Chapter

Sarcopenic Obesity: Focus on the Asian Population

Mukulesh Gupta and Tuhina Gupta

Abstract

Sarcopenic obesity (SO) is a condition observed in older adults, marked by a simultaneous presence of low muscle mass and high body fat mass. The document highlights the complex interplay of aging, hormonal changes, pro-inflammatory pathways, myocellular mechanisms, and oxidative stress as contributors to SO. It discusses the need for a standardized definition, as various criteria have been proposed over the years. The prevalence of SO varies in different populations, and its screening involves assessing body mass index (BMI) or waist circumference along with validated questionnaires. The document emphasizes the importance of accurate diagnostic methods, including measuring muscle mass, strength, and physical performance. The adverse health consequences of SO include increased risk of disability, cardiometabolic abnormalities, fractures, depression, mortality, and reduced quality of life. Lastly, the management of SO involves a multifaceted approach that focuses on gaining muscle mass while losing fat mass, primarily through resistance training, essential amino acid supplementation, dietary protein intake, and other emerging treatments.

Keywords: sarcopenic obesity, short physical performance battery (SPPB), appendicular lean mass, myosteatosis (MS), myofibrosis (MF)

1. Introduction

Normal aging is linked with 1% muscle loss from 30 years of age, which tends to accelerate after 70 years of age. In young adults, lean muscle mass, comprising around 50% of their overall bodyweight, declines to approximately 25% by the time they reach 75–80 years of age. After the age of 40, the rate of muscle loss can be as high as 8% per decade, and it increases to about 15% per decade after the age of 70. Individuals with diabetes experience a more significant reduction in muscle mass compared to others.

Hormones like total testosterone, which improves muscle protein synthesis, decrease by 1% per year, and the levels of dehydroepiandrosterone sulfate, a precursor to testosterone, also reduce with aging. Hyperthyroidism and chronic illness are also linked with muscle loss and reduced physical functioning. Sarcopenia was officially acknowledged as a medical condition in 2016 and was given a specific code in the International Classification of Diseases, tenth revision (ICD-10).

With age, apart from the development and progression of sarcopenia, the occurrence and prevalence of obesity also rise due to unhealthy diet and sedentary lifestyle [1]. The combination of high muscle mass and low fat mass is generally considered as healthy while the reverse as unhealthy. In obese individuals, metabolic change due to sedentary lifestyle, adipose tissue derangement, comorbidities, and so on can result in similar situation. A novel body composition category called sarcopenic obesity (SO) has emerged in recent times, characterized by the simultaneous presence of obesity and sarcopenia, encompassing both muscle mass and function [2]. This condition, also known as sarcopenic obesity, is gaining recognition as a clinical entity due to its substantial impact on patient-centered outcomes. It has multifactorial etiology, and its prevalence increases with age. SO is gaining attention because it is associated with many other age-related diseases that present as altered intercellular communication, dysregulated nutrient sensing, and mitochondrial dysfunction. Older adults identified with low muscle to fat ratio (MFR) have been found to have poor functional performance and high cardiometabolic risk. Higher cholecystectomy incidence is seen to be associated with low muscle mass, low muscle strength, sarcopenia, and sarcopenic obesity. Preliminary results suggest that SO may be associated with telomere shortening and may represent an important risk factor for accelerated aging than sarcopenia and obesity alone. Four body composition phenotypes have been proposed in older populations: normal, sarcopenic, obese, and sarcopenic obese. SO affects around 5–6% of Indian adults annually. SO is more common in older adults than in young adults. Both sarcopenia and obesity may individually cause threat for adverse health outcomes. But when combined, these two conditions can cause health threats that can be synergistically amplified. Studies have shown that SO is a better predictor of physical disability than sarcopenia or obesity alone.

