CANCER CACHEXIA AND SARCOPENIA: NUTRITIONAL STRATEGIES TO PRESERVE MUSCLE MASS AND AUTONOMY

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Abstract

Cancer cachexia and sarcopenia are complex, multifactorial, and highly prevalent syndromes in the oncological context, associated with metabolic, inflammatory, and functional alterations that negatively affect prognosis, treatment response, and quality of life in cancer patients. This chapter aimed to critically analyze the available scientific evidence on these conditions, with emphasis on nutritional strategies focused on preserving muscle mass and functional autonomy.

The study is characterized as a narrative literature review, developed from scientific articles, international consensus statements, and clinical guidelines indexed in the PubMed/MEDLINE, Scopus, Web of Science, and ScienceDirect databases. The analysis shows that muscle loss results from complex systemic mechanisms, including chronic inflammation, anabolic resistance, mitochondrial dysfunction, and increased protein catabolism — and cannot be explained solely by decreased food intake.

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Findings demonstrate a consistent association between muscle loss, decline in strength and functionality, reduced autonomy, and poorer quality of life, regardless of tumor site. Additionally, early assessment of body composition and functionality proved essential for identifying sarcopenia and cachexia, enabling more timely and individualized nutritional interventions.

It is concluded that appropriate nutritional strategies, when implemented early and integrated into a multidisciplinary care model, play a fundamental role in preserving muscle mass, mitigating functional decline, and promoting a more comprehensive, humanized, and evidence-based oncological approach.

Keywords: Cancer cachexia, Sarcopenia, Clinical nutrition, Muscle mass, Nutritional oncology.

INTRODUCTION

Cancer cachexia and sarcopenia are important clinical syndromes associated with cancer, characterized by the progressive loss of skeletal muscle mass, with or without concomitant loss of adipose tissue, exerting a significant negative impact on prognosis, treatment response, and quality of life among oncology patients (Fearon et al., 2011; Baracos et al., 2018). These conditions are linked to increased morbidity and mortality, reduced tolerance to antineoplastic therapies, longer hospital stays, and loss of functional autonomy, representing an increasing challenge in oncological and nutritional clinical practice (Argilés et al., 2014; Muscaritoli et al., 2021).

Cancer cachexia is recognized as a multifactorial metabolic syndrome resulting from the interaction between the tumor, the host's systemic inflammatory response, and profound alterations in energy and protein metabolism, and it is not fully reversible through conventional nutritional support alone (Fearon et al., 2011; Argilés et al., 2019). Sarcopenia, although initially described as an age-related condition, has been widely identified in cancer patients across different age groups and is aggravated by factors such as chronic inflammation, reduced food intake, physical inactivity, and adverse effects of oncological treatments, including chemotherapy and radiotherapy (Prado et al., 2008; Cruz-Jentoft et al., 2019).

Although they have different definitions and diagnostic criteria, cancer cachexia and sarcopenia share similar pathophysiological mechanisms, such as increased muscular protein catabolism, anabolic resistance, mitochondrial dysfunction, and activation of inflammatory pathways mediated by pro-inflammatory cytokines such as tumor necrosis factor-alpha and interleukin-6 (Baracos et al., 2018; Muscaritoli et al., 2021). These mechanisms contribute to accelerated loss of muscle mass and strength, compromising patient functionality and independence.

Given this scenario, the research problem addressed in this chapter focuses on the need to understand and systematize nutritional strategies capable of preventing or attenuating muscle loss, preserving functional autonomy, and improving clinical outcomes in cancer patients affected by cachexia and sarcopenia. Recent evidence indicates that reduced muscle mass should not be interpreted solely as a reflection of inadequate nutritional status, but as an independent prognostic factor associated with lower overall survival and greater treatment-related toxicity (Prado et al., 2016; Daly et al., 2021).

This chapter aims to analyze current scientific evidence and the main nutritional strategies applicable to the management of cancer cachexia and sarcopenia, with emphasis on preserving muscle mass and functional autonomy. The specific objectives include:

(i) describing the main pathophysiological mechanisms involved in the development of these syndromes;

(ii) discussing the importance of nutritional assessment and body composition analysis in oncology;

(iii) presenting evidence regarding nutritional interventions, including protein-energy adequacy, specific nutrients, and nutritional supplementation; and

(iv) highlighting the relevance of an individualized and multidisciplinary approach to cancer patient care (Muscaritoli *et al*., 2017; Arends *et al*., 2021).

