JOURNAL OF BONE AND MINERAL RESEARCH
Volume 23, Number 8, 2008
Published online on March 17, 2008; doi: 10.1359/JBMR.080316

Proximal Femoral Structure and the Prediction of Hip Fracture in Men: A Large Prospective Study Using QCT*

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ABSTRACT: The structure of the femoral neck contributes to hip strength, but the relationship of specific structural features of the hip to hip fracture risk is unclear. The objective of this study is to determine the contribution of structural features and volumetric density of both trabecular and cortical bone in the proximal femur to the prediction of hip fracture in older men. Baseline QCT scans of the hip were obtained in 3347 men ≥65 yr of age enrolled in the Osteoporotic Fractures in Men Study (MrOS). All men were followed prospectively for an average of 5.5 yr. Areal BMD (aBMD) by DXA was also assessed. We determined the associations between QCT-derived measures of femoral neck structure, volumetric bone density, and hip fracture risk. Forty-two men sustained incident hip fractures during follow-up: an overall rate of 2.3/1000 person-years. Multivariable analyses showed that, among the QCT-derived measures, lower percent cortical volume (hazard ratio [HR] per SD decrease: 3.2; 95% CI: 2.2–4.6), smaller minimal cross-sectional area (HR: 1.6; 95% CI: 1.2–2.1), and lower trabecular BMD (HR: 1.7; 95% CI: 1.2–2.4) were independently related to increased hip fracture risk. Femoral neck areal BMD was also strongly related to hip fracture risk (HR: 4.1; 95% CI: 2.7–6.4). In multivariable models, percent cortical volume and minimum cross-sectional area remained significant predictors of hip fracture risk after adjustment for areal BMD, but overall prediction was not improved by adding QCT parameters to DXA. Specific structural features of the proximal femur were related to an increased risk of hip fracture. Whereas overall hip fracture prediction was not improved relative to aBMD, by adding QCT parameters, these results yield useful information concerning the causation of hip fracture, the evaluation of hip fracture risk, and potential targets for therapeutic intervention.
J Bone Miner Res 2008;23:1326–1333. Published online on March 17, 2008; doi: 10.1359/JBMR.080316

Key words: men, hip fracture, hip structure, osteoporosis, BMD

INTRODUCTION

Fractures represent a major public health problem. Indeed, they are a leading cause of morbidity, mortality, and hospitalization, costing an estimated 17 billion dollars per year.[1] Particularly devastating, hip fractures account for ~80% of the costs and morbidity.

BMD assessed by DXA strongly predicts hip fractures in both women and men.[2–5] However, conventional DXA measures an integrated mineral content in the projected area of bone. It does not directly measure other elements that may contribute to bone strength, including the size, shape, geometry, and relative amounts of bone in the cortical and trabecular compartments. Because most fractures occur in those whose areal BMD (aBMD) is actually above the "osteoporosis" threshold,[6,7] it would seem that factors other than density may determine bone strength and, by extension, fracture risk. Moreover, whereas osteoporosis treatment raises BMD by DXA and reduces fracture risk, there has been increasing appreciation that the magnitude of change in aBMD does not adequately explain the effects of treatment on risk of fractures,[8] suggesting that treatment alters other important bone characteristics as well.

Laboratory studies have shown that aspects of femoral geometry along with BMD in cortical and trabecular bone contribute to femoral failure load.[9] Clinical studies have used pelvic radiographs to show that aspects of hip structure predict hip fracture independently of BMD.[10,11] Recent studies have found associations between structural properties derived from hip DXA scans and hip fracture. However, these DXA results are controversial because assessing 3D structures from 2D projections is problematic.[12] In all of these studies, the specific structural parameters assessed have varied. There remains no consensus as to which specific structural feature(s) of the proximal femur are the most important determinants of strength and risk of

*This article was presented in part at the 28th Annual Meeting of the American Society for Bone and Mineral Research, September 18, 2006, Philadelphia, PA, USA.

