Associations of sarcopenia and its components with bone structure and incident falls in Swedish older adults

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Conflict of Interest

David Scott, Jonas Johansson, Lachlan B. McMillan, Peter R. Ebeling, Peter Nordstrom and Anna Nordstrom declare that they have no conflict of interest.

Abstract

Purpose: To compare bone structure parameters and likelihood of falls across European Working Group on Sarcopenia in Older People (EWGSOP2) sarcopenia categories.

Methods: 3,334 Swedish 70-year-olds had appendicular lean mass (normalised to height; ALMHt), lumbar spine and total hip areal BMD (aBMD) estimated by dual-energy X-ray absorptiometry. Volumetric BMD (vBMD) and structure at the distal and proximal tibia and radius were estimated by peripheral quantitative computed tomography. Hand grip strength and time up-and-go were assessed, and sarcopenia was defined according to EWGSOP2 criteria. Incident falls were self-reported 6 and 12 months after baseline.

Results: Only 0.8% and 1.0% of participants had probable and confirmed sarcopenia, respectively. Almost one-third of participants with confirmed sarcopenia reported incident falls, compared with 20% for probable sarcopenia and 14% without sarcopenia (P=0.025). Participants with confirmed sarcopenia had poorer bone parameters (all P<0.05) except endosteal circumference at the proximal radius and tibia, while those with probable sarcopenia had lower cortical area at the proximal radius (B=-5.9; 95% CI -11.7, -0.1 mm^2) and periosteal and endosteal circumferences at the proximal tibia (-3.3; -6.4, -0.3 and -3.8; -7.5, -0.05 mm^2, respectively), compared with those without sarcopenia. Compared with probable sarcopenia, confirmed sarcopenic participants had significantly lower lumbar spine and total hip aBMD, distal radius and tibia total vBMD, and proximal radius and tibia cortical vBMD, area and thickness (all P<0.05).

Conclusions: Swedish 70-year-olds with confirmed sarcopenia demonstrate poorer BMD and bone architecture than those with probable and no sarcopenia, and have increased likelihood of incident falls.

Keywords: sarcopenia, muscle, falls, bone, osteoporosis, older adults

Introduction

Ageing is associated with increased susceptibility for osteoporosis and osteoporotic fracture [1] and the age-related decline in skeletal muscle mass and muscle strength (sarcopenia) may contribute to bone loss [2]. The European Working Group on Sarcopenia in Older People (EWGSOP) recently revised its consensus definition of sarcopenia, categorising low muscle strength alone as “probable sarcopenia”, combined low muscle strength and low muscle mass as “confirmed sarcopenia”, and combined low muscle strength, low muscle mass and poor physical performance as “severe sarcopenia” [3]. The combination of low muscle mass and low hand grip strength is associated with approximately 80% increased likelihood of osteopenia or osteoporosis in US and Chinese adults [4], and fracture risk may also be increased in sarcopenic individuals due to increased likelihood of falls [5]. However, given the recency of the revised EWGSOP criteria, associations of sarcopenia with osteoporosis and falls risk are unclear.

Moreover, while osteoporosis is most commonly diagnosed as low areal bone mineral density (aBMD) assessed by dual-energy X-ray absorptiometry (DXA), it is clear that structural measures including volumetric bone mineral density (vBMD) and bone architecture, which can be measured by peripheral quantitative computed tomography (pQCT), make additional important contributions to fracture risk beyond aBMD [6]. There is currently a lack of evidence on the associations of sarcopenia and its components with bone structure. It is particularly important to determine precise relationships between sarcopenia and poor bone structure given that it has been proposed that the combination of the two (“osteosarcopenia”) may synergistically increase fracture risk in older adults [7, 8].

The primary aim of this analysis was to determine cross-sectional associations of sarcopenia and its components with bone structure (aBMD, vBMD and bone architecture) in community-dwelling Swedish older adults. The secondary aims were to describe the

prevalence of sarcopenia according to the updated EWGSOP criteria, and its associations with incidence of falls over 12-months.

Methods

Study design and participants

This was an analysis of the Healthy Ageing Initiative (HAI) cohort study; an ongoing observational study of 70-year-old adults in the Umeå municipality in northern Sweden. The objectives of HAI are to investigate traditional and potentially novel risk factors for cardiovascular disease and injurious falls and fractures in 70-year-old men and women. Two eligibility criteria were applied: 1) Residence in the Umeå municipal area and, 2) 70 years of age at the time of testing. Using contact information drawn from population registers, all eligible individuals were sent written information about the study. A subsequent phone call was made, where individuals either accepted or declined to participate. The HAI participation rate was 69.5%. The study was approved by the Umeå University Research Ethics Committee and complied with the World Medical Association's Declaration of Helsinki. All participants provided written informed consent. The current analysis included the first 3,334 participants with complete data for demographics, components of sarcopenia and bone structure.

