



Associations of body mass index, body fat percentage and sarcopenia components with bone health estimated by second-generation high-resolution peripheral quantitative computed tomography in older adults with obesity

Anoohya Gandham^{a,b,*}, Jakub Mesinovic^{a,c}, Mavil May Cervo^a, Costas Glavas^c, Paul Jansons^{a,c}, Carrie-Anne Ng^a, Juan Pena Rodriguez^a, Ayse Zengin^a, Maxine P. Bonham^d, Peter R. Ebeling^a, David Scott^{a,c}

^a Department of Medicine, School of Clinical Sciences at Monash Health, Monash University, Clayton, Victoria, Australia

^b Mary MacKillop Institute for Health Research, Australian Catholic University, Victoria, Australia

^c Institute for Physical Activity and Nutrition (IPAN), School of Exercise and Nutrition Sciences, Deakin University, Geelong, Australia

^d Department of Nutrition, Dietetics and Food, Monash University, Notting Hill, Victoria, Australia

ARTICLE INFO

Section Editor: Carel Meskers

Keywords:

Obesity
Bone
Muscle
Older adults

ABSTRACT

Purpose: To investigate associations between body mass index (BMI), body fat percentage, and components of sarcopenia (muscle mass and muscle strength/power), with bone microarchitecture measured by high-resolution peripheral computed tomography (HR-pQCT) in older adults with obesity.

Methods: Seventy-four adults aged ≥ 55 years with body fat percentage ≥ 30 % (men) or ≥ 40 % (women) were included. Fat mass, lean mass and total hip, femoral neck, and lumbar spine areal bone mineral density (aBMD) were measured by dual-energy X-ray absorptiometry. Appendicular lean mass (ALM) was calculated as the sum of lean mass in the upper- and lower-limbs. BMI was calculated and participants completed physical function assessments including stair climb power test. Distal tibial bone microarchitecture was assessed using HR-pQCT. Linear regression (β -coefficients and 95 % confidence intervals) analyses were performed with adjustment for confounders including age, sex, smoking status, vitamin D and self-reported moderate to vigorous physical activity.

Results: BMI and ALM/height² were both positively associated with total hip, femoral neck and lumbar spine aBMD and trabecular bone volume fraction after adjusting for confounders (all $p < 0.05$). Body fat percentage was not associated with aBMD or any trabecular bone parameters but was negatively associated with cortical area ($p < 0.05$). Stair climb power (indicating better performance) was positively associated with cortical area and negatively associated with bone failure load (both $p < 0.05$).

Conclusion: Higher BMI, ALM/height² and muscle power were associated with more favourable bone microarchitecture, but higher body fat percentage was negatively associated with cortical bone area. These findings suggest that high BMI may be protective for fractures and that this might be attributable to higher muscle mass and/or forces, while higher relative body fat is not associated with better bone health in older adults with obesity.

1. Introduction

Obesity and osteoporosis are major public health concerns among older adults, contributing to poor quality of life and increased morbidity and mortality (Papageorgiou et al., 2020; Watts et al., 2012). It has been

projected that by 2025, more than three-quarters of Australian adults will be overweight or have obesity (Foundation VHP, 2014). Likewise, it is estimated that by 2022, 25 % of Australians aged >50 years will have osteopenia or osteoporosis (Watts et al., 2012).

The relationship between obesity and bone health is controversial (J.

* Corresponding author at: Department of Medicine, School of Clinical Sciences at Monash Health, Monash University, Clayton, Victoria 3168, Australia.

E-mail address: anoohya.gandham@monash.edu (A. Gandham).

<https://doi.org/10.1016/j.exger.2023.112227>

Received 7 April 2022; Received in revised form 28 May 2023; Accepted 29 May 2023

Available online 13 June 2023

0531-5565/© 2023 Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

J. C., 2011; Gandham et al., 2020; Palermo et al., 2016). Higher body mass index (BMI) is protective against osteoporosis due to greater mechanical loading (Gandham et al., 2020; Hoxha et al., 2014) and hormonal factors including enhanced peripheral androgen aromatisation (Kley et al., 1980; Ronde and Jong, 2011; Aguirre et al., 2015). BMI however does not differentiate between fat and lean mass and may underestimate the prevalence of obesity among older adults (Gandham et al., 2020; Nuttall, 2015; Shepherd et al., 2017). Body fat percentage assessed from dual-energy X-ray absorptiometry (DXA) is a direct measure of adiposity and higher body fat percentage, in contrast to BMI, has been found to be associated with increased risk for incident fracture in older adults (Gandham et al., 2020; Shepherd et al., 2017). Although, many studies have reported positive associations between BMI and areal bone mineral density (aBMD) among older adults, very few have explored associations between BMI and cortical and trabecular bone microarchitecture in this population (Lloyd et al., 2014; Evans et al., 2015; Jiang et al., 2015).

It is necessary to understand the underlying mechanisms contributing to adverse musculoskeletal health outcomes among this population of older adults as despite having high aBMD their bone microarchitecture may be compromised. It is therefore important to evaluate associations of BMI and body fat percentage with bone health using advanced bone imaging modalities (Gandham et al., 2021).

Sarcopenia is defined as an age-associated loss of skeletal muscle mass and function and older adults with sarcopenia and obesity ('sarcopenic obesity') have an increased risk for falls and fractures compared with those with obesity alone and healthy controls (with neither sarcopenia or obesity) (Gandham et al., 2021; Kirk et al., 2021; Scott et al., 2019). However, to date most research exploring relationships between sarcopenia, obesity and bone health have focused on two-dimensional aBMD measurements, while little is known about the influence of sarcopenia components and adiposity on volumetric BMD (vBMD) and bone microarchitecture variables in older adults with obesity.

The aim of this cross-sectional study of older adults with obesity was to explore associations of BMI, body fat percentage, and components of sarcopenia (muscle mass, function and power) with bone health measured by DXA and bone microarchitecture variables measured by second-generation high-resolution peripheral computed tomography (HR-pQCT), respectively.

2. Methods

2.1. Study design and participants

This cross-sectional analysis utilised a convenience sample of older adults with obesity with baseline data from three randomised controlled exercise trials conducted at the Monash Health Translation Precinct in Melbourne, Australia (ACTRN12618001146280; ACTRN12616000563460; ACTRN12618000192280). Seventy-four community-dwelling older adults aged 55–83 years, residing in Melbourne, Australia, were recruited via flyers and online advertisements. Participants with body fat percentage (assessed by DXA) $\geq 30\%$ (men) or $\geq 40\%$ (women) were included in this study (Scott et al., 2015). Exclusion criteria included inability to walk 400 m unassisted (without the use of walking aids); inability to speak English, diagnosis of any progressive neurological disorders, severe knee or hip osteoarthritis (awaiting joint replacement), lung diseases requiring the use of oxygen, renal kidney disease requiring dialysis or any other disorder of severity that life expectancy was <12 months.

The studies were conducted according to the principles of the Declaration of Helsinki and were approved by the Monash Health Human Research Ethics Committee (Protocol ID: HREC/15/MonH/182; HREC/17/MonH/613; HREC/18/MonH/399) and all participants provided written informed consent.

2.2. Questionnaires

At baseline, participants completed self-administered questionnaires including questions on demographics, smoking status, and moderate to vigorous physical activity. Total number of days of moderate to vigorous physical activity was assessed using the International Physical Activity Questionnaire for the Elderly (IPAQ-E) (Hurtig-Wennlof et al., 2010; Craig et al., 2003).

2.3. Anthropometry

Weight (kg) was measured to the nearest 0.1 kg using an electronic scale (Seca 804 electronic scales, Seca, Hamburg, Germany) and height (m) was measured to the nearest 0.1 m using a stadiometer (Seca 213 wall-mounted stadiometer, Seca, Hamburg, Germany) with footwear and heavy items of clothing removed. BMI was calculated as weight (kg)/ height (m²). Waist and hip circumference were measured three times and the average of the three measurements was calculated to the nearest 0.1 cm using a measuring tape (Seca 203) and used to calculate waist/hip ratio. Waist circumference was measured at the level of the mid-point between the inferior margin of the last rib and the crest of the ilium in the mid-axillary plane. Hip circumference was measured at the level of the greatest posterior protuberance of the buttocks.

2.4. Blood biochemistry

Blood samples were collected following an overnight fast of ≥ 10 h. Serum samples were analysed for levels of 25-hydroxyvitamin D (25 (OH)D) (Han et al., 2014) using a DiaSorin Liaison (DiaSorin Inc., Stillwater, MN, USA) direct competitive chemiluminescent immunoassay with inter-assay and intra-assay coefficient of variation (%CV) of 10.7 % and 6.5 %, respectively.

2.5. Physical function

Hand grip strength was measured using a hydraulic dynamometer (Jamar Plus dynamometer, Patterson Medical, Bolingbrook, IL, USA). Participants gripped the dynamometer with maximal force in a seated position with their elbow at a 90° angle. Participants repeated this measurement three times in the dominant arm with a 30s rest between trials and the mean force of the second two trials was used to calculate average hand grip strength.

Participants completed the Short Physical Performance Battery (SPPB) test which consists of gait speed, chair stand and standing balance assessments and a composite score of 0–12 (higher score indicating better function) was given based on the performance in three assessments (Freiberger et al., 2012; Guralnik et al., 2000). For chair stand test, participants were instructed to stand up straight from a seated position five times as quickly as possible and the time taken (seconds) was recorded. Tests were aborted after 1 min, or if the participants utilised their arms and failed to come to a complete standing position. Balance assessments consisted of semi-tandem and full-tandem stand. For the semi-tandem position, participants were required to stand with the heel of one foot placed beside the big toe of the opposite foot and hold that position for 10 s. For the full-tandem position, participants were required to place their preferred foot in front of the other with the back of the heel of one foot touching the toes of the other foot. Participants who were unable to complete the semi-tandem stand for 10 s were required to stand with both feet side-by-side instead (Gandham et al., 2019). Gait speed was assessed over different walking course distances in the three studies. A correction factor was therefore applied to studies that measured gait speed over a 2.44 m distance to convert to 4 m gait speed using previously developed methodologies (Guralnik et al., 2000). As an additional functional measure of muscle power, participants also completed a 10-step stair climb power test (Bean et al., 2007). In a safe manner, participants were instructed to climb the stairs as fast as

possible (participants were allowed to use the handrail if required). This assessment was completed twice after a 1-minute recovery period after the first trial, and the average of the time taken was recorded using a stopwatch. The following formula was utilised to calculate stair climb power: force X velocity (Bean et al., 2007). Force was calculated as the product of participants body mass (kg) and acceleration due to gravity (9.8 m/s^2). Velocity was calculated as the vertical height of stairs (1.75 m) divided by stair climb power test time (s) (Bean et al., 2007).

