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Sarcopenic obesity in ageing: cardiovascular outcomes and mortality

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Abstract

Obesity is a major public health issue with prevalence increasing worldwide. Obesity is a well-established risk factor for CVD and mortality in adult populations. However, the impact of being overweight or obese in the elderly on CVD and mortality is controversial. Some studies even suggest that overweight and obesity, measured by BMI, are apparently associated with a decreased mortality risk (known as the obesity paradox). Ageing is associated with an increase in visceral fat and a progressive loss of muscle mass. Fat mass is positively associated and lean mass is negatively associated with risk of mortality. Therefore, in older adults BMI is not a good indicator of obesity. Sarcopenia has been defined as the degenerative loss of muscle mass, quality and strength with age and is of major concern in ageing populations. Sarcopenia has previously been associated with increased risks of metabolic impairment, cardiovascular risk factors, physical disability and mortality. It is possible for sarcopenia to co-exist with obesity, and sarcopenic obesity is a new class of obesity in older adults who have high adiposity levels together with low muscle mass, quality or strength. Therefore, sarcopenia with obesity may act together to increase their effect on metabolic disorders, CVD and mortality. This review will discuss the available evidence for the health implications of sarcopenic obesity on CVD and mortality in older adults.

Key words: **Sarcopenia: Muscle: Obesity: CVD: Mortality: Older adults**

Obesity is defined as abnormal or excessive body fat, and it is a major public health problem. In recent times, the prevalence of obesity has increased dramatically and it continues to increase in middle-aged and older adults worldwide, with a doubling in prevalence since 1980[1,2]. With age, obesity prevalence also increases, so in an ageing population this obesity epidemic represents a mounting financial concern in regard to healthcare resources[3–6]. Obesity is a well-established risk factor for CVD and mortality in adult populations[7–10]; typically 'U' or 'J' shaped curves are seen between obesity (measured by BMI) and CVD or mortality, with increased risks in underweight and overweight middle-aged adults. However, there is controversy surrounding the effects of overweight and obesity on CVD and mortality in older people. Some studies even suggest that overweight and obesity, measured by BMI, are apparently associated with a lower mortality risk[11] (known as the obesity paradox). A previous large meta-analysis, including thirty-two studies, of almost 200 000 individuals aged 65 years and older, showed a U-shaped relationship between BMI and mortality, with the lowest risk in those with a BMI between 24 and 30 kg/m^2, and mortality risk only began to increase when BMI exceeded 33 kg/m^2[12]. This obesity paradox may be partly explained by the fact that BMI is an imprecise measure of body fat which does not distinguish between fat and lean body mass, with have opposing effects on mortality risk; fat mass is positively associated and lean mass is negatively associated with mortality risk[13].

As people age, some important changes to body composition occur, which includes a relative increase in visceral abdominal fat and a gradual loss of muscle mass[14–16]. Increased visceral fat is a risk factor for developing metabolic disorders, such as hypertension, dyslipidaemia and insulin resistance, and also CVD. The progressive loss of muscle strength and mass which happens with age is known as sarcopenia[17]. Many factors contribute to the development of sarcopenia but its aetiology is not completely understood. A number of pathological mechanisms have been suggested to underlie age-related muscle loss including neuronal and hormonal changes, being underweight, undernutrition including low protein intake, physical inactivity and inflammation[6,18–22]. Sarcopenia is of major concern in ageing populations as it is associated with metabolic impairment, cardiovascular risk factors and physical disability[23–25]. Although sarcopenia has been less extensively studied in relation to incident CVD morbidity and mortality, there is increasing evidence that muscle mass or muscle strength components of

Abbreviations: BIA, bioimpedance analysis; DXA, dual-energy X-ray absorptiometry; EWGSOP, European Working Group on Sarcopenia in Older People; HR, hazard ratio.

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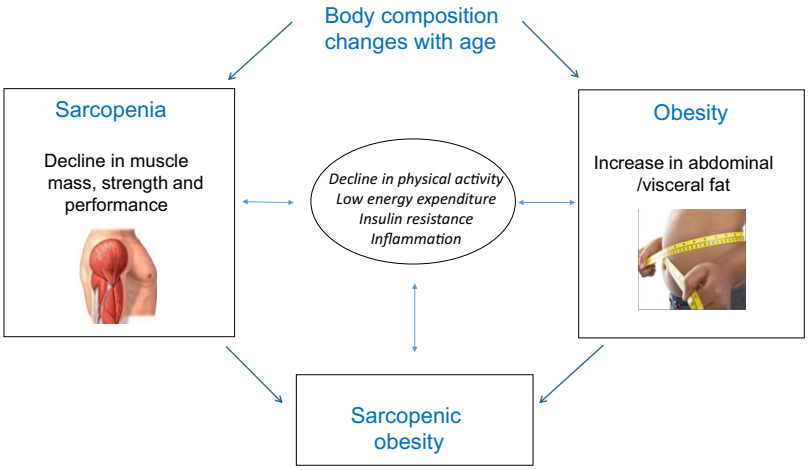

Fig. 1. Body composition changes with age and the interplay between sarcopenia and obesity. Adapted from Wannamethee & Atkins[35].

sarcopenia are associated with increased risk of CVD[26–30]. It is well documented that sarcopenia is a significant predictor of death in older adults, including those who are community-dwelling, care home residents or hospitalised patients[31–33]. A recent meta-analysis of six prospective cohort studies examined the association between sarcopenia and mortality, including 7367 community-dwelling older adults[31]. The pooled estimate showed that sarcopenic individuals had a 60 % increase in the risk of mortality (hazard ratio (HR) 1·60, 95 % CI 1·24, 2·06) compared with those without sarcopenia. Sarcopenia is also a significant predictor of all-cause mortality among older nursing home residents, with a meta-analysis of six studies showing an 86 % increase in risk (pooled HR 1·86, 95 % CI 1·42, 2·45)[32].

