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Review Article

The Connection Between Sarcopenia and Trismus and Their Impact on Survival Outcomes in Curatively Treated Head and Neck Cancer Patients

Efsun Somay[1]*, Erkan Topkan[2], Nilüfer Kılıç Durankus[3], Sibel Bascil[4] and Ugur Selek[3]

[1]Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Baskent University, Ankara, Turkey

[2]Department of Radiation Oncology, School of Medicine, Baskent University, Adana, Turkey

[3]Department of Radiation Oncology, School of Medicine, Koc University, Istanbul, Turkey

[4]Department of Periodontology, Faculty of Dentistry, Baskent University, Ankara, Turkey

***Corresponding Author:** Efsun Somay, Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Baskent University, Ankara, Turkey

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Abstract

Head and neck cancers (HNCs) rank as the ninth most prevalent malignancy on a global scale. These cancers encompass various malignancies from different anatomical sites, including the oral cavity, pharynx, larynx, and paranasal sinuses. Despite significant advancements in treatment methodologies, HNCs continue to represent a critical public health challenge due to their high morbidity and mortality rates. Sarcopenia, characterized by a progressive decline in skeletal muscle mass, strength, and contraction capacity, has emerged as a critical factor influencing the prognosis of individuals diagnosed with HNC. The prevalence of sarcopenia among this patient population ranges from 35.5% to 54.5%. Sarcopenia is increasingly recognized for its association with greater treatment intolerance, reduced survival rates, and diminished quality of life in patients with HNC. Trismus, characterized by a restricted ability to open the mouth, frequently manifests as a long-term complication in patients undergoing treatment for HNC. This condition has the potential to trigger or exacerbate the nutritional and functional challenges associated with sarcopenia. Conversely, sarcopenia can also significantly contribute to the onset or worsening of trismus, primarily due to associated muscle loss and weakness. Sarcopenia and trismus likely have a reciprocal relationship, significantly influencing one another and impacting survival outcomes in patients with HNC. Hence, this review seeks to clarify the intricate relationships between sarcopenia and trismus, and how these conditions influence the survival outcomes of HNCs.

Keywords: Sarcopenia; Trismus; Survival; Head and Neck Cancer

Abbreviations

HNCs: Head and Neck Cancers; RT: Radiotherapy; CCRT: Concurrent Chemotherapy

Introduction

Sarcopenia is derived from the Greek term meaning "scarcity of flesh." In 1988, the term was coined by Rosenberg to describe a clinical condition characterized by a progressive decline in skeletal muscle mass and strength, primarily due to aging [1]. This decline is typically associated with various adverse health outcomes, including increased frailty, risk of falls, and reduced quality of life. The concept of sarcopenia is focused explicitly on skeletal muscle and deliberately excludes other muscle types, including smooth muscle, which is found in the walls of hollow organs; myocardium, the specialized cardiac muscle that composes the heart; and myoepithelium, which is located in specific glandular tissues. A crucial aspect of skeletal muscle physiology is that each skeletal muscle fiber operates as a multinucleated syncytium; this unique structure arises from the fusion of multiple myoblasts during development [2]. As a result of this multinucleation, skeletal muscle fibers lose the ability to undergo mitosis after they have formed. Instead, while they cannot divide, these fibers can undergo hypertrophy, increasing in size and volume in response to stimuli such as resistance training, or they can experience atrophy-leading to a decrease in size-due to factors such as disuse, aging, or certain diseases [2].

Sarcopenia is a significant factor that markedly impacts the prognosis, treatment response, and overall quality of life for patients diagnosed with head and neck cancer (HNC). This condition is characterized by progressive muscle mass and strength loss, often associated with aging and various medical conditions, suggesting a gradual and natural decline over time. Research has shown a notable variation in the prevalence of preoperative sarcopenia among HNC patients, with studies reporting figures ranging from 15.6% to a concerning 79.2% [3]. In a pooled analysis that aggregates data from multiple studies, the overall prevalence of sarcopenia in this population was found to be 37.7% [3].