2.6. Dual energy X-ray absorptiometry (DXA)

Whole-body DXA scans measured body composition parameters including body fat percentage and lean mass (Hologic Discovery A, Hologic, USA). Appendicular lean mass (ALM) was calculated as the sum of lean mass in the upper- and lower-limbs. All scans were performed in the morning with participants either fasted or having consumed a light snack. The DXA scanner was calibrated daily using the manufacturer's spine phantom. DXA scans also measured aBMD at the lumbar spine, femoral neck and non-dominant total hip. Osteopenia was defined as a T-score between -1 and -2.5 and osteoporosis as a T-score of ≤ -2.5 at the total hip (Kanis, 1994). Lumbar spine trabecular bone score (TBS) was determined using TBS iNight software version 3.0.2 (Medimaps, Switzerland). Individuals with $\text{BMI} \geq 37 \text{ kg/m}^2$ were excluded from the analysis using the TBS data (Bonaccorsi et al., 2020). %CV for scans repeated on 30 individuals in our laboratory was 0.90 % for aBMD at the whole-body and 0.96 % for whole-body total fat.

2.7. Sarcopenia definition

Sarcopenia was defined using both the Sarcopenia Definitions and Outcomes Consortium (SDOC) and revised European Working Group on Sarcopenia in Older People (EWGSOP2) definitions (Kirk et al., 2021; Cruz-Jentoft et al., 2019). SDOC is defined as low hand grip strength, with cut points of $<35.5 \text{ kg}$ for men and $<20 \text{ kg}$ for women, and low gait speed ($<0.8 \text{ m/s}$) (Kirk et al., 2021). EWGSOP2 is defined as low appendicular lean mass index ($<7 \text{ kg/m}^2$ for men and $<5.50 \text{ kg/m}^2$ for women) and low hand grip strength ($<27 \text{ kg}$ for men and $<16 \text{ kg}$ for women) or slow chair stands time ($>15 \text{ s}$ for five rises) (Cruz-Jentoft et al., 2019). Two definitions were utilised to compare differences in prevalence of sarcopenia in this group of older adults.

2.8. High-resolution peripheral quantitative computed tomography (HR-pQCT)

HR-pQCT scans were performed on the non-dominant distal tibia to estimate bone microarchitecture and strength (XtremeCT II, ScanCo, Switzerland) (Bouxsein et al., 2010; Cheung et al., 2013). A two-dimensional scout view scan was used to identify the region of interest (22.5 mm proximal to the reference line placement at the end plate of the tibia). Participant's leg was positioned into the scanner using the manufacturer-provided cast to prevent movement artifact. One hundred and sixty-eight parallel computed tomography slices were obtained over a 10.20 mm region of the distal tibia using an isotropic resolution of 61 μm .

HR-pQCT images were analysed according to the manufacturer evaluation protocol to measure cortical and trabecular bone variables using software version 6.1 (Nishiyama and Shane, 2013). Scans were graded according to a 5-point scale to account for any motion artifacts (1 = perfect, 5 = severe motion artifact) (Karasik et al., 2017). A semi-automated slice-by-slice contouring was also performed on all scans to extract the bone region from the surrounding soft tissue and manual corrections were applied where necessary (Whittier et al., 2020). Bone variables included: cross-sectional area (CSA) (mm^2), total volumetric BMD (vBMD; mg HA/cm^3), cortical area (mm^2), cortical vBMD (mg HA/cm^3), cortical porosity (%), cortical thickness (mm), trabecular area (mm^2), trabecular vBMD (mg HA/cm^3), trabecular thickness (mm),

trabecular separation (mm), trabecular bone volume fraction (BV/TV) (%) and trabecular number (1/mm) (Whittier et al., 2020). Additional analyses were performed using two computed variables: trabecular area/CSA and cortical area/CSA. Micro-finite element analysis was performed for bone strength estimates such as bone stiffness (N/mm) (total reaction force of the model divided by the applied displacement) and bone failure load (N) (an indirect estimate from linear finite element models using a yield criterion) (Bouxsein et al., 2010; Cheung et al., 2013; Whittier et al., 2020). %CV, estimated by repeated scans performed on 30 individuals in our laboratory, was 0.62 % for total vBMD, 1.10 % for cortical area, 0.71 % for cortical vBMD, 1.34 % for cortical thickness, 1.07 % for trabecular area, 0.59 % for trabecular vBMD, 0.97 % for trabecular thickness, 2.47 % for trabecular separation, 3.37 % for trabecular number, and 0.82 % for trabecular bone volume.

2.9. Statistical analysis

All data analyses were performed using SPSS Statistics 25 (IBM, NY, USA). Participant characteristics were reported as mean and standard deviations for continuous variables, or as percentages for categorical variables. Mean and standard deviations for all bone parameters determined by the DXA and HR-pQCT were presented for all participants (Supplementary Table 1).

Scatterplots and Pearson's correlation analyses were performed with no adjustment for confounders to evaluate relationships between BMI, body fat percentage, ALM/height^2 and HR-pQCT-determined bone parameters. Linear regression analysis was performed to evaluate the associations between components of obesity, sarcopenia, and physical function with DXA- and HR-pQCT-determined bone parameters. Adjustment for confounders included age, sex, smoking status, vitamin D and self-reported moderate to vigorous physical activity.

Mediation analysis was performed to evaluate whether muscle mass/forces mediated associations between BMI and bone microarchitecture (trabecular vBMD, trabecular BV/TV and trabecular number). Path X corresponds to the effect of BMI on (a) muscle mass (ALM/height^2) (b) muscle force (stair climb power test). Path Y corresponds to the effects of (a) muscle mass (ALM/height^2) (b) muscle force (stair climb power test) on bone microarchitecture. The total effect captured by direct (Z) and indirect (Z') effects with the mediator muscle mass/force. The percentage mediation was used to calculate the effect size using the formula: $P_M = XY/(XY + Z')$ (MacKinnon et al., 2002).

For all analyses, $p < 0.05$ or 95 % confidence intervals not including the null point was considered statistically significant.

3. Results

In total, 74 participants (62 % women) were included in this cross-sectional study with an age range of 55 to 83 years (Table 1). Twenty-eight (38 %) participants had a SPPB score of 12/12. Ten participants did not have TBS, total hip, femoral neck or lumbar spine aBMD data and were therefore excluded in analyses using those data. In addition, 16 participants had a $\text{BMI} \geq 37 \text{ kg/m}^2$ and were therefore excluded in analyses using the TBS data. Six participants had confirmed sarcopenia according to the EWGSOP2 definition (both low ALM and low hand grip strength). Three participants had slow chair stand time and no participants had both low ALM and low chair stand time according to the EWGSOP2 definition. However, only 3 (4 %) participants had sarcopenia defined by the SDOC definition (both low hand grip strength and low gait speed).

Fig. 1 presents correlations for ALM/height^2 , BMI and body fat percentage with tibial trabecular and cortical vBMD estimated by HR-pQCT. There was a positive correlation between ALM/height^2 and tibial trabecular vBMD ($p = 0.037$). However, after adjusting for confounders in linear regression analyses (Table 2), the associations between BMI and tibial trabecular vBMD were significant ($R^2 = 0.094$) nevertheless the associations between ALM/height^2 and tibial

Table 1
Descriptive characteristics.

	Mean ± SD or N (%)
Age (years)	67.7 ± 6.2
Women (%)	46 (62 %)
Weight (kg)	91.0 ± 14.9
Height (m)	1.7 ± 0.1
BMI (kg/m ²)	33.1 ± 4.1
Waist circumference (cm)	109.0 ± 15.2
Waist/hip ratio	0.94 ± 0.11
Current or previous smoker (%)	29 (40 %)
Whole-body aBMD (g/cm ³)	1.075 ± 0.111
Body composition	
ALM (kg)	20.4 ± 5.0
Body fat (%)	44.5 ± 5.7
Physical function	
Gait speed (m/s)	0.99 ± 0.23
SPPB score	10.8 ± 1.2
Sarcopenia (%)	
EWGSOP2 definition	
Low ALMI	8 (11 %)
Low HGS	11 (15 %)
Low ALMI + HGS	6 (8 %)
SDOC definition	
Low HGS	28 (38 %)
Low gait speed	13 (18 %)
Low HGS + gait speed	3 (4 %)

Abbreviations: BMI, body mass index; aBMD, areal bone mineral density; ALMI, appendicular lean mass index; SPPB, short physical performance battery; HGS, hand grip strength; EWGSOP2, European Working Group on Sarcopenia in Older People revised definition; SDOC, Sarcopenia Definitions and Outcomes Consortium.

trabecular vBMD were no longer significant ($R^2 = 0.104$). In addition, after adjusting for confounders, BMI and ALM/height² were both positively associated with total hip, lumbar spine and femoral neck aBMD and tibial trabecular bone volume fraction. Conversely, body fat percentage was negatively associated with tibial cortical area. Components of sarcopenia including muscle strength, function and power had varying associations with bone parameters. Stair climb power test was positively associated with total hip aBMD, cortical area and bone stiffness after adjusting for confounders and hand grip strength was positively associated with tibial cross-sectional area. However, gait speed and chair stand test times were not associated with any bone micro-architectural variables. In addition, SPPB was positively associated with tibial bone failure load, bone stiffness and cortical porosity. Additionally, no significant associations were found for any of the sarcopenia and obesity components with trabecular area/CSA after adjusting for confounders (all $p > 0.05$; data not shown). A sensitivity analysis exploring the associations of BMI with bone parameters after further adjustment for ALM/height² and stair climb power test resulted in all associations being non-significant (all $p > 0.05$; data not shown).

