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Differences in bone mineral density, bone mineral content, and bone areal size in fracturing and non-fracturing women, and their interrelationships at the spine and hip

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Abstract Osteoporotic fractures are a major public health problem, particularly in women. Bone mineral density (BMD), bone mineral content (BMC), and bone size have been regarded as important determinants of osteoporotic fractures. In 1449 women over age 30 years, we studied the detailed relationship, at the spine and hip, between BMD, BMC, and bone areal size (all measured by dual-energy X-ray absorptiometry) and compared their relative magnitudes in fracturing and non-fracturing individuals. We find that, (1) BMD and BMC are significantly higher at the spine and hip in non-fracturing women. Bone areal size is significantly larger at the spine in non-fracturing women; however, the significance disappears when adjustment is made for the significant difference of height (stature) between fracturing and non-fracturing women. In contrast to the spine, bone areal size is always significantly *larger* in fracturing women at the hip. (2) The relationship among BMD, BMC, and bone areal size is different at the spine and hip. Specifically, at the spine, BMD increases with bone areal size linearly. At the hip, BMD has a quadratic relationship with bone areal size, so that BMD increases at lower bone areal sizes, then (after an intermediate zone of values) decreases with increasing bone areal size. However, BMD adjusted for BMC always decreases with increasing bone areal size, as expected by the definition of BMD. With no adjustment for BMC, the increase in BMD with bone areal size is due to a more rapid increase of BMC than increasing bone areal size, thus explaining the observations of association of both larger BMD and larger bone areal size with stronger bone. (3) At the spine, 86.2% of BMD variation is attributable to BMC and 12.6% to bone areal size. At the hip, 98.0% of BMD variation is due to BMC and 1.1% due to bone areal size. The current study may be important in understanding the relationship among BMD, BMC, and bone size as risk determinants of osteoporotic fractures.

Key words bone size · BMD · BMC · DEXA · osteoporotic fractures

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Introduction

Osteoporosis results in more than 1.3 million fractures per year in the United States, with an estimated direct cost of 13.8 billion dollars in 1995 [1]. Bone mineral density (BMD), bone mineral content (BMC), and bone size are important risk determinants for osteoporotic fractures [2–9]. Patients with osteoporotic fractures have reduced BMD and BMC compared with non-fracturing controls [2–4]. Patients with spine fractures have reduced bone size [6,8,9]. A deficit in bone size may partly account for both the increased bone fragility and the deficit in BMD and BMC compared with age-matched controls [5]. Bone loss associated with aging may be offset partially by an increase in bone size, tending to preserve bone strength [7–11].

BMD is the ratio of BMC to bone size. Thus, simply *by this mathematical definition alone*, the larger the bone size, the smaller the BMD should be under constant BMC. This expectation seems to create an apparent conflict with previous findings that larger bone sizes and higher BMD values are both associated with stronger bone [2–10]. Although BMD, BMC, and bone sizes have all been studied individually as risk factors for osteoporotic fractures, the relationship among these phenotypes is unclear. For example, we do not know how much variation in BMD, as a composite phenotype, is attributable to variations in the component phenotypes BMC and bone size. We lack data on the interrelationship between BMD, BMC, and bone size. Further, we do not know whether the relationships among BMD, BMC, and bone size are similar across various skeletal sites. In addition, the relative magnitudes of bone size in fracturing and non-fracturing groups are compared in many studies without adjusting for important covariates, such as age, height, and/or weight [5,6,8–11]. These important covariates may differ significantly among fracturing and non-fracturing groups. Whether or not we adjust for these important

covariates may lead to quantitatively, or even qualitatively, different conclusions, as will be shown in this study. The conclusion that larger bone is stronger is largely obtained from studies of the spine [5,6,8–10]. Whether this conclusion is general across skeletal sites needs to be examined.