Despite it being the case that body composition can greatly change with age, the fact that visceral fat tends to increase and muscle mass tends to decrease means that there may be no significant change to an individual's overall body weight or BMI[6,11]. Body composition changes with age can see the co-occurrence of sarcopenia with increases in fat mass. Sarcopenic obesity has recently emerged as a new category of body composition[6] (Fig. 1). The body composition of older adults can therefore be categorised as: normal, sarcopenic, obese or sarcopenic obese. Visceral fat and muscle mass are connected pathogenically and share common pathways including decline in physical activity, low energy expenditure, increase in insulin resistance and inflammation[6,34–37]. The co-existence of both sarcopenia and obesity in older adults may therefore interact and increase their effects on risk of CVD and mortality, which may result in older adults with a sarcopenic obese body composition having the worse disease and mortality outcomes[6,38–40].

Sarcopenic obesity

The term 'sarcopenic obesity' was first coined by Baumgartner[41] and combines the body composition categories of both sarcopenia and obesity. BMI (weight divided by height squared) is the most commonly used measure of adiposity, with obesity defined as greater than or equal to 30 kg/m^2[42]. However, the validity of BMI in adequately measuring adiposity has been questioned, especially in older age, as BMI does not differentiate between fat mass and lean mass[13]. Alternative obesity definitions have therefore focused on the distribution of body fat, with central or visceral obesity being commonly measured[15]. Fat mass can be assessed using bioimpedance analysis (BIA) or dual-energy X-ray absorptiometry (DXA)[16]. Computerised tomography or MRI can also be used to evaluate adipose tissue or its quality[43] (Table 1). Measures of central obesity have also been shown to be stronger predictors of CVD and mortality than BMI in older adults[44,45]. Two such anthropometric measures of central adiposity are waist:hip ratio (≥0·90 cm for men; ≥0·85 cm for women) and waist circumference (>102 cm for men; >88 cm for women), as defined by the WHO[46].

Sarcopenia has been defined using many different measurement methods (Table 1), and the diagnostic criteria are not uniform[47]. Sarcopenia was originally defined by Baumgartner *et al.*[19] as appendicular skeletal muscle mass two SD below the sex-specific reference for a young healthy person, assessed using DXA and height adjusted. Janssen *et al.*[48] developed an alternative sarcopenia definition of skeletal muscle mass measured by BIA. DXA and BIA are more commonly used to assess muscle mass in research settings, but some clinical setting may also use computerised tomography or MRI scans. In 2010, The European Working Group on Sarcopenia in Older People (EWGSOP) published a sarcopenia definition to assist in case finding in older adults[49]. This definition included the presence of both low muscle function (low strength and/or low physical performance) and low muscle mass. The EWGSOP sarcopenia definition recommended measuring physical performance using gait speed and measuring muscle strength using handgrip strength[49]. In 2014, an alternative and more specific sarcopenia definition was recommended by the Foundation for the National Institutes of Health Sarcopenia Project; appendicular lean mass cut-points adjusted for BMI (<0·789 for men; <0·512 for women) and for grip strength cut-points (<26 kg for men; <16 kg for women)[50]. Recently, there has been much increased acknowledgement of the importance of sarcopenia in older adults, and in 2016 sarcopenia was officially recognised as a disease and assigned an International Classification of Disease-10

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Table 1. Methods for measuring sarcopenia and obesity

Sarcopenia			Obesity	
Muscle mass	Muscle strength	Muscle performance	Fat mass	Adipose tissue
Anthropometry, for example, calf circumference, MAMC Bioimpedance analysis Computerised tomography Dual-energy X-ray absorptiometry MRI	Grip strength Chair stand test Knee flexion/extension	Gait speed Timed-up-and-go test Short physical performance battery	Anthropometry, for example, BMI, skinfold thickness, WC, WHR Bioimpedance analysis Dual-energy X-ray absorptiometry	Computerised tomography MRI

MAMC, midarm muscle circumference; WC, waist circumference; WHR, waist:hip ratio.

code[51]. In 2019, the EWGSOP published an updated sarcopenia definition and cut-points (the EWGSOP-2) which focused on low muscle strength as a key sarcopenia characteristic, used detection of low muscle quantity and quality to confirm the diagnosis and used poor physical performance to indicate severe sarcopenia[52]. Comparison of the old and new EWGSOP definitions of sarcopenia in the UK Biobank cohort study suggests that the new EWGSOP-2 definition recognises fewer people as sarcopenic (0·36 %) compared with the old definition (8·14 %)[53].

