Acta Orthopaedica et Traumatologica Turcica 50 (2016) 548–553

Contents lists available at ScienceDirect

Acta Orthopaedica et Traumatologica Turcica

journal homepage: https://www.elsevier.com/locate/aott

Discriminative ability of calcaneal quantitative ultrasound compared with dual-energy X-ray absorptiometry in men with hip or distal forearm fractures

Fatih Cesme, Sina Esmaeilzadeh*, Aydan Oral

Istanbul University, Istanbul Faculty of Medicine, Istanbul, Turkey

ARTICLE INFO

Article history:
Received 1 September 2015
Accepted 25 December 2015
Available online 25 September 2016

Keywords:
Calcaneal quantitative ultrasound
Distal forearm fractures
Dual-energy X-ray absorptiometry
Hip fractures
Osteoporosis

ABSTRACT

Objectives: The aim of this case–control study was to compare the discriminatory ability of bone mineral density (BMD) measurements and calcaneal quantitative ultrasound (QUS) parameters for fractures and to determine fracture thresholds for each variable in men with hip or distal forearm fractures.
Patients and methods: A total of 20 men with hip and 18 men with distal forearm fractures and 38 age-matched controls were included in this study. Dual-energy X-ray absorptiometry (DXA) BMD (spine and hip) and calcaneal QUS measurements were made. Area under the curves (AUCs) were calculated to assess fracture discriminatory power of DXA and QUS variables.
Results: Quantitative Ultrasound Index (QUI) T-score and Speed of Sound (SOS) were found to be the best parameters for the identification of hip and distal forearm fractures, respectively, with AUCs greater than those of DXA BMD and other QUS parameters. While a QUI T-score of ≤ -1.18 could identify and rule out hip fracture cases with approximately 80% sensitivity and specificity, a SOS value of ≤ 1529.75 reached to almost 90% for ruling in and out distal forearm fractures.
Conclusion: The discriminatory performance of calcaneal QUS variables between fractured and non-fractured men was as good as those of the DXA BMD and even better. Since men appear to sustain fractures at closer QUS variable levels than those of the DXA BMD regardless of the fracture type, it may be speculated that calcaneal QUS may be more helpful in predicting the risk of fractures when BMD alone does not demonstrate impaired bones.
Level of Evidence: Level III, Study of Diagnostic Test

Introduction

The most common osteoporotic fractures include distal forearm fractures (DFFs), hip fractures (HFs), and vertebral fractures with an estimated number of 1.7, 1.6, and 1.4 million, respectively, in 2000.[1] The remaining life-course probability of a HF and a DFF at age 50 was estimated as 10.7% and 22.9% in men, respectively.[2]

The association between HFs and mortality is well established in both genders, being higher in males.[3] Increasing evidence also suggests an increased risk for premature mortality in those with DFFs.[4] Osteoporotic fractures may also cause significant disability[5] as well as tremendous societal and economic impact.[1] Therefore, it is crucial to predict the risk of osteoporotic fractures and/or to identify bone characteristics of fracturers to apply evidence-based pharmacological and non-pharmacological treatment options for prevention.[5,6]

While dual energy X-ray absorptiometry (DXA) bone mineral density (BMD) measurement is the gold standard for predicting HFs,[7] two meta-analyses of prospective studies showed that calcaneal quantitative ultrasound (cQUS) variables were strong predictors of non-spinal fracture risk, in both men and women usually in a way comparable to DXA-BMD measurements.[8,9] cQUS studies are not as many as in men than they are in women.[9] A number of case–control studies provided evidence on the fracture discriminatory ability of cQUS in men[10–14] however, very few of them assessed cut-off values for QUS variables for fractures providing us with any osteoporotic fracture thresholds while not defining separate cutoff points for HFs or DFFs.[15,16]

* Corresponding author. Istanbul University, Istanbul Faculty of Medicine, Department of Physical Medicine and Rehabilitation, Millet Cad, Capa, Fatih, 34093, Istanbul, Turkey.
E-mail address: sinabox@gmail.com (S. Esmaeilzadeh).
Peer review under responsibility of Turkish Association of Orthopaedics and Traumatology.

http://dx.doi.org/10.1016/j.aott.2016.08.006

The aim of this case–control study was two-fold: to compare the fracture discriminatory ability of cQUS parameters and DXA-BMD measurements and to determine fracture thresholds for DXA-BMD and cQUS variables separately for HFs or DFFs in men.

