

Surgical Management of Unilobar Budd-Chiari Syndrome Following Orthotopic Liver Transplantation

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Background	Vascular complications are among the most serious complications following orthotopic liver transplantation (OLT). While inflow complications affecting the hepatic artery and the portal vein are well studied, outflow complications involving the hepatic veins and the inferior vena cava (IVC) are relatively uncommon and associated with a wider range of clinical presentations. Additionally, data on these complications and their management in whole liver transplantation is limited compared to split liver transplantations. To date, the gold-standard treatment for vascular complications remains controversial and ranges from an observational approach to re-transplantation with a high rate of morbidity and graft loss. While surgical and interventional radiologic management of inflow complications is widely described, management of outflow complications remains varied depending on the etiology. This report describes a unique graft-saving surgical approach to a liver transplant patient who developed unilobar Budd-Chiari syndrome (BCS).
Summary	Herein we describe a case of de-novo unilobar BCS after hepatic transplantation, which was treated by major hepatic resection. The patient is a 66-year-old male with a history of alcoholic cirrhosis complicated by hepatocellular carcinoma (HCC), for which he underwent OLT from a donor after brain death. Postoperatively, he was noted to have persistent fever, delirium, agitation, inability to follow commands, and a radiological picture compatible with left lobe graft outflow obstruction involving the left and middle hepatic veins. Attempted interventional radiologic approach and operative thrombectomy were unsuccessful, leading to left hepatectomy. The final pathology of the left lobe was consistent with BCS.
Conclusion	While there have been cases of de-novo BCS after OLT, hepatic resection as a graft rescue therapy for hepatic vein thrombosis has not been described. Given the continued organ shortage, every possible attempt should be made to preserve each donor allograft. Here we present the first such case of major hepatectomy as graft salvage following unilateral BCS.
Key Words	Budd-Chiari syndrome; hepatic vein thrombosis; orthotopic liver transplant; hepatic resection; left hepatectomy

DISCLOSURE STATEMENT:

The authors have no conflicts of interest to disclose.

FUNDING/SUPPORT:

The authors have no relevant financial relationships or in-kind support to disclose.

RECEIVED: July 18, 2020

REVISION RECEIVED: October 30, 2020

ACCEPTED FOR PUBLICATION: November 24, 2020

To Cite: Rahman U, Bevilacqua LA, Shaheen O, Bodzin AS, Frank AM, Maley WR. Surgical Management of Unilobar Budd-Chiari Syndrome Following Orthotopic Liver Transplantation. *ACS Case Reviews in Surgery*. 2022;3(6):51-56.

Case Description

The patient is a 66-year-old male with a history of alcoholic cirrhosis complicated by hepatocellular carcinoma (HCC), who presented in December 2019 to our center for liver transplantation after a suitable donor was identified. The donor liver had a short supra-hepatic vena cava related to cardiac procurement, ultimately requiring closure with a running polypropylene suture instead of a vascular stapler. The graft was implanted utilizing a side-to-side cavocavostomy with a partial caval clamp per our center's standard technique. The remainder of the case was completed without untoward event, with three units of packed red blood cells and four units of fresh frozen plasma transfused in total.

