Five-year incident fracture risk assessed by quantitative multisite ultrasound: the Canadian Multicentre Osteoporosis Study.

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Background

There is need to identify additional variables other than bone mineral density (BMD) and the other variables already integrated into popular fracture risk models (ie. FRAX) that are easily measured in the clinic that can provide additional information to better stratify individual fracture risk.

Quantitative ultrasound (QUS) has been used to assess bones with the hopes of being able to identify those individuals who are at an increased risk for fracture. QUS devices are attractive as they are portable, comparatively inexpensive, require little training for their use, and emit no ionizing radiation.

The majority of QUS devices assess bone at the calcaneus, but there are other QUS devices that can assess bone at the kneecap, tibia, radius, and phalanx as well. One QUS device is capable of providing measurements from a number of different sites including the tibia, distal radius and phalanx.

Purpose

This investigation assessed the capability of a multisite QUS device (BeamMed Omnisense MultiSite Quantitative Ultrasound) to prospectively assess fracture risk over five years in a large cohort of randomly selected men and women from the Canadian Multicentre Osteoporosis Study (CaMOS).

Participants

The Canadian Multicentre Osteoporosis Study (CaMos) is a prospective study that has the mandate to better understand the factors that lead to osteoporosis and fractures in Canadians. CaMos has collected ten years of prospective data in almost 10,000 randomly-selected individuals and is ongoing. In year 5 of CaMOS 4124 men and women were assessed by both DXA and QUS in six centres from CaMOS equipped with both a Sunlight QUS and a DXA (Calgary, Halifax, Hamilton, Saskatoon, Ste-Foy, and St. John's).

Methods

QUS estimated bone strength (SOS; speed of sound in m/s) at three anatomical sites: distal radius, tibia and phalanx. After QUS assessment, all participants were prospectively followed for five years during which incident fractures were recorded. Further, extensive questionnaires were employed at the time of QUS measurement.

Analyses

Only low-trauma factures were included in the analyses, with the exception of any fractures of the skull, face, hands, or feet.

There were two separate survival analyses (proportional hazards regression) done for each skeletal site grouping (all clinical fractures, all non-vertebral fractures and all hip fractures) – an uncontrolled univariate analysis and a multivariate analysis controlling for a large number of clinical risk factors for fracture. In the multivariate model, adjustments were made for age, anti-resorptive use, femoral neck BMD, number of diseases, previous fractures, body mass index, sex (in model with both men and women), parental history of hip fracture, current smoking, current alcoholic drinks >3 per day, current use of glucocorticoids, and diagnosis of rheumatoid arthritis. Many of these variables were selected for control because they are used in the FRAX fracture stratification tool now used world-wide. Further, all analyses were completed on the cohort as a whole and for men and women separately.

For each participant, the follow-up time corresponded to the number of days between the randomization date and the earliest date for one of the following events: the date of fracture (event of interest), date of death (censored), the date of the ten year follow-up interview (censored), or the date of last correspondence (censored).

All analyses were completed on a Windows-based workstation with SAS 9.3. Statistical significance was considered to have occurred at an alpha of 0.05.

Results

A total of 4123 patients had QUS performed during their year five evaluation. However, 382 participants had no follow-up after the QUS measurement and were therefore excluded from the analyses, leaving a total of 2633 (70.4%) women and 1108 (29.6%) men (total sample of 3741).

Table 1. provides the general characteristics of the participants assessed. The average age was approximately 65 years old, with the men on average younger than the women. The men possessed higher SOS values at all three investigated sites and had a higher femoral neck BMD as compared to the women.

The uncontrolled results of the univariate proportional hazard model for all three fracture groupings are provided in Table 2. For the combined group, an increase of 150 m/s in the SOS measurement was associated with a significant decrease in the risk of any clinical fracture, hip fracture or non-vertebral fracture (27-49% decreased risk). Similar predictive power for all three sites was observed when the women were analysed separately from the men (25-48% decreased risk). However, when the men were analysed separately, none of the mQUS measures significantly predicted fracture risk in any of the three skeletal groupings.

The adjusted proportional hazard models for all three fracture groupings are provided in Table 3. After adjustment for other known variables that predict fracture risk, there was a general attenuation of the predictive ability of the QUS measures. When assuming a SOS increase of 150 m/s, the distal radius and tibia measures were significantly associated with a decreased risk of any clinical fracture or non-vertebral fracture in the combined cohort (17-19% decreased risk of fracture). For women alone, the results were similar (21-22% decreased risk of fracture). As in the unadjusted model, the QUS measures did not significantly stratify fracture risk in men.

Table 1. Basic demographic information of cohort.