The management of Sarcopenic Obesity involves implementing effective dietary and exercise strategies to counteract the negative outcomes. Additionally, there are various potential and developing treatments for SO, such as pharmacological interventions (including testosterone supplementation, selective androgen receptor modulators, myostatin inhibitors, and anti-obesity drugs), electrical acupuncture, whole-body electro-myo-stimulation, and the use of A2B agonists.

Conclusion: Sarcopenic obesity is emerging as a new and distinct category of obesity across the globe, which is clinically important. A theoretical methodological work (with a special focus on Asian population) aiming at providing practical-application guidelines is proposed.

2. Sarcopenic obesity (SO): an emerging challenge

Sarcopenic obesity is a new category of obesity in older adults who have high adiposity with low muscle mass. With aging, a progressive increase in fat mass, which normally peaks at about age 65 years in men and later in women, is observed. Aging is also associated with body fat distribution changes, visceral abdominal fat increase, and subcutaneous abdominal fat decrease. Moreover, in the elderly, ectopic fat deposition within non-adipose tissue such as the skeletal and cardiac muscle, liver, and pancreas has been observed. This phenomenon occurs even without significant changes in body mass index (BMI) or body weight. However, sarcopenia may arise in individuals with obesity at any age. The presence of obesity can cause a decline in muscle mass and function on its own, primarily because of the detrimental effects of metabolic disorders associated with adipose tissue. These disorders include oxidative

stress, inflammation, insulin resistance, and a higher occurrence of chronic noncommunicable diseases.

2.1 Definition

BMI does not distinguish between fat mass and lean mass. In 2000, Baumgartner introduced the term of sarcopenic obesity (SO), a condition characterized by the coexistence of low muscle mass and a high body fat mass [3]. But it may underestimate sarcopenia in overweight and obese subjects, thus leading to an underdiagnosis of SO. Hence, more definitions of SO have been proposed.

In 2009, the European Working Group on Sarcopenia in Older People (EWGSOP) put forward a clinical definition of sarcopenia to facilitate its identification in older individuals. This definition suggested that sarcopenia should be diagnosed based on the simultaneous presence of two factors: low muscle mass and impaired muscle function, indicated by either low strength and/or low physical performance. The International Working Group on Sarcopenia proposed a similar definition in 2011, based on a low appendicular or whole-body fat-free mass combined with poor physical functioning [4]. In 2014, the Foundation for the National Institutes of Health Sarcopenia Project recommended defining sarcopenia using specific cut points for low lean mass (appendicular lean mass adjusted for BMI: 0.789 for men and 0.512 for women) and for muscle weakness (grip strength: 26 kg for men and 16 kg for women) [5]. However, to date, there is no universally accepted definition or classification for sarcopenia, or for sarcopenic obesity [6]. Studies have shown that SO is a better predictor of physical disability than sarcopenia or obesity alone. In 2022, European Society for Clinical Nutrition and Metabolism (ESPEN) and the European Association for the Study of Obesity (EASO) defined Sarcopenic obesity as the coexistence of obesity and sarcopenia (includes mass and function) [2].

2.2 Etiology and pathogenesis of SO

SO is a result of many complex interrelated mechanisms as mentioned below:

i. *Aging:* Many changes in body composition on aging due to lifestyle and reduced physical activity result in increased accumulation of fat, leading to SO phenotype.

ii. *Hormonal changes:* Hormonal changes that occur with aging result in insulin resistance, reduced thyroid hormone, increased cortisol levels, reduced growth hormones (GH), reduced insulin growth factor I (IGF-I), decreased sex steroids, and so forth, resulting in development of SO phenotype.

iii. *Pro-inflammatory pathways:* Aging results in increased levels of pro-inflammatory cytokines like TNF-α, IL-6, IL-1, and so forth. These inflammatory mediators cause muscle atrophy (increased catabolism) and adipocyte hypertrophy (infiltration of immune cells), both leading to SO.

iv. *Myocellular mechanisms:* One of the important parameter leading to SO is intramyocellular deposition of lipids (IMCLs), which promotes lipogenesis, inflammation, muscle insulin resistance, oxidative stress, and mitochondrial