Mediation analysis (Figs. 2 and 3) investigated the relationships between BMI and trabecular bone microarchitecture with ALM/height² (Fig. 2) and stair climb power test (Fig. 3) as the mediator. After adjusting for age, the percentage mediation (P_M) effect between 49 % to 58 % suggested that stair climb power test was a strong mediator of the association between BMI and trabecular bone microarchitecture. However, ALM/height² did not mediate the effect of BMI on trabecular bone microarchitecture ($p > 0.05$).

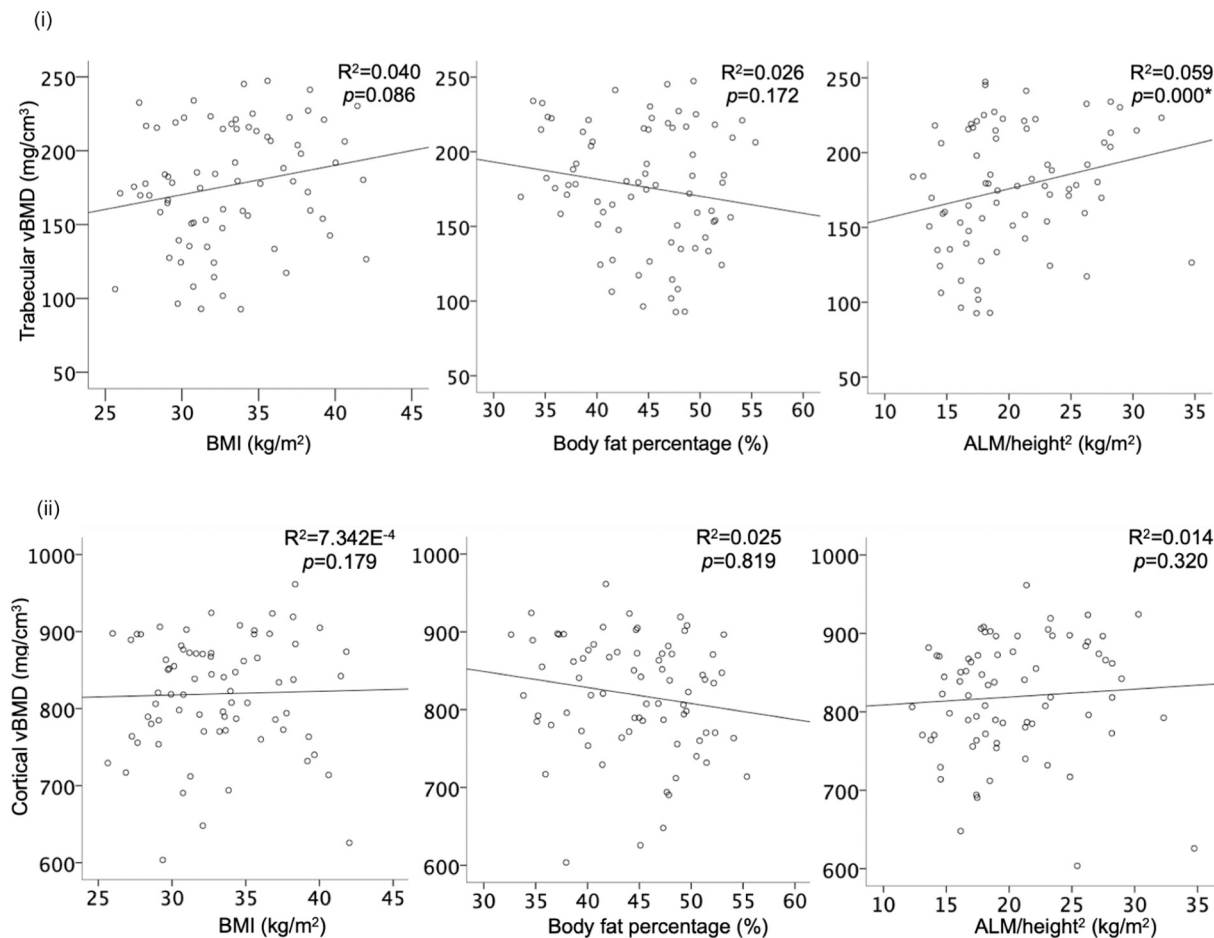


Fig. 1. Scatter plots showing the correlation between body mass index, body fat percentage, ALM/height² and HR-pQCT (i) trabecular and (ii) cortical vBMD at the distal tibia. Abbreviations: BMI, body mass index; ALM, appendicular lean mass; vBMD, volumetric bone mineral density; R^2 , coefficient of determination.

Table 2

Linear regression analysis showing associations between components of obesity and sarcopenia with DXA-determined areal bone mineral density and HR-pQCT bone parameters at the distal tibia.

	Waist circumference (cm)	BMI (kg/m ²)	Body fat percentage (%)	ALM/height ² (kg/m ²)	HGS (kg)	Gait speed (m/s)	Chair stand time (s)	SPPB	Stair climb power test (100W)
DXA bone parameters									
Total hip aBMD (g/cm²)									
Unadjusted	0.003* (0.000, 0.006)	0.016* (0.007, 0.025)	-0.009* (-0.016, -0.002)	0.072* (0.045, 0.099)	0.004* (0.001, 0.008)	-0.025 (-0.195, 0.146)	0.012 (-0.004, 0.028)	0.002 (-0.028, 0.033)	0.088* (0.055, 0.121)
R ²	0.124	0.160	0.158	0.376	0.030	0.000	0.044	0.000	0.260
Adjusted	0.002 (0.000, 0.005)	0.012* (0.004, 0.020)	-0.005 (-0.013, 0.004)	0.071* (0.040, 0.102)	-0.001 (-0.005, 0.004)	-0.019 (-0.169, 0.131)	0.010 (-0.004, 0.024)	-0.004 (-0.033, 0.025)	0.058* (0.015, 0.101)
R ²	0.400	0.415	0.346	0.492	0.364	0.331	0.364	0.324	0.396
Femoral neck aBMD (g/cm²)									
Unadjusted	0.002 (0.000, 0.004)	0.014* (0.007, 0.022)	-0.005 (-0.011, 0.001)	0.051* (0.027, 0.076)	0.003 (-0.001, 0.006)	0.006 (-0.155, 0.167)	0.013 (0.000, 0.026)	-0.005 (-0.031, 0.022)	0.062* (0.032, 0.091)
R ²	0.066	0.456	0.089	0.268	0.042	0.042	0.068	0.004	0.170
Adjusted	0.002 (0.000, 0.004)	0.012* (0.005, 0.019)	-0.001 (-0.08, 0.007)	0.055* (0.026, 0.083)	-0.001 (-0.005, 0.004)	-0.007 (-0.150, 0.137)	0.013* (0.001, 0.025)	-0.013 (-0.040, 0.013)	0.033 (-0.007, 0.072)
R ²	0.283	0.330	0.246	0.352	0.257	0.244	0.290	0.250	0.283
Lumbar spine aBMD (g/cm²)									
Unadjusted	0.002 (-0.002, 0.005)	0.014* (0.007, 0.022)	-0.008 (-0.017, 0.002)	0.051* (0.027, 0.076)	0.005* (0.001, 0.010)	0.006 (-0.239, 0.251)	0.028* (0.009, 0.047)	-0.031 (-0.071, 0.008)	0.038 (-0.013, 0.090)
R ²	0.038	0.043	0.080	0.148	0.043	0.002	0.120	0.037	0.049
Adjusted	0.002 (-0.002, 0.005)	0.012* (0.005, 0.019)	-0.003 (-0.016, 0.010)	0.055* (0.026, 0.083)	0.005 (-0.003, 0.012)	0.024 (-0.215, 0.263)	0.026* (0.007, 0.045)	-0.037 (-0.079, 0.005)	-0.002 (-0.072, 0.068)
R ²	0.159	0.158	0.141	0.187	0.160	0.137	0.222	0.176	0.140
TBS									
Unadjusted	-0.001 (-0.003, 0.001)	-0.005 (-0.015, 0.004)	-0.003 (-0.008, 0.001)	0.007 (-0.018, 0.033)	0.001 (-0.002, 0.005)	0.057 (-0.063, 0.178)	-0.001 (-0.012, 0.011)	0.013 (-0.008, 0.033)	0.012 (-0.015, 0.038)
R ²	0.011	0.027	0.044	0.008	0.041	0.009	0.000	0.028	0.014
Adjusted	0.000 (-0.003, 0.002)	-0.006 (-0.015, 0.004)	-0.004 (-0.012, 0.003)	0.000 (-0.034, 0.002)	0.002 (-0.001, 0.004)	0.053 (-0.067, 0.174)	0.001 (-0.011, 0.013)	0.009 (-0.014, 0.032)	0.001 (-0.032, 0.033)
R ²	0.077	0.087	0.087	0.061	0.083	0.075	0.062	0.074	0.061
HR-pQCT bone parameters									
Cross-sectional area (mm²)									
Unadjusted	2.549 (-4.289, 9.387)	1.127 (-8.074, 10.328)	-14.609* (-20.399, -8.818)	64.039* (36.408, 91.669)	9.620* (6.955, 12.284)	24.551 (-132.149, 181.250)	15.928* (0.797, 31.060)	-17.405 (-48.666, 13.856)	44.440* (6.859, 82.022)
R ²	0.066	0.000	0.261	0.225	0.071	0.018	0.066	0.017	0.083
Adjusted	0.806 (-8.549, 10.160)	2.549 (-4.289, 9.387)	0.529 (-6.895, 7.953)	15.204 (13.983, 44.390)	5.380* (1.551, 9.209)	66.196 (-54.601, 186.992)	10.276 (-1.634, 22.185)	-1.681 (-26.881, 23.520)	18.188 (-16.253, 52.628)
R ²	0.489	0.470	0.468	0.475	0.528	0.476	0.488	0.430	0.475
Total vBMD (mg/cm³)									
Unadjusted	0.279 (-0.729, 1.288)	2.638 (-0.815, 6.092)	-2.439 (-6.056, 1.178)	12.586* (8.65, 24.308)	0.706 (-0.624, 2.035)	-2.307 (-67.469, 62.854)	-4.363 (-9.858, 1.133)	6.235 (-4.962, 17.432)	241.364 (10.625, 37.647)
R ²	0.006	0.044	0.038	0.060	0.019	0.000	0.031	0.015	0.123
Adjusted	0.369 (-0.639, 1.376)	3.171 (-0.189, 6.530)	-2.212 (-4.819, 0.394)	12.491 (-1.465, 26.448)	-0.590 (-2.559, 1.378)	6.948 (-53.952, 67.847)	-3.383 (-8.937, 2.171)	2.659 (-9.084, 14.403)	16.856 (-1.856, 3.118)
R ²	0.114	0.493	0.067	0.151	0.126	0.118	0.135	0.120	0.177
Cortical Area (mm²)									
Unadjusted	0.305 (-0.213, 0.822)	1.199 (-0.661, 3.059)	-3.358* (-4.458, -2.258)	13.723* (8.447, 18.999)	1.486* (0.887, 2.085)	-8.284 (-41.918, 25.351)	-0.391 (-3.458, 2.677)	3.318 (-2.985, 9.262)	16.847* (10.385, 23.309)
R ²	0.006	0.044	0.038	0.060	0.019	0.000	0.031	0.015	0.123
Adjusted	0.102 (-0.323, 0.526)	1.188 (-0.226, 2.601)	-1.647* (-3.127, -0.167)	5.635 (-0.183, 11.453)	-0.102 (-0.890, 0.685)	1.759 (-23.734, 27.252)	-1.048 (-3.410, 1.315)	4.571 (-0.269, 9.411)	9.100* (1.422, 16.777)
R ²	0.470	0.493	0.461	0.497	0.531	0.476	0.481	0.499	0.533
Cortical vBMD (mg/cm³)									
Unadjusted	-0.085 (-1.351, 1.182)	0.669 (-3.831, 0.000)	-1.575 (-4.865, 0.000)	5.760 (-9.257, 0.000)	0.095 (-1.512, 0.000)	-21.875 (-102.752, 0.000)	-2.202 (-9.215, 0.000)	6.682 (-7.384, 0.000)	18.254* (0.263, 0.000)

