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Original Article

Ultrasound Measurements for the Prediction of Osteoporotic Fractures in Elderly People

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Abstract. In this prospective study we investigated the predictive value of quantitative ultrasound (QUS) measurements and other potential predictors of osteoporotic fractures in the elderly. During a 1-year period, 710 participants (132 men and 578 women), aged 70 years and older (mean age ± SD: 82.8 ± 5.9), were recruited from seven homes and apartment houses for the elderly. QUS measurements (broadband ultrasound attenuation (BUA) and speed of sound (SOS)) were assessed with a clinical bone densitometer. A structured questionnaire was used to collect information on other potential predictors. Follow-up of fractures was done each half year by telephone interviews. During the study period (median follow-up 2.8 years, maximum 3.7 years), 30 participants had a first hip fracture and 54 suffered from a first other nonspinal fracture. Cox regression analyses, adjusted for age and sex, showed that the relative risk (RR) of hip fracture for each standard deviation reduction was 2.3 (95% CI, 1.4–3.7) for BUA and 1.6 (95% CI, 1.1–2.3) for SOS. Slightly weaker relationships were found for any fracture (BUA: RR, 1.6; 95% CI, 1.2–2.1; SOS: RR, 1.3; 95% CI, 1.0–1.6). Multivariable analyses identified low BUA values and immobility as the strongest predictors for hip fractures and any fracture. Female gender proved to be the strongest predictor for other nonspinal fractures. It can be concluded that QUS measurements can predict the risk for hip fracture and any fracture in elderly people.

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Introduction

Osteoporosis has become a major public health issue, because world-wide the number of fractures is increasing due to the increasing number of elderly people [1]. Fractures, particularly hip fractures, often result in decreased physical functioning, and permanent institutional care. Important consequences are an impaired quality of life, impaired survival and increasing costs of health care [2–4]. The identification of predictors for fractures is necessary for the implementation of effective preventive strategies.

The risk for fractures is strongly related to bone mineral density (BMD), which is usually measured with dual-energy X-ray absorptiometry (DXA) [5–7]. Currently, there is increasing interest in the use of quantitative ultrasound (QUS) measurements of the heel bone for predicting the risk of fractures. It has been suggested that the QUS parameters of broadband ultrasound attenuation (BUA) and speed of sound (SOS) depend not only on bone density but also on bone structure and elasticity [8–10]. QUS offers several other advantages over DXA, since the apparatus is free of ionizing radiation, relatively inexpensive and simple to apply [11].

Several cross-sectional and retrospective studies have demonstrated lower QUS values in persons with osteoporosis or fractures compared with controls [12–18]. Recently, the results of three prospective studies have shown that QUS measurements of the heel can indeed be used to predict the risk for fractures in elderly women [19–21]. However, these studies all used a water-based QUS system. The predictive value of a dry system has not yet been examined prospectively. A dry system has the advantage that it is portable, which makes it possible to measure elderly people at home. A disadvantage may be less efficient coupling by a coupling gel instead of water, which may influence the predictive value. Furthermore, the independent contribution of QUS to the prediction of fracture risk compared with other potential risk factors, such as decreased physical activity, recurrent falls, low body weight or history of fractures, is not clear. This knowledge is important for the identification of high-risk groups and for adequately targeting preventive strategies.

The main objective of this prospective study was to examine the value of QUS measurements with a portable dry system for the prediction of osteoporotic fractures. A secondary objective was to compare the predictive value of QUS parameters with that of some other potential predictors for fractures in elderly people.

Subjects and Methods

Study Population

Between October 1993 and December 1994, 710 elderly (132 men and 578 women) were recruited from seven homes and seven apartment houses for the elderly in Amsterdam and its vicinity (The Netherlands) to participate in this prospective study. In Dutch homes for the elderly some care is provided, but less than in a nursing home. People who live in apartment houses for the elderly live independently, but they can ask for help when necessary, meals are served on demand and their houses offer special protection against falls and accidents and are equipped with an alarm system. The people are less independent than elderly people living in the community. Inclusion criteria were age 70 years or older and no severe cognitive impairment as judged by the personnel of the care facility. Informed consent was asked from the participants. Measurements were performed at baseline and thereafter follow-up of fractures was performed each half year. The protocol was approved by the Medical Ethics Committee of the Academic Hospital of the Vrije Universiteit, Amsterdam.