Apart from age-related primary sarcopenia, which naturally occurs due to the aging process, secondary sarcopenia can also develop as a result of various systemic diseases and conditions that trigger inflammatory responses. Examples of such conditions include malignancies, where tumors secrete proinflammatory substances; neurological disorders that affect muscle innervation; and osteoarthritis, which often leads to chronic pain and decreased physical activity [4]. Research has demonstrated a significant correlation between tumor-induced systemic inflammation and the progression of sarcopenia. This relationship is chiefly mediated by proinflammatory cytokines, particularly interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α). These cytokines play a crucial role in muscle metabolism, as they can induce muscle proteolysis, decreasing muscle mass [5-7]. They may additionally trigger or contribute to metabolic dysfunctions that hinder the body's ability to repair and build muscle tissue. Besides, the presence of these inflammatory cytokines is often associated with clinical symptoms such as anorexia and fatigue, which exacerbate muscle loss and contribute to the development of cachexia, a complex syndrome characterized by weight loss and muscle wasting typically observed in cancer patients [5-7]. Understanding the mechanisms by which these systemic inflammatory responses affect muscle health is essential for developing targeted interventions to prevent and treat sarcopenia, especially in patients with underlying chronic illnesses.

Trismus, a restriction in the ability to fully open the jaws, is often characterized by muscle discomfort, involuntary spasms, or fibrosis. This condition frequently arises as a complication in patients undergoing treatment for HNC, significantly affecting their quality of life. The context of trismus in HNC patients is particularly concerning, as it not only complicates routine functions such as eating, speaking, and dental hygiene but also has profound implications for their overall survival and functional independence. Research indicates that the prevalence of trismus in this population may lead to increased physical discomfort and can hinder effective treatment modalities, ultimately worsening patient outcomes [8,9]. Moreover, trismus may directly threaten the affected patient's life in emergencies, requiring prompt airway maintenance.

Sarcopenia and trismus, two potentially interrelated conditions sharing various pathophysiological mechanisms, may impact each other's development and progression, which may ultimately affect the treatment outcomes in HNC patients. The presence of sarcopenia may hinder a patient's ability to perform jaw exercises or eat adequately, further compounding the effects of trismus. Conversely, limited jaw mobility can lead to difficulties in swallowing and reduced oral intake, contributing to muscle wasting. Therefore, recognizing and addressing sarcopenia and trismus through early screening and interventions such as nutritional support, physical therapy, and resistance training is crucial to optimizing the patient prognosis and quality of life of HNC patients [10]. Considering these facts, this review will focus on the complex pathophysiological connections between sarcopenia and trismus and their individual and combined impacts on the survival of patients with HNC.

Sarcopenia, head and neck cancer and survival

HNCS represent a critical global health challenge, with over 650,000 new diagnoses and approximately 330,000 fatalities each year [11,12]. The prognosis for patients diagnosed with HNC is intricately linked to various factors, including the patient's age, performance status, body weight, the stage of the cancer at the time of diagnosis, and the presence of Human Papillomavirus (HPV) [13]. Additionally, radiologically defined decreased skeletal muscle mass has been associated with unfavorable survival outcomes in cancer patients, marking it as a critical indicator for oncologists [13]. Several studies have rigorously examined the complex relationship between HNC and sarcopenia, revealing alarming insights. A notable study by Stones et al. focused on a cohort of HNC patients and revealed striking disparities in survival rates [14]. Among the 23 patients classified as sarcopenic, only 36.5% survived over 5 years, compared to a more favorable survival rate of 60.5% among the 26 patients without sarcopenia. The researchers employed multivariate analysis, underscoring sarcopenia as a significant negative

predictor of overall survival, with odds ratios indicating a 67% and 62% reduction in survival rates at 2-year (OR = 0.33; 95% confidence interval [CI], 0.14-0.77) and 5-year (OR = 0.38; 95% CI, 0.17-0.84) time points, respectively. In a complementary study, Nagpal., *et al*. [15]. investigated the treatment outcomes in 300 patients suffering from advanced head and neck squamous cell carcinoma. These patients underwent a comprehensive treatment strategy that included a radical radiotherapy (RT) protocol delivering a total dose of 70 Gy over 35 fractions alongside concurrent chemotherapy, namely concurrent chemo-RT (CCRT), spanning seven weeks. The study meticulously assessed how sarcopenia impacted various treatment outcomes, disease-free survival, and toxicity levels experienced by patients. The findings were compelling; sarcopenic patients faced considerably poorer treatment outcomes, as evidenced by lower rates of disease-free survival, higher rates of treatment-related toxicity, and prolonged treatment interruptions.