The operational definition of sarcopenic obesity is still under discussion[36] and hence there is no universally accepted classification[24,40,52]. There is a marked heterogeneity in definitions and approaches to diagnose sarcopenic obesity[54]. The threshold values used in previous literature to define both sarcopenia and obesity have varied significantly depending on population, age, sex and ethnicity[55]. It is therefore a challenge to compare the results of findings between studies using different sarcopenic obesity definitions. Prevalence estimates for sarcopenic obesity have therefore also differed greatly, from 0 to 25 % in older adults across different studies, with an average prevalence of 5–10 %[55]. In a review of eight sarcopenic obesity definitions, Batsis *et al.*[56] estimated that prevalence can vary up to 26-fold depending on definition used. Such a high degree of variability is suggestive of a need to establish a consensus definition that can be reliably applied across different clinical and research settings[36].

Sarcopenic obesity and cardiovascular risk factors

There has been a rapid growth in the literature in the last couple of decades which has examined the associations between sarcopenic obesity and cardiovascular risk factors[35,39,57]. Table 2 summarises relevant studies, discussed below, that investigate the associations of sarcopenic obesity and cardiovascular risk factors in older people. In Korean older adults, several cross-sectional studies have shown that sarcopenic obese individuals have the highest cardiovascular risk; sarcopenic obesity (classified by skeletal muscle mass assessed by DXA and obesity assessed by either DXA, BMI or waist circumference) was associated with up to an 8-fold increase in the risk of the metabolic syndrome, an increased risk of hypertension, insulin resistance, dyslipidaemia, higher fasting glucose levels and a lower cardiorespiratory fitness, compared with the non-sarcopenic, non-obese group[58–66]. A study in Taiwanese older adults (defined by BIA-measured muscle mass and BMI) is also comparable in that the sarcopenia obese group also had the highest risk of the metabolic syndrome, with a 12 times increased risk, compared with the non-sarcopenic, non-obese group[67]. A large cross-sectional study of over 14 000 adults in the National Health and Nutrition Examination Survey showed that sarcopenic obese individuals (defined by BIA-measured muscle mass and BMI) also have the highest risk of dysglycaemia and insulin resistance[68].

Not all studies, however, show that sarcopenic obese older adults have the highest cardiovascular risks, with some studies suggesting that obese older adults have higher levels of cardiovascular risk factors. The New Mexico Aging Process Study examined older adults aged 60 years and over, and found that the prevalence of hypertension and the metabolic syndrome was highest in the non-sarcopenic obese group, followed by the sarcopenic obese group (assessed using DXA measurements)[69]. Studies in older, postmenopausal women have also shown that sarcopenic obese individuals did not have a worse metabolic profile compared with non-sarcopenic obese individuals[70] and that glucose level, lipid profile and blood pressure were not significantly higher in sarcopenic obese compared with non-sarcopenic, non-obese people[71].

In spite of inflammation being on a common pathway for both sarcopenia and obesity, differing results have been found regarding the association between sarcopenic obesity and inflammatory or haemostatic markers. The 'Invecchiare in Chianti' (InCHIANTI) study of older adults, aged 65 years and older, showed that sarcopenic obesity (defined using grip strength and waist circumference measurements) was associated with higher levels of inflammatory markers including IL-6 and C-reactive protein in cross-sectional analysis[72]. Similarly, a study found that in older Korean women, the sarcopenia obese group had the highest C-reactive protein levels[64]. However, baseline analysis of the Trial of Angiotensin Converting Enzyme Inhibition and Novel Cardiovascular Risk Factors study found that although obesity and sarcopenia were both significantly associated with higher C-reactive protein and IL-6 levels, the relationship of inflammation with sarcopenia was not independent of the relationship with obesity[73]. A study of postmenopausal women also found that C-reactive protein levels were not significantly different between the sarcopenic obese and non-sarcopenic, non-obese groups[71].

The 5th Korean National Health and Nutrition Examination Survey (n 3320; ≥40 years) assessed the association between sarcopenic obesity and a number of cardiovascular risk factors, encapsulated within the Framingham risk score[74]. The Framingham risk score was calculated based on age, sex, total

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Table 2. Summary of studies examining the association between sarcopenic obesity and cardiovascular risk factors in older people*

