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Unit No. 2

DIAGNOSIS AND MANAGEMENT OF SARCOPENIC OBESITY

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ABSTRACT

While obesity has garnered significant attention as one of the most common chronic diseases, the awareness and scientific understanding around the role of sarcopenia in obesity remains lacking. Sarcopenic obesity (SO) is characterised by the co-existence of sarcopenia (loss of skeletal muscle mass and function/strength) and obesity (excess or abnormally distributed body adiposity, which impairs health), which can impact people of all ages. SO warrants attention as it serves as an independent risk factor for poorer health and outcomes including increased frailty and mortality, and more adverse metabolic outcomes. With the increasing use of obesity management interventions that result in significant weight loss, SO can either develop in susceptible individuals or worsen in those with pre-existing SO. Management of SO poses unique challenges as it mandates a balance of adequate weight loss with the preservation of skeletal muscle mass and strength. This article provides an overview of SO and its management.

Keywords: Sarcopenia, obesity, prevention, diagnosis, management

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INTRODUCTION

Sarcopenic obesity (SO) is the co-existence of sarcopenia (loss of skeletal muscle mass (SMM) and physical function or strength) and obesity (excess or abnormally distributed body adiposity, which impairs health).

With the advent of a rapidly ageing population, increasing life expectancy and the rising prevalence of obesity in Singapore, SO warrants urgent attention as it is associated with poorer health outcomes for frailty and geriatric syndromes, for comorbidities of various chronic conditions and increased mortality, compared to either sarcopenia or obesity alone.[1-3] In Singapore, the prevalence of sarcopenia ranges from 13.6 percent to 25 percent among community-dwelling older adults.[4] The National Population Health Survey 2022 (Singapore) revealed that abdominal (central) obesity increased with age, particularly in women, with the highest prevalence (57.4 percent) among women aged 60-74 years old compared to women 18-29 years old (23.1 percent).[5] In the Geri-LABS study, which studied Singapore adults 50 years and older, the prevalence of SO was 6.2 percent in men and 12.4 percent in women.[6]

SO can develop under various clinical scenarios. Sarcopenia develops typically as a consequence of ageing, which sees a paralleled change in body composition favouring relative or absolute body fat accrual, setting the metabolic milieu for the development of SO. Furthermore, adipose tissue-associated inflammation of muscle can exacerbate the process of sarcopenia. On the other hand, sarcopenia can develop in people with obesity due to changes in skeletal muscle metabolism, a very sedentary lifestyle, inadequate protein intake and malnourishment (e.g., from chronic dieting or after metabolic bariatric surgery) or after an acute illness that induces skeletal muscle loss. While SO is more common in people of older age, it is also highly prevalent in people with obesity across the lifespan.

In addition, with the availability and use of obesity treatments that can result in significant and rapid weight loss as seen with the newer incretin-based therapies and metabolic bariatric surgery, SO can worsen in those with undiagnosed and untreated SO or develop in at-risk individuals.

Primary care physicians play a pivotal role in the early detection and management of SO to reduce the risk of health sequelae from untreated SO. This article aims to provide an overview of the screening, diagnosis, mechanisms, and management of SO.

PREVALENCE OF SARCOPENIC OBESITY

The prevalence of SO is variable due to the inconsistencies in definitions used and populations studied, highlighting the challenges faced in the diagnostic criteria used for SO. In a study of 535 community-dwelling Singaporean adults aged 21-90 years (the Yishun study), the overall prevalence of SO ranged from 0.4 percent to 7.6 percent, when BMI and waist circumference (WC) were respectively used to define obesity.[7] Among Singaporean adults aged 50 years and above (Geri-LABS study), the prevalence of SO was lowest for BMI (0.5 percent) compared to fat mass percentage (10.0 percent) and WC (10.5 percent), with WC correlating with worse functional outcomes, underscoring the need to prioritise assessment of central obesity over BMI for the diagnosis of obesity in Singaporeans.[6]

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SO is highly prevalent among people with obesity and type 2 diabetes (T2D). Among Singaporean adults with a mean age of 61 years and T2D, prevalence of SO was nearly 20 percent.[8] In a cohort of 599 people with obesity (mean age 51 years, mean BMI 43.1 kg/m^2) presenting for obesity treatment, SO was present in nearly 50 percent. The prevalence increased with age, with 31 percent of those aged 18-40 years old having SO compared to ~60 percent in those 60 years and above, with SO being twice more prevalent among women (~51 percent) than in men, and in those with lower BMI.[9] These variable prevalence rates inform us that we need to be vigilant with case-finding not just among people of older age but also among people with co-existing chronic diseases which can predispose to sarcopenia (e.g., T2D) and obesity.