Systemic inflammation associated with sarcopenia has been shown to impact survival rates in patients with various cancers significantly [16]. For example, a detailed study conducted by Cho et al. involving 221 HNC patients treated with CCRT showed that patients diagnosed with sarcopenia exhibited markedly worse OS and PFS than their non-sarcopenic counterparts [16]. Notably, this adverse effect was more pronounced in patients exhibiting a high neutrophil-to-lymphocyte ratio, a well-recognized marker of systemic inflammation. The authors of the study asserted that sarcopenia could critically influence treatment tolerance, potentially leading to increased rates of treatment-related toxicity. This assertion is especially relevant for patients undergoing CCRT, as both sarcopenia and systemic inflammation may compromise the body's ability to withstand the rigorous demands of the aggressive CCRT, thereby impacting the overall effectiveness and safety of the therapeutic regimen. In this context, the direct effects of tumor-derived factors on muscle tissue have been extensively investigated in preclinical models, focusing primarily on the mechanisms of tumor-induced systemic inflammation and altered metabolism. These studies provide critical insights into how tumors can negatively impact muscle health and function, lending support to the hypothesis that the presence of tumors may lead to muscle wasting and weakness [17,18]. In particular, various types of cancer have been shown to enhance the upregulation of pro-inflammatory cytokines, such as interleukin-6 (IL-6), tumor necrosis factor-alpha (TNFα), and interferon-gamma. These cytokines play a significant role in the inflammatory response associated with cancer. Notably, many of these molecules are known to be anorexigenic, meaning they can suppress appetite and are proteolytic, leading to muscle protein breakdown. This dual action of promoting inflammation while contributing to muscle degradation helps to explain the muscle loss observed in cancer patients, ultimately impacting their quality of life and treatment outcomes.

For patients diagnosed with malignant tumors, the issues of weight loss and malnutrition are prevalent challenges that significantly affect individuals at every stage of cancer. These factors complicate treatment efforts and adversely influence overall prognosis [3]. As such, it becomes imperative in clinical practice to consider a multifaceted approach encompassing tumor progression, antitumor therapy types (such as chemotherapy or RT), individual nutritional assessments, and comprehensive supportive therapies. The relationship between sarcopenia and survival rates in cancer patients is complex and involves various biological, nutritional, and treatment-related factors that are still under active research. In particular, patients with HNC frequently encounter substantial difficulties in eating and swallowing as a result of tumor-related complications, such as obstruction of the esophagus, pain, and dysphagia. These challenges lead to significant nutritional deficiencies, which further exacerbate muscle wasting and contribute to a decline in physical function, namely sarcopenia [19]. Malnutrition impacts the body profoundly: it diminishes muscle mass and weakens the immune system's ability to combat infections. This impaired immunity can complicate recovery from aggressive treatments, including surgical interventions, RT, or chemotherapy. As a result, patients may experience prolonged hospital stays and an increased risk of postoperative complications, such as infections or delayed healing.

Sarcopenia is often intricately linked with cachexia, a more severe syndrome marked by significant weight loss and muscle wasting that frequently occurs in the advanced stages of cancer. In individuals with HNC, the presence of cachexia accelerates the depletion of muscle mass and functional capacity, contributing to a decline in both performance status and survival outcomes [20]. Furthermore, patients suffering from sarcopenia may face poorer outcomes following surgical procedures, including extended recovery periods and an elevated incidence of complications. Sarcopenia can also hinder the timely initiation of adjuvant treatments, such as chemotherapy or radiation, which are critical for prolonging survival. Delays in treatment not only compromise immediate therapeutic effectiveness but may also impact long-term survival rates, underscoring the importance of addressing nutritional health and muscle preservation in the management of cancer patients [21].