Author	Year published	Study type	Participants and sample	Measurement of sarcopenic obesity	Main results
Khadra *et al.*[75]	2019	Meta-analysis	*n* 60 118 Eleven studies (mainly cross-sectional) Men and women	Various measurements	The pooled OR showed that sarcopenic obesity was associated with a 38 % increase in odds of type 2 diabetes compared with those without sarcopenic obesity
Khadra *et al.*[76]	2020	Meta-analysis	*n* 11 308 Twelve studies Men and women	Various measurements	Pooled analysis showed that sarcopenic obese participants did not have a significantly increased risk of the MetS compared with those with obesity only
Baumgartner *et al.*[69]	2004	Cross-sectional analysis at baseline of a prospective cohort (8 years follow-up)	*n* 451 New Mexico Aging Process Study Men and women Aged ≥60 years	DXA (ASM; % body fat)	The prevalence of MetS and hypertension was highest in the non-sarcopenic obese group, followed by the sarcopenic obese group
Cesari *et al.*[73]	2005	Cross-sectional	*n* 286 Trial of Angiotensin Converting Enzyme Inhibition and Novel Cardiovascular Risk Factors study Men and women Aged >55 years	DXA (appendicular lean mass; % FM)	No significant interactions were found between sarcopenia and obesity with CRP or IL-6
Schrager *et al.*[72]	2007	Cross-sectional	*n* 871 InCHIANTI study Men and women Aged ≥65 years	Grip strength; WC; BMI ≥ 30 kg/m^2	Sarcopenic obesity was associated with higher levels of inflammatory markers including CRP and IL-6
Kim *et al.*[66]	2009	Cross-sectional	*n* 526 Korean Sarcopenic Obesity Study Men and women Aged ≥20 years	DXA (ASM; SMI; % body fat)	Women with sarcopenic obesity (identified using SMI) have three times the risk of MetS and non-sarcopenic obese had two times the risk of MetS compared with non-sarcopenic, non-obese participants. Similar associations found in men although not significant
Messier *et al.*[70]	2009	Cross-sectional	*n* 136 Healthy overweight or obese postmenopausal women Aged 46–70 years	DXA (ASM); CT	Sarcopenic overweight/obese women did not show a higher risk metabolic profile compared with non-sarcopenic overweight/obese women
Srikanthan *et al.*[68]	2010	Cross-sectional	*n* 14 528 National Health and Nutrition Examination Survey III Men and women Aged >20 years	BIA (SMI); BMI ≥ 30 kg/m^2	The sarcopenic obese group had the highest risk of insulin resistance and dysglycaemia
Lim *et al.*[59]	2010	Cross-sectional	*n* 565 Korean Longitudinal Study on Health and Aging Men and women Aged ≥65 years	DXA (ASM); CT (VFA)	The sarcopenic obese group was at the highest risk of insulin resistance and Mets, with eight times the risk of MetS compared with non-sarcopenic, non-obese
Chung *et al.*[60]	2013	Cross-sectional	*n* 2943 Korea National Health and Nutrition Examination Survey Men and women Aged ≥60 years	DXA (ASM); BMI ≥ 25 kg/m^2	The sarcopenic obese group was associated with a higher risk of insulin resistance, MetS and CV risk factors than any other group

Table 2. (*Continued*)

Author	Year published	Study type	Participants and sample	Measurement of sarcopenic obesity	Main results
Hwang *et al.*[61]	2012	Cross-sectional	*n* 2221 Korea National Health and Nutrition Examination Survey Men and women Aged ≥60 years	DXA (ASM); WC (WC ≥90 cm for men; ≥85 cm for women)	Sarcopenic obesity was associated with higher fasting glucose level and TAG level in women, and higher serum insulin levels
Kim *et al.*[64]	2013	Cross-sectional	*n* 493 Korean Sarcopenic Obesity Study Men and women Aged ≥20 years	DXA (ASM); CT (VFA)	In women, the sarcopenic obese group had higher levels of insulin resistance and CRP compared with the non-sarcopenic, obese group. In men, the sarcopenic obese group had higher levels of insulin resistance compared with the non-sarcopenic obese group
Lu *et al.*[67]	2013	Cross-sectional	*n* 600 Community-dwelling Taiwanese adults Men and women Aged 63·6 (SD 10·1) years	BIA (skeletal muscle mass); BMI ≥ 25 kg/m^2	The sarcopenic obese group was at highest risk of MetS, with twelve times the risk compared with non-sarcopenic, non-obese
Park *et al.*[62]	2013	Cross-sectional	*n* 6832 Korea National Health and Nutrition Examination Survey Men and women Aged ≥19 years	DXA (ASM); WC (WC ≥ 90 cm for men; ≥85 cm for women)	The odds of hypertension were higher in the sarcopenic obese group compared with the obese, sarcopenic and non-sarcopenic, non-obese groups
Baek *et al.*[58]	2014	Cross-sectional	*n* 3483 Korea National Health and Nutrition Examination Survey Men and women Aged ≥65 years	DXA (ASM); BMI ≥ 25 kg/m^2	Sarcopenic obesity was associated with an increased risk of dyslipidaemia compared with sarcopenia or obesity alone
Han *et al.*[65]	2014	Cross-sectional	*n* 4846 Korea National Health and Nutrition Examination Survey Men and women Aged ≥60 years	DXA (ASM); BMI ≥ 25 kg/m^2	The odds of hypertension were highest in the sarcopenic obese group compared with all other groups
Kim *et al.*[63]	2014	Cross-sectional	*n* 298 Korean patients visiting hospital for a regular checkup Men and women Aged 20–70 years	DXA (SMI); CT (VFA)	Sarcopenic obesity was strongly associated with low cardiorespiratory fitness
dos Santos *et al.*[71]	2014	Cross-sectional	*n* 149 Postmenopausal Brazilian women Aged 67·2 (SD 6·1) years	DXA (appendicular FFM; FM)	No significant difference in BP, glucose level, TC, HDL, LDL and CRP between the sarcopenic obese and non-sarcopenic obese groups
Kim *et al.*[74]	2015	Cross-sectional	*n* 3320 Korea National Health and Nutrition Examination Survey Men and women Aged ≥40 years	DXA (ASM); BMI ≥ 25 kg/m^2	The sarcopenic obese group was associated with a significantly increased 10-year CVD risk score (based on the Framingham risk score) compared with the non-sarcopenic, non-obese group (OR 2·49, 95 % CI 1·53, 4·06 in men; OR 1·87, 95 % CI 1·02, 3·41 in women)