DIAGNOSING SARCOPENIC OBESITY

The diagnosis of SO begins with high vigilance and an approach of case-finding (rather than universal screening).[4,10,11] Locally, the Singapore Clinical Practice Guidelines for Sarcopenia 2022 recommends case-finding for sarcopenia in adults aged 65 years and above.[4] In addition, screening for SO is recommended for all individuals with risk factors or with signs or symptoms of SO regardless of age (see **Table 1**).[4,11]

Commonly encountered clinical scenarios include someone with a very high BMI who loses a disproportionately higher amount of SMM during weight loss (e.g., from physical inactivity and inadequate dietary protein intake) or someone with a pre-disposing chronic disease or frailty who gains weight mainly in ectopic sites and develops central obesity.

There is a lack of a universally established SO definition and diagnostic criteria especially among Asians. Regardless, the diagnosis of SO remains as the establishment of a loss of SMM coupled with reduction in muscle strength or function in people with obesity (including those with central obesity), based on ethnic/population-specific established criteria.[12]

For obesity, screening and diagnosis involve establishing the presence of excess adiposity using ethnic-specific BMI cutoffs (e.g., Asians in Singapore: BMI ≥27.5 kg/m^2) and/or abnormally distributed adiposity using ethnic and gender-specific anthropometric measurements such as waist circumference (e.g., Asians in Singapore: males ≥90 cm; females ≥80 cm) or waist-hip ratio (e.g., Asians in Singapore: males ≥1.0; females ≥0.85). The use of BMI alone can often underdiagnose SO particularly in older adults and in Asians. Hence, adding a surrogate assessment of excess or abnormal distribution of adiposity is highly recommended.[6,7] In addition to anthropometrics, measurement of percent body fat has been advocated by some experts for diagnosis of obesity in SO although there is no standardisation at present.[13] The WHO uses body fat cutoffs of >25 percent in males and >35 percent in females while recent studies used >30 percent and >40 percent in males and females respectively to define excess total body fat.[6,14]

The presence of any of the following clinical conditions that predispose to sarcopenia (e.g., functional decline or limitation; recurrent falls; malnutrition or chronic conditions such as chronic heart, lung, liver, and kidney disease) serves as a positive screening and will warrant confirmation of sarcopenia with further assessments.

In the absence of clinical signs or symptoms of sarcopenia, the Singapore Clinical Practice Guidelines for Sarcopenia (2022) and the Asian Workgroup for Sarcopenia (AWGS) 2019 Consensus call for the adoption of a case-finding approach in adults ≥60 years old with the measurement of the calf circumference, CC (in the standing position) or the use of questionnaires (e.g., SARC-F or SARC-CaIF).[10] If any of the following parameters are met CC (M: <34 cm, F: <33 cm) or SARC-F ≥4 or SARC-CalF ≥11 – further assessments must be carried out to confirm the diagnosis of sarcopenia. The SARC-CaIF adds 10 points to the SARC-F scoring for CC below cutoffs. In an individual with a high BMI, an increase in accumulation of fat in the calf might falsely increase the CC, which may result in an under-diagnosis of sarcopenia. The use of adjusted CC has been recommended by experts to circumvent this; a subtraction of 3, 7, or 12 cm (for BMI 23-27.4, 27.5-37.4, and ≥37.5 kg/m^2, respectively, for Asians) from the CC measurement.[2]