(continued on next page)

Table 2 (continued)

	Waist circumference (cm)	BMI (kg/m ²)	Body fat percentage (%)	ALM/height ² (kg/m ²)	HGS (kg)	Gait speed (m/s)	Chair stand time (s)	SPPB	Stair climb power test (100W)
R ²		5.224	1.715	20.777	1.701	59.003	4.811	20.748	36.245
Adjusted	0.038	0.000	0.025	0.014	0.061	0.005	0.006	0.012	0.261
R ²	(-1.174, 1.250)	-0.531	-3.868	6.314	-1.214	-16.026	0.441	-1.555	14.073
R ²	0.171	3.689	0.516	23.735	1.170	58.421	7.281	12.658	37.692
R ²		0.171	0.195	0.173	0.181	0.173	0.171	0.179	0.175
Cortical thickness (mm)		0.014	-0.021*	0.090*		-0.047	-0.013	0.043	0.128*
Unadjusted	0.002	(-0.004, 0.008)	(-0.034, -0.009)	(0.031, 0.149)	0.008	(-0.388, 0.293)	(-0.043, 0.017)	(-0.017, 0.104)	(0.057, 0.198)
R ²	0.016	0.040	0.139	0.131	0.056	0.003	0.008	0.023	0.143
Adjusted	0.001	0.014	-0.017	0.057	-0.002	0.015	-0.015	0.047	0.078
R ²	(-0.004, 0.006)	(-0.004, 0.031)	(-0.035, 0.001)	(-0.016, 0.129)	(-0.012, 0.009)	(-0.299, 0.328)	(-0.044, 0.014)	(-0.013, 0.108)	(-0.019, 0.175)
R ²	0.181	0.219	0.222	0.213	0.212	0.190	0.202	0.213	0.241
Cortical porosity (%)		-0.019	-0.019	-0.010	0.005	0.064	-0.012	0.104	-0.150
Unadjusted	-0.004	(-0.022, 0.014)	(-0.066, 0.028)	(-0.232, 0.211)	(-0.019, 0.030)	(-1.071, 1.200)	(-0.122, 0.098)	(-0.116, 0.323)	(-0.423, 0.122)
R ²	0.002	0.000	0.003	0.002	0.5	0.000	0.002	0.014	0.019
Adjusted	0.000	-0.026	0.013	0.013	0.017	0.096	-0.047	0.249	-0.008
R ²	(-0.017, 0.018)	(-0.090, 0.039)	(-0.240, 0.266)	(-0.240, 0.266)	(-0.017, 0.052)	(-0.966, 1.159)	(-0.151, 0.057)	(0.032, 0.466)	(-0.312, 0.297)
R ²	0.186	0.189	0.196	0.189	0.205	0.191	0.200	0.257	0.189
Trabecular area (mm ²)		0.176	-10.638*	49.515*	7.798*	-4.127	16.319*	-20.544	32.102
Unadjusted	2.194	(-9.400, 9.753)	(-17.129, -4.147)	(20.069, 78.962)	(4.722, 10.874)	(-175.456, 167.202)	(1.943, 30.695)	(-50.274, 9.187)	(-4.009, 68.224)
R ²	0.052	0.000	0.170	0.150	0.043	0.002	0.073	0.025	0.039
Adjusted	1.471	2.4258	2.771	12.873	4.509	34.053	11.323	-6.251	-6.511
R ²	(-0.814, 3.757)	(-5.485, 10.341)	(-5.637, 11.178)	(-19.853, 45.599)	(-0.002, 9.021)	(-105.839, 173.944)	(-1.221, 23.866)	(-32.904, 20.402)	(-51.073, 38.051)
R ²	0.370	0.350	0.351	0.353	0.407	0.358	0.377	0.363	0.351
Trabecular vBMD (mg/cm ³)		2.357	-1.377	9.716*	0.649	3.666	-2.449	2.128	16.115*
Unadjusted	0.265	(-0.039, 4.752)	(-3.147, 0.393)	(1.868, 17.565)	(-0.258, 1.557)	(-40.426, 47.759)	(-6.291, 1.393)	(-5.703, 9.960)	(6.828, 25.401)
R ²	0.006	0.040	0.026	0.059	0.000	0.002	0.018	0.004	0.108
Adjusted	0.341	2.581*	-0.672	9.369	-0.182	-10.036	-2.212	0.906	11.133
R ²	(-0.350, 1.032)	(0.296, 4.866)	(-3.188, 1.844)	(-0.185, 18.922)	(-1.556, 1.191)	(-31.786, 51.858)	(-6.197, 1.773)	(-7.469, 9.280)	(-1.924, 24.190)
R ²	0.058	0.094	0.076	0.104	0.065	0.068	0.078	0.073	0.135
Trabecular bone volume fraction (%)		0.287	-0.161	1.202*	0.048	0.769	-0.325	0.239	1.905*
Unadjusted	0.025	(-0.028, 0.601)	(-0.388, 0.067)	(0.159, 2.245)	(-0.070, 0.166)	(-4.760, 6.297)	(-0.855, 0.204)	(-0.841, 1.318)	(0.642, 3.168)
R ²	0.007	0.047	0.021	0.059	0.000	0.002	0.017	0.2	0.104
Adjusted	0.028	0.286	-0.160	1.347*	-0.049	0.977	-0.283	0.040	1.813*
R ²	(-0.065, 0.121)	(-0.024, 0.595)	(-0.501, 0.180)	(0.042, 2.652)	(-0.231, 0.134)	(-4.647, 6.601)	(-0.834, 0.267)	(-1.153, 1.233)	(0.256, 3.370)
R ²	0.050	0.091	0.065	0.100	0.055	0.057	0.069	0.064	0.127
Trabecular thickness (mm)		0.001*	-0.001	0.005*		0.002	-0.013	0.000	0.006*
Unadjusted	0.000	(0.000, 0.000)	(-0.001, 0.000)	(0.001, 0.009)	0.000	(-0.020, 0.024)	(-0.043, 0.017)	(-0.003, 0.004)	(0.001, 0.010)
R ²	0.000	0.064	0.005	0.051	0.000	0.002	0.000	0.000	0.041
Adjusted	0.000	0.002	0.000	0.006*	0.000	0.004	-0.015	0.001	0.004
R ²	(0.000, 0.000)	(0.000, 0.003)	(-0.002, 0.001)	(0.001, 0.011)	(0.000, 0.001)	(-0.018, 0.026)	(-0.044, 0.014)	(-0.003, 0.005)	(-0.002, 0.011)
R ²	0.016	0.076	0.026	0.092	0.023	0.017	0.015	0.028	0.101
Trabecular separation (mm)		-0.010	0.002	-0.027	-0.001	-0.049	0.010	-0.006	-0.051*
Unadjusted	-0.001	(-0.020, 0.000)	(-0.006, 0.009)	(-0.061, 0.006)	(-0.005, 0.003)	(-0.233, 0.135)	(-0.006, 0.025)	(-0.038, 0.026)	(-0.091, -0.011)
R ²	0.002	0.040	0.003	0.030	0.000	0.012	0.016	0.002	0.079
Adjusted	-0.001	-0.010	-0.002	-0.026	0.002	-0.062	0.009	0.000	-0.027
R ²	(-0.004, 0.002)	(-0.019, 0.000)	(-0.013, 0.009)	(-0.067, 0.016)	(-0.004, 0.008)	(-0.240, 0.116)	(-0.007, 0.025)	(-0.035, 0.034)	(-0.082, 0.028)
R ²	0.057	0.088	0.060	0.075	0.060	0.070	0.075	0.064	0.100
Trabecular number (1/mm)		0.018*	-0.002	0.049	0.001	0.094	-0.023	0.014	0.084*
	0.000	(-0.014, 0.000)	(-0.002, 0.000)	(-0.005, 0.000)	(-0.005, 0.000)	(-0.203, 0.000)	(-0.048, 0.000)	(-0.038, 0.000)	(0.000, 0.000)