ASM, appendicular skeletal muscle mass; BIA, bioelectrical impedance analysis; BP, blood pressure; CRP, C-reactive protein; CT, computerised tomography; DXA, dual-energy X-ray absorptiometry; FFM, fat-free mass; FM, fat mass; MetS, metabolic syndrome; SMI, skeletal muscle mass index; TC, total cholesterol; VFA, visceral fat area; WC, waist circumference.
* Table adapted from Atkins & Wannamethee[82]. Studies arranged by type (meta-analysis, cross-sectional) and by year.

Table 3. Summary of studies examining the association between sarcopenic obesity and risk of CVD in older people*

Author	Year published	Study type	Participants and sample	Measurement of sarcopenic obesity	Main results
Stephen & Janssen[79]	2009	Prospective cohort (8-year follow-up)	*n* 3366 Cardiovascular Health Study Men and women Aged ≥65 years	BIA (skeletal muscle mass); grip strength; WC	Sarcopenic obesity, based on muscle strength but not muscle mass, was associated with a 23 % increase in CVD risk
Atkins *et al.*[80]	2014	Prospective cohort (11-year follow-up)	*n* 4111 British Regional Heart Study Men Aged 60–79 years	MAMC; BIA (FM; FFM); WC	Sarcopenic obesity (defined based on WC > 102 cm and lowest two quintiles of MAMC, or defined by BIA) was not associated with CVD events or CVD mortality
Farmer *et al.*[81]	2019	Prospective cohort (5·1-year follow-up)	*n* 452 931 UK Biobank Men and women Aged 40–70 years	Grip strength; BMI	Sarcopenic obesity was associated with the highest risk of CVD events, compared with the other three body composition categories, with no clear differences between those with and without a history of CVD
Baumgartner *et al.*[69]	2004	Cross-sectional analysis at baseline of a prospective cohort (8-year follow-up)	*n* 451 New Mexico Aging Process Study Men and women Aged ≥60 years	DXA (ASM; % body fat)	Participants with sarcopenic obesity did not have a higher CVD prevalence
Chin *et al.*[78]	2013	Cross-sectional	*n* 1578 Korea National Health and Nutrition Examination Survey Men and women Aged ≥65 years	DXA (ASM); BMI ≥ 25 kg/m^2	The sarcopenic obese group had a higher prevalence of CVD (12·4 %) compared with non-sarcopenic obese (10·1 %), but the difference was non-significant

ASM, appendicular skeletal muscle mass; BIA, bioelectrical impedance analysis; DXA, dual-energy X-ray absorptiometry; FFM, fat free mass; FM, fat mass; MAMC, midarm muscle circumference; WC, waist circumference.
* Table adapted from Atkins[39]. Studies arranged by type (prospective cohort, cross-sectional) and by year.

cholesterol, HDL-cholesterol, systolic blood pressure, smoking and diabetes. The sarcopenic obese group was associated with a significantly increased 10-year CVD risk (OR 2·49, 95 % CI 1·53, 4·06 in men; OR 1·87, 95 % CI 1·02, 3·41 in women) compared with the non-sarcopenic, non-obese group. However, sarcopenic non-obese and non-sarcopenic obese participants were not associated with an increased 10-year CVD risk.

More recently, a meta-analysis of studies examining the associations between sarcopenia obesity and type 2 diabetes has been performed, with eleven studies including a total of 60 118 adults who were overweight or obese[75]. Sarcopenic obesity was significantly associated with a 38 % increase in risk of type 2 diabetes compared with those without sarcopenic obesity (OR 1·38, 95 % CI 1·27, 1·50), but results should be interpreted with caution as the majority of studies were cross-sectional. A meta-analysis has also been carried out to synthesise the results of studies assessing the associations between sarcopenia obesity and the metabolic syndrome, including twelve studies with a total of 11 308 overweight or obese adults[76]. Pooled analysis showed that sarcopenic obese participants did not have a significantly increased risk of the metabolic syndrome (risk ratio 1·08, 95 % CI 0·99, 1·17) compared with those with obesity only.

