META-ANALYSIS

Diagnostic Value of Quantitative Ultrasound for Osteoporosis in Elderly Women: A Meta-Analysis

Yi Jiang, MM; Haifan Wu, MM; Dan Yang, BM; Wenyi Wang, MM; Jiahao Chu, MM; Jing Tang, MM; Xinmiao Yao, MM

ABSTRACT

Objective • To assess the reliability of quantitative ultrasound (QUS) in diagnosing and screening osteoporosis in elder women.

Methods • We conducted a systematic search of the online databases, including PubMed, Embase, Web of Science, and China National Knowledge, and screened the studies according to the inclusion criteria. We directly extract or calculate the value of true positive (TP), false positive (FP), false negative (FN), and true negative (TN) from eligible studies. We sought to evaluate the diagnostic parameters of QUS, containing the pooled sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR), diagnostic odds ratio (DOR), and area under the curve (AUC).

Results • Twelve studies were included in this study with a total of 2260 women. QUS showed a pooled diagnostic odds ratio of 5.07 (95% CI 3.28-7.84), sensitivity of 0.69 (95% CI 0.65-0.72), specificity of 0.67 (95% CI 0.64-0.69), and an AUC of 0.7523 (Q^*=0.6953). There was no obvious heterogeneity and threshold effect according to the Spearman correlation coefficient (P = 0.059). No significant publication bias was found through the Deek's funnel.

Conclusion • Our study suggested that the diagnostic value of QUS for osteoporosis in elder women was acceptable, but the accuracy still needed to be improved, QUS can be recommended as a pre-screening tool for osteoporosis to determine whether DXA measurement was needed. (*Altern Ther Health Med.* 2024;30(1):226-231).

Yi Jiang, MM, Resident doctor; **Haifan Wu, MM,** Resident doctor; **Wenyi Wang, MM,** Resident doctor; **Jiahao Chu, MM,** Resident doctor; **Jing Tang, MM,** Associate chief physician; **Xinmiao Yao, MM,** Chief physician; Department of Orthopedics, Zhejiang Chinese Medicine University Third Clinical Medical College, Hanzhou, Zhengjiang, China; **Dan Yang, BM,** Resident doctor; TCM Internal Medicine, Wenling Traditional Chinese Medicine Hospital, Wenling, Zhengjiang, China.

Corresponding author: Xinmiao Yao, MM
E-mail: yxmtcm@aliyun.com
Corresponding author: Jing Tang, MM
E-mail: tangjing3333@163.com

INTRODUCTION

Osteoporosis is a kind of systemic bone disease with bone mass reduction and bone microstructure destruction, which increases the bone fragility and risk of fracture.[1,2] It has been recognized as one of the problems that seriously affect public health.[3,4] For the diagnosis of osteoporosis, WHO recommends the detection of lumbar spine bone mineral density (BMD) by Dual-energy X-ray absorptiometry (DXA) as the gold standard.[5,6]

DXA is the preferred technique for evaluating BMD, which has the characteristics of fast, good accuracy, repeatability, and flexibility, and it is carried out at low radiation doses.[5] However, DXA equipment is not portable, expensive, and involves ionizing radiation exposure, so in many geographic regions, it is usually limited to tertiary health care hospitals because of the need for specialized and trained personnel.[7,8]

Quantitative ultrasound (QUS), which developed in recent years, has gradually become one of the preferred tools for many doctors and researchers to diagnose and screen osteoporosis with its advantages of non-radiation, non-invasive, portable, low examination cost, and providing information on bone quality and strength.[9-11]

Considering the considerable health problems caused by osteoporosis in postmenopausal women, it was necessary to choose a low-cost screening method to identify the disease.[12,13] In recent years, there have been a lot of clinical controlled studies on QUS and DXA in the diagnosis of osteoporosis around the world.[14-16] However, the sensitivity and specificity of each research institution were quite different, and there was less systematic evaluation of such data.[17-20]

Our study aimed to comprehensively evaluate the clinical value of QUS in the diagnosis of osteoporosis in elder women by using the method of evidence-based medicine.

METHODS

Literature Search Strategy

We systematically searched online databases, including PubMed, Embase, Web of Science (WOS), and China National Knowledge Infrastructure, to identify correlative studies published before August 2022. We used the following keywords: (1) quantitative ultrasound (QUS); (2) osteoporosis; (3) diagnostic, search words were combined using Boolean operators "and". No restrictions regarding the year of publication, language, or publication status were applied and no gray literature search was conducted. Hand searches of the reference lists of the relevant reports were carried out to identify any relevant studies that were missed with the search strategy.

