The Clinical Use of Ultrasound

ABSTRACT

Since the introduction of dual x-ray absorptiometry (DXA) in 1987, adoption of osteoporosis testing has steadily increased worldwide. In recent years, guidelines for testing and treatment have been published by recognized organizations, including the World Health Organization (WHO), the National Osteoporosis Foundation (NOF), and the International Osteoporosis Foundation (IOF). Concurrently, a growing number of therapeutic options have become available, each of which has been shown in large-scale international clinical trials to effectively build bone mass and to prevent fractures. The availability of effective testing technology and therapeutic agents offers great hope in the fight against osteoporosis, a disease that causes fractures in half of Caucasian women. Despite this great progress, however, it is estimated that 77% of women at risk for this condition remain undiagnosed and untreated.[1]

While DXA is established as the gold standard for diagnosis, portable technologies such as quantitative ultrasound (QUS) now offer low-cost options for screening a large number of people at risk for osteoporosis. QUS does not require radiation, and can be used in a primary care, mobile, or pharmacy setting to determine fracture risk. Those at risk can be referred for a full diagnostic work-up, including a DXA test for diagnosis and to establish a baseline for monitoring disease progression or treatment response. Effective utilization of screening by QUS can help address the problem of a large, untested population at risk for osteoporotic fracture.

QUANTITATIVE ULTRASOUND AND HIP FRACTURE RISK

UNLIKE IMAGING ULTRASOUND, which is widely used for such applications as fetal imaging, Quantitative Ultrasound (QUS) assesses bone status by measuring the speed and amount of sound transmitted through bone. QUS is typically used to measure skeletal sites with little overlying soft tissue, such as the calcaneus, or heel. "Dry" ultrasound devices, such as the Hologic Sahara, utilize a coupling gel to provide sound transmission, while other systems use water based "wet" coupling technology.

Heel ultrasound has been shown in numerous large-scale studies to be highly predictive of hip fracture risk,[2-6] making it a valuable screening tool to accurately triage those in need of further assessment. In one of the largest studies of quantitative ultrasound to date, over 7000 postmenopausal women were evaluated by three different QUS devices and then followed to determine hip fracture rates.[6] Results from this study indicate that heel ultrasound is a strong predictor of hip fracture risk, with a 2.4-fold increase in hip fracture risk for every standard deviation (T-score) decrease in Sahara ultrasound results (Figure 1). This same study also demonstrated that ultrasound of the heel is a significantly better predictor of fracture risk than ultrasound of the phalanges.

A large observational study in the United States found that risk for all fractures increased by a factor of 3.94 for patients with Sahara T-scores less than -2.5, and by a factor of 1.82 for T-
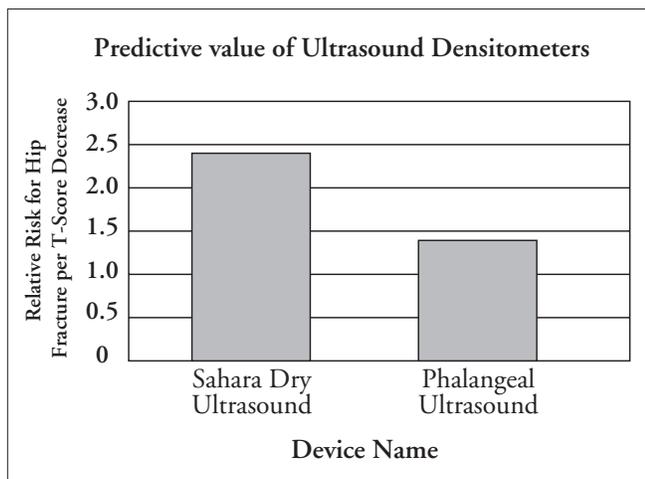

Predictive value of Ultrasound Densitometers

Figure 1

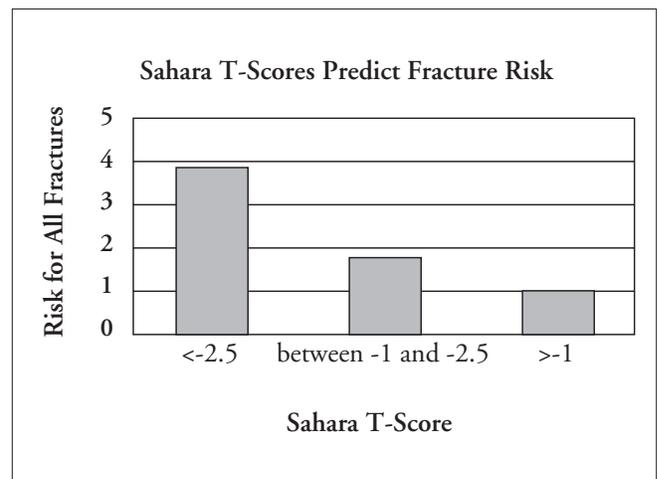Sahara T-Scores Predict Fracture Risk

Figure 2

scores between -1 and -2.5 (Figure 2).[4] These relative risks were calculated after adjustment for age and prior fracture history. Other peripheral devices are also available to assess fracture risk, such as DXA and radiographic absorptiometry of the phalanges, tibia, forearm, etc. However, these devices tend to have inferior fracture risk prediction capabilities and utilize ionizing radiation, limiting their accessibility and broad use as screening tools in the population at risk for osteoporosis.[5-8]

INTERPRETATION OF ULTRASOUND RESULTS

As new techniques for measuring bone mass and fracture risk have been introduced into the medical community, there has been confusion regarding the proper interpretation of the results from different devices. Organizations such as the International Society for Clinical Densitometry (ISCD), the National Osteoporosis Foundation (NOF), and the World Health Organization (WHO) have provided guidance for the interpretation of these measurements.[8-12]

In 1994, the WHO published criteria to categorize populations with osteoporosis and osteopenia (low bone mass).[9] These definitions of disease severity were based upon central (spine and hip) DXA T-score results, which report the measured bone mineral density (BMD) in terms of the number of standard deviations below (Figure 3) the young adult mean value.
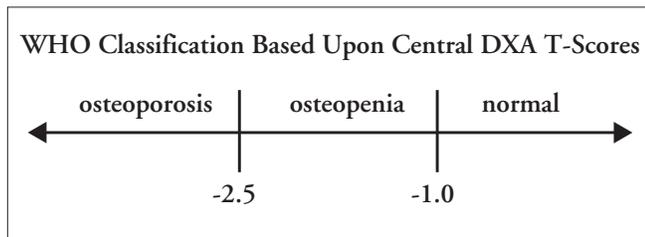

WHO Classification Based Upon Central DXA T-Scores

osteoporosis | osteopenia | normal

-2.5   -1.0

Figure 3

As other technologies were introduced, there was a tendency to apply these same diagnostic thresholds from central DXA measurements to devices that assess other sites ("peripheral" skeletal sites). However, with the increasing use of both central and peripheral devices, strong evidence emerged that the WHO diagnostic criteria did not apply to peripheral devices, such as QUS[13,14]. For example, Sahara QUS and central DXA T-scores for an individual can differ by up to 1 T-Score, a significant difference that can affect diagnosis and treatment decisions. These differences arise not from the technology, but from the bone density differences found in an individual patient at different skeletal sites. Similar variability from central DXA T-scores is seen with peripheral DXA and QUS devices.

Due to the differences in bone densitometry results from central vs. peripheral measurements, the ISCD and NOF have provided guidelines for the use of bone densitometry systems for diagnosis versus screening.[8-12] Central DXA remains the gold standard for diagnosis, and can be effectively utilized for monitoring of serial changes in bone density. Ultrasound is valuable in screening and identifying those at risk for fracture, but it is not a diagnostic tool.

Peripheral DXA, QUS = Screening for high-risk patients

Spine and Hip DXA = Diagnosis of osteoporosis, monitoring of change

QUS thresholds specific to Sahara have been developed to accurately identify those at risk for fracture who should receive a more thorough exam and diagnosis by central DXA. In a study of 319 postmenopausal women (mean age 63 years), both hip DXA and Sahara QUS measurements were made to assess risk thresholds.[15] Of those with a QUS T-score of –1.0 or less, 90% had a diagnosis of osteoporosis or osteopenia by central DXA and only 10% had normal BMD. This threshold also captured 82% of all patients with osteoporosis. Therefore, patients with a QUS score more than one standard deviation below the young adult mean were classified as having a high fracture risk. Those with a QUS T-score greater than 0 were classified as low-risk, as very few (6%) in this group were diagnosed with osteoporosis. The majority of those in the moderate risk group (between 0 and –1) had osteopenia. Studies by other investigators have validated these thresholds to help establish proper guidance for QUS screening.[16-20] Figure 4 illustrates the risk stratification based upon QUS T-score using a Hologic Sahara system.

Risk Stratification Based Upon QUS T-Scores

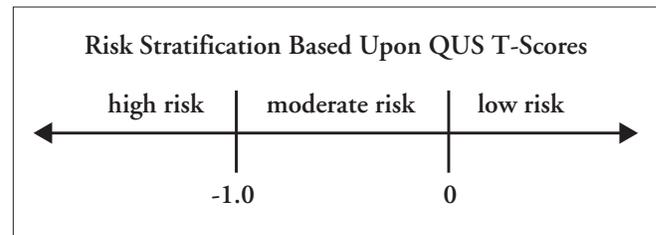high risk | moderate risk | low risk

-1.0   0

Figure 4

- *In the high-risk category, Sahara QUS has a sensitivity of 82% in identifying those with steoporosis by central DXA.*

- *90% of those in the high-risk category were identified as either osteoporotic or osteopenic by central DXA*

- *Only 6% of patients in the low risk category had a diagnosis of osteoporosis by central DXA*

SAHARA AS A SCREENING TOOL

The medical community has routinely used low-level screening tests to target those in need of a more detailed assessment. For example, mammography and breast exams are accepted methods to screen for potential signs of breast cancer, but these evaluations are not used to make a diagnosis regarding tumor malignancy. Blood pressure measurement is another routine test, conducted using a stethoscope and blood pressure cuff. Because high blood pressure can be a sign of heart or kidney disease, additional follow-up is often required to make a proper diagnosis.

Sahara screening provides valuable information for healthcare providers and patients to determine if a more detailed osteoporosis assessment is warranted. Because no radiation is used, Sahara can be used in almost any setting, making it a practical and accurate way to screen the large population of individuals at risk for osteoporosis. The figure below shows the value of Sahara in identifying postmenopausal women who are in need of follow-up DXA testing and clinical evaluation. It is important to note that proper diagnosis includes not only DXA, but also an assessment of other risk factors such as age, the presence of existing fractures, and family history of fracture. Such a thorough diagnostic assessment is necessary to provide the best individual therapy for the prevention or treatment of osteoporosis.
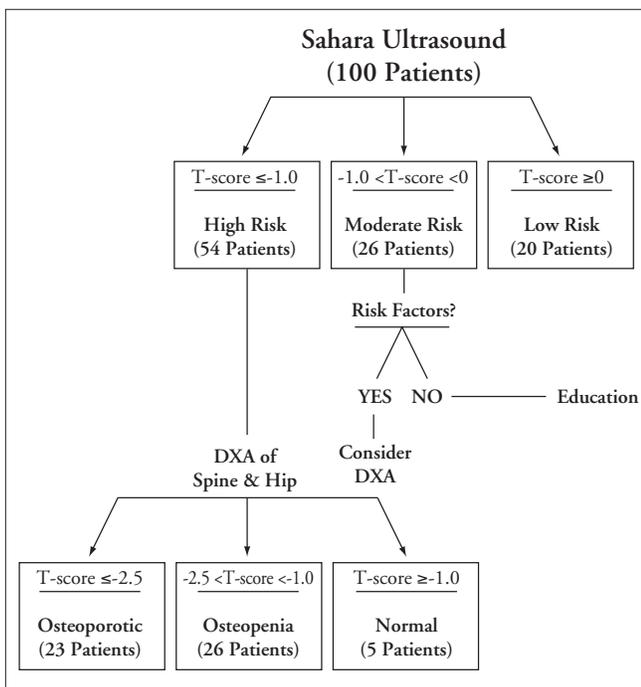
Patient Evaluation Flowchart for Sahara

Figure 5

• *Roughly one-half of all postmenopausal women tested by Sahara have a high risk for fracture and should be referred for DXA testing.*

• *This result is consistent with data from the National Institutes of Health (NIH) indicating that 55% of women over the age of 50 have low bone mass or osteoporosis.[21]*

Risk assessment based on Sahara T-scores can be accomplished utilizing the flow-chart (Figure 5). The number of patients is given in each subgroup, indicating excellent sensitivity (82%) for the T=-1 threshold, and excellent specificity (94%) for the T=0 threshold.

• **High fracture risk (Sahara T-score <-1):** 54% of postmenopausal women have a Sahara T-score less than –1.0.

– 90% in this group are osteoporotic or osteopenic based upon subsequent DXA diagnosis

– 82% of patients with osteoporosis (defined by central DXA) are included in this group (Sensitivity = 82%)

• **Moderate-to-high fracture risk (Sahara T-score <0):** 80% of postmenopausal women have a Sahara T-score less than 0.

– 85% in this group have osteoporosis or osteopenia based upon subsequent DXA diagnosis

• **Low fracture risk (Sahara T-score > 0):** 20% of postmenopausal women have a T-score more than 0.

– 6% of this group have osteoporosis based upon subsequent DXA diagnosis

Sahara Meets the need for Increased Access to Testing

Access to testing is a major challenge in the battle against osteoporosis. Despite the proliferation of central DXA testing equipment, many postmenopausal women are not tested. Even with the availability of therapies that significantly reduce fracture risk, only 23% of women at risk for osteoporosis are diagnosed and less than half of those diagnosed are treated.[1] The Sahara system provides a portable, radiation free technique for identifying those at high risk. The test can be conducted almost anywhere, such as a primary care office, a mobile testing van, a pharmacy, or a health fair. With Sahara, the procedure takes only 10 seconds and no water bath is required, so that the set-up time between exams is negligible. Those at high risk can then be counseled and referred for a full DXA examination. The consequences of this under-recognized condition are apparent, given that one out of two women over the age of 50 will suffer an osteoporosis-related fracture in their lifetime.[22] Early recognition and intervention are important, especially for postmenopausal women, who lose on average 20% of their bone mass in the first five to seven years following menopause.[22] Therefore, the use of ultrasound as a screening tool has great promise as simple, economical method to address the large undiagnosed and untreated population at risk for osteoporotic fracture.

Benefits of Sahara for Screening

Sahara provides a low-cost, reliable method to identify those in need of more detailed diagnostic evaluation.

• Sahara is highly predictive of hip fracture.

• The system is portable and radiation free, so the test can be conducted anywhere

• There is no need for an x-ray technician, and x-ray regulations to not apply

• With Sahara's dry technology, the procedure is fast (10 sec) with little set-up required between tests

• Sahara filters out those at low risk for fracture and identifies those in need of additional testing

• Sahara provides a manageable way to address the large undiagnosed and untreated population at risk for osteoporotic fracture.