In conclusion, sarcopenia represents a significant factor influencing survival outcomes in patients diagnosed with HNC. This

condition arises from a complex interplay of multiple factors, including nutritional deficiencies due to reduced oral intake, adverse effects of cancer treatments, functional impairments, systemic inflammation, immune suppression, and metabolic dysregulation. Nutritional deficiencies often occur as patients struggle with dysphagia (difficulty swallowing) or loss of appetite, leading to unintended weight loss and muscle depletion. Impaired treatment tolerance may stem from a reduced physiological reserve, limiting patients' ability to endure aggressive modalities such as chemotherapy and RT. Additionally, decreased functional capacity can hinder daily activities and adversely impact quality of life. Systemic inflammation, a common feature in cancer patients, can further exacerbate muscle loss by promoting catabolic processes that outpace muscle synthesis. Immune suppression may compromise patients' ability to fight infections, complicating their treatment regimen and recovery. Moreover, metabolic dysregulation can lead to altered energy expenditure and an imbalance in nutrient utilization, contributing to the progression of sarcopenia. Early intervention is critical; addressing sarcopenia can be achieved through individualized nutritional support, tailored exercise programs, and potential pharmacological treatments for muscle preservation. Such strategies improve patient outcomes and enhance their ability to undergo and tolerate cancer treatments, ultimately leading to better survival rates. Consequently, identifying patients with sarcopenia-particularly those who exhibit signs of systemic inflammation-can be a vital step in stratifying risk and providing targeted interventions for individuals at an elevated risk of poor survival outcomes (Figure 1). By doing so, healthcare providers can optimize treatment approaches and improve the overall prognosis for patients with HNC.

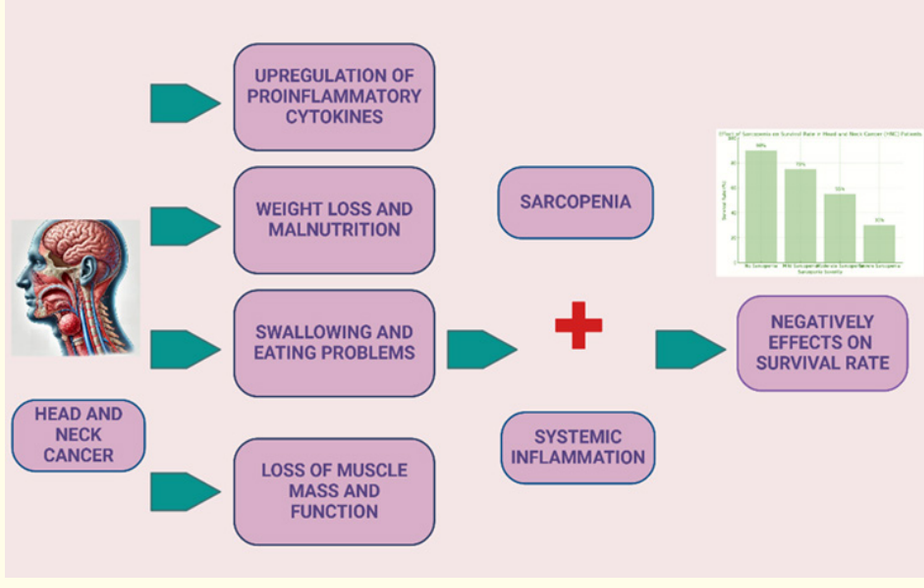

Figure 1: The potential effect of sarcopenia on survival of head and neck cancer patients.

Trismus, head and neck cancer and survival

Despite significant advancements in oncological treatments, such as intensity-modulated RT (IMRT) and volumetric-modulated arc therapy (VMAT), as well as rehabilitation strategies that incorporate prophylactic swallowing exercises and jaw-opening exercises designed to mitigate functional complications related to both the tumor and its treatment, the occurrence of adverse side effects remains a concern [22]. instance, trismus-a condition characterized by restricted mouth opening-affects an estimated 28% to 42% of HNC patients who undergo RT or C-CRT [23,24]. Several risk factors have been identified in the literature contributing to trismus's onset. These include pre-treatment measurements of mouth opening, the clinical T stage of the tumor, the volumetric dose of radiation received by the masticatory apparatus, and the levels of inflammatory biomarkers in the patient. Recently, there has been increasing recognition of sarcopenia emerging as a significant risk factor for trismus in these patients [9,25-27]. Understanding the interplay of sarcopenia and trismus is crucial for developing effective prevention and management strategies to improve the quality of life for individuals undergoing treatment for HNCs.

