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Muscle loss and obesity: the health implications of sarcopenia and sarcopenic obesity

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This paper reviews the health implications of obesity, sarcopenia and sarcopenic obesity on CVD and mortality in older adults and discusses the obesity paradox seen in patients with CVD. Obesity is a major public health problem with increasing prevalence worldwide. It is an established risk factor for cardiovascular morbidity and mortality in adult populations. However, there is controversy surrounding the effects of obesity as measured by BMI in older people, and overweight and obesity ($\text{BMI} \geq 25 \text{ kg/m}^2$) are apparently associated with increased survival in those with CVD (obesity paradox). Ageing is associated with an increase in visceral fat and a progressive loss of muscle mass which have opposing effects on mortality. Thus BMI is not a good indicator of obesity in older adults. Sarcopenia, the age-associated loss of skeletal muscle mass, is a major concern in ageing populations and has been associated with metabolic impairment, CVD risk factors, physical disability and mortality. Sarcopenia often coexists with obesity. Sarcopenic obesity is a new category of obesity in older adults who have high adiposity coupled with low muscle mass. To fully understand the effect of obesity on mortality in the elderly it is important to take muscle mass into account. The evidence suggests that sarcopenia with obesity may be associated with higher levels of metabolic disorders and an increased risk of mortality than obesity or sarcopenia alone. Efforts to promote healthy ageing should focus on both preventing obesity and maintaining or increasing muscle mass.

Obesity: Muscle: Sarcopenia: CVD: Mortality: Older adults

Obesity, i.e. excess body fat usually defined as $\text{BMI} \geq 30 \text{ kg/m}^2$, is a major public health problem and is well recognised as a risk factor for cardiovascular morbidity and mortality in adult populations. Obesity prevalence in middle-aged and older adults continues to increase worldwide and has doubled since 1980^(1,2). However, there is controversy surrounding the effects of overweight and obesity in older people, with many studies showing that being overweight, as defined by BMI of 25–29 kg/m^2 , does not appear to be as harmful in the elderly as in middle-aged populations and may even be associated with lower, rather than higher, mortality^(3–5). In addition, a large body of evidence indicates that

overweight and obesity ($\text{BMI} \geq 25 \text{ kg/m}^2$) are associated with increased survival in patients with CVD and in particular those with heart failure, an unexpected finding termed the obesity paradox^(6–10). The mechanisms of these paradoxical association remain largely unexplained but a number of explanations have been proposed^(11,12). Part of the explanation may be that BMI is an imprecise measure of body fat and does not distinguish between fat and lean body mass, the latter having been negatively associated with increased mortality⁽¹³⁾. Important changes in body composition occur with age, including a relative increase in fat tissue and a gradual decline in muscle mass, meaning that overall body weight and

Abbreviations: BIA, bioelectrical impedance analysis; DXA, dual energy X-ray absorptiometry; HF, heart failure; WC, waist circumference.
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BMI may remain relatively unchanged^(3,14,15). Since BMI does not distinguish between fat mass and fat-free mass, which have opposing effects on the risk of morbidity and mortality, the use of BMI in the elderly may have limitations. Therefore to fully understand the effect of obesity in the elderly, it is important to also take both fat mass and lean mass into account.

Sarcopenia, the age-associated loss of muscle mass and function, is a major concern in ageing populations and is often associated with visceral fat⁽¹⁵⁾. A new concept of sarcopenic obesity refers to sarcopenia coupled with increased body fat^(14,15). Recent reviews have highlighted the impact of sarcopenic obesity on general health outcomes and metabolic risk^(15–20). The present paper discusses the health implications of obesity and sarcopenia and sarcopenic obesity on CVD and mortality in older adults and discusses the obesity paradox seen in patients with CVD, highlighting the role of diminished muscle mass (sarcopenia) in explaining the obesity paradox.

Obesity and mortality in older adults

The most commonly used measure of overweight and obesity is BMI, defined by WHO as cut-off points of ≥ 25 and ≥ 30 kg/m², respectively⁽²¹⁾. However, the relationship between BMI and mortality in older age is controversial. A systematic review of older adults aged ≥ 65 years found that BMI in the overweight range is not associated with a significantly increased mortality risk, and BMI in the moderately obese range is only associated with a modest increase in mortality risk⁽⁴⁾. Similarly, a more recent large meta-analysis of nearly 200 000 individuals aged 65 or older showed a U-shaped relationship between BMI and mortality, with the lowest risk seen in those with a BMI between 24.0 and 30.0 kg/m² and risk only began to increase when BMI exceeded 33 kg/m²⁽⁵⁾. Ageing is associated with significant changes in body composition with a substantial reduction in fat-free mass and muscle mass and an increase in visceral fat, even if the body weight remains unchanged^(3,14,15). Thus BMI depends not only on adiposity but also on the loss of muscle mass which has opposing effects on mortality⁽¹³⁾, so that BMI may not be a good indicator of obesity in the elderly. It is suggested that measures of adiposity such as waist circumference (WC) or the waist:hip ratio, which better reflect visceral fat, may be more useful at assessing obesity risk as they are better at predicting CVD and mortality in older subjects^(22–26). Central obesity has been defined as a WC > 102 cm for men and > 88 cm for women, or a waist:hip ratio ≥ 0.9 for men and ≥ 0.85 for women⁽²⁷⁾.