Patients and methods

Participants

The study participants consisted of 38 men with low-energy fractures in the period of 6 months after fracture, 20 having HFs and 18 having DFFs and 38 age-matched men (±2 years than each fracturer) without any fracture, disease, or medications known to affect bone metabolism as the control group. All of the subjects filled out a questionnaire including information such as age, height and weight, handedness, smoking status, physical activity level (the time spent for walking before the fracture categorized as <1, 1–2, and >2 h a week), a family or own history of osteoporotic fracture, and information for fracturers such as type and side of fracture, and time since fracture. Participants had cQUS and DXA-BMD measurements. The study protocol was approved by the local Ethics Committee and written informed consent was obtained from all of the participants.

DXA measurements

DXA-BMD measurements were made using a Hologic QDR 1000 DXA device (Hologic, Waltham, MA, USA) at posteroanterior spine and hip (at the non-fractured side in the fracturers and at the non-dominant side in the controls). Hip fractured men were ambulatory, being able to come to our bone densitometry unit for testing. The BMD of the vertebrae from L1 to L4 at the lumbar spine (LS) and femoral neck (FN), and total femur BMD at the hip were included in the data analysis. The presence of osteoporosis at any region of interest (ROI) was defined as a T-score ≤ -2.5. A T-score between -1 and -2.5 was classified as low bone mass/osteopenia and a T-score ≥ -1 was classified as normal.[17] However, Z-scores of ≤ -2.0 were used for defining BMD "below the expected range for age," (osteoporosis), while Z-scores > -2.0 were considered "within the expected range for age" (normal) in those <50 years.[18] An individual was considered as osteoporotic in the presence of a T-score ≤ -2.5 or a Z-score ≤ -2.0 (<50 years) in any of the ROI.

QUS measurements

Acoustic parameters of bone were measured using a portable, gel-coupled cQUS device (Sahara® Clinical Bone Sonometer, Hologic, Waltham, MA, USA). This device measures broadband ultrasound attenuation (BUA) (dB/MHz) and the speed of sound (SOS) (m/s) and calculates Quantitative Ultrasound Index (QUI) as well as a QUI T-score and estimated heel BMD (eBMD) (g/cm^2). Daily quality control was performed using a phantom provided by the manufacturer. Given the findings that considerable differences may exist between sides as found in women[19] both heel measurements were made and repeated with repositioning of the feet. The mean of the two measurements were calculated for both feet and the lowest mean value of QUS variables obtained for the two sides was included in statistical analyses, except for the hip fractured men in whom the mean of QUS measurements of the non-fractured side was used.

Precision of cQUS parameters

The short-term precision of the QUS variables was examined as recommended by Glüer et al using the double measurements obtained in all subjects with repositioning of the feet as the root-mean-square coefficient of variation (RMS-%CV) according to the following formula: RMS-%CV $= \sqrt{\sum CVi^2/n} \times 100$ (CV: coefficient of variation).[20]

Statistical analysis

For statistical analyses, SPSS software, version 17.0 (SPSS Inc., Chicago, IL, USA) was employed. We used Student's t-test and Chi square tests to compare continuous and dichotomous variables, respectively, in fracturers and non-fracturers. Receiver operating characteristic (ROC) analysis was used to determine fracture discriminatory ability of QUS and BMD variables. Areas under the ROC curves (AUCs) were calculated for each variable. The sensitivity and specificity of various cut-off points for each variable in ROC curves showing the best balance were used to determine fracture thresholds for variables. Significance was set at $p < 0.05$.

Results

One participant with a HF and a HF control did not have a spine BMD measurement due to metal implants in one and positioning difficulties in the other. A man with a HF and the other with a DFF did not have a hip DXA measurement due to positioning problems. Characteristics of study participants are shown in Table 1. BMD and QUS variables are displayed in Table 2. AUCs are given in Table 3. Various cut-off values for BMD and QUS variables and their sensitivity and specificity are shown in Table 4. The precision of QUS variables are shown in Table 5.

Discussion

As expected, the results of this study revealed significantly lower values for both DXA-BMD and cQUS variables in those with fractures when compared with those without (Table 2) in line with other studies comparing DXA and QUS variables for the identification of hip,[11,21,22] lower extremity,[14] or all osteoporosis-related fractures.[23,24] Studies using only QUS in men also demonstrated significantly lower QUS variables in fracturers than non-fracturers.[10,12,13,15,16]