(continued on next page)

Table 2 (continued)

	Waist circumference (cm)	BMI (kg/m ²)	Body fat percentage (%)	ALM/height ² (kg/m ²)	HGS (kg)	Gait speed (m/s)	Chair stand time (s)	SPPB	Stair climb power test (100W)
Unadjusted	(-0.005, 0.005)	(0.002, 0.034)	0.010	0.102	0.007	0.390	0.003	0.065	(0.020, 0.148)
R ²	0.000	0.055	0.00	0.035	0.004	0.021	0.033	0.003	0.087
Adjusted	0.000	0.019*	0.003	0.058	-0.003	0.106	-0.023	0.009	0.053
R ²	(-0.005, 0.005)	(0.003, 0.034)	(-0.015, 0.020)	(-0.009, 0.126)	(-0.013, 0.007)	(-0.184, 0.397)	(-0.050, 0.003)	(-0.047, 0.066)	(-0.036, 0.142)
	0.045	0.084	0.043	0.078	0.039	0.058	0.082	0.050	0.109
Bone failure load (N)									
Unadjusted	21.0	52.2	-262.3*	1096.2*	128.2*	306.0	-156.2	752.7*	1563.1*
R ²	(-23.5, 65.5)	(-124.5, 229.0)	(-145.1, -367.9)	(540.5, 1651.9)	(71.4, 184.1)	(2901.3, 3513.2)	(-451.1, 138.8)	(209.4, 1295.9)	(986.3, 2139.9)
	0.023	0.007	0.328	0.232	0.024	0.003	0.017	0.134	0.376
Adjusted	5.07	48.3	-93.9	206.6	31.7	413.5	-145.3	586.4*	872.6*
R ²	(-27.6, 37.8)	(-76.9, 173.6)	(-242.3, 54.5)	(-377.2, 790.4)	(-38.2, 101.7)	(-1954.3, 2781.2)	(-366.2, 75.6)	(139.3, 1033.5)	(275.0, 1470.2)
	0.525	0.530	0.539	0.529	0.532	0.525	0.540	0.591	0.594
Bone stiffness (N/mm)									
Unadjusted	248	892	-4850*	20295*	2437	662	-3033	14522*	30395*
R ²	(-691, 1187)	(-2696, 4479)	(-7001, -269)	(8739, 31851)	(1353, 3521)	(-3783, 2459)	(-8665, 2598)	(4152, 24891)	(18487, 42302)
	0.021	0.008	0.315	0.228	0.020	0.004	0.017	0.136	0.375
Adjusted	236	1559	-1634	4708	554	7985	-2774	11447*	15498
R ²	(-478, 951)	(-1050, 4167)	(-4752, 1485)	(-7230, 16647)	(-923, 2031)	(-58991, 43022)	(-7103, 1555)	(2686, 20207)	(85, 30911)
	0.500	0.506	0.517	0.506	0.510	0.501	0.516	0.571	0.575

Data presented as unstandardised β -coefficients with 95% confidence intervals and R² value. Adjusted for age, sex, smoking status, vitamin D and self-reported MVPA. * indicates significance at $p < 0.05$. Abbreviations: BMI, body mass index; ALM, appendicular lean mass; HGS, hand grip strength; MVPA, moderate to vigorous physical activity; TBS, trabecular bone score; aBMD, areal bone mineral density; vBMD, volumetric bone mineral density; DXA, dual energy X-ray absorptiometry; HR-pQCT, high resolution peripheral quantitative computed tomography; R², coefficient of determination

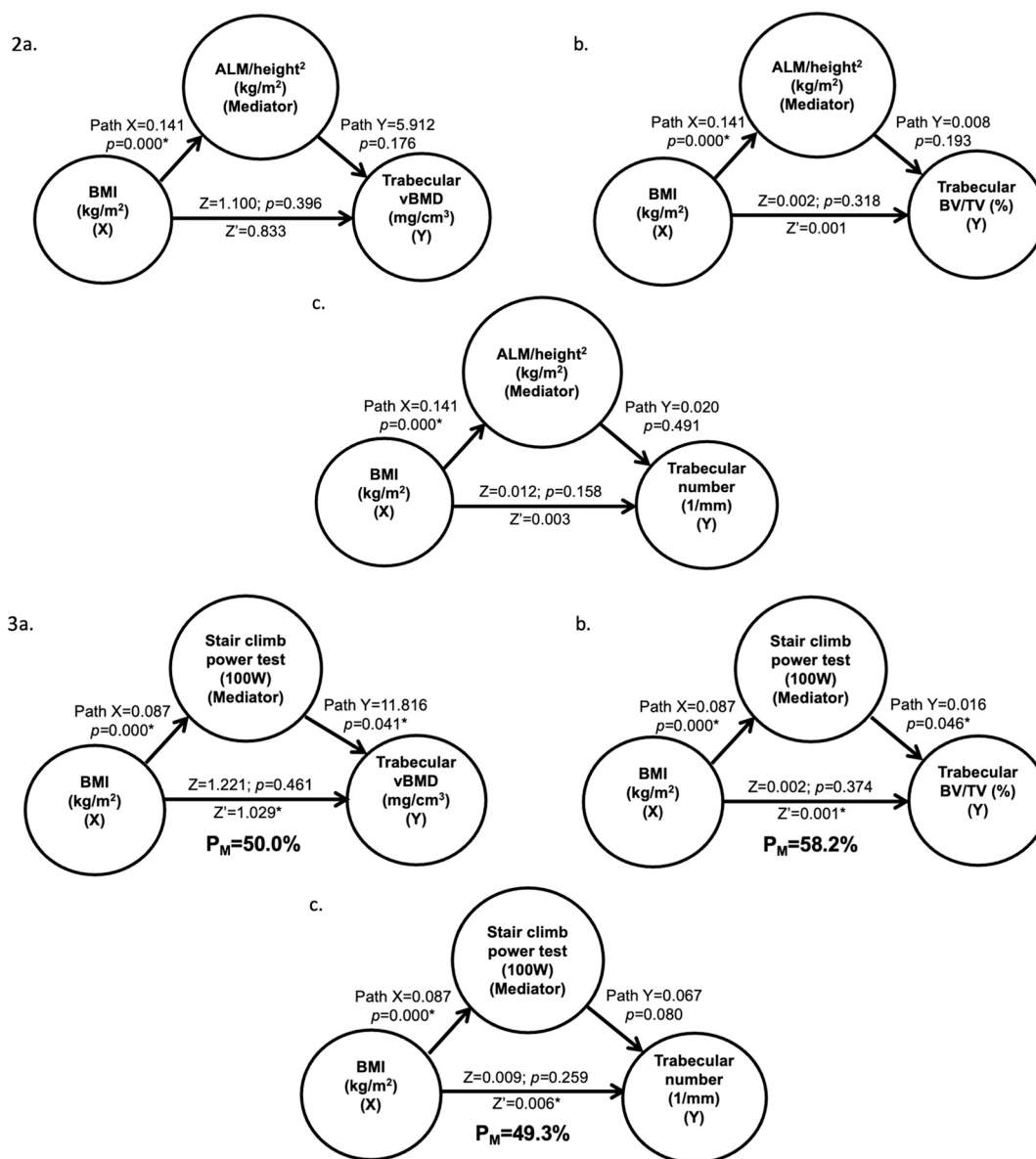
4. Discussion

In this population of older adults with obesity, BMI, ALM/height² and stair climb power were associated with more favourable aBMD and tibial bone microarchitecture. Body fat percentage was negatively associated with tibial cortical area, suggesting higher body fat may be detrimental on bone. These results indicate associations between BMI, body fat percentage and bone health in older adults with obesity are divergent, and that positive associations between BMI and bone health may be explained by higher muscle mass and/or muscular power.

Obesity defined by BMI is positively associated with bone mass and is protective on bone health and fractures (Gandham et al., 2020; Palermo et al., 2016; Lloyd et al., 2014). In the current study, BMI was positively associated with total hip, femoral neck, and lumbar spine aBMD and tibial trabecular vBMD, thickness, number, and bone volume fraction. In addition, as evident from the sensitivity analysis and mediation analysis, stair climb power mediated the associations between BMI on the trabecular bone microarchitecture. Similarly, a study of 200 community-dwelling adults aged 25 to 75 years demonstrated that those with obesity defined by BMI had favourable bone microarchitecture and greater bone strength at the distal radius and tibia compared to individuals without obesity (Evans et al., 2015). This is likely because of increased mechanical loading on bone from additional body weight (Evans et al., 2015; Liu et al., 2017; Litwic et al., 2021; Lagerquist et al., 2021; Gower and Casazza, 2013). In the above study, those with high BMI also had greater cortical thickness and vBMD estimated by the HR-pQCT, however, in the current study, BMI was not associated with any cortical bone variables (Evans et al., 2015). This finding could be explained by different population groups or differences in physical activity levels, but further research is required to confirm associations of BMI with cortical bone parameters in older adults with and without obesity.

