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ASSOCIATION OF SARCOOPENIC OBESITY WITH BMD AND FRACTURE <zaq;1>

Sarcopenic Obesity and Its Temporal Associations With Changes in Bone Mineral Density, Incident Falls, and Fractures in Older Men: The Concord Health and Ageing in Men Project

David Scott,^{1,2} Markus Seibel,³ Robert Cumming,^{4,5,6} Vasi Naganathan,⁵ Fiona Blyth,⁵ David G Le Couteur,⁷ David J Handelsman,⁸ Louise M Waite,⁵ and Vasant Hirani^{5,9}

¹School of Clinical Sciences at Monash Health, Monash University, Clayton, Australia

²Department of Medicine and Australian Institute of Musculoskeletal Science, Melbourne Medical School – Western Campus, The University of Melbourne, St Albans, Australia

³Bone Research Program, ANZAC Research Institute, and Department of Endocrinology and Metabolism, Concord Hospital, The University of Sydney, Sydney, Australia

⁴School of Public Health, University of Sydney, Sydney, Australia

⁵Centre for Education and Research on Ageing, Concord Hospital, University of Sydney, Sydney, Australia

⁶The ARC Centre of Excellence in Population Ageing Research, University of Sydney, Sydney, Australia

⁷ANZAC Research Institute and Charles Perkins Centre, University of Sydney, Sydney, Australia

⁸Department of Andrology, Concord Hospital and ANZAC Research Institute, University of Sydney, Sydney, Australia

⁹School of Life and Environmental Sciences, Charles Perkins Centre, University of Sydney, Sydney, Australia

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Address correspondence to: David Scott, PhD, School of Clinical Sciences at Monash Health, Monash University, Clayton, Victoria, Australia 3168. E-mail: david.scott@monash.edu

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ABSTRACT

Body composition and muscle function have important implications for falls and fractures in older adults. We aimed to investigate longitudinal associations between sarcopenic obesity and its components with bone mineral density (BMD) and incident falls and fractures in Australian community-dwelling older men. A total of 1486 men aged ≥ 70 years from the Concord Health and Ageing in Men Project (CHAMP) study were assessed at baseline (2005–2007), 2-year follow-up (2007–2009; $n = 1238$), and 5-year follow-up (2010–2013; $n = 861$). At all three time points, measurements included appendicular lean mass (ALM), body fat percentage and total hip BMD, hand-grip strength, and gait speed. Participants were contacted every 4 months for 6.1 ± 2.1 years to ascertain incident falls and fractures, the latter being confirmed by radiographic reports. Sarcopenic obesity was defined using sarcopenia algorithms of the European Working Group on Sarcopenia (EWGSOP) and the Foundation for the National Institutes of Health

(FNIH) and total body fat $\geq 30\%$ of total mass. Sarcopenic obese men did not have significantly different total hip BMD over 5 years compared with non-sarcopenic non-obese men ($p > 0.05$). EWGSOP-defined sarcopenic obesity at baseline was associated with significantly higher 2-year fall rates (incidence rate ratio [IRR] 1.66; 95% confidence interval [CI] 1.16–2.37), as were non-sarcopenic obesity (1.30; 1.04–1.62) and sarcopenic non-obesity (1.58; 1.14–2.17), compared with non-sarcopenic non-obese. No association with falls was found for sarcopenic obesity using the FNIH definition (1.01; 0.63–1.60), but after multivariable adjustment, the FNIH-defined non-sarcopenic obese group had a reduced hazard for any 6-year fracture compared with sarcopenic obese men (hazard ratio 0.44; 95% CI 0.23–0.86). In older men, EWGSOP-defined sarcopenic obesity is associated with increased fall rates over 2 years, and FNIH-defined sarcopenic obese men have increased fracture risk over 6 years compared with non-sarcopenic obese men. © 2016 American Society for Bone and Mineral Research.

KEY WORDS: SARCOPENIA; OBESITY; OSTEOPOROSIS; FALLS; FRACTURE

Introduction

Sarcopenia, the age-related decline in skeletal muscle mass and function, is an independent predictor of incident falls⁽¹⁾ and poorer bone health in older adults.⁽²⁾ A recent study demonstrated that low muscle mass predicts incident fractures in older adults independently of FRAX, a fracture risk calculator promoted by the World Health Organization.⁽³⁾ Conversely, obesity is generally considered to be protective against fracture, although half of all fractures in older adults occur in the overweight and obese population.⁽⁴⁾

In cross-sectional studies, Korean older men with both sarcopenia and obesity (“sarcopenic obesity”) had eightfold higher likelihood for osteoporosis compared with those without

sarcopenia or obesity,⁽⁵⁾ and sarcopenic obese older Australians attending a falls clinic had significantly lower hip bone mineral density (BMD) *T*-scores compared with those with obesity alone.⁽⁶⁾ Sarcopenic obese patients also reported significantly more falls in the past 6 months than non-sarcopenic obese and non-sarcopenic non-obese counterparts in this study. Two prospective studies in community-dwelling Australian older adults have demonstrated that those with low muscle strength combined with obesity have significantly greater increases in falls risk (determined by physiological assessments) over 5 years⁽⁷⁾ compared with non-sarcopenic non-obese, whereas men with low muscle mass and obesity have approximately threefold higher rates of self-reported non-vertebral fractures over 10 years compared with non-sarcopenic non-obese and non-sarcopenic obese counterparts.⁽⁸⁾ However, no prospective study has examined associations of sarcopenic obesity with incident falls and radiographically confirmed fractures. The coexistence of sarcopenia and obesity (“sarcopenic obesity”) conceivably increases fracture risk because both sarcopenia and obesity increase falls risk, whereas low muscle mass may counteract the potential benefit of obesity on BMD. The aims of the present study were to determine whether community-dwelling older men with sarcopenic obesity are at increased risk of greater declines in BMD, falls, and fractures.