Our purposes here are largely twofold. First, we will compare BMD, BMC, and bone areal size at the spine and hip between fracturing and non-fracturing female groups. Second, we will investigate the detailed relationship among BMD, BMC, and bone areal size at the spine and hip in women and quantify the percentage of variation of BMD, as a composite phenotype, that can be attributable to the component phenotypes, BMC and bone areal size. This study should aid in understanding the interrelationship among BMD, BMC, and bone size as risk determinants of osteoporotic fractures.

Subjects and methods

Subjects

Extensive data for 1449 women came from study subjects who participated in various projects conducted, or being conducted, during the past decade at the Osteoporosis Research Center (ORC) of Creighton University. We have obtained data on BMD, BMC, and bone areal size at the spine and/or hip, along with atraumatic fracture status ascertained through questionnaire during studies for individual projects. Among these female subjects, 1081 were ascertained for general fracture status at the hip, spine, ankle, elbow, humerus, clavicle, pelvis, and wrist, etc., without specific fracture type identified. From here on, we will refer to these subjects collectively as the "all-fracture study group". Unless otherwise specified as hip fractures, fractures will refer to all those fracture types ascertained. Three hundred sixty-eight additional subjects were ascertained specifically for hip fracture status only, and these subjects will be referred to collectively as the "hip-fracture study group". The hip-fracture study group was studied so that the finding (see Results section) that the hip bone areal size is larger in fracturing individuals is not confounded by the non-specificity of identification of fracture types in the all-fracture study group. All the subjects are Caucasian and were at least 30 years of age at the time the measurements were taken. Some of the studies from which some of the subjects come from have been reported [12–19] and others are in preparation for publication [20]. All of the individual studies were approved by the Creighton University Institutional Review Board. All the study subjects signed informed-consent documents before entering the individual projects.

Measurement

BMD, BMC, and bone areal size of spine and hip were measured by a Hologic 1000, 2000+, or 4500 scanner (Hologic, Waltham, MA, USA). Measurement of bone phenotypes in the ORC has been documented in detail in our previous studies [12–17]. Briefly, all the dual-energy X-ray absorptiometry (DEXA) machines are calibrated daily, and long-term precision is monitored with external spine and hip phantoms. We maintain constant quality assurance procedures that track potential confounding events, such as X-ray tube replacement, arm realignments, collimator changes, and software version updates. Technicians maintain scan-by-scan surveillance for quality control. For the spine, our quantitative phenotype is for the combined measurements of L_1–L_4. For the hip, it is the combined phenotypes of the femoral neck, trochanter, and intertrochanteric region. All DEXA machines report BMD in grams per square centimeter (g/cm^2), BMC in grams and bone size as area measurements in square centimeters (cm^2). Usually, for the hip, the non-dominant body side is measured. The coefficient of variation (CV) across the scanners for measurements of BMD, BMC, and bone areal size were, respectively, 1.28%, 1.74%, and 1.11% for the spine and 1.36%, 2.51%, and 1.94% for the hip. Height and weight are measured and age ascertained on the same visit at which the bone areal size measurements are taken. Measurement by different machines for various subjects will introduce a source of random errors in subsequent statistical analyses and render our tests less powerful. Hence, significant results found from our statistical analyses should be conservative and thus robust. In addition, although our phenotype measurements are from different models of the Hologic DEXA machines, the measurements are actually highly comparable (see Appendix A).

DEXA has been the most commonly used technique to assess bone phenotypes (BMD, BMC, and bone areal size) in epidemiological studies. It involves relatively weak radiation and provides shortened scan times, enhanced image definition, and improved precision compared with dual-photon absorptiometry [21]. Another significant advantage of DEXA is the relative stability of calibration in clinical use [22,23]. DEXA has been an accepted method for measuring bone size, with the advantages of relatively low cost and small radiation dose [24,25,28,37,38]. Areal bone size (in cm^2) measured by DEXA, may be used to approximate volumetric bone size in cubic centimeters (cm^3) by a transformation of 3/2th power [28,38]. This approximation needs a crucial assumption of cylindrical bone shape, which is only crude at the spine and not applicable to the hip at all. Our analyses, not shown here, found that our conclusions reached in this study were not changed by the

approximation of volumetric bone size with areal bone size. In addition, the unmeasured bone depth has an effect on bone size measurement. Therefore, we retained the original areal bone size measurement by DEXA as our study phenotype. Volume, area, and length (or diameter) are all legitimate measures of bone size in different dimensions, and thus all deserve individual studies.