Body fat percentage, unlike BMI, is not protective on aBMD or bone microarchitecture (Sukumar et al., 2011). Many studies have previously investigated the associations between body fat percentage and bone health but were however limited to two-dimensional measures of aBMD

assessed by DXA (Kim et al., 2019; Hilton et al., 2022; Ma et al., 2022; Deng et al., 2021). No studies have previously investigated the effects of obesity defined by body fat percentage on bone structural parameters including cortical and trabecular bone microarchitecture using three-dimensional imaging modalities such as HR-pQCT among older adults. In the current study, body fat percentage was negatively associated with poorer tibial cortical area. In a study of 115 adolescent women, body fat percentage was inversely associated with cortical bone area and cortical bone mineral content (BMC) at the tibia measured by peripheral quantitative computed tomography (pQCT) (Pollock et al., 2007). It seems that higher body fat percentage is associated with bone microarchitecture degradation, with cortical bone being more affected than trabecular bone (Pollock et al., 2007; Hayon-Ponce et al., 2021). An explanation for this finding could be that individuals with higher fat mass may be more likely to have hormonal imbalance including higher levels of parathyroid hormone and lower levels of circulating 25-hydroxy-vitamin D which may cause excess bone resorption and poor bone health (Sukumar et al., 2011). Additionally, it is also possible that estrogens produced by peripheral aromatisation in the adipose tissue may help mitigate bone loss therefore causing smaller damage on trabecular bone than cortical bone (Manolagas et al., 2013). In addition, it is also plausible that excess adipose tissue leads to an increase in bone marrow adipose tissue which may offset potential benefits of mechanical loading on bone growth (Liu et al., 2017; Pollock et al., 2007; Hardouin et al., 2016). This was evident in a study of 35 men with obesity with a mean age of 34 years which reported excess bone marrow fat was negatively associated with bone microarchitecture estimated by the HR-pQCT (Bredella et al., 2012). Excess adiposity, particularly visceral adiposity, may also lead to systemic inflammation promoting the activity of cytokines and adipokines and subsequently inducing bone loss (Liu et al., 2017; Kurgan et al., 2020; Ellulu et al., 2017). However, the underlying mechanisms contributing to the associations between body fat percentage and cortical, rather than trabecular bone microarchitecture among older adults with obesity warrants further investigation.



Figs. 2 and 3. Mediation analysis of the effects of BMI on bone microarchitecture (a. trabecular vBMD, b. trabecular BV/TV and c. trabecular number) and the mediating effect of ALM/height² (Fig. 2) and stair climb power test (Fig. 3). Path (X) corresponds to the effect of BMI on muscle mass (Fig. 2) and muscle power (Fig. 3). Path (Y) corresponds to the effect of muscle mass (Fig. 2) and muscle power (Fig. 3) on bone microarchitecture. The direct (Z) and indirect (Z') pathways corresponds to the effect of BMI and bone microarchitecture with muscle mass (Fig. 2) and muscle power (Fig. 3) as the mediators. Data presented as β -coefficients and adjusted for age. * indicates significance at $p < 0.05$. Abbreviations: BMI, body mass index; ALM, appendicular lean mass; vBMD, volumetric bone mineral density; BV/TV, bone volume fraction.

Muscle mass is a strong determinant of bone health among older adults (Evans et al., 2015; Madeira et al., 2014; Ilesanmi-Oyelere et al., 2018; Wagner et al., 2021; Lebrasseur et al., 2012). In the current study, similar to BMI, ALM/height² was positively associated with aBMD at all sites and bone microarchitectural parameters including trabecular bone volume fraction and trabecular thickness at the distal tibia. Similarly, in a study of 50 individuals with obesity defined by BMI and metabolic syndrome aged under 50 years, total body lean mass was positively correlated with aBMD at the total femur and bone microarchitecture including trabecular bone volume fraction, trabecular number, trabecular thickness and cortical thickness at the distal radius and tibia measured by HR-pQCT (Madeira et al., 2014). Additionally, in a prospective study including 821 men aged 60 years and older, low appendicular lean mass was associated with an age-related decline in HR-pQCT determined bone microarchitecture (Wagner et al., 2021). A plausible explanation for this is that higher amounts of lean mass induce

greater mechanical forces on adjacent bone during locomotion, which stimulates improvements in bone density and microarchitecture (Ilesanmi-Oyelere et al., 2018; Lebrasseur et al., 2012; Moradell et al., 2020; Kim et al., 2018; Pomeroy et al., 2018). Future studies should therefore develop interventions targeting improvements in lean mass and muscle function to prevent bone microarchitecture deterioration among older adults with obesity (Marin-Mio et al., 2018).

Muscle strength has been found to be positively associated with bone health (Chen et al., 2020; Snow-Harter et al., 1990). Likewise, in the current study, handgrip strength was associated with tibial cross-sectional area after adjusting for confounders. The lack of associations between hand grip strength and other bone parameters assessed in this study could be due to the fact that bone microarchitecture in this study was assessed at the distal tibial site only. In support, a study including 508 men and 651 women with the mean age of 70 years showed that grip strength was positively associated with radial cross-sectional area

measured by HR-pQCT (McLean et al., 2021). In addition, SPPB score was also positively associated with tibial cortical porosity and was the only sarcopenia component associated with bone failure load and bone stiffness after adjusting for confounders. In this study, higher SPPB score was associated with better bone strength which may therefore be protective against fractures. However, in our previous study including 50 community-dwelling postmenopausal women aged between 49 and 82 years, SPPB score was not associated with any of the bone strength estimates (Gandham et al., 2019). These differences may be explained due to the fact that the current study includes individuals with obesity unlike the abovementioned study which includes individuals with normal BMI. Examination of SPPB may therefore be a more important tool for screening individuals with poor bone health and may have a utility in predicting fractures among older adults with obesity compared to those without. In the current study, gait speed was however not associated with any of the bone variables. This may be attributed to the fact that gait speed was performed at usual pace in this study and was likely not challenging enough for the vast majority of these community-dwelling older adults. Previous research has suggested that physical performance may be associated with bone health only in older adults with functional deficits (Mikkilä et al., 2022; Blaizot et al., 2012). Our findings are similar to a study with 313 older men and 318 women with the mean age of 69.2 and 69.5 years respectively, which also found no apparent relationship between gait speed (measured over a 3 m distance) and bone microarchitecture assessed by pQCT (Edwards et al., 2013). However, another study with 129 older adults with the mean age of 76.2 years found that gait speed was positively associated with cortical BMD measured by pQCT (Moradell et al., 2020). These contradictory findings may be explained by the use of maximum walking speed in the abovementioned study which may be more closely associated with muscle power than usual gait speed which was used in the current study (Moradell et al., 2020). Likewise, no associations were found between chair stand test and tibial bone microarchitecture. In contrast, in a study including 230 women aged 21 to 87 years, chair stand test maximum force (kN) which was performed using a ground reaction force plate was strongly associated with tibial bone microarchitecture at cortical sites (Simon et al., 2022). These contradictory findings may be explained by the fact that our chair stand test assessed total time to completion rather than maximum force generated. However, further research is required to better understand the associations between chair stand test and bone microarchitecture.

Indeed, higher muscle power (assessed using a stair climb power test) in this study was strongly associated with better cortical bone area and bone stiffness among older adults with obesity. Previously, no studies have investigated the associations between muscle power and bone microarchitecture in older adults with obesity but in our previous study of 50 postmenopausal women, muscle power assessed by the stair climb power test was consistently associated with HR-pQCT bone variables measured at the distal tibia (Gandham et al., 2019). Similarly, in another study including 1171 men aged 65 years and over, men with the highest leg power assessed by Nottingham Power Rig had larger total bone area and cortical area compared with men who had the lowest leg power (Cousins et al., 2010). A possible explanation for this finding could be that muscle power from increased physiological mechanical loading may lead to changes in morphology of the bone, particularly the cortical bone contributing to better overall bone microarchitecture (Cousins et al., 2010; Chang et al., 2008; Gianoudis et al., 2012). Examination of muscle power may therefore be a useful tool in clinical practice for screening individuals at increased risk of poor bone health among older adults with obesity.

This study provides important insights into associations between obesity, sarcopenia, and bone microarchitecture in older adults. There are however some limitations. Firstly, this was a cross-sectional analysis from three studies with a relatively small sample size and due to insufficient power, we may have had limited our ability to detect some associations, so our analyses could not be stratified based on age groups or

sex. Hence, longitudinal studies should be conducted in larger populations to identify any sex-specific associations as recent evidence has demonstrated that there are likely differences in bone size, trabecular BV/TV and thickness among men and women (Amin and Khosla, 2012). Furthermore, the cross-sectional design of this study limits inferences of causation in the associations of sarcopenia and obesity with bone health. It should also be noted that genetics, nutrition status and hormonal factors not evaluated in this study, could have influenced the associations between components of obesity and sarcopenia on bone health. In regard to hormonal factors, it is not clear how menopause status may have affected associations for women however given the minimum age for inclusion in the study was 55 years it is expected that most women would have been postmenopausal. In addition, the associations between TBS and bone parameters were only investigated in a sub-group of older adults with obesity in this study ($n = 48$) due to recommendations that TBS data should not be performed in individuals with BMI ≥ 37 kg/m² (Bonaccorsi et al., 2020). Future studies exploring associations of body composition with lumbar spine microarchitecture in individuals with obesity should consider the use of computed tomography (CT) imaging. In addition, it should also be noted that this study did not distinguish between android and gynoid obesity phenotypes which may have differing associations with overall bone health and bone microarchitecture. It should also be noted that individuals included in this study had obesity but otherwise were healthy community-dwelling older adults which may have explained the low prevalence of sarcopenia. Furthermore, since there is no consensus definition for sarcopenia, the current study used both the SDOC and EWGSOP2 definitions and the use of different sarcopenia definitions could influence its observed prevalence and associations with bone health.

In conclusion, higher BMI, ALM and muscle power were associated with more favourable bone microarchitecture, but higher body fat percentage was negatively associated with cortical bone area, among older adults with obesity. These findings suggest that high BMI is protective for aBMD and bone microarchitecture, which is explained by higher muscle forces, but higher relative body fat is not associated with/beneficial for bone health. Further longitudinal studies are required to understand the underlying mechanisms contributing to poor bone microarchitecture among older adults with sarcopenia and obesity.