The ability of DXA-BMD measurements in separating men with HF or DFFs from those without could be considered as "fair" or "good" with AUCs ranging from 0.772 (for FN T-score) to 0.838 (for L1–L4 T-score) for HFs and 0.775 (for L1–L4 BMD) to 0.891 (for FN T-score) for DFFs (Table 3). It was interesting to note that discriminative power of L1–L4 BMD was higher than that of the FNBMD for HFs as reflected by AUCs (0.836 vs. 0.778) and vice versa for DFFs (0.775 vs. 0.876), despite the findings of a strong association with risk of HF, and FNBMD in men and weaker association with LSBMD.[25] However, another study did show the equally good predictive ability of LS and FNBMD for various types of fractures in women.[26] Supporting this finding, two studies in men with any osteoporotic fractures demonstrated a better discrimination power of LSBMD than that of FNBMD, AUC values for LS vs. FNBMD being 0.800 vs. 0.730 and 0.668 vs. 0.643, possibly resulting from the inclusion of relatively fewer number of men with non-spinal fractures. Whether these findings apply to HFs alone in men remains to be further investigated in large-scale prospective studies. As for DFFs, in parallel with our findings, FNBMD was found a significant risk factor.[23,27,28]

cQUS variables discriminated men with HFs or DFFs in a way comparable to DXA-BMD measurements with similar or slightly greater AUCs varying from 0.819 (for BUA) to 0.841 (for QUI T-score), implying "good" discriminatory ability. For men with DFFs, all QUS variables, with the exception of BUA, could be considered as

Table 1
Characteristics of the participants.

Characteristics	Hip fracture (n. 20)	Controls (n. 20)	p value	Forearm fracture (n. 18)	Controls (n. 18)	p value	p value
Age (years)	69.30 ± 10.75	68.85 ± 10.39	0.894	54.78 ± 8.61	54.83 ± 7.88	0.984	<0.001
Age range (years)	47–82	47–83		44–73	44–71		
Weight (kg)	69.80 ± 12.89	76.55 ± 14.01	0.121	77.78 ± 9.43	77.83 ± 8.60	0.985	0.038
Height (m)	1.68 ± 0.08	1.69 ± 0.07	0.473	1.73 ± 0.07	1.71 ± 0.06	0.345	0.045
BMI (kg/m^2)	24.80 ± 3.80	26.59 ± 3.37	0.124	26.03 ± 2.24	26.75 ± 2.30	0.348	0.227
Time since fx (mo)	4.08 ± 1.67			2.86 ± 1.27			
Smoking status	8 (40.0)/12(60.0)	0 (0.0)/20 (100.0)	0.003	7 (38.9)/11(61.1)	3 (16.7)/15(83.3)	0.137	0.944
Cigarettes smoked	26.25 ± 9.16	–		28.57 ± 9.00	33.33 ± 11.55	0.497	0.630
Years smoked	42.25 ± 8.31	–		33.86 ± 10.96	30.00 ± 10.00	0.616	0.116
Physical activity (walking)							
<1 h/week	12 (60.0)	4 (20.0)	0.023	9 (50.0)	0 (0.0)	<0.001	0.353
1–2 h/week	7 (35.0)	10 (50.0)		5 (27.8)	3 (16.7)		
>2 h/week	1 (5.0)	6 (30.0)		4 (22.2)	15 (83.3)		
Previous fracture	3 (15.0)/17(85.0)	0 (0.0)/20(100.0)	0.231	4 (22.2)/14(77.8)	0 (0.0)/18(100.0)	0.104	0.687
Parent history of fracture	1 (5.0)/19(95.0)	0 (0.0)/20(100.0)	1.000	1 (5.6)/17(94.4)	3 (16.7)/15(83.3)	0.603	1.000
Bone status							
Osteoporosis	11 (55.0)	1 (5.0)	0.001	7 (38.9)	0 (0.0)	<0.001	0.725
Osteopenia	7 (35.0)	9 (45.0)		9 (50.0)	6 (33.3)		
Normal	2 (10.0)	10 (50.0)		2 (11.1)	12 (66.7)		
OP in any ROI	11 (55.0)/9 (45.0)	1 (5.0)/19(95.0)	0.001	7 (38.9)/11(61.1)	0 (0.0)/18(100.0)	0.008	0.321
Spinal OP	10 (52.6)/9(47.4)	1 (5.3)/18(94.7)	0.001	7 (38.9)/11(61.1)	0 (0.0)/18(100.0)	0.008	0.402
Femoral neck OP	6 (31.6)/13(68.4)	1 (5.0)/19(95.0)	0.044	1 (5.9)/16(94.1)	0 (0.0)/18(100.0)	0.486	0.092
Total hip OP	4 (21.1)/15(78.9)	0 (0.0)/20(100.0)	0.047	1 (5.9)/16(94.1)	0 (0.0)/18(100.0)	0.486	0.342

BMI: Body mass index; Fx: fracture; mo: months; OP: osteoporosis; ROI: Region of interest.
Mean ± SD are shown for continuous variables; Number of participants (%) are shown for categorical variables as YES/NO; p values for variables for hip fracture vs. distal forearm fracture cases ($p < 0.05$).

