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Research paper

Sarcopenia and the cardiometabolic syndrome: A narrative review

G. Bahat *, B. İlhan

Istanbul University, Istanbul Medical School, Department of Internal Medicine, Division of Geriatrics, Çapa, 34093 Istanbul, Turkey

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ABSTRACT

Sarcopenia is a prevalent problem in the older population that is commonly considered for its well-known adverse functional associations. Cardiovascular diseases and metabolic syndrome are also significant problems whose prevalence dramatically increase with age and remain the main cause of mortality in older adults. These two entities have recently been suggested to be inter-related and significant evidence has accumulated. In this article, we review the current evidence on this proposed association and the possible related pathophysiologic mechanisms. In summary, it seems that lower muscle mass is associated with higher cardiometabolic diseases (CMD) when adjusted for weight, but lower CMD when adjusted for height squared. Sarcopenic obesity – obesity and sarcopenia combined – might be associated with a greater risk of CMD than sarcopenia and obesity alone. Sarcopenia and CMD seem to share a common pathway and interact with each other to facilitate mutual abnormalities.

Sarcopenia is a prevalent problem in older age with reported frequencies of 10–26% [1–4]; it may affect as much as 50% of people aged over 80 years [4,5]. It is defined as age-related decline in muscle mass and function [6] and is well-known for its associations with functional outcomes such as frailty, decreased mobility, disability, decreased strength, risk of falling, impaired respiratory function tests, and mortality [7–9]. Cardiovascular disease (CVD) and metabolic syndrome are other highly prevalent problems that cause disability and premature mortality worldwide. Their prevalences increase dramatically with age. Hence, CVD represents the main cause of mortality in the aged population.

Sarcopenia and CVD, apart from being two highly prevalent problems in the older adults, have recently been suggested to be inter-related and significant evidence has accumulated. In this article, we narratively review the current evidence on this proposed association and the possible related pathophysiologic mechanisms.

Obesity and related dysregulations were considered the major pathophysiologic contributing factor for CVD until the recent past [10,11]. Obesity is universally evaluated using body mass index (BMI) [12]. However, for a given body weight, BMI increases as the individual ages because of degenerative thinning of intervertebral cartilage and/or common osteoporotic vertebral compression fractures. Moreover, the percentage of body fat increases in older adults compared with young adults, yet the effects of increasing BMI on mortality are less pronounced in older adults than in middle-aged adults [13]. In addition to increased fat mass, age-related changes in body composition include sarcopenia. Other than the traditional risk factors for insulin resistance, i.e., obesity and physical inactivity, muscle-centred dysregulations also contribute to reduced insulin signalling and action in skeletal muscle. Hence, sarcopenia may be an important actor for CVD, which suggests that body composition analysis of fat mass and fat-free mass may be a better risk predictor than BMI in these individuals [13–15].

We searched Pubmed for English language studies of sarcopenia, sarcopenic obesity and cardiometabolic syndrome, cardiovascular disease, metabolic syndrome in August 2015. From this search, we identified following numbers of articles: ‘sarcopenia, cardiovascular disease, elderly’: 141 articles (50 were review); ‘sarcopenia, cardiometabolic syndrome, elderly’: 6 articles (3 were review); ‘sarcopenia, metabolic syndrome, elderly’: 58 articles (20 were review); ‘sarcopenic obesity, cardiometabolic syndrome, elderly’: 3 articles (1 was review); ‘sarcopenic obesity, cardiovascular disease, elderly’: 20 articles (5 were review); ‘sarcopenic obesity, metabolic syndrome, elderly’: 19 articles (6 were review). We excluded duplicated and/or unrelated studies and got the eligible 37 cross-sectional and longitudinal studies below. The related review articles have also been reviewed.

First, cross-sectional studies signalled the association between sarcopenia and CVD, and metabolic syndrome. More than 10 years ago, Jurca et al. cross-sectionally examined the association of

* Corresponding author. Tel.: +90 212 414 20 00; fax: +90 212 532 42 08.
E-mail addresses: gbahatozturk@yahoo.com (G. Bahat), birkanilhan@hotmail.com (B. İlhan).