The authors state that they have no conflicts of interest.

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fracture, nor to the relative importance of cortical versus trabecular bone.

Unlike estimating femoral geometry from 2D DXA or radiograph images, QCT allows reconstruction of the 3D structure of the hip and therefore offers the potential to more precisely assess aspects of structure and to assess separately the contribution of cortical and trabecular bone to hip fracture risk. Whereas QCT has been previously used in studies with cadeveric bones as well as cross-sectional studies, it has not been used in prospective studies of fracture risk.

In this paper, we report results from a prospective study in which proximal femoral QCT scans were obtained from 3347 men enrolled in Osteoporotic Fractures in Men Study (MrOS) who were subsequently followed for occurrence of hip fracture. We determined the association between hip fracture and features of femoral geometry, along with cortical and trabecular BMD. In addition, we compared the abilities of QCT-derived variables and femoral neck areal BMD to predict hip fracture risk in men.

MATERIALS AND METHODS

Study participants

MrOS is a prospective cohort study designed to examine the extent to which fracture risk is related to skeletal characteristics, lifestyle factors, anthropometric and physical performance measures, fall propensity, and other factors. Design and recruitment have been previously described in detail.[13,14] From March 2000 through April 2002, 5995 community-dwelling, ambulatory U.S. men ≥65 yr of age were recruited from six geographically and ethnically diverse academic medical centers in the United States (Birmingham, AL; Minneapolis, MN; Palo Alto, CA; Pittsburgh, PA; Portland, OR; and San Diego, CA). Men were not enrolled if they were unable to walk without assistance, had a life-threatening medical condition, or had undergone previous bilateral hip replacements. All patients provided written informed consent, and the study was approved by the Institutional Review Board (IRB) at each site.

Baseline assessments

A variety of measurements were made at the baseline visit, including height, weight, and areal BMD by DXA. At all clinical sites, DXA BMD measures were performed using machines of the same model and manufacturer (4500W; Hologic, Waltham, MA, USA) and using a uniform procedure that included centralized standardization and monitoring of quality.

QCT scanning

The first 650 participants enrolled at each site along with all men from minority backgrounds were referred for QCT scans of the hip (3786 or 63% of the MrOS population). Of these, 122 were not eligible for hip scans because of hip replacement. Of the 3664 scans performed, 101 (2.8%) were not available for processing because they were lost or corrupted during transfer to University of California, San Francisco (UCSF), leaving 3563 hip scans for processing.

Scans were acquired using a standardized protocol and extended from the femoral head to 3.5 cm below the lesser trochanter at settings of 80 kVp, 280 mA, 3-mm slice thickness, and 512 × 512 matrix in spiral reconstruction mode. Scanner models used at the sites were GE Prospeed (Birmingham), GE Hispeed Advantage (Minneapolis), Phillips MX-8000 (Palo Alto), Seimans Somatom +4 (Pittsburgh), Phillips CT-Twin (April–July, 2000, 190 participants), Toshiba Acquilion (December 2000–March 2002, 467 participants; Portland), and Picker PQ-5000 (San Diego). Calibration standards with known hydroxyapatite concentrations (150, 75, and 0 mg/cm^3; Image Analysis) were included with the participant in each scan. Quality review, processing, and collation occurred centrally at UCSF and the Oregon Health & Science University.

QCT-derived femoral neck measures

Of the initial 3563 hip scans available for processing, 133 (3.7%) failed image processing. Reasons for failure were insufficient number of images, interference from metal implants, calibration standard not visible, or unrecorded cause. Eighty-three men were excluded for having missing data for the total hip, femoral neck, or trochanter, leaving a total of 3347 men available for analysis.

