Sarcopenic obesity and associations with mortality in old women and men – a prospective observational study

Åsa von Berens (asa.von.berens@pubcare.uu.se)
Department of public health and caring sciences, clinical nutrition and metabolism
https://orcid.org/0000-0001-8653-8028

Sine R Obling
Department of Medical Gastroenterology, Odense University Hospital

Margaretha Nydahl
Department of Food Studies, Nutrition and Dietetics, Uppsala University

Afsaneh Koochek
Department of Food Studies, Nutrition and Dietetics, Uppsala University

Lauren Lissner
Department of Public Health and Community Medicine, Sahlgrenska Academy, University of Gothenburg

Ingmar Skoog
Institute of Neuroscience and Physiology, Neuropsychiatric Epidemiology Unit, University of Gothenburg

Kerstin Frändin
Institute of Neuroscience and Physiology, Neuropsychiatric Epidemiology Unit, University of Gothenburg

Elisabeth Skoglund
Department of Public Health and Caring Sciences, Clinical Nutrition and Metabolism, Uppsala University

Elisabet Rothenberg
Kristianstad University, Food and Meal Science

Tommy Cederholm
Department of Public Health and Caring Sciences, Clinical Nutrition and Metabolism, Uppsala University

Research article

Keywords: Older adults, sarcopenic obesity, EWGSOP2, prevalence, mortality

Posted Date: July 3rd, 2019

DOI: https://doi.org/10.21203/rs.2.10873/v1

Version of Record: A version of this preprint was published at BMC Geriatrics on June 9th, 2020. See the published version at https://doi.org/10.1186/s12877-020-01578-9.

Abstract

Background The combined effect of sarcopenia and obesity, i.e., sarcopenic obesity, has been associated with disability and worse outcomes in older adults, but results are conflicting. The objectives of this study were to describe the prevalence of sarcopenic obesity (SO) in older adults, and to examine how the risk of mortality is associated with different body composition phenotypes. Methods Data were obtained from two Swedish population studies, the Gothenburg H70 Birth Cohort Studies of 521 women and men at the age of 75, and the Uppsala Longitudinal Study of Adult Men (ULSAM), which included 288 men aged 88 years. Sarcopenia was defined using the EWGSOP2 definition. Obesity was defined by any of three established definitions: body mass index ≥30 kg/m2, fat mass >30%/ >42% or waist circumference ≥88 cm/≥102 cm for women and men, respectively. The Kaplan-Meier survival curve and the Cox proportional hazard model were used for 10-year and 4-year survival analyses in the H70 and ULSAM cohorts, respectively. Results SO was observed in 4% of the women and 11% of the men in the H70 cohort, and in 10% of the ULSAM male cohort. The 75-year-old women with SO had a higher risk (HR 3.25, 95% confidence interval (1.2-8.9)) of dying within ten years compared to those with a “normal” phenotype. A potential similar association with mortality among the 75-year-old men was not statistically significant. In the older men aged 88 years, obesity was associated with increased survival. Conclusions SO was observed in 4-11% of community-dwelling older adults. In 75-year-old women SO appeared to associate with an increased risk of dying within ten years. In 88-year-old men, the results indicated that obesity was related to a survival benefit over a four year period.

Background

The aging of the global population provides both opportunities and challenges. The overall prevalence of obesity in society is currently increasing and a greater proportion of the surviving older population is also becoming overweight and obese [1]. Aging is *per se* associated with changes in body composition, which are mainly expressed as increase in fat mass, changes in body fat distribution, and loss of muscle mass. The combination of low muscle mass and poor muscle function, i.e., sarcopenia, has recently gained increasing attention [2]. The condition of sarcopenia combined with increased fat mass is termed sarcopenic obesity (SO) [3, 4]. Sarcopenia, a term first introduced in 1988 [5], is a geriatric condition associated with adverse effects on function, quality of life and survival [6-9]. Various definitions of the condition have subsequently been proposed. A decade ago, the European Working Group on Sarcopenia in Older People (EWGSOP) proposed that the combination of low muscle mass and low strength/physical function should define sarcopenia [8]. Recently, the EWGSOP published an updated consensus definition (EWGSOP2) [2]; Sarcopenia was highlighted as a muscle disease, and the new definition emphasizes poor muscle function as the major determinant for the condition rather than low muscle mass.

For middle-aged individuals, the cardio-metabolic risks of overweight and obesity are well established [10]. However, for older individuals there is an ongoing debate concerning the health consequences of obesity, and whether excessive weight might even be beneficial; what is sometimes called the obesity paradox, but the data are contradictory [11-15]. There are indications that obesity-related comorbidities

vary with age, e.g., optimal body mass index (BMI) values for older adults might be higher than for younger adults [11, 16, 17]. Studies have also shown that the risk of physical disabilities is greater, particularly among obese older individuals[18-20].

Sarcopenia and obesity potentially affect health and physical function. Thus, the combination of the two conditions, i.e., sarcopenic obesity (SO), might be important in its own right. There is an increasing awareness of the potential negative impact of SO in older adults, but results from studies are conflicting [3, 21-23] .

The objective of this study was to describe the prevalence of sarcopenic obesity using the recently launched EWGSOP2 definition of sarcopenia in combination with various definitions of obesity in three Swedish cohorts of older adults. A further objective was to examine how the risk of mortality was associated with different body composition phenotypes, including sarcopenic obesity.

Methods

Participants

Data were extracted from two Swedish population studies: the H70 Study from Gothenburg (i.e., the Gothenburg H70 Birth Cohort Studies, including both women and men)[24] and the Prospective Population Study of Women in Gothenburg (PPSW)[25]), and the Uppsala Longitudinal Study of Adult Men (ULSAM) [26] (see also http://www.pubcare.uu.se/ ULSAM).

In the H70 cohorts, all participants were born in 1930 and data on sarcopenia, obesity, mortality and related covariates for a total of 521 individuals (n=319 women and n=202 men) were collected from the examinations conducted in 2005 when participants were 75 years old (defined as baseline in this study). In the ULSAM cohort, data from 288 community-dwelling men aged 87 years were collected in 2008-2009 (defined as baseline in this study).

