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Research Article

Differential contributions of lean and fat mass on bone mineral density in Asian women of reproductive age: the Singapore Preconception Study of Long-Term Maternal and Child Outcomes study

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Abstract

The relationships between fat mass (FM), lean mass (LM), and bone mass are complex with significant implications for obesity, sarcopenia, and osteoporosis later in life. While greater LM is associated with higher BMD, the association between FM and BMD is less clear. Such relationships warrant further investigation, especially in Asians, who have a higher risk of metabolic diseases and osteoporotic fractures compared to Western populations. This study investigated the associations of LM, FM, and modifiable risk factors with BMD in Asian women aged 18-45 yr. A total of 191 women from the Singapore Preconception Study of Long-Term Maternal and Child Outcomes (S-PRESTO) cohort study underwent DXA scanning at the first study visit for BMD and body composition measurements. LM, FM, and four body composition phenotypes derived from dichotomizing LM and FM were related to cohort-specific Z-scores of BMD at FN (BMD_{FN}), LS (BMD_{LS}), and whole body (BMD_{WB}). Adjusting for covariates, LM showed positive associations with Z-BMD_{FN}, [β (95%CI)], [0.38 (0.22, 0.55)], Z-BMD_{LS} [0.43 (0.25, 0.62)], and Z-BMD_{WB}, [0.63 (0.44, 0.81)]. Fat mass by contrast showed an inverse association only with Z-BMD_{WB}, [−0.39 (−0.58, −0.20)]. Compared to women with healthy body composition (higher LM-lower FM), women with lower LM-higher FM had similar BMI, mean (SD) 20.9 (1.5) kg/m^2 but

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disproportionately higher percent fat, 38.4 (2.2%), and lower Z-BMD_{FN} [−0.58 (−0.97, −0.18)], Z-BMD_{LS} [−0.41 (−0.81, 0.00)], and Z-BMD_{WB} [−0.66 (−1.06, −0.25)]. Chinese women had lower BMD than Malay women. Physical activity and education attainment were positively, while the age of menarche was negatively associated with BMD. These findings in young women underscore the importance of early interventions recognizing ethnic differences in BMD to improve lifecourse musculoskeletal health. Most importantly, intervention strategies for Asian women should focus on healthy body composition beyond BMI, with a goal to preserve or increase LM.

Keywords: osteoporosis, sarcopenia, general population studies, human association studies, lean mass, Asian women

Lay Summary

The relationships between fat mass (FM), lean mass (LM), and bone mass are complex with significant implications for obesity, frailty, and bone fractures later in life. While greater LM is recognized to be associated with higher BMD, a measure of bone mass, higher adiposity measured by BMI has been conventionally shown to be associated with BMD. This study investigated these complex relationships in young Asian women, the population with a higher risk of metabolic diseases and osteoporotic fractures compared to those of Western populations. Among these young women aged 18-45 yr, ethnic variations in BMD were observed with Chinese women having a lower BMD than Malay women. Among Chinese women, women with lower LM had lower BMD regardless of level of adiposity. Women who were physically more active and who had higher educational attainment had higher BMD. These findings in young women underscore the importance of early interventions recognizing ethnic differences in BMD to improve lifecourse musculoskeletal health. Most importantly, intervention strategies for Asian women should focus on healthy body composition beyond BMI, with a goal to preserve or increase LM.

Introduction

Obesity and osteoporosis present enormous global health and economic challenges with their escalating prevalence rates along with an aging population.[1] Osteoporosis, which is characterized by low BMD and poor bone microarchitecture, is the most common skeletal disorder in aging populations. Globally almost 9 million osteoporotic fractures are reported annually, and the number is expected to surge further. The prevalence of osteoporotic hip fractures worldwide is projected to escalate from 26% in 1990 to nearly 50% in 2050 with more than half of these fractures expected to occur in Asia.[2,3]

The relationships between the major components of body composition, that is, lean mass (LM), fat mass (FM), and bone mass are complex with significant implications for obesity, sarcopenia, frailty, and osteoporosis later in life. While LM correlates positively with BMD, the association between FM and BMD is less clear. Obesity, conventionally defined by higher BMI, has been suggested to be associated with higher BMD mediated via greater mechanical loading[4] and, in women, by promoting osteoblastic activity through greater estrogen levels.[5,6] However, the association between BMI and BMD varies according to geographical location, ethnicity and skeletal sites. While higher BMI has been associated with higher BMD of the femur, lower BMI is shown to be linked to higher BMD at other bone sites.[7,8] In Chinese populations with lower BMD at the FN (BMD_{FN}), a higher BMD at the LS (BMD_{LS}) has been reported compensating for smaller bone size through differences in hip geometry and microstructural skeletal organization.[8] Recent epidemiological studies have suggested that obesity, type 2 diabetes, and metabolic syndrome are associated with lower bone strength and a higher risk of fracture challenging the traditional view of a positive association between BMI and BMD.[9–11] These controversial findings reflect the complex nature of the association between adiposity and bone health. However, BMI is a crude measure of adiposity and masks the contribution of the individual LM and FM compartments. On the contrary, LM is recognized as a strong determinant of bone accrual over the life course. Lower whole-body LM and lower appendicular skeletal muscle mass index (ASMI) coexist with low BMD[12] and are often associated with falls and functional disability in aging population.[13] The complex interplay between LM and FM with bone health is not fully understood and warrants further investigation.[14] Such data are sparse in younger populations, especially in Asians, who are recognized to have unique thin-outside-fat-inside body composition phenotypes (Asian phenotype), higher metabolic risk at similar BMI, and greater incidence of osteoporotic fractures compared to Western populations.[15]