Statistical analyses

The basic characteristics of the subjects in the all-fracture study group and the hip-fracture study group are summarized and are available from the authors upon request. Unless otherwise specified, the following analyses were performed for each of the two groups, respectively, for comparison. We compared the basic characteristics between fracturing and non-fracturing subjects (Table 1) with *t*-tests. Multiple regression analyses were performed, using BMD, BMC, and bone areal size at the spine and hip as the dependent variables, respectively, and age, height, and weight as predictor variables (Table 2). BMD, BMC, and bone areal size were then compared, with *t*-tests, after adjusting for significant covariates of age, height, and/or weight (Table 3), by multiple regression. Because the all-

Table 1. Comparison of basic characteristics in fracturing and non-fracturing women

Fracture status	Age (years)	Height (m)	Weight (kg)	Spine BMD (g/cm^2)	Spine BMC (g)	Spine Area (cm^2)	Hip BMD (g/cm^2)	Hip BMC (g)	Hip Area (cm^2)
All-fracture study group									
Non-fracture	63.47 (9.82) [752]	1.61 (0.06) [741]	68.91 (15.01) [741]	0.90 (0.17) [656]	51.42 (12.97) [656]	56.51 (6.39) [656]	0.79 (0.15) [751]	26.44 (5.38) [751]	33.36 (3.04) [751]
Fracture	70.06 (8.26) [86]	1.59 (0.06) [84]	64.20 (11.85) [84]	0.79 (0.12) [78]	43.46 (9.43) [78]	54.79 (6.64) [78]	0.68 (0.12) [85]	23.18 (4.61) [85]	34.25 (3.54) [85]
t-Test *P* value	0.0000	0.0010	0.0010	0.0001	0.0001	0.0258	0.0000	0.0000	0.0269
Hip-fracture study group									
Non-fracture	50.06 (13.58) [359]	1.64 (0.07) [357]	69.67 (14.99) [358]				0.85 (0.15) [359]	28.15 (6.04) [305]	32.98 (3.22) [305]
Fracture	69.18 (18.54) [9]	1.59 (0.11) [9]	66.19 (15.61) [9]				0.61 (0.19) [9]	22.92 (7.14) [9]	37.14 (3.49) [9]
t-Test *P* value	0.003	0.08	0.49				0.005	0.06	0.0001

Within each cell with three numbers, data values are the means, the standard deviations (numbers in parentheses), and the sample sizes (numbers brackets)
BMD, Bone mineral density; BMC, bone mineral content

Table 2. Results of multiple regression and *P* values of the partial regression coefficient of age, height, weight, and adjusted R^2

Regression	Age	Height	Weight	Adj. R^2
The all-fracture study group				
Spine				
BMD = 0.652 − 0.004age + 0.15height + 0.004weight	0.000	0.071	0.000	0.261
BMC = −36.9 − 0.243age + 54.5height + 0.229weight	0.000	0.000	0.000	0.308
Bone size = −29.5 + 0.0003age + 53.2height + 0.002weight	0.986	0.000	0.855	0.339
Hip				
BMD = 0.691 − 0.005age + 0.051height + 0.004weight	0.000	0.435	0.000	0.337
BMC = −13.7 − 0.0519age + 19.9height + 0.162weight	0.000	0.000	0.000	0.372
Bone size = −14.1 + 0.125age + 23.6height + 0.023weight	0.000	0.000	0.000	0.288
The hip-fracture study group				
Hip				
BMD = 0.867 − 0.006age − 0.051height + 0.0049weight	0.000	0.594	0.000	0.466
BMC = −14.5 − 0.105age + 21.4height + 0.184weight	0.000	0.000	0.000	0.446
Bone size = −16.5 + 0.099age + 26.4height + 0.021weight	0.000	0.000	0.043	0.343