Femoral neck and total hip regions of interest (ROIs) were used to derive density and structural measures. Image processing was performed using the methods of Lang and colleagues.[15,16] Images were converted from the native scanner Hounsfield units (HU) to equivalent concentration (g/cm^3) of calcium hydroxyapatite contained in the calibration standard. ROIs in the left proximal femur were identified in QCT images reformatted along the neutral axis of the femoral neck. The periosteal boundary of the femur was determined with a threshold-based region growing algorithm. Using this boundary, the cross-sectional area in each slice along the neutral axis of the femoral neck between the proximal femoral neck and the lateral edge of the trochanter was calculated, and the minimum and maximum areas were determined. The femoral neck ROI was defined as at the portion of the neck extending from the slice with minimum cross-sectional area (medial boundary) to a point 25% of the distance toward the maximal cross-sectional area. The total hip ROI was defined as portion of scan bounded medially by the femoral neck cross-sectional area and laterally by the limit of the cross-sectional area plot. This ROI encompasses both the femoral neck and trochanter.

The following measures were obtained within the femoral neck ROI. The cross-sectional area (cm^2) was computed as the area within the periosteal boundary at the minimum cross-section. Integral volume (cm^3) of the ROI was computed as the total volume within the periosteal boundary. A trabecular volume of the ROI was obtained by applying an erosion process to the integral volume to retain the same shape in a region fully contained within the medullary space. The cortical volume was defined by applying a threshold of 0.35 g/cm^3 to all voxels between the periosteal boundary and the outer boundary of the trabecular volume. Medullary volume was computed by subtracting the cortical volume from the integral volume. The percent cortical volume was computed as cortical volume divided by integral

Table 1. Baseline Characteristics of MrOS Participants With QCT (n = 3347)

		Mean	*SD*	*n*	*Percentage*
Age at baseline (yr)	Mean	73.5	5.9		
	65–69			1019	30.4
	70–74			957	28.6
	75–79			799	23.9
	80+			572	17.1
Race/ethnicity	White			2924	87.4
	Black			170	5.1
	Asian			121	3.6
	Hispanic			90	2.7
	Other			42	1.3
Body mass index (kg/m^2)		27.3	3.8		
Height (cm)		174	6.9		
BMD from DXA (g/cm^2)	Lumbar spine	1.17	0.25		
	Total hip	0.96	0.14		
	Femoral neck	0.79	0.13		
BMD from QCT of femoral neck (g/cm^3)	Integral	0.289	0.057		
	Cortical	0.526	0.062		
	Trabecular	0.073	0.044		
Volumetric properties from QCT	Percent cortical bone of femoral neck	44.4	6.6		
	Minimum cross-sectional area of femoral neck (cm^2)	12.7	1.7		
	Percent cortical bone of total femur	38.8	4.8		
	Medullary volume of femoral neck (cm^3)	11.7	3.5		

volume times 100. Volumetric BMD for integral, trabecular, and cortical compartments was computed over all voxels in the respective volumes. Cortical and trabecular parameters were defined for the total hip region using parallel methods to those for the femoral neck.

In a group of postmenopausal women, CVs for the QCT analysis used ranged from 0.6% to 3% for vBMD measures and 1% to 4% for cross-sectional areas, tissue volumes, and other geometric measures.[17]

Follow-up

After baseline evaluation, participants were followed for an average of 5.5 yr. At 4-mo intervals, each man was queried by mail concerning the presence of fractures. Any reported fracture was verified by obtaining medical records including reports of radiographic results.