Study Selection

Articles were included in our review if they met the following inclusion criteria: (1) Focus on the value of quantitative ultrasound in the diagnosis of osteoporosis in elder women; (2) Directly or indirectly provided the following data: true positive (TP), false positive (FP), false negative (FN) and true negative (TN); (3) Diagnosed osteoporosis based on widely recognized gold standards, such as DXA; (4) Full-text articles were available. Studies would be excluded for the reasons as follows: (1) Researches not meet the inclusion criteria; (2) The outcomes of interest were not reported or impossible to use; (3) Review, abstract, or duplicate publication.

Data extraction

Two review authors independently screened the titles and abstracts of search results for relevance, acquired and screened the full texts of potentially eligible articles, and extracted data from included studies as follows: first author's name, year of publication, country of origin, sample size, patient's age and BMI, test location, gold standard and corresponding cut-off value, primary outcome (TP, FP, FN, TN).

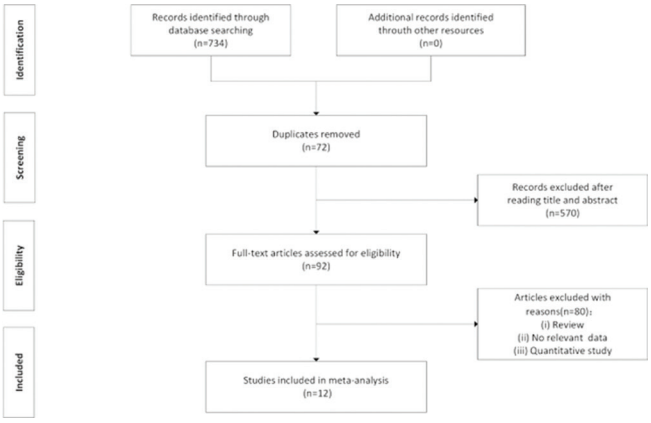
Quality assessment

The methodological quality of the included publications was assessed using the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) tool in the Revman software (version 5.4), which contained four domains, including "patient selection", "index test", "reference standard", and "flow and timing". Two review authors independently appraised the quality of the included studies, and a third reviewer assisted in the event of a discrepancy.

Statistical Analysis

Meta-analysis was performed by using Meta-DiSc (Version 1.4, Madrid, 2006), Stata software (Version 14.0, Stata Corporation), and Review Manager (Version 5.4, Cochrane Collaboration, 2020). The I^2 was used to assess the heterogeneity among the studies. If $P < .05$ or $I^2 > 50\%$, a random effect model would be used for analysis; if $P \geq .05$ and $I^2 \leq 50\%$, a fixed effect model would be used for analysis.

Figure 1. Flow diagram of study selection



Forest plots were conducted to evaluate pooled estimates, sensitivity analysis was conducted by eliminating individual studies one by one, and Deeks' funnel plots were used to identify the publication bias.

RESULTS

Search Process

Altogether 734 potentially relevant articles were identified through a primary literature search using the described search strategy and inclusion/exclusion criteria. By carefully reading the titles and abstracts, 570 studies were excluded because they did not meet the inclusion criteria. From these, 80 articles were further excluded due to various reasons including different study designs or insufficient data available. Ultimately, 12 studies that met the selection criteria were included in the present meta-analysis.[21-31] Figure 1 illustrates the search process, with the associated inclusion and exclusion criteria.

Characteristics of Included Studies

Table 1 shows the principal characteristics of the 12 included studies. The published year was between 2001 and 2018. These studies were from nine countries and contained a total of 2260 women. In all studies, the test location of quantitative ultrasound was calcaneus, and the gold standard was DXA (cut-off value: $T \leq -2.5$ or $T < -2.5$).

Results of Quality Assessment

As shown in Figure 2, the QUADAS-2 tool was used to assess the quality of included studies. The risks of clinical applicability were low in all studies, and so was the risk of the reference standard. Two studies showed a high risk of patient selection, and the other two articles showed a high risk of index test and flow and timing. Figure 3 presented a summary of bias risk and applicability concerns for each included study.

Results of Diagnostic accuracy

The random effect model was used to evaluate the heterogeneity due to the significant heterogeneity in all outcomes. The overall pooled sensitivity and specificity of

