

Contributions of bone density and structure to fracture risk assessment in men and women

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Abstract Although bone mineral density (BMD) is a strong predictor of fractures, it is only a surrogate for bone strength. Bone structural parameters can now be measured on BMD scans, but it is unclear whether they would be more useful for risk assessment. We measured structural parameters using the Hip Structural Analysis Program and evaluated their association, compared with standard hip BMD, with fracture risk in a population-based sample of 213 postmenopausal women and 200 men ≥ 50 years of age. Altogether, 38% of the women and 27% of the men had experienced a fracture due to moderate trauma (half involved hip, spine or distal forearm), while 23% and 36%, respectively, had a previous fracture due to severe trauma. In logistic regression analyses adjusted for age, the hip BMD and structural parameters were all associated with moderate trauma fractures generally, and osteoporotic fractures specifically, in women, but the best predictor in a multivariate model was femoral neck BMD (odds ratio [OR], 2.8;

95% confidence interval [CI], 1.9–4.0). BMD and the structural parameters were strongly correlated, however, and could be interchanged with little reduction in predictive power. These variables were less predictive of moderate trauma fractures in men. The best model included age (OR per 10 years, 1.5; 95% CI, 1.1–2.1), femoral neck section modulus (OR, 1.6; 95% CI, 1.1–2.5) and intertrochanteric buckling ratio (OR, 1.6; 95% CI, 1.3–2.0). Correction for body size did not alter these relationships. Fractures due to severe trauma were best predicted by structural parameters: in women, femoral neck buckling ratio (OR, 1.2; 95% CI, 1.04–1.5) and, in men, intertrochanteric buckling ratio (OR, 1.4; 95% CI, 1.2–1.6). These data suggest that selected structural variables as assessed by dual-energy X-ray absorptiometry would be as good as standard BMD measurements for predicting fracture risk. Because of the strong correlations, however, some judgment can be used in selecting the variables easiest to measure.

Keywords Biomechanics · Bone density · Bone structure · Epidemiology · Fractures · Gender · Osteoporosis

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Introduction

Observational studies show clearly that bone mineral density (BMD) is a strong predictor of future fracture risk [1]. It is generally understood, however, that areal BMD as assessed by dual-energy X-ray absorptiometry (DXA) is only a surrogate for factors less easily assessed in vivo (i.e., bone structural dimensions and tissue material properties [2]), which are actually responsible for bone strength and resistance to fracture [3]. Indeed, it has been suggested that the association of greater BMD levels with lower fracture risk might really result from the confounding of BMD values by bone size [4], insofar as areal BMD overestimates volumetric density in larger, and therefore stronger, bones [5]. On the other hand, our

group has shown that correcting for bone size degraded fracture prediction by BMD only slightly in women and improved it somewhat in men [6]. However, that analysis was based on a rough adjustment for bone volume (i.e., bone mineral apparent density), and biomechanically relevant effects of greater bone size were not addressed. It has now become possible to estimate skeletal structural parameters from DXA scans of the proximal femur [7], and there is obvious intellectual appeal in assessing measures of bone strength more directly. However, DXA-derived BMD measurements are already widely used in clinical practice, and while it is possible to compute structural properties from the same data, the scanners and scan protocols were not designed to do so. Since precision for measuring structural properties from DXA data is worse than for assessing BMD from the same data, it is unclear whether expressing measurements in terms of structure rather than density provides any practical advantage for determining fracture risk. This question was evaluated in a cross-sectional study that included older men as well as postmenopausal women.