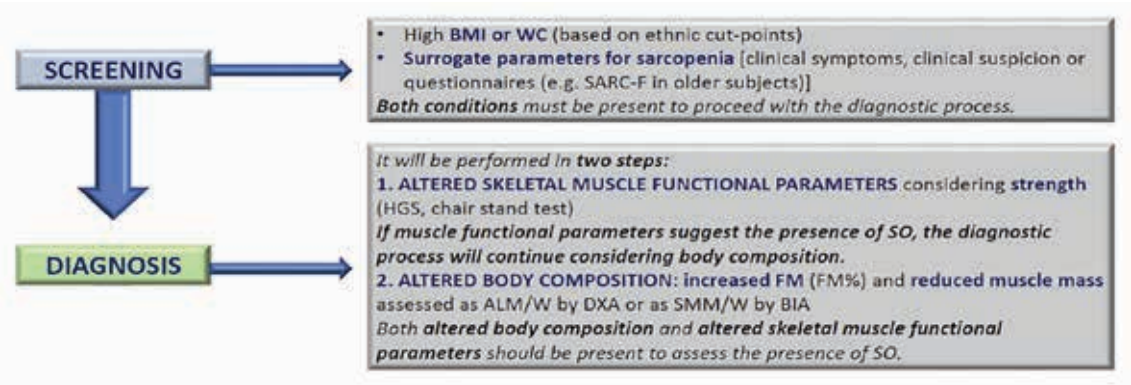
Table 1. Clinical Symptoms or Risk Factors for Sarcopenic Obesity

Age >70 years
Chronic disease diagnosis (e.g., inflammatory diseases and organ failure or chronic disease) including but not limited to:
Chronic heart failure
Chronic kidney disease (particularly renal replacement therapy)
Chronic bowel failure or dysfunction
Chronic liver disease (particularly NASH and liver cirrhosis)
Chronic respiratory disease
Chronic neurologic and neurodegenerative diseases
Chronic cognitive impairment
Depression
Organ transplantation
Endocrine diseases (e.g., metabolic syndrome, diabetes mellitus, hypercortisolism, hypogonadism and corticoid treatment)
Osteoarthritis
Cancer (especially but not limited to chemotherapy of breast or prostate cancer)
Recent acute disease/nutritional events:
Recent hospitalization (particularly but not limited to COVID-19, ICU stay, surgery)
Recent major surgery or trauma with/without complications
Recent sustained immobilization or reduced mobility (e.g., trauma, fracture, orthopaedic disease)
Recent history of reduced food intake (e.g., <50% for >2 weeks)
Recent weight loss (including diet-induced voluntary weight loss and weight cycling syndrome)
Recent rapid increase in weight
Long-standing restrictive diets and bariatric surgery
History – complaint of:
Repeated falls
Weakness, exhaustion
Fatigability
Perceived progressive movement limitations

Adapted from Definition and Diagnostic Criteria for Sarcopenic Obesity: ESPEN and EASO Consensus Statement. Donini LM, Busetto L, Bischoff SC, et al. Definition and Diagnostic Criteria for Sarcopenic Obesity: ESPEN and EASO Consensus Statement. Obes Facts. 2022;15(3):321-35[11]

Following a positive screening for sarcopenia, the diagnosis of sarcopenia requires the confirmation of both (1) reduced skeletal muscle function or strength and (2) reduced SMM, in a 2-stage approach (refer to **Figure 1**).

Figure 1. Diagnostic procedure for the assessment of sarcopenic obesity



Legend:
ALM/W = appendicular lean mass adjusted to body weight
BIA = bioelectrical impedance analysis
BMI = body mass index
DXA = dual X-ray absorptiometry
FM = fat mass
HGS = handgrip strength
SMM/W = total skeletal muscle mass adjusted by weight
SO = sarcopenic obesity
WC = waist circumference
SARC-F = strength, assistance with walking, rising from a chair, climbing stairs, and falls

Adapted from Definition and Diagnostic Criteria for Sarcopenic Obesity: ESPEN and EASO Consensus Statement. Donini LM, Busetto L, Bischoff SC, et al. Definition and Diagnostic Criteria for Sarcopenic Obesity: ESPEN and EASO Consensus Statement. Obes Facts. 2022;15(3):321-35[11]

For Asians, sarcopenia should be diagnosed using the AWGS 2019 criteria.[10] Poor physical function (performance) is defined as 6-metre walk (gait speed) <1.0 m/s or 5-time chair stand test ≥12 seconds or Short Physical Performance Battery (SPPB) ≤9 while reduced muscle strength is defined as handgrip strength (HGS) of <28 kg and <18 kg for men and women respectively (refer to **Table 2**). However, the validation of these cutoffs is not available for younger people with obesity.