Singapore is one of the countries with the highest prevalence of osteoporotic hip fractures in the world.[16] Ethnic and sex differences in BMD have been reported in individuals over 50 yr of age in the three major ethnic groups in Singapore, Chinese (74.3%), Malay (13.5%), and Indians (9%). Chinese compared to Malay and Indians, and women compared to men, have a higher prevalence of hip fractures.[17,18] Women lose bone earlier and at a faster rate. They also go through different life stages, including pregnancy, breastfeeding, and menopause, after which bone loss accelerates over time. Most importantly, bone density trait of women is heritable and hence can pass down to their offspring. However, current research on bone health focuses primarily on prevention, diagnosis, and treatment of osteoporosis in older age. There is a scarcity of research aimed at better understanding of the epidemiology of bone health in early adulthood. Hence, to address these critical knowledge gaps, this study aimed to simultaneously evaluate the associations between major components of body composition (ie, FM and LM) with BMD and to determine the factors associated with BMD in Asian women of reproductive age.

Materials and methods

Study population

Participants were a subset of women from the Singapore Preconception Study of Long-Term Maternal and Child Outcomes (S-PRESTO), a longitudinal cohort study.[19] The S-PRESTO study recruited 1039 women of Chinese, Malay, Indian, or mixed ethnicity aged 18-45 yr between February 2015 and October 2017 at a preconception clinic in KK Women's and Children's Hospital in Singapore. Women who had been actively trying to conceive for more than 18 mo, who were currently pregnant, or who were using oral or implanted contraception at the time of recruitment were excluded from the study. Details of inclusion and exclusion criteria for S-PRESTO study have been previously presented.[19] A total of 191 women of Chinese, Malay, and Indian ethnicity consented to undergo DXA scans at a preconception study visit. Women with mixed ethnicity were excluded from these analyses.

Ethics approval

This study was approved by the Central Institutional Review Board of SingHealth (CIRB2019/2143). All women gave voluntary written informed consent.

Study measurements

During the first study visit at preconception, detailed sociodemographic data, such as ethnicity, age, age at menarche, education attainment, obstetric and medical history, occupation, and lifestyle behaviors such as dietary habits, physical activity, smoking, and alcohol intake were collected using interviewer-administered questionnaires. Participants reported the frequency and duration of their light-moderate, moderate, and vigorous intensity physical activities to which an absolute metabolic equivalent of task (MET) value was assigned. Total physical activity intensity in MET hours per week was calculated by multiplying total hours spent on a specific intensity per week with its corresponding MET value.[20] Dietary dairy score was one of the 11 components of the modified healthy eating index for pregnant women in Singapore (HEI-SGP).[21] This dairy component measures the adherence to serving recommendations of dietary guidelines with a maximum score of 10. Score-0 is given for no consumption of dairy while a score of 10 is given when serving recommendations were met, and with intermediate scores assigned proportionately for partial adherence.[21] Height and weight were measured in duplicate according to standardized protocol by trained research staff. The average of 2 measurements were taken for analysis. 25OHD concentrations were measured by liquid chromatography/tandem mass spectrometry (Bevital AS, https://bevital.no/vitamin-d/, coefficients of variation 7.2% for D3 and 10% for D2).

DXA scans

Dual energy X-ray absorptiometry scans were undertaken at the Department of Diagnostic and Interventional Imaging, KKH. A Hologic Discovery W DXA scanner, QDR 4500 A, fan-beam densitometer with Apex software version: 13.4.2:7 was used to assess bone mineral content (g), BMD (g/cm^2), and body composition. Quality control assessments were performed by certified technologists using standard protocols. Daily calibration of the densitometer was performed using Hologic phantoms at the beginning of the day before scanning the participants for the day. The daily phantom plots were reviewed to verify that the spine, hip, and whole-body phantom for BMD, BMC, and area values of the scanner were within normal limits. DXA scans of hip, LS, and whole body were performed to measure BMD of FN (BMD_{FN}), LS (BMD_{LS}), and whole body (BMD_{WB}). Cohort-specific Z-scores of BMD (Z-BMD) values were derived to compare the magnitude of associations between risk factors and three bone sites.