Statistical analysis

The overall analysis used variables from QCT and DXA as predictors of fracture. For QCT, the analysis focused on parameters from the femoral neck, although the total femur measurements were used in some analyses. We first plotted survival curves of time to first fracture within quartiles (defined within each clinical site) for each variable. We then performed adjusted analyses using Cox proportional hazards models[18] and expressed hazard ratios (HRs; and 95% CIs) per SD decrease in the parameters. All analyses were adjusted for age (continuous), BMI, and clinical center (six categorical variables) because each of these three variables was strongly related to the QCT parameters. Because the initial analysis indicated a threshold effect in the lowest quartile compared with the higher three, in addition to HR per SD decrease, we calculated the relative hazard for the lowest risk quartile compared with the three highest combined. We used stepwise multiple predictor proportional hazards models to examine the interdependence of hip geometric and density parameters. These analyses included all QCT-assessed variables at the femoral neck. For any variables correlated >0.7, only one was included (the one with the higher univariate relationship). After the best set of significant QCT variables were chosen, an additional multivariate analysis was performed in which femoral neck DXA was added. Receiver operating characteristic (ROC) curves were used to examine whether the addition of QCT measures improves the prediction of hip fracture over DXA measures alone.[19]

RESULTS

Table 1 shows baseline characteristics of the 3347 men in the QCT cohort. There were no differences between the men in the QCT cohort and the overall MrOS group, except that the proportion of minority men was somewhat higher in the QCT cohort.

Forty-two hip fractures occurred during the period of follow-up (overall rate: 2.3 per 1000 person-years); about two thirds were femoral neck fractures. For several of the bone density and structural parameters, the risk of hip fracture was substantially higher in the lowest quartile compared with the higher quartiles (Table 2; Fig. 1). For example, for femoral neck integral volumetric density, the 5-yr risk of hip fracture in the lowest quartile was >15 times

TABLE 2. HIP FRACTURE INCIDENCE RATE BY QUARTILE OF QCT AND DXA IN 3347 MEN (42 HIP FRACTURES, OVERALL RATE 2.3 PER 1000 PERSON-YEARS)

	Quartile 1		*Quartile 2*		*Quartile 3*		*Quartile 4*	
	Fractures	*Rate*	*Fractures*	*Rate*	*Fractures*	*Rate*	*Fractures*	*Rate*
Femoral neck								
Integral bone, volumetric BMD (g/cm^3)	30	6.6	5	1.1	5	1.1	2	0.4
Cortical bone, volumetric BMD (g/cm^3)	19	4.1	7	1.5	7	1.5	9	2.0
Trabecular bone, volumetric BMD (g/cm^3)	23	5.1	10	2.2	8	1.7	1	0.2
Integral volume (cm^3)	4	0.9	13	2.8	13	2.8	12	2.6
Cortical volume (cm^3)	18	4.0	12	2.6	8	1.7	4	0.9
Percent cortical volume	30	6.6	7	1.5	3	0.6	2	0.4
Medullary volume (cm^3)	0	0.0	10	2.2	12	2.6	20	4.4
Minimum cross-sectional area (cm^2)	11	2.4	7	1.5	15	3.3	9	1.9
Areal BMD from DXA (g/cm^2)	30	6.7	8	1.7	1	0.2	3	0.6
Total femur								
Integral bone, volumetric BMD (g/cm^3)	30	6.7	7	1.5	3	0.6	2	0.4
Cortical bone, volumetric BMD (g/cm^3)	21	4.6	9	1.9	6	1.3	6	1.3
Trabecular bone, volumetric BMD (g/cm^3)	31	6.9	7	1.5	2	0.4	2	0.4
Cortical bone, BMC (g)	19	4.2	15	3.3	4	0.9	4	0.9
Integral volume (cm^3)	7	1.5	9	1.9	14	3.0	12	2.6
Cortical volume (cm^3)	18	4.0	14	3.0	5	1.1	5	1.1
Percent cortical volume	33	7.4	3	0.6	3	0.6	3	0.6
Areal BMD from DXA (g/cm^2)	31	6.9	8	1.8	0	0.0	3	0.6

