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Review Article

Sarcopenic Obesity: Pathophysiology, Clinical Impact, and Current Strategies for Prevention and Treatment.

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Abstract

Purpose of Review: *Sarcopenic obesity (SO) describes the coexistence of obesity and sarcopenia, two conditions that together amplify the risk of adverse health outcomes. This review draws on the most recent evidence to explore the underlying mechanisms, diagnostic challenges, clinical implications, and emerging treatments for SO.*

Recent findings: *We conducted a comprehensive review of the literature published between 2021 and 2025, focusing on randomized controlled trials, systematic reviews, and consensus guidelines. The global prevalence of SO is rising, driven by ageing populations and increasing obesity rates. Effective management requires resistance training, optimised nutrition, and emerging pharmacological therapies.*

Summary: *Timely identification and a multimodal treatment approach are essential to mitigate the health risks associated with SO.*

Keywords: *Sarcopenic obesity, muscle mass, resistance training, GLP-1 receptor agonists, sarcopenia, obesity treatment, and ageing.*

Introduction

The global burden of obesity and sarcopenia has reached unprecedented levels. According to the World Health Organization, as of 2022, more than one billion individuals globally are classified as obese, with adult obesity prevalence nearly tripling since 1975 (1). Concurrently, the ageing population has contributed to the growing incidence of sarcopenia, a progressive and generalized skeletal muscle disorder characterised by a decline in muscle strength, quantity, and quality, recognized by the European Working Group on Sarcopenia in Older People (EWGSOP2) as a distinct clinical entity (2).

Sarcopenic obesity (SO) is defined by the coexistence of excess adiposity and sarcopenia, combining two metabolic and functional burdens that synergistically heighten the risk of disability, frailty, falls, cardiometabolic disease, and premature mortality (3,4). Evidence suggests a pathophysiological interaction between adipose and muscle tissues that accelerates catabolic processes in both compartments (5). The increasing prevalence of SO has made it a major focus in geriatric, metabolic, and rehabilitation medicine. Although sarcopenia and obesity each have distinct diagnostic criteria, their overlapping clinical

manifestations often lead to underdiagnosis of SO. In clinical practice, patients with SO may present with preserved or even elevated body mass index (BMI), masking the concurrent loss of muscle mass and function. This highlights the inadequacy of BMI as a sole metric for risk stratification and underscores the importance of body composition assessment and functional testing in at-risk populations (6).

The implications of SO extend beyond physical disability. A growing body of literature has linked sarcopenic obesity to impaired glucose metabolism, systemic inflammation, reduced response to physical therapy, diminished vaccine response in older adults, and increased postoperative complications (7–10). In cancer patients, SO has emerged as an independent predictor of chemotherapy toxicity and poor oncologic outcomes (11). Despite its clinical importance, SO remains underrecognized and undertreated, in part due to the absence of universally accepted diagnostic thresholds and limited awareness among healthcare providers. Furthermore, the evidence base for targeted therapies in SO, particularly pharmacologic interventions, remains in its infancy. However, recent advances in exercise science, nutritional biochemistry, and metabolic pharmacology offer promising avenues for intervention.

In this review, we synthesise recent evidence (2021–2025) concerning the pathogenesis, epidemiology, diagnostic strategies, clinical consequences, and current treatment options for sarcopenic obesity. Our goal is to inform clinical decision-making and identify areas for future research in the management of this increasingly prevalent and complex condition.

Literature search

A comprehensive search was performed across multiple databases, including MEDLINE (via PubMed), Embase, Web of Science, and the Cochrane Library, covering recent studies (2021-2025). Search terms included combinations of Sarcopenic obesity, muscle mass, resistance training, GLP-1 receptor agonists, sarcopenia, obesity treatment, and ageing. No restrictions on study design were applied. The search was limited to English-language publications to ensure accessibility of full texts, and reference lists of included articles were manually screened to identify additional relevant studies.

In order to ensure the quality of the included studies, a quality assessment was performed using the Newcastle-Ottawa Scale for cohort studies and the Jadad scale for randomised controlled trials.