Materials and Methods

Study design and population

CHAMP is an epidemiological study of Australian men aged 70 years and older. The selection of study subjects has been described in detail elsewhere.⁽⁹⁾ Briefly, men living in a defined urban geographical region (the Local Government Areas of Burwood, Canada Bay, and Strathfield) near Concord Hospital in Sydney, Australia, were recruited. The sampling frame was the New

South Wales Electoral Roll, on which registration is compulsory. The only exclusion criterion was living in a residential aged care facility. Eligible men were sent a letter describing the study and, if they had a listed telephone number, were telephoned about 1 week later. Of the 2815 eligible men with whom contact was made, 1511 participated in the study (54%). An additional 194 eligible men living in the study area heard about the study from friends or the local media and were recruited after contacting the study investigators before being identified through electoral rolls, yielding a total cohort of 1705 subjects.

Baseline data were collected between January 2005 and June 2007. Men completed a questionnaire at home, including questions on demographics, health status, and physical activity. Subsequently, participants attended a study clinic at Concord Hospital for assessment of body composition, physical performance, medication use, and blood biochemistry. These measurements were repeated at follow-up clinics conducted 2 years (between January 2007 and October 2009) and 5 years (between January 2012 and October 2013) after baseline. Of the 1705 subjects who completed the baseline assessments, 1366 had 2-year follow-up assessments and 954 had 5-year follow-up assessments. Fully trained staff collected data and the same equipment was used for all measurements and assessments, which were carried out in a single clinic.

Additionally, participants were contacted by telephone every 4 months from baseline until January 2014 to ascertain incident falls and fractures, as described below. All participants gave written informed consent. The study complied with the World Medical Association Declaration of Helsinki and was approved by the Sydney South West Area Health Service Human Research Ethics Committee, Concord Repatriation General Hospital, Sydney, Australia.

Anthropometrics, body composition, and bone mineral density

Height was measured using a Harpenden stadiometer and weight using Wedderburn digital scales; body mass index (BMI) was calculated as kg/m^2 . Whole-body and total hip dual-energy X-ray absorptiometry (DXA) scans were performed using a Hologic Discovery-W scanner (Hologic Inc., Bedford, MA, USA). Men removed jewelry and wore light cotton gowns free from metal. The same DXA scanner was used for all scans. Quality-control scans were conducted daily using the Hologic whole-body phantom and indicated no shifts or drifts. From whole-body DXA, appendicular lean mass (ALM) was calculated as the sum of lean mass of arms and legs (kg), and total body fat percentage was determined as the proportion of body fat relative to total body mass. Total hip BMD (g/cm^2) was estimated from total hip DXA. The coefficient of variation (CV%) for scans duplicated on 30 men from the study cohort was 1.6% for the total hip, 1.0% for whole-body lean mass, and 2.5% for whole-body fat mass.

Hand-grip strength and physical performance

Hand-grip strength (kg) of the dominant hand (best of two trials) was assessed using a Jamar dynamometer (Promedics, Blackburn, UK). Self-selected usual gait speed was measured on a 6-meter course at usual pace and timed from the first footfall. To maintain consistency with current low gait speed cut-points for sarcopenia, 6-meter gait speed was converted to estimate 4-meter gait speed using a previously published formula.⁽¹⁰⁾ Time to successfully complete five chair stands was also assessed using a chair without a backrest but with armrests and a seat height of 40 cm.

Definitions of sarcopenia and sarcopenic obesity

The European Working Group on Sarcopenia in Older People (EWGSOP) and Foundation for the National Institutes of Health (FNIH) Sarcopenia Project criteria were used to define

sarcopenia in this study. The EWGSOP defines sarcopenia in men as ALM adjusted for height squared $<7.25 \text{ kg/m}^2$ combined with low hand-grip strength ($<30 \text{ kg}$) and/or low gait speed ($\leq 0.8 \text{ m/s}$).⁽¹¹⁾ The FNIH derived ALM and hand-grip strength cut-points from nine different population-based studies and defines low lean mass criteria as $\text{ALM/BMI} < 0.789$ for men and hand-grip strength $< 26 \text{ kg}$.⁽¹²⁾ There are currently no consensus definitions for sarcopenic obesity. Obesity was defined in this study as body fat percentage $\geq 30\%$ because body fat percentage is a more appropriate indicator of obesity than BMI.⁽¹³⁾ Using both EWSOP and FNIH definitions, participants were allocated to the following categories: non-sarcopenic non-obese (referent), non-sarcopenic obese, sarcopenic non-obese, and sarcopenic obese.

Sociodemographic and lifestyle measures

Sociodemographic variables included age and living arrangements (lives alone versus lives with others). Smoking status (never smoker, ex-smoker, current smoker) was assessed. Physical activity was measured using the Physical Activity Scale for the Elderly (PASE) for individuals aged 65 years or older.⁽¹⁴⁾

Medication assessment

Trained personnel conducted a medication inventory of each participant during the baseline clinic visit. Participants were instructed to bring all the prescription and over-the-counter medications they were taking to the clinic visit for review. They were also asked whether they had taken any prescription or non-prescription medications during the past month. Details of all medications and prescription patterns were recorded. Reported medicines were coded using the Iowa Drug Information Service code numbers.⁽¹⁵⁾ The medications included in the analysis were

grouped into classes: psychotropic medications, bisphosphonates, and corticosteroids because these are known to influence falls, BMD, and fractures.