Table 1. Characteristics of eligible studies

Study	Country	No. of participants	Age	BMI (kg/m²)	Test location	Gold standard	Cut-off value	TP	FP	FN	TN
Dubois 2001	Netherlands	137	63±8	25±4	Calcaneus	DXA	T ≤ -2.5	30	20	13	74
Pearson 2003	UK	99	69±8	25.6±5.4	Calcaneus	DXA	T < -2.5	33	15	20	31
Pérez 2003	Spain	265	72.6±5.3	27.2±4.14	Calcaneus	DXA	T ≤ -2.5	65	55	42	103
Panichkul 2004	Thailand	300	57.91±8.16	23.9±3.39	Calcaneus	DXA	T ≤ -2.5	83	78	24	115
Boonen 2005	Belgium	221	50~75	24.2±4.1	Calcaneus	DXA	T < -2.5	27	53	41	127
Cook 2005	UK	208	59.7(20,87)	25.4±5.2	Calcaneus	DXA	T < -2.5	41	80	4	83
Pongchaiyakul 2007	Thailand	300	57.9±8.7	23.3±3.2	Calcaneus	DXA	T ≤ -2.5	23	36	15	226
Dane 2008	Turkey	186	59.5±4.8	27.5±6.2	Calcaneus	DXA	T ≤ -2.5	55	63	18	50
Jin 2010	China	106	50.2±10.9	24.82±3.86	Calcaneus	DXA	T < -2.5	32	4	13	57
Schafer 2011	Germany	43	62~87	27.2±4.5	Calcaneus	DXA	T ≤ -2.5	8	12	0	23
Vallipakorn 2016	Thailand	161	70(65,94)	23.24±5.8	Calcaneus	DXA	T ≤ -2.5	39	61	9	52
Steiner 2018	Austria	234	58.7±8.7	24.9±4.4	Calcaneus	DXA	T ≤ -2.5	22	63	10	139

Abbreviations: BMI, body mass index; TP, true positive; FP, false positive; FN, false negative; TN, true negative; DXA, dual-energy X-ray absorptiometry.

Figure 2. Proportion of studies with low (green), high (red), or unclear (yellow) risk of bias