Participants attended a hospital clinic near Umeå University for a baseline clinic appointment where they completed assessments detailed below and also had fasting blood tests from which plasma glucose was analysed. Height and weight were assessed by stadiometer (Holtain Limited, Crymych, Dyfed, UK) and scales (Avery Berkel HL 120, Taiwan), respectively, and body mass index (BMI; kg/m^2) was calculated. Participants also completed a questionnaire which assessed demographics, lifestyle and medical history. Six and 12 months after the baseline clinical appointment, participants were contacted by a research nurse to determine incident falls since the appointment [9]. Participants were asked: "During the past 6 months, have you experienced a fall at the same level?" This question was further clarified by explaining that qualifying falls were low energy, where the participant had unexpectedly come to rest on the ground by him/herself.

Bone parameters and body composition

aBMD (g/cm^2) was measured at the lumbar spine (L1–L4) and non-dominant total hip and femoral neck, and T-scores were estimated for lumbar spine and total hip, using a Lunar iDXA (GE Healthcare Lunar, Madison, WI, USA). Osteoporosis was defined as a T-score at the lumbar spine or total hip of ≤-2.5 SD [1]. Whole-body soft-tissue composition (total fat mass and appendicular lean mass; ALM) was assessed using the same machine. The machine was calibrated using a phantom each morning before measurements were obtained. Coefficients of variation (CVs) for in-vivo measurements of the iDXA are 0.4% for the lumbar spine and 1.4% for the femoral neck [10].

A peripheral quantitative computed tomography (pQCT) device (XCT-2000; Stratec Medizintechnik, Pforzheim, Germany) was used to measure total, cortical and trabecular vBMD (mg/cm^3) and area (mm^2), cortical thickness (mm), periosteal and endosteal circumferences (mm), and stress-strain index (SSI polar) of the non-dominant tibia and radius. Slice thickness was set at 2.0 mm, with a voxel size of 0.5 mm. Total and trabecular vBMD and area were measured at scan sites in the metaphysis located at 4% (distal site) of total tibial bone length in the distal–proximal direction, and cortical vBMD, area, thickness, periosteal and endosteal circumferences, and SSI polar were measured at diaphyseal scan sites located at 66% (proximal site) of total bone length in the same trajectory. Measurements were repeated in the event of motion artefacts. Reported CVs for the Stratec XCT-2000 pQCT device are 1.6% for trabecular density and 0.3% for cortical density, measured *in-vivo* [11].

Physical performance

Hand grip strength was assessed using an isokinetic hand dynamometer (Jamar; Patterson Medical, Warrenville, IL, USA). Research nurses instructed the participant to hold the hand dynamometer in their non-dominant hand, maintain a 90° angle in the elbow joint and to keep the elbow in close proximity to the waist. The research nurses further instructed the participant to, on command, start squeezing the hand dynamometer as forcefully as possible. The best of two attempts was subsequently recorded. The Timed Up-and-Go (TUG) test assessed physical performance; participants were asked to rise unaided from an armchair and walk forward 3 meters, then to turn around and return to a seated position in the chair. Research nurses provided instructions and measured TUG time using a stopwatch.

Definition of sarcopenia

In 2010, the EWGSOP initially defined pre-sarcopenia as low muscle mass, and sarcopenia as low muscle mass with the addition of low muscle strength and/or low physical performance [12]. Low muscle mass and strength criteria for EWGSOP1 were ALM adjusted for height squared (ALMHt) <7.26 kg/m^2 (men) or <5.50 kg/m^2 (men) and hand grip strength <30 kg (men) or <20 kg (women), respectively. [12]. While the TUG was recommended as an assessment of physical performance in EWGSOP1, no cut-point was provided for slow TUG time. The proposed conceptual stages of sarcopenia were pre-sarcopenia (low muscle mass alone), sarcopenia (low muscle mass with low muscle strength or poor physical performance) and severe sarcopenia (all of low muscle mass, low muscle strength and poor physical performance) [12].

In 2018, the EWGSOP published a revised definition and criteria for sarcopenia case-finding (EWGSOP2), which categorises probable sarcopenia as low muscle strength only, confirmed sarcopenia as low muscle strength and low muscle mass, and severe sarcopenia as low muscle strength and muscle mass and poor physical performance [3]. For EWGSOP2,

low muscle strength criteria include hand grip strength <27kg (men) or <16 kg (women), low muscle mass criteria include ALMHt <7.0 kg/m^2 (men) or <6.0 kg/m^2 (men) and low physical performance criteria include TUG time ≥ 20 s [3]. In the present study, sarcopenia status was defined according to the EWGSOP2 criteria and for comparison, according to EWGSOP1 criteria. Given EWGSOP1 did not provide a cut-point for slow TUG time, the EWGSOP2 criterion (≥20 s) was used for this component of sarcopenia.