Table 2
DXA BMD and QUS variables in participants with hip or distal forearm fractures and controls.

BMD and QUS variables	Hip fracture (n. 20)	Controls (n. 20)	p value	Forearm fracture (n. 18)	Controls (n. 18)	p value	p value
L1–L4 BMD (g/cm^2)	0.845 ± 0.165	1.069 ± 0.145	<0.001	0.899 ± 0.105	1.026 ± 0.102	0.001	0.235
L1–L4 T-score	−2.23 ± 1.53	−0.19 ± 1.32	<0.001	−1.78 ± 0.97	−0.59 ± 0.97	0.001	0.286
Femoral neck BMD (g/cm^2)	0.635 ± 0.111	0.794 ± 0.160	0.001	0.724 ± 0.103	0.876 ± 0.080	<0.001	0.018
Femoral neck T-score	−2.15 ± 0.86	−1.03 ± 1.17	0.002	−1.52 ± 0.75	−0.33 ± 0.60	<0.001	0.027
Total hip BMD (g/cm^2)	0.757 ± 0.118	0.956 ± 0.176	<0.001	0.856 ± 0.124	0.999 ± 0.086	<0.001	0.019
Total hip T-score	−1.81 ± 0.79	−0.53 ± 1.16	<0.001	−1.18 ± 0.82	−0.16 ± 0.56	<0.001	0.024
QUI	75.90 ± 17.91	100.61 ± 17.38	<0.001	73.67 ± 8.56	94.83 ± 13.68	<0.001	0.624
QUI T-score	−1.83 ± 1.02	−0.47 ± 1.00	<0.001	−2.02 ± 0.53	−0.77 ± 0.80	<0.001	0.473
BUA (dB/MHz)	57.01 ± 20.03	79.99 ± 16.05	<0.001	56.58 ± 8.87	74.26 ± 14.76	<0.001	0.931
SOS (m/s)	1520.84 ± 24.80	1557.82 ± 28.16	<0.001	1514.58 ± 13.97	1549.52 ± 20.03	<0.001	0.339
eBMD (g/cm^2)	0.404 ± 0.113	0.560 ± 0.110	<0.001	0.388 ± 0.056	0.524 ± 0.086	<0.001	0.579

DXA: dual-energy X-ray absorptiometry; BMD: Bone mineral density; QUS: Quantitative ultrasound; L1–L4: lumbar vertebrae 1 to 4; QUI: Quantitative ultrasound index; BUA: Broadband ultrasound attenuation; SOS: Speed of sound; eBMD: estimated heel BMD.
Mean ± SD are shown for continuous variables; p values for variables for hip fracture vs. distal forearm fracture cases ($p < 0.05$).

Table 3
Area under the ROC curves for fracture discrimination power of variables.

BMD and QUS variables	Hip fracture					Distal forearm fracture				
	Area	SE	p value	95% CI		Area	SE	p value	95% CI	
				Lower	Upper				Lower	Upper
L1–L4 BMD (g/cm^2)	0.836	0.066	<0.001	0.708	0.965	0.775	0.078	0.006	0.621	0.928
L1–L4 T-score	0.838	0.065	<0.001	0.710	0.965	0.788	0.076	0.004	0.639	0.936
Femoral neck BMD (g/cm^2)	0.778	0.075	0.004	0.630	0.925	0.876	0.064	<0.001	0.751	1.001
Femoral neck T-score	0.772	0.076	0.005	0.623	0.921	0.891	0.058	<0.001	0.776	1.005
Total hip BMD (g/cm^2)	0.822	0.068	0.001	0.689	0.954	0.827	0.073	0.001	0.684	0.970
Total hip T-score	0.801	0.072	0.002	0.660	0.942	0.851	0.068	<0.001	0.718	0.985
QUI	0.836	0.067	<0.001	0.704	0.968	0.918	0.046	<0.001	0.829	1.008
QUI T-score	0.841	0.067	<0.001	0.710	0.972	0.918	0.045	<0.001	0.830	1.007
BUA (dB/MHz)	0.819	0.072	0.001	0.677	0.960	0.840	0.067	0.001	0.708	0.971
SOS (m/s)	0.825	0.069	0.001	0.689	0.961	0.938	0.042	<0.001	0.856	1.019
eBMD (g/cm^2)	0.836	0.067	<0.001	0.704	0.968	0.922	0.044	<0.001	0.835	1.008

ROC: Receiver operating characteristic; SE: Standard error; BMD: Bone mineral density; QUS: Quantitative ultrasound; L1–L4: lumbar vertebrae 1 to 4; QUI: Quantitative ultrasound index; BUA: Broadband ultrasound attenuation; SOS: Speed of sound; eBMD: estimated heel BMD.