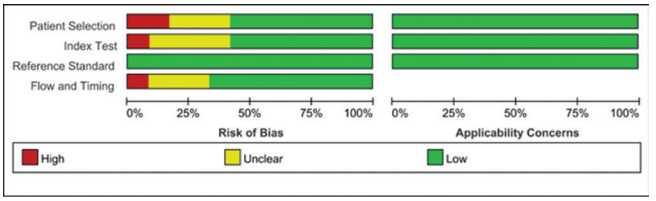


Figure 3. Summary of QUADAS-2 assessments of included studies

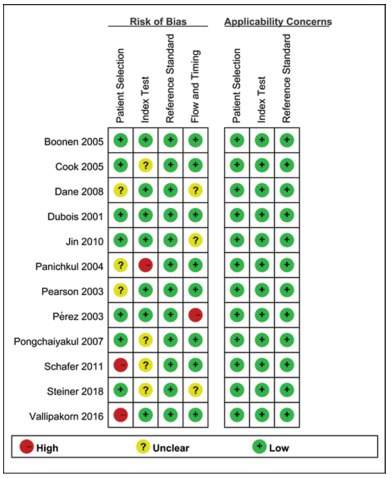


Figure 4. Forest plot: sensitivity of QUS for osteoporosis

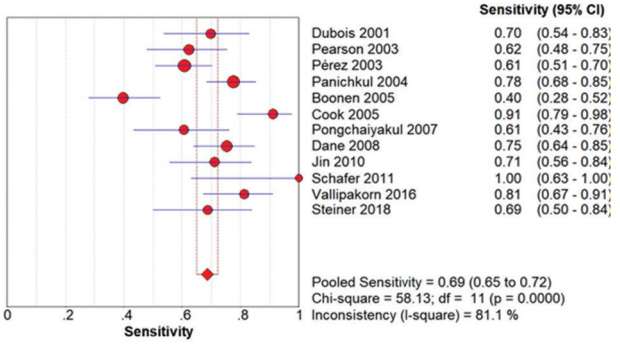


Figure 5. Forest plot: specificity of QUS for osteoporosis

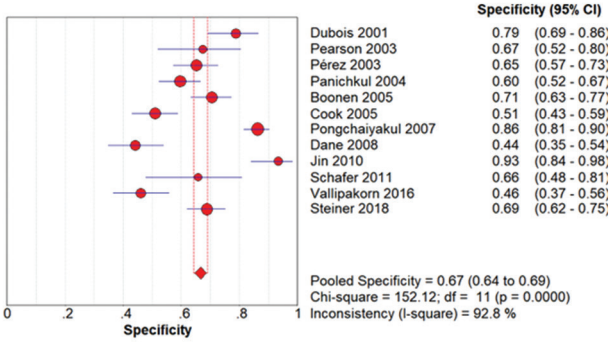


Figure 6. Forest plot: positive likelihood ratio of QUS for osteoporosis

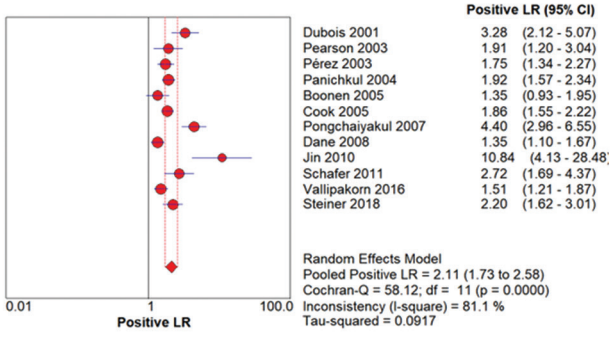


Figure 7. Forest plot: negative likelihood ratio of QUS for osteoporosis

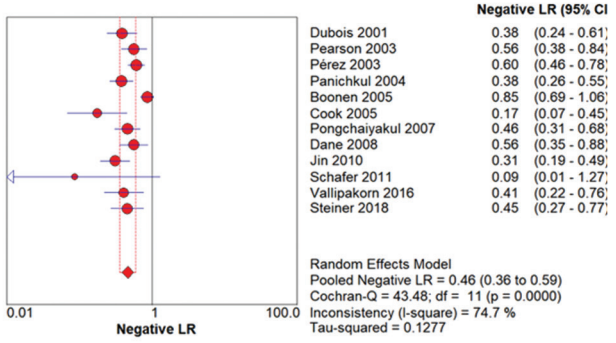


Figure 8. Forest plot: diagnostic odds ratio of QUS for osteoporosis

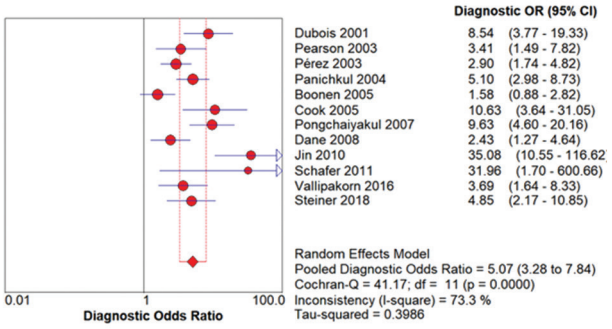


Figure 9. Summary receiver operating characteristic (SROC) curve of QUS for osteoporosis

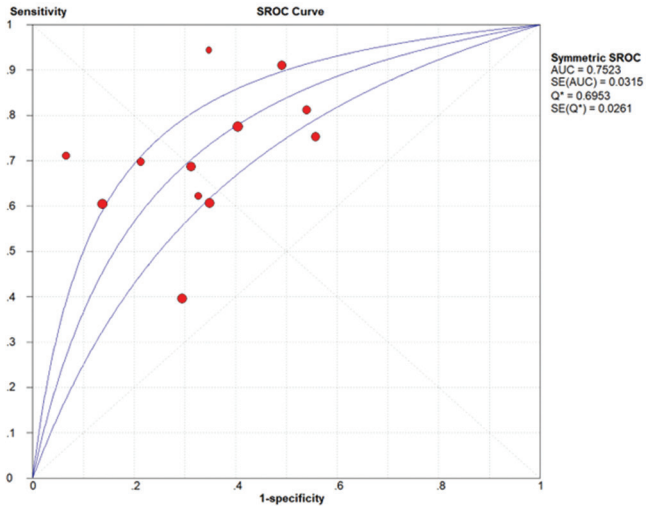
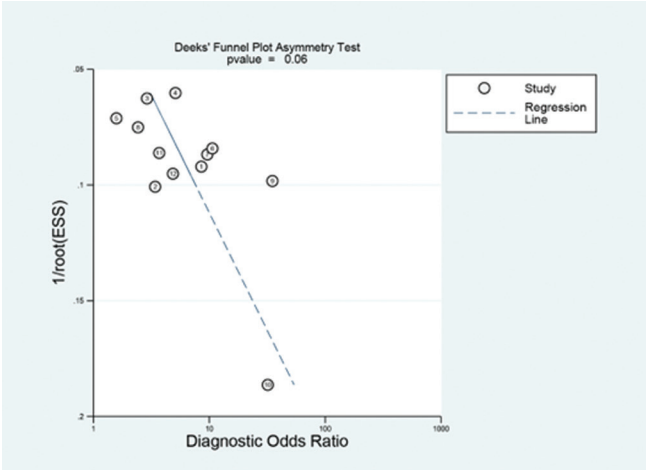


Figure 10. Deeks' funnel plot for evaluating potential publication bias



QUS for osteoporosis diagnosis were 0.69 (95%CI[0.65, 0.72], I^2 = 81.1%, P < .00001, Figure 4) and 0.67 (95%CI[0.64, 0.69], I^2 = 92.8%, P < .00001, Figure 5). The pooled PLR, NLR and DOR were 2.11 (95%CI[1.73, 2.58], I^2 = 81.1%, P < .00001, Figure 6), 0.46 (95%CI[0.36, 0.59], I^2 = 74.7%, P < .00001, Figure 7), and 5.07 (95%CI[3.28, 7.84], I^2 = 73.3%, P < .00001, Figure 8), respectively. The area under the curve was 0.7523 (Q* = 0.6953) (Figure 9).