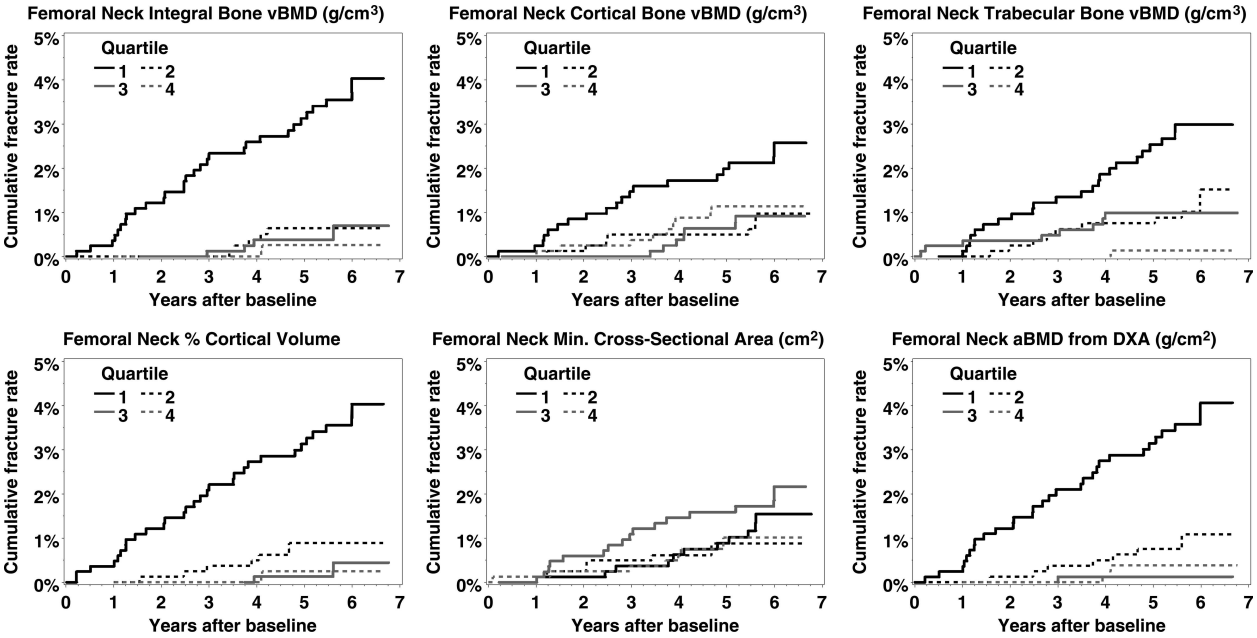

FIG. 1. Relationship of quartile of structure and density to hip fracture risk, unadjusted.

that in the highest quartile (3.6% versus 0.2%; Table 2). The association was similar in magnitude and steepness for percent cortical volume in the femoral neck, trabecular BMD, and for femoral neck areal BMD assessed by DXA. Other parameters such as cross-sectional area of the femoral neck and cortical BMD were not strongly related to hip fracture risk.

Table 3 shows the relationship of individual bone density and geometry parameters at the femoral neck to risk of hip fracture adjusted for age, BMI, and clinical center. Most parameters were strongly related to hip fracture. For example, for percent cortical volume in the femoral neck, there was a 3-fold increased risk of hip fracture ($p < 0.001$) for each SD decrease, whereas risk was increased 4-fold for each SD reduction in femoral neck aBMD. Femoral neck integral volume and minimum cross-sectional area were not significantly associated with hip fracture risk in these analyses. The relationship of parameters in the total hip (data not shown), including areal BMD, was generally similar to the comparable parameters at the femoral neck.