Whole-body DXA scans provide total and segmental LM and FM measurements. Total LM assessed by DXA includes whole-body fat free mass components, that is, muscle, organs, and connective tissues except bone mass.[22] Segmental body composition includes LM and FM of the head, arms, legs, trunk, and pelvis. Appendicular skeletal muscle mass (ASM) is the sum of LM of upper and lower extremities, which accounts for approximately three-quarters of whole-body lean muscle mass.[23] Low ASM is the indicator of sarcopenia and a predictive measure of hip fracture.[23] ASM-Index (ASMI), ASM divided by height in meter square (ASM/m^2), is one of the criteria used to define sarcopenia or low muscle mass with the cut-off value of 5.4 kg/m^2 for women according to the 2019 Asian working group of sarcopenia guidelines.[24]

Body composition phenotypes

These phenotypes were derived to examine the differential contribution of LM and FM to BMD. ASMI was dichotomized into lower LM ($<$5.4 kg/m^2) and higher LM ($\geq$5.4 kg/m^2).[24] To dichotomize FM, a threshold of 35% percent body fat (PBF) was used according to the American Association of Clinical Endocrinology/American College of Endocrinology 2004 guideline to define obesity in women.[25] The same threshold (35% PBF) was also reported as the cut-off for prediction of metabolic syndrome in Chinese women in a study including 3916 Chinese adults (58.6% women).[26] Women with PBF $\leq$35% were categorized as "lower adiposity" and those with PBF $>$35% as "higher adiposity." These dichotomized ASMI and adiposity categories were combined to derive 4 distinct body composition phenotypes: higher LM-lower FM, higher LM-higher FM, lower LM-lower FM, and lower LM-higher FM, (Figure S1). Only Chinese women ($N = 139$) were included in the analyses, which included body composition phenotypes, as the number of Malay ($N = 34$) and Indian ($N = 18$) women were small, and these women were not represented across all 4 phenotypes.

Statistics

Differences in the characteristics of participants by ethnicity were determined using ANOVA omnibus F test for normally distributed continuous variables, non-parametric Kruskal–Wallis test for variables not normally distributed, and the chi-square test for categorical variables (Table 1). Based on prior knowledge from the literature, factors that were known to be associated with BMD or potentially influence the associations between LM, FM, and BMD were included in the statistical models described below. These included ethnicities, age, age at menarche, education, MET values for physical activities, serum 25OHD concentrations, and dietary dairy scores. Among these covariates, missing data were minimal; 1 subject for physical activity and only 5% for 25OHD concentration, hence no data imputation was undertaken.

Multiple response regression analyses were performed where cohort-specific Z-BMD of FN, LS, and whole body (responses) were simultaneously regressed on the risk factors, accounting for joint contributions and the correlation among risk factors on the responses. Two multiple response regression models were utilized. In the first model, LM and FM were used as separate body composition components to investigate their associations with BMD (Table 2). BMI was also used to investigate whether its association with BMD in these women was consistent with the findings reported in the previous studies. The rest of the variables used in both models were the same. The estimated regression coefficients and the 95% CIs β (95% CI) are presented in Table 2.

Exploratory multiple response regressions analyses were also performed for women of Chinese ethnicity ($N = 139$), investigating the association of body composition phenotypes, specifically the differential contributions of LM and FM to BMD adjusting for age. Analyses were performed within the software environment R-Studio.[27]

Table 1. Characteristics of study participants.

	N	All 191	Chinese 139 (72.8)	Malay 34 (17.8)	Indian 18 (9.4)	p
Age at recruitment (yr)	191	32 (4)	33 (4)	31 (4)	31 (4)	.101
Age at menarche (yr)		12 (1)	13 (2)	12 (1)	12 (1)	.073
Height (m)	191	1.59 (0.06)	1.60 (0.06)	1.57 (0.06)	1.58 (0.05)	**.029**
Highest education	191					**<.001**
University and higher		111 (58.1)	92 (66.2)	6 (17.7)	13 (72.2)	
Polytechnic/diploma/advanced diploma		71 (37.2)	42 (30.2)	24 (70.6)	5 (27.8)	
Below secondary		9 (4.7)	5 (3.6)	4 (11.8)	0 (0.0)	
Physical activity	190					
Metabolic equivalent of tasks (hr/wk)		24.0 (41.8)	21.6 (34.7)	40.4 (40.6)	51.1 (37.1)	**.007**
Moderate and vigorous activity per week (min)†		120 (0, 270)	80 (0, 180)	310 (79, 653)	120 (0, 375)	**<.001**
Dietary dairy scores†	191	6.9 (4.0, 10.0)	6.2 (3.8, 10.0)	8.2 (4.6, 10)	9.7 (6.1, 10.0)	.069
Body composition	191					
BMI (kg/m^2)		23.5 (4.8)	22.5 (4.0)	26.8 (5.8)	24.5 (6.0)	**<.001**
Fat mass (kg)		21.82 (7.96)	20.23 (6.57)	26.63 (9.43)	25.0 (10.32)	**<.001**
Lean mass (kg)		36.44 (5.91)	36.27 (5.67)	37.86 (7.03)	35.03 (5.27)	.213
Vitamin D concentration (nmol/L)	181	50.88 (16.61)	56.14 (14.3)	34.84 (12.14)	37.89 (14.99)	**<.001**
Deficiency (≤50 nmol/L)		78 (43.1)	38 (28.4)	27 (87.1)	13 (81.3)	**<.001**
Insufficiency (>50 to 75 nmol/L)		89 (49.2)	82 (61.2)	4 (12.9)	3 (18.8)	
Sufficiency (>75 nmol/L)		14 (7.7)	14 (10.4)	0 (0.0)	0 (0.0)	
Areal BMD	191					
Femoral neck BMD (g/cm^2)		0.75 (0.11)	0.74 (0.11)	0.82 (0.10)	0.74 (0.09)	**<.001**
Lumbar spine BMD (g/cm^2)		0.99 (0.11)	0.99 (0.11)	1.05 (0.10)	0.93 (0.11)	**<.001**
Whole-body BMD (g/cm^2)		1.08 (0.08)	1.08 (0.08)	1.13 (0.07)	1.05 (0.08)	**<.001**