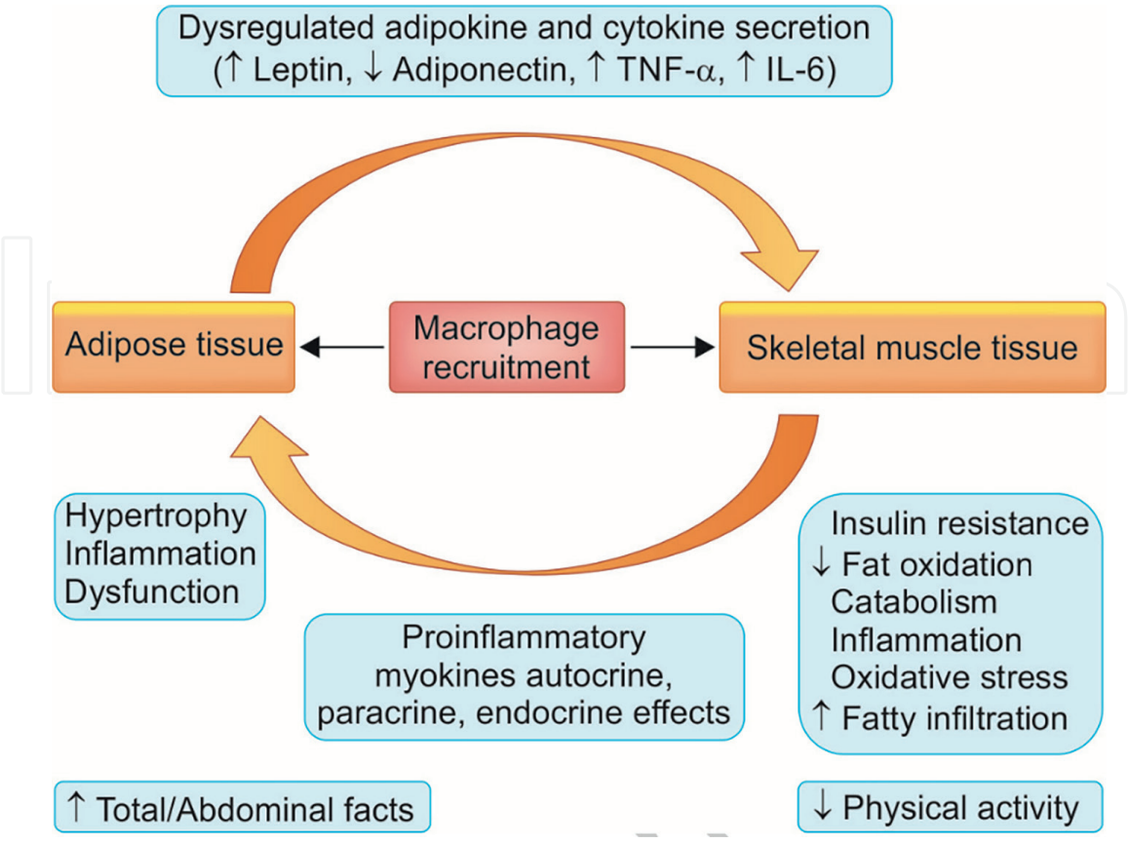

Figure 1.
Pathophysiology leading to Sarcopenic obesity.

dysfunction. This leads to impaired myocyte satellite cells differentiation/proliferation, leading to sarcopenia due to obesity.

v. *Oxidative stress:* Oxidative stress (OS) leads to an accumulation of ROS/RNS, accompanied by cellular damage. OS leads to infiltration of immune cells in the adipose tissue, leading to obesity and IR. OS also causes damage to the myocyte/satellite cells, leading to sarcopenia. Thus, OS can lead to sarcopenic obesity (**Figure 1**).