Pathophysiology of Sarcopenic Obesity

The pathogenesis of sarcopenic obesity reflects a multifactorial process involving metabolic, inflammatory, hormonal, and neuromuscular mechanisms. It is now well-recognized that adipose tissue is not an inert energy reservoir but an active endocrine organ that secretes cytokines and adipokines capable of influencing muscle metabolism. Conversely, skeletal muscle also produces myokines that modulate systemic energy homeostasis, suggesting a bidirectional cross-talk known as the adipose–muscle axis (12).

In obesity, the chronic low-grade inflammatory milieu is driven by macrophage infiltration of visceral adipose tissue and subsequent release of pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and monocyte chemoattractant protein-1 (MCP-1) (13). These cytokines induce muscle catabolism by activating the ubiquitin-proteasome pathway, impairing insulin signaling, and inhibiting the mTOR pathway responsible for protein synthesis (14). In parallel, obesity-induced insulin resistance diminishes glucose uptake in skeletal muscle, further promoting atrophy and metabolic inflexibility (15).

Aging exacerbates these metabolic disturbances. Sarcopenia is characterized by mitochondrial dysfunction, increased oxidative stress, and reduced satellite cell regenerative capacity in skeletal muscle. These alterations contribute to a progressive decline in muscle quality and contractile function (16). Moreover, physical inactivity, common among individuals with obesity and older adults, leads to disuse atrophy and further diminishment of neuromuscular integrity (17).

Hormonal dysregulation is a core feature of SO. Levels of anabolic hormones such as testosterone, growth hormone (GH), and insulin-like growth factor 1 (IGF-1) decline with age and are often further suppressed in obesity. This creates an anabolic resistance state, in which the muscle becomes less responsive to protein intake and exercise-induced stimuli (18). Leptin resistance and reduced adiponectin levels—both common in obesity—have also been implicated in impairing muscle metabolism and increasing ectopic fat accumulation within muscle fibers (19).

The infiltration of adipose tissue into muscle, termed myosteatosis, not only reduces muscle quality but also contributes to local inflammation and fibrosis. This phenomenon has been associated with poor muscle strength and functional outcomes independent of muscle mass (20). Intramyocellular lipid accumulation further interferes with insulin signaling and mitochondrial function, exacerbating metabolic inflexibility (21).

In summary, sarcopenic obesity arises from a convergence of obesity-related metabolic derangements and age-associated sarcopenia. These factors interact through shared pathways—including inflammation,

hormonal imbalance, and insulin resistance—to produce a phenotype marked by low muscle mass, high fat mass, and diminished physical function. Figure 1 illustrates the interconnected mechanisms underlying this condition.