Methods

Study subjects

Following approval by Mayo Clinic's Institutional Review Board, subjects were recruited from an age-stratified random sample of Rochester, Minnesota, residents that was selected using the medical records linkage system of the Rochester Epidemiology Project [8]. Over half of the Rochester population is attended annually at Mayo, and the majority of people are seen in any 3-year period. Thus, the enumerated population (Rochester women seen in 1990 ± 1 year and men seen in 1991 ± 1 year) approximates the underlying population of the community, including both free-living and institutionalized individuals. Altogether, 1,138 men were approached for this study, but 239 of them were ineligible, mostly as a consequence of dementia [6]. Of the 899 eligible men, 348 (39%) participated, and bone structural data were available for 343. Similarly, 938 women were approached for study, but 126 were ineligible. Of the eligible women, 351 participated (43%), and bone structural data were available for 349. All but 13 men and two women were white, reflecting the ethnic composition of the population (96% white in 1990). This analysis was based on the 213 postmenopausal women (mean age, 67.8 ± 13.2 years; range, 34–93 years) and the 200 men ≥ 50 years of age (69.9 ± 11.3 years; range, 50–90).

Fracture ascertainment

All subjects were interviewed in accordance with a standard protocol in order to collect clinical data, including a comprehensive fracture history that was then

verified by review of each subject's complete (inpatient and outpatient) medical records in the community. The records contained the clinical history and the radiologist's report of each fracture, but the original roentgenograms were not available for review. Consequently, the diagnosis of vertebral fracture was accepted on the basis of a radiologist's report of compression, wedging or collapse of one or more thoracic or lumbar vertebrae. There was generally good agreement between interview and medical record data [9]. The duration of contemporary medical record documentation prior to baseline that was available for review averaged 30.8 years (median, 29 years; range, 1–81 years), and ascertainment of clinically evident fractures is believed to be complete. The subset of "osteoporotic" fractures was defined as clinically recognized fractures of the hip, spine or distal forearm that resulted from minimal or moderate trauma (e.g., a fall from standing height or less) among persons 35 years of age or older. At the time of the interview, each subject also underwent anthropometric assessment, which included measurement of height to the nearest 0.1 cm and weight in light clothes without shoes to the nearest 0.1 kg.

Bone densitometry

Areal BMD (g/cm^2) was determined for the proximal femur (total, femoral neck and intertrochanteric regions) using dual energy X-ray absorptiometry with the Hologic QDR-2000 instrument (Hologic, Waltham, MA, USA) and software version 5.67. The coefficient of variation (CV) for the total hip BMD measurement was 0.6%. We also estimated volumetric bone mineral apparent density (BMAD, g/cm^3) as previously described [10], using the following formula: femoral neck $BMAD = BMC / A^2$; where BMC is the bone mineral content and A is the projected bone area (since region length is usually fixed by the software, this effectively corrects for differences in neck width). Sex-specific, young normal means and SDs were derived from 50 Rochester women and 48 Rochester men in the original sample who were 20–29 years of age at baseline [6]. Total lean body mass (LBM, kg) was determined from a whole body scan using the same instrument (CV, 0.6%).

Bone structural analysis

As described in detail previously [7, 11], an interactive computer program (Hip Structural Analysis) was used to derive a number of structural variables from the femoral DXA scans. The regions assessed were the narrowest width of the femoral neck, which overlaps or is proximal to the standard Hologic femoral neck region; an intertrochanteric region located along the bisector of the neck-shaft angle; and the femoral shaft 2 cm distal to the midpoint of the lesser trochanter. The measurements included cross-sectional area, outer cortical diameter, cross-sectional moment of inertia,

centroid position and areal BMD for each region. The section modulus, a measure of bending and torsional strength, was computed as the cross-sectional moment of inertia divided by the maximum distance from the center of mass to the medial or lateral bone edge. Estimates of cortical thickness were computed using models of cross-sections: Neck and shaft cross-sections were modeled as circular annuli with 60% and 100%, respectively, of the bone mass in the cortex; the intertrochanteric region was modeled as an elliptical annulus with 70% of the mass in the cortex. This approach results in cortical thickness values within the expected range [12] but can only be regarded as a crude estimate given the limitations of the available information. Because age-related increases in outer diameter and decreases in cortical thickness may lead to local instability in bending, we also computed buckling ratios, defined as the maximum distance from the center of mass to the medial or lateral bone edge, divided by the estimated mean cortical thickness. Coefficients of variation for the different component variables were previously reported to range from 2.4% to 4.7% but were 7.7% and 5.4%, respectively, for section moduli at the femoral neck and shaft [13]. Sex-specific normative data were derived from the 20–29 year-old Rochester women and men. These were generally comparable to previously reported values for 20-to-29-year-old white males and females [7].