Sarcopenia is primarily driven by systemic inflammation and the excessive release of cytokines, often referred to as cytokine storms [28]. In patients with HNC, assessing sarcopenia is critical for un-

derstanding their nutritional status and overall health outcomes. This evaluation frequently involves imaging-based studies that measure the skeletal muscle index, which is calculated by dividing the cross-sectional area of skeletal muscle at specific anatomical levels, such as the cervical (C3) or lumbar (L3) vertebrae, by the square of the individual's height in meters [28,29]. Recent research has shifted some focus toward the masseter muscle, a vital player in the process of mastication. In addition to its role in chewing, the masseter muscle serves as an indicator of sarcopenia due to its significance in oral function and nutrition [30]. A decrease in masseter muscle volume can reduce mastication efficiency, potentially leading to difficulties in proper food intake and consequently increasing the risk of malnutrition [30]. Furthermore, disuse of the masseter muscle and other masticatory muscles can lead to muscular atrophy, which results in a reduction of muscle volume and strength. This muscular degeneration may manifest as varying degrees of difficulty in open mouth fully. As a result, individuals may experience heightened vulnerability to developing trismus, further complicating their ability to eat and maintain adequate nutrition (Figure 2).

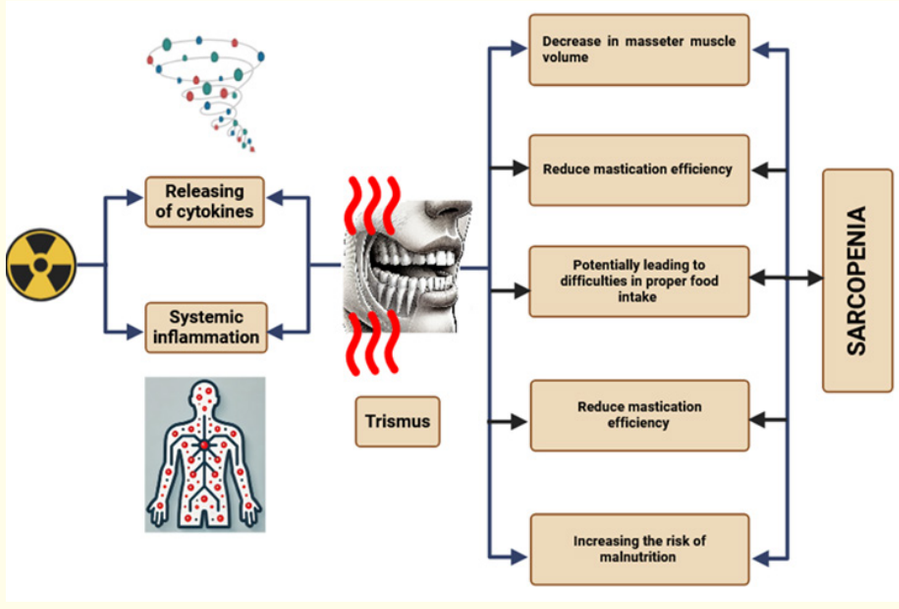

Figure 2: The potential effect of trismus on sarcopenia.

While the precise relationship between sarcopenia and trismus remains to be fully defined, researchers have sought to articulate the potential mechanisms linking these two complications. A primary focus has been on the physiological processes involved, particularly the significant loss of muscle mass associated with cancer cachexia, as well as treatment-related side effects, such as radiation-induced fibrosis and specific pathophysiologic mechanisms of trismus development. Recent studies suggest that the loss of skeletal muscle could trigger the production and release of pro-inflammatory cytokines, including interleukin (IL)-1 and IL-6, alongside adipokines such as leptin and tumor necrosis factor-alpha (TNF-α). These inflammatory agents may substantially exacerbate both sarcopenia and trismus, contributing to their interconnected nature [31,32]. For example, a pivotal study conducted by Somay et al. investigated whether pretreatment measurements of total masseter muscle volume (TMMV) could serve as a predictive biomarker for radiation-induced trismus (RIT) in patients diagnosed with locally advanced nasopharyngeal carcinoma undergoing C-CRT [9]. The findings indicated that a smaller TMMV before treatment correlates strongly with a higher incidence of RIT in this specific patient group. The authors hypothesized that these results might indicate a progressive state of cancer cachexia within this cohort, characterized by significant muscle atrophy [9]. This weakened muscle mass could, in turn, enhance the risk of developing trismus, thereby initiating a feedback loop, that inflammatory mediators like IL-1, IL-6, and TNF-α drive. In support of this claim, studies have found that cancer-induced cachexia, a condition sharing many features with sarcopenia, and associated pro-inflammatory cytokines may significantly increase radiation-related toxicities such as trismus [33,34]. In the study conducted by Cho et al., it was demonstrated that patients diagnosed with sarcopenia not only faced more frequent interruptions during RT but also exhibited a marked decrease in their tolerance to ongoing treatment [16]. This suggests that sar-