Accelerometer-determined physical activity

Participants wore a triaxial accelerometer (GT3X+; Actigraph, Pensacola, FL, USA) for seven days following the clinic appointment as described previously [13]. Accelerometer data were collected at a frequency of 30 Hz and data were transformed into "counts" of movement with an activity threshold of 100 counts per min (CPM). Collected data were downloaded using ActiLife 6.11.2 software (Actigraph, Pensacola, FL, USA) in epoch lengths of 60 seconds with subsequent wear time validation performed. Periods ≥60 min characterized by <100cpm were marked as non-wear time, facilitating the exclusion of sleep time from further analyses. Sedentary time was classified as 1 to 99 CPM for periods >60min, while physical activity was classified as light (100 to1951 cpm), moderate (1952 to 5724 cpm), or vigorous (≥5725 cpm), as proposed by Freedson, et al. [14]. Due to low amounts of vigorous intensity activity, moderate and vigorous intensity physical activity (MVPA) were combined into a single variable [15]. Participants were instructed to wear the accelerometer on their non-dominant hip and to remove it only when showering, swimming or in bed at night. They were also instructed to be normally active in accordance with their current lifestyle, to obtain representative accelerometer measurements. Participants who did not provide at least 4 days of at least 10 hours per day of valid measurements had accelerometer data excluded [16].

Statistical Analyses

All statistical analyses were performed using SPSS Version 25 (IBM Corp, Armonk, NY, USA). Descriptive data were presented as mean ± SD for continuous variables or frequencies for categorical variables. We initially generated frequency tables to compare proportions of participants who met EWGSOP2 and EWGSOP 1 criteria for sarcopenia and its components. We compared differences in participant characteristics according to EWGSOP2 sarcopenia status using one-way ANOVA (continuous variables) and Chi-square tests (categorical variables) with Bonferroni post-hoc tests and column proportion Z-tests, respectively, to determine between group differences. A Chi-square test was also used to determine the proportion of participants who reported falls over the 12-month follow-up period according to EWGSOP2 sarcopenia categories. Receiver operating characteristic (ROC) curves were obtained for each component of sarcopenia (ALMHt, hand grip strength and TUG) to determine their ability to classify osteoporosis. In the SPSS ROC curve procedure, smaller values for sarcopenia components were considered more indicative of a positive test for osteoporosis. Generalised linear models were used to compare differences in bone health parameters across EWGSOP2 and EWGSOP1 sarcopenia categories. Non-standardised regression coefficients were obtained. Due to low numbers of sarcopenic participants according to EWGSOP2 criteria, these analyses were minimally adjusted for sex and daily percentage of MVPA. The no sarcopenia group was set as the referent group in the primary analyses. Post-hoc analyses with the confirmed sarcopenia group set as referent were performed in order to allow comparisons of bone parameters between probable and confirmed sarcopenic participants (EWGSOP2), and with the sarcopenia group set as referent to allow comparisons between pre-sarcopenia and sarcopenia (EWGSOP1).

Multivariable linear regression models also explored associations of components of sarcopenia (continuous variables) with bone parameters. These analyses were adjusted for sex, fasting glucose, percentage MVPA, and smoking status, as well as for other components of sarcopenia. Collinearity diagnostics including variance inflation factors and tolerance values were checked to ensure these models were not influenced by collinearity. Standardised beta coefficients were presented for this analysis. For all analyses, P-values <0.05 or 95% confidence intervals (95% CI) not including the null point were considered statistically significant.

Results

Figure 1 describes sarcopenia classifications of 3,334 HAI participants (50.6% women) according to EWGSOP2 criteria. Only 34 (1.0%) participants had confirmed sarcopenia and 27 (0.8%) had probable sarcopenia. No participant in this cohort had severe sarcopenia, while 3,273 (98.2%) met criteria for no sarcopenia. Similarly, according to EWGSOP1 criteria, 14.4% of participants had pre-sarcopenia and 2.1% had sarcopenia, but no participant had severe sarcopenia, Comparing EWGSOP1 and EWGSOP2 individual criteria, the more conservative EWGSOP2 criteria resulted in decreases of 41%, 54% and 72% in the prevalence of low ALMHt in men, low hand grip strength men, and low hand grip strength in women, respectively, compared with EWGSOP1. Conversely, the less conservative criteria for low ALMHt in women resulted in an increase in the prevalence of low ALMHt of 93% compared with EWGSOP1.

Table 1 presents baseline participant characteristics according to EWGSOP2 sarcopenia categories. There were no differences in sex proportions across sarcopenia categories, but participants with confirmed sarcopenia were more likely to be current smokers and had lower MVPA compared to those without sarcopenia. BMI, ALM and ALMHt were all significantly lower in those with confirmed sarcopenia compared to those with probable and no sarcopenia. As expected, hand grip strength was significantly lower in confirmed and probable sarcopenia compared to no sarcopenia, but TUG time was significantly slower for probable sarcopenia compared with confirmed sarcopenia. Total hip and lumbar spine aBMD were significantly lower for confirmed sarcopenia, and prevalence of osteoporosis was significantly higher, compared to probable and no sarcopenia. In the 12 months following baseline, a total of 2,554 participants provided responses to falls questions at six-month intervals, and of these, 354 (14%) reported at least one fall. According to EWGSOP2 sarcopenia categories, 13.8% of participants without sarcopenia reported at least one fall,

while 20.0% and 32.0% of participants with probable and confirmed sarcopenia had falls. A Chi-square test revealed a significant difference in the incidence of falls across these categories (P=0.025).