Table 3. Comparison of BMD, BMC, and bone size in fracturing and non-fracturing women after adjusting for significant effects of age, height, and/or weight

Traits	Spine BMD		Spine BMC		Spine bone size		Hip BMD		Hip BMC		Hip bone size	
The all-fracture study group												
Fracture status	NF	F	NF	F	NF	F	NF	F	NF	F	NF	F
Sample size	642	77	642	77	642	77	740	83	740	83	740	83
Adjusted mean	0.895	0.833	51.31	47.14	56.55	55.89	0.79	0.73	26.44	24.82	33.31	33.99
SD	0.145	0.116	10.74	7.99	4.81	5.01	0.12	0.10	4.31	3.36	2.55	2.94
t-Test *P* value	0.0002		0.001		0.314		6.02×10^{-6}		0.001		0.024	
The hip-fracture group												
Fracture status							NF	F	NF	F	NF	F
Sample size							357	9	303	9	303	9
Adjusted mean							0.847	0.733	28.18	26.47	49.35	52.40
SD							0.115	0.114	4.54	4.23	2.72	2.80
t-Test *P* value							0.003		0.264		0.001	

For the all-fracture study group, the regression equations employed to adjust for significant age, height, and/or weight effects are as follows:
Spine BMD = 0.652 − 0.0043age + 0.151height + 0.0041weight
Spine BMC = −36.9 − 0.243age + 54.53height + 0.23weight
Spine bone size = − 28.9 + 53.0height
Hip BMD = 0.776 – 0.0046age + 0.0044weight
Hip BMC = −13.7 − 0.0519age + 19.9height + 0.162weight
Hip bone size = −14.1 + 0.125age + 23.6height + 0.023weight
For the hip fracture group, the regression equations employed to adjust for significant age, height, and/or weight effects are as follows:
Hip BMD = 0.783 − 0.0055age + 0.0048weight
Hip BMC = −14.5 − 0.105age + 21.4height + 0.18weight
Hip bone size = −16.5 + 0.099age + 26.4height + 0.021weight
SD, Standard deviation; NF and F, non-fracturing and fracturing women, respectively

Table 4. Percentages of variation in BMD explained by BMC and/or bone size

Regression	R^2	BMC	Bone size
Spine			
BMD = 0.86 + 0.018BMC − 0.015bone size	98.8	86.2	12.6
BMD = 0.26 + 0.012BMC	86.2		
Hip			
BMD = 0.759 + 0.030BMC − 0.023bone size	99.1	98.0	1.1
BMD = 0.146 + 0.0244BMC	98.0		

Note, R^2 is the approximate percentage of variation explained by the regression model. The data in the BMC column are obtained from the regression equation of BMD with BMC, and are the approximate percentages of variation in BMD explained by that of BMC. The data in the bone-size column are obtained from the difference of the R^2*s* associated with the regression equation of BMD with BMC and bone size, and the regression of BMD with BMC, and are the approximate percentages of variation in BMD explained by that of bone size

fracture study group is a large sample, the following analyses that do not involve comparisons between the two study groups were performed for the all-fracture study group only. At the spine and hip, multiple regression analyses were performed, respectively, with BMD as the dependent variable and BMC and bone areal size as predictor variables (Table 4). To estimate the approximate percentage variation in BMD that is attributable to BMC or bone areal size, separate regression analyses were conducted with BMD as the dependent variable and BMC as the predictor variable. From the adjusted R^2 values and their differences in these regression analyses, the percentage variation in BMD that is attributable to BMC and bone areal size can be approximated (Table 4) [15,26,27]. Polynomial regression analyses were performed between each pair of phenotypes of BMD, BMC, and bone areal size at the spine and hip, and significant relationships (linear and/or quadratic) are reported (Figs. 1, 2). The normality of data (for the *t*-test) and residuals (for regression analyses) was tested by graphical analyses and no significant deviation from normality was found. In this study, unless otherwise specified, the significance level refers to $P = 0.05$ or smaller in a statistical test.