Baseline Measurements

The baseline examination was performed by trained research assistants at the residence of each participant, and included the completion of a structured questionnaire during a personal interview, QUS measurements and body weight assessment. The questionnaire was used to collect information on age, gender, residence, fracture history since age 50 years, the use of a walking aid, the level of daily physical activity, mobility, and recurrent falls ($\geq$2 falls) in the previous year. Daily physical activity in the previous year was ascertained by means of a validated questionnaire for elderly persons regarding household, sports and leisure activities [22]. To assess the level of mobility in the previous year, participants were asked whether there had been a period in that year in which they had not been able to walk or had been confined to bed. Participants were classified as immobile if this period had been longer than 4 weeks.

QUS measurements were obtained using the CUBA Clinical instrument (McCue Ultrasonics, Winchester, UK). The ultrasound system consists of two transducers (emitting and receiving) faced with silicone rubber coupling pads. These are placed in direct contact on either side of the heel using a coupling gel. BUA (dB/MHz) and speed of sound SOS (m/s) were measured twice in both the right and left calcaneus. Mean BUA and SOS were calculated from these four measurements. The coefficient of variation (CV), calculated in 20 healthy volunteers measured on 5 occasions consecutively within 1 h, was 3.4% for BUA and 1.3% for SOS [23].

Follow-up of Fractures

Participants were contacted by telephone every half year to ask whether they had had a fracture in the previous half year. Participants were sent a self-administered questionnaire on fractures if they could not be reached by telephone. Caregivers were interviewed if participants were not able to respond. When participants died, their primary care physician or caregiver was contacted to supply information on whether a fracture had occurred since the last telephone contact. Each reported hip fracture was verified with the general practitioner.

Data Analysis

A Cox proportional-hazard regression model was used to estimate the relationship between QUS parameters and fractures and to identify other potential predictors of fracture risk. A stepwise backward Cox regression model was used to identify the independent risk factors.

The duration of follow-up was recorded for each participant from the date of enrolment in the study to the date of the first fracture, the date of death or the date of the last follow-up. Separate analyses were performed for participants with one or more hip fractures (vs participants with no hip fracture), participants with other nonspinal fractures (vs participants with no other nonspinal fractures) and these both groups combined (participants with any fracture vs participants with no fracture at all) as outcome measures. Hazard ratios are reported as the relative risk (RR) with 95% confidence intervals (95% CIs). Age, body weight and total activity score were entered as continuous variables when they were linearly related to fracture risk.

Table 1. Baseline characteristics of the study population (n = 710)

Characteristic	Unit	Value
Age (years)	Mean (SD)	82.8 (5.9)
Female	%	81.4
BUA (dB/MHz)[a]	Mean ± SD	60.8 (20.6)
SOS (m/s)[a]	Mean ± SD	1468.6 (34.3)
Body weight (kg)[b]	Mean ± SD	67.7 (12.7)
Recurrent falls in previous year	%	19.2
Any fracture since age 50 years[c]	%	34.2
Physical activity score[d]	Median (range)	3.0 (0.0–22.8)
Immobile period (>4 weeks) in previous year	%	3.1
Use of a walking aid	%	49.2
Living in a home for the elderly	%	48.3

[a] BUA (broadband ultrasound attenuation) and SOS (speed of sound) were not measured in 2 participants.
[b] Body weight was not measured in 4 participants.
[c] Two hundred and forty-three respondents suffered 296 fractures after the age of 50 years, of which 47 were hip fractures, 61 other lower extremity fractures (femur, tibia, ankle and foot fractures), 104 wrist fractures, 62 other upper extremity fractures (humerus, clavicle, hand fractures) and 22 other fractures (pelvic, rib, skull and known vertebral fractures).
[d] According to a questionnaire on household, sports and leisure activities.

In the first analyses, the crude relative risks of hip fractures, other nonspinal fractures and any fracture were assessed for a 1 standard deviation (SD) decrease in BUA and SOS. Additionally, the same analyses were performed after adjustment for age and sex. After that, each other potential predictor was entered in a single Cox regression model. Multivariable models were used to identify the strongest predictors for fractures. Those variables that were significantly ($p<0.05$) related to fracture risk in the univariate analyses were included in stepwise backward Cox regression models. Because SOS and BUA showed collinearity, the significant predictors were entered in two different multivariable Cox regression models: one with BUA and one with SOS. Variables with a p value smaller than 0.05 were included and those with a p value greater than 0.10 were eliminated from the models.