The assessment of muscle mass can be performed using dual energy X-ray absorptiometry (DEXA) for the analysis of appendicular skeletal mass (ASM) corrected for height (ASM/height^2). A low ASM is defined as <7.0 and <5.4 kg/m^2 in men and women respectively, as measured by DXA (refer to **Table 2**).[10] While DEXA is the recommended modality, it is not as accessible in the primary care setting and not every diagnostic facility has the capability to perform a body composition analysis with a DEXA scan. DEXA incurs higher cost (compared to bioelectrical impedance analysis (BIA)) and X-ray exposure, which may impose a barrier for the uptake of assessment. Recognising these challenges, some experts recommend the use of BIA, which is more readily available in most clinical settings. When performed under controlled conditions (e.g., fasted state with light clothing) and in subjects without fluid overload (or issues with lower extremity swelling), BIA can be a practical and reproducible assessment for monitoring of treatment.

Table 2. Cutoffs for the Screening and Diagnosis of Sarcopenia in Asians[10]

Screening		
Clinical Situation	**Measurements/Assessment**	**Positive Cutoff(s)**
Presence of any clinical condition or, signs or symptoms of sarcopenia	Functional decline or limitation; unintentional weight loss; depressive mood; cognitive impairment; repeated falls; malnutrition OR Chronic conditions (as listed in **Table 1**)	Presence of any
Without clinical conditions, signs or symptoms of sarcopenia	Calf circumference **or**	M <34 cm, F <33 cm*
	SARC-F **or**	≥4
	SARC-CalF	≥11
Diagnosis**		
Muscle strength	Handgrip strength	M <28 kg, F <18 kg
Physical performance (function)	6-metre walk **or**	<1.0 m/s
	5-time chair stand test **or**	≥12 s
	Short Physical Performance Battery	≤9
Appendicular skeletal muscle mass (ASM)#	Dual-energy X-ray absorptiometry **or**	M<7.0 kg/m^2 F <5.4 kg/m^2
	Bioelectrical impedance analysis	M <7.0 kg/m^2 F <5.7 kg/m^2

M = males; F = females

*can consider adjusted CC using subtraction of 3, 7, or 12 cm (BMI 23-27.4, 27.5-37.4, and ≥37.5 kg/m^2 respectively for Asians) from the CC measurement.

**Assessments must be performed in sequence and all three criteria must be present/positive for the diagnosis of sarcopenia.

#Use of appendicular lean mass (ALM) or SMM corrected for weight (ALM/weight for DEXA or SMM/weight by BIA) has been alternatively recommended [cutoffs of 35.7% (M) and 30.7% (F) by BIA has been used for a predominantly East Asian population.[15]

In people with obesity, in whom total body mass can be high, the use of ASM for SMM assessment can under-diagnose sarcopenia. Relatively reduced SMM in the presence of high fat and total body mass can have clinical implications including functional impact, even in the absence of absolute SMM loss. Hence, the use of appendicular lean mass (ALM) or SMM corrected for weight (ALM/weight[W] for DEXA or SMM/weight[W] by BIA) is recommended.[2,11] Cutoffs of 1-2 standard deviations corresponding to 31.5-37.0 percent (males) and 22.1-27.6 percent (females) have been recommended,[16] while in the Korean SO Study cutoffs of 35.7 percent (males) and 30.7 percent (females) by BIA have been used for a predominantly East Asian population.[15]

In the primary care setting, screening is encouraged using a case-finding approach via a BMI and waist circumference measurement followed by sarcopenia screening in those with signs or symptoms (refer to **Table 1**), a calf circumference measurement, or a SARC-F questionnaire in those with very high BMI or history of lower extremity oedema (in whom a calf circumference will not be accurate). Confirmation of sarcopenia can be done using a step-wise approach; firstly, to confirm reduced muscle strength or function using a hand-held dynamometer to measure handgrip strength repeated at least twice (for assessment of muscle strength) or the 5-time chair stand test or 6-m walk test (for assessment of muscle function). If reduced muscle function or strength is detected, it is required to confirm a reduced SMM (body composition) using a BIA scan, provided the patient does not have fluctuating body fluid issues, or a DEXA body composition scan.