Statistical analysis

Pearson correlations were used to relate bone structural parameters to each other and to measures of height and

bone density. The relative risk of various fractures was estimated by odds ratios (OR) obtained from multiple logistic regression models where fracture was the dependent variable and age, gender, BMD or BMAD (per SD decrease) and the structural parameters (per SD increase) were the potential predictors. Variables were selected in a stepwise fashion, entering only those that were significant at the 0.05 level after adjusting for the other variables in the model. Interactions and higher ordered terms were investigated. The *c*-index was used to compare logistic models when substituting different variables one for another [14]. This is a rank correlation that compares the predicted probabilities from a model with the observed responses (whether or not fracture was detected). It is a useful statistic for comparing models—the higher the *c*, the better the model does at predicting the event.

Results

Prior to the baseline assessment, 81 (38%) of the 213 postmenopausal women and 54 (27%) of the 200 men age 50 years and over had experienced one or more fractures due to minimal or moderate trauma that occurred on or after age 35 years (thereby excluding childhood fractures). Fifty percent of all moderate trauma fractures observed (83 of 166) involved the hip, spine or distal forearm. Altogether, 46 postmenopausal women (22%) and 33 men ≥ 50 years of age (17%) had one or more “osteoporotic” fractures as defined in “Methods.” In addition, 48 (23%) of the postmenopausal women and 71 (36%) of these older men had at least one fracture after age 35 years that resulted from

Table 1 Relative risk of various fractures estimated by univariate or age-adjusted odds ratios (OR) per 1 SD change in femoral bone mineral density (BMD), bone mineral apparent density (BMAD) or

hip structural parameter among postmenopausal Rochester, Minnesota women (*IT* intertrochanteric, *FN* femoral neck, *SM* section modulus, *BR* buckling ratio)

Variable	Any moderate trauma		Hip, spine, forearm only		Any severe trauma	
	Unadjusted OR	Adjusted OR	Unadjusted OR	Adjusted OR	Unadjusted OR	Adjusted OR
Bone density parameters (per SD decrease)						
FN BMD	2.8***	2.5***	3.3***	2.9***	1.4	1.4
FN BMAD	2.5***	2.2***	2.4***	2.0**	1.5*	1.5*
IT BMD	2.2***	2.0***	2.7***	2.5***	1.2	1.2
Shaft BMD†	1.9***	1.8***	2.0***	1.8***	1.1	1.0
Total hip BMD	2.4***	2.2***	3.0***	2.8***	1.2	1.2
Bone structural parameters (per SD increase)						
FN SM†	0.4***	0.5**	0.4***	0.4**	0.7	0.7
FN BR†	1.5***	1.4***	1.6***	1.4**	1.2*	1.3*
IT SM†	0.4***	0.5***	0.5***	0.5**	1.0	1.0
IT BR†	1.7***	1.6***	1.7***	1.6***	1.1	1.1
Shaft SM†	0.5***	0.6**	0.5**	0.6*	1.0	1.0
Shaft BR†	1.5***	1.4***	1.5***	1.4**	1.1	1.0

†Measurements are from the Hip Structural Analysis Program

* $P < 0.05$

** $P < 0.01$

*** $P < 0.001$

severe trauma (e.g., motor vehicle and recreational accidents and falls from a height).