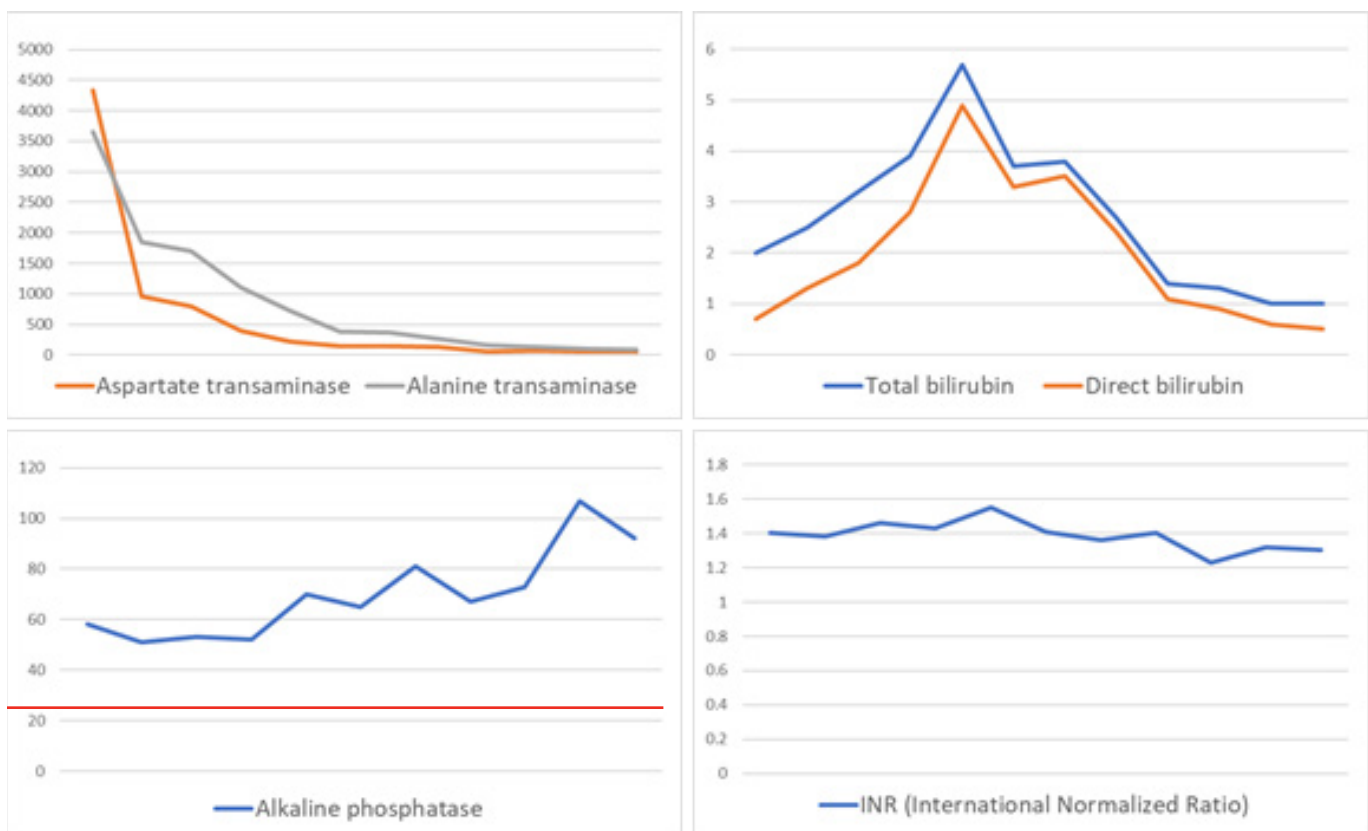
Postoperatively, the patient was transferred to the ICU intubated. His first posttransplant Doppler ultrasound on postoperative day (POD) 1 was unremarkable. Initially, he remained agitated and febrile postoperatively, despite broad-spectrum antibiotics and required vasopressor support. Of note, his transaminases peaked over 3,500 IU/L

but came down over the first week (Figure 1). An extensive evaluation for infectious and neurologic etiology was performed and negative. His mental status was attributed to multifactorial delirium.

With this clinical status, a CT scan with contrast was obtained on POD 7, which demonstrated left-sided unilobar swelling and possible occlusion of the left and middle hepatic veins, consistent with findings of reversal of flow in the left portal vein. Given these findings, retrograde venography was pursued with interventional radiology (IR) but was unable to access the left and middle hepatic veins despite multiple maneuvers. Biopsy of the left hepatic lobe showed Zone 2 and 3 hepatocyte necrosis and mild acute cellular rejection, for which the patient was treated with steroids.

The patient continued to be agitated and intermittently unresponsive to commands despite extensive negative infectious and neurologic workup. Additionally, he had multiple failed attempts at extubation, ultimately requiring tracheostomy placement. CT abdomen/pelvis was

Figure 1. Trend of Liver Function Tests Post-OLT. Published with Permission



repeated, which re-demonstrated the previously noted stable hypoattenuation of the left lobe and non-opacification of the middle and left hepatic veins (Figure 2).