PATHOGENESIS AND AETIOLOGY OF SARCOPENIC OBESITY

The aetiology and pathophysiology of SO is complex. Different factors that can trigger the development of SO include ageing (age-related changes in body composition), hormonal imbalances, dietary and lifestyle factors (e.g., malnutrition, physical activity and mental stress), presence of co-existing acute or chronic conditions, and systemic inflammation to myocellular mechanisms (e.g., oxidative stress).[2,11] Regardless of the metabolic scenario, the main mechanism of pathogenesis is the cross-talk between adipose tissue and skeletal muscle inflammation, and both weight gain and weight loss can contribute to the development of SO.

In people with obesity, the constellation of systemic inflammation, insulin resistance, and oxidative stress, systemically and within the muscles, can lead to a muscle-catabolic state, potentially promoting a "resistance to anabolism" in the skeletal muscle (i.e., reduced muscle protein synthesis in response to nutrients is blunted).[2,17] In response to weight gain, this leads to a preferential increase in fat mass with proportionately reduced SMM accrual, favouring the development of SO.

Ectopic fat deposition in the muscle (myosteatosis), commonly seen in people with central obesity and insulin resistance, can lead to muscle oxidative stress with reduction in SMM and strength.[1] Reduced physical activity, a pertinent risk factor of weight gain and aetiology of obesity, can have further direct negative impact on muscle protein synthesis and muscle function. Obesity is associated with a myriad of other acute and chronic conditions/diseases (e.g., T2D, heart failure, chronic kidney disease, obstructive sleep apnoea, asthma, musculoskeletal conditions, prolonged hospital stays) that can perpetuate the process of SO either through further reduction in physical activity and/or through systemic inflammation and oxidative stress.[2,11,13,14]

Weight loss (interventions) inevitably results in SMM loss, especially with rapid or large amounts of weight loss such as those seen with metabolic bariatric surgery, very-low calorie diets, and when protein intake and physical activity are lacking during weight loss.[11] Body weight cycling and inadequate nutrition, as often seen in chronic dieting in the process of management of obesity, can lead to development of or perpetuate pre-existing SO.[11,12] Hence, SO is rather prevalent even in younger individuals with obesity. Regardless, as people with obesity increase in age, the physiologic changes in body composition favouring a loss in SMM and function with preferential fat mass gain and aggravate pre-existing SO, especially in the presence of risk factors (see **Table 1**).

Ageing is associated with physiologic body composition changes involving SMM loss (beginning in middle age) along with the development of myosteatosis and oxidative stress within the muscles, an increase in fat mass, and propensity for visceral adiposity, which favour the development of SO. These changes result from hormonal changes (e.g., reduced growth hormone, testosterone, and estrogen), low levels of physical activity, changes in energy metabolism, and diet (e.g., low protein, calcium, vitamin D intake). When older adults are inflicted with acute or chronic conditions, the above factors are augmented through increased inflammation, immobility, or changes in nutrition, which can lead to either weight gain or weight loss, triggering the onset or accelerating the development of SO.[2,16]

In people with T2D, in whom obesity is common, the presence of diabetes micro- and macrovascular complications along with poor glycaemic control may accelerate the onset of and perpetuate sarcopenia.

CLINICAL IMPLICATIONS OF SARCOPENIC OBESITY

The co-existence of obesity and sarcopenia synergistically creates a vicious twin-cycling of SMM loss and adipose tissue gain with further aggravation of SO if untreated. Multiple studies demonstrate an increased risk of metabolic disorders, geriatric syndromes, morbidity, and mortality related to SO.

