Review Article

Sarcopenia and sarcopenic obesity in cardiovascular disease: a comprehensive review

Li Feng Tan[1,2], MRCP(UK), FAMS, Ching Hui Sia[2,3], MRCP(UK), FAMS, Reshma Aziz Merchant[2,4], FRCPEd, FAMS

[1]Healthy Ageing Programme, Alexandra Hospital, National University Health System, [2]Department of Medicine, Yong Loo Lin School of Medicine, National University of Singapore, [3]Department of Cardiology, National University Heart Centre, Singapore, [4]Division of Geriatric Medicine, Department of Medicine, National University Hospital, Singapore

Abstract

Sarcopenia is the loss of muscle strength, mass and function. It is often exacerbated by chronic comorbidities such as cardiovascular diseases (CVDs). There is a bidirectional relationship between sarcopenia and CVD. Sarcopenia can lead to increased adiposity, insulin resistance and chronic inflammation, predisposing adults to developing cardiovascular events. Chronic inflammation and decreased physical activity observed in cardiac patients can lead to accelerated muscle loss and the development of sarcopenia. Sarcopenia is linked to faster CVD progression, higher mortality and reduced quality of life. The co-occurrence of obesity with sarcopenia is termed sarcopenic obesity (SO). This condition is associated with worse outcomes than either condition individually. Early detection is crucial, as interventions can slow or reverse sarcopenia and improve cardiovascular outcomes. This review summarises evidence on the interplay between CVD and sarcopenia, discusses diagnostic approaches and management strategies, and identifies knowledge gaps for future research.

Keywords: Cardiovascular disease, myosteatosis, obesity, sarcopenia, sarcopenic obesity

INTRODUCTION

With the rise of ageing populations globally, the prevalence of non-communicable diseases (NCDs), such as cardiovascular disease (CVD), diabetes mellitus, obesity, cancer, frailty, sarcopenia and dementia, continues to grow.[1] The hallmarks of ageing — chronic inflammation, mitochondrial dysfunction, genomic instability, telomere attrition, epigenetic alterations, cellular senescence and loss of proteostasis — contribute to the onset and progression of NCDs.[2] These biological changes lead to a decline in cellular and organ function, increasing vulnerability to diseases. Cardiovascular disease is a major cause of mortality and disability worldwide, accounting for a third of global deaths.[3] There is a bidirectional association between sarcopenia and CVD. The term sarcopenia was first coined by Dr Irvin Rosenberg in 1988. Sarcopenia was initially defined as the age-related loss of muscle mass. The definition has since evolved to encompass muscle strength and poor physical performance, in addition to low muscle mass.[4] Reduced muscle strength and mass in sarcopenia impairs physical function, leading to increased risks of falls, fractures and disability. This physical decline further exacerbates the risk of NCDs, creating a vicious cycle of declining physical function, poor physical activity and adverse outcomes. Sarcopenia also contributes to metabolic dysfunction, promoting insulin resistance and systemic inflammation, both of which are underlying mechanisms in the development of diabetes mellitus, hepatic steatosis and CVDs. The combined impact of sarcopenia and NCDs accelerates adverse outcomes, including higher morbidity and mortality, and reduced quality of life among older adults.[5] Sarcopenia was recognised as an official medical disease in the International Classification of Diseases, Tenth Revision (M62.84) in 2016.[6] It is a progressive condition, and although its prevalence increases with age,[7] it is not solely a disease of ageing. It can be caused by chronic diseases that affect muscle mass and function, such

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Correspondence: A/Prof. Reshma Aziz Merchant, Head and Senior Consultant, Division of Geriatric Medicine, Department of Medicine, National University Hospital, 1E Kent Ridge Road, 119228, Singapore. E-mail: reshmaa@nuhs.edu.sg

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as hypertension, chronic heart failure and diabetes mellitus.[5] Individuals with CVD are more likely to have sarcopenia than age-matched controls, independent of cardiovascular risk factors and after adjusting for renal function and medications.[8-10] Sarcopenia is also associated with worse outcomes and faster progression in individuals with CVD.

