Module: Cachexia, Anorexia, Asthenia (Wasting Syndromes)

Learning Objectives

Attitudes

- Recognize the multifactorial nature of wasting syndromes in regards to pathophysiology and treatment options.
- Awareness that wasting cannot always be reversed by meeting caloric goals or supplementing nutrition.
- Recognize Cachexia, sarcopenia ,anorexia, and asthenia impact clinical outcomes such as QoL (Quality of Life) and may limit therapeutic options, including surgery.

Knowledge

- Review the non-pharmcological and pharmcological interventions for wasting syndromes
- Enumerate common factors contributing towards wasting syndromes
- Describe clinical outcomes affected by wasting syndromes

Skills

- Construct a multidisciplinary approach targeting factors which contribute towards wasting syndrome
- Develop an individualized care plan for patients with wasting syndromes.
- Consider use of artifical nutrition in terms of risk vs benefit, context

Sudeep Pandey, MD, Egidio Del Fabbro, MD

Module: Cachexia, Anorexia, Asthenia (Wasting Syndromes)

Definitions

Cachexia: A multifactorial syndrome characterized by loss of weight (including muscle, adipose tissue) and often accompanied by anorexia, increased inflammatory markers and fatigue.

Anorexia: Lack of appetite

Asthenia: Weakness.

Sarcopenia: A Loss of muscle mass and function, especially strength and gait speed, primarily associated with aging. Secondary sarcopenia occurs when other conditions are the cause, such as Cancer or Heart failure.

Differential Diagnosis

Cachexia, anorexia, asthenia, frailty and sarcopenia often overlap. The key is to identify the condition, and then manage modifiable contributing causes with a multidisciplinary approach, using pharmacological and non-pharmacological interventions.

Causes

Endocrine abnormalities - Hypothyroidism, Hypogonadism, Adrenal insufficiency
Neurologic and muscular disorders – Dementia, Stroke, Multiple Sclerosis, Myopathies etc.
Congestive heart failure
Chronic obstructive pulmonary disease
Chronic kidney disease
Cancer (solid and hematological malignancies)
Liver disease, including cirrhosis
Chronic Inflammatory state– Infectious, Autoimmune
Medication side effects (e.g. some anti-neoplastic agents)
Lack of support or access to nutrition, care
Uncontrolled symptoms such as nausea, pain, depression, anxiety

The reversibility of these conditions is variable, and the primary disease process may not be curable. In addition, disease-specific therapy may contribute to the problem e.g., anti-neoplastic therapy causing nausea or fatigue.

Key point in evaluating patients with cachexia

Identifying weight loss and/or poor appetite is an important initial step. Weight loss of ≥5% within 6 months is a poor prognostic factor in patients with Cancer, and Heart failure. Patients with poor metabolic reserve are at greater risk e.g., in oncology patients with BMI<20, weight loss of only 2% increases mortality. Identifying Nutrition Impact Symptoms (NIS) contributing to decreased oral intake such as pain, nausea, and depression are often treatable with relatively inexpensive medications. Patients may also benefit from taking conscious control of their meals by scheduling a snack or small calorie dense meal every few hours, ensuring adequate protein intake e.g., 1-1.5 gram /kg/day.

While it is important to address insufficient calorie / protein intake, the wasting syndrome may only be partially modifiable because of metabolic abnormalities such as impaired cellular uptake and intracellular utilization of nutrients. The metabolic dysfunction is usually driven by a cytokine-mediated inflammatory state and will not respond to nutrition supplementation alone.

Treatment

Cachexia is a multifactorial syndrome that require a multidisciplinary, multimodal approach. Since no pharmacological therapies are considered standard of care in the U.S, attention to nutritional intake and physical activity are critical. If resources are available, then co-management of patients with a dietician and a physical therapist is ideal. Psychosocial support, physical therapy, structured exercise programs, and a review of medications are often useful.

Pharmacologic considerations

Medications such as Megestrol and Corticosteroids stimulate appetite and produce weight gain in patients, but do not affect lean body mass, overall quality of life, strength, endurance or enhance survival.