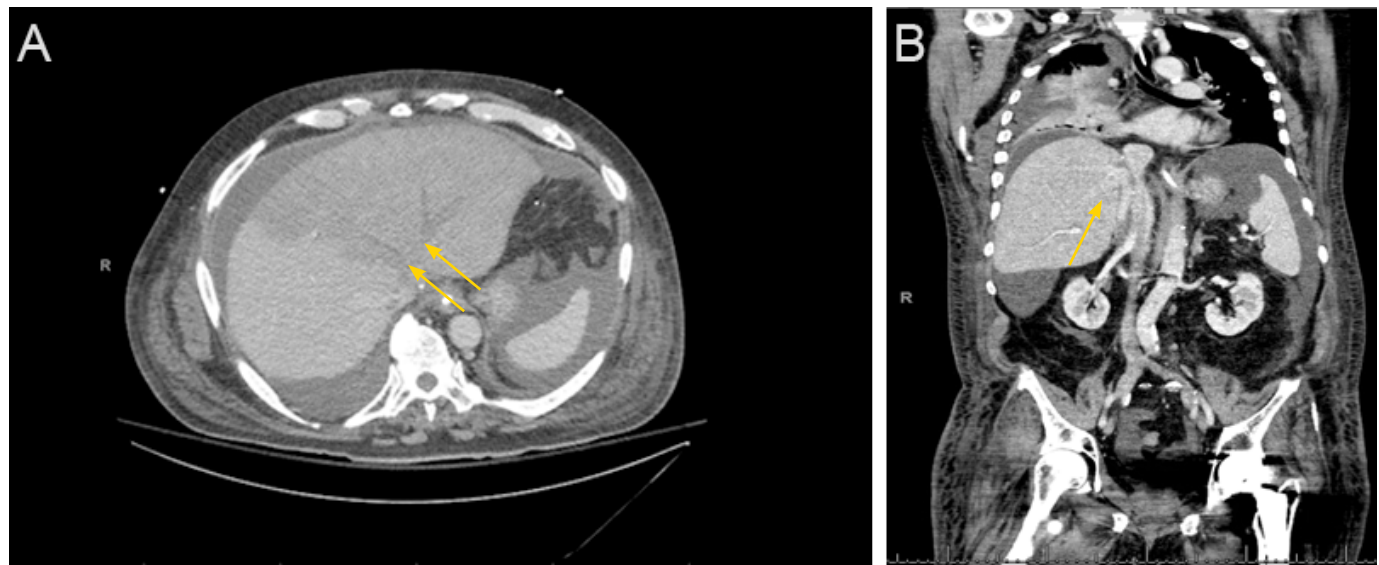
Given these image findings and failed IR thrombectomy, the decision was made to return to the operating room to perform surgical hepatic vein thrombectomy or salvage left hepatectomy. Intraoperatively, the left lobe of the liver was more edematous compared to the right, with large volume ascites present upon entry. The left and middle hepatic veins were dissected to achieve proximal and distal control. A repair suture from the initial transplant was seen and appeared to have potentially narrowed the confluence of the veins. An embolectomy catheter was passed retrograde into the hepatic veins via a venotomy with a large clot burden removed; however, no outflow was present after clot evacuation. Given the findings, a decision was made to proceed with left hepatectomy.

The final pathology of the explanted left lobe was consistent with Budd-Chiari syndrome showing central vein thrombosis with zone 3 necrosis and hepatocytes dropout, and moderate acute cellular rejection with the progression of rejection activity index from 4 to 6. Post-resection, he was weaned from the ventilator and was fully alert and oriented. A follow-up ultrasound and CT scan showed patent vessels with normal waveforms, and he was eventually discharged to acute rehab.

Discussion

The incidence of vascular complications after liver transplantation is approximately 7%, and they may severely compromise graft function and patient survival if not managed expeditiously.¹⁶ Arterial complications, such as hepatic artery thrombosis, are more common (5-10%) than venous complications, with an incidence of venous complications estimated to be around 3% (portal vein

Figure 2. CT Scans. Published with Permission



A) Axial CT showing hypoattenuation and increased periportal edema in left lobe of liver, and nonopacification of middle and left hepatic veins (arrows); and B) coronal CT showing patency of the right hepatic vein and inferior vena cava (arrow).

Figure 3. Sequence of Events. Published with Permission



1-3% and caval <2%).^{16,19,20} Occlusions from cavocaval thrombosis or stenosis are less frequent, and hepatic vein thrombosis is rare in adult patients undergoing OLT.^{9,12,16-18} Hepatic venous outflow obstruction (HVOO) may occur due to venous thrombosis, stenosis of suprahepatic IVC, or compression of vessels from a large graft, fluid collection or hematoma. As a result of obstruction, the sinusoidal pressure becomes elevated, causing hepatic congestion and ischemic injury leading to Budd-Chiari syndrome (BCS), as seen in our patient. Subsequently, centrilobular fibrosis and nodular regenerative hyperplasia occur when all hepatic veins are involved, leading to liver dysfunction and eventual cirrhosis.¹ Some studies also suggest that a hypercoagulable state that may ensue after OLT can contribute to vascular thromboses.^{30,31} Regardless of the etiology, HVOO can cause severe allograft dysfunction and affect graft and patient survival. Therefore, timely diagnosis and management are required to prevent allograft loss.