Sarcopenia

Sarcopenia, the age-related loss of muscle mass and decline in muscle strength, is strongly associated with physical disability, poor quality of life and frailty⁽²⁸⁾. Several different definitions of sarcopenia have been used in the literature but to date no consensus definition has been

universally adopted⁽²⁹⁾. Measurement methods such as computerised tomography, dual energy X-ray absorptiometry (DXA) and bioelectrical impedance analysis (BIA) have been used to assess total or skeletal muscle mass⁽¹⁵⁾. Sarcopenia was originally defined on the basis of appendicular skeletal muscle mass, assessed by DXA and adjusted for height. Those whose height-adjusted appendicular skeletal muscle mass were two standard deviations below the reference for healthy younger persons were considered to be sarcopenic⁽²⁸⁾. Subsequently, the definition of sarcopenia has evolved from a focus on muscle mass to muscle strength and physical function. Recently, a definition of sarcopenia has been suggested by The European Working Group on Sarcopenia in Older People which proposed the presence of both low muscle mass and low muscle function (strength or performance)⁽²⁹⁾.

Sarcopenia and mortality and cardiovascular risk

Prospective studies have shown consistent associations between low muscle mass (as measured by DXA), BIA and mid-arm muscle circumference) or muscle strength as measured by hand grip and an increased risk of mortality^(30–37). Some studies suggest that decline in muscle strength is a stronger independent risk factor for mortality compared with muscle mass^(38,39).

Several mechanisms underlying age-related muscle loss have been recognised, including neuronal and hormonal changes, poor nutrition, physical inactivity and inflammation^(15,40). Thus sarcopenia shares many pathological mechanisms with atherosclerosis, including insulin resistance and inflammation⁽¹⁵⁾. Population studies have shown sarcopenia to be associated with metabolic impairments, including insulin resistance^(15,28,39). Low muscle mass has also been associated with CVD risk factors, including arterial stiffness and blood pressure^(41,42). However, the association with CVD disease is uncertain and few studies have examined the association between sarcopenia and CVD^(43,44). In those that have there is suggestion that sarcopenia is associated with increased risk of CVD mortality⁽⁴³⁾.

Sarcopenic obesity

Given the age-related changes in body composition, sarcopenia often coexists with an increase in fat mass (Fig. 1). Visceral fat and muscle mass are known to be interrelated from a pathogenic point of view and are reported to share common inflammatory pathways⁽¹⁵⁾. In addition, sarcopenia reduces physical activity which results in decreased energy expenditure leading to increased risk of obesity⁽¹⁵⁾. Alternatively, visceral fat induces inflammation which may contribute to the development of sarcopenia⁽⁴⁵⁾. The interplay between sarcopenia and rising trends in obesity in an ageing population is emerging as an important public health concern in the elderly. The term sarcopenic obesity was first introduced by Baumgartner⁽¹⁴⁾ and is defined by the combination of

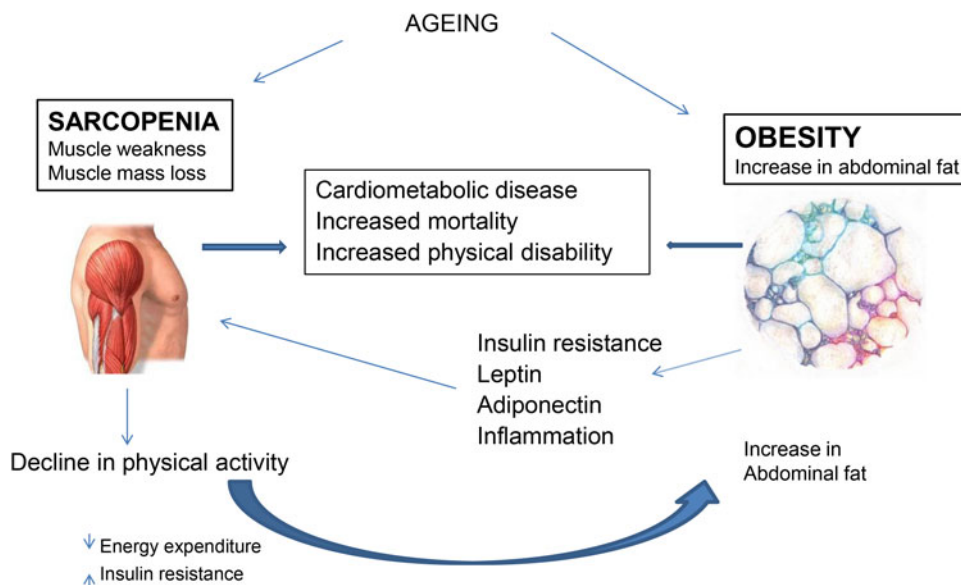


Fig. 1. (Colour online) Sarcopenic obesity with ageing. The interplay between sarcopenia and obesity. Adapted from Zamboni *et al.* (15).