Health, medical, and physical measurements

Data on medical conditions were obtained from self-report of whether a doctor or a health care provider had told them that they had any of the following diseases: diabetes, thyroid dysfunction, osteoporosis, Paget's disease, stroke, Parkinson's disease, epilepsy, hypertension, heart attack, angina, congestive heart failure, intermittent claudication, chronic obstructive lung disease, liver disease, cancer (excluding non-melanoma skin cancers), osteoarthritis, and gout. Physical disability was assessed by seven items from a modified version of the Katz activities of daily living (ADL) scale, including walking across a small room, bathing, grooming, dressing, eating, transferring from a bed to a chair, and using the toilet. ADL disability was defined as needing help with one or more activities.⁽¹⁶⁾ Self-rated general health was assessed using the 12-Item Short Form Health Survey (SF-12).⁽¹⁷⁾ This provided data for self-rated health status. Men were asked to compare their health status with other people their own age and rate their health on a five-point scale as excellent, good, fair, poor, or very poor. Health status was categorized as poor if health was rated as poor or very poor. The presence of chronic pain was assessed through the question: "In the last 6 months, have you experienced pain in any part of your body which has lasted for 3 months or more, that is pain experienced every day for at least 3 months?"

Blood tests

All blood tests were performed at the Diagnostic Pathology Unit of Concord RG Hospital, which is a National Australian Testing Authority (NATA)-accredited pathology service, using a MODULAR Analytics system (Roche Diagnostics, Castle Hill, Australia). Fasting serum 25-

hydroxyvitamin D levels (25OHD) were measured by RIA (DiaSorin Inc., Stillwater, MN, USA), as described previously.⁽¹⁸⁾ The assay for 25OHD has a sensitivity of <3.75 nmol/L with an intra-assay precision of 7.6% and an interassay precision of 9.0%. All assays were carried out in duplicate. Of note, because of complete cross-reactivity of the antibody, the assays measure total circulating vitamin D levels, including both vitamin D2 and vitamin D3. Hemoglobin was measured by absorption spectrophotometry on the Abbott Diagnostics Cell Dyn Sapphire instruments. Serum albumin level was also measured in the same laboratory at Concord RG Hospital and was used as a continuous measure.

Assessment of incident falls and fracture

After the baseline assessment, men were contacted by telephone every 4 months until January 2014 and administered a questionnaire to retrospectively determine falls and fractures. The following questions were asked: “Have you fallen in the past 4 months? If yes, how many times have you fallen?” and “Have you broken or fractured a bone in the past 4 months?” If a fracture was reported, radiology reports were obtained either from the participant or from hospital medical records and radiology practices. Additional manual searching for fractures was conducted by accessing medical records within our health district. Only fractures confirmed by radiographic reports were included in the present analysis. Pathological fractures and fractures of hands, fingers, feet, toes, and the skull were excluded. Only the first incident fracture that met the inclusion criteria was included, regardless of trauma level or any additional subsequent fractures reported.⁽¹⁹⁾ Fractures were classified as any, non-vertebral, or a hip fracture. Time to censorship was either date of death, date of official withdrawal from the study, or date of the last telephone contact. The date of first fracture was the date on the radiology report.

Statistical analyses

Baseline descriptive characteristics were compared across categories of sarcopenic obesity using one-way ANOVA for continuous variables and chi-square tests for categorical variables.

Bonferroni post hoc tests were performed for these analyses. Paired *t* tests also compared baseline and follow-up differences in components of sarcopenic obesity. To study the longitudinal association between change in total hip BMD (in mg/cm^2) and change in sarcopenia components and body fat status, we used generalized estimating equation (GEE) analyses.⁽²⁰⁾

GEE takes into account the time-varying nature over multiple time points of both the outcome and the exposure and provides an estimated population average model by using all longitudinal data. With GEE analysis, the association between two longitudinally measured variables can be studied using all longitudinal data simultaneously and adjusting for within-person correlations caused by repeated measurement on each participant using robust estimation of the variances of the regression coefficients. GEE is also robust with regard to data missing at random. Models were initially unadjusted and then adjusted for age, income, smoking status, physical activity, and corticosteroid use number of comorbidities. In these and subsequent analyses, gait speed was converted to units of 0.1 m/s.

Associations between sarcopenic obesity categories and its components at baseline with incident falls were assessed with negative binomial regression adjusting for age, income, living alone, smoking status, psychotropic medication use, physical activity, vitamin D, and number of comorbidities examined. Given falls are relatively common in older age and sarcopenia and obesity are likely to have immediate to short-term effects on falls risk, only falls occurring up to 2 years after baseline were included. To minimize issues with multicollinearity between the

continuous sarcopenic obesity component variables, residuals were calculated for each participant by subtracting the overall mean for each variable from the actual value. Interaction terms were included for each of ALM, hand-grip strength, and gait speed with body fat percentage.

Unadjusted and adjusted Cox proportional hazards regression models examined associations of baseline sarcopenic obesity categories and its components with incident any, non-vertebral, and hip fracture, with adjustment for age, income, living alone, psychotropic medication use, smoking status, physical activity, 25OHD, and number of comorbidities. For these fracture outcome analyses, we also performed sensitivity analyses using multiple imputation for missing data in 1673 participants who attended baseline clinics.⁽²¹⁾ Furthermore, falls and fracture outcome analyses were repeated with the sarcopenic obesity group set as the referent to determine potential differences in fall rates and fracture incidence between this group and the non-sarcopenic obese and sarcopenic non-obese groups. Any p values < 0.05 or 95% confidence intervals not including the null point were considered statistically significant. Analyses were performed in SPSS Statistics 23 (IBM, Armonk, NY, USA).