Table 2 reports regression coefficients from multivariable generalised linear models (adjusted for sex and MVPA) indicating the differences in bone parameters, assessed by DXA at the hip and lumbar spine, and by pQCT at the proximal and distal tibia and radius, according to EWGSOP2 sarcopenia categories. Participants with confirmed sarcopenia demonstrated significantly lower values than those with no sarcopenia for all bone parameters except endosteal circumference at the proximal radius and tibia. Furthermore, compared with participants with probable sarcopenia, those with confirmed sarcopenia had significantly lower lumbar spine and total hip aBMD and T-scores, distal radius total and trabecular vBMD, proximal radius cortical vBMD, area, thickness and SSI, distal tibia total vBMD and trabecular area, and proximal tibia total and cortical vBMD, cortical area and thickness, and periosteal circumference. There were generally no significant differences in bone parameters between participants with no sarcopenia and probable sarcopenia, although those with probable sarcopenia had lower proximal radius cortical area, and proximal tibia periosteal and endosteal circumference. The same analyses were performed for EWGSOP1 criteria to compare bone parameters amongst participants without sarcopenia, and those with pre-sarcopenia and sarcopenia. These analyses are presented in the supplementary table. Generally, these results indicated that participants with pre-sarcopenia or sarcopenia both had poorer bone health than those without sarcopenia. Furthermore, similar bone parameters were significantly poorer for pre-sarcopenia and sarcopenia, with the only exception being proximal radius cortical vBMD which was significantly lower for the sarcopenia group but not the pre-sarcopenia group, compared to those without sarcopenia. Nevertheless, compared with the pre-sarcopenia group, the sarcopenia group did demonstrate significantly lower

distal radius total and trabecular area and vBMD, proximal radius total and cortical area, cortical thickness, SSI and periosteal circumference, distal tibia total vBMD, and proximal tibia total area, cortical area and thickness, SSI and periosteal circumference.

We obtained ROC curves to compare the ability of components of sarcopenia to classify osteoporosis at baseline (Figure 2). The AUCs for both baseline ALMHt (AUC: 0.77; 95% CI 0.75, 0.80) and hand grip strength (0.71; 95% CI 0.68, 0.74) were significantly different from 0.5 (both P<0.001), whereas the AUC for TUG time (0.53; 0.49-0.56) was non-significant (P=0.097).

Table 3 reports standardised beta coefficients from multivariable linear regression models examining associations of components of sarcopenia (continuous variables) with bone parameters. These analyses were adjusted for sex, fasting plasma glucose, percentage MVPA, smoking status, and the other components of sarcopenia. Amongst DXA bone parameters, higher ALMHt was associated with significantly higher lumbar spine, total hip and femoral neck aBMD and T-scores, while hand grip strength was positively associated with femoral neck aBMD only.

At the distal radius, ALMHt and hand grip strength were positively associated with total and trabecular area, and total vBMD, and ALMHt was additionally positively associated with trabecular vBMD. At the proximal radius, ALMHt and hand grip strength were positively associated with total and cortical area, cortical thickness, SSI and periosteal and endosteal circumference in both models. However, hand grip strength had a positive association, while ALMHt had a negative association, with cortical vBMD. Slower TUG time was associated with lower total vBMD and cortical thickness, but with higher endosteal circumference.

At the distal tibia, ALMHt was positively associated with all bone parameters, whereas higher hand grip strength was associated with higher total and trabecular area, and

slower TUG time was associated with lower trabecular vBMD. At the proximal tibia, higher hand grip strength and ALMHt were associated with greater total and cortical area area, SSI and periosteal circumference. As observed for the radius, hand grip strength had a positive association, while ALMHt had a negative association, with cortical vBMD. ALMHt also had a positive association with cortical thickness, and hand grip strength had a positive association with endosteal circumference, at the proximal tibia. Slower TUG time was associated with greater total area, periosteal and endosteal circumference at the proximal tibia, but lower total and cortical VBMD, and lower cortical area and thickness.

Discussion

The primary findings of this analysis of a community-dwelling population of Swedish 70-year-olds were that participants with confirmed sarcopenia (low muscle strength and mass) according to the EWGSOP2 definition generally had poorer bone health than those with probable sarcopenia (low muscle strength only) and those without sarcopenia. Furthermore, individual components of sarcopenia demonstrated independent relationships with aBMD, vBMD and bone architecture. We also observed low prevalence of sarcopenia (and no participant with severe sarcopenia) according to updated EWGSOP2 guidelines. Nevertheless, confirmed sarcopenia was associated with significantly increased likelihood of 12-month incident falls.

Age-related declines in skeletal muscle may contribute to bone loss through reductions in biomechanical stimuli and growth factors [17], and studies have reported that both mass and strength are positively associated with bone structure in older adults [2, 18]. It follows that older adults with sarcopenia would have increased likelihood of osteoporosis, and some experts have proposed that the two conditions should be combined into the single condition of “osteosarcopenia” [7, 8]. In support, the Osteoporotic Fractures in Men (MrOS) study showed that hazard for fracture compared with healthy controls was substantially greater for men with both low aBMD and sarcopenia than those with only one condition [19]. Conversely, the Women’s Health Initiative and Concord Health and Ageing in Men Project have reported that participants with osteopenia have increased fracture risk regardless of sarcopenia status [20, 21]. Thus, the clinical utility of osteosarcopenia for fracture prediction remains unclear. However, the present findings indicate that simple functional assessments for sarcopenia such as hand grip strength and TUG may predict poor bone structure independently of the traditional risk factors for osteoporosis.