sarcopenia and obesity. Both obesity and sarcopenia are associated with metabolic disorders and are important causes of disability, morbidity and mortality⁽¹⁵⁾. Therefore it is hypothesised that obesity and sarcopenia may act synergistically; sarcopenic obesity may have a greater effect on metabolic disorders, CVD and mortality than either obesity or sarcopenia alone. However, there are limited studies which have investigated the joint effect of sarcopenia and obesity on CVD and mortality, the majority of which have been cross-sectional studies or have focused on disability or physical function as outcomes^(15,19,20,46).

Sarcopenic obesity and mortality

Only a few population prospective studies have examined the association between sarcopenic obesity and the risk of all-cause mortality and there is suggestion that sarcopenic obese adults have the highest mortality risk. In an earlier report from the British Regional Heart study involving over 4000 men, aged 60–79 years followed up for 6 years, men with high WC (>102 cm) and low mid-arm muscle circumference (sarcopenic obese) showed a 55% increase in mortality risk compared with non-sarcopenic, non-obese individuals⁽³³⁾. Similar findings were observed with extended 11-year follow-up with the sarcopenic obese group showing the highest mortality risk⁽⁴³⁾ (Fig. 2). A 14-year prospective study of participants from the National Health and Nutrition Examination Survey III found a similar association in sarcopenic obese women (based on skeletal muscle mass and body fat measurement from BIA), with a 29% increase in mortality risk compared with those without sarcopenia or obesity⁽⁴⁷⁾. However, no significant association was seen in this cohort between sarcopenic obesity and mortality in men. In the InCHIANTI

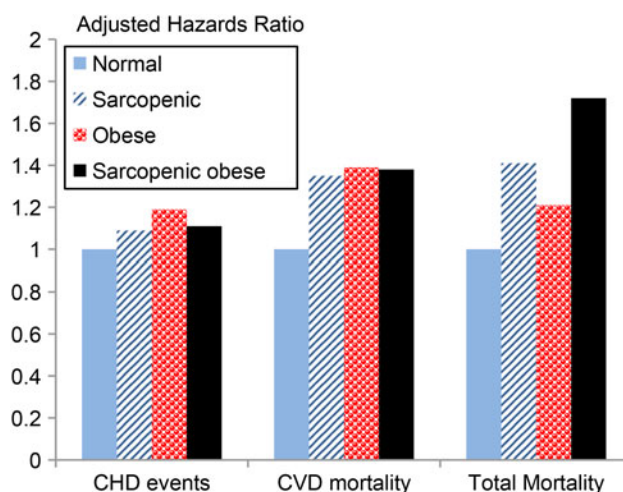


Fig. 2. (Colour online) Adjusted hazards ratio for major CHD events, cardiovascular mortality and total cause mortality according to sarcopenic obesity groups (defined according to waist circumference (>102 cms) and mid-arm muscle circumference (lowest 2 quintiles)). Hazards ratios adjusted for age, smoking status, alcohol intake, physical activity and social class. The British Regional Heart Study. Data extracted from Atkins *et al.*⁽⁴³⁾.

study of 934 male and female participants aged 65 years and over followed for 6 years, no significant difference in mortality risk was reported across six sarcopenic obesity groups (defined using calf skeletal muscle and BMI) although sarcopenic obese adults showed the lowest survival⁽³⁵⁾. A study which defined sarcopenic obesity using a measure of muscle strength instead of muscle mass showed a significant association between sarcopenic obesity and risk of mortality; adult men who were overweight (BMI ≥ 25) and in the lowest grip strength tertile had the highest mortality risk⁽³⁶⁾.

Sarcopenic obesity and cardiovascular risk factors

Numerous studies have examined the association of sarcopenic obesity with established cardiovascular risk factors. Several cross-sectional studies in Korean populations of older adults have found that sarcopenic obese individuals had the worse cardiovascular risk profile. Sarcopenic obesity (based on skeletal muscle assessed by DXA and obesity measured by either computerised tomography, DXA, BMI or WC) was associated with lower cardiorespiratory fitness, higher fasting glucose levels, a higher risk of hypertension, dyslipidaemia and insulin resistance, and up to an 8-fold increase in risk of the metabolic syndrome compared with non-sarcopenic, non-obese^(48–55). Similar findings were reported in a community-dwelling sample of Taiwanese older adults; sarcopenic obesity (defined by BIA-measured muscle mass and BMI) was associated with the highest risk of metabolic syndrome⁽⁵⁶⁾. In a large cross-sectional analysis of over 14 000 adults from the National Health and Nutrition Examination Survey III, the sarcopenic obese group (defined by BIA-measured muscle mass and BMI) had the highest risk of insulin resistance and dysglycaemia⁽⁵⁷⁾. However, not all studies have shown sarcopenic obese individuals to have the worst profile and some cross-sectional studies have suggested that obese older adults may have higher cardiovascular risk factors than sarcopenic obese subjects^(58–60). Conflicting results have also been shown regarding the relationship between inflammatory markers and sarcopenic obesity. While some cross-sectional studies have shown sarcopenic obese adults to have the highest level of inflammatory markers as measured by C-reactive protein^(47,61) others have found no significant interactions between sarcopenia and obesity with C-reactive protein⁽⁶²⁾.