3. Sarcopenia in Asian populations: a distinct entity

Asian people have been seen to have lower muscle mass, weaker grip strength, slower gait speed, and greater body fat mass with central distribution; however, the intensity of age-associated muscle mass decline in the older Asian population remains comparatively unaltered, but the decline rate in muscle strength or physical performance with aging was more noteworthy. Additionally, Asian people showed greater elevation in fat mass and higher incidence of central obesity with aging, particularly in women.

3.1 Prevalence of sarcopenic obesity

The prevalence of sarcopenic obesity exhibits significant variation depending on the definitions used, assessment methods employed, and the specific

populations under consideration.SO prevalence generally varies from 0 to 25% in older adults in different studies. The prevalence of sarcopenia in Indian population is approximately 39% [7]. A study conducted in Indian population in 2015 by ICMR concluded that the prevalence rate of obesity and central obesity varies from 11.8 to 31.3% and 16.9 to 36.3%, respectively [8]. SO affects around 5–6% of Indian adults annually.

4. Screening

It is based on concomitant presence of an elevated body mass index (BMI) or waist circumference (WC) with ethnicity specific cutoff points. Validated questionnaires, for example, SARC-F in older subjects [9]. The Asian Working Group for Sarcopenia (AWGS) recommends several preliminary screening methods for sarcopenia. These include measuring calf circumference (less than 34 cm in men and less than 33 cm in women), utilizing the SARC-F scale (≥4), or employing the SARC-Calf scale (≥11). During hospitalization, DXA or BIA can be used to enhance the accuracy of skeletal muscle mass (SMM) measurements (**Table 1**).

5. Diagnosis and method of assessment

According to the consensus of the Asian Working Group for Sarcopenia (AWGS) [11], the diagnosis of this ailment necessitates analysis of

a. Muscle mass

b. Muscle strength

c. Physical performance

5.1 Body composition

a. Dual-Energy X-ray Absorptiometry (DEXA),

b. Bioelectrical Impedance Analysis (BIA),

c. Ultrasound, computed tomography, and magnetic resonance imaging

In fact, both Dual Energy X-ray Absorptiometry (DXA) and Bioelectrical impedance analysis (BIA), the body composition methods which are usually recommended for definition of sarcopenia, are not able to recognize either myosteatosis (MS) or myofibrosis (MF) and also do not take into account muscle function in terms of strength and performance, and it is important because both muscle strength and performance decline quicker than muscle mass with aging.

To accurately diagnose SO, quantitative assessment of SMM and fat mass (FM) is vital. Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) are considered as gold standard for accurate diagnosis of SMM and FM, but their use is limited due to high cost, limited availability, and radiation exposure in case of CT (**Table 2**).

SARC-F screen for sarcopenia: component question scoring

Strength: How much difficulty do you have in lifting and carrying 10 pounds?

- None 0
- Some 1
- A lot or unable 2

Assistance in walking: How much difficulty do you have walking across a room?

- None 0
- Some 1
- A lot, use aids, or unable 2

Rise from a chair: How much difficulty do you have transferring from a chair or bed?

- None 0
- Some 1
- A lot or unable without help 2

Climb stairs: How much difficulty do you have climbing a flight of 10 stairs?

- None 0
- Some 1
- A lot or unable 2

Falls: How many times have you fallen in the past year?

- None 0
- 1ess than 3 falls 1
- 4 or more falls 2

Data suggests that a SARC-F score of ≥4 best predicts the need for further, more comprehensive evaluation.

Table 1.
Validity of SARC-F Score: The SARC-F scale has demonstrated internal consistency and validity in identifying individuals at risk of experiencing negative outcomes associated with sarcopenia in various studies, including AAH, BLSA, and NHANES [10].