Results of Heterogeneity analysis

We conducted the threshold analysis through Meta-DiSc to explore the threshold effect, the Spearman correlation coefficient was 0.559 (P = .059), indicating that there was no obvious heterogeneity and threshold effect. Meanwhile, the forest plot of DOR showed that Cochran Q was 41.17 (P < .00001), suggesting there may be some threshold effect, and the random effect model should be used to analyze.

Sensitivity analysis

For the heterogeneity of the above analysis, to observe the stability level of the synthesis results, we performed a sensitivity analysis and the results showed that there was no obvious change. Therefore, it can be judged that the conclusion was reliable.

Publication Bias

A Deeks' funnel plot was performed to qualitatively evaluate the publication bias, and the P value was 0.06, which indicated no significant publication bias existed in this meta-analysis (Figure 10).

DISCUSSION

Osteoporosis has become a very serious public health problem, with the increase of life expectancy and the change of lifestyle. Early detection of high-risk groups of osteoporosis is the key to preventing and reducing the occurrence of osteoporosis fractures.[19,32,33] Therefore, efforts should be made to find more effective methods to prevent and detect osteoporosis in the early stage.[34,35]

DXA screening was most commonly used in patients who have had brittle fractures or who have begun osteoporosis treatment. However, prevention of the first brittle fracture should be the primary goal to reduce the disability burden, increased costs, and increased risk of death caused by brittle fractures.[36,37] Therefore, it was neither recommended nor feasible to use DXA widely in the whole population to screen osteoporosis.[7,38]

Quantitative ultrasound (QUS) has been widely used in bone health assessment in primary medical and health institutions due to its advantages of good repeatability, non-radiation injury, and non-invasive.[39,40] However, there were potential sources of error in the measurement of QUS in vivo, including soft tissue thickness, temperature, and anthropometric parameters, which may lead to the misclassification of individuals.[41,42] Therefore, QUS had not been used as the gold standard for the diagnosis of

osteoporosis.[19,37] However, QUS could be used as an alternative screening tool for osteoporosis, and some studies have shown that QUS can predict measurements of BMD and fracture risk.[43-46]

Our study showed that the combined sensitivity of QUS in the diagnosis of osteoporosis was 69%, indicating that there was a certain under-diagnosis rate (31%). The specificity was 67%, indicating that the misdiagnosis rate was relatively high (33%). Likelihood ratio (LR) was a composite index that can reflect sensitivity and specificity at the same time, which was not affected by the prevalence of the disease and can reflect the diagnostic value of detection technology.

Jaeschke suggested that when PLR >10 and NLR < 0.1, it had a convincing diagnostic efficiency; when 5 < PLR ≤ 10 and 0.1 ≤ NLR < 0.2, it had a moderate diagnostic efficiency; when 2 < PLR ≤ 5 and 0.2 ≤ NLR < 0.5, the diagnostic efficiency was small, but it was important in some cases; when 1 < PLR ≤ 2 and 0.5 ≤ NLR < 1, the diagnostic efficiency was very small and it was not important.[48] The results of our study were 2.11 in PLR and 0.46 in NLR, so it was not considered that QUS has a strong diagnostic efficiency. In addition, another index to evaluate the value of the diagnostic test was the area under the SROC curve and its curve. In this study, AUC was 0.7523 and Q* was 0.6953, which were close to 1, indicating that the diagnostic ability was still acceptable, but it cannot be considered to be of high accuracy.

Our research had some limitations. First of all, the location of gold standard DXA in different studies was not consistent, spin, femoral neck, or total hip or their combination were selected as the detection sites respectively, which may cause some differences in the diagnostic accuracy of QUS in different studies. Secondly, the population included in this meta-analysis were all high-age or postmenopausal women, so the results may not apply to men or young women.

In conclusion, this study provided some information on a specific calcaneal QUS device as a screening tool for osteoporosis in elderly or postmenopausal women. Considering that the diagnostic ability was acceptable, but the accuracy needed to be improved, QUS can be recommended as a pre-screening tool for osteoporosis to determine whether DXA measurement was needed. To further support these findings, studies should be conducted in a larger female population.

CONFLICT OF INTEREST

The authors have no potential conflicts of interest to report relevant to this article.

AUTHOR CONTRIBUTIONS

Yi Jiang and Haifan Wu contributed equally to this work.