Sarcopenic obesity and CVD

Despite evidence on the relationships between sarcopenic obesity and cardiovascular risk factors, the association between sarcopenic obesity and CVD has been less studied. Two cross-sectional studies reported that older adults with sarcopenic obesity (based on appendicular skeletal muscle mass and per cent body fat from DXA) did not show significantly higher prevalence of CVD compared with non-sarcopenic, non-obese adults^(58,63). Prospective studies examining the association between sarcopenic obesity and CVD are limited and we have identified only two such studies to date. In the Cardiovascular Health Study, a large prospective study of community-dwelling older men and women (age ≥ 65 years), sarcopenic obesity based on WC and muscle strength, was associated with the highest risk of CVD and congestive heart failure. Sarcopenic obese adults showed a 23 % increase in risk of CVD and a 42 % increase in risk of congestive heart failure over 8 years of follow-up compared with non-obese non-sarcopenic subjects⁽⁴⁴⁾. However, the risk of CVD events was not significantly greater in the sarcopenic obese group, when defined using BIA-measured muscle mass, implying

that muscle strength may be more important than muscle mass. These results are broadly comparable with a prospective study of older men (age 60–79 years), from the British Regional Heart Study which also showed no excess risk of CHD events (fatal or non-fatal myocardial infarction) in sarcopenic obese men (defined by WC and mid-arm muscle circumference) over 11 years of follow-up (Fig. 2)⁽⁴³⁾. Sarcopenic obese men showed increased risk of CVD mortality but risk of CVD mortality was similar to those with sarcopenia or obesity alone. However, this study did not consider muscle strength in defining sarcopenic obesity. Overall, findings from cross-sectional and prospective studies do not provide strong evidence for a synergistic effect of sarcopenic obesity on risk of developing CVD.

The inconsistencies in the observed associations of sarcopenic obesity with cardiovascular risk and mortality risk may be explained by the large variability between studies in their sample size and population characteristics, and also due to the heterogeneity in the definition and classification of sarcopenic obesity. To further assess the association between sarcopenic obesity and risk of CVD and mortality there is a need for larger, prospective studies to be carried out which use a standardised definition of sarcopenic obesity.

The obesity paradox in those with CHD

Despite the potential adverse effects of overweight and obesity on CVD risk factors and incidence, numerous investigators and meta-analysis of studies in cohorts with CHD have shown increased survival in those who are overweight or obese^(6–10) when defined by high BMI, the obesity paradox, although this has not been seen in all studies after adjustment for confounders^(64,65). In the RICO Survey, a study of over 2000 patients with acute myocardial infarction, an inverse association was seen between BMI and mortality but this was attenuated after adjustment for factors associated with survival, including prior myocardial infarction, hypertension, diabetes, hyperlipidaemia, smoking and left ventricular ejection fraction⁽⁶⁴⁾. In the Secondary Manifestations of ARterial disease study no association was seen at all between BMI and mortality in patients with CVD⁽⁶⁵⁾. Part of the explanation for the obesity paradox may be due to the use of BMI to define obesity, which does not take into account lean muscle mass. BMI is a poor marker of body fat and does not distinguish between fat and lean body mass which has been associated with increased mortality⁽¹³⁾. Abdominal obesity has been suggested as a better marker of obesity risk. Indeed, meta-analysis of cohorts in CHD has shown positive associations between WC and mortality⁽⁶⁶⁾. However, few population studies to date have examined the possible role of lean muscle mass in explaining the obesity paradox in those with CHD. In a recent report from the British Regional Heart Study, it was shown that the vast majority of men with normal body weight had low muscle mass and the prevalence of low muscle mass increased appreciably in the presence of CHD and heart failure (HF)

Table 1. BMI and adjusted hazards ratio (95% CI) total mortality in men by CHD and heart failure (HF) status