The elaboration of this chapter is based on the high prevalence of cachexia and sarcopenia among oncology patients and on the growing body of evidence demonstrating the direct relationship between

muscle mass, functionality, and clinical outcomes. Despite advances in cancer treatment, these syndromes remain frequently underdiagnosed and undertreated, limiting therapeutic effectiveness and compromising patient quality of life (Argilés et al., 2019; Arends et al., 2021). Therefore, the systematization of available scientific knowledge is essential to support evidence-based clinical practice and strengthen the work of nutritionists and physicians in comprehensive oncology care.

From a theoretical standpoint, studies show that systemic inflammation plays a central role in the pathophysiology of cachexia and sarcopenia, promoting an imbalance between muscle protein synthesis and degradation (Baracos et al., 2018). In addition, resistance to the action of insulin and essential amino acids — especially leucine — compromises the muscle anabolic response, even when protein intake appears adequate (Phillips & Martinson, 2019). Recent evidence indicates that early nutritional interventions, combined with strategies that stimulate muscle anabolism, may contribute to preserving lean mass, functionality, and autonomy, reinforcing the importance of an integrated, patient-centered therapeutic approach (Daly et al., 2021; Muscaritoli et al., 2021).

METHODOLOGY

TYPE OF RESEARCH AND STUDY DESIGN

This chapter is characterized as a descriptive, qualitative, and exploratory study, developed from a narrative review of the scientific literature. This methodological approach was adopted because it allows for critical and integrated analysis of different types of evidence, including original studies, systematic reviews, narrative reviews, international consensus statements, and clinical guidelines, enabling a broad and in-depth understanding of cancer cachexia, sarcopenia, and nutritional strategies aimed at preserving muscle mass and functional autonomy in oncology patients.

The choice of a narrative review is justified by the multifactorial complexity of the syndromes addressed, which involve pathophysiological, clinical, nutritional, and functional aspects often investigated through different methodological designs. This type of review enables the integration of

knowledge from diverse scientific approaches, promoting the construction of an interpretative, critical text applicable to clinical practice.

SEARCH STRATEGY AND INFORMATION SOURCES

The literature search was conducted systematically in the PubMed/MEDLINE, Scopus, Web of Science, and ScienceDirect databases, internationally recognized for indexing high-impact scientific journals in the areas of health, nutrition, and oncology. These databases were selected for their breadth, reliability, and academic relevance, ensuring access to updated and methodologically consistent evidence.

Controlled descriptors and keywords in English were used, according to the Medical Subject Headings (MeSH) terms, combined with Boolean operators (“AND” and “OR”). The main search terms included: cancer cachexia, sarcopenia, muscle wasting, oncology nutrition, protein intake, nutritional intervention, and functional decline. Search strategies were adapted to the characteristics of each database to increase sensitivity and relevance of the results.

STUDY SELECTION CRITERIA

Inclusion criteria consisted of scientific articles published predominantly in the last ten years, regardless of methodological design, provided they addressed aspects related to the pathophysiology of cancer cachexia and sarcopenia, body composition assessment, clinical impact of muscle loss, and nutritional interventions in oncology. International consensus statements, clinical guidelines, and classic articles widely cited in the literature were included regardless of publication year due to their scientific relevance.

Study selection occurred in two stages: screening of titles and abstracts, followed by full-text reading of potentially eligible articles.

ANALYSIS TECHNIQUES AND INSTRUMENTS USED

Analysis of the selected studies was performed through critical and interpretative reading, considering methodological aspects, consistency of results, and clinical applicability of the evidence presented. Information extracted from the articles was organized into thematic categories, including: pathophysiological mechanisms of cachexia and sarcopenia, methods of nutritional and body composition assessment, nutritional strategies, and the impact of muscle loss on functionality and autonomy.

Thematic synthesis charts were used to support the analysis, enabling comparison among studies and identification of convergences, divergences, and gaps in scientific knowledge. This process allowed for the construction of an integrated, coherent approach aligned with the most current evidence.