Corticosteroids:

In patients with advanced cancer, appetite, and energy are improved within 2 weeks. Because prolonged use increases side-effects and reduces benefit, patients with limited life expectancy of weeks to months are most appropriate. Adverse effects include insomnia, glucose intolerance, steroid myopathy, and osteoporosis.

Megestrol (Megace):

Exercise caution in patients at risk for thromboembolic events by using a lower dose since this side-effect may be dose dependent. The optimal dose is uncertain, however clinical trials using doses of 480mg to 800 mg/day showed improved appetite and weight gain. Other important endocrine side-effects include adrenal suppression and decreased testosterone.

Cannabinoids (for example dronabinol):

Their evidence for efficacy is limited since higher doses cause side-effects such as dysphoria or delirium, particularly in elderly patients. Dronabinol may improve taste in oncology patients with dysgeusia and reduce chemotherapy induced nausea and vomiting but has not produced weight gain or improved appetite in randomized controlled trials.

Olanzapine

An update of the ASCO guideline for cancer cachexia in 2023, recommended low dose olanzapine (2.5mg daily) based on a RCT showing appetite and weight gain compared to placebo in patients with advanced Lung or GI cancer. All patients were receiving chemotherapy and their olanzapine doses increased to 5mg daily during the 4 days after chemotherapy.

Promising therapeutic agents

Ideally an intervention should improve physical function and/or quality of life in addition to appetite and weight. Newer agents showing promise in improving lean body mass are under investigation but not yet approved in the U.S. Anamorelin, a Ghrelin agonist, approved in Japan, produced an increase in lean body mass in addition to improved appetite and weight gain in patients with Lung cancer. Two placebo controlled phase II trials recently reported improved physical performance in patients with cancer. Ponsegromab, a GDF-15 inhibitor, improved appetite, weight and physical activity, while Espindolol, a non-selective β blocker reversed weight loss, improved fat free mass, and increased strength.

Module: Cachexia, Anorexia, Asthenia (Wasting Syndromes)

Pre/Post Test

Questions

1. Which of the following are not likely to be mechanisms of wasting in Tuberculosis, Cancer, COPD and Heart Failure.
2. Sarcopenia is associated with the following outcomes after surgery
3. Dexamethasone, a commonly used appetite stimulant is shown to:
4. Which of the following interventions for wasting increase the risk of thromboembolism?

Answers

1. Decreased levels of Interleukin 6(IL-6) and growth differentiation factor 15 (GDF-15)
2. Significantly lower survival rates at 1, 3, and 5 years after surgery.
3. Improve both appetite and fatigue in patients with advanced cancer
4. Megestrol acetate

Module: Cachexia, Anorexia, Asthenia (Wasting Syndromes)

Cachexia, Anorexia, Asthenia and Fatigue (Wasting Syndromes) Learner Assessment Form

Content Checklist: Make an "X" if the resident did this without prompting, mark with "✓" if the resident did this only after prompting and leave blank if this was not done.

_____ Can differentiate between terms Cachexia, Anorexia, Asthenia and Sarcopenia.

_____ Able to identify different causes.

_____ Classify reversible and non-reversible causes of Wasting syndrome.

_____ Able to identify Nutrition Impact Symptoms.

_____ Can create a multimodal treatment plan to address the syndrome.

_____ Able to pick a preferred pharmacologic agent based on patients' clinical condition and assessment.

Please provide your overall assessment.

_____ Competent to perform independently

_____ Needs close supervision

_____ Needs basic instruction

NOTES

Module: Cachexia, Anorexia, Asthenia (Wasting Syndromes)

Bibliography

Bruera E, Beattie-Palmer LN. Pharmacologic management of nonpain symptoms in surgical patients. Surg Oncol Clin N Am. 2001 Jan;10(1):89-107. PMID: 11406453.

Del Fabbro E, Dalal S, Bruera E. Symptom control in palliative care--Part II: cachexia/anorexia and fatigue. J Palliat Med. 2006 Apr;9(2):409-21. doi: 10.1089/jpm.2006.9.409. PMID: 16629571.