Table 4
Various cutoff values for fractures with their sensitivity and specificity.

BMD and QUS variables	Hip fracture			Distal forearm fracture		
	Cut-off values	Sensitivity	Specificity	Cut-off values	Sensitivity	Specificity
L1–L4 BMD (g/cm^2)	0.954	0.667	0.789	0.948	0.588	0.722
	0.966	**0.722**	**0.737**	**0.956**	**0.588**	**0.611**
	0.984	0.778	0.737	0.970	0.647	0.611
L1–L4 T-score	−1.26	0.667	0.789	−1.30	0.588	0.667
	−1.14	**0.722**	**0.737**	**−1.23**	**0.588**	**0.611**
	−0.97	0.778	0.737	−1.10	0.647	0.611
Femoral neck BMD (g/cm^2)	0.673	0.556	0.632	0.773	0.765	0.833
	0.679	**0.611**	**0.632**	**0.795**	**0.824**	**0.833**
	0.684	0.667	0.632	0.814	0.824	0.778
Femoral neck T-score	−1.90	0.556	0.632	−1.16	0.715	0.833
	−1.85	**0.611**	**0.632**	**−0.98**	**0.824**	**0.833**
	−1.81	0.667	0.632	−0.82	0.882	0.833
Total hip BMD (g/cm^2)	0.799	0.667	0.737	0.909	0.706	0.778
	0.812	**0.667**	**0.684**	**0.934**	**0.706**	**0.722**
	0.824	0.667	0.632	0.947	0.765	0.722
Total hip T-score	−1.47	0.611	0.684	−0.76	0.706	0.778
	−1.39	**0.611**	**0.632**	**−0.64**	**0.706**	**0.722**
	−1.32	0.611	0.579	−0.54	0.824	0.722
QUI	83.38	0.722	0.779	81.50	0.765	0.833
	88.03	**0.778**	**0.779**	**81.95**	**0.765**	**0.778**
	92.10	0.833	0.779	82.33	0.824	0.778
QUI T-score	−1.45	0.722	0.779	−1.58	0.765	0.833
	−1.18	**0.778**	**0.779**	**−1.53**	**0.765**	**0.778**
	−0.93	0.833	0.779	−1.45	0.882	0.778
BUA (dB/MHz)	67.38	0.667	0.737	63.85	0.706	0.778
	68.33	**0.722**	**0.737**	**64.87**	**0.765**	**0.778**
	68.68	0.778	0.737	65.55	0.765	0.722
SOS (m/s)	1532.15	0.722	0.779	1528.60	0.882	0.944
	1537.50	**0.778**	**0.779**	**1529.75**	**0.882**	**0.889**
	1540.65	0.833	0.779	1530.80	0.882	0.833
eBMD (g/cm^2)	0.451	0.722	0.779	0.439	0.765	0.833
	0.480	**0.778**	**0.779**	**0.442**	**0.765**	**0.778**
	0.506	0.833	0.779	0.445	0.824	0.778

BMD: Bone mineral density; QUS: Quantitative ultrasound; L1–L4: lumbar vertebrae 1 to 4; QUI: Quantitative ultrasound index; BUA: Broadband ultrasound attenuation; SOS: Speed of sound; eBMD: estimated heel BMD (Values providing the best compromise between sensitivity and specificity are marked in bold).

Table 5
Short-term precision of QUS variables expressed as RMS CV%.

	QUI	BUA	SOS	eBMD
Right heel	2.73	5.33	0.26	3.17
Left heel	2.76	5.85	0.25	3.08

QUS: Quantitative ultrasound; RMS CV: root-mean-square coefficient of variation; BMD: QUI: Quantitative ultrasound index; BUA: Broadband ultrasound attenuation; Bone mineral density; SOS: Speed of sound; eBMD: estimated heel BMD.