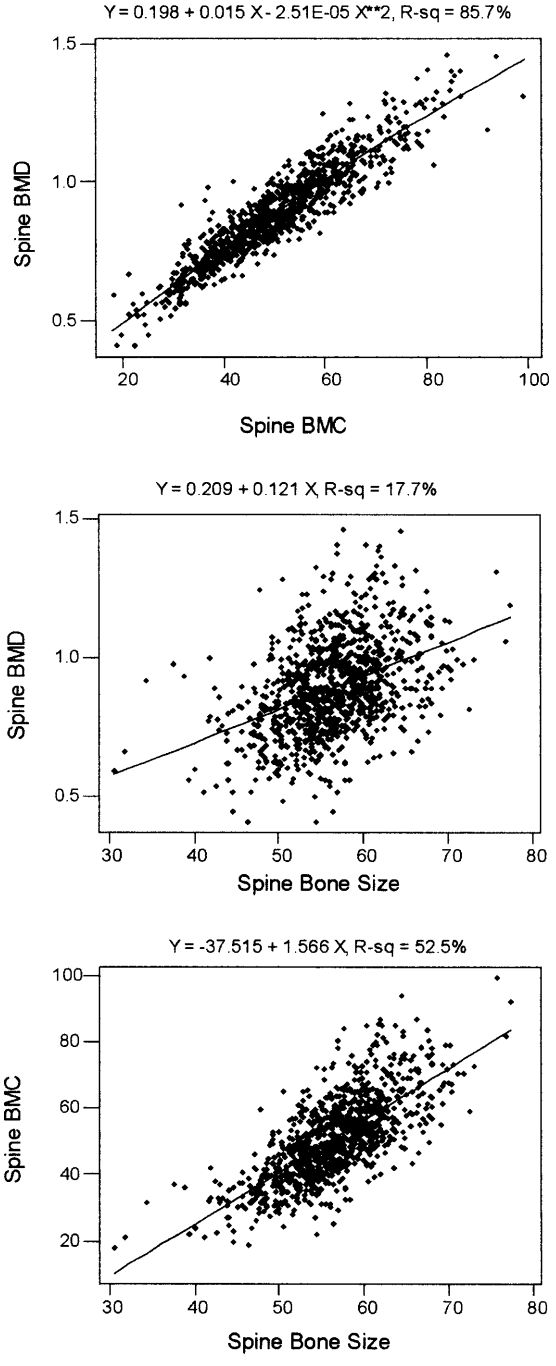

Fig. 1. Relationships of spine bone mineral density (*BMD*), spine bone mineral content (*BMC*), and spine bone size