	BMI (kg/m ²)			P for trend
	18.5–24.9	25–29.9	30+	
No CHD and no HF (n 3174)				
% low muscle mass	56.7	20.9	7.8	
Model 1	1.00	0.88 (0.76, 1.02)	1.01 (0.83, 1.24)	P = 0.67
Model 2	1.00	0.99 (0.84, 1.16)	1.25 (1.00, 1.59)	P = 0.13
CHD and no HF (n 860)				
% low muscle mass	66.4	26.4	7.3	
Model 1	1.00	0.71 (0.56, 0.91)	0.77 (0.57, 1.04)	P = 0.04
Model 2	1.00	0.80 (0.62, 1.03)	0.96 (0.68, 1.35)	P = 0.60
HF (N 86)				
% low muscle mass	73.9	31.1	27.8	
Model 1	1.00	0.57 (0.28, 1.16)	0.41 (0.16, 1.09)	P = 0.04
Model 2	1.00	0.66 (0.29, 1.52)	0.47 (0.17, 1.35)	P = 0.09

Model 1=adjusted for age, smoking, alcohol intake, social class, physical activity, prevalent diabetes and stroke.

Model 2=Model 1 + low muscle mass.

Low muscle mass defined as lowest quartile of mid-arm muscle circumference.

Source: adapted from Wannamethee *et al.*⁽⁶⁷⁾.

(Table 1). Low muscle mass was shown to be associated with increased mortality in those without HF irrespective of CHD status. The lower risk associated with overweight and obesity in those with CHD was attenuated after adjustment for muscle mass suggesting that the lower risk of mortality associated with excess body weight in men with CHD without HF appears largely associated with higher muscle mass (Table 1)⁽⁶⁷⁾. The inverse association seen in those with HF persisted after adjustment for muscle mass. Although one study showed the obesity paradox to persist in those with CHD even after taking into account muscle mass⁽⁸⁾, patients with CHD in that study included those with HF. Thus the persistence of lower risk associated with obesity may have been due to the high prevalence of patients with HF in this group. In HF, the obesity paradox may be driven by the deleterious effects of cardiac cachexia (wasting) reflecting the combined loss of muscle and adipose tissue⁽⁶⁸⁾. Cardiac cachexia observed in end stage HF is associated with a decrease of fat mass in addition to a reduced lean muscle mass⁽⁶⁹⁾. It has also been postulated that several physiologic mechanisms may explain the protective effect of a higher BMI on mortality⁽¹¹⁾. NT-proBNP levels, a marker of cardiac dysfunction, are lower in overweight and obese patients; lower NT-proBNP predicts lower mortality^(66,70). Another possible explanation for the obesity paradox directly involves the functions of adipose tissue^(11,66). Adipose tissue produces leptin which experimental studies suggest may have protective effects in HF⁽⁷¹⁾ and adiponectin is decreased in obesity; lower concentrations of adiponectin have been associated with lower mortality in patients with CHD or HF^(72–74).

The association between WC and mortality in CHD patients in contrast to BMI have found to be positive⁽⁶⁷⁾ or null⁽⁶⁵⁾. The positive association between central adiposity and mortality in those with CHD is in keeping with the findings that the inverse association seen for BMI in those with CHD may reflect reduced muscle mass.

Conclusions

BMI is not a good indicator of obesity in older adults because it does not take into account the loss of muscle mass with increasing age. Muscle mass and visceral fat have opposing effects on mortality. The increased mortality in normal weight subjects compared with overweight and obese subjects in those with CHD (obesity paradox) appears to be associated to some extent with low muscle mass. Sarcopenia is associated with increased mortality and is often associated with visceral obesity. Sarcopenic obesity is a new category of obesity in older adults and there is some evidence that it is associated with higher levels of cardiovascular risk factors and an increased risk of mortality than obesity or sarcopenia alone. This highlights the need to take muscle mass and function into account when assessing the effects of obesity in older adults. Several different definitions of sarcopenia have been used in the literature but to date no consensus definition has been agreed. There is a need for a universal standardised definition of sarcopenia and sarcopenic obesity to improve identification and management in clinical practice. Efforts to promote healthy ageing and to reduce the risk of morbidity and mortality should focus not only on preventing obesity but also on maintaining or increasing muscle mass and strength.

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Conflicts of Interest

None.

Authorship

S. G. W. initiated the design of the manuscript. J. L. A. carried out the literature review on the influence of sarcopenic obesity on cardiovascular risk. S. G. W. and J. L. A. both contributed to the writing of the manuscript.