Sarcopenic obesity (SO) is the occurrence of both sarcopenia and obesity in an individual. In 2020, 58% of adults in Singapore were classified as overweight or obese based on the Asian body mass index (BMI) cut-off of ≥23 kg/m² and 40.6% based on abdominal circumference (male >90 cm and female >80 cm).[11] While many studies on cardiovascular outcomes have used physical function and/or low muscle strength and BMI or waist and arm circumference to define SO,[12-14] high BMI alone in older adults may be protective. The 'obesity paradox' refers to the phenomenon where BMI, which encompasses both fat and fat-free mass, displays a 'U'-shaped relationship with physical function and mortality in older adults.[15,16] A meta-analysis by Winter *et al.*[17] reported increased mortality in individuals with BMI < 23 kg/m² or > 33 kg/m². Another potential explanation for this paradox is the height loss commonly experienced by older adults as they age. Other measures such as waist circumference and hip–waist ratio may better predict poor outcomes in these group of patients.[15,16] Both sarcopenia and obesity are considered independent risk factors for poor health outcomes and increased risk of NCDs, but together, they cause more harm synergistically than the sum of their individual effects. Individuals with SO often have multiple cardiometabolic diseases, insulin resistance, hepatic steatosis, lipotoxicity, mitochondrial dysfunction and ongoing chronic inflammation, which leads to an increased risk of mortality[18] [Figure 1].

Myosteatosis, defined as excessive fat infiltration within skeletal muscle, is commonly used to describe poor muscle quality.[19] It is frequently seen in persons with cardiometabolic disease or older adults with ectopic fat deposition. Fat infiltration in muscle is a source of proinflammatory cytokines. Combined with inflammaging[20] and CVD risk factors, this can affect muscle composition, quality and elasticity, and interfere with muscle contraction even before the onset of loss of muscle mass.[21] The concomitant presence of sarcopenia and obesity is associated with myosteatosis, and together with low physical activity levels, it can lead to a vicious downward spiral of fat gain and muscle loss, functional decline and disability.[22,23] Besides the liver and muscle, ectopic fat also gets deposited in the epicardium, known as epicardial adipose tissue (EAT).[24] Epicardial adipose tissue is associated with presence, severity and progression of coronary artery disease, atrial fibrillation and arrhythmias.[25] Elevated EAT volumes are associated with impaired endothelial function, arterial stiffness, increased left ventricular mass and diastolic dysfunction.[26] They are also associated with idiopathic ventricular tachycardia and atrial fibrillation recurrence after ablation.[27]

Despite their high prevalence and health impact, there is a lack of awareness, knowledge, diagnosis and management of sarcopenia and SO in clinical practice, especially in the management of chronic conditions such as CVD. In this review, we (1) summarise the current evidence on the complex interplay of CVD, sarcopenia and SO; (2) discuss its diagnostic evaluation; (3) explore management strategies in the context of CVD; and (4) outline key gaps in knowledge with implications for the future of the field.

PREVALENCE

The prevalence of sarcopenia ranges from 9% to 86.5% depending on the context and diagnostic criteria used.[28] A systematic review of 41 studies with 34,955 participants found that the prevalence of sarcopenia was higher in institutionalised (51% in men and 31% in women) and hospitalised (23% in men and 24% in women) adults compared to community-dwelling adults (11% in men and 9% in women).[29] The prevalence of sarcopenia in patients with CVD varies across the globe depending on the diagnostic tool used and the age and population studied, as shown by Pacifico *et al*.,[30] who pooled data from 63 studies. The study reported a prevalence of 40.4% based on the the Asian Working Group for Sarcopenia (AWGS) criteria, and 20.7% based on the European Working Group on Sarcopenia in Older People (EWGSOP) criteria.[30] Another systematic review of 38 studies found a pooled prevalence of sarcopenia in patients with CVDs of 36% (95% confidence interval [CI] 27%–46%) in Asia, 31% (95% CI 16%–45%) in Europe, 35% (95% CI 14%–57%) in South America and 39% (95% CI 21%–57%) in Oceania.[31] Sarcopenia in patients with CVD was more prevalent in Asia (44.7%) compared to Europe (15.5%). Sarcopenia is common among patients with congestive heart failure (CHF) and hypertension. It is associated with recurrent hospitalisations, increased length of stay and higher mortality. The prevalence of sarcopenia ranges from 34% to 66% and is highest among hospitalised patients with acute decompensated heart failure.[32] In coronary artery disease (CAD), it ranges from 12% to 25%.[10] In patients undergoing aortic valve replacement, its prevalence is between 21% and 70%.[10] As no agreed definition for SO exists, many studies have used muscle strength or physical performance, along with various measures of obesity.[12-14] A 2023 meta-analysis of adults aged ≥50 years found a SO prevalence of 9% in men and women across 48 studies from 2000 to 2020.[33] The study also observed SO was associated with 51% and 63% increased risks of all-cause and CVD-related mortality, respectively, compared to healthy controls.