Data shown are *N* (%) for categorical variables and mean (SD) and median (IQR) as indicated by † for continuous variables. *p* values were determined with the use of ANOVA omnibus F test for normally distributed continuous variables, non-parametric Kruskal–Wallis test for variables indicated by †, and the chi-square test for categorical variables. Bold text indicates statistical significance i.e., *p* value <0.05.

Table 2. Risk factors associated with bone mineral density at different sites in Asian women of reproductive age.

	Cohort-specific Z-scores of femoral neck BMD aβ (95% CI)	Cohort-specific Z-scores of lumbar spine BMD aβ (95% CI)	Cohort-specific Z-scores of whole-body BMD aβ (95% CI)
Body composition			
Lean mass (kg)	**0.38 (0.20, 0.55)**	**0.43 (0.25, 0.62)**	**0.63 (0.44, 0.81)**
Fat mass (kg)	0.10 (−0.08, 0.28)	−0.03 (−0.22, 0.17)	**−0.39 (−0.58, −0.20)**
Ethnicity			
Chinese	Reference	Reference	Reference
Malay	**0.45 (0.08, 0.83)**	**0.40 (0.01, 0.80)**	**0.73 (0.34, 1.13)**
Indian	−0. 13 (−0.54, 0.28)	**−0.51 (−0.95, −0.08)**	−0.14 (−0.57, 0.30)
Age (yr)	−0.10 (−0.22, 0.02)	0.03 (−0.09, 0.16)	−0.07 (−0.19, 0.06)
Age at menarche (yr)	−0.04 (−0.16, 0.08)	**−0.13 (−0.26, −0.02)**	−0.12 (−0.24, 0.01)
Education			
University and higher	Reference	Reference	Reference
Polytechnic/diploma/advanced diploma	−0.22 (−0.45, 0.01)	−0.16 (−0.40, 0.09)	**−0.30 (−0.54, −0.06)**
Below secondary	0.19 (−0.37, 0.74)	0.38 (−0.21, 0.97)	0.15 (−0.44, 0.74)
Vitamin D: 25-OH cholecalciferol (nmol/L)	−0.00 (−0.14, 0.14)	−0.02 (−0.16, 0.13)	−0.01 (−0.16, 0.14)
Physical activity (MET hr/wk)	**0.21 (0.09, 0.33)**	0.10 (−0.02, 0.23)	0.08 (−0.04, 0.21)
Dietary dairy score	0.07 (−0.05, 0.19)	0.07 (−0.06, 0.20)	0.12 (−0.01, 0.24)

Abbreviations: 25-OH cholecalciferol, 25-hydroxy cholecalciferol; aβ, adjusted beta-coefficient; MET, metabolic equivalent of task. aβs and 95% CIs were derived from multiple response regression analyses with cohort-specific Z-scores of femoral neck, lumbar spine, and whole body as the dependent variables, and the joint contributions of lean mass and fat mass, ethnicity, age on the day of DXA scan, age at menarche, education, vitamin D concentrations, physical activity and dietary dairy scores as the independent variables. Values in bold indicate the significant associations between the risk factors and cohort-specific Z-scores of BMD.

Results

A total of 139 (72.8%) Chinese, 34 Malay (17.8%), and 18 Indian (9.4%) women were included in this study (Table 1). Mean (min-max) of Z-scores of FN (generated by manufacturer) were −0.49 (−2.50, 2.60), 0.26 (−1.40, 2.50), and −0.48 (−2.60, 0.90) for Chinese, Malay, and Indians, respectively. Mean (min-max) of Z-scores of LS (generated by manufacturer) were −0.05 (−2.10, 2.30), 0.56 (−0.70, 2.80), and −0.56 (−2.90, 2.80) for Chinese, Malay, and Indians, respectively. Six Chinese and two Indian women had BMD_{FN} z-scores (manufacturer generated) −2.0 or lower which is defined as "BMD lower than expected" for women prior to menopause according to the recommendation by the International Society for Clinical Densitometry (ISCD).[28] There were 1 Chinese and 2 Indian women with Z-scores $BMD_{LS} \leq -2.0$. Malay women did not have Z-scores BMD ≤ −2.0 either at FN or LS.