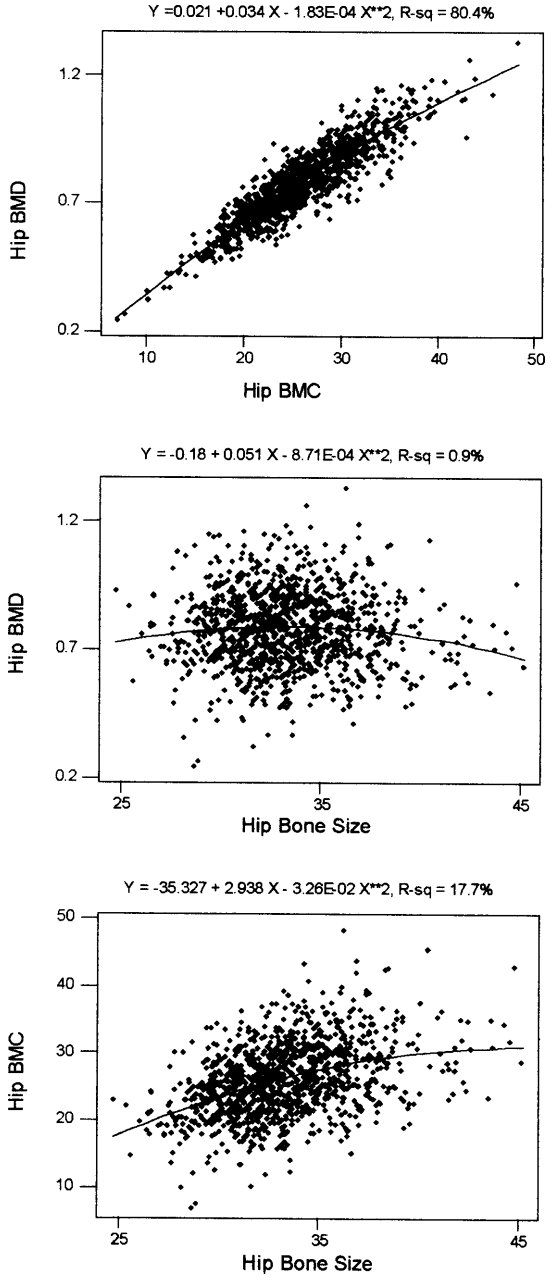

Fig. 2. Relationships of hip BMD, hip BMC, and hip bone size

Results

Comparison of BMD, BMC, and bone areal size in fracturing and non-fracturing individuals

Without adjusting for any covariate that may be significant, bone areal size is significantly larger in non-fracturing individuals at the spine; however, bone areal size is significantly larger in fracturing individuals at the hip (Table 1). BMD and BMC are both significantly larger in non-fracturing individuals at both the spine and hip. Age is lower, and weight and height are greater in non-fracturing individuals, and these differences are significant (Table 1).

Age, height, and weight generally have significant effects on BMD, BMC, and bone areal size at the spine and hip (Table 2), except for the following. Height does not significantly affect BMD variation, particularly at the hip (Table 2). Age and weight do not significantly affect bone areal size variation at the spine in our

subjects, aged over 30 years (Table 2). After adjusting for age, height, and/or weight that are significantly different between fracturing and non-fracturing individuals, BMD and BMC generally remain significantly higher in non-fracturing individuals (Table 3). The exception is hip BMC in the hip fracture study group, which may be attributable to the small sample size (nine individuals) with hip fractures in this group (Table 3). The significant difference in bone areal size at the hip remains after the adjustment (Table 3). However, the significant difference in spine bone areal size between the fracturing and non-fracturing individuals disappears after the adjustment (Table 3). This may be largely due to the significant effect of height on spine bone areal size (Table 2) and the significant difference in height between fracturing and non-fracturing individuals (Table 1).

Relationship between BMD, BMC, and bone areal size

At the spine (Fig. 1), BMD increases with increasing BMC, having a significant quadratic relationship that is dominated by the linear term. The coefficient (−2.51E-5) for the quadratic term of BMC, although significant, is very small compared with the significant coefficient (0.015) for the linear term of BMC. Because BMD has a linearly increasing relationship with BMC, spine BMC also increases linearly with increasing spine bone areal size, noting that BMC increases at a more rapid rate than the increase in bone areal size, as reflected by the linear term coefficient of 1.5. In a linear relationship, a coefficient of 1.0, greater than 1.0, or smaller than 1.0 indicates that the dependent variable increases, respectively, at a rate similar to, greater than, or smaller than the predictor variable.