THEORETICAL SAMPLE AND SCIENTIFIC FOUNDATION

The theoretical sample consisted of scientific articles selected according to the established criteria, representing a set of relevant, current, and high-impact evidence in the field of nutrition and oncology. Although not a numerical sample, the rigorous selection of studies allowed the construction of a solid conceptual foundation grounded in literature widely recognized and cited in the international scientific community.

This approach is appropriate for scientific book chapters whose main objective is the critical synthesis of available knowledge, rather than statistical quantification of results, as done in systematic reviews or meta-analyses.

METHODOLOGICAL DISCUSSION

The choice of a narrative review made it possible to address cancer cachexia and sarcopenia comprehensively, integrating pathophysiological, clinical, and nutritional evidence. Considering the multifactorial nature of these syndromes and the heterogeneity of available studies, this design was

adequate to discuss nutritional strategies relevant to clinical practice, respecting the complexity of oncological care.

Furthermore, the use of recognized scientific databases and prioritization of high-impact journals contributed to the reliability of the information presented. Critical literature analysis enabled not only description of findings but also contextualization of the evidence, highlighting clinical implications and reinforcing the importance of individualized and multidisciplinary approaches in managing cachexia and sarcopenia.

RESULTS AND DISCUSSION

PATHOPHYSIOLOGICAL ALTERATIONS ASSOCIATED WITH CANCER CACHEXIA AND SARCOPENIA

The studies analyzed consistently demonstrate that cancer cachexia and sarcopenia are associated with a persistent systemic inflammatory state, characterized by elevated pro-inflammatory cytokines such as tumor necrosis factor-alpha, interleukin-1, and interleukin-6, which play a central role in activating muscle catabolic pathways. These findings show that muscle loss in oncology patients does not result exclusively from reduced food intake, but from profound metabolic alterations induced by tumor–host interactions (Fearon et al., 2011; Argilés et al., 2014; Baracos et al., 2018).

Chronic inflammation promotes activation of the ubiquitin–proteasome system, increasing degradation of myofibrillar proteins and reducing muscle protein synthesis. At the same time, inhibition of anabolic pathways — particularly the mTOR pathway, essential for maintaining skeletal muscle mass — contributes to the progression of cachexia even in the presence of adequate nutritional support (Baracos et al., 2018; Argilés et al., 2019).

Beyond inflammation, hormonal and metabolic alterations such as insulin resistance and reduced activity of anabolic hormones including testosterone and insulin-like growth factor-1 significantly contribute to muscle loss in cancer. Anabolic resistance — the reduced muscle response to amino acid

availability, especially leucine — emerges as a critical factor, reinforcing the need for specific and early nutritional interventions (Muscaritoli et al., 2021; Phillips & Martinson, 2019).

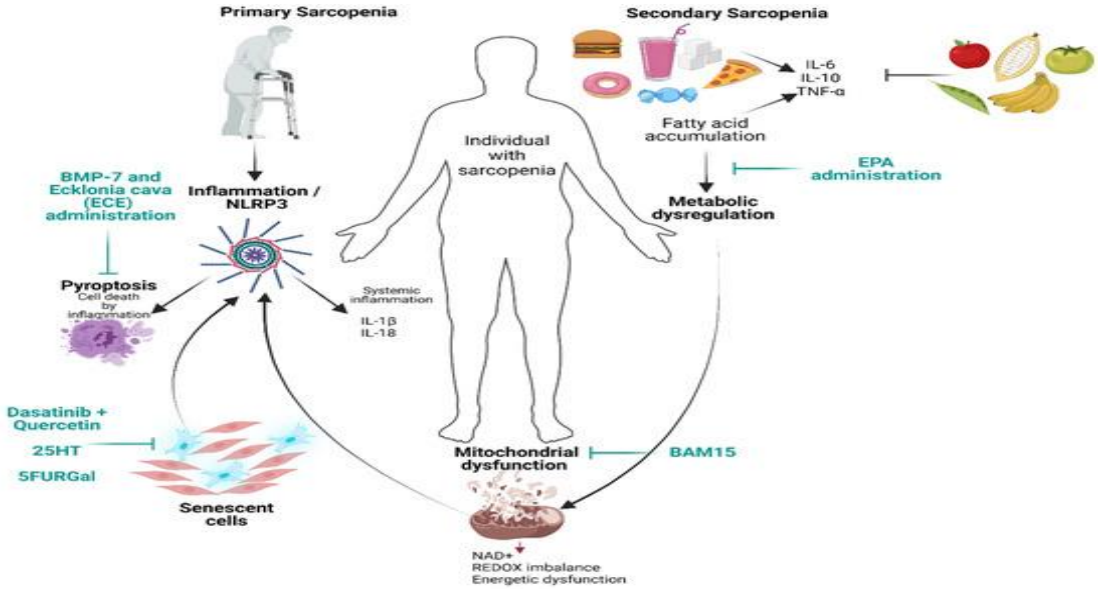
These results show that cancer cachexia and sarcopenia must be understood as complex systemic syndromes in which muscle loss represents only one clinical manifestation of broader metabolic imbalance.