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.exger.2023.112227>.

Funding

This work was supported by a 2018 Rebecca L. Cooper Foundation-Project Grant and 2017 American Society of Bone and Mineral Research Rising Star Award awarded to Dr. David Scott, and Monash University's School of Clinical Sciences "Near-Miss" grant Scheme awarded to Professor Peter Ebeling. Dr. David Scott is supported by an Australian National Health and Medical Research Council (NHMRC) Investigator Grant (GNT1174886).

Declaration of competing interest

Authors declare no conflicts of interest.

CRediT authorship contribution statement

Anoohya Gandham: Writing – original draft, Writing – review & editing, Formal analysis, Data collection. **Jakub Mesinovic:** Writing – review & editing, Data collection. **Mavil May Cervo:** Writing – review & editing, Data collection. **Costas Glavas:** Writing – review & editing, Data collection. **Paul Jansons:** Writing – review & editing, Data collection. **Carrie-Anne Ng:** Writing – review & editing, Data collection. **Juan Pena Rodriguez:** Writing – review & editing, Data collection. **Ayse Zengin:** Writing – review & editing, Supervision. **Maxine P. Bonham:** Writing – review & editing, Supervision. **Peter R. Ebeling:**

Writing – review & editing, Supervision, Conceptualization. **David Scott:** Writing – review & editing, Supervision, Conceptualization.

Consent to participate

All participants included in the study provided informed consent.

Acknowledgements

We acknowledge the efforts of all study participants and students.

References

- Aguirre, L.E., Colleluori, G., Fowler, K.E., Jan, I.Z., Villareal, K., Qualls, C., et al., 2015. High aromatase activity in hypogonadal men is associated with higher spine bone mineral density, increased truncal fat and reduced lean mass. *Eur. J. Endocrinol.* 173 (2), 167–174.
- Amin, S., Khosla, S., 2012. Sex- and age-related differences in bone microarchitecture in men relative to women assessed by high-resolution peripheral quantitative computed tomography. *J. Osteoporos.* 2012, 129760.
- Bean, J.F., Kiely, D.K., LaRose, S., Alian, J., Frontera, W.R., 2007. Is stair climb power a clinically relevant measure of leg power impairments in at-risk older adults? *Arch. Phys. Med. Rehabil.* 88 (5), 604–609.
- Blaizot, S., Boutroy, S., Vilaythiou, N., Boonen, S., Chapurlat, R., Szulc, P., 2012. Poor bone microarchitecture in older men with impaired physical performance—the STRAMBO study. *Osteoporos. Int.* 23 (12), 2785–2796.
- Bonaccorsi, G., Cafarelli, F.P., Cervellati, C., De Guio, F., Greco, P., Giganti, M., et al., 2020. A new corrective model to evaluate TBS in obese post-menopausal women: a cross-sectional study. *Aging Clin. Exp. Res.* 32 (7), 1303–1308.
- Bouxsein, M.L., Boyd, S.K., Christiansen, B.A., Guldborg, R.E., Jepsen, K.J., Muller, R., 2010. Guidelines for assessment of bone microstructure in rodents using micro-computed tomography. *J. Bone Miner. Res.* 25 (10), 1568–1576.
- Bredella, M.A., Lin, E., Gerweck, A.V., Landa, M.G., Thomas, B.J., Torriani, M., et al., 2012. Determinants of bone microarchitecture and mechanical properties in obese men. *J. Clin. Endocrinol. Metab.* 97 (11), 4115–4122.
- Chang, G., Pakin, S.K., Schweitzer, M.E., Saha, P.K., Regatte, R.R., 2008. Adaptations in trabecular bone microarchitecture in Olympic athletes determined by 7T MRI. *J. Magn. Reson. Imaging* 27 (5), 1089–1095.
- Chen, F., Su, Q., Tu, Y., Zhang, J., Chen, X., Zhao, T., et al., 2020. Maximal muscle strength and body composition are associated with bone mineral density in chinese adult males. *Medicine (Baltimore)* 99 (6), e19050.
- Cheung, A.M., Adachi, J.D., Hanley, D.A., Kendler, D.L., Davison, K.S., Josse, R., et al., 2013. High-resolution peripheral quantitative computed tomography for the assessment of bone strength and structure: a review by the Canadian bone strength working group. *Curr. Osteoporos. Rep.* 11 (2), 136–146.
- Cousins, J.M., Petit, M.A., Paudel, M.L., Taylor, B.C., Hughes, J.M., Cauley, J.A., et al., 2010. Muscle power and physical activity are associated with bone strength in older men: the osteoporotic fractures in men study. *Bone* 47 (2), 275–281.
- Craig, C.L., Marshall, A.L., Sjostrom, M., Bauman, A.E., Booth, M.L., Ainsworth, B.E., et al., 2003. International physical activity questionnaire: 12-country reliability and validity. *Med. Sci. Sports Exerc.* 35 (8), 1381–1395.
- Cruz-Jentoft, A.J., Bahat, G., Bauer, J., Boirie, Y., Bruyere, O., Cederholm, T., et al., 2019. Sarcopenia: revised European consensus on definition and diagnosis. *Age Ageing* 48 (1), 16–31.
- Deng, K.L., Yang, W.Y., Hou, J.L., Li, H., Feng, H., Xiao, S.M., 2021. Association between body composition and bone mineral density in children and adolescents: a systematic review and meta-analysis. *Int. J. Environ. Res. Public Health* 18 (22), 11722.
- Edwards, M.H., Gregson, C.L., Patel, H.P., Jameson, K.A., Harvey, N.C., Sayer, A.A., et al., 2013. Muscle size, strength, and physical performance and their associations with bone structure in the Hertfordshire Cohort Study. *J. Bone Miner. Res.* 28 (11), 2295–2304.
- Ellulu, M.S., Patimah, I., Khaza'i, H., Rahmat, A., Abed, Y., 2017. Obesity and inflammation: the linking mechanism and the complications. *Arch. Med. Sci.* 13 (4), 851–863.
- Evans, A.L., Paggiosi, M.A., Eastell, R., Walsh, J.S., 2015. Bone density, microstructure and strength in obese and normal weight men and women in younger and older adulthood. *J. Bone Miner. Res.* 30 (5), 920–928.
- Foundation VHP, 2014. Negative growth: the future of obesity in Australia. *VicHealth.* Freiberger, E., de Vreede, P., Schoene, D., Rydwik, E., Mueller, V., Frandin, K., et al., 2012. Performance-based physical function in older community-dwelling persons: a systematic review of instruments. *Age Ageing* 41 (6), 712–721.
- Gandham, A., McMillan, L.B., Ng, C.A., Humbert, L., Bonham, M.P., Zengin, A., et al., 2019. Associations of health-related quality of life, fear of falling and objective measures of physical function with bone health in postmenopausal women with low bone mass. *J. Clin. Med.* 8 (9), 1487–1495.
- Gandham, A., Zengin, A., Bonham, M.P., Winzenberg, T., Balogun, S., Wu, F., et al., 2020. Incidence and predictors of fractures in older adults with and without obesity defined by body mass index versus body fat percentage. *Bone* 140, 115546.
- Gandham, A., Mesinovic, J., Jansons, P., Zengin, A., Bonham, M.P., Ebeling, P.R., et al., 2021. Falls, fractures, and areal bone mineral density in older adults with sarcopenic obesity: a systematic review and meta-analysis. *Obes. Rev.* 22 (5), e13187.
- Gianoudis, J., Bailey, C.A., Sanders, K.M., Nowson, C.A., Hill, K., Ebeling, P.R., et al., 2012. Osteo-cise: strong bones for life: protocol for a community-based randomised controlled trial of a multi-modal exercise and osteoporosis education program for older adults at risk of falls and fractures. *BMC Musculoskelet. Disord.* 13 (78), 1–12.
- Gower, B.A., Casazza, K., 2013. Divergent effects of obesity on bone health. *J. Clin. Densitom.* 16 (4), 450–454.
- Guralnik, J.M., Ferrucci, L., Pieper, C.F., Leveille, S.G., Markides, K.S., Ostir, G.V., et al., 2000. Lower extremity function and subsequent disability: consistency across studies, predictive models, and value of gait speed alone compared with the short physical performance battery. *J. Gerontol.* 55 (2), 231–236.
- Han, S.S., Kim, M., Lee, S.M., Lee, J.P., Kim, S., Joo, K.W., et al., 2014. Association between body fat and vitamin D status in Korean adults. *Asia Pac. J. Clin. Nutr.* 23 (1), 65–75.
- Hardouin, P., Rharass, T., Lucas, S., 2016. Bone marrow adipose tissue: to be or not to be a typical adipose tissue? *Front. Endocrinol. (Lausanne)* 7, 85.
- Hayon-Ponce, M., Garcia-Fontana, B., Aviles-Perez, M.D., Gonzalez-Salvatierra, S., Andujar-Vera, F., Moratalla-Aranda, E., et al., 2021. Lower trabecular bone score in type 2 diabetes mellitus: a role for fat mass and insulin resistance beyond hyperglycaemia. *Diabetes Metab.* 47 (6), 101276.
- Hilton, C., Vasani, S.K., Neville, M.J., Christodoulides, C., Karpe, F., 2022. The associations between body fat distribution and bone mineral density in the Oxford Biobank: a cross sectional study. *Expert. Rev. Endocrinol. Metab.* 17 (1), 75–81.
- Hoxha, R., Islami, H., Qorraj-Bytyqi, H., Thaci, S., Bahtiri, E., 2014. Relationship of weight and body mass index with bone mineral density in adult men from Kosovo. *Mater. Soc.* 26 (5), 306–308.
- Hurtig-Wennlof, A., Hagstromer, M., Olsson, L.A., 2010. The international physical activity questionnaire modified for the elderly: aspects of validity and feasibility. *Public Health Nutr.* 13 (11), 1847–1854.
- Ilesanmi-Oyelere, B.L., Coad, J., Roy, N., Kruger, M.C., 2018. Lean body mass in the prediction of bone mineral density in postmenopausal women. *Biores. Open Access.* 7 (1), 150–158.
- J.J. C., 2011. Effects of obesity on bone metabolism. *J. Orthop. Surg. Res.* 6, 1–10.
- Jiang, Y., Zhang, Y., Jin, M., Gu, Z., Pei, Y., Meng, P., 2015. Aged-related changes in body composition and association between body composition with bone mass density by body mass index in Chinese Han men over 50-year-old. *PLoS One* 10 (6), e0130400.
- Kanis, J.A., 1994. Assessment of fracture risk and its application to screening for postmenopausal osteoporosis: synopsis of a WHO report. *Osteoporos. Int.* 4 (2), 162–170.
- Karasik, D., Demissie, S., Lu, D., Broe, K.E., Boyd, S.K., Liu, C.T., et al., 2017. Bone strength estimated by Micro-finite element analysis (microFEA) is heritable and shares genetic predisposition with areal BMD: the Framingham study. *J. Bone Miner. Res.* 32 (11), 2151–2156.
- Kim, J., Kwon, H., Heo, B.K., Joh, H.K., Lee, C.M., Hwang, S.S., et al., 2018. The association between fat mass, lean mass and bone mineral density in premenopausal women in Korea: a cross-sectional study. *Korean J. Fam. Med.* 39 (2), 74–84.
- Kim, D.H., Lim, H., Chang, S., Kim, J.N., Roh, Y.K., Choi, M.K., 2019. Association between body fat and bone mineral density in normal-weight middle-aged Koreans. *Korean J. Fam. Med.* 40 (2), 100–105.
- Kirk, B., Zanker, J., Bani Hassan, E., Bird, S., Brennan-Olsen, S., Duque, G., 2021. Sarcopenia definitions and outcomes consortium (SDOC) criteria are strongly associated with malnutrition, depression, falls, and fractures in high-risk older persons. *J. Am. Med. Dir. Assoc.* 22 (4), 741–745.
- Kley, H.K., Deselaers, T., Peerenboom, H., Kruskemper, H.L., 1980. Enhanced conversion of androstenedione to estrogens in obese males. *J. Clin. Endocrinol. Metab.* 51 (5), 1128–1132.
- Kurgan, N., McKee, K., Calleja, M., Josse, A.R., Klentrou, P., 2020. Cytokines, adipokines, and bone markers at rest and in response to plyometric exercise in obese vs normal weight adolescent females. *Front. Endocrinol. (Lausanne)* 11, 513926.
- Lagerquist, M.K., Gustafsson, K.L., Henning, P., Farman, H., Wu, J., Sjogren, K., et al., 2021. Acute fat loss does not affect bone mass. *Sci. Rep.* 11 (1), 14177.
- Lebrasseur, N.K., Achenbach, S.J., Melton 3rd, L.J., Amin, S., Khosla, S., 2012. Skeletal muscle mass is associated with bone geometry and microstructure and serum insulin-like growth factor binding protein-2 levels in adult women and men. *J. Bone Miner. Res.* 27 (10), 2159–2169.
- Litwic, A.E., Westbury, L.D., Ward, K., Cooper, C., Dennison, E.M., 2021. Adiposity and bone microarchitecture in the GLOW study. *Osteoporos. Int.* 32 (4), 689–698.
- Liu, C.T., Broe, K.E., Zhou, Y., Boyd, S.K., Cupples, L.A., Hannan, M.T., et al., 2017. Visceral adipose tissue is associated with bone microarchitecture in the Framingham osteoporosis study. *J. Bone Miner. Res.* 32 (1), 143–150.
- Lloyd, J.T., Alley, D.E., Hawkes, W.G., Hochberg, M.C., Waldstein, S.R., Orwig, D.L., 2014. Body mass index is positively associated with bone mineral density in US older adults. *Arch. Osteoporos.* 9, 175.
- Ma, M., Liu, X., Jia, G., Geng, B., Xia, Y., 2022. The association between body fat distribution and bone mineral density: evidence from the US population. *BMC Endocr. Disord.* 22 (1), 170.
- MacKinnon, D.P., Lockwood, C.M., Hoffman, J.M., West, S.G., Sheets, V., 2002. A comparison of methods to test mediation and other intervening variable effects. *Psychol. Methods* 7 (1), 83.
- Madeira, E., Mafort, T.T., Madeira, M., Guedes, E.P., Moreira, R.O., de Mendonca, L.M., et al., 2014. Lean mass as a predictor of bone density and microarchitecture in adult obese individuals with metabolic syndrome. *Bone* 59, 89–92.
- Manolagas, S.C., O'Brien, C.A., Almeida, M., 2013. The role of estrogen and androgen receptors in bone health and disease. *Nat. Rev. Endocrinol.* 9 (12), 699–712.
- Marin-Mio, R.V., Moreira, L.D.F., Camargo, M., Perigo, N.A.S., Cerondoglo, M.S., Lazaretti-Castro, M., 2018. Lean mass as a determinant of bone mineral density of proximal femur in postmenopausal women. *Arch. Endocrinol. Metab.* 62 (4), 431–437.