5.2 Skeletal muscle functional parameters

- Hand-grip strength (HGS),
- Knee extensor strength (adjusted for body mass in relevant populations),
- Chair-stand tests (5-time sit-to-stand test and the 30-second chair stand test)
- Gait speed test (GS) EWGSOP threshold <0.8 m/s
- Timed up and go (TUG)
- Short physical performance battery (SPPB)

Muscle functional cutoff points need to be validated as reference values for sex, ethnicity, and age stratum. Moreover, studies suggest the necessity to adjust hand-grip strength (HGS) to body mass.

Technique	Benefits	Limitations
Dual energy X-ray absorptiometry (DEXA)	Rapid Noninvasive Minimal radiation High precision Simultaneously measures SMM and FM	Portability Cost Limited access Dependent on patient hydration Does not distinguish between fat & lean mass
Computed axial tomography (CAT)	Identifies and quantifies myosteatosis High precision Differentiates between fat and lean mass	Portability Cost Limited access Radiation
Magnetic resonance imaging (MRI)	No radiation Identifies and quantifies myosteatosis High precision Differentiates between fat and lean mass	Portability Cost Limited access Long duration of test
Muscle tissue Ultrasound (US)	Low cost No radiation Real time imaging Inflammation and infiltration of muscle tissue can be differentiated	Dependent on type of ultrasound device and examiner's skill

Table 2.
Diagnosis techniques for Sarcopenic obesity.

5.3 Biomarkers for sarcopenia

Several Biomarkers have been studied. Irisin, a myokine that is released by skeletal muscles, is a potential biomarker for sarcopenia. Low irisin levels (<9.49 ng/mL) in T2DM patients is an independent risk factor for SO.

6. Staging

- *Stage-I*: No complications attributable to altered body composition and skeletal muscle functional parameters;
- *Stage-II*: Presence of at least one complication attributable to altered body composition and skeletal muscle functional parameters (e.g., metabolic diseases, disabilities resulting from high FM and-or low muscle mass, and cardiovascular and respiratory diseases).

7. Adverse health consequences of SO

7.1 SO has been associated with major clinical implications

Increased risk of disability, mobility limitations, and overall impaired physical capacity; elevated risk of cardiometabolic abnormalities such as insulin resistance, dyslipidaemia, hypertension, type 2 diabetes, and low-grade inflammation; increased risk of fractures; depression and compromised overall psychological health; poor outcomes in cancer; increased mortality risk; reduced health-related quality of life;