Definitions and cut-offs for sarcopenia, obesity and sarcopenic obesity

Prevalence figures were calculated by using the EWGSOP2 definition for sarcopenia, combined with three different definitions for obesity (see Table 1).

The updated EWGSOP2 definition advocates the use of reduced chair-stand capacity (time to perform five repeated chair stands >15 seconds) or reduced hand grip strength (<16 kg for women and <27 kg for men) in combination with low muscle mass for the diagnosis of sarcopenia.

In the H70 Study, bioelectrical impedance spectroscopy (BIS, see below) was used to calculate skeletal muscle mass index (SMI). No cut-offs for SMI are proposed in the EWGSOP2, which is why we chose to use the cut-offs from Janssen et al. for H70 (as in EWGSOP [8] $\leq$5.75 kg/m^2 for women and $\leq$8.5 kg/m^2 for men [27]). In the ULSAM cohort, muscle mass was measured by Dual-energy X-ray absorptiometry

(DXA) and the EWGSOP2 recommended cut-off for appendicular skeletal muscle index (ASMI) of <7 kg/m^2 was used.

To define SO, the definitions for sarcopenia were combined with any of three measures of obesity, i.e., BMI ≥30 kg/m^2, fat mass >42% (women) and >30% (men), or waist circumference ≥88 cm (women) and ≥102 cm (men) [10, 28, 29]. If any of the obesity criteria were fulfilled, the individual was defined as obese.

Measurements

Body composition: Body composition was measured by BIS using Xitron Hydra 4200 devices (Xitron technologies, San Diego, USA) in the H70 cohorts. Skeletal muscle mass (SMM) from BIS was estimated using the equation (Total Body Skeletal Muscle Mass, no Body weight ($TBSMM_{noBW)}$ = -24.05 + (0.365*height)+(-0.005*Ri)+(-0.012*Re)+(-1.337*gender)(R_i and R_e=Intra- and extracellular resistance)) developed and validated by Tengvall et al. [30]. Skeletal muscle index (SMI) was calculated as the ratio of SMM to height in meters squared.

In the ULSAM cohort, DXA (DPX Prodigy, Lunar corp., Madison, WI, USA) was performed and ASMI was calculated using total muscle mass from arms and legs divided by height in meters squared.

Strength and function: Grip strength was measured using a Jamar dynamometer in H70 and the Baseline hydraulic hand dynamometer in the ULSAM cohort. The highest value from the strongest hand was used in the analyses, and the thresholds were 16 kg and 27 kg for women and men, respectively. To measure leg strength, the participants were asked (both in H70 and in ULSAM) to perform five repeated chair stands without using their hands. The threshold value for reduced strength was >15 seconds [2].

Co-variates: In the regression analyses of body composition phenotypes as exposure for mortality various co-variates were accessible for the two cohorts. In the analyses of the H70 women and men, comorbidities and smoking (number of cigarettes/day) were adjusted for. For the corresponding analyses in the ULSAM male cohort the following factors were adjusted for; age, comorbidities, education, exercise, living conditions (living alone: yes/no) and smoking (current smoker or non-smoker). When adjusting for co-morbidities, the un-weighted Charlson Comorbidity Index was used in both cohorts. The index was based on in-patient diagnoses (ICD9 - ICD10) in the patient register before the dates of the examinations [31, 32]. In the ULSAM cohort education was assessed by number of years in school divided into categories (7, 8 or 12 years), college education, or graduate exam. Regular exercise was defined as doing sports/heavy gardening more than three hours per week.

Statistical analyses

All values are presented as means± SD, median or percentage, as appropriate. In the survival analyses, the cohorts were divided into four groups based on body phenotype: sarcopenic obesity, sarcopenia (without obesity), obesity (without sarcopenia), and no sarcopenia or obesity (i.e “normal” phenotype) as

indicated above. In the analysis of the potential association between SO and all-cause mortality, we examined the 10-year survival in the 75 year old participants of the H70 cohorts (depending on date of examination, maximum years at risk was 9.7) and 4-year survival in the 87 year old participants of the ULSAM cohort (maximum years at risk 4.0). The log-rank test, the Kaplan-Meier survival curve and the Cox proportional hazard model were used. The Cox regression analyses were presented as hazard ratios with 95% confidence intervals. A p-value of <0.05 was considered statistically significant. Relevant multivariable co-variates for the associations of interest were included in the models. When finding the best fitting model, a likelihood ratio test was performed and a test for proportional hazard assumption including plots of Schoenfeld residuals. All analyses were conducted using STATA15 [33].

Sensitivity analyses: In sensitivity analyses (Cox regression for survival), individuals within the H70 cohort who had passed away within a year after the examination (2005-2006) were excluded. We also performed sensitivity analyses where the mortality for the women with obesity (no sarcopenia) defined as BMI ≥30 kg/m^2 was compared to the mortality for the group with no sarcopenia or obesity, and where women with obesity by any of the definitions (irrespective of sarcopenia) were compared to women without obesity.

The exercise-related co-variate in H70, "*spare time activity during the last year*", was missing for almost half of the H70 sample. For this reason complementary sensitivity analyses were performed by adding this co-variate in models that only included individuals with this data available.In the ULSAM cohort, mortality was also compared between the group with obesity (without sarcopenia) defined as waist circumference ≥102 cm and those with no sarcopenia or obesity, and between the group with obesity by any definition (irrespective of sarcopenia) and the group without obesity (irrespective of sarcopenia).

Results

Basic characteristics, i.e. anthropometry, body composition and tests of functional performance are presented in Table 2. In the H70 cohorts, the mean age was 75.6 years for both women and men, and in the ULSAM cohort mean age was 87 years.

In the two cohorts elevated body fat mass was the measure which defined the majority of the individuals with obesity. In the H70 cohorts, the mean BMIs were 26 kg/m^2 and 27 kg/m^2 for women and men, respectively. Obesity prevalence by any of the factors BMI, body fat mass or waist circumference was 60% in women and 68% in men in the H70 cohorts. In the ULSAM cohort, average BMI was 26 kg/m^2, and corresponding obesity prevalence was 55%.