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muscular strength with metabolic syndrome in 8570 men and revealed an independent, inverse association. The authors assessed muscular strength in the upper and lower body using a standardized strength testing protocol of variable resistance weight machines [16]. Later, there were studies from Asian populations showing the association of low muscle mass with metabolic syndrome especially, and reporting on the association of sarcopenia adjusted by body weight and metabolic syndrome components [17–20]. In their study evaluating skeletal muscle mass by dual X-ray absorptiometry, Kim et al. examined 526 participants (328 women, 198 men) and reported that the lowest quintile of skeletal muscle mass index (skeletal mass adjusted for body weight) was associated with a greater presence of metabolic syndrome among both men and women [17]. From Japan, Ochi et al. reported a significant and negative association between muscle mass and indicators of atherosclerosis. They studied the cross-sectional area (CSA) of mid-thigh muscle that was measured using computed tomography corrected by body weight (CSA/BW), and carotid intima media thickness (IMT) with brachial-ankle pulse wave velocity (baPWV) in apparently healthy 496 middle-aged to elderly people. The authors reported a significant and negative association between thigh muscle CSA/BW and carotid IMT and baPWV in men [20]. The authors also suggested that testosterone accounted for the sex difference owing to its effect on both muscle mass and atherosclerosis. In another cross-sectional study, Kato et al. included 161 patients undergoing haemodialysis with changes of arteriosclerosis to investigate the association between abdominal visceral adiposity, atherosclerosis, and thigh sarcopenia. After multiple regression analyses, the authors observed standardized computed tomography-measured CSA, which had been corrected for femoral shift, was significantly associated with carotid IMT, baPWV, cardio-ankle vascular index, and ankle-brachial pressure index. They concluded that sarcopenia was closely and independently associated with systemic changes of atherosclerosis in patients undergoing haemodialysis [21]. Similarly, Ohara et al. reported lower CSA, which was assessed by computed tomography was significantly associated with higher arterial stiffness, pressure wave reflection, and central pulse pressure in their cross-sectional J-SHIPP 2014 study [22]. In 2015, the same authors reported portable-simple non-invasive techniques, i.e. handgrip strength and bioimpedance, were also observed as risk factors for CMD in 1593 patients who were middle-aged and older [23]. Very recently, Kim et al. evaluated sarcopenia adjusted by body weight and CVD risk using the Framingham risk score, and noted that obese subjects had increased 10-yr CVD risk only when there was accompanying sarcopenia. In their study, sarcopenia was considered as appendicular skeletal muscle mass divided by body weight <1 standard deviation below the mean reference value (i.e., aged 20–39 yr) [19]. Recently, Hamasaki et al. observed that the ratio of lower extremity muscle mass to body weight was significantly and negatively correlated with body mass index, waist circumference, waist-to-hip ratio, body fat mass, body fat percentage, subcutaneous fat area, and serum free fatty acid concentration, was positively correlated with daily physical activity. And the ratio of lower extremity muscle mass to upper extremity muscle mass was significantly and positively correlated with serum high-density lipoprotein cholesterol. They measured body composition by bioelectrical impedance [24]. Byeon et al. recently measured appendicular skeletal muscle mass adjusted for body weight using dual X-ray absorptiometry and reported that sarcopenia itself was associated with higher Framingham risk score for CVD and may be an early predictor of its susceptibility in both elderly and middle-aged subjects in their KNHANES survey [25]. Positive associations between sarcopenia which was defined lower muscle mass adjusted by body weight and insulin resistance, diabetes, and metabolic syndrome, stroke risk, cardiovascular disease, nonalcoholic fatty liver disease (NAFLD) and all-cause mortality have been showed in multiple KNHANES surveys [26–32]. Also several other cross-sectional studies from different countries reported the associations between sarcopenia and mortality, probable greater risk for aortic calcification, hypertensive target organ damage and other traditional CV risk factors [33–36]. One of the KNHANES surveys which is 2008–2011 cross-sectional study showed skeletal muscle index which had been corrected for total body weight was inversely correlated with all nonalcoholic fatty liver disease (NAFLD) predicting scores and advanced fibrosis [30]. Another retrospective study of 11,116 participants stated that bioelectric impedance analysis -measured skeletal muscle mass which had been corrected for total body weight was significantly associated with NAFLD using by the fatty liver index (greater fatty liver index sign the probability of having fatty liver). Skeletal muscle to visceral fat ratio (SVR) and skeletal muscle index had inverse correlations with fatty liver index [37]. Dynapenia might also be an associated factor with metabolic risk factors. A total of 3007 men and women from the National Health and Nutrition Examination Survey investigated the additive effect of dynapenia and abdominal obesity on metabolic risk factors in older adults. The odds of having metabolic syndrome, cardiovascular diseases, and type II diabetes were higher in DYN/AO compared with dynapenic/non-abdominally obese and non-dynapenic/non-abdominally obese people [38].

Several prospective studies have revealed increased CVD risk in adults/older people who have lower muscle strength or muscle mass [39–41]. In a 27-year follow-up study that included 4912 people aged 35 to 74 years at baseline from the Adult Health Study (AHS) cohort, Sasaki et al. reported that the multivariate-adjusted relative risk of CVD was lower in men with greater handgrip strength [39]. Stephen and Janssen reported that low muscle strength predicted the higher CVD among obese participants in their cohort study of 3366 community-dwelling men and women aged ≥ 65 years, who were free of CVD at baseline and monitored for CVD development over 8 years. In their study, waist circumference, bioimpedance analysis, and grip strength were used to measure abdominal obesity, whole-body muscle mass, and muscular strength, respectively [40]. In another prospective observational cohort study, Heitmann and Frederiksen examined the associations between thigh circumference and incidental CVD over 10 years among 1436 men and 1380 women in Denmark [41]. The authors reported that the lower muscle mass, which was indicated by a small thigh circumference, was associated with an increased risk of CVD in both men and women. A threshold effect for thigh circumference was evident, with greatly increased risk of premature death below 60 cm. These findings were independent of abdominal and general obesity, lifestyle, and cardiovascular risk factors such as blood pressure and lipid concentration. Recently, prospective cohort data from older men in the British Regional Heart Study demonstrated that sarcopenia assessed using the mid-arm muscle circumference was associated with increased CVD mortality [42–44].

In contrast, studies that suggest an association of sarcopenia with lower metabolic syndrome prevalence have also been reported. Longitudinal data from the New Mexico Aging Process Study reported that the prevalence of metabolic syndrome was lowest in the sarcopenic group, as defined by appendicular skeletal muscle mass adjusted by height squared [45]. This finding was similar to the results of a small cross-sectional study of 22 obese postmenopausal women [46]. Aubertin-Leheudre et al. compared sarcopenic-obese and non-sarcopenic-obese postmenopausal women for risk factors predisposing to CVD and reported that sarcopenia seemed to be associated with fewer CVD risk factors in obese postmenopausal women. Of note, sarcopenia was defined as fat-free muscle mass index of <14.30 kg, measured using dual