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Review

Sarcopenic obesity: A Critical appraisal of the current evidence

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SUMMARY

Sarcopenic obesity (SO) is assuming a prominent role as a risk factor because of the double metabolic burden derived from low muscle mass (sarcopenia) and excess adiposity (obesity). The increase in obesity prevalence rates in older subjects is of concern given the associated disease risks and more limited therapeutic options available in this age group.

This review has two main objectives. The primary objective is to collate results from studies investigating the effects of SO on physical and cardio-metabolic functions. The secondary objective is to evaluate published studies for consistency in methodology, diagnostic criteria, exposure and outcome selection. Large between-study heterogeneity was observed in the application of diagnostic criteria and choice of body composition components for the assessment of SO, which contributes to the inconsistent associations of SO with cardio-metabolic outcomes.

We propose a metabolic load:capacity model of SO given by the ratio between fat mass and fat free mass, and discuss how this could be operationalised. The concept of regional fat distribution could be incorporated into the model and tested in future studies to advance our understanding of SO as a predictor of risk for cardio-metabolic diseases and physical disability.

1. Introduction

Healthy ageing is associated with physiological, gender-specific changes in body composition which impose an overall minimal load on the control of metabolic and cardiovascular functions.[1,2] A significant deviation from a healthy trajectory of body composition may increase the incidence rate of adverse health events.[3] The assessment of body composition is commonly performed by quantifying fat (FM) and fat free mass (FFM) components. These components are often utilized to assess the risk for adverse health outcomes in conditions characterized by abnormal modifications of body composition (e.g., obesity, anorexia, cancer).[4] However, in recent years the study of the loss of muscle mass (sarcopenia) has experienced a revitalized research interest,[5] promoted by the specific application of *in vivo* body composition methods (dual energy X-ray absorptiometry (DXA), imaging and spectroscopic methods) for the assessment of the quantitative and qualitative characteristics of skeletal muscle mass.[6–8]

The predictive value of sarcopenia for health outcomes relates to the metabolic and functional relationship between muscle mass (MM) and physical strength, mobility and vitality.[9–11] Sarcopenia is associated with an increased risk for age-related decline in muscular strength and functional ability,[12,13] as such as it has been labelled a “silent crippler” because of its association with physical disability, falls, fractures and frailty.[9–11,14,15] Loss of MM in older individuals is significantly associated with extended hospital stays, infectious and non-infectious complications and overall mortality.[9,14,16–18]

However, sarcopenia often co-occurs with an increase in FM, a scenario termed **sarcopenic obesity (SO)**, which may carry the cumulative risk derived from each of the two individual body composition phenotypes.[19,20] On its own, excess adiposity may generate significant adverse health effects (e.g., hypertension, dyslipidaemia, insulin resistance). However, evidence increasingly suggests that these risks may be elevated with the addition of low MM.

The prevalence of SO in older-aged individuals is increasing[21–23] and its impact on physical, metabolic and cardiovascular functions is becoming a primary concern amongst nutritionists, geriatricians and public health officers. The ethio-pathogenesis of SO is complex

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and multi-factorial factors can interplay, including lifestyle (diet, physical activity, smoking), endocrine (corticosteroids, growth factors, insulin, catecholamines), vascular (endothelial function, coagulation), and immunological (inflammation, reactive oxygen species) factors.[24,25] A unanimous view on the direction of the causality of the associations between these factors is not established.

A simple example of the multi-factorial origin of SO is illustrated in Fig. 1. The diagram describes two hypothetical metabolic scenarios conducive to the onset of the same sarcopenic obese phenotype, which is, however, derived from two different metabolic trajectories, i.e., weight gain and weight loss. Weight gain normally occurs alongside a variable rate of accretion of FFM which can potentially give origin to either an obese (normal FFM accretion) or to a SO (low FFM accretion) phenotype. The direction of the model can be reversed when, for example, morbidly obese subjects (body mass index (BMI) $>$ 40 kg/m^2) lose a significant amount of weight but not sufficient to move subjects into the overweight category (BMI $<$ 30 kg/m^2), a scenario habitually observed with non-surgical weight loss treatments. Weight loss in these subjects could induce a variable rate of FFM loss and therefore determine the onset of a SO phenotype in obese subjects with more prominent losses in lean tissue mass. The between-subject variability in the composition of the tissue in both positive and negative energy balance has been demonstrated in overfeeding and underfeeding experimental, controlled studies able to control for potential confounding factors such as physical activity or dietary intake. For example, Siervo et al.,[26] showed that lean healthy subjects gained 6.0 $\pm$ 1.3 kg in body weight after a 9-week stepwise overfeeding and the contribution of FM, measured using a 4-compartment model, to total weight change varied between 11% and 98%. Similarly, two groups of obese men who lost 10% ($-$10.9 $\pm$ 2.6 kg) of their baseline weight following either a VLCD or LCD and the contribution of FM to total weight loss varied between 73% and 106%.[27] Additional factors can further add to the variability of body composition changes in states of energy imbalance such as physical activity, dietary macronutrient composition, rate of weight loss, genetics, menopausal state, immobilization, endocrine dysfunctions, inflammatory disorders or pharmacological treatments.[28–32] Recent advances in the allometric modelling of these changes could provide a roadmap for the evaluation of the effects of interventions on body composition.[33] These models, along with models of the change in visceral fat with weight/fat change could define the trajectory of the expected changes in fat and lean with weight gain and loss and the ability of specific interventions to modify body composition when weight changes. Unfortunately, these models have not been validated in SO and this should be a priority for future clinical studies.