Prevalence of sarcopenic obesity

The H70 cohorts: SO was observed in 4% (n=13) of women and 11% (n=23) of men (Table 2). For sarcopenia only, i.e. without obesity, the prevalence was around 1% (n=4) for women and <1% (n=1) for men. Based on the total sample (SO included), 41 subjects (7.8%) were defined as sarcopenic.

The ULSAM cohort: The prevalence of SO was 10%, and the prevalence of sarcopenia only was also 10% (Table 2).

Association with mortality

The H70 cohorts: The association with mortality varied with gender, thus the results are presented for women and men separately (Table 3). Since very few were defined as sarcopenic (n=5) (without obesity), this group was excluded from further analyses. Compared to the group with "normal" body phenotype, i.e., "no sarcopenia or obesity", the women with SO in the H70 cohort had a 3-fold increased risk of dying during the ten years of follow-up. This result was significant in the crude model, whereas the CIs became wider in the adjusted model (Table 3). The women with obesity only, i.e. without sarcopenia, also had an increased risk (although non significant) of mortality during the follow-up period compared to the women who had "no sarcopenia or obesity" (Table 3, Fig 1a). There were only five fatal events among the smaller group of women with SO, whereas among the women with obesity only there were 41 events. In the H70 male cohort, no significant association was found between SO and 10-year survival (Table 3), although the pattern of mortality (Figure 1b) was similar to that of the women. When performing the survival analyses for women and men together (n = 521) SO was associated with an increased risk of mortality during the ten years of follow-up (HR 2.46, 1.3- 4.6, crude model). This finding remained significant when adjusted for comorbidities and smoking (HR 2.23, 1.1-4.6).

The ULSAM cohort: There was no significant difference in survival between participants with SO compared to those with a "normal" body phenotype, i.e. no sarcopenia or obesity (Table 3, Fig 1c). In the adjusted model, men with obesity only; i.e. without sarcopenia, had a 40% lower mortality risk compared to those with "no sarcopenia or obesity".

Sensitivity analyses

The H70 cohorts: Exclusion of individuals that died within one year after baseline did not alter the results. Moreover, analyses showed that women with a BMI >30 kg/m^2 (without sarcopenia) had a significantly higher mortality than the women with "no sarcopenia or obesity" (HR 3.4 95% CI (1.4-8.4)). However, this association did not remain after adjustment for comorbidities. On the other hand, the women with obesity irrespective of sarcopenia displayed increased 10 year mortality even after adjustment for comorbidities and smoking; i.e. HR 1.7 95% CI (1.0-3.0) compared to the women without obesity.

Adding the covariate "spare time activities during the last year"to the model did not alter the results.

The ULSAM cohort: When comparing mortality for men with obesity defined as a waist circumference ≥102 cm to those with "normal" body phenotype ("no sarcopenia or obesity"), the obese men still had a 40% (HR 0.6, 95% CI (0.4-1.1)) lower risk of dying within the follow-up time (although a wide confidence interval). When adjusted for comorbidities, education, exercise, living conditions, and smoking, this association became even stronger (HR 0.4, 95% CI (0.2-0.8)). When comparing the individuals with obesity by any definition (irrespective of sarcopenia) to the those without obesity (irrespective of

sarcopenia), results showed a lower risk of mortality in the group with obesity in both the age-adjusted and the fully adjusted model (HR 0.5 95% CI (0.3-0.9)).

Discussion

This study is one of the first to examine the prevalence of SO in older adults using the updated EWGSOP2 definition. Among interesting results is the finding that the 75-year-old women with SO appeared to have a higher risk of dying during the ten years of follow-up compared to those with “normal” body phenotype (“no sarcopenia or obesity”). No similar association was obvious among the 75-year-old men. In contrast, in the 88 year old men obesity (irrespective of sarcopenia) appeared to be associated with prolonged survival.

The prevalence of SO for the cohorts in this study is currently difficult to compare with similar studies, since no studies have so far been published using the EWGSOP2 definition of sarcopenia. In a cross-sectional analysis in an American population using eight different definitions for SO, the prevalence varied up to 26 fold depending on the definition [21]. In a systematic review from 2014, the EWGSOP group reported prevalences of sarcopenia of 1-29% using the previous EWGSOP definition from studies of home-dwelling older adults [34]. It is noteworthy that many studies in this field do not distinguish between sarcopenia and sarcopenic obesity. It cannot be ruled out that a proportion of the samples identified as having sarcopenia in previous reports were actually sarcopenic obese, a distinct phenotype with specific clinical and metabolic characteristics.

The results of our analyses indicate that, for the 75-year-old women, the risk of dying within the ten-year follow-up period was three-fold for those with SO. However, sample sizes were small, and only five fatal events were observed among the women with SO, producing wide confidence intervals. When combining women and men the association between mortality and SO became stronger.

Three measures, i.e. BMI, waist circumference and proportion of fat mass, were used to define obesity. Interestingly, the mean BMI in the groups of 75-year-old women with either SO or any type of obesity were below 30 kg/m^2. In the sensitivity analysis, where mortality was compared between the groups of women with obesity defined as a high BMI only and the women with “no sarcopenia or obesity”, the women with obesity by BMI had a higher risk of mortality. However, this association became non-significant after adjustment for co-morbidities. Furthermore, the sensitivity analyses revealed an increased mortality risk in the women with any type of obesity, irrespective of sarcopenia and adjusted for comorbidities and smoking, compared to the women without obesity (irrespective of sarcopenia).

No clear corresponding association between SO or obesity and mortality was found among the 75-year-old men. A possible explanation could be that the health consequences of obesity differ between the genders. The male pattern of obesity is usually more related to increased risks, e.g., the metabolic syndrome, contributing to the fact that men have a shorter life expectancy than women [35]. It is possible, therefore, that many men at increased risk had died before the age of 75. Thus a selection of men with

less metabolically active obesity could have been included in this study. A corresponding selection may not have occurred yet in the 75-year-old women. A study from 2012 examining the relationship between body composition and mortality in Swedish older adults, mean age 72 years, also found a gender difference. However, these data displayed a U-shaped relationship between total fat mass and mortality in men. In women, in contrast to our finding total fat mass was negatively associated with mortality, indicating a protective effect in the women [36].