Results

Characteristics of participants

After excluding participants who did not attend baseline ($n = 32$) and those with incomplete anthropometric ($n = 27$), DXA ($n = 21$), and physical performance ($n = 139$) data at baseline, a total of 1486 participants were included in the analysis. Compared with excluded participants, included participants were significantly younger (76.6 ± 5.3 versus 79.0 ± 6.4 years; $p < 0.001$) and had fewer comorbidities (2.4 ± 1.7 versus 3.2 ± 2.0 ; $p < 0.001$). Among included

participants, 48% were non-sarcopenic non-obese, 36% were non-sarcopenic obese, 9% were sarcopenic non-obese, and 7% were sarcopenic obese according to the EWGSOP definition. According to the FNIH definition, 54% were non-sarcopenic non-obese, 38% were non-sarcopenic obese, 4% were sarcopenic non-obese, and 4% were sarcopenic obese. Table 1{TBL 1} presents baseline characteristics of participants according to EWGSOP sarcopenic obesity categories. Sarcopenic obese men were significantly older and had more self-reported comorbidities than non-sarcopenic non-obese men. Sarcopenic obese men had significantly lower self-reported physical activity compared with both non-sarcopenic non-obese and non-sarcopenic obese. Total hip BMD was significantly lower in sarcopenic obese men compared with non-sarcopenic non-obese men. Furthermore, sarcopenic obese men took significantly longer to complete the chair stand task than all other groups. Similar results were observed when sarcopenic obesity categories were defined using the FNIH definition (data not shown). Supplemental Fig. S1 is a flowchart of participation according to EWGSOP sarcopenic obesity categories in this study. Of the 1486 participants with complete baseline data, 1238 (83%) completed the 2-year follow-up and 861 (58%) completed the 5-year follow-up. At both 2 and 5 years, significantly greater proportions of sarcopenic obese (26% and 42%) and sarcopenic non-obese (29% and 45%) men were excluded compared with non-sarcopenic non-obese (14% and 32%) and non-sarcopenic obese (15% and 26%; p value for trend < 0.001). At baseline, men lost to follow-up were significantly older (78.5 ± 6.0 years versus 75.4 ± 4.5 years; $p < 0.001$), had more comorbidities (2.8 ± 1.8 versus 2.2 ± 1.6 ; $p < 0.001$) and lower total hip BMD (0.92 ± 0.15 versus 0.95 ± 0.13 ; $p < 0.001$) but similar body fat percentage ($28.1 \pm 5.8\%$ versus $28.1 \pm 5.4\%$; $p = 0.854$). Table 2{TBL 2} reports baseline and follow-up values for components of sarcopenic

obesity according to the EWGSOP definition. ALM, hand-grip strength, and gait speed were all lower at baseline in sarcopenic obese men compared with non-sarcopenic non-obese and non-sarcopenic obese, whereas body fat percentage was significantly higher compared with non-sarcopenic non-obese and sarcopenic non-obese. ALM and hand-grip strength significantly decreased after 5 years for all groups, but gait speed was significantly reduced only in men who were non-sarcopenic non-obese or non-sarcopenic obese at baseline. Body fat percentage significantly increased over 5 years only for men who were non-sarcopenic non-obese at baseline and increased significantly more in this group than for non-sarcopenic obese and sarcopenic obese men.

BMD

GEE analysis determined longitudinal population average associations between sarcopenic obesity and total hip BMD (in mg/cm^2), adjusting for age, physical activity, smoking, income, and number of comorbidities over three time points (Table 3).{TBL 3} Using both EWGSOP and FNIH sarcopenic obesity definitions with non-sarcopenic non-obese as the referent group, non-sarcopenic obesity was associated with an increase in total hip BMD over time, whereas sarcopenic non-obesity was associated with a decline in total hip BMD over time. Sarcopenic obesity according to both FNIH and EWGSOP definitions was not associated with a difference in total hip BMD over time compared with non-sarcopenic non-obese in the multivariable analysis. Conversely, for components of sarcopenic obesity, population average increases in ALM, body fat percentage, hand-grip strength, and gait speed were all associated with increased total hip BMD over 5 years (Table 3).

Falls

Falls recorded up to 2 years after baseline were included in these analyses. Thirty percent of men reported at least one fall and 10% reported multiple falls over two years. According to the EWGSOP definition, 48% of men with sarcopenic obesity fell within 2 years compared with only 26% of non-sarcopenic non-obese men. The population attributable risk fraction for sarcopenic obesity and 2-year falls was 9.4%.

Table 4{TBL 4} reports the mean number of falls over 2 years and incidence rate ratios (IRRs) from negative binomial regression according to sarcopenic obesity status at baseline. Compared with non-sarcopenic non-obese men, all of non-sarcopenic obese, sarcopenic non-obese, and sarcopenic obese had significantly higher IRRs for falls, according to the EWGSOP definition. The highest IRR (2.4-fold) was observed for sarcopenic obese men, although this was moderated but remained significant after multivariable adjustment, and incidence rates for falls were also higher for non-sarcopenic obese and sarcopenic non-obese. Conversely, according to the FNIH definition, sarcopenic obesity was not associated with increased rates for falls compared with non-sarcopenic non-obese, whereas non-sarcopenic obese and sarcopenic non-obese men had higher fall rates in unadjusted and multivariable analyses. When the sarcopenic obese group was set as the referent group in these analyses, there were no significant differences in falls incidence for the non-sarcopenic obese (IRR 0.78; 95% CI 0.55–1.12) or sarcopenic non-obese (0.95; 0.63–1.43) groups, according to the EWGSOP definition. Similarly, compared with FNIH-defined sarcopenic obesity, there were no differences in incident falls for the FNIH-defined non-sarcopenic obese (1.28; 95% CI 0.80–2.05) or sarcopenic non-obese (1.61; 0.90–2.90) groups. Negative binomial regression determined associations of baseline sarcopenic obesity components with incident falls at 2 years. As reported in Supplemental Table S1, higher ALM, hand-grip

strength, and gait speed were associated with significantly reduced rate of falls in unadjusted models, but after adjustment a significant association was observed for gait speed only; a 0.1 m/s higher baseline gait speed was associated with 7% reduced rate of falls over 2 years. There were no interactions in the relationship of components of sarcopenic obesity with incident falls.