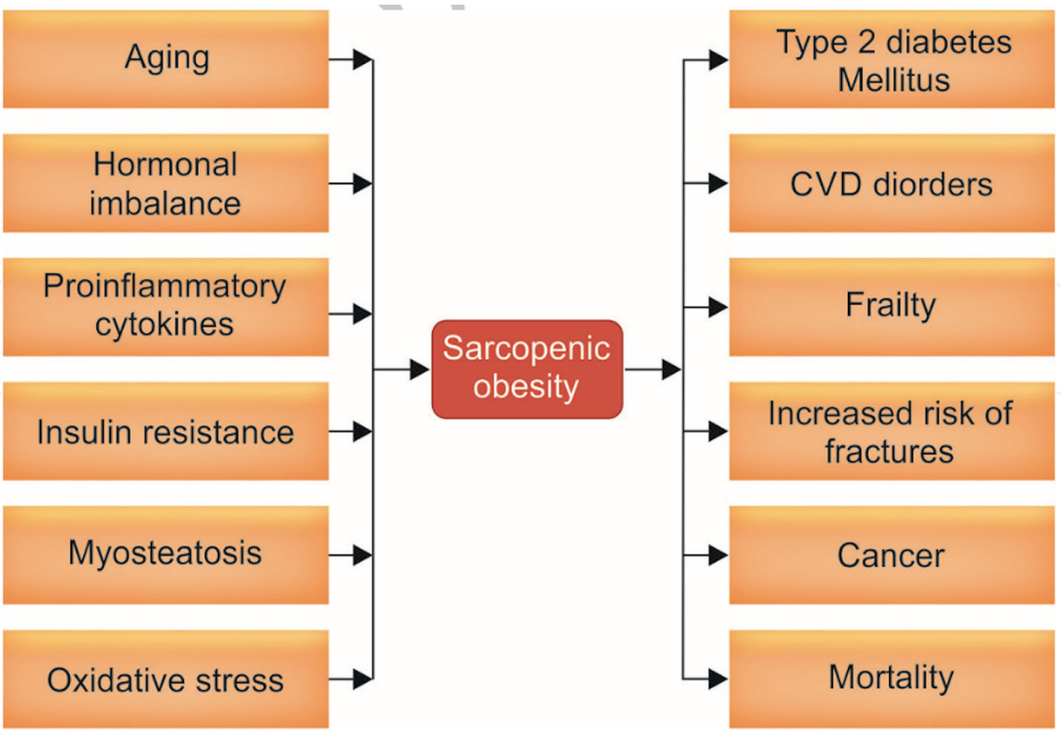

Figure 2.
Sarcopenic obesity: causes and consequences (CVD: cardiovascular disease).

and institutionalization and expanded healthcare costs. However, the cross-sectional design of related studies fails to provide solid information on causal relationships. This highlights the need for longitudinal studies to elucidate the real impact of SO on the onset and progression of specific diseases (**Figure 2**).

8. Management of sarcopenic obesity

Two approaches need to be pursued at the same time:

Gaining SMM while losing FM: The effects of any intervention should focus on changes in body composition and functional parameters and not be measured as changes of body weight alone. If the treatment strategy is limited to only weight loss interventions, there can be inevitable health risks for elderly individuals, mainly related to the concomitant loss of bone and skeletal muscle mass and exacerbation of osteosarcopenia [12].

Therefore, it is very important to focus on body fat loss and maintenance or accretion of muscle mass, so as to maintain strength, function, and resting metabolic rate (RMR). Combined therapy of nutrition along with exercise is the most accepted strategy for these goals [13].

8.1 Resistance training

Resistance training is one the most accepted training for older adults that can improve body composition without weight loss.

Fiatarone and colleagues showed that an eight-week training program of resistance training led to an increase in muscle mass in even frail, institutionalized 90-year-old men and women [14]. Weight training (resistance training) for three days

a week increases muscle mass, with a decrease in fat mass in healthy men and women aged 50–75 years, with body weight remaining unchanged [15].

Resistance training also induces changes in muscle fiber in healthy men and women aged 60 years or older.

Along with severe calorie restriction, resistance training is beneficial. Calorie restriction usually leads to a reduction in both fat and lean mass. Resistance exercise, when prescribed along with calorie restriction, can help prevent muscle loss. As a result, this can lead to a decrease in fat mass along with maintaining muscle mass.

8.2 Essential amino acids (EAA) supplementation

EAA supplementation along with resistance exercise can enhance muscle protein synthesis and can improve body composition by increasing lean mass, not fat mass [16]. In men and women aged 25–35 years, ingestion of essential amino acids before intense resistance exercise resulted in significant increase in muscle protein synthesis and an increase in lean mass [17]. Similarly, 12 weeks of resistance training with the consumption of protein supplement (17 g of essential amino acids) twice a day by healthy young men stimulated greater gain in lean mass compared with resistance training alone [18]. Administration of 15 g of essential amino acids to healthy middle-aged men, along with resistance training program, resulted in attenuation of loss of muscle and gains in fat.