References

- World Health Organisation (2014) Obesity and Overweight. Fact Sheet Number 311. <http://www.who.int/mediacentre/factsheets/fs311/en/> (accessed 17 October 2014).
- Department of Health (2011) *Healthy Lives, Healthy People: a Call to Action on Obesity in England*. London: Department of Health.
- Zamboni M, Mazzali G, Zoico E *et al.* (2005) Health consequences of obesity in the elderly: a review of four unresolved questions. *Int J Obes* **29**, 1011–1029.
- Janssen I & Mark AE (2007) Elevated body mass index and mortality risk in the elderly. *Obes Rev* **8**, 41–59.
- Winter JE, MacInnis RJ, Wattanapenpaiboon N *et al.* (2014) BMI and all-cause mortality in older adults: a meta-analysis. *Am J Clin Nutr* **99**, 875–890.
- Oreopoulos A, Padwal R, Kalantar-Zadeh K *et al.* (2008) Body mass index and mortality in heart failure: a meta-analysis. *Am Heart J* **56**, 13–22.
- Romero-Corral A, Montori VM, Somers VK *et al.* (2006) Association of bodyweight with total mortality and with cardiovascular events in coronary artery disease: a systematic review of cohort studies. *Lancet* **368**, 666–678.
- Angerås O, Albertsson P, Karason K *et al.* (2013) Evidence for obesity paradox in patients with acute coronary syndromes: a report from the Swedish Coronary Angiography and Angioplasty Registry. *Eur Heart J* **34**, 345–353.
- Oreopoulos A, McAlister FA, Kalantar-Zadeh K *et al.* (2009) The relationship between body mass index, treatment and mortality in patients with established coronary artery disease: a report from APPROACH. *Eur Heart J* **30**, 2584–2592.
- Lavie CJ, de Schutter A, Patel DA *et al.* (2012) Body composition and survival in stable coronary heart disease. *J Am Coll Cardiol* **60**, 1374–1380.
- Dorner TE & Rieder A (2012) Obesity paradox in elderly patients with cardiovascular diseases. *Int J Cardiol* **155**, 56–65.
- Lavie CJ, Milani RV & Ventura HO (2011) Impact of obesity on outcomes in myocardial infarction: combating the “obesity paradox”. *J Am Coll Cardiol* **58**, 2651–2653.
- Allison DB, Zhu SK, Plankey M *et al.* (2002) Differential associations of body mass index and adiposity with all-cause mortality among men in the first and second National Health and Nutrition Examination Surveys (NHANES I and NHANES II) follow-up studies. *Int J Obes Relat Metab Disord* **26**, 410–416.
- Baumgartner RN (2000) Body composition in healthy aging. *Ann N Y Acad Sci* **904**, 437–448.
- Zamboni M, Mazzali G, Fantin F *et al.* (2008) Sarcopenic obesity: a new category of obesity in the elderly. *Nutr Metab Cardiovasc Dis* **18**, 388–395.
- Choi KM (2013) Sarcopenia and sarcopenic obesity. *Endocrinol Metab (Seoul)* **28**, 86–89.
- Kohara K (2014) Sarcopenic obesity in aging population: current status and future directions for research. *Endocrine* **45**, 15–25.
- Stenholm S, Harris TB, Rantanen T *et al.* (2008) Sarcopenic obesity: definition, cause and consequences. *Curr Opin Clin Nutr Metab Care* **11**, 693–700.
- Waters DL & Baumgartner RN (2011) Sarcopenia and obesity. *Clin Geriatr Med* **27**, 401–421.
- Prado CM, Wells JC, Smith SR *et al.* (2012) Sarcopenic obesity: a critical appraisal of the current evidence. *Clin Nutr* **31**, 583–601.
- World Health Organization (2000) *Obesity: Preventing and Managing the Global Epidemic. Report of a WHO Consultation. WHO Technical Report Series, No 894*. Geneva: WHO.
- Czernichow S, Kengne AP, Stamatakis E *et al.* (2011) Body mass index, waist circumference and waist-hip ratio: which is the better discriminator of cardiovascular disease mortality risk? Evidence from an individual-participant meta-analysis of 82 864 participants from nine cohort studies. *Obes Rev* **12**, 680–687.
- Donini LM, Savina C, Gennaro E *et al.* (2012) A systematic review of the literature concerning the relationship between obesity and mortality in the elderly. *J Nutr Health Aging* **16**, 89–98.
- de Koning L, Merchant AT, Pogue J *et al.* (2007) Waist circumference and waist-to-hip ratio as predictors of cardiovascular events: meta-regression analysis of prospective studies. *Eur Heart J* **28**, 850–856.
- Decaria JE, Sharp C & Petrella RJ (2012) Scoping review report: obesity in older adults. *Int J Obes (Lond)* **36**, 1141–1150.
- de Hollander EL, Bemelmans WJ, Boshuizen HC *et al.* (2012) The association between waist circumference and risk of mortality considering body mass index in 65- to 74-year-olds: a meta-analysis of 29 cohorts involving more than 58 000 elderly persons. *Int J Epidemiol* **41**, 805–817.
- World Health Organization (2008) *Waist Circumference and Waist-hip Ratio: Report of a WHO Expert Consultation*. Geneva: World Health Organization.
- Baumgartner RN, Koehler KM, Gallagher D *et al.* (1998) Epidemiology of sarcopenia among the elderly in New Mexico. *Am J Epidemiol* **147**, 755–763.
- Cruz-Jentoft AJ, Baeyens JP, Bauer JM *et al.* (2010) Sarcopenia: European consensus on definition and diagnosis: report of the European Working Group on Sarcopenia in Older People. *Age Ageing* **39**, 412–423.
- Wijnhoven HA, Snijder MB, van Bokhorst-de van der Schueren MA *et al.* (2012) Region-specific fat mass and muscle mass and mortality in community-dwelling older men and women. *Gerontology* **58**, 32–40.
- Han SS, Kim KW, Kim KI *et al.* (2010) Lean mass index: a better predictor of mortality than body mass index in elderly Asians. *J Am Geriatr Soc* **58**, 312–317.
- Landi F, Russo A, Liperoti R *et al.* (2010) Midarm muscle circumference, physical performance and mortality: results from the aging and longevity study in the Sirente geographic area (ILSIRENTE study). *Clin Nutr* **29**, 441–447.
- Wannamethee SG, Shaper AG, Lennon L *et al.* (2007) Decreased muscle mass and increased central adiposity are independently related to mortality in older men. *Am J Clin Nutr* **86**, 1339–1346.

