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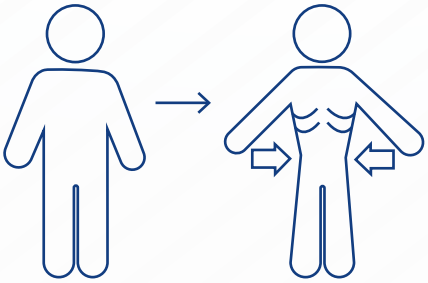
# Cancer Cachexia: Importance of Early Recognition and Intervention

## Insights into pathophysiology, early recognition, diagnostic criteria, and management of cachexia

## Cancer cachexia[1,2,3,4,5]



- Cancer cachexia is a multifactorial syndrome characterized by progressive and unintentional weight loss and muscle atrophy, which diminishes both the quality of life and overall lifespan of patients
- The European Society for Medical Oncology (ESMO) defines cachexia as disease-related malnutrition accompanied by the presence of systemic inflammation

### Prevalence of cachexia

**30%** of all patients with cancer[1]

Patients with breast cancer, sarcoma, leukemia, and Hodgkin lymphoma: **40%**[3]

Patients with colon, lung, and prostate cancer and non-Hodgkin lymphoma: **61%**[3]

Patients with pancreatic and gastric cancer: **87%**[3]

### Clinical impact and disease burden of cancer cachexia

Impaired physical functioning

Increased drug toxicity and decreased chemotherapy efficacy

Higher risk of post-surgical complications

Higher medical costs

**Despite the widespread occurrence of cachexia and international guidelines, challenges regarding its prevention, early identification, intervention, and management persist due to the lack of routine screening for malnutrition and suboptimal integration of nutrition and metabolic care into clinical oncology practice**

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# Pathophysiology of cancer cachexia[1,6,7]

Energy imbalance in the presence of an inflammatory environment causes weight loss and muscle wasting in cachexia. Anorexia-cachexia signaling mediators, such as activin A, myostatin, growth differentiation factor 15, and lipocalin-2, have also been implicated

## Decreased energy intake

Patients with cancer cachexia have a variety of nutritional impact symptoms (NIS) that limit nutrient intake

Certain cancers, such as head and neck cancers or tumors in the gastrointestinal tract, affect energy intake by causing:

- Dysphagia
- Early satiety
- Malabsorption of nutrients

NIS caused by chemotherapy and radiation include:

- Decreased appetite due to altered taste and smell
- Food aversions
- Nausea
- Diarrhea

**Increased energy expenditure and decreased energy intake over time lead to significant weight loss**

**Role of inflammatory cytokines in cachexia[6]**

- Upregulation of catabolic pathways
- Affects the regeneration of skeletal muscle, leading to muscle wasting

## Comparison of the effects of cachexia, anorexia, and sarcopenia[8]

| | Cachexia | Anorexia | Sarcopenia |
|---|---|---|---|
| **Decreased appetite** | Yes | Yes | No |
| **Decreased protein synthesis** | Yes | Yes | Yes |
| **Proteolysis** | Yes | No | Yes |
| **Lipolysis** | Yes | Yes | No |
| **Cytokine excess** | Excessive | Minimal | Mild |
| **Total energy expenditure** | Increased | Decreased | Decreased |

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# Clinical symptoms, diagnostic criteria, and staging of cachexia[3,7,9,10]

## Symptoms of cancer cachexia

### Physical

- Pain/hyperalgesia
- Lack of appetite/anorexia
- Nausea and vomiting
- Early satiety
- Changes in taste and smell
- Fatigue/exhaustion
- Fever and oral mucositis are associated with cancer cachexia
- Muscle wasting

### Psychological

- Anxiety
- Delirium
- Depression
- Drowsiness/ hypersomnia
- Insomnia

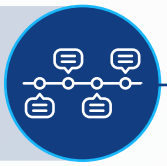
## Barriers to the diagnosis of cachexia

**Several diagnostic criteria are available but not widely used in daily practice for the following reasons:**

- Lack of awareness of cachexia and its diagnosis
- Difficulty in assessing the loss of skeletal muscle mass
- Assessment methods, such as weight and body mass index (BMI), are not suitable for obese patients with sarcopenia and patients with severe edema due to the effects of ascites
- Complexity in the etiology of cachexia and differences in the phenotype and progression rate of cachexia across diseases

**Stages of cachexia are determined according to the clinical characteristics of the patient**

**The risk of progression from one stage to another depends on:**



- Cancer type and stage
- Food intake
- Presence of systemic inflammation
- Physical inactivity
- Poor treatment response or surgical complications

## Clinical criteria for staging of cachexia

### Pre-cachexia

- Patients with minimal weight loss (2%–5%)
- Clinical and metabolic signs predictive of future weight loss are observed

### Cachexia

- Weight loss >5% over the previous six months
  or
- BMI of <20 kg/m$^2$ with ongoing >2% weight loss
  or
- Depletion of muscle mass and >2% weight loss

### Refractory cachexia

- Clinically resistant catabolic state
- Characterized by poor performance status, progressive cancer, and a life expectancy of <3 months