PATHOGENESIS

Skeletal muscle changes in ageing, cardiovascular disease and congestive cardiac failure

With ageing, there is a progressive decline in type II muscle fibres and muscle fibre satellite cells, which are essential for

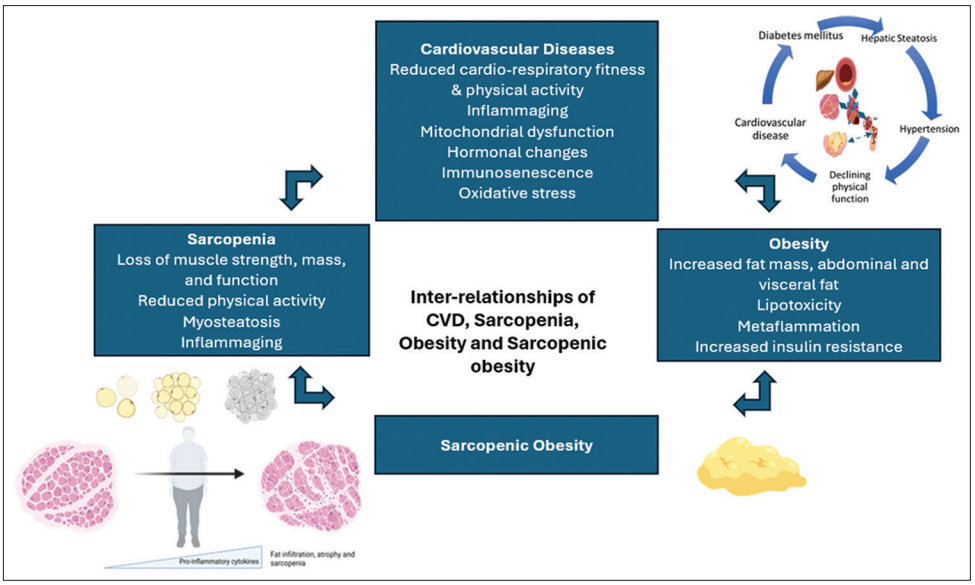

Figure 1: Diagram shows the interrelationships of cardiovascular disease (CVD), sarcopenia, obesity and sarcopenic obesity. [Created in BioRender. Sia C. (2024) https:// BioRender.com/d17b111]

fast and powerful movements. This decline, compounded by low physical activity, significantly contributes to reduced muscle strength and function, accelerating the progression of sarcopenia.[34] In addition, CVDs can accelerate the onset of sarcopenia by impairing blood flow and nutrient delivery to muscles, exacerbating muscle atrophy and functional decline.[35] A gradual reduction in the size and number of muscle fibres begins at 50 years, and approximately 50% of the fibres are lost by the age of 80. While some type II fibres can convert to type I fibres due to changes in nerve supply, the overall number of muscle fibres decreases, leading to muscle atrophy and reduced muscle function. Type I muscle fibres influence peripheral resistance, affecting blood pressure (BP). Lower levels of these fibres in hypertensive individuals correlate with higher BP, making sarcopenia a contributor to poor BP control and cardiovascular risk.[36,37] Low skeletal muscle mass in community-dwelling older adults has been found to be associated with subclinical atherosclerosis, increased coronary artery calcium score, arterial stiffness and carotid artery wall thickening.[38]