At the hip (Fig. 2), similar to the spine, BMD increases with increasing BMC, exhibiting a significant quadratic relationship that is dominated by the linear term. The significant coefficient (−1.83E-4) for the quadratic term of BMC is small compared with the significant coefficient (0.034) for the linear term of BMC. In contrast to spine BMD (Fig. 1), hip BMD has a significant quadratic relationship with hip BMC (Fig. 2). Particularly, at the hip, BMD first increases with increasing bone areal size values; then, after an intermediate zone of values, BMD decreases with increasing bone areal size. Within the normal range of bone areal size, hip BMC increases with increasing bone areal size in a quadratic fashion, which is also different from the spine. The linear term coefficient of BMC with bone areal size is 2.9, which may explain the increase in hip BMD with hip bone areal size at low to intermediate bone areal size values.

The above relationships between BMD, BMC, and bone areal size were obtained without adjustment for any other phenotype. For example, the relationship between BMD and bone areal size is obtained without adjusting for BMC. If adjusted for BMC or bone areal size in multiple regression analyses (Table 4), it is apparent that BMD increases with BMC, and BMD decreases with increasing bone areal size, as reflected by the sign of the associated partial regression coefficients in the multiple regression analyses. From the associated adjusted R^2 values of the regression results and their differences (Table 4), it is estimated that, at the spine, about 86.2% of the BMD variation is explained by the BMC variation, and about 12.6% of the BMD variation is explained by the bone areal size variation. At the hip, 98% of the BMD variation is explained by the BMC variation and only about 1.1% of the BMD variation is explained by the bone areal size variation.

Discussion

Osteoporotic fractures are a major public health problem, particularly in women. BMD, BMC, and bone areal size, which can all be measured by DEXA, have been regarded as important determinants of osteoporotic fractures [2–10]. BMD is the ratio of the BMC to bone size. Given a constant BMC, the larger the bone size is, the smaller the BMD should be. This expectation seems to be in apparent conflict with clinical observations that both larger bone size and higher BMD values are associated with stronger bones [2–10]. We have studied the detailed relationships between BMD, BMC, and bone areal size at the hip and spine in 1449 women aged at least 30 years. In addition, the relative magnitudes of BMD, BMC, and bone areal sizes in fracturing and non-fracturing women were also studied.

The relationships among BMD, BMC, and bone size have seldom been studied, especially with regard to the homogeneity of the relationship across different skeletal sites. This study, for the first time, to the best of our knowledge, demonstrates the heterogeneity of the relationship among BMD, BMC, and bone, areal size at the spine and hip. The study reconciles the apparent dilemma of some of the observations that larger BMD and bone size are both associated with stronger bone, and *the mathematical expectation* that smaller bone sizes lead to larger BMD (given constant BMC). Indeed, when adjusting for BMC, larger BMD is associated with smaller bone areal size, as is clear from the partial regression coefficient of the multiple regression analyses, which is consistent with the mathematical expectation that BMD and bone size have an inverse relationship. However, without adjustment for BMC, BMD may increase with increasing bone areal size simply because of the more rapid increase of BMC than of bone

areal size, which is consistent with some observations [2–10,33,34] that both larger BMD and larger bone size are associated with stronger bones.

In additional to the heterogeneity of the relationship of BMD, BMC, and bone areal size across different skeletal sites, the heterogeneity of the relative magnitudes of bone areal size at the spine and hip revealed here in fracturing and non-fracturing women is also noteworthy. The observations that larger bone size renders stronger bone largely come from studies of the spine [6,8,9,33]. The generality of this observation to various skeletal sites has seldom been questioned, despite some exceptions [30–32,37,38] found at the hip. In addition, these observations are often made without adjusting for important covariates, such as age, height, and/or weight [5,6,8–10], despite the importance of these covariates, as demonstrated in several studies [6,11,33–35]. We show here that, for spine BMD, fracturing and non-fracturing women differ significantly in height. Without adjusting for height, spine bone areal size is 3% larger (significantly) in non-fracturing women than in fracturing women (Table 1). After adjusting for height, spine bone areal size is still 1% larger in non-fracturing women (Table 3); however, the difference does not remain significant despite our relatively large sample size ($n = 1081$). Therefore, it appears that the significant difference in spine bone areal size between fracturing and non-fracturing women in our sample is largely due to the significant difference in height between these two groups of study subjects. In contrast to the spine, the hip bone areal size was always about 2%–12% larger (Tables 1 and 3) in fracturing women in the two study groups. This conclusion holds whether adjusting for significant covariates or not and whether the fracture type identified is general, including various types of fractures, or specific for hip fracture. The association between larger bone size and weaker bone has also been observed earlier at the hip [30–32,36,37].