copenic patients are more susceptible to the adverse effects of RT, potentially leading to suboptimal treatment regimens. Moreover, the findings imply that a stratified approach, one that classifies patients based on the presence or absence of sarcopenia, could provide valuable insight, enabling clinicians to identify individuals at a higher risk for experiencing toxicities associated with treatment, while also recognizing those who may better withstand the rigors of therapy [35]. This differentiation could ultimately enhance personalized treatment plans and improve patient outcomes.

In conclusion, significant progress has been achieved in the field of oncology, particularly with the development of advanced treatment modalities such as IIMRT and VMAT. These techniques enhance the precision of radiation delivery, thereby minimizing collateral damage to surrounding healthy tissues. Furthermore, rehabilitative interventions, including prophylactic swallowing exercises and jaw-opening programs, have been implemented to mitigate the risks of post-treatment complications. However, despite these advancements, patients with HNC continue to encounter substantial severe long-term complications, including trismus and sarcopenia, which significantly impair essential daily functions and the overall quality of life. Emerging evidence highlights the significance of sarcopenia as a potential risk factor for trismus, driven by systemic inflammation and cytokine storms. Imaging-based evaluations, including assessments of skeletal muscle index and masseter muscle volume, play a critical role in identifying patients who are at an elevated risk for these complications. Furthermore, the complex interplay between muscle loss, pro-inflammatory cytokines, and treatment-related toxicities underscores the necessity for early detection and stratification of sarcopenic patients to enhance treatment tolerance and outcomes. Future research should prioritize clarifying the precise mechanistic relationship between sarcopenia and trismus while investigating tailored interventions aimed at mitigating the impact of these debilitating conditions in patients with HNC.

Discussion

Clinically, sarcopenia is defined by low muscle strength, reduced muscle quantity, quality, and/or physical performance [36]. It is a condition particularly prevalent among patients with HNC, with studies indicating that approximately 50% of these individuals are afflicted by sarcopenia [37]. This condition significantly heightens their risk of experiencing severe toxicity from chemotherapy or RT, with sarcopenic patients facing double the likelihood of such adverse effects compared to their non-sarcopenic counterparts [37]. Sarcopenia has emerged as a critical determinant of survival outcomes in HNC patients [38]. The link between muscle wasting and decreased survival can be attributed to several interrelated factors, including systemic inflammation, cancer cachexia, and various metabolic dysfunctions that collectively diminish the body's resilience to the toxic effects of cancer treatments. Moreover, patients with sarcopenia often demonstrate a reduced tolerance to RT, which is evidenced by frequent treatment interruptions and an increased incidence of complications, such as mucositis or infections. The literature consistently identifies sarcopenia as a significant negative prognostic factor, adversely impacting both overall survival rates and progression-free survival [39].

Trismus is a serious yet often overlooked complication in HNC patients following oncologic treatment modalities such as surgery, RT, and chemotherapy. Trismus impairs quality of life substantially by disrupting essential functions including eating, speaking, and swallowing, which can lead to malnutrition and social isolation [40]. The underlying mechanisms that contribute to the development of trismus are not fully elucidated; however, it is often reported in conjunction with sarcopenia. This coincidence exacerbates the already challenging nutritional and functional issues faced by HNC patients, thereby contributing to a cycle of declining health. Recent scholarly interest has focused on the masseter muscle, an integral component of the masticatory apparatus that plays a crucial role in the chewing process. Studies indicate that a decrease in masseter muscle volume may serve as a useful biomarker for sarcopenia. Furthermore, this reduction in muscle volume has been linked to an increased risk of developing trismus [41].