Although risks associated with obesity are well described in the literature, there is an ongoing debate as to whether this risk weakens with age and whether “the obesity paradox” exists for older adults [16, 37, 38]. In our study, the 88-year-old men with obesity (with or without sarcopenia) appeared to have a lower risk of dying within the 4 year follow-up time, even when obesity was defined as a high waist-circumference only. Mechanisms explaining the obesity paradox are not clear, but it is hypothesized that obesity is accompanied by an increase in muscle mass which could mediate the protective effect [12] [39, 40]. Other explanations include that obesity may merely reflect an absence of chronic disease, whereas lower BMI at older age is often associated with chronic catabolic illnesses, triggering unintentional weight loss that contributes to premature death [16, 41].

Reports on risks associated with SO are also conflicting. A recent meta-analysis reported SO to be associated with an increased risk of mortality (24%), especially in men [42]. However, the heterogeneity among the compiled studies was substantial. One of the studies, based on the National Health and Nutrition Examination Survey III (NHANESIII, Batsis et al.), reported results according to gender aspects that were in line with those found in the current study. Thus, the prevalence of SO was higher in men, and SO in women was associated with a higher risk of mortality [43]. In this still young area of research, conflicting results are probably partly due to the heterogeneity of definitions of sarcopenia and SO, as well as the measuring techniques and cut-offs chosen [35, 44].

A general limitation of observational studies, especially when examining older adults, is the risk of selection bias, the “healthy participant effect” [45]. It is reasonable to expect that the older adults that were well enough to participate in the H70 and ULSAM examinations were healthier than the general older population in Sweden. Other limitations of the study include the relatively small sample sizes with few fatal events and a subsequent risk of type 2 errors. The fact that we reported different follow-up times for the two cohorts could be viewed as a short-coming. Still, we found it feasible to have a longer (10 year) follow-up period in the considerably younger participants of the H70 cohorts compared to the 4 years of follow-up in the 88 year old ULSAM cohort. Furthermore, most covariates were based on self-reported data (e.g., smoking, education, living alone) and, due to study design, we cannot rule out residual confounding. In the H70 cohorts, due to few events in the group with SO, we limited the inclusion of covariates in the model. The assessment methods, such as that for body composition, were not the same in the various cohorts. Interestingly though, the prediction equation for estimating total body skeletal muscle mass by BIS, used in this study for the two H70 cohorts, has been validated against DXA also using the H70 population with only a small systematic bias being reported [30].

The strengths of this study include the choice of cohorts, which include both women and men, and men at different ages, i.e., 75 and 88 years. The study is also based on the most recent consensus sarcopenia definition by EWGSOP2. In addition, since BMI has some limitations when used in older populations [39, 40], we chose to include also measures of body fat and waist circumference for the assessment of obesity.

In conclusion, this study illuminates the importance of considering obesity when studying sarcopenia. The results show that SO defined by EWGSOP2 in combination with three different measures of obesity, was more prevalent among 75-year-old men than among women of the same age. In contrast to the 75-year-old men, the 75-year-old women with SO seemed to have an increased risk of dying within ten years compared to women who did not have sarcopenia or obesity. The prevalence of SO in men was higher in the 88 year olds than in the 75 year olds, but no association between SO and mortality was found in any of the two groups of men. On the contrary, in the oldest men the results indicated that obesity could be protective. More studies in this emerging research field, based on larger samples and with special focus on gender and age, are warranted.

Abbrevations

ASMI: Appendicular Skeletal Muscle Index

BIS: Bioelectrical Impedance Spectroscopy

DXA: Dual-energy X-ray Absorptiometry

EWGSOP: European Working Group of Sarcopenia in Older People

H70: The Gothenburg H70 Birth Cohort Studies

PPSW: Prospective Population Study of Women in Gothenburg

SMI: Skeletal Muscle Index

SMM: Skeletal Muscle Mass

SO: Sarcopenic Obesity

ULSAM: Uppsala Longitudinal Study of Adult Men

Declarations

Ethics approval and consent to participate

The study was approved by the Ethics Committee of the University of Gothenburg, Sweden (Dnr S377-99/T45 304) and the Regional Ethical Committee of Uppsala, Sweden (Dnr 2007/338). All methods were

performed in accordance with relevant guidelines and regulations, e.g., the Helsinki Declaration. Informed consent was obtained from all participants and/or their relatives.

Consent for publication

Not applicable.

Availability of data and material

The data used and analysed during the current study are available from the author on reasonable request.

Competing interests

ÅvB has received grants from Nestlé Health Science and the Geriatric Fund whilst conducting the study. TC has received unconditional research grants and speaking engagement honoraries from Nestle Health Science and Nutricia, and speaking engagement honoraries from Fresenius-Kabi and Arla Food. AK has been employed as a Nutritional translator at Nestlé Health Science (September 2016 to October 2017), no other competing interests are declared. MN reports receiving grant support from Nestle Health Science, no other competing interests are declared. ES has received grants from the Geriatric Fund and Thureus Uppsala. SRO, LL, IS, KF and ER report no potential conflict of interest.

Funding

The H70 study was supported by grants from the Swedish Research Council (2015-02830, 2013-8717), Swedish Research Council for Health, Working Life and Welfare (2013-2300, 2006-1506, 2013-2496), and the Swedish state under the agreement between the Swedish government and the county councils, the ALF-agreement (ALF 716681). The ULSAM study was funded by Uppsala University and Uppsala University Hospital.

Authors´ contribution

ÅvB has substantially contributed to the analysis and interpretation of the data in this study and to the writing and revision of the manuscript. SRO, ER, ES and TC have substantially contributed to the design of the study and to the revision of the manuscript. LL has contributed to the interpretation of the data and to the revision of the manuscript, and AK, MN, KF and IS have also contributed to the revision of the manuscript. All authors have contributed to and approved the final version of this manuscript.