Sarcopenic obesity and CVD

In spite of the growth of literature on the associations between sarcopenic obesity and cardiovascular risk factors in recent years, to date only a limited number of studies have assessed the associations between sarcopenic obesity and CVD risk in older adults[35,39,57,77]. Table 3 summarises relevant studies, discussed below, that investigate the associations of sarcopenic obesity and the risk of CVD in older people. Cross-sectional studies have yielded inconsistent results. A cross-sectional analysis in the New Mexico Aging Process Study compared CVD prevalence across body composition groups in older adults, aged 60 years and older[69]. The prevalence of CVD was not higher in sarcopenic obese individuals (11·5 %), defined with appendicular skeletal muscle and percentage body fat from DXA, compared with non-sarcopenic, non-obese individuals (13·7 %). Conversely, a cross-sectional study of older adults aged 65 years and older, in the Korea National Health and Nutrition Examination Survey, found that the sarcopenic obese group (based on appendicular skeletal muscle from DXA and BMI ≥ 25 kg/m^2) showed a slightly higher but non-significant prevalence of CVD (12·3 %) compared with non-sarcopenic obese (10·0 %)[78].

There are a small number of prospective studies that have examined the association between sarcopenic obesity and CVD risk over time. Stephen & Janssen[79] analysed data from a prospective study of 3366 community-dwelling older adults (aged 65 years and over) followed over 8 years, in the Cardiovascular Health Study. The risk of CVD events was not significantly raised in the sarcopenic obese group (defined using waist circumference and BIA-measured muscle mass) compared with the normal body composition group. However, it seems that muscle strength could be better measure of sarcopenia than muscle mass in predicting CVD risk, as within the same study population, when sarcopenic obesity was defined by grip

strength and waist circumference, there was a 23 % increase in CVD risk in the sarcopenic obese group, compared with the non-sarcopenic, non-obese group[79]. The sarcopenic obese group also had the highest risk of CVD compared with the sarcopenic group and the obese group[79]. A prospective study of 4111 men from the British Regional Heart Study, aged 60–79 years and followed-up for 11 years, showed no association between sarcopenic obesity (defined by midarm muscle circumference and waist circumference) and CVD events or CVD mortality[80]. However, this study did not examine muscle strength measures when defining sarcopenic obesity. Recently, Farmer *et al.*[81] explored the association between sarcopenic obesity and CVD in the largest prospective study of its kind to date in UK Biobank (452 931 community volunteers, aged 40–70 years, followed up for 5·1 years). Sarcopenic obesity (defined by hand grip strength and BMI) was associated with the highest risk of CVD events, compared with the other three body composition categories, with no clear differences between those with and without a history of CVD. However, there is no clear evidence of an interaction between obesity and sarcopenia for CVD events. Overall, it seems that research to date from these cross-sectional and prospective studies shows heterogeneity in associations between sarcopenic obesity and risk of CVD; the literature is not consistent as to whether the sarcopenic obese group has the highest risk of CVD, but these inconsistencies are perhaps due to the different sarcopenic obesity definitions used between studies.

Sarcopenic obesity and mortality

Recently, there has been a growing number of prospective studies which have examined the risk of all-cause mortality in sarcopenic obese older adults[39,82,83]. Table 4 summarises relevant studies, discussed below, that investigate the associations of sarcopenic obesity and mortality risk in older people. In a community-based study of 4107 men, aged 60–79 years (the British Regional Heart Study) the risk of all-cause mortality was increased in sarcopenic obese individuals; those with a high waist circumference (>102 cm) and in the lowest quartile of midarm muscle circumference had a 55 % increase in mortality risk compared with non-sarcopenic, non-obese individuals over a follow-up period of 6 years[84]. This same population was re-examined more recently after 11 years of follow-up[80]. The risk of mortality was increased in the sarcopenic group (41 % increase in risk) and the obese group (21 % increase), with the highest risk in sarcopenic obese men (72 % increase) compared with the non-sarcopenic, non-obese group, after adjustment for lifestyle and cardiovascular risk factors[80].

The National Health and Nutrition Examination Survey has also assessed the association between sarcopenic obesity and mortality in more than 4000 participants, aged 60 years or above, followed-up for 14 years[85]. Sarcopenic obesity was classified according to BIA-measured skeletal muscle mass and body fat, and sarcopenic obese women had a significantly increased mortality risk of 29 % compared with those with no sarcopenia or obesity, after adjustment for age, sex, ethnicity and cardiovascular risk factors[85]. However, there was no significant increase in mortality risk in sarcopenic obese men in this cohort[85]. The InCHIANTI study assessed risk of mortality in 934 males and females aged 65 years and above, across six different sarcopenic obesity combinations, combining sarcopenia (measured with calf skeletal muscle) or no sarcopenic with three adiposity categories (obese, overweight or normal body weight measured by BMI)[86]. Over a follow-up period of 6 years, no significant difference in risk of mortality was observed across the six sarcopenic obesity groups. Similarly, a recent small study in 954 men (aged 70 years and above, followed-up for over 7 years) from the Concord Health and Ageing in Men Project, categorised sarcopenic obesity based on DXA-measured lean mass and body fat, also found no significant association between sarcopenic obesity and mortality risk after adjustment for confounders[87].