The characteristics of the study participants are described in Table 1. In general, Chinese women were older at the time of the study visit and older at menarche, were taller and had

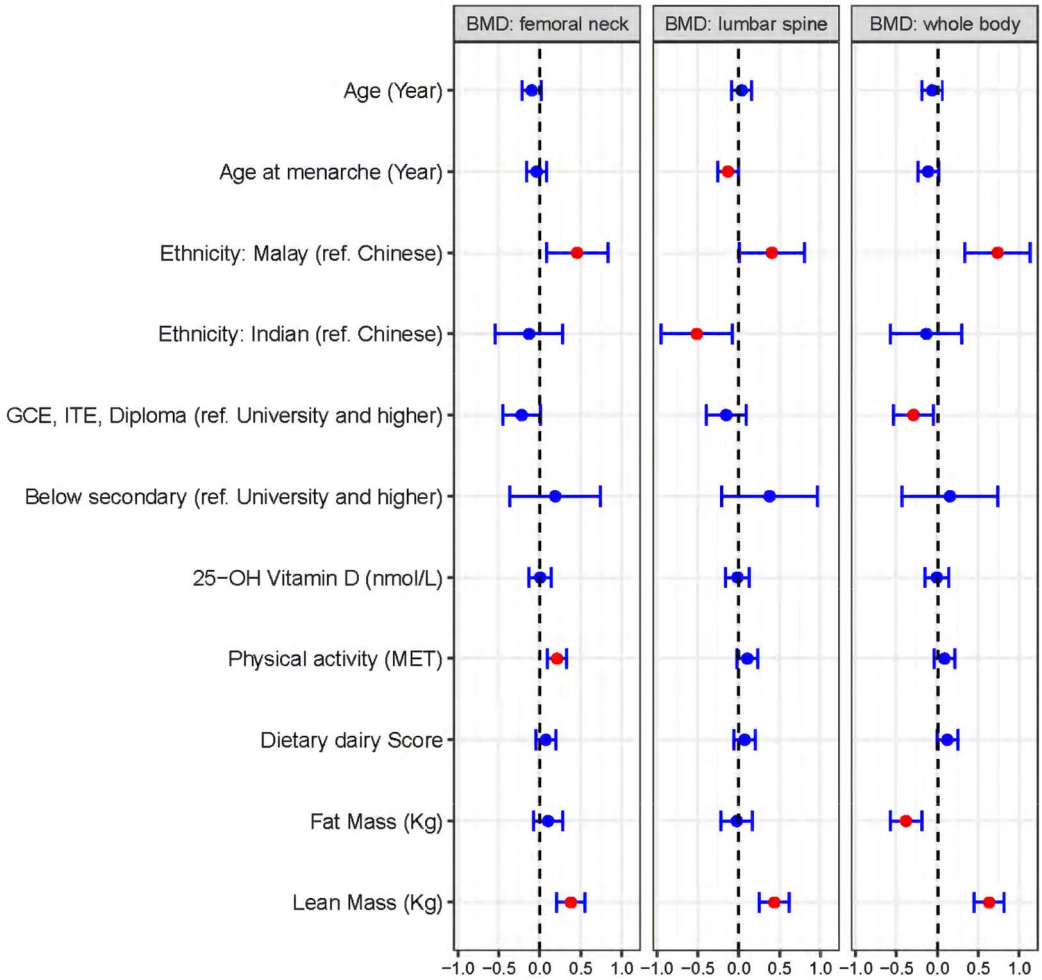

Figure 1. Joint contribution of risk factors related to BMD of femoral neck, lumbar spine, and whole body. The x-axis shows the adjusted β coefficients (aβ) of cohort-specific Z-scores of BMD based on the multiple response regression analysis. The dots indicate the adjusted ß which is the effect size and the error bars represents the corresponding 95% confidence interval. The y-axis shows risk factors that jointly contributed to BMD of femoral neck, lumbar spine, and whole body.

lower BMI and lower consumption of dairy products, and were less physically active especially moderate to vigorous physical activity compared to Malay and Indian women. Malay and Indian women had higher FM when compared to Chinese women. Malay women had higher LM than women of the other 2 ethnic groups. Only 7.7% of 191 women had sufficient 25OHD concentration (>75 nmol/L) and all these women were of Chinese ethnicity. Malay and Indian women had either insufficient (>50 to 75 nmol/L) or deficient (≤50 nmol/L) 25OHD concentrations (Table 1).