All of the standard hip bone density measures, as well as femoral neck BMAD, were strongly associated with moderate trauma fractures in postmenopausal women (Table 1). There was little difference in the influence of femoral neck BMD as assessed in the original DXA scan or in the Hip Structural Analysis Program. Because the standard deviations were larger in the latter analysis (0.140 g/cm² vs 0.119 g/cm² in young women), the odds ratio per 1 SD decline was slightly higher (OR, 3.1; 95% confidence interval [CI], 2.1–4.6) compared with the original scan (OR, 2.8; 95% CI, 1.9–4.0). For this reason, the more precise femoral neck BMD data obtained from the Hologic software were used in the remainder of this analysis. Relationships were even stronger for the subset of moderate trauma fractures linked to osteoporosis. Similarly, increasing section modulus measured at the different hip sites (femoral neck, intertrochanteric region, proximal femur shaft) was strongly protective of all moderate trauma fractures together and of osteoporotic fractures alone, while increases in the various buckling ratios were all associated with significantly greater fracture risk (Table 1). None of these relationships was substantially changed by adjustments for height (or arm span), weight or lean body mass (data not shown).

In a multivariate model, the only independent predictor of a moderate trauma fracture among the postmenopausal women was femoral neck BMD (OR, 2.8; 95% CI, 1.9–4.0). As shown in Table 2, however, femoral neck BMD was strongly, though inversely, correlated with the femoral neck buckling ratio ($r = -0.87$; $p < 0.001$), and the predictive power changed little if the latter were substituted in the model (c , 0.75 vs 0.71). For the osteoporotic fractures alone, the best predictor among the postmenopausal women was again femoral neck BMD (OR, 3.3; 95% CI, 2.0–5.2). If the femoral neck buckling ratio were substituted for femoral neck BMD in this model, the model c -index declined only from 0.77 to 0.73.

Among men 50 years of age and over, the hip bone density measures were all associated with the likelihood of any moderate trauma fracture (Table 3), but the relationships were much weaker than those seen for women. Indeed, some of the associations with the subset of osteoporotic fractures were not statistically significant. Again, because the standard deviations were larger (0.122 g/cm² vs 0.109 g/cm² in young men), there was a slightly stronger relationship between fractures and BMD as assessed by the Hip Structural Analysis Program (OR, 1.6; 95% CI, 1.2–2.1) compared with the standard femoral neck BMD (OR, 1.4; 95% CI, 1.1–1.9), but the more precise original measurements were used in subsequent analyses. As with the women, there were also significant associations of fracture risk with increases in the various femoral buckling ratios. However, greater section modulus values were not as protective for moderate trauma fractures in men as they

Table 2 Pearson correlations among femoral bone mineral density (BMD), bone mineral apparent density (BMAD) and hip structural parameters among postmenopausal Rochester, Minnesota, women and men ≥ 50 years of age [men in brackets] (IT intertrochanteric, FN femoral neck, SM section modulus, BR buckling ratio)

Variable	Bone density parameters				Bone structural parameters					
	FN BMD	FN BMAD	IT BMD	Total hip BMD	FN SM	FN BR	IT SM	IT BR	Shaft SM	Shaft BR
Bone density parameters										
FN BMD	-	[0.89]***	[0.83]***	[0.89]***	[0.63]***	[-0.80]***	[0.54]***	[-0.73]***	[0.36]***	[-0.61]***
FN BMAD	0.88***	-	[0.70]***	[0.74]***	[0.37]***	[-0.80]***	[0.28]***	[-0.70]***	[0.09]	[-0.62]***
IT BMD	0.88***	0.72***	-	[0.98]***	[0.50]***	[-0.73]***	[0.55]***	[-0.82]***	[0.35]***	[-0.77]***
Shaft BMD†	0.83***	0.69***	0.93***	[0.90]***	[0.43]***	[-0.67]***	[0.52]***	[-0.84]***	[0.25]***	[-0.90]***
Total hip BMD	0.93***	0.77***	0.99***	-	[0.56]***	[-0.75]***	[0.62]***	[-0.84]***	[0.37]***	[-0.76]***
Bone structural parameters										
FN SM†	0.56***	0.31***	0.51***	0.54***	-	[-0.26]***	[0.66]***	[-0.27]***	[0.68]***	[-0.18]*
FN BR†	-0.87***	-0.81***	-0.81***	-0.82***	-0.34***	-	[-0.34]***	[0.76]***	[-0.10]	[0.66]***
IT SM†	0.52***	0.26***	0.60***	0.62***	0.52***	0.41***	-	[-0.44]***	[0.75]***	[-0.27]***
IT BR†	-0.81***	-0.72***	-0.90***	-0.91***	-0.37***	0.79***	-0.56***	-	[-0.02]	[0.89]***
Shaft SM†	0.45***	0.15*	0.55***	0.54***	0.61***	-0.29***	0.78***	-0.37***	-	[0.05]
Shaft BR†	-0.73	-0.65***	-0.85***	-0.83***	-0.31***	0.71***	-0.42***	0.91***	-0.34***	-