Comorbid sarcopenia and osteoporosis appears to be a common public health issue in older adult populations. Amongst almost 18,000 US and Chinese adults, sarcopenia, defined as low muscle mass and hand grip strength, was associated with 80% increased likelihood of osteopenia or osteoporosis [4] while in older Finnish women, sarcopenia (defined as the lowest quartiles of ALM and muscle strength and/or gait speed) was associated with almost 13-fold increased odds for osteoporosis [22]. In the present analysis of Swedish 70-year-olds, 47% of participants with confirmed sarcopenia had osteoporosis, compared with 8% for probable sarcopenia and 13% for participants without sarcopenia. The fact that osteoporosis is more prevalent in older adults with confirmed sarcopenia compared with probable sarcopenia suggests that muscle mass is a more important contributor to age-related bone loss than muscle function. Indeed, while ROC curves demonstrated that hand grip strength was significantly associated with osteoporosis, the AUC for grip strength was slightly lower than that observed for ALMHt, and TUG time did not classify osteoporosis. This is consistent with data from the Hertfordshire Cohort Study, which reported muscle cross-sectional area substantially attenuates associations of hand grip strength with pQCT-determined bone size and strength in 631 older adults, and inconsistent associations between gait speed and bone parameters [2]. It was also notable in the present study that pre-sarcopenia, defined used the EWGSOP1 criteria, was more consistently associated with poorer bone health than probable sarcopenia, defined according to EWGSOP2 criteria. The differences in these associations may be explained by the significantly lower muscle mass of pre-sarcopenic individuals given that pre-sarcopenia is defined as the presence of low lean mass alone [12], whereas probable sarcopenia is defined as the presence of low hand grip strength alone [3]. This supports the concept that muscle mass is more closely associated with bone health than muscle function.

Nevertheless, in multivariable analyses investigating associations of sarcopenia components with DXA- and pQCT-determined bone parameters, slower TUG time was

independently associated with lower proximal radius total vBMD and cortical thickness, distal tibia trabecular vBMD, and proximal tibia total and cortical vBMD, cortical area and thickness. In fact, amongst pQCT variables, slower TUG time appeared to be more consistently associated with poorer peripheral vBMD, whereas lower ALMHt and hand grip strength were most consistently associated with poorer peripheral structural variables such as bone area and SSI. It is unclear why there are divergent associations between components of sarcopenia and pQCT-determined bone parameters. It may be that development of lean mass and muscle strength are more closely associated with development of structural bone parameters which peak in early adulthood and only change incrementally thereafter [23], whereas physical performance assessments may be more reflective of current levels of physical activity which potentially influence BMD more than bone structure during older age. In support, a study which assessed self-reported bone-specific physical activity in women reported that physical activity was positively associated only with vBMD in middle-aged women, but with all bone geometry variables in young women, suggesting a greater effect of physical activity on BMD than bone structure in older age [24]. Nevertheless, the associations of TUG with vBMD in our study remained significant even after adjustment for MVPA, and so further investigations are required.

This study is one of the first we are aware of to report prevalence of sarcopenia according to EWGSOP2 criteria in community-dwelling older adults. Recently, Phu et al reported in a population of 228 Australian older adults that prevalence of severe sarcopenia was lowest when using TUG as opposed to other measures of physical performance [25], and so the use of TUG may partly explain the lack of severe sarcopenia cases in our cohort. Prevalence of severe sarcopenia (low hand grip strength, low ALMHt and slow TUG) according to EWGSOP2 criteria was 5% in the previous cohort, which differs from our own in that participants in that study had a history or risk of falls [25]. Similarly, in the

SarcoPhAge cohort, prevalence of sarcopenia was 13.6% according to EWGSOP1, but only 7.4% according to EWGSOP2 [26]. This reduction in prevalence is consistent with our own observation of substantial reductions in the prevalence of men classified as having low ALMHt, and both men and women classified as having low hand grip strength, as a result of the lower revised cut-points of EWGSOP2 compared with EWGSOP1 [3, 12]. The overall prevalence of confirmed sarcopenia was only 1%, suggests that the EWGSOP2 criteria are too conservative for sarcopenia case-finding in this population of community-dwelling Swedish 70-year-olds. This finding supports the need to validate sarcopenia definitions in population-specific settings and potentially to develop relevant local cut-points for low muscle mass and function [27].

Our findings suggest that sarcopenia may be an important independent risk factor for fracture in older adults, although prospective studies are required to determine whether the bone deficits identified in confirmed sarcopenic participants confer increased incident fracture rates. Nevertheless, these results support the need for increased attention to assessment of risk factors for fracture in confirmed sarcopenic older adults, and also interventions which simultaneously target improvements in bone health, muscle mass and function. Exercise interventions, particularly those involving concurrent weight-bearing impact and high-intensity progressive resistance training, appear most beneficial for reversing osteoporosis and sarcopenia in older adults. For example, high-intensity impact and progressive resistance training resulted in significant 8-month improvements in lumbar spine and femoral neck aBMD in postmenopausal women, and also improvements in a range of functional performance measures including muscle strength and TUG time (17). Improvements in these functional components are likely to reduce falls rates [28], and given that we observed a greater than two-fold higher likelihood of 12-month falls in confirmed

sarcopenic participants, may therefore contribute to fracture prevention through both reductions in falls risk and improvements in bone health.