Fractures

Over a mean follow-up period of 6.1 ± 2.1 years, 152 (10%) participants reported any fracture, 125 (8%) reported a non-vertebral fracture, and 37 (3%) reported a hip fracture. The respective incidences of any and non-vertebral fracture according to sarcopenic obesity status are reported in Table 5. {TBL 5} Table 5 also reports Cox proportional hazards regression models for fracture across categories of sarcopenic obesity. In unadjusted models, there was no increased hazard for any fracture according to EWGSOP-defined sarcopenic obesity, but men with sarcopenic obesity defined by FNIH had more than twofold increased hazard ratios for any fracture, but after multivariable adjustment, the higher hazard ratio for FNIH-defined sarcopenic obese compared with non-sarcopenic non-obese was non-significant. However, post hoc analyses with sarcopenic obesity set as the reference group revealed a significantly decreased hazard for any fracture for FNIH-defined non-sarcopenic obese men compared with sarcopenic obese men in both unadjusted (hazard ratio 0.38; 95% CI 0.20–0.71) and adjusted analyses (0.44; 0.23–0.86), whereas there was no difference in hazard for sarcopenic non-obese men compared with sarcopenic obese men in multivariable analyses (0.58; 0.31–1.11). There were no differences in hazard for non-vertebral fracture across FNIH-defined sarcopenic obesity categories or for any or non-vertebral fracture across EWGSOP-defined sarcopenic obesity categories, after multivariable adjustment (all $p > 0.05$). Multiple imputation analyses (Supplemental Table S2)

including 1673 men who attended baseline clinics revealed similar associations; after multivariable adjustment, a significantly decreased hazard for any fracture in the non-sarcopenic obese group compared with the sarcopenic obese group (0.53; 0.28–0.99) was observed. Cox proportional hazards regression models determined associations of baseline ALM, hand-grip strength, gait speed, and body fat percentage with incident fracture. After multivariable adjustment, there were no significant associations or interactions for baseline components of sarcopenic obesity with any, non-vertebral, or hip fracture (Supplemental Table S3).

Discussion

This prospective population-based study demonstrated that sarcopenic obese older men had significantly higher 2-year fall rates compared with non-sarcopenic non-obese counterparts, although only according to the EWGSOP definition. Increases in muscle and fat mass, and also muscle function, predicted increases in hip BMD, and FNIH-defined sarcopenic obese men had significantly increased risk of incident fractures after compared with non-sarcopenic obese but not sarcopenic non-obese or non-sarcopenic non-obese men.

This is the first study to our knowledge to use radiographically confirmed fracture data to demonstrate that non-sarcopenic obese men have less than half of the risk of any fracture over 6 years compared with sarcopenic obese men. A previous analysis of the Tasmanian Older Adult Cohort (TASOAC) Study similarly demonstrated that sarcopenic obese men had 3.6-fold higher rates of non-vertebral fractures over 10 years compared with non-sarcopenic obese men, although fractures in this study were self-reported only.⁽⁸⁾ Sarcopenic obese men in TASOAC also had threefold higher rates of non-vertebral fracture than non-sarcopenic non-obese men, whereas in the present study, the higher rate of fracture for sarcopenic obese men was not

significantly different from non-sarcopenic non-obese men after multivariable adjustment. In the previous study, sarcopenia was defined by low muscle mass alone⁽⁸⁾ rather than the EWGSOP or FNIH definitions, and differences in criteria for sarcopenia likely explain differences in associations of sarcopenic obesity with incident fracture.

It is somewhat surprising that FNIH-defined non-sarcopenic obese men had significantly reduced incident fracture risk compared with sarcopenic obese men over 6 years given that non-obese but not sarcopenic obese men had significantly higher 2-year fall rates compared with non-sarcopenic non-obese men (albeit there were no significant differences in fall rates between sarcopenic obese and non-sarcopenic obese). It is possible that the ALM/BMI definition for low muscle mass proposed by FNIH is a stronger predictor of fracture risk than the ALM adjusted for height squared definition recommended by EWGSOP, and indeed a similar method of adjusting ALM for body size revealed significant associations for sarcopenic obesity and fractures previously.⁽⁸⁾ Although obese older adults generally fall more often, they may have reduced risk of fall-related injuries,⁽²²⁾ but the presence of low muscle mass relative to body size might reduce the protective effect through reductions in BMD or poorer shock absorption during a fall impact. EWGSOP- but not FNIH-defined sarcopenic obese had significantly increased 2-year fall rates compared with non-sarcopenic non-obese counterparts but not compared with non-sarcopenic obese or sarcopenic non-obese men. The differences in associations of EWGSOP- and FNIH-defined sarcopenic obesity with incident falls may be related to the smaller number of FNIH-defined sarcopenic obese participants. In the present study, the prevalence of sarcopenia at baseline was substantially higher for the EWGSOP definition (16%) compared with the FNIH definition (8%). A previous study of 1566 British men and women aged 60 to 64 years also

observed a higher prevalence of sarcopenia when defined according to the EWGSOP definition, which appeared attributable to the differences in criteria for low muscle mass between these definitions.⁽²³⁾ More individuals will potentially be diagnosed as sarcopenic using the EWGSOP than FNIH definition given that the low hand-grip criteria (<30 versus <26 kg) are less conservative, and also because individuals without low hand-grip strength may still be considered sarcopenic under the EWGSOP definition if gait speed is low.^(11,12) However, given that the IRR for 2-year falls in FNIH-defined sarcopenic obese men was approximately 1.0, it is unlikely that larger sample sizes would reveal a significant association.