†Measurements are from the Hip Structural Analysis Program

* $p < 0.05$

** $p < 0.01$

*** $p < 0.001$

were in women (Table 3). Again, none of the associations of fracture risk with the structural parameters in men were altered by adjustment for height, weight or lean body mass (data not shown).

In a multivariate analysis, the independent predictors of any moderate trauma fracture in men were age (OR per 10-year increase, 1.5; 95% CI, 1.1–2.1), femoral-neck section modulus (OR, 1.6; 95% CI, 1.1–2.5) and the intertrochanteric buckling ratio (OR, 1.6; 95% CI, 1.3–2.0). As shown in Table 2, the intertrochanteric buckling ratio was correlated with the femoral neck buckling ratio ($r = 0.76$; $p < 0.001$), and little degradation was seen if the latter was substituted in the model (c , 0.76 vs 0.70). Thus, fracture prediction could be carried out using only femoral neck variables but with some reduction in predictive power. If femoral neck BMD were forced into the model first, the intertrochanteric buckling ratio was still significantly associated with the risk of a moderate trauma fracture in men (OR, 1.9; 95% CI, 1.4–2.5). The model for osteoporotic fractures alone was similar, with age (OR per 10 years, 1.7; 95% CI, 1.2–2.5), femoral neck section modulus (OR, 1.9; 95% CI, 1.2–3.0) and intertrochanteric BMD (OR, 1.8; 95% CI, 1.2–2.6) as the independent predictors.

In a separate analysis that combined men and women, male gender was associated with a lower risk of moderate trauma fracture (OR, 0.6; 95% CI, 0.4–0.9) and some reduction in osteoporotic fracture risk (OR, 0.7; 95% CI, 0.4–1.2). The associations with moderate trauma fractures (OR, 0.8; 95% CI, 0.4–1.9) and osteoporotic fractures (OR, 0.8; 95% CI, 0.3–2.2) were attenuated somewhat after adjustment for femoral neck BMD and femoral neck buckling ratio.

Among both the postmenopausal women and older men, femoral bone density and structural parameters

were less strongly associated with the fractures due to severe trauma (Tables 1 and 3). In multivariate analyses, the femoral neck buckling ratio was the only independent predictor of severe trauma fractures in women (OR, 1.2; 95% CI, 1.04–1.5), and the intertrochanteric buckling ratio was the only predictor in men (OR, 1.4; 95% CI, 1.2–1.6). If the femoral neck buckling ratio were substituted in the model for men, the c -index declined only from 0.64 to 0.62. In either women or men, no structural parameter independently predicted a severe trauma fracture if age and femoral neck BMD were forced into the model first. In a model that contained both women and men, male gender was associated with an increased likelihood of a severe trauma fracture (OR, 1.9; 95% CI, 1.2–2.9) that was not attenuated by adjustment for femoral neck BMD and buckling ratio (OR, 2.1; 95% CI, 0.9–4.7), although the adjusted odds ratio was no longer statistically significant.