Anabolic resistance and imbalance between muscle protein anabolism and catabolism are caused by many interrelated factors such as hormonal changes (reduction in growth hormone, testosterone, thyroid hormone and insulin-like growth factor), inflammaging, mitochondrial dysfunction, impaired nutrient sensitivity and reduced physical activity.[39] Ageing muscle becomes less sensitive to anabolic stimuli such as amino acids from protein intake, which further exacerbates mitochondrial dysfunction. Mitochondrial dysfunction is consistently reported in CVD[40] and has been implicated in myocyte dysfunction and viability. The mechanisms that maintain homeostasis, atrophy and regeneration of skeletal muscle are complex, and studies suggest that epigenetic changes, microRNAs[41] and mitochondrial activity[42] play important roles in muscle function. Similar changes have been observed in cardiomyocytes, which ultimately lead to cardiomyocyte death and CVD.[43,44]

Cardiac dysfunction significantly contributes to sarcopenia. Conditions such as chronic heart failure, cardiomyopathies and valvular heart diseases impair cardiac function, leading to a decline in cardiorespiratory fitness and, consequently, reduced physical activity, which is a precursor for sarcopenia. Moreover, cardiac dysfunction is associated with systemic low-level inflammation and oxidative stress, which cause muscle tissue damage. Hormonal imbalances, overactivation of the ubiquitin–proteasome system, endothelial dysfunction and diminished muscle blood flow further exacerbate muscle degradation and fat infiltration. Collectively, these factors result in the progressive loss of muscle mass and strength, characteristic of sarcopenia.[45] Sex differences in CHF are well recognised, with women having greater symptom burden and lower quality of life than men. Recent studies have found that muscle pathology relating to muscle transcriptome, myofibre size and phenotype, capillarity, molecular signalling and circulating factors[46] might account for these observed sex differences.

Sarcopenic obesity

Fat infiltration and sarcopenia impact on multiple organs cumulatively give rise to negative outcomes.[47] Besides obesity, other risk factors include sedentary lifestyle, mismatch between caloric intake and expenditure, inadequate protein and micronutrient intake, stress and environment. The mechanism is not well understood, and there may be two groups of individuals at high risk of SO. The first group comprises individuals who

have been obese in midlife with cardiometabolic diseases,[48] while those in the second group may have increased ectopic fat deposition with ageing itself.[47] Although the mechanisms may be similar between the two groups, obesity may be the root cause in the former. In both situations, there may be an imbalance between proinflammatory adipokines and anti-inflammatory myokines, oxidative stress and mitochondrial dysfunction. The adipose tissue responds to proinflammatory cytokines with fibrosis, lipolysis, fat redistribution and central obesity, whereas the skeletal muscle tissue responds to proinflammatory cytokines with atrophy and sarcopenia.[49] Sarcopenic obesity shares common aetiological mechanisms with CVD, such as insulin resistance, hepatic steatosis, increased visceral adipose tissue and atherosclerosis. A recent meta-analysis by Liu *et al*.[33] found that SO is associated with higher risk for CVD events, stroke and myocardial infarction, angina pectoris and heart failure.

Emerging role of epicardial adipose tissue in cardiovascular disease

Epicardial adipose tissue[25] is a unique fat depot located between the myocardium and the visceral layer of the epicardium that is supplied by branches of coronary arteries. This is in contrast to the pericardial adipose tissue (PAT), which is located externally and supplied by non-coronary arteries.[50] Epicardial adipose tissue has a unique proximity to the heart and has a transcriptome and secretome that differ from those of other fat deposits. Epicardial adipose tissue exerts local paracrine and autocrine effects, resulting in local inflammation, which is associated with atherosclerosis, myocardial fibrosis, higher coronary artery calcium scores, impaired coronary vasomotion, atrial fibrillation and impaired endothelial function. These contribute to ischaemic heart disease even without significant luminal stenosis. Epicardial adipose tissue is frequently observed in individuals with obesity or diabetes mellitus,[51] although it has been found to predict early stages of atherosclerosis independent of obesity. Further studies on EAT and its relationships with obesity and SO are warranted.