Rather, we believe the lack of association is likely explained by the fact that gait speed assessment is not included in the FNIH definition. Poor gait performance and lower-limb function are consistent independent predictors of incident falls over several years in older adults.^(24–27) Indeed, in the present study, multivariable negative binomial regression revealed baseline gait speed was the only independent predictor of incident falls amongst all sarcopenic obesity components, with higher gait speed predicting reduced incidence of falls. The finding that higher gait speed but not hand-grip strength was associated with reduced falls is consistent with lower-limb muscle function being more relevant for falls than upper-limb strength; however, higher gait speed may also reflect better function in other physiological dimensions (eg, cognition) important for preventing falls.⁽²⁸⁾

To the best of our knowledge, this is the first study to prospectively investigate the effects of sarcopenic obesity on incident falls. A greater than 60% increased incidence of 2-year falls was observed in sarcopenic obese men according to the EWGSOP definition, and the population attributable risk fraction for 2-year falls was 9.4%, indicating that almost 1 in 10 older men could

avoid 2-year falls if sarcopenic obesity was prevented. A previous study of 183 older adults living in New Zealand revealed that self-reported number of falls in the previous 12 months was higher (although not significantly) in those with sarcopenic obesity, but sarcopenia was defined by low muscle mass alone.⁽²⁹⁾ However, a recent study of 680 older adults attending an Australian falls and fracture clinic, which also defined sarcopenia based on low muscle mass only, demonstrated significantly higher mean number of self-reported falls over the past 6 months in sarcopenic obese (4.4) compared with non-sarcopenic non-obese (3.2) and non-sarcopenic obese (2.8).⁽⁶⁾ In TASSOAC, which included almost 700 community-dwelling older adults, those with sarcopenic obesity (when sarcopenia was defined by lower-limb muscle strength but not when defined by ALM) had significant increases in fall risk over 5 years, estimated by a validated physiological profile assessment.⁽⁷⁾ These data indicate that the effects of sarcopenic obesity on fall risk are likely to be influenced by the definitions applied.

Our study has some limitations. The conclusions may be limited to relatively healthy community-dwelling older men because we did not include institutionalized older men, those included in the analysis were younger and demonstrated better health compared with excluded participants at baseline, and there was substantial loss to follow-up with greater loss of sarcopenic obese and sarcopenic non-obese men, which may have contributed to a lack of sufficient statistical power to detect increased fall and fracture rates in these groups.

Nevertheless, sensitivity analyses using multiple imputation in the entire baseline cohort revealed similar associations between sarcopenic obesity and incident fracture as those observed for analyses in included participants. Differences may exist between older men and women for associations of sarcopenic obesity and fracture risk⁽⁸⁾ and so prospective studies of older women

are required. Circumstances leading to falls and fractures were not ascertained, and the lack of a fall definition as well as four-monthly retrospective ascertainment may have resulted in misclassification and recall errors. However, fall recall appears to be acceptable up to 12 months in older adults using simple fall ascertainment questions.⁽³⁰⁾ Furthermore, although DXA is an accepted technique for assessing body composition and BMD, its assumptions may influence interpretation of results,⁽³¹⁾ so future studies using imaging techniques such as magnetic resonance imaging and computed tomography may shed further light on the effects of sarcopenic obesity on fracture risk in older adults. The strengths of this study include its large sample size, measurements of sarcopenia consistent with current recommended operational definitions, and long-term follow-up for fractures with radiographic confirmation.

In conclusion, in community-dwelling older men, EWGSOP-defined sarcopenic obesity is associated with increased fall rates over 2 years, and FNIH-defined sarcopenic obese men have increased fracture risk over 6 years compared with non-sarcopenic obese men.

Disclosures

All authors state that they have no conflicts of interest.

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Authors' roles: DS and VH completed data analysis and interpretation and drafted the manuscript. MS, RC, VS, FB, DGLC, DJH, and LMW contributed to study conception and design and revised the manuscript. DS accepts responsibility for the integrity of the data analysis.

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Table 1. Baseline Characteristics According to Sarcopenic Obesity Status Using the EWGSOP Definition of Sarcopenia

	Non-sarcopenic non-obese <i>n</i> = 718	Non-sarcopenic obese <i>n</i> = 531	Sarcopenic non-obese <i>n</i> = 137	Sarcopenic obese <i>n</i> = 100
Age (years)	75.8 ± 4.8 ^{c,d}	75.9 ± 4.7 ^{c,d}	80.7 ± 6.1 ^{a,b}	80.3 ± 6.5 ^{a,b}
Lives alone (%)	16.0	17.6	22.6	25.5
Pension (%)	38.9 ^{b,c}	46.5 ^a	58.4 ^a	44.9
Current smoker (%)*	6.3	4.2	13.2 ^{a,b,d}	3.1
No. of comorbidities	2.2 ± 1.6 ^{b,c,d}	2.6 ± 1.7 ^a	2.7 ± 1.7 ^a	3.1 ± 1.9 ^a
Chronic pain (%)*	22.3 ^b	32.1 ^a	26.5	29.3
ADL disability (%)*	3.1 ^{c,d}	4.3 ^d	8.8 ^a	15.0 ^{a,b}
Self-rated health excellent/good (%)*	78.8 ^{b,c}	67.1 ^a	61.3 ^a	69.1
Psychotropic medication (%)*	9.7 ^c	11.5	19.3 ^a	15.3
Bisphosphonate medication (%)*	4.2	2.4	5.8	4.0
Corticosteroid medication (%)*	6.3 ^c	9.2 ^c	19.0 ^{a,b}	13.0
25OHD (nmol/L)	58.7 ± 23.2 ^b	54.2 ± 20.1 ^a	59.4 ± 23.8	54.6 ± 22.2
Hemoglobin (g/L)	14.4 ± 1.3 ^{c,d}	14.5 ± 1.3 ^{c,d}	13.8 ± 1.6 ^{a,b}	13.8 ± 1.4 ^{a,b}
Albumin (g/L)	44.1 ± 2.6 ^c	44.1 ± 2.6 ^c	43.4 ± 3.0 ^{a,b}	43.5 ± 3.0
PASE score	140.3 ± 57.1 ^{b,c,d}	127.4 ± 61.7 ^{a,c,d}	99.6 ± 59.4 ^{a,b}	88.5 ± 54.9 ^{a,b}
BMI (kg/m ²)	26.4 ± 2.8 ^{b,c}	30.9 ± 3.3 ^{a,c,d}	23.3 ± 2.5 ^{a,b,d}	27.2 ± 2.4 ^{b,c}
Chair rise time (s)	15.7 ± 5.4 ^{b,c,d}	16.6 ± 6.1 ^{a,d}	17.7 ± 5.3 ^{a,d}	20.8 ± 6.6 ^{a,b,c}
Total hip BMD (g/cm ²)	0.94 ± 0.13 ^{b,c,d}	0.97 ± 0.13 ^{a,c,d}	0.85 ± 0.14 ^{a,b}	0.90 ± 0.14 ^{a,b}