Results

Baseline characteristics of the study population are shown in Table 1. Ultrasound parameters were not obtained in 2 participants, and in 7 participants only on one side, due to oedema, a fractured calcaneus and other disabilities. During 1818 person-years of follow-up (median 2.8 years, maximum 3.7 years) 168 (23.7%) participants died and 5 (0.7%) were lost to follow-up. Those who died were older, fell more often, had a lower physical activity score and lower baseline BUA and SOS values compared with the survivors.

Table 2 shows the types and numbers of the various fractures sustained during the total follow-up period. During this period, 96 nonspinal fractures occurred in 77 participants. Thirty-one hip fractures occurred in 30 participants; 1 had a hip fracture on each side. Fifty-four participants sustained 65 other nonspinal fractures, including 23 Colles' fractures and 8 humerus fractures. Seven participants sustained both a hip fracture and another nonspinal fracture.

Table 2. Number of fractures sustained during follow-up at different skeletal sites in men and women (n = 710)

Type of fracture	Women (n = 578)	Men (n = 132)
Hip fracture	27	4
Other lower extremity[a]	10	1
Wrist	23	0
Humerus	8	0
Other upper extremity[b]	12	0
Other[c]	11	0
Total	91	5

[a] Femur, tibia, ankle, foot fractures.
[b] Clavicle, hand fractures.
[c] Pelvic, rib and skull fractures.

In Table 3, the associations between ultrasound parameters and fracture risk are presented. After adjustment for age and sex, both ultrasound parameters were associated with increased risk for hip fracture and for any fracture, but not for other nonspinal fractures. A decrease of 1 SD in BUA was associated with a more than 2-fold increase in risk for hip fracture (RR, 2.3; 95% CI, 1.4–3.7) and a 60% increase in the risk for any fracture (RR, 1.6; 95% CI, 1.2–2.1). The associations between SOS and fractures were slightly weaker: each 1 SD reduction in SOS was associated with a 60% increase in the risk for hip fracture (RR, 1.6; 95% CI, 1.1–2.3) and a 30% increase in the risk for any fracture (RR, 1.3; 95% CI, 1.0–1.6).

Table 4 shows the relative risks of hip fractures, other nonspinal fractures and any fracture for each single other potential predictor. Increasing age, low body weight and an immobile period of more than 4 weeks in the previous year were related to risk for hip fracture. A lower body weight and female sex were related to risk for other nonspinal fractures, whereas increasing age, female sex, a lower body weight and an immobile period were significantly associated with risk for any fracture.

Table 3. Relative risk of hip fracture, other nonspinal fractures and any fracture for a 1 standard deviation (SD) decrease in ultrasonographic measurements, according to Cox regression analyses

QUS parameter[a]	Hip fracture (n = 30)		Other nonspinal fractures (n = 54)		Any fracture (n = 77)	
	RR	(95% CI)	RR	(95% CI)	RR	(95% CI)
BUA (dB/MHz)						
Unadjusted	2.3	(1.5–3.7)*	1.5	(1.1–2.1)*	1.8	(1.4–2.4)*
Adjusted[b]	2.3	(1.4–3.7)*	1.3	(0.9–1.8)	1.6	(1.2–2.1)*
SOS (m/s)						
Unadjusted	1.8	(1.2–2.5)*	1.3	(1.0–1.7)	1.4	(1.1–1.8)*
Adjusted[b]	1.6	(1.1–2.3)*	1.1	(0.9–1.5)	1.3	(1.0–1.6)

QUS, quantitative ultrasound measurements; BUA, broadband ultrasound attenuation; SOS, speed of sound; n = number of participants; RR, relative risk; CI, confidence interval.
*p<0.05.
[a] BUA and SOS were not obtained in two participants.
[b] Adjusted for age and sex.

Table 4. Relative risks (RR) and 95% confidence intervals (95% CI) for several predictors of hip fracture, other nonspinal fractures and any fracture, according to Cox regression analysis