FUNDING

This study was supported by the science and technology Traditional Chinese Medicine Plan of Zhejiang Province, China (No. 2021ZB149, No. 2022ZA091), And the support of the Traditional Chinese Medicine studio of Dr. XM Yao (No. 20- 2014, No. 70-2018).

REFERENCES

1. Chen Y, Guo Y, Zhang X, Mei Y, Feng Y, Zhang X. Bone susceptibility mapping with MRI is an alternative and reliable biomarker of osteoporosis in postmenopausal women. *Eur Radiol*. 2018;28(12):5027-5034. doi:10.1007/s00330-018-5419-x
2. Guglielmi G, Scalzo G, de Terlizzi F, Peh WCG. Quantitative ultrasound in osteoporosis and bone metabolism pathologies. *Radiol Clin North Am*. 2010;48(3):577-588. doi:10.1016/j.rcl.2010.02.013
3. Sherchan B, Lamichhane A, Mahara DP. Osteoporosis Self Assessment Tool for Asian (OSTA) Index in Comparison to Quantitative Ultrasound of the Calcaneal in Predicting Low Bone Density. *Nepal Orthopaedic Association Journal*. 2014;3(2):20-25. doi:10.3126/noaj.v3i2.9524
4. Reid IR, Billington EO. Drug therapy for osteoporosis in older adults. *Lancet*. 2022;399(10329):1080-1092. doi:10.1016/S0140-6736(21)02646-5
5. Muftic M, Selimovic EK, Miladinovic K. Osteoporosis--comparative study between quantitative ultrasound of calcaneus and DXA. *Med Arh*. 2013;67(4):289-291. doi:10.5455/medarh.2013.67.289-291
6. Naseed M, Mir F, Nazir I. Comparison of Radiographic Singh Index with Dual-Energy X-Ray Absorptiometry Scan in Diagnosing Osteoporosis. *Matrix Science Medica*. 2021;5(1):17. doi:10.4103/MTSM.MTSM_41_20
7. Dane C, Dane B, Cetin A, Erginbas M. The role of quantitative ultrasound in predicting osteoporosis defined by dual-energy X-ray absorptiometry in pre- and postmenopausal women. *Climacteric*. 2008;11(4):296-303. doi:10.1080/13697130802178471
8. Wan H, Yang D, Shen J. Comparison between SOS of Quantitative Ultrasound and BMD Measured by DXA in Diagnosing Osteoporosis. *Bone*. 2008;43(S1):S91. doi:10.1016/j.bone.2008.07.122
9. Beattie A, Cournane S, Finucane C, Walsh JB, Stassen LFA. Quantitative Ultrasound of the Mandible as a Novel Screening Approach for Osteoporosis. *J Clin Densitom*. 2018;21(1):110-118. doi:10.1016/j.jocd.2017.08.001
10. Tao B, Liu JM, Li XY, Wang JG, Wang WQ, Ning G. An assessment of the use of quantitative ultrasound and the Osteoporosis Self-Assessment Tool for Asians in determining the risk of nonvertebral fracture in postmenopausal Chinese women. *J Bone Miner Metab*. 2008;26(1):60-65. doi:10.1007/s00774-007-0798-0
11. Liu C, Li D, Fan Y. The Possibility of Diagnosing Osteoporosis by Quantitative Ultrasound under Loading Conditions: preliminary Study. *Bone*. 2010;47(1):S392-S393. doi:10.1016/j.bone.2010.09.161
12. Abdulameer SA, Sahib MN, Sulaiman SAS. The Prevalence of Osteopenia and Osteoporosis Among Malaysian Type 2 Diabetic Patients Using Quantitative Ultrasound Densitometer. *Open Rheumatol J*. 2018;12(1):50-64. doi:10.2174/1874312901812010050
13. Bonte D, Ilie AC, Iacob RE, et al. The Evaluation of the Leptin Implication in Postmenopausal Osteoporosis. *J Food Agric Environ*. 2013;11. doi:10.1234/4.2013.3833
14. Olszynski WP, Brown JP, Adachi JD, Hanley DA, Ioannidis G, Davison KS; CaMos Research Group. Normative data for multisite quantitative ultrasound: the Canadian Multicenter Osteoporosis Study. *J Clin Densitom*. 2014;17(4):534-540. doi:10.1016/j.jocd.2013.09.017
15. Pennisi P, Pizzarelli G, Spina M, Riccobene S, Fiore CE. Quantitative ultrasound of bone and clodronate effects in thalassemia-induced osteoporosis. *J Bone Miner Metab*. 2003;21(6):402-408. doi:10.1007/s00774-003-0435-5
16. Pongchaiyakul C, Panichkul S, Songpatanasilp T, Nguyen TV. A nomogram for predicting osteoporosis risk based on age, weight and quantitative ultrasound measurement. *Osteoporos Int*. 2007;18(4):525-531. doi:10.1007/s00198-006-0279-7
17. Biino G, Casula L, de Terlizzi F, et al. Epidemiology of osteoporosis in an isolated Sardinian population by using quantitative ultrasound. *Am J Epidemiol*. 2011;174(4):432-439. doi:10.1093/aje/kwr106
18. Sofka CM. Quantitative Ultrasound in the Assessment of Osteoporosis. *Ultrasound Q*. 2010;26(2):117. doi:10.1097/01.ruq.0000377232.72440.90
19. Stewart A, Reid DM. Quantitative ultrasound in osteoporosis. *Semin Musculoskelet Radiol*. 2002;6(3):229-232. doi:10.1055/s-2002-36720
20. Nayak S, Olkin I, Liu H, et al. Meta-analysis: accuracy of quantitative ultrasound for identifying patients with osteoporosis. *Ann Intern Med*. 2006;144(11):832-841. doi:10.7326/0003-4819-144-11-200606060-00009
21. Edelmann-Schäfer B, Berthold LD, Stracke H, Lührmann PM, Neuhäuser-Berthold M. Identifying elderly women with osteoporosis by spinal dual X-ray absorptiometry, calcaneal quantitative ultrasound and spinal quantitative computed tomography: a comparative study. *Ultrasound Med Biol*. 2011;37(1):29-36. doi:10.1016/j.ultrasmedbio.2010.10.003
22. Boonen S, Nijs J, Borghs H, Peeters H, Vanderschueren D, Luyten FP. Identifying postmenopausal women with osteoporosis by calcaneal ultrasound, metacarpal digital X-ray radiogrammetry and phalangeal radiographic absorptiometry: a comparative study. *Osteoporos Int*. 2005;16(1):93-100. doi:10.1007/s00198-004-1660-z
23. Cook RB, Collins D, Tucker J, Zioupos P. Comparison of questionnaire and quantitative ultrasound techniques as screening tools for DXA. *Osteoporos Int*. 2005;16(12):1565-1575. doi:10.1007/s00198-005-1864-x
24. Díez-Pérez A, Marín F, Vila J, et al. Evaluation of calcaneal quantitative ultrasound in a primary care setting as a screening tool for osteoporosis in postmenopausal women. *J Clin Densitom*. 2003;6(3):237-245. doi:10.1385/JCD:6:3:237
25. Dubois EF, van den Bergh JP, Smals AG, van de Meerendonk CW, Zwinderman AH, Schweitzer DH. Comparison of quantitative ultrasound parameters with dual energy X-ray absorptiometry in pre- and postmenopausal women. *Neth J Med*. 2001;58(2):62-70. doi:10.1016/S0300-2977(00)00102-9
26. Jin N, Lin S, Zhang Y, Chen F. Assess the discrimination of Achilles InSight calcaneus quantitative ultrasound device for osteoporosis in Chinese women: compared with dual energy X-ray absorptiometry measurements. *Eur J Radiol*. 2010;76(2):265-268. doi:10.1016/j.ejrad.2009.05.046
27. Panichkul S, Sripramote M, Sriussawaamorn N. Diagnostic performance of quantitative ultrasound calcaneus measurement in case finding for osteoporosis in Thai postmenopausal women. *J Obstet Gynaecol Res*. 2004;30(6):418-426. doi:10.1111/j.1447-0756.2004.00224.x
28. Pearson D, Masud T, Sahota O, Earnshaw S, Hosking D. A comparison of calcaneal dual-energy X-ray absorptiometry and calcaneal ultrasound for predicting the diagnosis of osteoporosis from hip and spine bone densitometry. *J Clin Densitom*. 2003;6(4):345-352. doi:10.1385/JCD:6:4:345
29. Pongchaiyakul C, Panichkul S, Songpatanasilp T. Combined clinical risk indices with quantitative ultrasound calcaneus measurement for identifying osteoporosis in Thai postmenopausal women. *J Med Assoc Thai*. 2007;90(10):2016-2023.
30. Steiner B, Dimai HP, Steiner H, Cirar S, Fahrleitner-Pammer A. Prescreening for Osteoporosis With Quantitative Ultrasound in Postmenopausal White Women. *J Ultrasound Med*. 2019;38(6):1553-1559. doi:10.1002/jum.14844
31. Vallipakorn SA-O, Vallipakorn O, Sophonsritsuk A, Jirapinyo M, Sritara C. The Optimal Cut-Points for Weight and Non-Weight Quantitative Ultrasound of the Calcaneus to Screen Osteoporosis in Postmenopausal Women. *J Med Assoc Thai*. 2016;99(3):249-256.
32. Moayyeri A, Bingham SA, Luben RN, Wareham NJ, Khaw KT. Respiratory function as a marker of bone health and fracture risk in an older population. *J Bone Miner Res*. 2009;24(5):956-963. doi:10.1359/jbmr.081231
33. Wu XP, Liao EY, Luo XH, Dai RC, Zhang H, Peng J. Age-related variation in quantitative ultrasound at the tibia and prevalence of osteoporosis in native Chinese women. *Br J Radiol*. 2003;76(909):605-610. doi:10.1259/bjr/56839904
34. Wang T, Li S, Yi C, Wang X, Han X. Protective Role of β-Sitosterol in Glucocorticoid-Induced Osteoporosis in Rats Via the RANKL/OPG Pathway. *Altern Ther Health Med*. 2022;28(7):18-25.