ASSESSMENT AND DIAGNOSIS

There are multiple consensus guidelines from across the globe for the diagnosis of sarcopenia, with the EWGSOP2[5] and AWGS[26,52] diagnostic algorithms being the most widely used in clinical practice. As shown in Figure 2, low muscle strength or physical function together with low muscle mass is required to diagnose sarcopenia. The presence of all three would indicate severe sarcopenia.[5,52] The use of blood biomarkers in sarcopenia is a fast-evolving field.

Screening tools

The guidelines[5,52,53] recommend a case-finding approach by utilising screening questionnaires, such as Strength, Assistance with walking, Rising from a chair, Climbing stairs, and Falls (SARC-F),[54] for individuals without secondary risk factors or age-related conditions such as falls or functional decline. SARC-F is a simple questionnaire [see Supplemental Digital Appendix] with low–moderate sensitivity and high specificity for case detection in the community settings. The addition of calf circumference measurement to SARC-F (termed SARC-CalF) has been found to increase the sensitivity in diagnosis of sarcopenia.[52,55] SARC-F using a lower cut-off score of ≥2 in older adults with CVD was shown to be associated with increased all-cause mortality and rehospitalisation.[56] Okoye *et al*.[57] recently showed that both handgrip strength (HGS) and SARC-F, including its individual components such as limited physical function and history of falls, independently predicted 30-day mortality in patients with acute heart failure.

Muscle strength and physical performance

Low muscle strength is a cardinal feature of sarcopenia, and

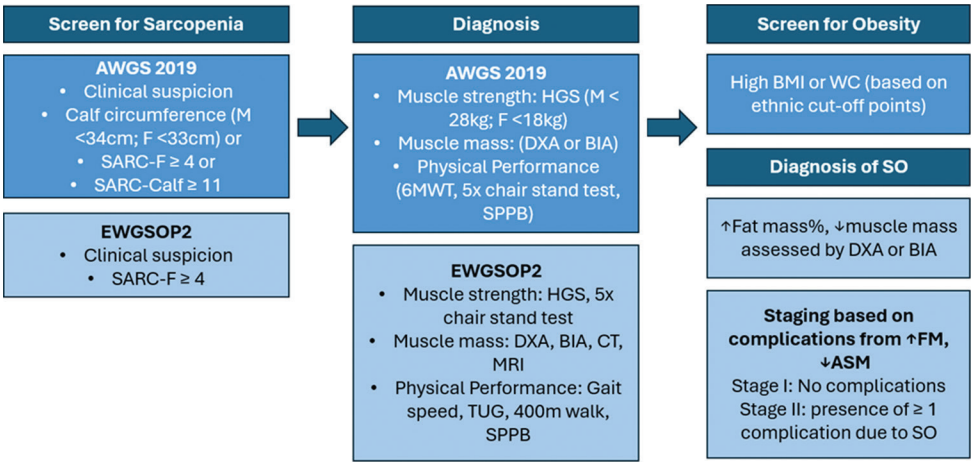

Figure 2: Diagnostic algorithm for sarcopenia and sarcopenic obesity. 6MWT: 6-minute walk test, ASM: appendicular skeletal muscle mass, AWGS 2019: Asian Working Group for Sarcopenia 2019 guidelines, BIA: bioelectrical impedance analysis, BMI: body mass index, CT: computed tomography, FM: fat mass, DXA: dual-energy X-ray absorptiometry, EWGSOP2: European Working Group on Sarcopenia in Older People 2018 guidelines, HGS: handgrip strength, MRI: magnetic resonance imaging, SARC-F: Strength, Assistance with walking, Rising from a chair, Climbing stairs, and Falls, SO: sarcopenic obesity, SPPB: Short Physical Performance Battery, TUG: timed up and go, WC: waist circumference.