Our findings should be considered in the context of the study's limitations. The primary analysis of bone health outcomes was cross-sectional and so causality cannot be conferred. In particular, longitudinal studies are required to determine the effects of probable, confirmed and severe sarcopenia on long-term changes in BMD and bone structure. While falls were prospectively assessed, the relatively low incidence is likely attributable to the definition used; low-energy falls resulting in coming to rest at ground level, rather than ground or other lower level as commonly defined in other studies [29]. Furthermore, given falls were self-reported only at six-month intervals following baseline, it is possible that low prevalence was influenced by recall bias. Finally, this is a population of relatively healthy older adults, as evidenced by low prevalence of sarcopenia and falls, and so the observed associations are not necessarily generalisable to other populations. The low prevalence of probable and confirmed sarcopenia also limited our ability to adjust for multiple covariates in generalised linear models, and so we cannot exclude the possibility of residual confounding.

In conclusion, while prevalence is low, Swedish 70-year-olds with confirmed sarcopenia according to the EWGSOP2 definition generally demonstrate poorer BMD and bone structure, and higher incidence of falls, than those with probable sarcopenia and without sarcopenia. Interventions which can increase muscle mass, function and bone health should be targeted at older adults with confirmed sarcopenia.

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Table 1. Participant characteristics at baseline according to EWGSOP2 sarcopenia status.

	No sarcopenia (N=3273)	Probable sarcopenia (N=27)	Confirmed Sarcopenia (N=34)	P-value for trend
Age (years)	70.0±0.1	70.0±0.2	70.0±0.0	0.251
Women (%)*	50.1	59.3	55.9	0.546
Current smoker (%)*	5.8[c]	7.4	23.5[a]	**<0.001**
Diabetes (%)*	8.1	11.1	9.1	0.836
Fasting plasma glucose (mmol/L)	5.66±1.15	5.45±0.66	5.67±1.38	0.649
MVPA (%)	4.04±3.04[c]	3.27±2.99	2.21±2.59[a]	**0.001**
BMI (kg/m^2)	26.4±4.1[c]	28.0±4.9[c]	23.4±3.2[a,b]	**<0.001**
Total fat mass (kg)	27.4±8.8	29.8±11.2[c]	23.8±7.2[b]	**0.023**
ALM (kg)	21.0±4.7[c]	20.1±3.6[c]	15.7±2.8[a,b]	**<0.001**
ALMHt (kg/m^2)	7.18±1.11[c]	7.29±0.70[c]	5.66±0.66[a,b]	**<0.001**
Hand grip strength (kg)	34.7±10.6[b,c]	16.4±5.3[a]	16.6±6.2[a]	**<0.001**
Timed up-and-go (s)	9.89±2.32[b]	12.39±4.82[a,c]	10.72±2.50[b]	**<0.001**
Left total hip aBMD (g/cm^2)	0.95±0.15[c]	0.94±0.13[c]	0.83±0.13[a,b]	**<0.001**

Lumbar spine aBMD (g/cm^2)	1.15±0.21[c]	1.15±0.21[c]	1.01±0.22[a,b]	**0.001**
Osteoporosis (%)	12.8[c]	8.0[c]	46.9[a,b]	**<0.001**

*Note: Bold values are significant. ± standard deviation; all tests are one-way ANOVA, except * (z-tests). [a]denotes significantly different to no sarcopenia; [b]denotes significantly different to probable sarcopenia; [c]denotes significantly different to confirmed sarcopenia (Bonferroni post-hoc tests). Bold values are significant (P<0.05). Abbreviations: BMI; body mass index, ALM; appendicular lean mass, ALMHt; appendicular lean mass normalised to height, aBMD; areal bone mineral density, MVPA; moderate/vigorous physical activity.*

Table 2. Generalised linear models for associations between EWGSOP2 sarcopenia status and bone health parameters.

Outcome	No sarcopenia	Probable sarcopenia B (95% CI)	Confirmed sarcopenia B (95% CI)
DXA			
Lumbar spine			
L1-L4 aBMD (g/cm^2)	REF	0.007 (-0.064, 0.079)	**-0.139 (-0.203, -0.075)***
L1-L4 T-score	REF	0.079 (-0.499, 0.656)	**-1.096 (-1.612, -0.580)***
Left hip			
Femoral neck aBMD (g/cm^2)	REF	-0.014 (-0.062, 0.033)	**-0.080 (-0.127, -0.034)**
Total hip aBMD (g/cm^2)	REF	0.004 (-0.047, 0.055)	**-0.117 (-0.165, -0.068)***
Total hip T-score	REF	0.047 (-0.330, 0.425)	**-0.810 (-1.174, -0.446) ***
pQCT - Radius			
4% site			
Total area (mm^2)	REF	-25.78 (-51.64, 0.083)	**-30.25 (-52.49, -8.00)**
Total vBMD (mg/cm^3)	REF	-2.49 (-21.82, 16.85)	**-44.43 (-61.06, -27.80)***
Trabecular area (mm^2)	REF	-11.60 (-23.24, 0.038)	**-13.61 (-23.63, -3.60)**