Acknowledgments

We would like to acknowledge the Nordic Nutrition Academy and especially Sanna Hedman and Anton Kinnander who worked on the original idea and abstract for this manuscript. We would also like to thank Valter Sundh, University of Gothenburg for helping with the H70 data and Vilmantas Giedraitis, Uppsala University for support regarding ULSAM.

References

1. Global Health Observatory data https://www.who.int/gho/ncd/risk_factors/overweight_text/en/. Accessed 2018-02-11.

2. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, Cooper C, Landi F, Rolland Y, Sayer AA *et al*: Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing. 2018; doi: 10.1093/ageing/afy169

3. Cederholm T, Barazzoni R, Austin P, Ballmer P, Biolo G, Bischoff SC, Compher C, Correia I, Higashiguchi T, Holst M *et al*: ESPEN guidelines on definitions and terminology of clinical nutrition. Clin Nutr. 2017; doi: 10.1016/j.clnu.2016.09.004

4. Guo SS, Zeller C, Chumlea WC, Siervogel RM: Aging, body composition, and lifestyle: the Fels Longitudinal Study. Am J Clin Nutr. 1999; doi: 10.1093/ajcn/70.3.405

5. Rosenberg IH: Sarcopenia: origins and clinical relevance. J Nutr. 1997; doi: 127 990S-991S

6. Pagotto V, #xe9, ria, Silveira EA: Methods, Diagnostic Criteria, Cutoff Points, and Prevalence of Sarcopenia among Older People. The Scientific World Journal. 2014; doi: 10.1155/2014/231312

7. Fielding RA, Vellas B, Evans WJ, Bhasin S, Morley JE, Newman AB, Abellan van Kan G, Andrieu S, Bauer J, Breuille D *et al*: Sarcopenia: an undiagnosed condition in older adults. Current consensus definition: prevalence, etiology, and consequences. International working group on sarcopenia. J Am Med Dir Assoc. 2011; doi: 12 249-256. http://www.ncbi.nlm.nih.gov/pubmed/21527165

8. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, Martin FC, Michel JP, Rolland Y, Schneider SM *et al*: Sarcopenia: European consensus on definition and diagnosis: Report of the European Working Group on Sarcopenia in Older People. Age Ageing. 2010; doi: 10.1093/ageing/afq034

9. Beaudart C, Zaaria M, Pasleau F, Reginster J-Y, Bruyère O: Health Outcomes of Sarcopenia: A Systematic Review and Meta-Analysis. PLoS ONE. 2017; doi: 10.1371/journal.pone.0169548

10. Organization WH: Obesity: Preventing and Managing the global epidemic. Report of a WHO Consultation. In: WHO Technical Report Series 894. 10-12. www.who.int/nutrition/publication/obesity/WHO_TRS_894/en/; 2000: 10-12.

11. Canning KL, Brown RE, Jamnik VK, Kuk JL: Relationship between obesity and obesity-related morbidities weakens with aging. J Gerontol A Biol Sci Med Sci. 2014; doi: 10.1093/gerona/glt026

12. Bischoff SC, Boirie Y, Cederholm T, Chourdakis M, Cuerda C, Delzenne NM, Deutz NE, Fouque D, Genton L, Gil C *et al*: Towards a multidisciplinary approach to understand and manage obesity and related diseases. Clin Nutr. 2016; doi: 10.1016/j.clnu.2016.11.007

13. Grabowski DC, Ellis JE: High body mass index does not predict mortality in older people: analysis of the Longitudinal Study of Aging. J Am Geriatr Soc. 2001; doi: 49 968-979

14. Zamboni M, Mazzali G, Zoico E, Harris TB, Meigs JB, Di Francesco V, Fantin F, Bissoli L, Bosello O: Health consequences of obesity in the elderly: a review of four unresolved questions. Int J Obes (Lond). 2005; doi: 10.1038/sj.ijo.0803005

15. Masters RK, Reither EN, Powers DA, Yang YC, Burger AE, Link BG: The impact of obesity on US mortality levels: the importance of age and cohort factors in population estimates. Am J Public Health. 2013; doi: 10.2105/ajph.2013.301379

16. Winter JE, MacInnis RJ, Wattanapenpaiboon N, Nowson CA: BMI and all-cause mortality in older adults: a meta-analysis. The American Journal of Clinical Nutrition. 2014; doi: 10.3945/ajcn.113.068122

17. Dey DK, Rothenberg E, Sundh V, Bosaeus I, Steen B: Body mass index, weight change and mortality in the elderly. A 15 y longitudinal population study of 70 y olds. Eur J Clin Nutr. 2001; doi: 10.1038/sj.ejcn.1601208

18. Al Snih S, Ottenbacher KJ, Markides KS, Kuo YF, Eschbach K, Goodwin JS: The effect of obesity on disability vs mortality in older Americans. Arch Intern Med. 2007; doi: 10.1001/archinte.167.8.774

19. Vincent HK, Vincent KR, Lamb KM: Obesity and mobility disability in the older adult. Obes Rev. 2010; doi: 10.1111/j.1467-789X.2009.00703.x

20. Schaap LA, Koster A, Visser M: Adiposity, muscle mass, and muscle strength in relation to functional decline in older persons. Epidemiol Rev. 2013; doi: 10.1093/epirev/mxs006

21. Batsis JA, Barre LK, Mackenzie TA, Pratt SI, Lopez-Jimenez F, Bartels SJ: Variation in the prevalence of sarcopenia and sarcopenic obesity in older adults associated with different research definitions: dual-energy X-ray absorptiometry data from the National Health and Nutrition Examination Survey 1999-2004. J Am Geriatr Soc. 2013; doi: 10.1111/jgs.12260

22. Zamboni M, Mazzali G, Fantin F, Rossi A, Di Francesco V: Sarcopenic obesity: a new category of obesity in the elderly. Nutr Metab Cardiovasc Dis. 2008; doi: 10.1016/j.numecd.2007.10.002

23. Baek SJ, Nam GE, Han KD, Choi SW, Jung SW, Bok AR, Kim YH, Lee KS, Han BD, Kim DH: 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. 2014; doi: 10.1007/s40618-013-0011-3