The clinical consequences of SO include worsening metabolic dysfunction with development of metabolic syndrome, T2D, increased risk of geriatric syndromes (further reduction in

physical activity with functional limitation and disability, increased frailty, cognitive impairment and dementia, risk of falls and fractures, depression), prolonged hospital length of stay, increased risk of all-cause mortality, and mortality from various conditions such as cardiovascular disease, heart failure, post-hospitalisation, worse morbidity outcomes of various chronic diseases (e.g., stroke, lung diseases), and cancer outcomes (e.g., reduced overall disease-free survival), and development of various clinical conditions (e.g., hospitalisation, reduced quality of life, poor nutritional status).[2,3,8,15,16]

MANAGEMENT OF SARCOPENIC OBESITY

Regardless of the phenotypic presentation or primary aetiology of SO, the overall management of SO requires an approach of vigilance and case-finding in susceptible individuals with early detection and halting of the process, along with management strategies that address fat loss without further SMM loss (preservation), and where possible, increase in SMM.

However, the treatment of SO poses unique challenges. By reducing fat mass, intramyocellular inflammation can be lessened. Yet, with weight loss, there is inevitable concurrent muscle loss. Hence, effective management strategies of SO will need to focus on combining exercise and nutritional interventions targeted at reducing fat (weight) while preserving or increasing muscle mass and function. This approach aims to create a negative energy balance, leading to adipose tissue reduction, improved adipose markers, and decreased inflammation, while also enhancing muscle mass.

Interventions with Exercise and Physical Activity

Exercise is essential for the prevention and management of SO.[18] Regular physical activity, particularly resistance and aerobic exercises, has been shown to improve muscle mass, strength, and overall physical function. Resistance training, in particular, is highly effective in enhancing muscle quality, function, strength, and flexibility in older adults, and it is recommended for at least two non-consecutive days per week, gradually increasing intensity and volume over time.[19,20]

Aerobic exercise, such as walking, cycling, or swimming, is also important as it improves muscle aerobic capacity and cardiovascular function, increases insulin sensitivity, promotes mitochondrial adaptation, increases capillary density of muscle tissue, and reduces oxidative stress and adipose tissue.[21,22] A combination of resistance and aerobic exercises is more effective in improving muscle mass and function and reducing fat than either form of exercise alone.[2] High-intensity interval training (HIIT), which alternates between short bursts of intense exercise and recovery periods, has been particularly noted for its ability to stimulate muscle protein synthesis and improve muscle function and insulin sensitivity.[23]

The Singapore Physical Activity Guidelines (SPAG), developed by the Health Promotion Board and SportSG, advise adults to engage in 150 to 300 minutes of moderate-intensity aerobic activity weekly, which can be spread across any duration throughout the week.[24] SPAG encourages incorporating various activities, such as strength training and light-intensity exercises, to break up sedentary periods and enhance overall physical and mental well-being. For older adults, staying active while enhancing muscular strength and functional balance is crucial, as it aids in managing frailty and common chronic conditions like diabetes and hypertension.

Nutritional Interventions

Nutritional strategies play a vital role in preventing and treating SO. While hypocaloric diets can effectively reduce fat mass, they might also lead to muscle loss by downregulating muscle protein synthesis and increasing proteolysis. There is also a risk of micronutrient deficiencies and bone loss.[25] Currently, there is insufficient evidence regarding the impact of macronutrient manipulation (such as fat versus carbohydrate restriction) compared to conventional calorie restriction (total calorie intake) on weight loss and body composition, particularly in relation to the SO phenotype.[26]

A modest reduction in calorie intake, typically between 200-700 kcal per day, is recommended to achieve gradual weight loss of 0.5-1 kg per week, while minimising muscle loss.[27] Protein intake is particularly important in preserving muscle mass, especially in older adults who are at higher risk of anabolic resistance. A daily protein intake of 1.0-1.2 g/kg body weight is generally recommended to maintain and recover muscle mass and function, with higher amounts (1.2-1.5 g/kg) suggested for individuals with multiple co-morbidities.[28,29] Additionally, protein intake should be spread evenly across meals to optimise muscle protein synthesis, as no significant anabolic benefits have been observed with protein intake exceeding 30 g per meal.[30]