Trabecular vBMD (mg/cm^3)	REF	-3.90 (-18.81, 11.02)	**-23.30 (-36.13, -10.47)***
66% site			
Total area (mm^2)	REF	-9.33 (-20.75, 2.09)	**-15.26 (-25.09, -5.43)**
Total vBMD (mg/cm^3)	REF	-12.09 (-51.65, 27.47)	**-57.84 (-91.87, -23.81)**
Cortical area (mm^2)	REF	**-5.91 (-11.70, -0.12)**	**-15.24 (-20.22, -10.26)***
Cortical vBMD (mg/cm^3)	REF	2.77 (-15.64, 21.17)	**-26.83 (-42.66, -11.00)***
Cortical thickness (mm)	REF	-0.10 (-0.26, 0.07)	**-0.36 (-0.50, -0.21)***
SSI Polar (mm^3)	REF	-26.72 (-60.10, 6.65)	**-74.01 (-102.72, -45.30)***
Periosteal circumference (mm)	REF	-1.18 (-2.73, 0.38)	**-2.12 (-3.46, -0.78)**
Endosteal circumference (mm)	REF	-0.56 (-2.51, 1.40)	0.12 (-1.57, 1.80)
pQCT – Tibia			
4% site			
Total area (mm^2)	REF	-68.16 (-143.12, 6.80)	**-73.75 (-139.57, -7.93)**
Total vBMD (mg/cm^3)	REF	-1.74 (-18.51, 15.04)	**-40.44 (-55.17, -25.72)***
Trabecular area (mm^2)	REF	-30.67 (-64.40, 3.07)	**-33.21 (-62.83, -3.59)***
Trabecular vBMD (mg/cm^3)	REF	-9.57 (-25.49, 6.36)	**-29.00 (-42.99, -15.02)**

66% site			
Total area (mm^2)	REF	-40.67 (-81.98, 0.64)	**-57.98 (-94.26, -21.71)**
Total vBMD (mg/cm^3)	REF	30.79 (-5.02, 66.60)	**-39.24 (-70.68, -7.79)***
Cortical area (mm^2)	REF	-4.91 (-24.18, 14.36)	**-52.29 (-69.22, -35.37)***
Cortical vBMD (mg/cm^3)	REF	10.77 (-4.38, 25.91)	**-16.58 (-29.88, -3.28)***
Cortical thickness (mm)	REF	-0.07 (-0.20, 0.34)	**-0.55 (-0.79, -0.31)***
SSI Polar (mm^3)	REF	-106.22 (-304.91, 92.47)	**-376.64 (-551.12, -202.17)***
Periosteal circumference (mm)	REF	**-3.33 (-6.37, -0.28)**	**-4.55 (-7.22, -1.87)***
Endosteal circumference (mm)	REF	**-3.76 (-7.48, -0.05)**	-1.13 (-4.39, 2.14)

*Note: Adjusted for sex and percentage MVPA. Bold text indicates significantly different to no sarcopenia (referent); * indicates significantly different to probable sarcopenia (P<0.05). Abbreviations: aBMD; areal bone mineral density, vBMD; volumetric bone mineral density; SSI; stress-strain index*

Table 3. Standardised beta-coefficients for associations between components of sarcopenia and bone structure parameters.

	Hand grip strength **β (P-value)**	**ALMHt** **β (P-value)**	**Timed up-and-go** **β (P-value)**
DXA			
Lumbar spine			
L1-L4 aBMD	0.049 (0.076)	**0.313 (<0.001)**	0.028 (0.067)
L1-L4 T-score	0.046 (0.106)	**0.325 (<0.001)**	0.029 (0.070)
Left hip			
Femoral neck aBMD	**0.082 (0.005)**	**0.253 (<0.001)**	0.014 (0.407)
Total hip aBMD	0.046 (0.095)	**0.357 (<0.001)**	-0.011 (0.471)
Total hip T-score	0.041 (0.173)	**0.394 (<0.001)**	-0.010 (0.564)
pQCT - Radius			
4% site			
Total area	**0.280 (<0.001)**	**0.136 (<0.001)**	0.008 (0.552)
Total vBMD	**0.095 (<0.001)**	**0.106 (<0.001)**	-0.028 (0.064)
Trabecular area	**0.280 (<0.001)**	**0.136 (<0.001)**	0.008 (0.551)