Understanding these pathophysiological mechanisms is essential for guiding integrated, individualized therapeutic strategies capable of attenuating muscle catabolism and improving clinical outcomes (Fearon et al., 2011; Muscaritoli et al., 2021).

The pathophysiological mechanisms underlying cancer cachexia and cancer-associated sarcopenia are outlined in Figure 1.

Figure 1

Pathophysiological mechanisms involved in cancer cachexia and cancer-associated sarcopenia, highlighting systemic inflammation, activation of muscle catabolic pathways, and inhibition of protein synthesis.



Source: Developed by the authors based on Fearon et al. (2011), Argilés et al. (2014), and Baracos et al. (2018).

BODY COMPOSITION ASSESSMENT IN THE ONCOLOGY CONTEXT

The reviewed literature demonstrates that body composition assessment is essential for identifying sarcopenia and cachexia in cancer patients. Studies indicate that traditional anthropometric parameters, such as body mass index, have low sensitivity for detecting muscle loss, especially in overweight or obese individuals — a condition referred to as hidden sarcopenia (Prado et al., 2008; Prado et al., 2016).

Computed tomography, particularly skeletal muscle area analysis at the level of the third lumbar vertebra, is described as the gold standard for assessing muscle mass in oncology. Studies show that this method enables early detection of body composition alterations, even before significant changes in body weight occur, allowing more timely and targeted nutritional interventions (Prado et al., 2009; Baracos et al., 2018).

In addition to tomography, complementary methods such as bioelectrical impedance analysis and functional assessment are highlighted, as long as they are interpreted in an integrated, contextualized manner. These findings reinforce that nutritional assessment in oncology must go beyond isolated parameters and incorporate body composition analysis as a central element for clinical decision-making (Cruz-Jentoft et al., 2019; Arends et al., 2021).

Clinically, early identification of muscle loss has direct implications for treatment, as sarcopenia is associated with greater toxicity to antineoplastic therapy, poorer therapeutic response, and reduced overall survival. Thus, the literature supports routine incorporation of body composition assessment in oncology practice (Prado et al., 2016; Daly et al., 2021).