34. Wijnhoven HA, van Bokhorst-de van der Schueren MA, Heymans MW *et al.* (2010) Low mid-upper arm circumference, calf circumference, and body mass index and mortality in older persons. *J Gerontol A Biol Sci Med Sci* **65**, 1107–1114.
35. Cesari M, Pahor M, Lauretani F *et al.* (2009) Skeletal muscle and mortality results from the InCHIANTI Study. *J Gerontol Ser A Biol Sci Med Sci* **64**, 377–384.
36. Rantanen T, Harris T, Leveille SG *et al.* (2000) Muscle strength and body mass index as long-term predictors of mortality in initially healthy men. *J Gerontol A Biol Sci Med Sci* **55**, M168–M173.
37. Arango-Lopera VE, Arroyo P, Gutiérrez-Robledo LM *et al.* (2013) Mortality as an adverse outcome of sarcopenia. *J Nutr Health Aging* **17**, 259–262.
38. Kim JH, Lim S, Choi SH *et al.* (2014) Sarcopenia: an independent predictor of mortality in community-dwelling older Korean men. *J Gerontol A Biol Sci Med Sci* **69**, 1244–1252.
39. Filippin LI, Teixeira VN, da Silva MP *et al.* (2014) Sarcopenia: a predictor of mortality and the need for early diagnosis and intervention. *Aging Clin Exp Res* [Epublication ahead of print version].
40. Jensen GL (2008) Inflammation: roles in aging and sarcopenia. *JPEN J Parenter Enteral Nutr* **32**, 656–659.
41. Han K, Park YM, Kwon HS *et al.* (2014) Sarcopenia as a determinant of blood pressure in older Koreans: findings from the Korea National Health and Nutrition Examination Surveys (KNHANES) 2008–2010. *PLoS ONE* **9**, e86902.
42. Snijder MB, Henry RM, Visser M *et al.* (2004) Regional body composition as a determinant of arterial stiffness in the elderly: The Hoorn Study. *J Hypertens* **22**, 2339–2347.
43. Atkins JL, Whincup PH, Morris RW *et al.* (2014) Sarcopenic obesity and risk of cardiovascular disease and mortality: a population-based cohort study of older men. *J Am Geriatr Soc* **62**, 253–260.
44. Stephen WC & Janssen I (2009) Sarcopenic-obesity and cardiovascular disease risk in the elderly. *J Nutr Health Aging* **13**, 460–466.
45. Gregor MF & Hotamisligil GS (2011) Inflammatory mechanisms in obesity. *Annu Rev Immunol* **29**, 415–445.
46. Dominguez LJ & Barbagallo M (2007) The cardiometabolic syndrome and sarcopenic obesity in older persons. *J Cardiometab Syndr* **2**, 183–189.
47. Batsis JA, Mackenzie TA, Barre LK *et al.* (2014) Sarcopenia, sarcopenic obesity and mortality in older adults: results from the National Health and Nutrition Examination Survey III. *Eur J Clin Nutr* **68**, 1001–1007.
48. Kim TN, Park MS, Lim KI *et al.* (2013) Relationships between sarcopenic obesity and insulin resistance, inflammation, and vitamin D status: the Korean Sarcopenic Obesity Study. *Clin Endocrinol (Oxf)* **78**, 525–532.
49. Lim S, Kim JH, Yoon JW *et al.* (2010) Sarcopenic obesity: prevalence and association with metabolic syndrome in the Korean Longitudinal Study on Health and Aging (KLoSHA). *Diab Care* **33**, 1652–1654.
50. Chung JY, Kang HT, Lee DC *et al.* (2013) Body composition and its association with cardiometabolic risk factors in the elderly: a focus on sarcopenic obesity. *Arch Gerontol Geriatr* **56**, 270–278.
51. Hwang B, Lim JY, Lee J *et al.* (2012) Prevalence rate and associated factors of sarcopenic obesity in Korean elderly population. *J Korean Med Sci* **27**, 748–755.
52. Park SH, Park JH, Song PS *et al.* (2013) Sarcopenic obesity as an independent risk factor of hypertension. *J Am Soc Hypertens* **7**, 420–425.
53. Park SH, Park JH, Park HY *et al.* (2014) Additional role of sarcopenia to waist circumference in predicting the odds of metabolic syndrome. *Clin Nutr* **33**, 668–672.
54. Baek SJ, Nam GE, Han KD *et al.* (2014) Sarcopenia and sarcopenic obesity and their association with dyslipidemia in Korean elderly men: the 2008–2010 Korea National Health and Nutrition Examination Survey. *J Endocrinol Invest* **37**, 247–260.