EWGSOP = European Working Group on Sarcopenia; ADL = activities of daily living; PASE = Physical Activity Scale for the Elderly; BMI = body mass index.

Values are ± standard deviation; all tests are one-way ANOVA except * (chi-square tests).

^aSignificant difference to non-sarcopenic non-obese.

^bSignificant difference to non-sarcopenic obese.

^cSignificant difference to sarcopenic non-obese.

^dSignificant difference to sarcopenic obese (Bonferroni post hoc tests).

Table 2. Baseline and Follow-up Means ($\pm$ Standard Deviation) for Components of Sarcopenic Obesity According to the EWGSOP Definition

	Non-sarcopenic non-obese	Non-sarcopenic obese	Sarcopenic non-obese	Sarcopenic obese
ALM (kg)				
Baseline	22.5 $\pm$ 2.8 ^{b,c,d} (n = 718)	23.0 $\pm$ 2.9 ^{a,c,d} (n = 531)	18.6 $\pm$ 2.1 ^{a,b} (n = 137)	18.9 $\pm$ 2.1 ^{a,b} (n = 100)
Year 2	22.3 $\pm$ 2.8* (n = 608)	22.7 $\pm$ 2.8* (n = 451)	18.2 $\pm$ 2.4* (n = 97)	19.2 $\pm$ 2.6 (n = 71)
Year 5	21.7 $\pm$ 2.8* (n = 453)	22.3 $\pm$ 2.8* (n = 307)	18.0 $\pm$ 2.2* (n = 48)	18.2 $\pm$ 2.3* (n = 40)
Hand-grip strength (kg)				
Baseline	36.4 $\pm$ 6.8 ^{c,d} (n = 718)	35.7 $\pm$ 6.4 ^{c,d} (n = 531)	27.2 $\pm$ 6.0 ^{a,b} (n = 137)	27.3 $\pm$ 6.9 ^{a,b} (n = 100)
Year 2	36.9 $\pm$ 7.5 (n = 587)	35.1 $\pm$ 7.2 (n = 432)	27.3 $\pm$ 6.2 (n = 90)	28.6 $\pm$ 7.0 (n = 68)
Year 5	34.4 $\pm$ 7.9* (n = 456)	32.8 $\pm$ 7.9* (n = 313)	26.1 $\pm$ 6.8* (n = 53)	25.4 $\pm$ 6.2* (n = 42)
Gait speed (m/s)				
Baseline	0.95 $\pm$ 0.19 ^{b,c,d} (n = 718)	0.90 $\pm$ 0.19 ^{a,c,d} (n = 531)	0.76 $\pm$ 0.17 ^{a,b} (n = 137)	0.71 $\pm$ 0.19 ^{a,b} (n = 100)
Year 2	0.99 $\pm$ 0.22* (n = 587)	0.93 $\pm$ 0.21 (n = 425)	0.84 $\pm$ 0.23 (n = 83)	0.80 $\pm$ 0.20 (n = 64)
Year 5	0.93 $\pm$ 0.22* (n = 456)	0.86 $\pm$ 0.22* (n = 313)	0.82 $\pm$ 0.22 (n = 52)	0.72 $\pm$ 0.20 (n = 39)
Body fat (%)				
Baseline	24.6 $\pm$ 3.6 ^{b,d} (n = 718)	33.1 $\pm$ 3.0 ^{a,c} (n = 531)	23.8 $\pm$ 4.4 ^{b,d} (n = 137)	33.7 $\pm$ 3.5 ^{a,c} (n = 100)
Year 2	25.1 $\pm$ 4.2* (n = 608)	33.1 $\pm$ 3.3 (n = 451)	24.5 $\pm$ 5.2 (n = 97)	33.4 $\pm$ 3.6 (n = 71)
Year 5	25.9 $\pm$ 4.5 ^{f,g*} (n = 453)	33.4 $\pm$ 3.9 ^e (n = 307)	24.7 $\pm$ 5.5 (n = 48)	32.9 $\pm$ 5.5 ^e (n = 40)

EWGSOP = European Working Group on Sarcopenia.

*Significantly different from baseline (paired *t* tests).

^aSignificant difference to non-sarcopenic non-obese at baseline.

^bSignificant difference to non-sarcopenic obese at baseline.

^cSignificant difference to sarcopenic non-obese at baseline.

^dSignificant difference to sarcopenic obese at baseline.

^eSignificant difference in change over 5 years to non-sarcopenic non-obese.

^fSignificant difference in change over 5 years to non-sarcopenic obese.

^gSignificant difference in change over 5 years to sarcopenic obese (Bonferroni post hoc tests).