Table 3. HRs of Skeletal Parameters at the Femoral Neck for Hip Fracture Adjusted for Clinic Site, Age, and Body Mass Index

	HR per SD decrease		
	HR	*95% CI*	*p*
Integral bone, volumetric BMD (g/cm^3)	3.55	2.33, 5.40	<0.001
Cortical bone, volumetric BMD (g/cm^3)	1.69	1.20, 2.37	0.003
Trabecular bone, volumetric BMD (g/cm^3)	2.21	1.55, 3.15	<0.001
Integral volume (cm^3)	0.76	0.58, 1.00	0.053
Cortical volume (cm^3)	1.62	1.10, 2.38	0.015
Medullary volume (cm^3)	0.64	0.52, 0.80	<0.001
Percent cortical volume	3.02	2.15, 4.23	<0.001
Minimum cross-sectional area (cm^2)	1.31	0.95, 1.80	0.101
Areal BMD from DXA (g/cm^2)	4.13	2.67, 6.38	<0.001

Multivariable analysis: independent contribution among parameters

Multivariable analyses that included all the QCT femoral neck structural and density measures showed that percent cortical volume, the minimum cross-sectional area, and trabecular BMD are independent predictors of hip fracture risk (Table 4, model B). Compared with the univariable, adjusted models, the point estimate for the HR increased for the minimum cross-sectional area and became significant.

Percent cortical volume and cross-sectional area of the femoral neck remained significant predictors, even after adjustment for areal BMD (Table 4, model C). In the presence of the QCT variables, the association of areal BMD with fracture was attenuated but remained statistically significant. Trabecular density was not associated with fracture risk after adjustment for aBMD.

When the analyses were limited to femoral neck fractures ($N = 24$), the results were similar for univariable and multivariable analyses, but because of the reduced numbers of fractures, the CIs were wider (data not shown).

Predictive value of QCT parameters versus DXA

ROC curves were used to examine whether the addition of QCT measures improves the prediction of hip fracture over DXA measures alone. Using femoral neck aBMD in ROC analyses yielded an area under the curve of 0.853, whereas ROC analyses using a combination of DXA and OCT measures (percent cortical volume, trabecular BMD, and minimal cross-sectional area) yielded an area under the curve of 0.860 (Table 4; Fig. 2).

DISCUSSION

This is the first prospective study to examine the relationship between QCT-derived structural and densitometric measures of the proximal femur and hip fracture risk. We found that the detailed information available from QCT provides insights into the pathophysiology of hip fractures. Three QCT-derived femoral neck parameters (percent cortical volume, minimal cross-sectional area, and trabecular BMD) were independent predictors of hip fracture risk. Furthermore, we found that femoral neck structure (percent cortical volume and minimum cross-sectional area) continued to make independent contributions after adjustment for aBMD, although overall fracture prediction was not improved compared with aBMD alone. These findings coming as they do from a prospective study and using 3D imaging advance a growing literature of primarily cross-sectional and case-control studies that have assessed hip structure from DXA images and radiographs. These findings may have important potential implications for understanding the pathophysiology of hip fracture, as well as for the diagnosis and treatment of osteoporosis.

The proximal femur is a complex structure, and identifying specific measurable parameters that reflect its strength is challenging. A variety of structural parameters have been identified as potential predictors of hip fracture, including bone width,[11,20] cortical thickness,[21–23] hip axis length,[10,24] neck shaft angle,[21] and trabecular density and structure.[25] In addition, some recent studies have suggested that it may be important to assess structure at specific regions of the hip[26]; others have integrated structural elements with density measures to construct composite bone strength estimates[27] or perform finite element analyses.[28,29] Whereas much additional work will be needed to identify the specific structure parameters and imaging techniques that are optimal for hip fracture prediction, our study confirms that structure of the hip plays an important role in the determination of hip fracture risk.