Trabecular vBMD	0.043 (0.128)	**0.090 (<0.001)**	-0.028 (0.077)
66% site			
Total area	**0.246 (<0.001)**	**0.195 (<0.001)**	0.026 (0.054)
Total vBMD	0.019 (0.543)	0.013 (0.597)	**-0.042 (0.016)**
Cortical area	**0.204 (<0.001)**	**0.171 (<0.001)**	-0.018 (0.082)
Cortical vBMD	**0.087 (0.006)**	**-0.066 (0.007)**	-0.034 (0.059)
Cortical thickness	**0.127 (<0.001)**	**0.115 (<0.001)**	**-0.039 (0.004)**
SSI Polar	**0.257 (<0.001)**	**0.153 (<0.001)**	-0.006 (0.639)
Periosteal circumference	**0.240 (<0.001)**	**0.200 (<0.001)**	0.020 (0.120)
Endosteal circumference	**0.165 (<0.001)**	**0.131 (<0.001)**	**0.049 (0.006)**
pQCT – Tibia			
4% site			
Total area	**0.276 (<0.001)**	**0.135 (<0.001)**	-0.015 (0.330)
Total vBMD	-0.053 (0.068)	**0.237 (<0.001)**	-0.031 (0.051)
Trabecular area	**0.276 (<0.001)**	**0.135 (<0.001)**	-0.015 (0.330)
Trabecular vBMD	-0.057 (0.074)	**0.216 (<0.001)**	**-0.039 (0.027)**

66% site			
Total area	**0.260 (<0.001)**	**0.178 (<0.001)**	**0.035 (0.015)**
Total vBMD	**-0.120 (<0.001)**	**0.132 (<0.001)**	**-0.088 (<0.001)**
Cortical area	**0.116 (<0.001)**	**0.253 (<0.001)**	**-0.043 (<0.001)**
Cortical vBMD	-0.001 (0.973)	-0.023 (0.369)	**-0.057 (0.002)**
Cortical thickness	-0.011 (0.700)	**0.223 (<0.001)**	**-0.075 (<0.001)**
SSI Polar	**0.211 (<0.001)**	**0.133 (<0.001)**	-0.003 (0.787)
Periosteal circumference	**0.247 (<0.001)**	**0.171 (<0.001)**	**0.033 (0.029)**
Endosteal circumference	**0.249 (<0.001)**	0.046 (0.075)	**0.073 (<0.001)**

Note: Adjusted for sex, fasting glucose, percentage MVPA, smoking status and other sarcopenia components. Bold values are significant (P<0.05). Abbreviations: ALMHt; appendicular lean mass normalised to height, TUG; timed up-and-go, aBMD; areal bone mineral density, vBMD; volumetric bone mineral density; SSI; stress-strain index.

Figure 1. Numbers of participants meeting EWGSOP2 criteria for sarcopenia categories and components.

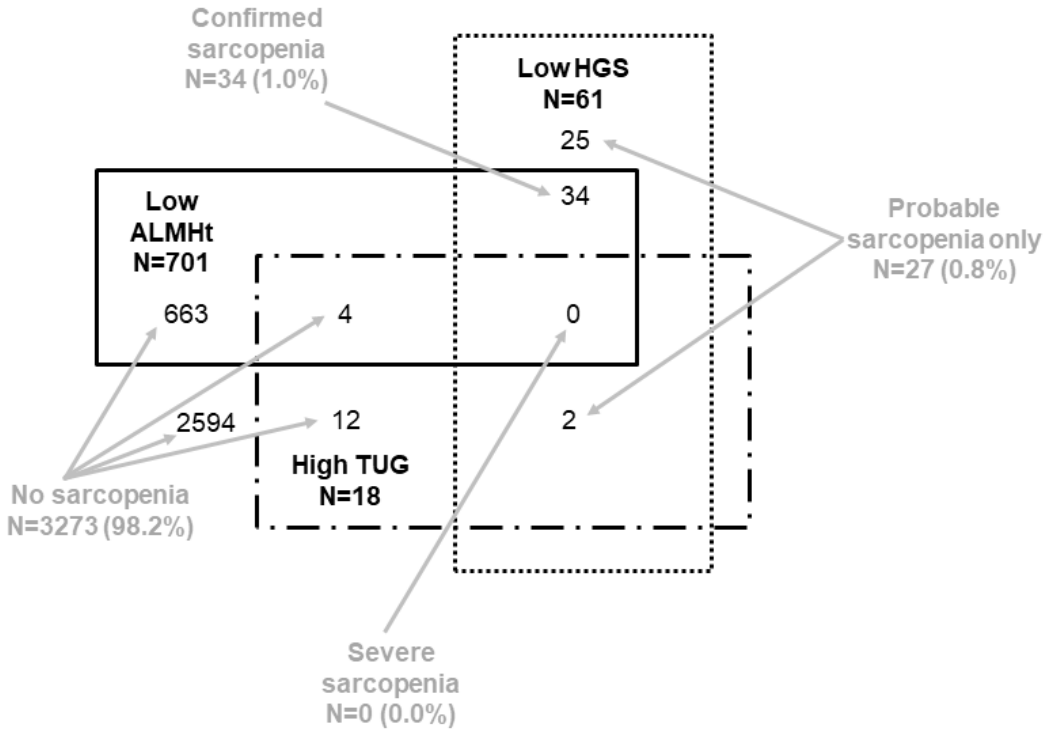

Figure 2. Receiver operator characteristic curves for classification of osteoporosis by individual sarcopenia components.