis

Ruptured HCC is the third-most common cause of death from HCC worldwide following tumor progression and liver failure.[3] While early studies reported a mortality of 25 to 75 percent from ruptured HCC, more recent studies have shown an overall mortality rate less than 25 percent, with the rate being as low as 1 percent in the setting of a successful hepatic resection.[5,14,30] Left untreated, median survival after ruptured HCC is between one and four months.[31] Among patients treated conservatively without any intervention, 30-day survival is less than 10 percent. Several studies have shown improved overall survival with a staged resection following TAE, mostly owing to the ability to achieve an R0 resection. Compared with emergency resection, which has a three-year survival of 34 percent, staged resection showed a three-year overall survival of 68 percent.[14] Although ruptured HCC is associated with worse survival compared with other HCC, this is confounded by worse baseline patient and tumor characteristics among those patients with a ruptured HCC. Recent studies have shown similar overall survival between ruptured and nonruptured HCC when controlling for these baseline factors.[32]

Conclusion

Ruptured HCC is a life-threatening complication and can be common in certain locales. Treatment consists of immediate resuscitation and stabilization followed by either immediate or staged resection following trans-arterial embolization. Despite its poor prognosis with conservative treatment, long-term survival is achievable in patients with resectable tumors and good underlying liver function. The most optimal treatment approach should be individualized for each patient and based on hemodynamic status, tumor stage, and liver function. Overall, hepatic resection is associated with increased survival and offers curative therapy in select patients.

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