Although there are a number of cross-sectional and retrospective, case-control studies, there are few large, prospective studies relating femoral geometry to hip fracture.[30] Moreover, the prospective studies to date have relied on 2D imaging techniques, such as pelvic radiographs[11] or DXA-based hip structural analysis (HSA)[24,31,32] to assess femoral structure. Whereas these studies have identified measures of femoral structure as predictors of hip fracture, in general, these parameters did not improve the prediction of hip fracture risk beyond that provided by femoral BMD.[24,31,32] This finding may be attributable to the observation that many of the femoral geometry measures derived from HSA are highly correlated to femoral BMD.[33] This study provides a unique opportunity to compare fracture risk predictions using femoral structure and volumetric BMD derived from 3D QCT to traditional aBMD measures from DXA. Furthermore, the assessment of femoral structure did not rely on any a priori assumptions about femoral geometry or the distribution of trabecular versus cortical bone, as is the case with HSA.[12]

Among a variety of structural elements examined, we found that a lower proportion of cortical bone, a smaller minimum size of the femoral neck, and lower trabecular BMD were independently associated with greater likelihood of hip fracture. From a biomechanical perspective, these findings are reasonable, because the size of the bone, the amount of cortical bone, and the integrity of trabecular bone component are predicted to affect overall resistance to fracture.[9,34,35] Our finding in the adjusted analysis that

TABLE 4. HRs OF MULTIVARIATE MODELS OF SKELETAL PARAMETERS AT THE FEMORAL NECK FOR HIP FRACTURE ADJUSTED FOR CLINIC SITE, AGE, AND BODY MASS INDEX

	Model A (HR per SD decrease)			*Model B (HR per SD decrease)*			*Model C (HR per SD decrease)*		
	HR	*95% CI*	*p*	*HR*	*95% CI*	*p*	*HR*	*95% CI*	*p*
Trabecular bone, volumetric BMD (g/cm^3)	—			1.65	1.15, 2.37	0.007	1.29	0.84, 1.98	0.250
Percent cortical volume	—			3.19	2.23, 4.57	<0.001	2.42	1.56, 3.76	<0.001
Minimum cross-sectional area (cm^2)	—			1.59	1.24, 2.05	<0.001	1.48	1.14, 1.94	0.004
Areal BMD from DXA (g/cm^2)	4.13	2.67, 6.38	<0.001	—			1.91	1.06, 3.46	0.033

Area under the ROC curve for Models A, B, and C were 0.853, 0.855, and 0.860, respectively.

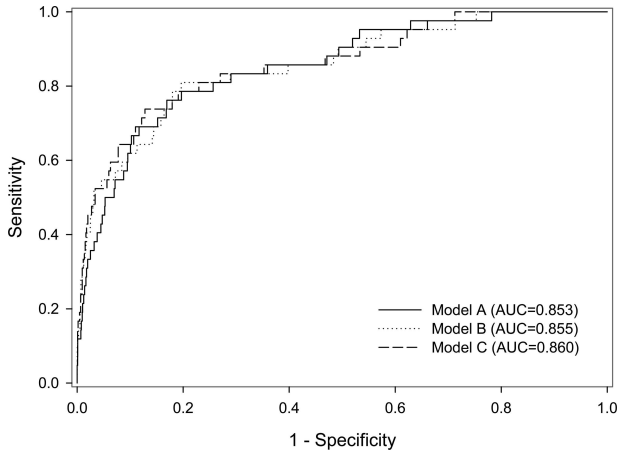

FIG. 2. ROC curves comparing DXA alone (model A), QCT parameters (model B), and QCT with DXA (model C).

smaller femoral neck size increases fracture risk is consistent with some reports,[31] but differs from other studies that have related larger femoral neck diameter to increased fracture risk.[16,32] This difference may reflect the incorporation of a variety of structural and densitometric measures in our final models, allowing the influence of smaller size to be identified as an independent predictor of fracture. Others have also reported low bone width as a risk factor for fracture.[36]