Predictor	Hip fracture		Other nonspinal fractures		Any fracture	
	RR	(95% CI)	RR	(95% CI)	RR	(95% CI)
Age (every 5 years older)	1.6	(1.1–2.2)*	1.1	(0.9–1.4)	1.2	(1.0–1.5)*
Female (vs male)	1.4	(0.5–4.0)	11.7	(1.6–84.9)*	4.1	(1.5–11.1)*
Body weight <67 kg (vs body weight ≥67 kg)	2.9	(1.3–6.6)*	1.3	(1.0–1.6)*[a]	1.4	(1.1–1.6)*[a]
Recurrent falls in previous year (vs ≤ 1 fall in previous year)	1.1	(0.5–2.8)	1.7	(0.9–3.1)	1.4	(0.9–2.5)
Any fracture since age 50 years (vs none)	1.6	(0.8–3.3)	0.9	(0.5–1.6)	1.2	(0.7–1.9)
Physical activity (every 2 points higher)	0.8	(0.6–1.0)	0.9	(0.8–1.1)	0.9	(0.7–1.0)
>4 weeks immobile in previous year (vs ≤4 weeks immobile)	3.9	(1.2–12.9)*	2.7	(1.0–7.5)	3.1	(1.4–7.2)*
Use of a walking aid (vs no use of a walking aid)	1.1	(0.6–2.3)	1.0	(0.6–1.7)	1.1	(0.7–1.7)
Living in a home for the elderly (vs apartment for the elderly)	2.0	(0.9–4.2)	1.2	(0.7–2.0)	1.4	(0.9–2.1)

*p<0.05.
[a] Since body weight was linearly related to other nonspinal fractures and to any fractures, body weight was entered as a continuous variable (RR per 10 kg decrease).

Table 5 shows the results of stepwise backward Cox regression analysis including QUS parameters and the other significant predictors of fracture risk. Model 1 shows the multivariable models that included BUA, while model 2 shows the multivariable models with SOS included. In model 1, low BUA values and immobility were identified as predictors for respectively hip fracture and any fracture. Female sex was a strong predictor for other nonspinal fractures and for any fracture, whereas low body weight remained a significant predictor only for hip fracture. In model 2, increasing age, a low body weight and an immobile period were identified as strong predictors for hip fracture and any fracture. Female sex was identified as a strong predictor both for other nonspinal fractures and any fracture. Low SOS value was only included in the model for hip fractures.

Discussion

The results of this prospective study showed that both BUA and SOS measurements of the calcaneus predict risk for hip fracture as well as for any fracture in elderly people. BUA was identified as a relatively strong predictor since the increased risk for hip and any fracture persisted in a multivariable model. In addition, other factors that can predict fracture risk in elderly people were identified. An immobile period of longer than 4 weeks was particularly related to increased risk for hip fracture and any fracture, whereas female sex was identified as the strongest predictor for other nonspinal fractures.

Our results support the previous finding from case–control studies that ultrasound measurements can

Table 5. Relative risks for each predictor, included in the multivariable models with broadband ultrasound attenuation (BUA) (model 1) and with speed of sound (SOS) (model 2), for hip fracture, other nonspinal fractures and any nonspinal fracture, after stepwise Cox regression analysis (backward elimination)[a]

	RR	(95% CI)
Model 1		
Hip fracture		
BUA (per 1 SD decrease)	2.1	(1.3–3.3)
Body weight <67 kg (vs ⩾67 kg)	2.2	(1.0–5.0)
Immobile >4 weeks in previous year (vs ⩽4 weeks)	3.6	(1.1–12.1)
Other nonspinal fractures		
Female (vs male)	11.6	(1.6–84.1)
Any fracture		
BUA (per 1 SD decrease)	1.6	(1.2–2.2)
Immobile >4 weeks in previous year (vs ⩽4 weeks)	2.6	(1.1–6.1)
Female (vs male)	2.3	(0.8–6.6)
Model 2		
Hip fracture		
SOS (per 1 SD decrease)	1.4	(1.0–2.1)
Age (every 5 years older)	1.4	(1.0–1.9)
Body weight <67 kg (vs ⩾67 kg)	2.2	(0.9–5.1)
Immobile >4 weeks in previous year (vs ⩽4 weeks)	4.1	(1.2–13.6)
Other nonspinal fractures		
Female (vs male)	11.6	(1.6–84.1)
Any fracture		
Age (every 5 years older)	1.2	(1.0–1.5)
Female (vs male)	3.4	(1.2–9.5)
Body weight (every 10 kg lower)	1.2	(1.0–1.5)
Immobile >4 weeks in previous year (vs ⩽4 weeks)	3.2	(1.4–7.3)

RR, relative risk; CI, confidence interval.
[a] Variables with a p value smaller than 0.05 were included and those with a p value greater than 0.10 were eliminated from the models.

discriminate between fracture and control groups [12–18]. The 2-fold increase in the relative risk of hip fracture for each 1 SD reduction in BUA is similar to the results found in other prospective studies [20,21]. The strength of the association between BUA and risk for any fracture was similar to that reported by Bauer et al. [21]. The association between QUS measurements and other nonspinal fractures was very weak and not significant. This may be due to the fact that a relatively large number of these fractures were less related to osteoporosis, such as fractures of the lower extremities and fractures of the fingers.