Discussion

It has long been recognized that bigger bones with larger diameters should be more resistant to fracture [15], but previous efforts to implement a width correction in two-dimensional areal BMD measurements by computing a three-dimensional equivalent (e.g., BMAD) did not greatly enhance fracture prediction in population studies [6, 16, 17]. Similar modest improvements in fracture risk prediction have been obtained using simple dimensions with some biomechanical relevance such as femoral neck width and hip axis length [18–23]. The present approach attacks the problem more directly by using the same bone mineral data used in bone density measurements to derive biomechanical parameters

Table 3 Relative risk of various fractures estimated by univariate or age-adjusted odds ratios (OR) per 1 SD change in femoral bone mineral density (BMD), bone mineral apparent density (BMAD) or

hip structural parameter among Rochester, Minnesota men ≥ 50 years of age (IT intertrochanteric, FN femoral neck, SM section modulus, BR buckling ratio)

Variable	Any moderate trauma		Hip, spine, forearm only		Any severe trauma	
	Unadjusted OR	Adjusted OR	Unadjusted OR	Adjusted OR	Unadjusted OR	Adjusted OR
Bone density parameters (per SD decrease)						
FN BMD	1.4*	1.3*	1.2	1.1	1.5**	1.5**
FN BMAD	1.6**	1.5*	1.3	1.1	1.5*	1.5*
IT BMD	1.7***	1.6**	1.5**	1.4*	1.4**	1.4**
Shaft BMD†	1.7***	1.6***	1.4*	1.3	1.4**	1.4**
Total hip BMD	1.6***	1.5**	1.5*	1.3	1.4**	1.4**
Bone structural parameters (per SD increase)						
FN SM†	1.1	1.2	1.2	1.3	0.8	0.8
FN BR†	1.3***	1.3**	1.2*	1.1	1.3**	1.3**
IT SM†	0.9	0.9	0.7	0.7*	0.8*	0.8*
IT BR†	1.5***	1.5***	1.2*	1.2	1.4***	1.4***
Shaft SM†	1.1	1.1	0.9	0.9	0.9	0.9
Shaft BR†	1.6***	1.5***	1.3**	1.2	1.3***	1.4***

†Measurements are from the Hip Structural Analysis Program

* $P < 0.05$

** $P < 0.01$

*** $P < 0.001$

commonly employed in engineering analyses. In this retrospective study, some of these skeletal structural parameters in the proximal femur (e.g., femoral neck buckling ratio) were strongly associated with fracture risk. Indeed, as one would expect, data from this cross-sectional sample suggest that selected structural variables would be at least as good as bone density measures for predicting osteoporotic fracture risk, and similar results were found for moderate trauma fractures in general and for fractures due to severe trauma. The buckling ratio is particularly attractive since it captures the geometric conditions that produce low bone density in a way that provides a mechanism for failure not evident in the BMD measurements per se. However, as one would also expect from different expressions of the same data, there were strong correlations among these parameters, and it may be possible to substitute one for another without much degradation in risk assessment.

Most of the structural parameters were correlated with body size, but adjustment for height, arm span, weight or lean body mass did not account for any of the associations of skeletal structural parameters with fracture risk. Likewise, previous work has shown that correction for body size explained most of the difference in proximal femur BMD between women and men [13, 24, 25] but did not eliminate men's biomechanical advantage [13]. The male advantage has been attributed to slower bone loss within a similarly expanding bone diameter that better preserves bending strength [7, 13, 26–28]. On the other hand, a recent report by Kaptoge and colleagues suggests that expansion of femoral neck diameter is actually faster in elderly women [29], supporting earlier observations on the metacarpal [30]. Loss of mass in a fixed diameter bone will reduce both BMD and strength, but the implications for fracture can be difficult to interpret when bone loss is combined with expansion of diameter. Thus, a larger diameter bone enclosing the same amount of mass would have a lower volumetric or areal BMD, because the bone volume is greater. However, it must be stronger from a mechanical perspective because the mass is farther from the neutral axis of bending. The patterns of change in bone structural parameters over life seem to correspond better with age-specific and gender-specific fracture rates than do changes in bone density measures alone [7]. However, in our analyses that combined men and women together, adjustment for structural parameters did not account for the lower risk of moderate trauma fractures in general, or osteoporotic fractures specifically, in men compared with women nor their greater risk of severe trauma fractures. Even with these more refined measures, then, it was still not possible to predict moderate trauma fracture risk as well in men.