24. Steen B, Djurfeldt H: The gerontological and geriatric population studies in Gothenburg, Sweden. Z Gerontol. 1993; doi: 26 163-169

25. Bengtsson C, Ahlqwist M, Andersson K, Bjorkelund C, Lissner L, Soderstrom M: The Prospective Population Study of Women in Gothenburg, Sweden, 1968-69 to 1992-93. A 24-year follow-up study with special reference to participation, representativeness, and mortality. Scand J Prim Health Care. 1997; doi: 15 214-219

26. Hedstrand H: A study of middle-aged men with particular reference to risk factors for cardiovascular disease. Ups J Med Sci Suppl. 1975; doi: 19 1-61

27. Janssen I, Baumgartner RN, Ross R, Rosenberg IH, Roubenoff R: Skeletal Muscle Cutpoints Associated with Elevated Physical Disability Risk in Older Men and Women. Am J Epidemiol. 2004; doi: 10.1093/aje/kwh058

28. Gallagher D, Heymsfield SB, Heo M, Jebb SA, Murgatroyd PR, Sakamoto Y: Healthy percentage body fat ranges: an approach for developing guidelines based on body mass index. The American Journal of Clinical Nutrition. 2000; doi: 10.1093/ajcn/72.3.694

29. Lean MEJ, Han TS, Morrison CE: Waist circumference as a measure for indicating need for weight management. BMJ. 1995; doi: 10.1136/bmj.311.6998.158

30. Tengvall M, Ellegård L, Malmros V, Bosaeus N, Lissner L, Bosaeus I: Body composition in the elderly: Reference values and bioelectrical impedance spectroscopy to predict total body skeletal muscle mass. Clin Nutr. 2009; doi: https://doi.org/10.1016/j.clnu.2008.10.005

31. Charlson ME, Pompei P, Ales KL, MacKenzie CR: A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987; doi: 40 373-383

32. Hude Q, Vijaya S, Patricia H, Andrew F, Bernard B, Jean-Christophe L, Saunders LD, Cynthia AB, Thomas EF, William AG: Coding Algorithms for Defining Comorbidities in ICD-9-CM and ICD-10 Administrative Data. Med Care. 2005; doi: 43 1130-1139. http://www.jstor.org/stable/3768193

33. StataCorp.: Stata Statistical Software: College Station, TX: StataCorp LP. In., Version Release 15 edn; 2015.

34. Cruz-Jentoft AJ, Landi F, Schneider SM, Zúñiga C, Arai H, Boirie Y, Chen L-K, Fielding RA, Martin FC, Michel J-P *et al*: Prevalence of and interventions for sarcopenia in ageing adults: a systematic review. Report of the International Sarcopenia Initiative (EWGSOP and IWGS). Age Ageing. 2014; doi: 10.1093/ageing/afu115

35. Mauvais-Jarvis F: Epidemiology of Gender Differences in Diabetes and Obesity. Adv Exp Med Biol. 2017; doi: 10.1007/978-3-319-70178-3_1

36. Toss F, Wiklund P, Nordström P, Nordström A: Body composition and mortality risk in later life. Age Ageing. 2012; doi: 10.1093/ageing/afs087

37. Oreopoulos A, Kalantar-Zadeh K, Sharma AM, Fonarow GC: The obesity paradox in the elderly: potential mechanisms and clinical implications. Clin Geriatr Med. 2009; doi: 10.1016/j.cger.2009.07.005

38. Villareal DT, Apovian CM, Kushner RF, Klein S: Obesity in older adults: technical review and position statement of the American Society for Nutrition and NAASO, The Obesity Society. Am J Clin Nutr. 2005; doi: 10.1093/ajcn/82.5.923

39. Gill LE, Bartels SJ, Batsis JA: Weight Management in Older Adults. Curr Obes Rep. 2015; doi: 10.1007/s13679-015-0161-z

40. Chapman IM: Obesity paradox during aging. Interdiscip Top Gerontol. 2010; doi: 10.1159/000319992

41. De Stefani FDC, Pietraroia PS, Fernandes-Silva MM, Faria-Neto J, Baena CP: Observational Evidence for Unintentional Weight Loss in All-Cause Mortality and Major Cardiovascular Events: A Systematic Review and Meta-Analysis. Sci Rep. 2018; doi: 10.1038/s41598-018-33563-z

42. Tian S, Xu Y: Association of sarcopenic obesity with the risk of all-cause mortality: A meta-analysis of prospective cohort studies. Geriatr Gerontol Int. 2016; doi: 10.1111/ggi.12579

43. Batsis JA, Mackenzie TA, Barre LK, Lopez-Jimenez F, Bartels SJ: Sarcopenia, sarcopenic obesity and mortality in older adults: results from the National Health and Nutrition Examination Survey III. Eur J Clin Nutr. 2014; doi: 10.1038/ejcn.2014.117

44. Gheller BJ, Riddle ES, Lem MR, Thalacker-Mercer AE: Understanding Age-Related Changes in Skeletal Muscle Metabolism: Differences Between Females and Males. Annu Rev Nutr. 2016; doi: 10.1146/annurev-nutr-071715-050901

45. Golomb BA, Chan VT, Evans MA, Koperski S, White HL, Criqui MH: The older the better: are elderly study participants more non-representative? A cross-sectional analysis of clinical trial and observational study samples. BMJ Open. 2012; doi: 10.1136/bmjopen-2012-000833

Tables

Table 1. Methods and cut-offs for sarcopenia and obesity.