Apart from the quantity of protein, the source of protein may also be vital for preserving muscle mass. Animal-based proteins, particularly whey, are more effective at promoting muscle protein synthesis due to their higher leucine content and faster digestion and absorption rates.[31] Supplementation with leucine, an essential amino acid, of 2.0-2.5 g per day has been associated with increased muscle protein synthesis in older adults, independent of other amino acid intake.[32]

Time-restricted eating (TRE) involves limiting food intake to specific periods of the day (e.g., an 8-hour feeding window over a 24-hour period). Some studies have suggested that TRE can promote weight loss while preserving muscle mass and improving cardiovascular health and other physiological markers.[33] Hence, TRE could be an appealing, safe, and practical dietary approach for patients with SO, but more research is needed.

The combination of exercise and nutrition interventions offers the best outcomes for individuals with SO. Existing studies suggest that combining exercise with adequate protein intake can lead to significant reductions in fat mass, increases in muscle mass, and improvements in physical function, such as handgrip strength and gait speed.[2]

Role of Nutritional Supplements

Several nutrients and dietary components have been proposed to support muscle health due to their anabolic, anti-inflammatory, anticatabolic, and antioxidant properties. These include omega-3 fatty acids, β-hydroxy β-methylbutyrate (HMB), carotenoids, selenium, and vitamins D, E, and C. However, the evidence supporting these interventions is inconclusive and sometimes conflicting due to limited studies and small sample sizes.[2] Further research is needed to clarify their roles in the treatment of SO.

IMPACT OF NOVEL GLP-1 BASED ANTI-OBESITY MEDICATIONS ON MUSCLE MASS AND FUNCTION

Newer glucagon-like peptide 1 (GLP-1) receptor agonist-based anti-obesity medications, such as semaglutide and tirzepatide, have garnered significant attention in recent years due to impressive weight loss of 17 percent with semaglutide and 21 percent with tirzepatide,[34,35] along with substantial improvements in both subjective and objective measures of physical function. However, these AOMs have not been specifically studied in populations with SO, and existing clinical trials have often limited the enrolment of older adults and individuals with chronic diseases. While semaglutide and tirzepatide can lead to significant adipose tissue loss, they can also result in concomitant muscle loss. In the STEP 1 trial, semaglutide treatment led to lean mass loss of 5.26 kg, representing ~38 percent of total weight loss[34] – exceeding the usual "quarter fat-free mass" rule.[36] Nonetheless, GLP-1 receptor agonists have not only been shown to improve glycaemic control, these agents have been observed to confer additional cardio- and reno-protective benefits in people with T2D.

Nevertheless, the extent of muscle mass loss relative to fat loss and the improvement in muscle composition, including reduction in myosteatosis and ectopic fat, remain unclear. These factors are crucial as they play a central role in the pro-inflammatory cycle driving SO.[2] Animal studies also suggest that GLP-1 may improve muscle cell function by enhancing blood flow, nutrient delivery, and even stimulating muscle growth through specific signalling pathways.[37]

METABOLIC BARIATRIC SURGERY

While metabolic bariatric surgery (MBS) is highly effective in treating severe obesity and obesity-related metabolic complications/comorbidities including T2D, and effecting significant fat loss and relative improvements in physical function, it also causes substantial loss of muscle mass and strength.[38] Research specifically targeting individuals with SO is limited and can be complex given the significant changes in overall body mass (weight) and body composition. In a study of 71 patients, sleeve gastrectomy was shown to better preserve bone and muscle compared to Roux-en-Y bypass.[39] However, remission rates for obesity-related complications/comorbidities were similar after surgery, regardless of sarcopenia.[40] Given the marked caloric deficit and weight loss in the first year after bariatric surgery, patients at risk of sarcopenia and undergoing MBS should be screened for and managed for SO even prior to MBS, and be managed at specialised multidisciplinary centres peri-operatively, with a focus on nutrition, exercise, and additional medical support.