"excellent" in identifying fractured and non-fractured men with AUCs ranging from 0.840 (for BUA) to 0.938 (for SOS). While QUI T-score showed the best HF discriminative capability, SOS was found to have the highest AUC for the identification of DFFs (Table 3). A number of studies reported a better discriminatory ability of SOS than those of BUA and stiffness index (SI) for all osteoporosis-related fractures in men.[10,15,23] Another study demonstrated the same AUC values for SOS and SI, higher than that for BUA for HFs.[11] One study demonstrated a better lower extremity fracture discrimination power of eBMD than that of BUA, SOS, or FNBMD.[14] However, a study indicated higher ORs for hip and other non-spinal fractures for BUA (2.24 and 1.38, respectively) than those for SOS (1.71 and 1.14) and SI (2.19 and 1.27) in elderly men.[12] Another one (MrOS study), using the Sahara®, pointed to QUI as the best parameter for the prediction of non-spine fractures (NSFs) in Chinese men.[24] On the contrary, the United States arm of this study revealed the same HR (1.6) for NSFs for all QUS variables and the same HR for SOS and QUI, higher than that for BUA (2.2 vs. 2.0) for the prediction of solely HFs in American men.[22] In a very large cohort, relative risk (RR) associated with any fracture for 1 SD decrease in BUA was higher than that of SOS (1.87 vs. 1.65).[29] While the discriminatory/predictive ability of DXA-BMD were similar with those of the QUS variables, AUCs ranging from 0.71 to 0.77 for BMD and 0.720 to 0.750 for QUS variables for the identification of any fracture in a study,[11] another study showed greater AUCs for SOS (0.750) than that for FNBMD (0.730).[23] Studies calculating RR or HR for fracture prediction also demonstrated varying results, the predictive ability of DXA-BMD being superior to QUS measurements in some studies[21,24] and being identical for any NSFs and superior for HFs in another study.[22] It seems that the results with regard to the discriminative ability of DXA BM in comparison to QUS measurements as well as those of the QUS parameters in comparison to each other are inconsistent across studies, possibly resulting from different QUS devices used in studies (technical differences among QUS devices known to affect values[30]), diverse ethnicities and geographical differences (affecting BMD values[31]), prediction of combined fractures-not separating each fracture type in some studies, and the age-range of men being relatively older in most of the studies.

The most important feature of this study is the calculation of cut-off values for each DXA-BMD and QUS variable for HFs and DFFs separately (Table 4). A QUI T-score of ≤ -1.18 provided the best compromise between sensitivity and specificity with ~80% (for both) to identify HFs and to detect true negatives. The optimal QUI T-score for the discrimination of DFFs was −1.53 with a sensitivity and specificity of ~78%. This cut-off level was comparable to that of ≤ 1.5 in a study using the same device and including mostly women (only 19 men) which assessed spine and NSFs.[32] In another study,

optimal cut-off levels were suggested as 1503.6 m/s for SOS and 107.1 dB/MHz for BUA in 30 individuals with various types of fractures[15] which did not coincide with the cut-off values in our study. A cut-off level of −1.30 for SI T-score was suggested for the prediction of NSFs in Chinese men.[16] The sensitivity and specificity of optimal cut-off values for the majority of QUS variables were higher than those of the DXA-BMD measurements for both types of fractures. An important finding of the present study was that both HFs and DFFs occurred at relatively similar/closer QUS thresholds contrary to those of the DXA-BMD measurements except for L1–L4 BMD and T-score. This finding provides implications that cQUS may predict fractures earlier than DXA, an issue that needs clarification in large sampled-sized prospective studies.

The prevalence of osteoporosis in any ROI in men with HFs was 55.0%; whereas, only 5.0% of the controls was osteoporotic. In those with DFFs, the prevalence of osteoporosis was 38.9%, while none in their controls. In parallel with our findings, a study found that while HFs were more common in men with osteoporosis, DFF rates were similar in those with osteopenia and osteoporosis.[13] It appears that DFFs in men occur more often in the non-osteoporotic BMD range than those of HFs, the absence of osteoporosis not precluding the occurrence of osteoporosis-related fractures in men. Thus, prediction of DFFs relying on BMD values seems more difficult and necessitates an alternative tool for which QUS appears to be a good candidate.

The magnitude of precision errors for QUS variables (Table 5) was lower for SOS and QUI and higher for BUA than those found in other studies employing the Sahara® in men[22,24]

Limitations of the study

The results of this study should be interpreted cautiously due to some limitations. The smallness of the number of men with HFs and DFFs may make generalizability of the results difficult. This small sample size did not allow us to calculate definitive ORs for variables for their discriminative power, yielding wide confidence intervals creating uncertainty (data not shown). Additionally, the design of the study, not being prospective, may have weakened the predictive power of variables. Furthermore, QUS parameters may have been biased by physical activity level, which significantly differed between the fractured and non-fractured men, given the positive linear relationship of BUA and SOS with physical activity levels.[33] It is also important to note that the measurement of DXA-BMD and QUS variables within 6 months after a hip fracture (mean post-fracture duration: 4.08 months) may have also contributed to lower BMD [shown to have been decreased after a hip fracture][34] and QUS values [shown to have been associated with physical activity][33] due to the immobilization period after hip surgery. However, considering the low level of physical activity in men before a HF, and the findings of a study demonstrating that current physical activity accounted for 14% of the variance in FNBMD in healthy middle-aged and older men,[35] we may speculate that DXA-BMD and QUS measurements at a relatively shorter time after a HF may not have obscured substantial differences regarding the relevant variables between hip fractured and non-fractured men to a significant extent.