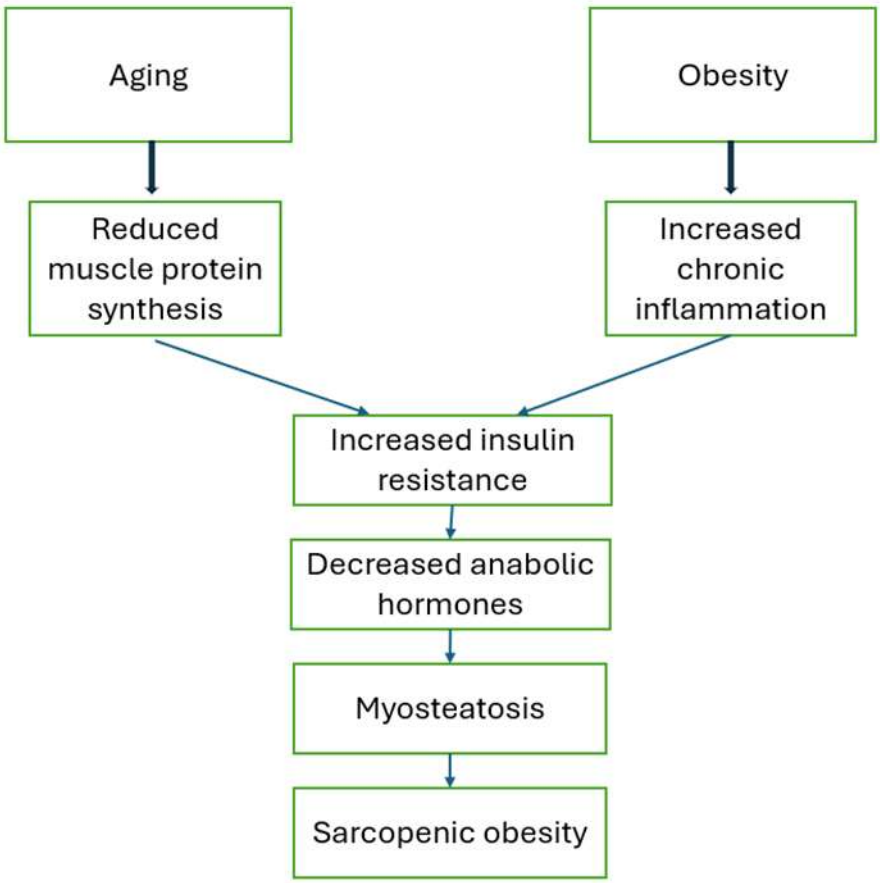

Figure 1: Interconnected mechanisms underlying sarcopenic obesity.

Epidemiology

Estimating the global prevalence of sarcopenic obesity is challenging due to the heterogeneity in diagnostic definitions and criteria used across studies. Prevalence estimates range widely, from approximately 5% to over 20% in community-dwelling older adults, depending on the population studied, sex, ethnicity, and whether sarcopenia is defined by muscle mass, strength, or physical performance (22,23).

A pooled analysis from the Global Burden of Disease (GBD) Study and systematic reviews of community and hospital-based cohorts suggests that sarcopenic obesity is particularly prevalent in older adults with sedentary lifestyles and chronic conditions such as type 2 diabetes, chronic kidney disease, and

cardiovascular disease (24,25). Women tend to have a higher prevalence, possibly due to sex differences in body composition, hormonal decline post-menopause, and greater longevity (26).

Geographically, the prevalence of SO appears to be increasing in both high-income and middle-income countries, mirroring global trends in aging and obesity. Data from the U.S. National Health and Nutrition Examination Survey (NHANES) and the Korean National Health and Nutrition Examination Survey (KNHANES) have both reported rising trends in SO prevalence in the last decade (27,28).

Diagnosis of Sarcopenic Obesity

Diagnosing sarcopenic obesity requires the integration of body composition and functional assessments. While sarcopenia is typically defined by reduced muscle mass and function, obesity is commonly assessed using BMI. However, BMI does not differentiate between lean and fat mass and may therefore underestimate risk in individuals with normal weight but high visceral adiposity (29). More accurate methods include dual-energy X-ray absorptiometry (DXA), which measures appendicular lean mass, and bioelectrical impedance analysis (BIA), which estimates body composition. Functional assessments such as handgrip strength (<27 kg for men and <16 kg for women), gait speed (<0.8 m/s), or the Short Physical Performance Battery (SPPB) are commonly used to assess sarcopenia per EWGSOP2 and AWGS2 guidelines (2,30).

Consensus on diagnostic cutoffs for sarcopenic obesity is still lacking, and this limits the comparability across studies and clinical utility. The SARC-F questionnaire is a practical screening tool, but its sensitivity in detecting SO is modest (31). Importantly, body composition tools must be paired with functional assessment to capture the full syndrome.

Clinical Impact of Sarcopenic Obesity

SO is associated with significantly higher morbidity and mortality than either condition alone. It predicts worse outcomes in terms of falls, fractures, functional dependence, and institutionalisation in older adults (32). In patients undergoing surgery, SO is linked with increased postoperative complications, delayed recovery, and prolonged hospitalisation (33).

The metabolic consequences are equally concerning. SO has been associated with insulin resistance, poor glycemic control, and an elevated risk of developing type 2 diabetes (34). It contributes to systemic

inflammation and oxidative stress, worsening cardiovascular and renal outcomes (35). In oncology, sarcopenic obesity is an independent predictor of chemotherapy toxicity, reduced treatment response, and poor survival in several malignancies, including breast, gastrointestinal, and lung cancers (36). Beyond medical outcomes, SO significantly impairs quality of life, increases healthcare costs, and imposes a major socioeconomic burden through increased disability and reduced workforce participation among aging populations (37).