Since we were not able to measure BMD in our study population, we cannot compare the predictive value of QUS parameters with that of BMD. However, the strength of the association between QUS and hip fracture risk seems similar to that previously reported for femoral neck BMD [6,20,21,24]. In addition, it has been shown that ultrasonographic measurements predict fracture risk independently of BMD [20,21].

The finding that age is especially related to risk for hip fracture in the very elderly, but not to other non-spinal fractures, confirms the results of other studies [25,26]. It is well established that the incidence of Colles' fracture reaches a plateau around age 50 years in men and around age 65 years in women, while hip fracture incidence increases exponentially throughout life [5,27,28]. Women have a higher risk for hip fractures and other types of fractures [29] than men. In this study, however, we did not observe a significant increase in hip fracture risk in women compared with men, which may be due to the low hip fracture incidence and the relatively small number of men participating in this study. Moreover, it is known that the sex ratio is more pronounced for Colles' fractures than for other types of fracture [30].

Our finding that people with a higher body weight had a lower risk for hip fracture than those with a lower body weight agrees with the findings reported in previous studies [31–33]. Fat tissue is positively related to estrogen activity in postmenopausal women, and may thus protect against bone loss. Furthermore, soft tissue around the hip may modify the impact of a fall.

Immobility has been shown to be associated with an increased risk for fracture in several studies [26]. Our results also showed an increased risk for fracture in those who were confined to bed or not able to walk for a period of more than 4 weeks. People who are immobile are more susceptible to falls as a consequence of muscle weakness or coordination problems. In addition, immobility results in increased bone resorption and a negative calcium balance leading to increased bone loss [34–36]. Since the method to measure immobility was not based on a validated questionnaire, it is uncertain how precisely it reflects immobility. Confinement to bed for a long period can also be due to other aspects of frailty, such as chronic illness.

Although 90% of hip fractures are the result of a fall, recurrent falls during the year preceding the study were not associated with increased risk for fracture. Furthermore, the results of this study do not confirm results of previous studies that daily physical activity protects against hip fracture [37] and that a history of fracture [33] increases the risk for fractures. However, the latter is probably due to the small sample size.

This is the first prospective study which demonstrates that a dry ultrasound system can predict fracture risk in elderly people. The dry, portable system permits measurement of elderly people at home or in an institution. In this way, risk assessment in the very elderly is feasible to identify those at high risk for fractures, so that preventive measures, such as hip protectors or medication, can be allocated efficiently [38,39]. The prospective design of this study avoids potential bias associated with case–control studies. On the other hand, our study also has several limitations, the most important of which is its limited power: in particular the incidence of a first hip fracture and the number of men participating in this study are rather small. Therefore, inferences about the predictors of fractures must be interpreted with caution. The estimate of the relative risks are less accurate and some relationships can only be detected with a larger sample and a higher incidence of fractures. Secondly, since the participants were 70 years old or older and living in apartment houses and homes for the elderly, these findings cannot automatically be generalized to younger people or elderly people living in the community. Furthermore, since people with severe cognitive impairments and those who were not able to participate were excluded, we must be careful to generalize the results of this study to the very frail elderly living in homes and apartment houses for the elderly. Thirdly, the ascertainment of fractures was based on self-report. Although this method has been shown to be accurate [40], there may have been misclassification in the ascertainment of fractures since radiographs were not checked. On the one hand, people may have overreported fractures. This may partly explain the small association found between QUS and other nonspinal fractures that included less osteoporotic fractures, such as those of the fingers, toes and ribs. On the other hand there may have been people who had a fracture that they never reported. This may have led to an underestimation of the fracture risk. In the fourth place, we could not compare the predictive value of QUS with that of BMD in this study. However, comparison with data from the literature shows that fracture prediction in this study was quite similar to that using BMD measured by DXA in other studies.

In conclusion, in this prospective study we found that low values of BUA and SOS can predict the risk for fractures in elderly people. In addition, some other easily measurable factors were identified as predictors for the different types of fractures. Because measurements can be performed with a dry portable instrument which is simple to apply, relatively inexpensive and free of ionizing radiation, QUS seems suitable for the identification of elderly with a high risk for osteoporotic fractures.

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