**Cancer stage and goal of treatment (curative vs palliative) are currently not considered for the staging of cachexia**

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## Tools for diagnosing and monitoring cachexia[3,10,11]

**Monitor the change in the body weight to screen patients for skeletal muscle loss**

**Nutrition questionnaires**

- Patient-Generated Subjective Global Assessment
- Mini Nutritional Assessment
- Malnutrition Screening Tool
- Nutritional Risk Screening 2002

**Other methods used to assess body composition in patients with cancer include:**

- Bioelectrical impedance analysis
- Computed tomography
- Magnetic resonance imaging
- Dual-energy X-ray absorptiometry

**Careful evaluation of cachexia is necessary to determine the overall health status of a patient and to optimize treatment decision**

## Management of cancer cachexia[7,10]

ESMO and European Society for Clinical Nutrition and Metabolism guidelines recommend the combination of nutrition, exercise, and pharmacotherapy for effectively managing cancer cachexia

Several studies highlight the benefits of nutritional counseling in cachexia management

Educating patients and caregivers to differentiate between normal weight loss and cachexia-related symptoms is key to improving treatment outcomes and enhancing the quality of life of patients with cancer cachexia

**Healthcare providers should consider discussing these key points with patients and their caregivers for optimal patient care**

- Loss of appetite is common in patients with advanced cancer
- Forcing a patient to eat is usually counterproductive, and can lead to increased nausea/vomiting, decreased social interactions, and increased patient distress
- Consulting a registered dietitian to discuss concerns and challenges related to nutrition, appetite, and meal planning is often recommended

## Key messages

- **Cancer cachexia is a multifactorial syndrome characterized by involuntary loss of weight and skeletal muscle, leading to progressive functional impairment, and is often diagnosed late**
- **Early diagnosis of cachexia enables timely nutritional interventions, improves conditions for chemotherapy or other anticancer therapies, and enhances patient outcomes**
- **Integration of a polymodal treatment strategy and early recognition of cachexia can help optimize aggressive cancer treatment, minimize toxicity, and improve patients' quality of life**


**References:**

1. Law, M. L. (2022). Cancer cachexia: Pathophysiology and association with cancer-related pain. *Frontiers in Pain Research, 3*, 971295.
2. Peixoto da Silva, S., Santos, J. M., Costa e Silva, M. P., Gil da Costa, R. M., & Medeiros, R. (2020). Cancer cachexia and its pathophysiology: links with sarcopenia, anorexia and asthenia. *Journal of Cachexia, Sarcopenia and Muscle, 11*(3), 619–635.
3. Ni, J., & Zhang, L. (2020). Cancer cachexia: definition, staging, and emerging treatments. *Cancer Management and Research*, 5597–5605.
4. Arends, J., Strasser, F., Gonella, S., Solheim, T. S., Madeddu, C., Ravasco, P., ... & ESMO Guidelines Committee. (2021). Cancer cachexia in adult patients: ESMO Clinical Practice Guidelines. *ESMO Open, 6*(3), 100092.
5. Arends, J., Muscaritoli, M., Anker, S., Audisio, R., Barazzoni, R., Bosnjak, S., ... & Aapro, M. (2023). Overcoming barriers to timely recognition and treatment of cancer cachexia: Sharing progress in cancer care task force position paper and call to action. *Critical Reviews in Oncology/Hematology, 185*, 103965.
6. Setiawan, T., Sari, I. N., Wijaya, Y. T., Julianto, N. M., Muhammad, J. A., Lee, H., ... & Kwon, H. Y. (2023). Cancer cachexia: molecular mechanisms and treatment strategies. *Journal of Hematology & Oncology, 16*(1), 54.
7. Nishikawa, H., Goto, M., Fukunishi, S., Asai, A., Nishiguchi, S., & Higuchi, K. (2021). Cancer cachexia: Its mechanism and clinical significance. *International Journal of Molecular Sciences, 22*(16), 8491.
8. Morley, J. E., Anker, S. D., & Evans, W. J. (2009). Cachexia and aging: An update based on the Fourth International Cachexia Meeting. *The Journal of Nutrition, Health and Aging, 13*(1), 47–55.
9. Amano, K., Hopkinson, J. B., Baracos, V. E., & Mori, N. (2023). Holistic multimodal care for patients with cancer cachexia and their family caregivers. *Asia-Pacific Journal of Oncology Nursing, 10*(Suppl 1), 100290.
10. Roeland, E. J., Bohlke, K., Baracos, V. E., Bruera, E., Del Fabbro, E., Dixon, S., ... & Loprinzi, C. L. (2020). Management of cancer cachexia: ASCO guideline. *Journal of Clinical Oncology, 38*(21), 2438–2453.
11. Bruggeman, A. R., Kamal, A. H., LeBlanc, T. W., Ma, J. D., Baracos, V. E., & Roeland, E. J. (2016). Cancer cachexia: Beyond weight loss. *Journal of Oncology Practice, 12*(11), 1163–1171.



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