Medical Treatments for Sarcopenic Obesity

Pharmacological Interventions

Several pharmacological options are being explored to manage SO, though most remain investigational. Testosterone replacement therapy can improve muscle mass and strength in hypogonadal men, but its cardiovascular risk profile limits widespread use (14). Selective androgen receptor modulators (SARMs), such as enobosarm, show promise in increasing lean mass with fewer side effects in early trials, but more data on long-term outcomes are needed (15).

GLP-1 receptor agonists, including semaglutide and tirzepatide, have demonstrated substantial weight loss and metabolic improvement in patients with obesity. Emerging evidence suggests that these agents may also preserve lean mass and improve physical function in selected populations (38). Growth hormone (GH) and insulin-like growth factor-1 (IGF-1) therapies have shown modest benefits but are constrained by adverse effects and cost (16).

Anti-inflammatory agents and myostatin inhibitors are under investigation, aiming to reduce muscle catabolism and improve muscle quality. However, these therapies are still in preclinical or early-phase human trials (18).

Nutritional Pharmacotherapy

Nutritional supplements with anabolic potential include leucine, omega-3 fatty acids, and vitamin D. Leucine and its metabolite HMB (β-hydroxy-β-methylbutyrate) stimulate mTOR signaling and enhance muscle protein synthesis (19). Omega-3 fatty acids exert anti-inflammatory effects and support anabolic signaling pathways (20). Vitamin D supplementation improves strength and physical performance, particularly in deficient individuals (21).

Non-Medical Treatments for Sarcopenic Obesity

Exercise Interventions

Exercise remains the cornerstone of SO treatment. Resistance training is the most effective modality for increasing muscle strength and mass, with evidence supporting benefits in both sarcopenia and obesity (22). Guidelines recommend at least 2–3 sessions per week, incorporating progressive overload principles. Aerobic training contributes to visceral fat reduction and cardiovascular health, while balance and flexibility training reduce fall risk (23).

Multicomponent interventions are superior to single-modality approaches and should be individualized based on baseline function, comorbidities, and preferences (24).

Dietary Strategies

Protein intake should meet or exceed 1.2 g/kg/day in older adults, with even higher targets (up to 1.5 g/kg/day) in those with catabolic conditions (25). Dietary patterns such as the Mediterranean diet, rich in plant-based foods, healthy fats, and antioxidants, have been associated with lower rates of sarcopenia and improved body composition (27). Caloric restriction must be approached cautiously to avoid muscle loss. Combining moderate energy deficits with adequate protein intake and resistance training is the preferred strategy (26).

Behavioral and Lifestyle Interventions

Behavioral approaches including motivational interviewing, self-monitoring, and goal setting can enhance adherence to exercise and nutrition programs. Sleep hygiene, smoking cessation, and stress reduction are additional modifiable factors that influence muscle and metabolic health (28).

Multimodal Approaches

Integrated programs combining exercise, nutrition, and behavioral strategies are more effective than monotherapies. Trials such as the Lifestyle Interventions and Independence for Elders (LIFE) study and the Vivifrail program demonstrate improvements in mobility, body composition, and quality of life (39,40).

Future interventions should be personalized, scalable, and culturally adapted.

Current Challenges and Future Directions

Challenges in SO management include the lack of standardized diagnostic criteria, insufficient awareness among clinicians, and limited high-quality intervention trials. Emerging technologies such as machine learning-based risk prediction, sarcopenia biomarkers, and precision nutrition hold promise for personalized approaches (41). Ongoing trials are evaluating new drug classes, including myostatin inhibitors, AMPK activators, and senolytic compounds. Cross-disciplinary collaboration between geriatricians, endocrinologists, nutritionists, and physiotherapists is essential to advance clinical care and research.

Conclusion

Sarcopenic obesity represents a critical intersection of two pandemics: aging and obesity. It poses serious risks to functional independence, cardiometabolic health, and survival. While our understanding of its pathophysiology has improved, gaps remain in effective and scalable treatments. Clinicians must prioritize early identification and adopt a holistic, evidence-based strategy that integrates lifestyle modification, medical therapy, and multidisciplinary care.

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Author contribution:

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by YS and AA. The first draft of the manuscript was written by MN, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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