Contribution of LM and FM to BMD

When the individual contribution of LM and FM to BMD were examined in the same multiple response regression model (Table 2), LM was positively associated with BMD at all 3 sites: β [95% CI], Z-BMD_{FN} [0.38 (0.22, 0.55)], Z-BMD_{LS} [0.43 (0.25, 0.62)], and Z-BMD_{WB} [0.63 (0.44, 0.81)]. On the other hand, FM was negatively associated with Z-BMD_{WB} [−0.39 (−0.58, −0.20)] (Table 2, Figure 1). When BMI was used as a combined measure of LM and FM, BMI showed a positive relationship with BMD: β [95% CI] were [0.39 (0.26, 0.52)], [0.34 (0.20, 0.48)], and [0.16 (0.02, 0.31)] for Z-BMD_{FN}, Z-BMD_{LS}, and Z-BMD_{WB}, respectively.

Risk factors associated with BMD

Ethnic variations in BMD at different bone sites were observed (Table 2). Compared to Chinese women, Malay women had higher Z-BMD_{FN}, β (95% CI), 0.45 (0.08, 0.83), Z-BMD_{LS} 0.40 (0.01, 0.80), and Z-BMD_{WB} 0.73 (0.34, 1.13). Indian women had significantly lower Z-BMD_{LS} −0.57 (−1.01, −0.12) than Chinese women. The older age of menarche was associated with lower Z-BMD_{LS} −0.13 (−0.26, −0.02).

Physical activity (MET hours per week) was positively associated with Z-BMD_{FN} [0.21 (0.09, 0.33)]. Higher dietary dairy scores appeared to be associated with higher Z-BMD_{WB} with the variability in associations reflected by wide 95% CI 0.14 (−0.01, 0.24) in these women (Figure 1 and Table 2). Compared to women who had higher educational attainment (university and above), women with diploma or technical education had significantly lower Z-BMD_{WB} −0.30 (−0.54, −0.06) and marginally lower Z-BMD_{FN} −0.22 (−0.45, 0.00). Although similar trend of association between women with higher educational attainment and women of secondary or lower education, the associations were not significant which may be attributed to the low numbers of women with secondary and below education ($N = 9$). 25OHD was not associated with BMD.

Table 3. Bone mineral density of different sites by body composition phenotypes in Chinese women.

	N (%)	BMI (kg/m^2) Median (IQR)	Cohort-specific Z-scores of femoral neck BMD aβ (95%CI)	Cohort-specific Z-scores of lumbar spine BMD aβ (95%CI)	Cohort-specific Z-scores of whole-body BMD aβ (95%CI)
Higher LM-lower FM	43 (30.9)	20.5 (19.3, 21.6)	Reference	Reference	Reference
Low LM-lower FM	16 (11.5)	17.5 (16.9, 19.0)	**−0.71 (−1.17, −0.26)**	**−0.74 (−1.21, −0.27)**	**−0.65 (−1.11, −0.18)**
Higher LM-higher FM	59 (42.4)	25.0 (23.3, 27.4)	**0.37 (0.14, 0.61)**	**0.31 (0.07, 0.55)**	0.17 (−0.07, 0.41)
Low LM-higher FM	21 (15.1)	21.0 (20.1, 22.0)	**−0.58 (−0.97, −0.18)**	−0.41 (−0.81, 0.00)	**−0.66 (−1.06, −0.25)**

Abbreviations: aβ, adjusted beta-coefficient; FM, fat mass; LM, lean mass. aβs and 95% CIs were derived from multiple response regression analyses with cohort-specific Z-scores of femoral neck, lumbar spine, and whole body as the dependent variables, and the joint contributions of body composition phenotypes (the reference healthy body composition group (higher LM-lower FM)) and age on the day of DXA scans as the independent variables. Values in bold font indicate the significant associations between body composition phenotypes and cohort-specific Z-scores of BMD.

Differential contribution of LM and FM to BMD

There were 80 (67.5%) Chinese women with PBF >35% and 37 (26.6%) with low muscle mass (ASMI < 5.4 kg/m^2). Women were categorized into 4 distinct body composition phenotypes: higher LM-lower FM, *N* (%), 43 (30.9%), higher LM-higher FM 59 (42.4%), lower LM-lower FM 16 (11.5%), and lower LM-higher FM 21 (15.1%) (Figure S1). Mean (SD) of BMI of the women in these groups were 20.6 (1.6), 25.7 (3.8), and 17.9 (1.3), and 20.9 (1.5) kg/m^2, respectively. Women with lower LM-higher FM had comparable BMI to women with higher LM-lower FM. Women with lower LM-higher FM had comparable PBF (%), 38.4 (2.2%) to women with higher LM-higher FM, 39.3 (2.8%) despite having lower BMI.