IMPACT OF MUSCLE LOSS ON FUNCTIONALITY AND AUTONOMY

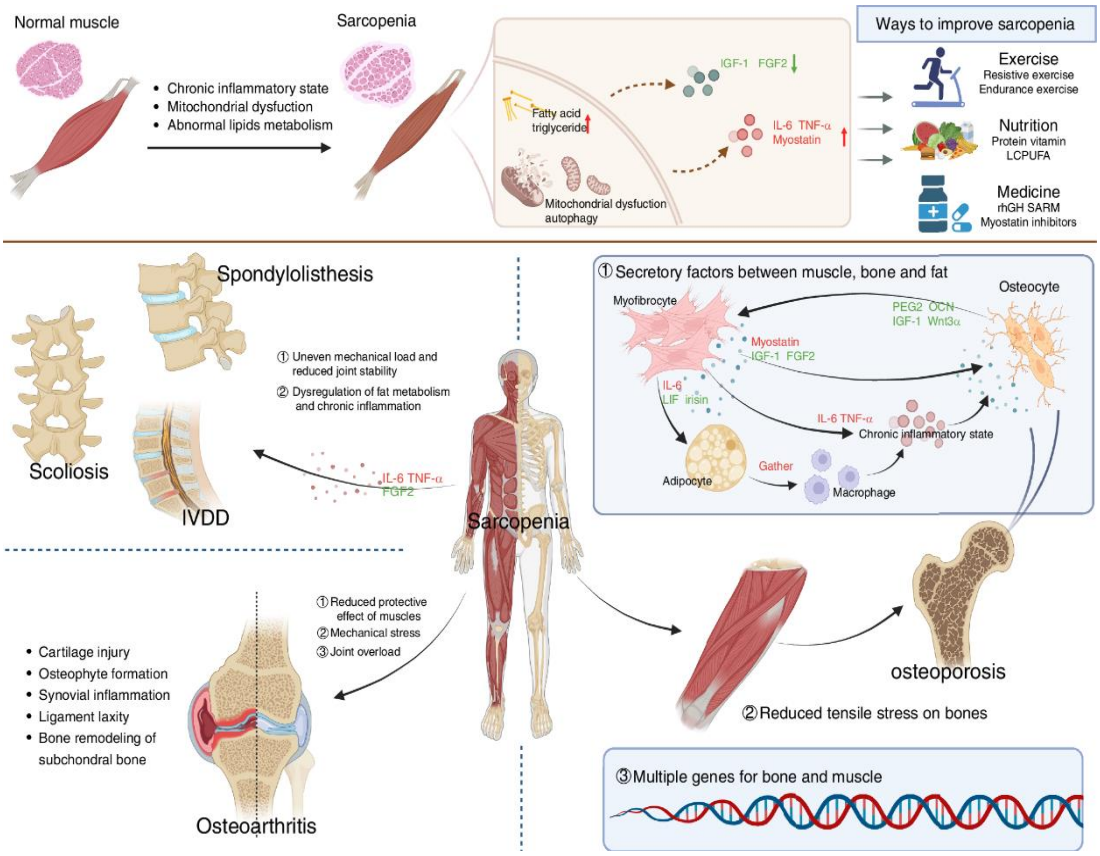
The reviewed literature shows a consistent association between muscle loss and impaired functionality in cancer patients, reflected in reduced muscle strength, increased fatigue, limited mobility, and decreased ability to perform activities of daily living. These findings reinforce that sarcopenia and cancer cachexia extend beyond the nutritional domain, acting as determinants of functional decline

capable of compromising patient autonomy and independence throughout cancer treatment (Cruz-Jentoft et al., 2019; Daly et al., 2021).

The results analyzed demonstrate a consistent relationship between muscle mass loss and functional impairment in cancer patients (Figure 2).

Figure 2

Conceptual representation of the relationship between muscle loss, functional decline, and reduced autonomy, including impacts on mobility, muscle strength, and food-related functions.



Source: Developed by the authors based on Cruz-Jentoft et al. (2019), Daly et al. (2021), and Ferreira et al. (2024).

Beyond locomotor outcomes, recent studies show that muscle loss also affects essential functions related to eating, with direct impact on the safety and efficiency of food intake. Evidence from hospitalized populations indicates that signs suggestive of sarcopenia are significantly associated with dysphagia risk and poorer nutritional status, suggesting that reduced muscle mass and strength

compromise not only mobility but also swallowing function (Wakabayashi, 2014; Nishida et al., 2021; Ferreira et al., 2024).

These findings show that muscle loss should be understood as a central factor in global functional decline, with consequences such as increased dependency, greater risk of clinical complications, prolonged hospitalization, and poorer quality of life. In oncology, these limitations may be intensified by systemic inflammation, treatment side effects, and reduced food intake (Baracos et al., 2018; Muscaritoli et al., 2021).

Thus, strategies aimed at preserving muscle mass should not focus exclusively on improving nutritional parameters or survival but also on maintaining functionality, autonomy, and dignity. An integrated approach to sarcopenia and cancer cachexia — emphasizing prevention of functional decline — reinforces the need for early nutritional interventions and continuous multidisciplinary care, tailored to patients' individual needs (Arends et al., 2017; Muscaritoli et al., 2021).

CONCLUSION

This study shows that cancer cachexia and sarcopenia are complex, multifactorial, and highly prevalent syndromes in oncology, associated with profound metabolic, inflammatory, and functional alterations. Muscle loss emerges as a central factor in this process, directly affecting prognosis, treatment response, functionality, autonomy, and quality of life — reinforcing its early recognition as an important clinical and functional marker.

Early assessment of body composition and functionality, combined with implementation of appropriate and individualized nutritional strategies, is essential for preserving muscle mass and mitigating functional decline, contributing to improved oncology care and a more comprehensive, evidence-based approach.

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