8.3 Dietary protein

Even without resistance exercise, a high protein diet may itself provide an anabolic environment for promoting retention or accretion of muscles over time. A study conducted by Solerte and colleagues concluded that in older men and women aged 64–84 years with sarcopenia, oral supplementation with 16 g per day of essential amino acids was sufficient to increase lean mass in 8 months [19]. This effect persisted over time and resulted in a decrease in TNFα, which is found to be elevated in sarcopenic process. Protein supplementation also prevents muscle loss during calorie restriction, with minimal energy deficit. Higher consumption of high-quality protein (aiming for 1–1.2 g/kg/d or even higher intake 1.2–1.5 g/kg/d) than the current RDA might be advantageous for older adults and malnourished medical in patients [20]. It is also seen that when an individual consumes insufficient diet, the loss of protein can be lessened or even stopped by the addition of carbohydrates or fats to the food and is regarded as the "protein-sparing action" of carbohydrates and fats.

8.4 Treatment strategies

See **Table 3**.

8.5 Newer emerging treatments

Electrical acupuncture and whole-body electro-myo-stimulation, in conjunction with nutritional supplementation, are emerging and effective approaches to bring about alterations in body composition. Whole body vibration therapy has also found to be a safe and convenient technique to cause neuromuscular activation and simulate the contraction of skeletal muscle. A recent study has demonstrated that the adenosine A2B receptor (A2B) is highly expressed in muscle tissue and brown adipose tissue (BAT) and may be a target for SO.

Treatment modality	Mechanism	Comments
Testosterone and Selective androgen receptor modulators (SARM)	Increase muscle mass by increasing IGF-1 decreasing inflammatory markers	Conflicting results Early studies showed good results in cancer patients
Myostatin inhibitors	Enhance skeletal muscle growth. Inhibiting SMM loss	Promising results in cancer related SMM loss
Mesenchymal stem cells	Precursors for skeletal muscle tissue	Promising result as an early treatment for sarcopenia Cost, regulatory, and ethical constraints.
Anamorelin (oral ghrelin analogue)	Anabolic effects Anti-inflammatory properties	Safe, well tolerated in cancer patients with cachexia
Anti-obesity medications	Promote weight loss. Minimal effects on SMM	Approved for non-geriatric population Not known in older adults
Bariatric surgery	Results in weight loss	Unknown safety and efficacy in older patients May exacerbate weight loss-induced sarcopenia and osteoporosis
Neuromuscular activation	Enhances muscle contraction efficiency and functions	Mixed data on efficacy and safety

Table 3.
Novel treatment strategies.

9. Unmet needs, challenges, and knowledge gaps

- To establish a robust and standardized definition of SO.
- To establish reliable techniques to assess body composition for diagnosing SO.
- Further elucidate on descriptive epidemiology of SO, beyond weight loss, morbidity, and mortality, focusing more on patient-centric outcomes like physical functionality and quality of life.
- At present, no specific dietary plans have been tested in populations suffering from SO. Several aspects like the type of protein, optimal concentration of amino acids to be given, and specificity of the amino acids needs to be established.
- To acquire more knowledge regarding optimal frequency, duration, and intensity of exercise (aerobic and resistance). Also, to evaluate if diet and exercise can be combined with pharmacotherapies such as testosterone supplements.

10. Conclusions and future directions

The convergence of two conditions – a growing aging population and increasing obesity rates – has led to an increase in the prevalence of SO, which is defined as the concurrent presence of sarcopenia and obesity in the same individual. SO can lead to an increase in risk of disability, CV disorders, hospitalization, and impaired quality

of life and mortality. Because of such negative effects of SO, its effective diagnosis, prevention, and treatment emerge as a top priority among researchers and clinicians.

Sarcopenic obesity (SO) carries significant implications for public health, as it is connected to frailty, falls, disability, and heightened risks of morbidity and mortality.

The thin fat Indian phenotype, characterized by higher body fat composition and lower muscle mass (sarcopenia), makes individuals of Asian Indian descent more susceptible to muscle loss and metabolic disorders. Compared to their white or African counterparts. The rising prevalence of this condition among younger populations is a cause for concern.

To further advance the current knowledge, the scientific community should try to establish a robust definition and a reliable assessment/diagnostic method, conduct more patient-centric trials, and, finally, obtain concluding evidences with the help of trials for dietary and resistance training interventions.

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