Variation in composite phenotype BMD has seldom, if ever, been partitioned into variation in the component phenotypes of BMC and bone size. We show that the majority of BMD variation, particularly at the hip, is attributable to BMC variation and only a small proportion is attributable to bone areal size variation. In light of this result, it can be expected that the correlation between BMD and BMC may be high and that between BMD and bone areal size may be low. Indeed, in the all-fracture study group, at the spine, the correlation between BMD and BMC is 0.93, the correlation between BMD and bone areal size is 0.43, and that between BMC and bone areal size is 0.72. At the hip, the correlation between BMD and BMC is 0.67, the correlation between BMD and bone areal size is −0.03 (not significant), and that between BMC and bone areal size is 0.41. Unless otherwise specified, all the above correlations are significant, with a *P*-value of less than 0.001. Some of the proportion of BMD variation attributable to bone areal size might be partially due to the edge detection effect of DEXA for measuring bone areal size. As BMD increases, edge detection becomes more effective, which may yield a larger measured bone areal size. On the other hand, it should not be unexpected that some of the BMD variation can be attributable to bone areal size, as it is a component (in the denominator) of the composite phenotype BMD. Given these results, it is not surprising that gene mapping may result in similar results for BMD and BMC and different results for bone size [39,42]. Separate mapping endeavors have to be made for BMD (or BMC) and bone areal size [40,41] if all these phenotypes are genetically important for osteoporotic fractures.

Finally, it is noted that the conclusions we reach here, especially for those concerning bone areal size, pertain to the measurement by DEXA. This study is important in demonstrating the relationships, and their heterogeneity, among the recognized fracture risk factors, BMD, BMC, and bone areal size, in demonstrating the potential heterogeneity of relative bone areal size across skeletal sites in fracturing and non-fracturing individuals, and in partitioning the variation in BMD into that due to BMC and that due to bone areal size.

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Appendix A

Although our phenotype measurements are from different models of the Hologic DEXA machines, the measurements are comparable, as they were carried out on our Hologic scanners by our expert scan technicians and analyzed according to the same procedures, which are uniform at our research center. Moreover, we have done cross-calibration studies, carried out by our scan technicians and using the concepts advanced by Glüer et al. [43] for accurate and stable results—namely, precision determined by addition in quadrature and at least 27 subjects. We found that the differences are minor. Briefly, we determined the precision in absolute terms and the coefficient of variation (CV) using Glüer's canonical methods [43]. We calculated the clinically

significant difference as $1.96*\sqrt{2}*$CV, and the correction between the Hologic 1000 and the Hologic 4500 value for a zero intercept fit of the cross-calibration data. The results are in the following two Tables.

Spine	Area	BMC	BMD
Precision	0.639	1.053	0.011
CV	1.13%	1.86%	1.08%
Clinically significant difference	3.14%	5.17%	3.00%
1000–4500 difference on zero intercept	0.18%	0.24%	0.21%
Hip	**Area**	**BMC**	**BMD**
Precision	0.379	0.618	0.018
CV	1.10%	1.92%	1.94%
Clinically significant difference	3.06%	5.33%	5.39%
1000–4500 difference on zero intercept	0.58%	2.60%	3.16%

The results for the Hologic 1000 and 2000+ studies are comparable. We are well inside the precision limits for the spine values and the hip area, and inside the clinical limits for the hip BMC and BMD. Our results here concur with the study of Ruetsche et al. [44] The variability in the total spine is mainly due to the mass determination rather than the area determination.

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