A number of prospective cohort studies examining mortality risk have defined sarcopenic obesity using a measure of muscle strength instead of muscle mass, with grip strength being a common measurement method. In over 6000 healthy adult men aged 45–68 years living in Hawaii, with follow-up of more than 30 years, mortality risk was significantly increased by 39 % in sarcopenic obesity men (BMI ≥ 25 kg/m^2; lowest tertile of grip strength)[88]. The Mini-Finland Health Examination Survey, including 3594 participants followed over 17 years, categorised sarcopenic obesity using BMI and grip strength (BMI ≥ 30 kg/m^2; lowest tertile of grip strength), found that sarcopenia and obesity each independently predicted mortality, but with an additive rather than a multiplicative effect[89]. A prospective study of 6864 older adults in the English Longitudinal Study of Ageing, which categorised sarcopenic obesity using BMI and grip strength (BMI ≥ 30 kg/m^2; lowest tertile of grip strength) found that sarcopenic obese individuals did not have a significantly greater risk of mortality than those with just sarcopenia, but the risk was higher than in those with just obesity[90]. Another prospective study, categorising sarcopenic obesity using tertiles of waist circumference and tertiles of grip strength (*n* 846 older adults from InCHIANTI), found that after adjustment for confounders, only the sarcopenic group (and not the obese group or the sarcopenic obese group) had a significantly increased mortality risk[91]. Although the above studies have all used tertiles of grip strength, this will have resulted in different grip strength cut-offs in different settings. This could confound results and makes valid comparison of findings problematic.

A recent meta-analysis by Tian & Xu in 2016[83] has amalgamated the results of twelve prospective studies, including 35 287 participants, assessing the association between sarcopenic obesity and risk of mortality. Analysis showed that sarcopenic obesity was associated with a 24 % increase in risk of all-cause mortality compared with those without sarcopenia or obesity (pooled HR 1·24, 95 % CI 1·12, 1·37).

However, this meta-analysis did not perform a subgroup analysis of types of participants and included both community-dwelling individuals and disease-specific populations. Zhang *et al.*[92] updated this meta-analysis in 2019, to include twenty-three prospective studies, with 50 866 participants aged 50–82 years. Similarly to the previous meta-analysis[83], a 21 % increase in mortality risk was seen in sarcopenic obese individuals (pooled HR 1·21, 95 % CI 1·10, 1·32) compared with non-sarcopenic, non-obese. This meta-analysis did not present

Table 4. Summary of studies examining the association between sarcopenic obesity and risk of mortality in older people*

Author	Year published	Study type	Participants and sample	Measurement of sarcopenic obesity	Main results
Tian & Xu[83]	2016	Meta-analysis	*n* 35 287 Twelve prospective cohort studies (including community-dwelling participants and disease specific populations) Men and women	Various measurements	The pooled HR showed that sarcopenic obesity was associated with a 24 % increase in risk of all-cause mortality compared with the non-sarcopenic, non-obese group
Zhang *et al.*[92]	2019	Meta-analysis	*n* 50 866 Twenty-three prospective cohort studies Men and women 50–82 years	Various measurements	The pooled HR showed that sarcopenic obesity was associated with a 21 % increase in risk of all-cause mortality compared with the non-sarcopenic, non-obese group (14 % increase in community-dwelling older people and 65 % increase in hospitalised patients)
Rantanen *et al.*[88]	2000	Prospective cohort (30-year follow-up)	*n* 6040 Healthy adults from Hawaii Men Aged 45–68 years	Grip strength; BMI	Sarcopenic obese mean (BMI $\geq$ 25 kg/m^2, lowest grip strength tertile) had a 39 % increased risk of mortality compared with normal weight men in the highest tertile
Wannamethee *et al.*[84]	2007	Prospective cohort (6-year follow-up)	*n* 4107 British Regional Heart Study Men Aged 60–79 years	MAMC; BIA (FM; FFM); WC; WHR	A combined measure of WC and MAMC was the strongest predictor of mortality. Sarcopenic obesity, based on high WC (>102 cm) and low MAMC (lowest quartile), showed a 55 % increase in risk of mortality compared with non-sarcopenic, non-obese
Cesari *et al.*[86]	2009	Prospective cohort (6-year follow-up)	*n* 934 InCHIANTI Study Men and women Aged $\geq$ 65 years.	CT (calf skeletal muscle; calf FM); BMI	No significant difference reported in mortality risk across six sarcopenic obesity groups
Batsis *et al.*[85]	2014	Prospective cohort (14-year follow-up)	*n* 4652 National Health and Nutrition Examination Survey III Men and women Aged $\geq$ 60 years	BIA (skeletal muscle mass; % body fat)	Sarcopenic obese women had a 29 % higher risk of mortality compared with those without sarcopenia or obesity. In men, mortality risk was not significantly associated with sarcopenic obesity
Stenholm *et al.*[89]	2014	Prospective cohort (17·9-year follow-up)	*n* 3594 Mini-Finland Health Examination Survey Men and women Aged 50–91 years	Grip strength; BMI	Both obesity and low handgrip strength independently predicted mortality risk, but with an additive pattern Among 50–69 year olds, the highest mortality risk was among obese participants with low handgrip strength
Atkins *et al.*[80]	2014	Prospective cohort (11-year follow-up)	*n* 4111 British Regional Heart Study Men Aged 60–79 years	MAMC; BIA (FM; FFM); WC	The sarcopenic obese group (based on WC > 102 cm and lowest two quintiles of MAMC) had a 72 % increase in risk of all-cause mortality compared with the non-sarcopenic, non-obese group. Sarcopenic obesity, based on BIA, was not associated with mortality
Hamer & O'Donovan[90]	2017	Prospective cohort (8·1-year follow-up)	*n* 6864 English Longitudinal Study of Ageing Men and women Mean age 66·2 (SD 9·5) years	Grip strength; BMI	Sarcopenic obesity did not confer any greater risk of mortality than sarcopenia alone
Hirani *et al.*[87]	2017	Prospective cohort (7-year follow-up)	*n* 954 Concord Health and Ageing in Men Project Men Aged $\geq$ 70 years	DXA (appendicular lean mass: BMI ratio; % body fat)	There was no significant association between sarcopenic obesity and mortality risk after adjustment for confounders
Rossi *et al.*[91]	2017	Prospective cohort (11-year follow-up)	*n* 846 InCHIANTI Study Men and women Aged 65–95 years	Grip strength; WC	Mortality risk was significantly higher in participants with sarcopenia (but not sarcopenic obesity) compared with the non-sarcopenic, non-obese group