Conclusions

The results of this small-sampled study demonstrated similar to or even better fracture discriminatory performance of cQUS variables when compared with those of the DXA-BMD with the QUI T-score as the best parameter for the identification of HFs and SOS as the best parameter for the discrimination of DFFs. It is important to note that DFFs in men do occur at younger ages and at high BMD values, slightly weakening the discrimination performance of DXA. Since men appear to fracture hips or forearms at similar QUS variable levels, it may be speculated that cQUS may be more helpful in predicting the risk of fractures when BMD alone does not demonstrate impaired bones. Prospective studies with much larger sample sizes separately evaluating the association between cQUS and different types of fractures may elucidate the role of cQUS in predicting fractures with more definitive conclusions.

References

1. Cummings SR, Melton LJ. Epidemiology and outcomes of osteoporotic fractures. *Lancet*. 2002;359:1761–1767.
2. Kanis JA, Johnell O, Oden A, Dawson A, De Laet C, Jonsson B. Ten year probabilities of osteoporotic fractures according to BMD and diagnostic thresholds. *Osteoporos Int*. 2001;12:989–995.
3. Johnell O, Kanis JA, Odén A, et al. Mortality after osteoporotic fractures. *Osteoporos Int*. 2004;15:38–42.
4. Bliuc D, Nguyen TV, Eisman JA, Center JR. The impact of nonhip nonvertebral fractures in elderly women and men. *J Clin Endocrinol Metab*. 2014;99:415–423.
5. Oral A, Kucukdeveci AA, Varela E, et al. The role of physical and rehabilitation medicine physicians. The European perspective based on the best evidence. A paper by the UEMS-PRM Section Professional Practice Committee. *Eur J Phys Rehabil Med*. 2013;49:565–577.
6. National Osteoporosis Foundation. *Clinician's Guide to Prevention and Treatment of Osteoporosis*. Washington, DC: National Osteoporosis Foundation; 2013.
7. Johnell O, Kanis JA, Oden A, et al. Predictive value of BMD for hip and other fractures. *J Bone Miner Res*. 2005;20:1185–1194.
8. Marín F, González-Macías J, Díez-Pérez A, Palma S, Delgado-Rodríguez M. Relationship between bone quantitative ultrasound and fractures: a meta-analysis. *J Bone Miner Res*. 2006;21:1126–1135.
9. Moayyeri A, Adams JE, Adler RA, et al. Quantitative ultrasound of the heel and fracture risk assessment: an updated meta-analysis. *Osteoporos Int*. 2012;23:143–153.
10. Pluskiewicz W, Drozdzowska B. Ultrasound measurements at the calcaneus in men: differences between healthy and fractured persons and the influence of age and anthropometric features on ultrasound parameters. *Osteoporos Int*. 1999;10:47–51.
11. Gonnelli S, Cepollaro C, Gennari L, et al. Quantitative ultrasound and dual-energy X-ray absorptiometry in the prediction of fragility fracture in men. *Osteoporos Int*. 2005;16:963–968.
12. Varenna M, Sinigaglia L, Adami S, et al. Association of quantitative heel ultrasound with history of osteoporotic fractures in elderly men: the ESOPO study. *Osteoporos Int*. 2005;16:1749–1754.
13. Maggi S, Noale M, Giannini S, et al, ESOPO Study Group. Quantitative heel ultrasound in a population-based study in Italy and its relationship with fracture history: the ESOPO study. *Osteoporos Int*. 2006;17:237–244.
14. Lee HD, Hwang HF, Lin MR. Use of quantitative ultrasound for identifying low bone density in older people. *J Ultrasound Med*. 2010;29:1083–1092.
15. Pluskiewicz W, Wilk R, Wielgórecki A, Golba KS, Drozdzowska B. Fracture status in men assessed by quantitative ultrasound measurements at the calcaneus. *J Ultrasound Med*. 2011;30:877–882.
16. Liu JM, Ma LY, Bi YF, et al. A population-based study examining calcaneus quantitative ultrasound and its optimal cut-points to discriminate osteoporotic fractures among 9352 Chinese women and men. *J Clin Endocrinol Metab*. 2012;97:800–809.
17. World Health Organisation. *Assessment of Fracture Risk and its Application to Screening for Postmenopausal Osteoporosis*. Geneva: WHO; 1994. WHO technical report series 843.
18. Schousboe JT, Shepherd JA, Bilezikian JP, Baim S. Executive summary of the 2013 International Society for Clinical Densitometry Position Development Conference on bone densitometry. *J Clin Densitom*. 2013;16:455–466. Available from the ISCD website at www.iscd.org. Accessed on April 13, 2014.
19. Oral A, Yaliman A, Sindel D. Differences between the right and the left foot in calcaneal quantitative ultrasound measurements. *Eur Radiol*. 2004;14:1427–1431.
20. Glüer CC, Blake G, Lu Y, Blunt BA, Jergas M, Genant HK. Accurate assessment of precision errors: how to measure the reproducibility of bone densitometry techniques. *Osteoporos Int*. 1995;5:262–270.
21. Ekman A, Michaelsson K, Petren-Mallmin M, Ljunghall S, Mallmin H. Dual X-ray absorptiometry of hip, heel ultrasound, and densitometry of fingers can discriminate male patients with hip fracture from control subjects: a comparison of four different methods. *J Clin Densitom*. 2002;5:79–85.
22. Bauer DC, Ewing SK, Cauley JA, Ensrud KE, Cummings SR, Orwoll ES. Osteoporotic Fractures in Men (MrOS) Research Group. Quantitative ultrasound predicts hip and non-spine fracture in men: the MrOS study. *Osteoporos Int*. 2007;18:771–777.
23. Mulleman D, Legroux-Gerot I, Duquesnoy B, Marchandise X, Delcambre B, Cortet B. Quantitative ultrasound of bone in male osteoporosis. *Osteoporos Int*. 2002;13:388–393.