	H70 women & men		ULSAM men	
Sarcopenia (1)	**Method**	**Cut-off**	**Method**	**Cut-off**
Chair stand (sec)	Five repeated chair stands	>15 (women & men)	Five repeated chair stands	>15
Grip strength (kg)	Jamar dynamometer	<16 (women) <27 (men)	Baseline hydraulic hand dynamometer	<27
Muscle Mass, kg/m^2	BIS	SMI <5.75(women)/ <8.5 (men) (27)	DXA	ASMI <7
Obesity				
BMI (kg/m^2)	Balance scale/ standing height	>30 (women & men) (10)	Balance scale/standing height	>30
Fat mass (%)	BIS	≥42 (women) ≥30 (men) (28)	DXA	>30
Waist circumference (cm)	Measuring tape[a]	>88 (women)/ >102 (men) (29)	Measuring tape[a]	>102

BIS=Bioelectrical impedance spectroscopy, DXA= Dual-energy X-ray absorptiometry, SMI= Skeletal Muscle Index, ASMI= Appendicular Skeletal Muscle Index.

[a] measured midway between the lowest rib bone and the iliac crest.

Table 2. Basic characteristics.

H70 (women)	**Total n=319**	**Sarcopenic obesity n=13 (4%)**	**Sarcopenia (without obesity) n=4 (1%)**	**Obesity (without sarcopenia) n=182 (57%)**	**No sarcopenia or obesity n=120 (38%)**
Age (yrs)	75.6± 0.3	75.7± 0.3	75.4± 0.2	75.5± 0.4	75.6± 0.3
Height (cm)	161± 6.1	162.5± 6.8	150.25± 2.8	162± 5.9	161± 6.1
Weight (kg)	66.5± 10.7	62.5± 9.9	48.8± 1.7	74.6± 10.5	61.2± 7.4
Body mass index (BMI) (kg/m^2)	25.7± 4.1	23.9± 5	21.5± 1.0	28.5± 3.8	23.6± 2.6
Proportion with BMI ≥ 30 kg/m^2	20%	7.7%	0	34.6%	0
Body fat mass (BF)(%)	39.7± 7.3	46± 5.9	38.1± 1.9	43.2± 5	35.6± 7.3
Proportion with BF >42%	46.6%	84.6%	0	69.8%	0
Waist circumference (WC) (cm)	86.9± 11.5	83.8± 12.8	70.2± 6.3	95.3± 9.5	78.5± 6.8
Proportion with WC≥88 cm	50%	46.1%	N/A	81.9%	0
Skeletal muscle index (SMI) (kg/m^2)	6.6± 0.9	5.2± 0.8	N/A	6.7± 0.8	6.6± 0.8
Grip strength (kg)	24.2± 4.3	19.8± 4.3	N/A	25.0± 3.8	24.1± 4.2
Time for five repeated chair stands (sec)	11.9± 3.3	19.7± 9.7	N/A	11.8± 1.7	11.1± 1.8
Gait speed (m/sec)	1.2±0.2	1.01±0.23	1.1±0.2	1.15±0.2	1.2±0.2
H70 (men)	**Total n=202**	**Sarcopenic obesity n=23 (11.4%)**	**Sarcopenia (without obesity) n=1 (0.5%)**	**Obesity (without sarcopenia) n=119 (59%)**	**No sarcopenia or obesity n=59 (29%)**
Age (yrs)	75.6± 0.3	75.4± 0.2	N/A	75.6± 0.4	75.6± 0.3
Height (cm)	174.9± 6.5	172.9± 7.7	N/A	176± 6.4	173.5± 5.5
Weight (kg)	82.2± 12.4	80.6± 11.1	N/A	86.1± 12.7	74.9± 8.5
Body mass index (BMI) (kg/m^2)	26.8± 3.6	26.9± 3.4	N/A	27.4± 3.6	24.8± 2.6
Proportion with BMI ≥30 kg/m^2	15.4%	13%	N/A	23%	0
Body fat mass (BF)(%)	31.5± 7.5	40.3± 4.6	N/A	33.6± 5.1	23.8± 6
Proportion with BF >30%	62%	100%	N/A	83%	0

Waist circumference (WC)(cm)	98.2± 10.5	99.8± 9.9	N/A	101.3± 9.8	91.5± 7.3
Proportion with WC ≥102 cm	35%	30%	N/A	52%	0
Skeletal muscle index (SMI) (kg/m^2)	8.6± 0.7	7.8± 0.6	N/A	8.6± 6	8.9± 0.5
Grip strength (kg)	38.5± 7.1	32.7± 8.0	N/A	39.5± 6.5	38.6± 7.5
Time for five repeated chair stands (sec)	12.5± 3.9	18.4± 5.5	N/A	12.1± 3	11± 2.7
Gait speed (m/sec)	1.2± 0.2	1.0± 0.3	1.43	1.2± 0.2	1.3± 0.1
ULSAM (men)	**Total n=288**	**Sarcopenic obesity n=29 (10%)**	**Sarcopenia (without obesity) n=29 (10%)**	**Obesity (without sarcopenia) n=128 (44%)**	**No sarcopenia or obesity n=102 (35%)**
Age (yrs)	86.6± 1	86.5± 0.9	86.5± 1.0	86.6± 1.0	86.6± 1.1
Height (cm)	172.4± 6	171.7± 5.4	171.1± 7.2	172.9± 6	172.3 ± 5.8
Weight (kg)	74.3± 7.8	73.8± 8.1	64± 7.9	83.7± 9.7	70.8± 7.9
Body mass index (BMI) (kg/m^2)	25.6± 3.5	25± 2.4	21.8± 2.0	28± 2.9	23.8± 2.6
Proportion with BMI ≥30kg/m^2	7%	3%	0	14%	0
Body fat mass (BF) (%)	28.6± 7.0	33.8± 3.4	22.4± 5.3	33.3± 4.6	23.1± 5.0
Proportion with BF > 30%	44%	90%	0	78.9%	0
Waist circumference (WC) (cm)	99.6± 9.7	100.2± 8.5	90.4± 6.9	106.5± 7.3	93.3± 6.7
Proportion with WC ≥102 cm	37%	41%	0	75%	0
Appendicular skeletal muscle index (ASMI) (kg/m^2)	7.45± 0.8	6.4± 0.5	6.5± 0.4	7.8± 0.6	7.5± 0.6
Grip strength (kg)	30.2± 6.5	25.8± 5.3	28.1± 5.6	30.4± 6.5	31.4± 6.5
Time for five repeated chair stands (sec)	18± 7	22± 10	17± 3	18± 7	17± 8
Gait speed (m/sec)	1.36± 0.3	1.2± 0.3	1.3± 0.3	1.4± 0.3	1.4± 0.3

Anthropometrics, body composition and functional characteristics at baseline. Sarcopenia is based on the EWGSOP2 definition (1), and obesity as BMI ≥30 kg/m^2, or percentage fat mass >30% (men) and 42% (women), or waist circumference ≥102 cm (men) and ≥88 cm (women). Data are presented as mean± SD.