Further exploratory analyses were performed to determine the differential contribution of LM and FM to BMD using body composition phenotypes (Table 3). Higher LM-lower FM phenotype was considered to have healthy body composition and was therefore used as the reference group. Compared to the reference group of women with high LM-lower FM, women with low LM, regardless of the degree of adiposity, that is, both lower LM-lower FM and lower LM-higher FM phenotypes, had lower Z-BMD$_{FN}$, Z-BMD$_{LS}$, and Z-BMD$_{WB}$. Women with higher LM-higher FM had higher Z-BMD$_{FN}$, and Z-BMD$_{LS}$ compared to the reference group of women with high LM-lower FM (Table 3).

Discussion

In this study of young Asian women, higher LM was associated with higher BMD$_{FN}$, BMD$_{LS}$, and BMD$_{WB}$, while higher FM was associated with lower BMD$_{WB}$. Ethnic variation in BMD were observed, with Chinese women having a lower BMD than Malay women. Among Chinese women, regardless of lower or higher adiposity, women with lower LM had lower BMD. Women who were physically more active, and who had higher educational attainment had higher BMD.

Our findings of positive associations between LM and BMD are consistent with the observations from recent studies that identified LM as the main determinant of BMD.[29–32] In general, a change in one SD of BMD is suggested to be associated with a 10% change in total BMD.[33] In older populations, a 2%-6% increase in BMD$_{FN}$ was reported to be associated with 16%-40% reduction in fracture risk.[33] Therefore, our observations of higher BMD at different skeletal sites ranging between 0.3 and 0.7 SD per 1 kg increase in LM could translate to a substantial reduction in fracture risk. On the other hand, we did not find any association between FM and BMD in the weight bearing femur, and LS except an inverse association between FM and BMD$_{WB}$. These observations further substantiate that it is LM and not FM that had a positive association with BMD in these young Asian women. Evidence on the contribution of FM or adiposity to BMD has been mixed in previous studies and these associations can be skeletal-site dependent. Many previous studies suggested that obesity is protective against osteoporosis and fracture risks[4] through greater mechanical loading and in women, through estrogen.[5,6] However, a meta-analysis of more recent prospective cohorts from 25 countries showed that high BMI in women was a risk factor for upper arm and other fractures, while low BMI was a risk factor for hip fracture, but was protective for other osteoporotic fractures.[7] A multinational, prospective, population-based observational study of 60 393 women aged 55 yr and older also reported that obesity is a risk factor for ankle and upper leg fractures.[34] Several potential mechanisms underlying the association between obesity and lower BMD have been proposed in recent studies. Obesity impairs glucose metabolism[35] and increases the production of inflammatory cytokines from adipose tissues which interfere with bone formation,[36,37] thus negatively influencing overall bone health.[38] In addition, fat deposition in muscles as a consequence of obesity leads to poor muscle quality and strength which may impose a negative impact on bone health.[39,40]

In our exploratory analyses in Chinese women, women with higher LM-higher FM had higher BMD compared to the reference group (women with higher LM-lower FM) and women with lower LM regardless of having lower or higher FM. We observed nil associations between FM with BMD$_{FN}$ and BMD$_{LS}$, and an inverse association with BMD$_{WB}$, these findings all together suggest that higher BMD in women with higher FM is likely due to the higher LM rather than FM. Tracking body composition in these young women is essential given the potential long term detrimental consequences of high adiposity on bone health, muscle quality, and function. These observations underscore the complex relationship between LM, FM, and BMD, which is the measurement of bone mass. Understanding such relationships is important in Asian women as Asians are recognized to have lower BMD and a higher risk of metabolic diseases at similar BMI, compared to Western populations. Moreover, Asians are known to have unique "thin outside-fat inside" phenotype.[41,42] Having clinically lower LM (ASMI < 5.4 kg/m^2) at reproductive age reflects that they may carry a higher risk of developing sarcopenia and osteoporosis later in life. More

importantly, women with lower LM-higher adiposity may indicate probable sarcopenic-osteopenic obesity phenotype and linked to elevated risk of developing not only sarcopenia and osteoporosis, but also metabolic diseases. The observation that over one quarter of the young Asian women in this study were of lower LM is concerning. These findings highlight that "healthy BMI" is insufficient to identify the risk of chronic metabolic diseases among Asian women. Women with lower LM-higher FM have comparable PBF to women of higher BMI while their BMI was similar to that of women with a healthy body composition. Hence, these women with lower LM-higher FM are unlikely to be identified by healthcare professionals due to a lean phenotype, potentially obscuring the need for earlier screening and intervention. Therefore, focusing on a "healthy body composition," that is, healthy range of FM and LM, is far more effective than BMI, specifically in identifying individuals at higher risk of osteoporosis and metabolic disease.