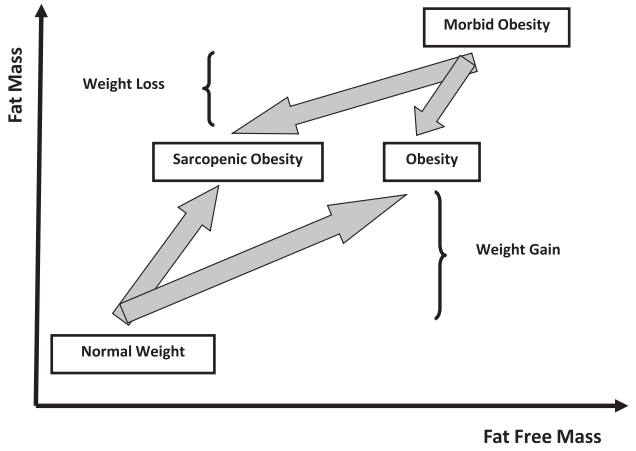

Fig. 1. Hypothetical metabolic scenarios conducive to the onset of the same sarcopenic obese phenotype but derived from two different metabolic trajectories, i.e., weight gain and weight loss.

2. Diagnosis of sarcopenic obesity

The lack of a unanimous view on the criteria to apply to define low MM and high FM in order to identify cases of SO represents a major clinical and research drawback. The criteria are somewhat arbitrary and study-specific, which may have minimized the predictive value of SO as a health risk factor.[12] One of the most commonly used indexes for the definition of sarcopenia is the total appendicular skeletal muscle (ASM) index assessed by DXA.[34] Individuals with either an ASM index (kg/m^2) lower than 7.26 kg/m^2 (men) and 5.45 kg/m^2 (women) or included in the lowest quantile group (ter-, quart-, quin-) were classified as sarcopenic.[9] A similar approach was used with MM and using the $-$2SD values of a gender-specific distribution of MM in a reference population of young, healthy subjects as cut-off points to identify sarcopenic cases.[14] Alternatively, the lowest quintile of the residual distribution derived from the regression of ASM on either height or FM was used to define sarcopenia.[35] More recently, muscle strength has been used as a criterion for the diagnosis of sarcopenia, defined as the lowest quantile of the muscle strength distribution.[36–39] The assessment of muscle strength has been proposed by some investigators based on the cost-effectiveness of the measurements, the widespread availability of the test in clinical settings and the close association with efficiency of neuromuscular functions.[40]

The identification of excess adiposity for the diagnosis of SO is also challenging. Despite being an imperfect measured of body fatness, BMI has been utilised in some studies.[41,42,59] Percent body fat (FM%) cut-off values adjusted for sex, age and ethnicity and measures of adipose tissue distribution (waist circumference (WC) or waist-hip-ratio) have also been proposed but they have rarely been applied for the diagnosis of SO.[43,44]

The lack of standardized diagnostic approaches is reflected in the variable combination of body composition indices and cut-offs that have been used to classify SO, which may be as limitative for the purpose of risk prediction as considering either sarcopenia or obesity in isolation. Baumgartner et al.[23] used DXA measurements to define SO if ASM was lower than $-$2 SD value obtained from a healthy population,[9] and FM% was greater than the 60th percentile of an age-matched population.[23] This approach has been followed in some studies[22,45,46] but not in others.[36–38,47,48] For example, Davison and colleagues[38] classified SO if cases were in the upper two quintiles for FM% and in the lowest quintile for MM whereas Schrager et al.[37] used BMI ($\geq$30 kg/m^2) and muscular strength (lowest tertile) to identify SO cases. The latter approach has recently been renamed “dynapenic-obesity” and it may have a greater risk predictive value.[45,49] Sternfeld et al. proposed a more integrative approach by examining the predictive value of lean body mass (LBM)/FM ratio for physical disability.[50] Multiple linear regression was also used to adjust ASM for differences in height and fat mass and used the residual distribution to classify subjects with sarcopenia (negative residual values).[35] Height-adjusted fat mass (FMI) and fat-free mass indexes (FFMI) have also been used[51,52] and more recently the muscle to fat ratio has been introduced to identify subjects with SO.[39,45]

Table 1 summarizes the design, population characteristics, methodological approaches and main results from studies investigating the relationship between SO and functional and cardiometabolic outcomes. Overall, a significant association between SO