Dev R, Amano K, Naito T, Del Fabbro E. Anamorelin for the Treatment of Cancer Anorexia-Cachexia Syndrome. Curr Oncol Rep. 2024 Jul;26(7):762-772. doi: 10.1007/s11912-024-01549-y

Fearon KC, Barber MD, Moses AG. The cancer cachexia syndrome. Surg Oncol Clin N Am. 2001 Jan;10(1):109-26. PMID: 11406454.

Groarke JD, Crawford J, Collins SM, Lubaczewski S, Roeland EJ, Naito T, Hendifar AE, Fallon M, Takayama K, Asmis T, Dunne RF, Karahanoglu I, Northcott CA, Harrington MA, Rossulek M, Qiu R, Saxena AR. Ponsegromab for the Treatment of Cancer Cachexia. N Engl J Med. 2024 Sep 14. doi: 10.1056/NEJMoa2409515. PMID: 39282907.

Hallenbeck J. Fast Fact and Concept #010: Tube Feed or Not Tube Feed. 2nd ed. End-of-Life Physician Education Resource Center. Available at: http://www.eperc.mcw.edu/fastFact/ff_010.htm.

Khorasanchi A, Nemani S, Pandey S, Del Fabbro E. Managing Nutrition Impact Symptoms in Cancer Cachexia: A Case Series and Mini Review. Front Nutr. 2022 Mar 3;9:831934. doi: 10.3389/fnut.2022.831934.

Pandey S, Bradley L, Del Fabbro E. Updates in Cancer Cachexia: Clinical Management and Pharmacologic Interventions. *Cancers*. 2024; 16(9):1696. https://doi.org/10.3390/cancers16091696.

Roeland EJ, Bohlke K, Baracos VE, Bruera E, Del Fabbro E, Dixon S, Fallon M, Herrstedt J, Lau H, Platek M, Rugo HS, Schnipper HH, Smith TJ, Tan W, Loprinzi CL. Management of Cancer Cachexia: ASCO Guideline. J Clin Oncol. 2020 Jul 20;38(21):2438-2453. doi: 10.1200/JCO.20.00611

Module: Cachexia, Anorexia, Asthenia (Wasting Syndromes)

Objectives

1. To identify multifactorial nature of wasting syndromes.
2. Acknowledging that cachexia cannot always be reversed by meeting caloric goals or supplementing nutrition.

Teaching Points

- Identifying various likely factors contributing towards wasting syndromes including Nutrition Impact Symptoms (NIS) and their management.
- Develop an individualized care plan for patients identified with wasting syndrome and when to engage palliative care consultant.

Case 1

A 60-year-old man underwent resection of a head and neck carcinoma, followed by radiation and chemotherapy. When he followed up with ENT postoperatively, he complains of sore throat, dry mouth, and difficulty swallowing. He takes Morphine for his pain and reports constipation. He is losing weight despite having a fair appetite. Also, complains of fatigue, tiredness and admits having a depressed mood.

Case 2

A 60-year-old woman with advanced pancreatic cancer is admitted to the surgical service with proximal small bowel obstruction likely secondary to her cancer. She is cachectic and mostly bedridden. She is alert and was able to inform that past several months she has suffered from loss of appetite, and past few weeks even got worse due to nausea. Laboratory examination show an albumin level of 1.2 gm/dl. Given the overall clinical condition, the team assess her as poor operative risk.

Questions

1. In both clinical scenarios identify the possible factors which could be contributing towards cachexia?
2. Categorize the above identified factors into two groups if they are reversible or non-reversible?
3. Consolidating on your future care plans for these patients, you might encounter some questions to which you do not know the answer. Example: What therapeutic options for xerostomia (dry mouth) in patients after head and neck surgery? Identify and discuss how you might pursue them. How much of this care would you as a surgeon be willing to initiate, and where might you want help from someone like a palliative care consultant?
4. Will you consider offering artificial nutrition to the patients in both cases? Contrast the patient where you expect more benefit from artificial nutrition and why?

Editorial Advisory Board: