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Original Article

Normative Data for Mulitsite Quantitative Ultrasound: The Canadian Multicenter Osteoporosis Study

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Abstract

Multisite quantitative ultrasound (mQUS) machines are attractive tools for assessing fragility fracture risk as they are often portable, comparatively inexpensive, require little training for their use, and emit no ionizing radiation. The primary objective of this investigation was to generate an mQUS normative database of speed of sound (SOS, in m/s) measures from a large sample of randomly selected community-based individuals. mQUS (BeamMed Omnisense MultiSite Quantitative Ultrasound 7000 S) measurements were obtained and assessed at the distal radius, tibia, and phalanx. All analyses were made separately for men and women and for each anatomical site. Scatterplots (SOS vs age) identified 30−39 yr of age as periods of both maximal SOS and of relative stability for all 3 sites over the age span investigated (30−96 yr of age; 2948 women and 1176 men) and, thus, was used as the "reference" population. For cross-sectional comparison of trends over aging, a number of age groupings were created: 30−39, 40−49, 50−59, 60−69, 70−79, and 80+ yr. In general, there were decreases in SOS over increasing age groupings. The normative data generated can be used to compare a given patient's mQUS measurement with reference to a young, healthy population, assigning them a gender-appropriate T-score.

Key Words: Fracture; normative data; quantitative ultrasound.

Introduction

In the recent past, the assessment of bone mineral density (BMD) by dual-energy X-ray absorptiometry (DXA) has served as an almost solitary pillar for the diagnosis of osteoporosis *(1)*. However, with the realization that the majority of women who do experience a fracture have a BMD above that which would be considered osteoporotic *(2,3)*, there has been a movement toward incorporating the valuable information provided by BMD with that of commonly assessed clinical risk factors to better estimate an individual's 10-yr fracture risk *(4,5)*.

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Although DXA-assessed BMD is of unquestionable value, machine availability or access can be limited in some regions and the release of low-dose radiation is a concern for some. Quantitative ultrasound (QUS) devices are attractive as they are often portable, comparatively inexpensive, require little training for their use, and emit no ionizing radiation. QUS has been used to estimate the mechanical integrity, or strength, of bone with the intent of being able to identify those individuals who are at an increased risk for fracture. The hope is that the fracture risk estimate provided from QUS can be used as a surrogate for BMD or that information gleaned through QUS can be input into one of the new 10-yr fracture risk assessments to provide a better estimate of future fracture risk.

For QUS to be able to assess a person's risk for fragility fracture, 2 milestones must be met: there must be a significant

relationship proven between the QUS measure of bone strength and future fracture risk, and there must be normative values available to compare a given individual's current estimate of bone strength to those who would be deemed at low risk for fracture and those at high risk for fracture.

A recent publication that assessed the 5-yr prospective utility of a multisite quantitative ultrasound (mQUS; BeamMed Omnisense MultiSite Quantitative Ultrasound 7000 S, Israel) concluded that mQUS was a significant predictor of clinical future risk in women, independent of BMD *(6)*.

Comparison of individuals to population norms allows the identification of those who may require intervention to minimize fracture risk. To establish a normative database for stratifying fracture risk, a reference population of sufficient sample size must be identified that has both the highest measure of bone strength and the lowest fragility fracture risk. Typically, these populations are selected to be around the age of attainment of peak bone mass during early adulthood (20−40 yr of age) *(7)* as this approximately coincides with the time of lowest fracture risk. Because osteoporotic fracture incidence increases with aging, the mQUS measures of bone strength should ideally decrease in a similar pattern to that of increasing fracture risk.

The primary objective of this investigation was to generate an mQUS normative database of speed of sound (SOS) measures from a large sample of randomly selected community-based individuals from the Canadian Multicentre Osteoporosis Study (CaMos). A secondary objective of this investigation was to assess whether mQUS SOS measures decreased in a pattern inverse to that of major osteoporotic fracture risks.

Materials and Methods

Participants

This investigation used a subset of participants from the CaMos cohort. The methods and objectives of the CaMos study have been previously published *(8)*. Briefly, CaMos is an ongoing, prospective cohort study involving 9423 randomly selected community-dwelling women (n = 6539) and men (n = 2884) aged 25 yr and older at baseline and who lived within 50 km of 9 major Canadian cities (St John's, Newfoundland and Labrador; Halifax, Nova Scotia; Quebec City, Quebec; Toronto, Hamilton and Kingston, Ontario; Saskatoon, Saskatchewan; Calgary, Alberta; and Vancouver, British Columbia). Households were randomly selected from a list of residential phone numbers, and participants were randomly selected from eligible household members using standard protocol. Of those selected, 42% agreed to participate and had a baseline interview. All researches carried out in the CaMos have been approved by local university ethics boards in each of the cities the study had centers in and have satisfied the criteria of the World Medical Association Declaration of Helsinki—Ethical Principles for Medical Research Involving Human Subjects. All participants provided informed consent.

Data collection at baseline and each follow-up visit included an extensive, standardized interviewer-administered questionnaire and a clinical assessment. Full assessments (clinical measures and questionnaires) occurred at baseline, after 3 yr (only for participants aged 40−60 yr at baseline), after 5 yr, and after 10 yr. In years that participants did not come to a study center, a self-administered fracture questionnaire was mailed out to identify incident fractures.

Table 1
Sample Sizes for Each Age Grouping by Gender and Site

	Women			Men		
Age grouping	DR	TIB	PX	DR	TIB	PX
30−39 yr	79	80	81	67	68	69
40−49 yr	104	102	115	86	88	89
50−59 yr	509	502	568	246	260	266
60−69 yr	723	731	794	272	278	278
70−79 yr	856	857	932	316	311	312
80+ yr	250	242	276	92	91	96

Abbr: DR, distal radius; PX, phalanx; TIB, distal tibia.

At the 5-yr follow-up investigation, a number of the clinical sites expanded their protocol by assessing participants with an mQUS (at the 5-yr follow-up Sunlight Omnisense MultiSite Quantitative Ultrasound 7000 S and now BeamMed Omnisense MultiSite Quantitative Ultrasound 7000 S, Petah Tikva, Israel), in addition to the normal CaMos assessments (Calgary, Saskatoon, Hamilton, Quebec City, Halifax, St John's). Because all participants were at least 25 yr of age at baseline, all the participants in this analysis were at least 30 yr of age (baseline plus and additional 5 yr).

mQUS Assessments

mQUS measurements were obtained and assessed at the distal radius (DR), tibia (TIB), and phalanx (PX) on the nondominant side of the participant and were recorded as the SOS in meters per second.

The mQUS was equipped with 2 handheld probes specifically designed for measurements of axial SOS along the surfaces of bone: 1 probe was suitable for measurements at the DRs and TIB, whereas the other assessed the PX. Details regarding the standard manufacturer-suggested techniques involved with bone measurement with the mQUS have been detailed previously, and these standards were employed in this investigation *(9−13)*. Briefly, the mQUS emits and detects acoustic waves at a frequency of 1.25 MHz. The SOS measure acquired is the time taken for the sound wave to travel from the time of sound wave emission to its detection. Quality control measurements were performed daily following procedures recommended by the manufacturer. Intraobserver in vivo short-term precision has been reported as 0.76% for the radius, 0.47% for the TIB, and 1.54% for the phalanges and interobserver precision from 0.77% to 2.39% *(14)*. Measures were taken by 1 technologist at each of the 6 study centers.

Analyses

For the normative data creation, a number of calculations and analyses were conducted. All calculations and analyses