We observed ethnic differences in BMD in these young Asian women, with lower BMD in Chinese women compared to Malay women. This observation is consistent with the findings in previous studies in Singapore that showed the highest prevalence of osteoporotic hip fractures among Chinese women and the lowest among Malay women ≥50 yr.[18,43] Chinese women in this study exhibited several characteristics associated with established risk factors of lower BMD, including a later onset of menarche, lower BMI, reduced physical activity, and lower consumption of dairy products. Notably, majority of Chinese women in this study had higher educational attainment, which may contribute to their sedentary lifestyle, as observed in previous studies in Singapore. The Chinese women also spent less time particularly on moderate and vigorous physical activity compared to the two other ethnic groups.[44] Their predominantly sedentary white-collar occupations, long working hours, and limited time for non-work-related activities, including physical activity, may also partly explain their lower BMD. Dietary patterns may also play a role in the lower BMD observed in Chinese women. Lower dairy consumption in Chinese women can be attributed to 2 primary factors. Firstly, traditional Chinese diets rarely consist dairy ingredients, such as milk, yoghurt, or cheese.[45] The Singapore's Total Diet Study (2021-2023) showed that Chinese individuals consumed less milk and dairy products compared to Malay and Indian individuals.[46] Furthermore, the high prevalence of lactose intolerance in South-East Asia and among Chinese individuals may lead to reduced or avoidance of dairy consumption, potentially affecting calcium intake and, subsequently, BMD. Collectively, these factors may contribute to the lower BMD observed in Chinese women in this study. These findings highlight that Chinese women in particular may improve their musculoskeletal health through healthy behavioral changes such as engaging health enhancing moderate and vigorous physical activity and increasing dairy consumption.

None of the Malay women in this study had sufficient 25OHD concentrations; 87% had deficiency and 13% had insufficiency. BMD at all three skeletal sites was, however, higher in Malay women than in Chinese women regardless of them having vitamin D insufficiency. However, this finding is aligned with those from previous studies in Singapore.[47,48] While vitamin D is well recognized to reduce bone resorption, lower risk for subsequent bone loss and osteoporotic fractures,[49,50] conflicting results have been reported in the associations between vitamin D and BMD in young women.[51,52] These observations suggest further studies are needed to investigate the role of vitamin D on bone health and potential underpinning mechanisms in this population. On the other hand, Indian women in this study had similar BMD_{FN} and BMD_{WB} but lower BMD_{LS} than Chinese women. However, in another study of women aged 45-69 yr in Singapore, Indian women had higher BMD_{FN} and similar BMD_{LS} compared to Malay and Chinese women.[48] Such differences in BMD observed in younger women in this study vs older women in the previous study of Indian ethnicity may indicate that the rate of bone loss may be slower with aging in Indian women compared to Malay and Chinese women. However, the number of Indian women in this study ($N = 18$) was small and these observations may be due to chance. Caution is thus warranted in interpreting these findings in Indian women.

Our study has several strengths. Bone health in Asian women of reproductive age is one area that has not widely been studied. Extensive demographic and lifestyle factors including physical activity and diet were comprehensively collected in this study. The major components of body composition, LM, FM, and bone mass were measured by "gold standard" DXA scans. Capturing a wide range of these measures in detail enabled us to examine complex relationships. In addition, we used a statistical approach considering the relationship between BMD at 3 different sites and potential predictors in the same model. The young women in this study were recruited from the general population and did not have major illnesses. Therefore, the findings in relation to unique body composition phenotypes and BMD help to identify at-risk stratification to develop early intervention strategies at a population level. This study has some limitations. First, it is a cross-sectional observation study in a modest sample. Therefore, our results cannot identify a causal relationship between determinants and BMD and may not be generalizable to the larger population in Singapore or other populations. In particular, the number of Indian women studied was small and caution is needed in interpreting the results in this ethnic group. However, the findings from this study, especially the contribution of LM to BMD and the ethnic differences in BMD, were consistent with other larger studies conducted in Singapore and in other populations of older age or wide-age range groups of women.

Bone health across lifespan is highly relevant as osteoporosis is one of the most prevalent skeletal disorders with aging and osteoporotic fractures represent a major public health burden with enormous societal and economic consequences.[2,3] Even though most individuals reach their peak bone mass between the age of 25 and 30 yr, existing studies have generally focused on bone loss later in life. Identifying determinants and risk factors of bone health and early interventions is of pivotal public health and clinical significance not only for the women themselves but also for the next generations due to heritability of bone density traits. Findings from the present study suggest that intervention strategies should focus on healthy body composition with a goal to preserve or increase LM from a younger age while reducing BMI. The observations from this study shed light on the limited information on epidemiology of bone health in women of reproductive age and modifiable factors which may aid to devise strategies for early intervention well before the development of osteoporosis.

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Supplementary material

Supplementary material is available at *JBMR Plus* online.

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Conflicts of interest

M.T.T., A.C., M.K.S.L., N.P., S.B.A., J.S.L., J.Y.B., P.D.G., F.M.-R., C.Z., M.D.I., and J.G.E. declare no potential conflict of interest that might bias the submitted work and no other relationships or activities that could appear to have influenced the submitted work.

Data availability

Some or all datasets generated during and/or analyzed during the current study are not publicly available but are available from the corresponding authors (J.G.E., M.T.T.) on reasonable request.

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