24. Kwok T, Khoo CC, Leung J, et al. Predictive values of calcaneal quantitative ultrasound and dual energy X ray absorptiometry for non-vertebral fracture in older men: results from the MrOS study (Hong Kong). *Osteoporos Int*. 2012;23:1001–1006.
25. Cummings SR, Cawthon PM, Ensrud KE, Cauley JA, Fink HA, Orwoll ES. Osteoporotic Fractures in Men (MrOS) Research Groups; Study of Osteoporotic Fractures Research Groups. BMD and risk of hip and nonvertebral fractures in older men: a prospective study and comparison with older women. *J Bone Min Res*. 2006;21:1550–1556.
26. Bagger YZ, Tanko LB, Alexandersen P, Hansen HB, Qin G, Christiansen C. The long-term predictive value of bone mineral density measurements for fracture risk is independent of the site of measurement and the age at diagnosis: results from the Prospective Epidemiological Risk Factors study. *Osteoporos Int*. 2006;17:471–477.
27. Szulc P, Munoz F, Duboeuf F, Marchand F, Delmas PD. Bone mineral density predicts osteoporotic fractures in elderly men: the MINOS study. *Osteoporos Int*. 2005;16:1184–1192.
28. Nguyen TV, Center JR, Sambrook PN, Eisman JA. Risk factors for proximal humerus, forearm, and wrist fractures in elderly men and women: the Dubbo Osteoporosis Epidemiology Study. *Am J Epidemiol*. 2001;153:587–595.
29. Khaw KT, Reeve J, Luben R, et al. Prediction of total and hip fracture risk in men and women by quantitative ultrasound of the calcaneus: EPIC-Norfolk prospective population study. *Lancet*. 2004;363:197–202.
30. Njeh CF, Hans D, Li J, et al. Comparison of six calcaneal quantitative ultrasound devices: precision and hip fracture discrimination. *Osteoporos Int*. 2000;11:1051–1062.
31. Nam HS, Shin MH, Zmuda JM, et al. Osteoporotic Fractures in Men (MrOS) Research Group. Osteoporotic Fractures in Men (MrOS) Research Group. Race/ethnic differences in bone mineral densities in older men. *Osteoporos Int*. 2010;21:2115–2123.
32. Lopez-Rodriguez F, Mezquita-Raya P, de Dios Luna J, Escobar-Jimenez F, Munoz-Torres M. Performance of quantitative ultrasound in the discrimination of prevalent osteoporotic fractures in a bone metabolic unit. *Bone*. 2003;32:571–578.
33. Graafmans WC, Bouter LM, Lips P. The influence of physical activity and fractures on ultrasound parameters in elderly people. *Osteoporos Int*. 1998;8:449–454.
34. Fox KM, Magaziner J, Hawkes WG, et al. Loss of bone density and lean body mass after hip fracture. *Osteoporos Int*. 2000;11:31–35.
35. Bolam KA, Beck BR, Adlard KN, et al. The relationship between BPAQ-derived physical activity and bone density of middle-aged and older men. *Osteoporos Int*. 2014;25:2663–2668.