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Table 4. (*Continued*)

Author	Year published	Study type	Participants and sample	Measurement of sarcopenic obesity	Main results
Farmer *et al.*[81]	2019	Prospective cohort (5·1-year follow-up)	*n* 452 931 UK Biobank Men and women Aged 40–70 years	Grip strength; BMI	In individuals without CVD at baseline, risk of mortality was increased in the sarcopenic obese group (HR 1·31, 95 % CI 1·18, 1·45) compared with the non-sarcopenic, non-obese group. This risk was fairly consistent with the sarcopenic group (HR 1·39, 95 % CI 1·30, 1·48) but higher than the obese only group (HR 1·14, 95 % CI 1·08, 1·21). When examining those without a history of CVD, there was minimal difference in risk

BIA, bioelectrical impedance analysis; CT, computerised tomography; DXA, dual-energy X-ray absorptiometry; FFM, fat free mass; FM, fat mass; HR, hazard ratio; MAMC, midarm muscle circumference; WC, waist circumference; WHR, waist:hip ratio.
* Table adapted from Atkins[39]. Studies arranged by type (meta-analysis, prospective cohort) and by year.

mortality risk in the sarcopenic obese group compared with the sarcopenic only group or the obese only group though. In subgroup analysis, sarcopenic obesity remained a significant predictor of all-cause mortality in community-dwelling older people (HR 1·14, 95 % CI 1·06, 1·23) and especially in hospitalised patients (pooled HR 1·65, 95 % CI 1·17, 2·33)[92]. However, the twenty-three studies included a range of countries and various adjustments for confounders, so there was significant heterogeneity across studies. Subgroup analysis by measurement type showed that sarcopenic obesity was associated with all-cause mortality when sarcopenic was measured by skeletal muscle mass (HR 1·12, 95 % CI 1·01, 1·23), muscle strength (HR 1·18, 95 % CI 1·05, 1·33) and skeletal muscle index (HR 1·53, 95 % CI 1·13, 2·07). Additionally, subgroup analysis showed a significant association between sarcopenic obesity and mortality when obesity was measured by waist circumference (HR 1·24, 95 % CI 1·09, 1·40), BMI (HR 1·29, 95 % CI 1·04, 1·59) and visceral fat area (HR 2·54, 95 % CI 1·83, 3·53). This suggests that using SMI and visceral fat to define sarcopenic obesity may be relevant diagnostic criteria to predict mortality risk in older adults.

More recently, Farmer *et al.*[81] explored the association between sarcopenic obesity and mortality using the UK Biobank, a very large community cohort study of 452 931 volunteers aged 40–70 years, who were followed-up for 5·1 years. Sarcopenic obesity was assessed by grip strength and BMI. In individuals without CVD at baseline, risk of mortality was increased in the sarcopenic obese group (HR 1·31, 95 % CI 1·18, 1·45) compared with the non-sarcopenic, non-obese group. This risk was fairly consistent with the sarcopenic group (HR 1·39, 95 % CI 1·30, 1·48) but higher than the obese only group (HR 1·14, 95 % CI 1·08, 1·21). When examining those without a history of CVD, there was minimal difference in risk.

Conclusion

Sarcopenic obesity is a new category of obesity in older adults, with the co-existence of low muscle mass and strength with high adiposity levels. Studies to date on sarcopenic obesity suggest that this body composition category is associated with higher levels of cardiovascular risk factors and an increased mortality risk in older adults compared with those without sarcopenia or obesity. Efforts to promote healthy ageing should therefore focus on both preventing obesity and maintaining muscle strength and muscle mass. There is some evidence to suggest that the sarcopenic obese group has even higher levels of cardiovascular risk factors and mortality than sarcopenic or obese groups alone. However, the evidence on whether sarcopenic obese have the highest risks of CVD and mortality varies between studies, which is likely to be due to the major differences in sarcopenic obesity classifications used. In recent times, sarcopenia has gained increased recognition as an important condition in older age which has helped to progress and expand the related field of research. However, there is still no universally accepted classification of sarcopenia, or hence therefore of sarcopenic obesity. Therefore, an important need exists to establish a consensus definition of sarcopenic obesity that can be reliably applied across different clinical and research settings.

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