Radiation-induced fibrosis is recognized as a primary contributor to trismus. When combined with factors such as muscle disuse and systemic inflammation, it creates a vicious cycle of progressive muscle atrophy that exacerbates trismus and associated morbidities [42]. Swallowing dysfunction is also linked to age-related primary or disease-related secondary muscle atrophy, or sarcopenia, particularly affecting the tongue, geniohyoid, and pharyngeal musculature [43-46]. The reduced tongue volume and strength hinder adequate swallowing due to the decreased ability to propel boluses [47]. The presence of trismus may lead to complications such as difficult intubation, cachexia resulting from significant weight loss, and an increased risk of mortality. Despite advancements in surgical techniques, RT, and systemic treatments, overall survival rates have plateaued, primarily due to disease recurrence. The current 5-year survival rate is approximately 60%, indicating a considerable opportunity to enhance diagnosis, prognosis, and treatment strategies [48]. Trismus, induced by radiation fibrosis [8], can be viewed as a complicating factor in the progression of sarcopenia, which diminishes the chance of a cure. Furthermore, trismus may

significantly impede oral intake, diminish calorie and protein consumption, and complicate dental care and prosthetic rehabilitation. Severe trismus may even obstruct endoscopic or surgical interventions, negatively affecting survival outcomes [9,40,49].

Nutritional issues are highly prevalent among HNC patients, affecting as many as 60% [50]. These problems can lead to significant complications, including trismus and/or odynophagia [50]. In these patients, it is essential to note that mild to moderate local and systemic inflammation, the seventh hallmark of cancer, can further alter physiological functions [51]. This inflammation may impact the immune response and significantly affect the oxygenation and vascularization of skeletal muscles, including the masticatory muscles, further exacerbating the complications [52]. As a result, sarcopenia, paired with the accompanying inflammation, can contribute to the onset of trismus. This cascade of effects not only imposes limitations on oral function but can also accelerate the progression of cachexia, a syndrome characterized by severe weight loss and muscle wasting, particularly in advanced stages of cancer. Ultimately, the interplay of these factors adversely affects patients' survival outcomes and quality of life.

The simultaneous occurrence of sarcopenia and trismus can create a detrimental feedback loop that significantly worsens outcomes for patients diagnosed with HNC. Sarcopenia may predispose patients to trismus by compromising the integrity of the muscles involved in jaw movement. This weakening of muscle function may impair patients' ability to perform essential rehabilitation exercises designed to maintain and improve mandibular mobility, which is crucial for proper eating and speaking. Conversely, trismus can lead to nutritional deficiencies due to difficulty ingesting adequate food. This reduced intake will not only impact overall health but also exacerbate the progression of sarcopenia by limiting essential nutrients that support muscle maintenance and growth. This cyclical relationship between sarcopenia and trismus highlights the complex interplay between these two conditions and emphasizes the critical need for a multidisciplinary approach to treatment. A coordinated care team involving nutritionists, physiotherapists, and oncologists can better address both sarcopenia and trismus, implementing strategies that improve muscle strength and mobility while ensuring patients receive the nutritional support necessary for their recovery

Conclusion

Sarcopenia and trismus are interrelated and serve as significant concerns in patients diagnosed with HNC. Both conditions profoundly impact treatment efficacy, survival outcomes, and quality of life. The pathophysiological mechanisms underlying these conditions are, to a large extent, shared, creating a reciprocal relationship. Sarcopenia may contribute to the onset of trismus by impairing the function of the masticatory muscles. Conversely, trismus can deteriorate sarcopenia by restricting nutritional intake if not addressed in a timely and appropriate manner. Recent research highlights the importance of early detection of sarcopenia, mainly through innovative biomarkers such as masseter muscle volume. Identifying changes in such biomarkers can provide significant prognostic information regarding an individual's overall health status and assist in more accurate risk stratification for related health complications. Moreover, the reciprocal relationship between sarcopenia and trismus underscores the need for a comprehensive, multidisciplinary approach to manage these interconnected disorders effectively. This approach should integrate various components, including tailored nutritional support designed to enhance muscle mass and strength, specialized exercise regimens that focus on resistance training and flexibility, and targeted pharmaceutical treatments to mitigate the progression of both conditions. By adopting a holistic strategy, healthcare professionals can improve patient outcomes and enhance the quality of life for those affected by sarcopenia and trismus. Therefore, future studies should focus on elucidating the intricate molecular pathways that connect sarcopenia with trismus. Such research effort is essential not only for understanding the underlying mechanisms but also for developing advanced preventive, diagnostic, and treatment measures that can precisely handle these conditions in patients battling HNC.

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NA.

Conflict of Interest

The authors declared that they have no conflict of interest.

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