measurement of HGS can easily be done in clinical practice.[58] Briefly, it is recommended to sit with 90° elbow flexion using the Jamar dynamometer, or stand with full elbow extension if using the Smedley dynamometer.[58] Most published studies measured both hands or the dominant hand for muscle strength and used the best performance of either two or three trials. Cut-offs for HGS are gender specific, and potential confounders such as hand osteoarthritis and neuromuscular disorders should be considered. Low HGS is linked to higher risks of adverse outcomes, including increased healthcare utilisation, myocardial infarction, strokes, disability and mortality.[59-62] In addition, gait speed (4 m or 6 m), Short Physical Performance Battery (SPPB) and/or the five-time sit-to-stand test can easily be performed in clinical practice.[63] Sarcopenia indices such as SPBB have been found to be associated with cardio-ankle vascular index, which is a measure of vascular stiffness in older patients with heart failure.[64] Presence of either low muscle strength or low physical performance is classified as probable or possible sarcopenia, and intervention should be offered regardless of low muscle mass.

Muscle mass

Several techniques are available, but all have limitations and variabilities. Use of dual-energy X-ray absorptiometry (DXA) and bioelectrical impedance analysis (BIA) is recommended in various guidelines for the measurement of appendicular skeletal muscle mass (ASM), but these have significant limitations such as requirement of specialised equipment and technicians, not being able to assess the muscle quality (e.g., myosteatosis) and inaccuracies in individuals with high levels of water, which would be of particular relevance in CHF.[65] The accuracy of BIA in obese individuals has also been questioned.[66] Studies have shown that phase angle measured using BIA is a useful prognostic measure for adverse events in CVD.[67] Sato *et al.*[68] showed that in patients with heart failure, mid-upper arm circumference or mid-upper arm muscle circumference was associated with higher CVD event rates compared to calf circumference and skeletal muscle index.

Computed tomography (CT) and magnetic resonance imaging (MRI) are gold standards for assessing muscle composition and quality,[69] particularly at the L3 level, which correlates well with total body skeletal muscle volume.[5] These imaging techniques provide detailed insights into muscle mass and myosteatosis, which can be quantified using Hounsfield units on CT. Assessment of mid-thigh muscles using CT or MRI effectively evaluates muscle quality and composition, correlating well with whole-body muscle mass. There is emerging literature on the use of ultrasonography of mid-thigh in diagnosing sarcopenia. The D3-creatine dilution method, involving deuterium-labelled creatine, provides direct and accurate muscle mass measurements, correlating well with MRI data and clinical outcomes such as falls and mobility issues.[70] Shi *et al.*[71] recently published a new estimation of muscle mass using an equation incorporating gender, height, weight, creatinine and cystatin C, which was found to accurately estimate muscle mass. Integrating these methods enhances the precision of muscle health assessments, allowing for early diagnosis and better management of sarcopenia and related conditions. However, its utilities need to be further validated in individuals with heart failure and CVD.

Sarcopenic obesity

There is currently no agreed definition for SO.[72] Most studies on SO, CVD and heart failure used muscle strength, SPPB and obesity defined by BMI. It is increasingly recognised that BMI-adjusted ASM may be a better measure of muscle mass in obese, older individuals.[66] The 2022 Sarcopenic Obesity Global Leadership Initiative, launched by the European Society for Clinical Nutrition and Metabolism and the European Association for the Study of Obesity consensus, recommends screening with BMI or waist circumference using ethnicity-specific cut-offs, followed by muscle strength and body composition assessment for the diagnosis of SO.[72] Sarcopenic obesity is then stratified into two stages based on the presence of complications resulting from high fat mass and low skeletal muscle mass [Figure 2]. The 2022 SO consensus recognises the limitations of BMI, but states that it is acceptable in the screening phase of SO due to its ease and accessibility. It recommends the use of waist circumference for the identification of excess abdominal visceral fat and increased cardiometabolic risk.

MANAGEMENT OF SARCOPENIA AND SARCOPENIA OBESITY IN CARDIOVASCULAR DISEASE

Managing sarcopenia and SO requires a holistic, multidisciplinary approach, and it is important to provide individualised treatment plans that address cardiovascular risk factors, physical fitness, frailty, cognition, depression, food access and polypharmacy. Specific interventions such as physical exercise, together with branched chain amino acids such as leucine and protein supplementation have been shown to improve muscle protein synthesis and reduce systemic inflammation.[73]

Physical activity and resistance training

Evidence-based clinical practice guidelines were published in 2018, providing strong recommendations for physical activity as the first-line treatment of sarcopenia.[74] Specifically, progressive resistance training (RT) has been demonstrated to have a dose–response effect on sarcopenia. Reduction in body fat percentage and total body fat mass has been demonstrated,[75] though more research is needed to strengthen the evidence of exercise and RT in SO.