N/A= Not applicable

Table 3. Associations with mortality.

Exposures	Model 1 HR (95% CI)	Model 2 HR (95% CI)	Model 3 HR (95% CI)
H70 (women)			
Sarcopenic obesity	3.25 (1.2-8.9)	2.7 (1.0-7.4)	2.6 (0.9-7.2)
Obesity (without sarcopenia)	1.7 (1.0-3.1)	1.6 (0.9-2.9)	1.6 (0.9-2.9)
H70 (men)			
Sarcopenic obesity	1.5 (0.7-3.5)	1.5 (0.6-3.5)	1.4 (0.6-3.3)
Obesity (without sarcopenia)	1.2 (0.7-2.1)	1.2 (0.7-2.2)	1.2 (0.7-2.1)
ULSAM (men)			
Sarcopenic obesity	0.7 (0.3-1.6)	0.65 (0.3-1.5)	0.8 (0.3-1.9)
Sarcopenia (without obesity)	1.5 (0.8-2.8)	1.35 (0.7-2.6)	1.4 (0.7-2.9)
Obesity (without sarcopenia)	0.7 (0.4-1.2)	0.6 (0.4-1.0)	0.6 (0.3-0.9)

Hazard ratios (HR) and 95% confidence intervals (CI) for mortality associated with various body composition phenotypes. Model 1 is crude analyses in H70 women and men, and adjusted for age in ULSAM men. Model 2 includes adjustments for comorbidities in H70, and in ULSAM, adjustments for age and comorbidities. Model 3 includes adjustments for comorbidities and smoking in H70 and, in ULSAM, adjustments for age, comorbidities, education, regular exercise, living conditions and smoking. The reference group was participants with “no sarcopenia or obesity”.

Figures

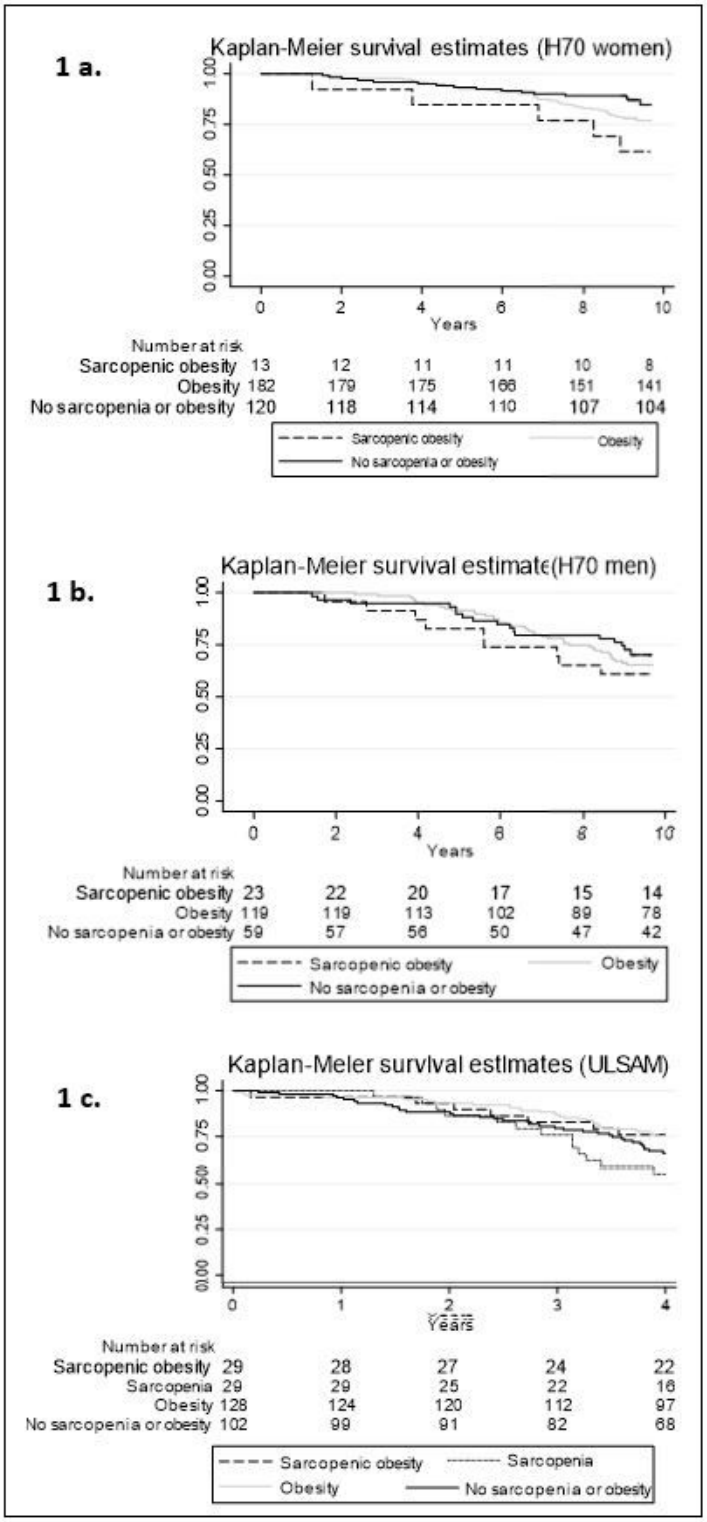

Figure 1

Panels a and b show survival rates in women and men from H70 stratified according to “sarcopenic obesity”, “obesity without sarcopenia” and “no sarcopenia or obesity”. Panel c displays corresponding data for ULSAM. In H70 (women and men), only five were defined as sarcopenic without obesity, and were consequently excluded from the survival analysis.