As an aid to diagnosis, the assessment of these structural components has the potential to improve identification of patients at high fracture for risk and improve fracture prediction.[21,36] However, there was a very strong relationship between aBMD and risk of hip fracture, and our ROC analysis showed that the QCT parameters yielded no overall advantage for fracture prediction relative to femoral neck areal BMD alone. Furthermore, combining QCT parameters with femoral neck aBMD similarly provided no advantage to DXA or QCT alone. Thus, whereas our results from QCT suggest that structure and density have independent roles, they indicate that aBMD at the hip is strongly predictive of hip fracture, presumably because of its fortuitous combination of density and structure into a single measurement. On the other hand, structural parameters might be predictive in subgroups of patients. For example, whereas BMD strongly predicts fractures, most nonvertebral fractures occur in those with BMD above the osteoporotic range.[6,7] Thus, structure may play a role in identifying non-osteoporotic patients at high risk for hip fracture. With continued follow-up of the MrOS cohort, future analyses will have greater power to test this hypothesis.

We were surprised by the sharpness of the risk gradient, particularly in the lowest quartile, for several of our parameters, assessed by both DXA and QCT. For example, for percent cortical volume in the total hip, 71% of fractures (30 of 42) occurred in the men with the lowest 25% of values. Our findings confirmed the similar pattern for areal hip BMD previously noted in the MrOS study[5]: for men with femoral neck aBMD in the lowest quartile (T-scores < –1.75), their hip fracture risk was about seven times higher than those above that value. The only other study to explore the shape of the relationship of density to hip fracture risk in men found a similar threshold-like gradient among men >75 yr of age.[37] However, studies in women[2,3] suggested more gradual gradients of risk. This unexpected pattern in men needs to be confirmed by longer follow-up and other studies. If there is a threshold value that identifies men at high risk of fracture, this would be a useful for selecting men most likely to benefit from treatment.

Because therapies may vary in their impact on components of structure despite having similar effects on aBMD, a better understanding of the role of hip structure in fracture risk may guide development of new osteoporosis treatments. For example, PTH seems to increase areal hip density less than bisphosphonates but increases trabecular density and cortical bone volume much more than bisphosphonates.[38–40] Some studies have suggested that PTH may also increase bone size,[40,41] whereas other studies have not.[38] These observations indicate that parameters such as cortical volume, trabecular density, or bone size should be specifically considered in evaluating potential new therapies.

Our study has a number of limitations. First, whereas this is the only prospective study of QCT and hip fracture risk, we had only 42 hip fractures among the men with QCT at baseline. However, while the results could change somewhat as more fractures accumulate over a longer follow-up period, we believe the general conclusions are robust. Second, the study was performed in men, most of whom were

white, and it is not certain the extent to which results are generalizable to women or other races. However, as mentioned previously, several recent prospective studies have shown that femoral geometry measures are predictive of hip fracture risk in women.[24,31,32] Third, we evaluated a limited number of QCT structural parameters and did not study all possible structural parameters, such as spatial distribution of cortical bone, that have recently been identified as potentially important for femoral fragility.[26] Last, this is the first study to use QCT of bone in a multicenter design. There were modest but significant differences in some QCT measures across clinical sites that could be caused by differences in QCT machines used at the sites.[42] Whereas we did adjust for these differences in all analyses, a further exploration of this issue may be important for implementation of QCT in future multicenter studies.

We conclude that specific elements of hip structure are predictive of hip fracture. While elements of hip structure did not improve overall prediction compared with areal BMD alone, understanding the role of hip structure may improve the understanding of the cause of fracture, the ability to identify those at higher risk, and the development of new therapies.

ACKNOWLEDGMENTS

DMB had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. MrOS is supported by the NIH. The following institutes provide support: the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), the National Institute on Aging (NIA), the National Center for Research Resources (NCRR), and NIH Roadmap for Medical Research under the following grant numbers: UO1 AR45580, UO1 AR45614, UO1 AR45632, UO1 AR45647, UO1 AR45654, UO1 AR45583, UO1 AG18197, U01 AG027810, and UL1 RR024140. The authors thank Benjamin Chan, MA, and Lori Lambert, MS, for data analysis assistance.

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Received in original form December 7, 2007; revised form March 7, 2008; accepted March 12, 2008.

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