Besides improving and maintaining muscle mass and strength, RT also has favourable physiological and clinical effects on CVD and risk factors.[76] Adults who participate in RT have 15% lower risk of all-cause mortality and 17% lower risk of CVD, compared to those who do not participate in it.[76,77] In older

adults with CVD and CHF, RT demonstrates improvements in glucose tolerance, lipids and lipoproteins, insulin resistance, vascular endothelial function[78] and resting BP,[79] with a dose–response association demonstrated. Physicians should be aware of guidelines when recommending exercise and RT for patients with CVD.[80]

Nutrition and protein supplementation

The evidence for nutrition interventions is less consistent.[75,81] While it is generally recommended that evaluation of protein and nutritional intake should be part of sarcopenia management,[53,74] the heterogeneity of nutritional interventions in trials makes it challenging to establish clear, standardised guidelines. The European Sarcopenia and Physical fRailty IN older people: multi-componenT Treatment strategies (SPRINTT) multicomponent, multicentre trial[82] found that a multicomponent intervention — comprising moderate-intensity physical activity with technological support and nutrition counselling — resulted in women having smaller declines in grip strength and appendicular lean mass at 24 and 36 months. There was no significant difference observed in men in the intervention versus the control group. Several cohort studies have found that lower protein intakes are related to a loss of lean mass and reduced grip strength.[83] However, most trials have combined exercise with increased protein intake when assessing the impact on muscle indices.[83,84] Most guidelines conditionally recommend protein supplementation, and that nutritional interventions should be paired with physical activity and RT.[53,74] However, trials of nutritional interventions addressing sarcopenia and SO in CVD, such as heart failure, are notably lacking.[85]

Weight loss in SO

Strong evidence and robust clinical trials on interventions in SO are lacking. While weight loss is recommended for obesity, a regimen of weight loss without exercise leads to a simultaneous reduction of both fat mass and lean mass, which further aggravates sarcopenia. Higher skeletal muscle losses have been reported in individuals with chronic diseases such as heart failure with preserved ejection fraction.[45] A systematic review by Weinheimer *et al*.[86] found that the addition of exercise to energy restriction attenuates the loss of lean mass, despite not appearing to have any significant additive effect on weight reduction. Thus, in SO, appropriate exercise prescription is key. While RT has been shown to be useful against sarcopenia, aerobic exercise has greater efficacy against obesity. Aerobic exercise improves cardiovascular function, reduces insulin resistance, enhances skeletal muscle capacity and reduces mortality. Their combination would provide the best results in SO, although robust evidence on this and its effect on specific subpopulations are lacking at present.

Anti-obesity medications

While currently, there is a paucity of evidence on the impact of anti-obesity medications such (e.g., incretin-based drugs), there is growing awareness of the importance of preserving skeletal muscle mass during weight loss treatment.[87] Encouragingly, Phase III trials have included muscle mass measurements in their outcomes,[87] although none have assessed muscle strength, which is a core component in the diagnosis of sarcopenia. Studies have found that a combination of anti-obesity medications such as glucagon-like peptide 1 receptor agonists and exercise (mostly aerobic training) led to the greatest weight loss, body fat percentage decrease (twice that of either intervention alone) and cardiorespiratory fitness improvement, in addition to preserving lean mass (by DXA).[88] Further studies exploring the impact of pharmacologic agents, coupled with diet and exercise interventions, on body composition, CVD events and survival in patients with SO will provide invaluable evidence to guide clinical practice on managing this complex condition.

RECOMMENDATIONS

Sarcopenia and SO are modifiable risk factors that have been linked to negative cardiovascular outcomes. Although there is no gold standard for diagnosing sarcopenia or SO, it is crucial to understand that BMI alone is not an accurate measure of obesity or cardiovascular risk in older adults. Simple clinical assessments such as HGS measurement, gait speed assessment or the five-times sit-to-stand test can be easily performed to identify high-risk individuals. Body composition analysis is also useful for diagnosing sarcopenia.