55. Kim TN, Park MS, Kim YJ *et al.* (2014) Association of low muscle mass and combined low muscle mass and visceral obesity with low cardiorespiratory fitness. *PLoS ONE* **9**, e100118.
56. Lu CW, Yang KC, Chang HH *et al.* (2013) Sarcopenic obesity is closely associated with metabolic syndrome. *Obes Res Clin Pract* **7**, e301–e307.
57. Srikanthan P, Hevener AL & Karlamangla AS (2010) Sarcopenia exacerbates obesity-associated insulin resistance and dysglycemia: findings from the National Health and Nutrition Examination Survey III. *PLoS ONE* **5**, e10805.
58. Baumgartner RN, Wayne SJ, Waters DL *et al.* (2004) Sarcopenic obesity predicts instrumental activities of daily living disability in the elderly. *Obes Res* **12**, 1995–2004.
59. Messier V, Karelis AD, Lavoie M-E *et al.* (2009) Metabolic profile and quality of life in class I sarcopenic overweight and obese postmenopausal women: a MONET study. *Appl Physiol Nutr Metab* **34**, 18–24.
60. dos Santos EP, Gadelha AB, Safons MP *et al.* (2014) Sarcopenia and sarcopenic obesity classifications and cardiometabolic risks in older women. *Arch Gerontol Geriatr* **59**, 56–61.
61. Schragger MA, Metter EJ, Simonsick E *et al.* (2007) Sarcopenic obesity and inflammation in the InCHIANTI study. *J Appl Physiol* **102**, 919–925.
62. Cesari M, Kritchevsky SB, Baumgartner RN *et al.* (2005) Sarcopenia, obesity, and inflammation – results from the Trial of Angiotensin Converting Enzyme Inhibition and Novel Cardiovascular Risk Factors study. *Am J Clin Nutr* **82**, 428–434.
63. Chin SO, Rhee SY, Chon S *et al.* (2013) Sarcopenia is independently associated with cardiovascular disease in older Korean adults: the Korea National Health and Nutrition Examination Survey (KNHANES) from 2009. *PLoS ONE* **8**, e60119.
64. Zeller M, Steg PG, Ravisy J *et al.* (2008) Relation between body mass index, waist circumference and death after acute myocardial infarction. *Circulation* **118**, 482–490.
65. Kanhai DA, Kapelle LJ, van der Graaf Y *et al.* (2012) The risk of general and abdominal adiposity in the occurrence of new vascular events and mortality in patients with various manifestations of vascular disease. *Int J Obes* **36**, 695–702.
66. Coutinho T, Goel K, Corrêa de Sá D *et al.* (2011) Central Obesity and survival in subjects with coronary artery disease: a systematic review of the literature and collaborative analysis with individual subject data. *J Am Coll Cardiol* **57**, 1877–1886.
67. Wannamethee SG, Shaper AG, Whincup PH *et al.* (2014) The obesity paradox in men with coronary heart disease and heart failure: the role of muscle mass and leptin. *Int J Cardiol* **171**, 49–55.
68. Marques MB & Langouche L (2013) Endocrine, metabolic and morphologic alterations of adipose tissue during critical illness. *Crit Care Med* **41**, 317–325.
69. Anker SD & Rauchhaus M (1999) Insights into the pathogenesis of chronic heart failure: immune activation and cachexia. *Curr Opin Cardiol* **14**, 211–216.



70. Clerico A, Giannoni A, Vittorini S *et al.* (2012) The paradox of low BNP levels in obesity. *Heart Fail Rev* **17**, 81–96.
71. McGaffin KR, Moravec CS & Mctiernan CF (2009) Leptin signalling in the failing and mechanically unloaded human heart. *Circ Heart Fail* **2**, 676–683.
72. Kistorp C, Faber J, Galatius S *et al.* (2005) Plasma adiponectin, body mass index and mortality in patients with chronic heart failure. *Circulation* **112**, 1756–1762.
73. Hascoet S, Elbaz M, Bongard V *et al.* (2013) Adiponectin and long term mortality in coronary artery disease participants and controls. *Arterioscler Thromb Vasc Biol* **33**, e19–e29.
74. Wannamethee SG, Whincup PH, Lennon L *et al.* (2007) Circulating adiponectin levels and mortality in elderly men with and without cardiovascular disease and heart failure. *Arch Intern Med* **167**, 1510–1517.