35. Asakawa K, Koyama K, Yamagata Z. Effect of educational intervention using the Internet on quantitative ultrasound parameters in prevention of osteoporosis: a randomized controlled trial in young Japanese women. *Int J Womens Health*. 2011;3:415-422. doi:10.2147/IJWH.S20225
36. Xu J, Sun M, Wang Z, et al. Awareness of osteoporosis and its relationship with calcaneus quantitative ultrasound in a large Chinese community population. *Clin Interv Aging*. 2013;8:789-796. doi:10.2147/CIA.S45874
37. Hollaender R, Hartl F, Krieg MA, et al. Prospective evaluation of risk of vertebral fractures using quantitative ultrasound measurements and bone mineral density in a population-based sample of postmenopausal women: results of the Basel Osteoporosis Study. *Ann Rheum Dis*. 2009;68(3):391-396. doi:10.1136/ard.2007.083618
38. Frost ML, Blake GM, Fogelman I. Can the WHO criteria for diagnosing osteoporosis be applied to calcaneal quantitative ultrasound? *Osteoporos Int*. 2000;11(4):321-330. doi:10.1007/s001980070121
39. Gambacciani M, de Aloysio D, Elia D, van der Mooren MJ, Hadji P, Wüster C. Quantitative ultrasound (QUS) of bone in the management of postmenopausal women. *Maturitas*. 2004;47(2):139-149. doi:10.1016/S0378-5122(03)00245-7
40. Pennington Z, Ehresman J, Lubelski D, et al. Assessing underlying bone quality in spine surgery patients: a narrative review of dual-energy X-ray absorptiometry (DXA) and alternatives. *Spine J*. 2021;21(2):321-331. doi:10.1016/j.spinee.2020.08.020
41. Chin KY, Low NY, Kamaruddin AAA, Dewiputri WI, Soelaiman IN. Agreement between calcaneal quantitative ultrasound and osteoporosis self-assessment tool for Asians in identifying individuals at risk of osteoporosis. *Ther Clin Risk Manag*. 2017;13:1333-1341. doi:10.2147/TCRM.S145519
42. Glüer CC; The International Quantitative Ultrasound Consensus Group. Quantitative ultrasound techniques for the assessment of osteoporosis: expert agreement on current status. *J Bone Miner Res*. 1997;12(8):1280-1288. doi:10.1359/jbmr.1997.12.8.1280
43. Thomsen K, Jepsen DB, Matzen L, Hermann AP, Masud T, Ryg J. Is calcaneal quantitative ultrasound useful as a prescreen stratification tool for osteoporosis? *Osteoporos Int*. 2015;26(5):1459-1475. doi:10.1007/s00198-014-3012-y
44. Vu TT, Nguyen CK, Nguyen TL, et al. Determining the prevalence of osteoporosis and related factors using quantitative ultrasound in Vietnamese adult women. *Am J Epidemiol*. 2005;161(9):824-830. doi:10.1093/aje/kwi105
45. Quiros Roldan E, Brianese N, Raffetti E, et al. Comparison between the gold standard DXA with calcaneal quantitative ultrasound based-strategy (QUS) to detect osteoporosis in an HIV infected cohort. *Braz J Infect Dis*. 2017;21(6):581-586. doi:10.1016/j.bjid.2017.08.003
46. Pumberger M, Palmowski Y, Strube P, et al. DXA Does not Represent Bone Structure in Patients with Osteoporosis. *Spine*. 2020;Publish Ahead of Print(13): Ahead of Print. doi:10.1097/BRS.0000000000003917
47. Guyatt GH, Meade MO, Jaeschke RZ, Cook DJ, Haynes RB. Practitioners of evidence based care. Not all clinicians need to appraise evidence from scratch but all need some skills. *BMJ*. 2000;320(7240):954-955. doi:10.1136/bmj.320.7240.954