Our patient's symptoms posttransplant were congruent with the usual symptoms of HVOO described in the literature. Patients with HVOO typically present with poor clinical status, abdominal ascites, and pleural effusion, which may cause respiratory complications.^{9,13} Doppler ultrasound is commonly used for the initial evaluation of hepatic vasculature after a liver transplant.¹⁴ Contrast-enhanced CT scan should be considered if ultrasound suggests venous outflow obstruction. With advances in endovascular intervention, most of these complications, particularly in living donor liver transplantation, are successfully managed with catheter-based thrombolytic therapy, balloon angioplasty, and stenting. Various studies have demonstrated the safety and efficacy of these interventions in HVOO occurring in living donor liver transplantations.^{35,36} Therefore, surgical intervention is less frequently needed to manage these vascular complications.¹⁶ Surgical treatment of venous outflow obstruction is limited to reconstruction of the anastomosis, creation of an additional anastomosis, or re-transplantation. One such technique to resolve acute or peri-operative BCS in the graft is to create an end-to-side cavocaval anastomosis between the graft infra-hepatic caval end and the recipient supra-renal caval trunk, in addition to the preexisting piggyback anastomosis.^{32,34} There have also been case reports of venous outflow obstruction in piggyback technique (PBT) grafts rescued by creating a side-to-side caval anastomosis.³³

The conventional bicaval technique of OLT involves hepatectomy of the native liver along with the retro-hepatic IVC, which requires cross-clamping of the IVC and some-

times venovenous bypass. The introduction of the PBT allowed the preservation of the recipient vena cava and direct anastomosis of the donor's vena cava with the recipient's hepatic veins. PBT obviated the need for a venovenous bypass but is associated with an increased risk of venous outflow obstruction (VOO).²⁴ This risk can be reduced by using the common orifice of all three hepatic veins for PBT anastomosis instead of using two hepatic veins (right and middle or left and middle).^{28,29} The increased risk of VOO with PBT is usually secondary to twisting or kinking of the anastomosis or due to the smaller caliber anastomosis between donor cava and recipient's hepatic veins.²⁵ The modified PBT, in which a side-to-side caval anastomosis is performed under partial caval clamping, has been shown to reduce the risk of VOO.²⁶ Studies have reported decreased rates of vascular complications, including BCS, with the side-to-side or an end-to-side cavocavostomy.^{25,27}

Literature on BCS after OLT is generally limited, specifically with hepatic vein thrombosis as the etiology. Karim et al. describe a case of BCS that occurred after OLT in an adult patient, secondary to IVC thrombus and supra-hepatic stenosis.⁸ The patient required percutaneous intervention with stenting after failing medical management with diuretics and anticoagulation, which mirrors other cases reported in the literature. Aucejo et al. report three cases of unilateral BCS secondary to isolated right hepatic vein obstruction after OLT using the piggyback technique for caval anastomosis.²³ All of these cases were managed endovascularly with angioplasty or stenting. Two of these grafts had short supra-hepatic cava.

Based on the literature and timing of the HVOO in our patient, the complication was most likely caused by technical factors.¹⁵⁻¹⁸ We used a side-to-side cavocavostomy associated with fewer anastomotic complications than an end-to-end cavocavostomy.¹⁸ However, the short supra-hepatic donor IVC, combined with perhaps hemostatic sutures placed after reperfusion, likely led to a stenotic left and middle vein outflow and/or thrombosis. Therefore, a bicaval anastomosis technique could have potentially avoided this complication. Alternatively, a donor vein graft for suprahepatic IVC reconstruction might have been used to avoid constricting the area near the hepatic vein orifices. To avoid this scenario, the suprahepatic IVC is usually cut approximately 2 to 2.5 cm above the level of the diaphragm to allow for an adequate suprahepatic IVC cuff to sew or close, depending on the implant method assuming the heart is being procured for transplant. During heart-liver procurements ensuring adequate IVC length for both

organs poses a challenge, as discussed by Waits et al.³⁷ If the heart is not being procured, it should be cut at the level of the right atrium. Ultimately, prompt surgical intervention after IR failed thrombectomy, instead of awaiting biopsy results and repeat CT scan, could have increased the likelihood of salvaging the whole liver allograft.

Literature on hepatic resection for hepatic vein thrombosis after OLT is scarce. The documented cases of hepatic resection in transplanted livers are in the setting of hepatic artery thrombosis, biliary stricture causing recurrent cholangitis, ischemic necrosis, and recurrent hepatocellular carcinoma.^{21,22} The rarity of Budd-Chiari syndrome secondary to hepatic vein thrombosis after OLT and with subsequent major hepatic resection makes this case unique.

Conclusion

There is a large volume of literature on orthotopic liver transplant as a treatment for Budd-Chiari syndrome; however, reports of de-novo unilateral BCS are scarce, especially left-sided. Depending on the severity, BCS after OLT can be managed with diuretics, anticoagulation, endovascular approaches, and in rare cases, more definitive treatment with hepatic resection may be required.

Lessons Learned

Venous outflow obstruction in a transplanted liver is not a common complication; however, it may severely threaten graft and patient survival if not diagnosed and treated promptly. Hepatic resection should be considered a definitive treatment option for graft salvage when endovascular interventions are unsuccessful.

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