Variable	All Mean±SD	Men Mean±SD	Women Mean±SD
Distal radius SOS in m/s	4043±150	4073±126.7	4031±156.9
Tibia SOS in m/s	3968±144	3935±117.5	3839±145.1
Phalanx SOS in m/s	3819±215	3883±192.5	3791±218.5
Age in years	65.3±12.0	63.3±12.9	66.1±11.5
Femoral neck BMD T-score	-1.02±1.01	-0.50±0.96	-1.25±0.95
Number of other diseases	0.84±1.01	0.66±0.92	0.91±1.05
Body mass index in kg/m^2	27.4±4.9	27.6±3.9	27.3±5.3
Mass in kg	73.5±15.4	83.2±13.7	69.6±14.4
Height in cm	163.7±9.3	173.7±7.0	159.7±6.8

Table 2. Results of univariate proportional hazards model for all fracture types (unadjusted model) assuming an increase in speed of sound of 150 m/s.

Fracture grouping	Measurement site	Combined Hazard Ratio (95% CI)	Women Hazard Ratio (95% CI)	Men Hazard Ratio (95% CI)
Any clinical fracture	Distal radius	0.549 (0.47, 0.64)	0.562 (0.48, 0.66)	0.877 (0.53, 1.44)
	Tibia	0.556 (0.48, 0.64)	0.597 (0.51, 0.70)	0.670 (0.41, 1.11)
	Phalanx	0.728 (0.66, 0.80)	0.751 (0.67, 0.84)	0.836 (0.62, 1.12)
Hip fracture	Distal radius	0.504 (0.36, 0.70)	0.516 (0.36, 0.73)	0.687 (0.24, 1.94)
	Tibia	0.511 (0.37, 0.71)	0.488 (0.34, 0.70)	0.958 (0.35, 2.65)
	Phalanx	0.586 (0.47, 0.73)	0.564 (0.44, 0.73)	0.739 (0.43, 1.27)
Non-vertebral fracture	Distal radius	0.550 (0.47, 0.64)	0.556 (0.47, 0.66)	0.932 (0.56, 1.55)
	Tibia	0.553 (0.48, 0.65)	0.588 (0.50, 0.70)	0.684 (0.41, 1.14)
	Phalanx	0.725 (0.65, 0.81)	0.743 (0.66, 0.83)	0.841 (0.62, 1.14)

Table 3. Results of adjusted* proportional hazards model for all fracture types assuming an increase in speed of sound of 150 m/s.

Fracture grouping	Measurement site	Combined Hazard Ratio (95% CI)	Women Hazard Ratio (95% CI)	Men Hazard Ratio (95% CI)
Any clinical fracture	Distal radius	0.825 (0.69, 0.98)	0.779 (0.65, 0.94)	1.05 (0.64, 1.73)
	Tibia	0.814 (0.68, 0.97)	0.791 (0.66, 0.95)	0.904 (0.52, 1.57)
	Phalanx	0.978 (0.87, 1.10)	0.964 (0.85, 1.09)	1.061 (0.76, 1.48)
Hip fracture	Distal radius	1.091 (0.76, 1.57)	1.077 (0.73, 1.59)	1.158 (0.38, 3.50)
	Tibia	0.882 (0.61, 1.27)	0.766 (0.52, 1.13)	2.692 (0.81, 9.00)
	Phalanx	0.952 (0.74, 1.23)	0.868 (0.65, 1.15)	1.649 (0.85, 3.20)
Non-vertebral fracture	Distal radius	0.824 (0.69, 0.99)	0.774 (0.63, 0.94)	1.094 (0.66, 1.83)
	Tibia	0.815 (0.68, 0.98)	0.785 (0.65, 0.95)	0.931 (0.53, 1.65)
	Phalanx	0.975 (0.86, 1.10)	0.961 (0.84, 1.10)	1.053 (0.75, 1.48)

*Adjusted for age, anti-resorptive use, femoral neck BMD, number of diseases, previous fractures, BMI, sex (in combined model), parental history of hip fracture, current smoking, current alcoholic drinks >3 per day, current use of glucocorticoids, and diagnosis of rheumatoid arthritis.

Conclusion

In conclusion, the BeamMed Omnisense MultiSite QUS provides significant five-year fracture prediction, independent of BMD and other significant risk factors for fracture, when measured at the distal radius and tibia sites. For the combined group, an increase of 150 m/s in at the distal radius and tibia would suggest a 17.5% and 18.6% lower clinical fracture risk, respectively, after control for all other variables (45% and 44% lower uncontrolled, respectively). Further investigation into the use of the BeamMed Omnisense MulitSite QUS for inclusion in 10-year fracture risk models and for its use in monitoring therapy is warranted.