Table 3. Associations Between Changes in Sarcopenic Obesity Status and Change in Total Hip BMD Over 5 Years

Total hip BMD (mg/cm ²)

	Unadjusted β coefficient (95% CI)	Adjusted ^a β coefficient (95% CI)
EWGSOP definition		
Non-sarcopenic non-obese	Ref.	Ref.
Non-sarcopenic obese	32.42 (17.68, 47.16)	37.63 (23.03, 52.23)
Sarcopenic non-obese	-88.83 (-113.06, -64.61)	-65.83 (-90.35, -41.32)
Sarcopenic obese	-41.95 (-69.34, -14.57)	-23.75 (-51.29, 3.79)
FNIH definition		
Non-sarcopenic non-obese	Ref.	Ref.
Non-sarcopenic obese	37.19 (22.88, 51.51)	40.33 (26.22, 54.44)
Sarcopenic non-obese	-62.94 (-98.87, -27.01)	-36.25 (-71.93, -0.59)
Sarcopenic obese	-33.58 (-68.1, -0.95)	-12.85 (-47.79, 22.09)
Sarcopenic obesity components		
ALM (kg)	11.5 (10.2, 12.8)	10.5 (9.14, 11.7)
Body fat (%)	2.60 (2.00, 3.21)	2.69 (2.13, 3.27)
Gait speed (0.1 m/s)	2.55 (1.58, 3.51)	1.93 (1.03, 2.83)
Grip strength (kg)	1.38 (1.02, 1.74)	1.07 (0.73, 1.41)

BMD = bone mineral density; EWGSOP = European Working Group on Sarcopenia; FNIH = Foundation for the National Institutes of Health;

ALM = activities of daily living.

^aAdjusted for age, income, smoking status, physical activity, number of comorbidities, and corticosteroid use.

Values are per 1 unit increase in sarcopenic obesity status/component. Bold values are significant. **Table 4.** Fall Rates and Incidence Rate Ratios (95% CI) for Falls 2 Years After Baseline, According to Sarcopenic Obesity Categories

	EWGSOP definition			
	Non-sarcopenic, non-obese (n = 718)	Non-sarcopenic obese (n = 531)	Sarcopenic non-obese (n = 137)	Sarcopenic obese (n = 100)
Mean ± SD falls	0.4 ± 0.7	0.5 ± 0.9	0.8 ± 1.2	0.9 ± 1.3
Unadjusted	Ref.	1.33 (1.08, 1.64)	2.28 (1.70, 3.04)	2.43 (1.76, 3.36)
Adjusted ^a	Ref.	1.30 (1.04, 1.62)	1.58 (1.14, 2.17)	1.66 (1.16, 2.37)
	FNIH definition			

	Non-sarcopenic, non-obese (n = 797)	Non-sarcopenic obese (n = 570)	Sarcopenic non-obese (n = 58)	Sarcopenic obese (n = 61)
Mean $\pm$ SD falls	0.4 $\pm$ 0.7	0.5 $\pm$ 1.0	0.9 $\pm$ 1.4	0.6 $\pm$ 1.0
Unadjusted	Ref.	1.36 (1.12, 1.65)	2.48 (1.68, 3.67)	1.50 (0.97, 2.32)
Adjusted ^a	Ref.	1.34 (1.09, 1.66)	1.69 (1.10, 2.61)	1.05 (0.66, 1.69)

EWGSOP = European Working Group on Sarcopenia; FNIH = Foundation for the National Institutes of Health.

^aAdjusted for age, income, living alone, psychotropic medication use, smoking status, physical activity, 25OHD, and number of comorbidities.

Bold values indicate significant difference to non-sarcopenic non-obese group.

Table 5. Hazards Ratios (95% CI) for Any and Non-vertebral Incident Fractures, According to Sarcopenic Obesity Categories in 1486 Men With Complete Baseline Data

	EWGSOP definition			
	Non-sarcopenic, non-obese (n = 718)	Non-sarcopenic obese (n = 531)	Sarcopenic non-obese (n = 137)	Sarcopenic obese (n = 100)
Any fracture (%)	10.3	9.4	9.5	15.0
Unadjusted	Ref.	0.90 (0.63, 1.29)	1.13 (0.63, 2.05)	1.67 (0.96, 2.91)
Adjusted ^a	Ref.	0.75 (0.51, 1.10)	0.74 (0.39, 1.40)	1.14 (0.63, 2.06)
Non-vertebral fracture (%)	8.4	8.5	8.0	9.0
Unadjusted	Ref.	1.01 (0.68, 1.48)	1.17 (0.62, 2.23)	1.19 (0.59, 2.40)
Adjusted ^a	Ref.	0.89 (0.59, 1.35)	0.75 (0.37, 1.51)	0.81 (0.39, 1.70)
	FNIH definition			
	Non-sarcopenic, non-obese (n = 797)	Non-sarcopenic obese (n = 570)	Sarcopenic non-obese (n = 58)	Sarcopenic obese (n = 61)
Any fracture (%)	10.0	9.3	12.1	19.7
Unadjusted	Ref.	0.90 (0.64, 1.28) ^b	1.46 (0.67, 3.15)	2.38 (1.29, 4.36)
Adjusted ^a	Ref.	0.76 (0.52, 1.10) ^b	0.90 (0.38, 2.11)	1.72 (0.90, 3.27)
Non-vertebral fracture (%)	8.4	8.1	6.9	13.1
Unadjusted	Ref.	0.93 (0.64, 1.36)	0.95 (0.35, 2.61)	1.81 (0.87, 3.78)
Adjusted ^a	Ref.	0.83 (0.56, 1.24)	0.52 (0.16, 1.68)	1.29 (0.60, 2.81)

EWGSOP = European Working Group on Sarcopenia; FNIH = Foundation for the National Institutes of Health.

^aAdjusted for age, income, living alone, psychotropic medication use, smoking status, physical activity, 25OHD, and number of comorbidities.

Bold values indicate significant difference to non-sarcopenic non-obese group.

^bIndicates significant difference to sarcopenic obese group.

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Author/s:

Scott, D;Seibel, M;Cumming, R;Naganathan, V;Blyth, F;Le Couteur, DG;Handelsman, DJ;Waite, LM;Hirani, V

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