Exercise and nutrition are two key intervention areas, with substantial evidence supporting their effectiveness in addressing possible sarcopenia, sarcopenia and SO. Resistance exercises, when paired with an adequate intake of protein and micronutrients, are essential for managing sarcopenia. Aerobic exercises, which enhance cardiovascular fitness and promote weight loss, are crucial for addressing obesity and SO. Familiarity with physical activity guidelines[89,90] is important for providing patients with specific, measurable exercise prescriptions.

Weight reduction is vital in the management of obesity and SO; however, it is important for physicians not to rely solely on BMI as a marker for weight loss, as losing muscle mass instead of fat can be harmful. Involvement of a multidisciplinary team to deliver multicomponent interventions is often necessary to effectively address SO in patients with CVD.

POTENTIAL BIOMARKERS

Multiple circulating biomarkers have been linked to sarcopenia, obesity and poor outcomes. They comprise myokines, adipokines, chemokines and cytokines such as interleukin (IL)-6, IL-8, tumour necrosis factor-α, growth differentiation factor-15 and circulating miRNA-1-3p levels.[91,92] High levels of proinflammatory cytokines from underlying obesity, ageing-related or cardiometabolic diseases negatively impact muscle metabolism and muscle mass through reduced activation of mechanistic target of rapamycin complex 1 signalling pathway and inhibiting

the release of myokines.[93] Besides blood biomarkers, EAT — especially thickness and volume — is recognised as an imaging biomarker that predicts major adverse cardiovascular events.[94]

FUTURE RESEARCH

The impact of sarcopenia and SO in CVD is significant, and there are many areas where further research is needed. Key areas include validation of body composition assessment tools and criteria, especially in the setting of obesity and heart failure, validation of diagnostic criteria and impact on outcomes in diastolic dysfunction, and optimisation of interventions for CVD patients with sarcopenia and SO. Further elucidation of the mechanisms of interaction among muscle, bone and adipose tissue in relation to sarcopenia, SO, obesity and CVD will help in understanding the complex metabolic crosstalk, risk factors and potential therapeutic targets for preventing and managing these interrelated conditions. The role of hormonal status (e.g., cortisol, testosterone, postmenopausal hormonal changes) and its impact on sarcopenia, SO and CVD are also relevant, given the CVD risks as hormonal changes affect muscle mass loss, fat redistribution, inflammation and metabolic dysfunction. Clinical trials that assess muscle mass, strength and quality (myosteatosis) — ideally using established diagnostic criteria[5,52,95] — are needed to evaluate the benefits and risks of pharmacological interventions, such as Sodium-Glucose Co-transporter 2 inhibitors and Glucagon-Like Peptide-1 receptor agonists, for these conditions in patients with CVD. Finally, we need rigorous studies that explore interventions that can reverse or delay the development of sarcopenia and SO, with attention to the specific types of exercise and their duration, nutritional supplementation, and various macro- and micronutrients.

CONCLUSION

Sarcopenia and SO are prevalent in patients with CVD, and these conditions have a bidirectional relationship with CVD. They are associated with faster progression, poorer prognosis and adverse health outcomes in patients with CVD. Tackling them is of public health importance, especially with the twin global trends of ageing and rising obesity. Sarcopenia and SO are potentially modifiable and have significant impact on outcomes in patients with CVD. However, validated biomarkers and evidence-based interventions for these conditions in this population are still lacking. Interventions such as RT and nutritional supplementation, as well as aerobic exercise for SO, are promising strategies, although specific details require further research. More work is needed in the area of skeletal muscle therapeutics and to elucidate the effects of anti-obesity medication on muscle and adiposity. Further research on effective strategies and approaches to manage these conditions in patients with CVD is needed to shape clinical practice and transform health policy.

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Conflicts of interest

Sia CH is a member of the SMJ Editorial Board and was thus not involved in the peer review and publication decisions of this article.

Supplemental digital content

Appendix at http://links.lww.com/SGMJ/A210

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