REFERENCES:

1 NHANES III. Osteoporosis among estrogen-deficient women—United States, 1988-1994. Morbidity and Mortality Weekly Report 1998; 47(45):969-973

2 Bauer DC, Gluer CC, Culey JA, Vogt TM, Ensrud KE, Genant HK, Black DM. Broadband ultrasound attenuation predicts fractures strongly and independently of densitometry in older women. Archives of Internal Medicine 1997; Vol 157:629-633

3 Hans D, Dargent-Molina P, Schott AM, et al. Ultrasonographic heel measurements to predict hip fracture in elderly women: the EPI-DOS prospective study. Lancet 1996; Vol 348:511-514

4 Siris ES, Miller PD, Barrett-Connor E, et al. Identification and fracture outcomes of undiagnosed low bone mineral density in postmenopausal women Results from the National Osteoporosis Risk Assessment. JAMA 2001; Vol 286(22):2815-2822

5 Miller PD, Siris ES, Barrett-Connor E, et al. Prediction of fracture risk in postmenopausal white women with peripheral bone densitometry: evidence from the national osteoporosis risk assessment. JBMR 2002; Vol 17(12):2222-2230

6 Krieg MA, Cornuz J, Ruffieux C, et al. Comparison of three bone ultrasounds for the discrimination of subjects with and without osteoporotic fractures among 7562 elderly women. JBMR 2003; Vol 18(7):1261-1266

7 Cummings SR, Black DM, Nevitt MC, et al. Bone density at various sites for prediction of hip fractures. Lancet 1993; Vol 341:72-75

8 Miller PD, Njeh CF, Jankowski LG, Lenchik L. What are the standards by which bone mass measurement at peripheral skeletal sites should be used in the diagnosis of osteoporosis. JCD 2002; Vol 5:S39-S45

9 Kanis JA. Assessment of fracture risk and its application to screening for postmenopausal osteoporosis: synopsis of a WHO report – WHO study group. Osteoporosis Int 1994; 4:368-381

10 Hamdy RC, Petak SM, Lenchik L. Which central dual x-ray absorptiometry skeletal sites and regions of interest should be used to determine the diagnosis of osteoporosis. JCD 2002; Vol 5:S11-S17

11 Lenchik L, Kiebzak GM, Blunt BA. What is the role of serial bone mineral density measurements in patient management. JCD 2002; Vol 5:S29-S38

12 National Osteoporosis Foundation. Physicians Guide to Prevention and Treatment of Osteoporosis. 2003

13 Faulkner KG, von Stetten E, Miller P. Discordance in patient classification using t-scores. JCD 1999; Vol. 2:343-350

14 Varney LF, Parker RA, Vincelette A, Greenspan SL. Classification of osteoporosis and osteopenia in postmenopausal women is

15 Goldstein SR, Nachtigall LE. Quantitative ultrasound of the calcaneus: comparison with dual energy x-ray absorptiometry (DXA) of the hip. Presented at the 9th Annual Meeting of the North American Menopause Society (Toronto, Sept. 16-19, 1998): Poster 70

16 Ayers M, Prince M, Ahmadi S, Baran D. Reconciling quantitative ultrasound of the calcaneus with x-ray-based measurements of the central skeleton. JBMR 2000; 15:1850-1855

17 Nairus J, Ellison B, Baker S, Ahmadi S, Baran D. Quantitative ultrasound: a cost effective screening technique for osteoporosis in perimenopausal women prior to dual energy x-ray absorptiometry. JBMR 1997; 12 (S1):S382-S387

18 Ikeda Y, Iki M, Morita A, et al. Age-specific values and cutoff levels for the diagnosis of osteoporosis in quantitative ultrasound measurements at the calcaneous with Sahara in healthy Japanese women: Japanese population-based osteoporosis (JPOS) study. Calcif Tissue Int 2002;71:1-9

19 Hans D, Hartl F, Krieg MA. Device-specific weighted t-score for two quantitative ultrasounds: operational propositions for the management of osteoporosis for 65 years and older women in Switzerland. Osteoporos Int 2003; 14:251-258

20 López-Rodríguez F, Mezquita-Raya P, de Dios Luna J, Escobar-Jiménez F, Muñoz-Torres M. Performance of quantitative ultrasound in the discrimination of prevalent osteoporotic fractures in a bone metabolic unit. Bone 2003; 32:571-578

21 National Osteoporosis Foundation. America's bone health: the state of osteoporosis and low bone mass in our nation. Feb 2002:1-15

22 National Institutes of Health, Fast Facts on Osteoporosis, 10/2000