- McLean, R.R., Samelson, E.J., Lobergs, A.L., Broe, K.E., Hannan, M.T., Boyd, S.K., et al., 2021. Higher hand grip strength is associated with greater radius bone size and strength in older men and women: the Framingham osteoporosis study. *JBM Plus* 5 (5), e10485.
- Mikkilä, S., Johansson, J., Nordstrom, A., Nordstrom, P., Emaus, N., Handegard, B.H., et al., 2022. A 15-year follow-up study of hip bone mineral density and associations with leisure time physical activity. *The Tromso Study 2001–2016*. *PLoS One* 17 (1), e0262228.
- Moradell, A., Gomez-Cabello, A., Gomez-Bruton, A., Muniz-Pardos, B., Puyalto, J.M., Matute-Llorente, A., et al., 2020. Associations between physical fitness, bone mass, and structure in older people. *Biomed. Res. Int.* 2020, 6930682.
- Nishiyama, K.K., Shane, E., 2013. Clinical imaging of bone microarchitecture with HR-pQCT. *Curr. Osteoporos. Rep.* 11 (2), 147–155.
- Nuttall, F.Q., 2015. Body mass index: obesity, BMI, and health: a critical review. *Nutr. Today* 50 (3), 117–128.
- Palermo, A., Tuccinardi, D., Defeudis, G., Watanabe, M., D'Onofrio, L., Lauria Pantano, A., et al., 2016. BMI and BMD: the potential interplay between obesity and bone fragility. *Int. J. Environ. Res. Public Health* 13 (6).
- Papageorgiou, M., Kerschan-Schindl, K., Sathyapalan, T., Pietschmann, P., 2020. Is weight loss harmful for skeletal health in obese older adults? *Gerontology*. 66 (1), 2–14.
- Pollock, N.K., Laing, E.M., Baile, C.A., Hamrick, M.W., Hall, D.B., Lewis, R.D., 2007. Is adiposity advantageous for bone strength? A peripheral quantitative computed tomography study in late adolescent females. *Journal of Clin. Nutr.* 86.
- Pomeroy, E., Macintosh, A., Wells, J.C.K., Cole, T.J., Stock, J.T., 2018. Relationship between body mass, lean mass, fat mass, and limb bone cross-sectional geometry: implications for estimating body mass and physique from the skeleton. *Am. J. Phys. Anthropol.* 166 (1), 56–69.
- Ronde, W., Jong, F.H., 2011. Aromatase inhibitors in men: effects and therapeutic options. *Reprod. Biol. Endocrinol.* 9.
- Scott, D., Daly, R.M., Sanders, K.M., Ebeling, P.R., 2015. Fall and fracture risk in sarcopenia and dynapenia with and without obesity: the role of lifestyle interventions. *Curr. Osteoporos. Rep.* 13 (4), 235–244.
- Scott, D., Johansson, J., McMillan, L.B., Ebeling, P.R., Nordstrom, P., Nordstrom, A., 2019. Associations of sarcopenia and its components with bone structure and incident falls in Swedish older adults. *Calcif. Tissue Int.* 105 (1), 26–36.
- Shepherd, J.A., Ng, B.K., Sommer, M.J., Heymsfield, S.B., 2017. Body composition by DXA. *Bone* 104, 101–105.
- Simon, A., Schafer, H.S., Schmidt, F.N., Sturznicke, J., Amling, M., Rolvien, T., 2022. Compartment-specific effects of muscle strength on bone microarchitecture in women at high risk of osteoporosis. *J. Cachexia. Sarcopenia Muscle* 13 (5), 2310–2321.
- Snow-Harter, C., Bouxsein, M., Lewis, B., Charette, S., Weinstein, P., Marcus, R., 1990. Muscle strength as a predictor of bone mineral density in young women.pdf. *J. Bone Miner. Res.* 5 (6).
- Sukumar, D., Schlüssel, Y., Riedt, C.S., Gordon, C., Stahl, T., Shapses, S.A., 2011. Obesity alters cortical and trabecular bone density and geometry in women. *Osteoporos. Int.* 22 (2), 635–645.
- Wagner, P.P., Whittier, D.E., Foesser, D., Boyd, S.K., Chapurlat, R., Szulc, P., 2021. Bone microarchitecture decline and risk of fall and fracture in men with poor physical performance—the STRAMBO study. *J. Clin. Endocrinol. Metab.* 106 (12) (e180–e194).
- Watts, J.J., Abimanyi-Ochom, J., Sanders, K.M., 2012. Osteoporosis costing all Australians a new burden of disease analysis. *Osteoporosis Australia*.
- Whittier, D.E., Boyd, S.K., Burghardt, A.J., Paccou, J., Ghasem-Zadeh, A., Chapurlat, R., et al., 2020. Guidelines for the assessment of bone density and microarchitecture in vivo using high-resolution peripheral quantitative computed tomography. *Osteoporos. Int.* 31 (9), 1607–1627.