Standard BMD measurements also have limitations, most notably variation in osteoporosis prevalence and fracture risk with BMD assessed by different devices or at different skeletal sites. Nonetheless, while areal BMD measurements are not themselves direct measures of mechanical strength, they do predict future fracture risk

comparably in men and women, despite the gender-specific discrepancies in bone size [31–33]. In the present study, the association of BMD with fracture risk in women was as strong as, and to some degree interchangeable with, that seen for the structural parameters. Consequently, if bone density were already known, hip structural parameters made a modest independent contribution to overall fracture prediction. In men, adding a structural parameter was helpful even if BMD was known, since the biomechanical variables were stronger predictors of fracture risk. These results should be confirmed in prospective studies, however. In addition, these site-specific structural parameters might be more strongly associated with hip fractures than with fractures at other skeletal sites [34]. Similarly, proximal femur BMD predicts hip fracture risk more strongly than the risk of moderate trauma fractures generally [1]. We had insufficient data to permit the study of separate fracture sites, and it would not have been possible in any event to identify the “best” variable for clinical application in a study of this limited size, given the highly correlated nature of the BMD and structural parameters.

The ability of BMD to predict fractures is due to the fact that a very low-density bone is in all probability a mechanically weak one, not that BMD per se is a mechanical characteristic. Fundamentally, mechanical strength depends on structural dimensions that govern the magnitude of loading stresses, as well as the material properties that define the ability to withstand those stresses. While aged bone tissue is more brittle, it is less clear that osteoporosis alters tissue properties to the extent that failure occurs at lower stresses [2, 26]. On the other hand, it is quite clear that osteoporosis alters bone structural geometry in ways that may alter stress magnitudes. Indeed, it can be argued that osteoporotic bone fragility is mainly evident in the structure. However, one must be cautious about making conclusions on the predictive value of bone geometry based on the relatively crude measurement method used here. Bones are complex three-dimensional entities, and there are limits on the structural information extractable from two-dimensional DXA images. For example, the Hip Structural Analysis Program measures section modulus in the image plane, but most bone cross-sections are not axially symmetric, so that the bone is stronger when bent in certain directions than in others. Moreover, inconsistent rotational positioning between patients, or between scans in the same patient, reduces precision, as reflected in relatively large coefficients of variation. The buckling ratio may be the parameter with the greatest promise for predicting fragility fracture [11, 12], although assumptions about shape and trabecular distribution required at the femoral neck and intertrochanteric regions introduce uncertainties. Shape assumptions are most valid at the purely cortical shaft region, where local buckling is unlikely, and shaft buckling ratios correlated strongly with buckling ratios at the other regions in our data.

All of them demonstrated a similar ability to predict fragility or moderate trauma fractures in both genders. The attractive feature of the buckling ratio is that it provides a potential mechanism to explain why greater bone loss and greater expansion of bone diameter both reduce BMD yet theoretically have opposing effects on strength: Bone expansion with cortical thinning may initially serve homeostasis, but if it proceeds to the point of local instability, fragility may ensue.

The analysis in this paper focused on an empirical discrimination of subjects with and without fracture rather than any exploration of the underlying etiologic mechanisms. Overall, one should regard the Hip Structural Analysis method as a means for supplementing BMD with structural geometry data in research studies using DXA scanners. While not an ideal method for measuring bone geometry, it can help account for the fragility underlying reduced BMD. Future advanced three-dimensional imaging methods, such as the latest generation multi-slice computed tomography scanners, may provide a more precise method for measuring the geometric variables shown to be predictive in these preliminary studies. Advanced methods should obviate the necessity of shape assumptions in the buckling ratio and permit the assessment of section modulus for bending in any direction. Indeed, it may ultimately be possible to use the geometric properties in an engineering analysis of strength by automated finite element analysis [35]. The potential for improved measures such as this to enhance the prediction of future fractures is a topic of urgent interest.

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