EMERGING MEDICAL THERAPIES

Myostatin Inhibitors

Myostatin inhibits skeletal muscle growth and development and elevated myostatin levels are observed in individuals with sarcopenia, making it a key target in SO treatment. Its inhibition leads to muscle cell hyperplasia and hypertrophy, suppresses irisin, and downregulates pro-inflammatory cytokines, with potential benefits to metabolism, adiposity, and insulin sensitivity.[41] Interestingly, myostatin levels can be decreased following a DASH diet, with improved body composition and cardiometabolic biomarkers in older adults.[42]

In a trial of the activin receptor type 2B inhibitor, bimagrumab, among 180 older adults with sarcopenia, bimagrumab improved functional parameters and lean mass, although no specific subanalysis for those with obesity was conducted.[43] In another trial involving adults with type 2 diabetes and BMI 28-40 kg/m^2, bimagrumab, combined with diet and exercise, led to significant adipose tissue loss, increased lean mass, and metabolic improvements.[43] However, there was no distinct analysis for those with SO.

Case Study

Mdm H is a 61-year-old woman who was referred to Dr N for treatment of obesity. She describes a gradual increase in weight since her early thirties, with difficulty sustaining weight loss via lifestyle measures. Her current weight is 92 kg (BMI 33.8 kg/m^2) and has a waist circumference of 92 cm. She also has hypertension, type 2 diabetes (diagnosed four years ago; latest HbA1c 7.3%), and obstructive sleep apnoea. Her medications include metformin 1 g BD, empagliflozin 25 mg OM, and losartan 50 mg OM.

On further history, she describes that she has tried to control her weight by limiting caloric intake. As she is a vegetarian, her current dietary intake consists mainly of vegetables and rice or noodles. She shares that it has been difficult for her to exercise as she gets tired easily. She also describes muscle fatigue even when playing with or carrying her baby grandson. She works as a part-time administrator (sedentary) and spends the rest of her day caring for her grandson at home. She does not smoke or drink alcohol.

Suspecting sarcopenic obesity, Dr N conducts the SARC-F screening questionnaire:

Question	Response	Points
How much difficulty do you have in lifting or carrying 4.5 kg?	Some	1
How much difficulty do you have walking across a room?	None	0
Rising from a chair: How much difficulty do you have transferring from a chair or bed?	Some	1
How much difficulty do you have climbing a flight of 10 stairs?	A lot	2
How many times have you fallen in the past year?	None	0
Total		**4**

Individual Item Scoring:
None = 0
Some = 1
A lot = 2

Total Score of ≥4 for SARC-F or ≥11 for SARC-CalF is a positive screening, which warrants confirmation of diagnosis of sarcopenia.

To confirm the diagnosis, further tests are performed:

Test	Result	Cutoff for Sarcopenic Obesity
Muscle Strength		
5-time chair stand test	16 seconds	≥12 seconds
Handgrip strength	15 kg	<18 kg (F)
Body Composition via Bioimpedance Analysis (BIA)		
Muscle mass (SMM/W)	26%	<30.7% (F)*
Fat mass	45%	>35% (F)

*via BIA based on an East Asian population

This confirms the diagnosis of sarcopenic obesity. Dr N explains to Mdm H the treatment goals will focus on reducing fat mass, while improving her muscle mass and strength, and improve control of her metabolic parameters. She is started on obesity pharmacotherapy and referred to the dietitian and physiotherapist to guide her on increasing protein intake and resistance exercises.

CONCLUSION

Sarcopenic Obesity poses a real threat to the health of rapidly ageing populations especially with concurrent high prevalence of central obesity. Early detection through screening with a case-finding approach is key to breaking the vicious cycle of SO, which can occur throughout the entire life-cycle. Despite challenges in diagnostic criteria, diagnosing SO involves the confirmation of excess or abnormal distribution of adiposity and loss of SMM and function/strength using the relevant population-specific cutoffs. The management of SO requires a multifaceted approach that includes exercise, nutrition, digital technology, and personalised care. Combining resistance and aerobic exercises with adequate protein intake and other nutritional strategies can effectively reduce fat, preserve or increase muscle mass, and improve overall physical function in individuals with SO. More research is needed to refine these interventions and explore the potential benefits of novel pharmacological agents and additional nutritional supplements to treat SO. In the meantime, it is essential to increase the awareness of SO and use simple screening tools in primary care to identify this important condition so that at-risk individuals can receive appropriate treatments to improve their clinical outcomes.

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