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Diagnostic value of calcaneal quantitative ultrasound in the evaluation of osteoporosis in middle-aged and elderly patients

Changzhou Li, MM[a], Jifeng Sun, MM[b], Li Yu, MM[c,*]

Abstract

To study the correlation between calcaneal quantitative ultrasound (QUS) and dual-energy X-ray absorptiometry (DXA), and analyze the diagnostic value of calcaneal QUS in the evaluation of middle-aged and elderly osteoporosis.

We assessed bone mineral density (BMD) at the femoral neck and intertrochanteric of left hip and lumbar spine (L1–L4) sites with DXA and QUS parameters of the right and left calcanei in a cohort of 82 patients over the age of 50 years. Using DXA parameters as the gold standard for the diagnosis of osteoporosis, the correlation coefficient between BMD and QUS parameters was calculated. Receiver operating characteristic curve was generated and areas under the curves were evaluated. Cut-off values for QUS were defined.

In men, there was a moderate correlation between calcaneal QUS and proximal femoral BMD ($P < .05$), but no significant correlation between calcaneal QUS and lumbar BMD ($P > .05$). In women, calcaneal QUS were moderately correlated with lumbar spine and proximal femoral BMD ($P < .05$). Using DXA as the gold standard, the accuracy, sensitivity, specificity, positive predictive value, and negative predictive value of calcaneal QUS in the diagnosis of osteoporosis were 90.2%, 89.2%, 100%, 100%, and 50.0%, respectively. According to the receiver operating characteristic curve, when the QUS T-score of calcaneum was –1.8, the area under the curve was 0.888, the sensitivity was 73.21%, and the specificity was 92.31% ($P < .05$). When the QUS T-score of calcaneum was –2.35, the sensitivity was 37.2% and the specificity was 100%.

Calcaneal QUS can be used to predict proximal femoral BMD in middle-aged and elderly people, as well as lumbar BMD in women. As a screening method for osteoporosis, calcaneal QUS has good specificity, so it can be recommended to use it as a pre-screening tool to reduce the number of DXA screening. When the QUS T-score of calcaneum is –1.8, it has the greatest diagnostic efficiency for osteoporosis; when the QUS T-score of calcaneum is ≤–2.35, it can be diagnosed as osteoporosis.

Abbreviations: BMD = bone mineral density, BUA = broadband ultrasound attenuation, DXA = dual-energy X-ray absorptiometry, QCT = quantitative computed tomography, QUS = quantitative ultrasound, ROC = receiver operating characteristic, SOS = speed of sound.

Keywords: bone mineral density, dual-energy X-ray absorptiometry, middle-aged and elderly, osteoporosis, quantitative computed tomography, quantitative ultrasound

1. Introduction

Osteoporosis is a systemic metabolic bone disease characterized by reduced bone mass and damaged normal structure of bone tissue resulting in reduced bone strength and easy fracture, which is one of the main causes of bone pain, fracture and disability, and death caused by fracture in elderly patients.[1] With the increase in people's life expectancy and the rapid increase of the aging population, the incidence of osteoporosis, which is closely related to aging, is increasing continuously and it has become the 7th common disease in the world.[2] Studies have shown that the lifetime risk of fragility fracture is about 50% for women and 25% for men over 50 years old.[3] The prevalence of osteoporosis in the European Union is estimated at 27.6 million and is 3 to 4 times higher in women over the age of 50 than in men. It is estimated that by 2050, the worldwide incidence of fragility fractures will increase 310% in men and 240% in women compared to 1990 rates.[4,5] These alarming increases pose a major public health concern and justify the need for better screening and early identification during healthcare encounters.

Bone mineral density (BMD) is an important means to diagnose osteoporosis and predict fracture and is most commonly measured by dual-energy X-ray absorptiometry (DXA) currently. It emits 2 kinds of X-ray with different energy after penetrating the human body measurement part. Due to the difference of attenuation and absorption of bone tissue, the data are generated and analyzed automatically on the computer, so as to obtain the bone mineral content of the measured bone.[6] The advantages of

Editor: Roxana Covali.

The authors have no funding and conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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How to cite this article: Li C, Sun J, Yu L. Diagnostic value of calcaneal quantitative ultrasound in the evaluation of osteoporosis in middle-aged and elderly patients. Medicine 2022;101:2(e28325).

Received: 24 July 2021 / Received in final form: 17 October 2021 / Accepted: 28 November 2021

http://dx.doi.org/10.1097/MD.0000000000028325

DXA are simple operation, fast scanning speed, low radiation dose, low price. However, DXA is only a cross-sectional mean BMD and cannot distinguish between cortical or cancellous BMD.[7] DXA also has variable measurement reliability at different skeletal sites and there is controversy regarding its accuracy in the lumbar spine. Due to the 2D nature of DXA imaging, factors such as metallic foreign bodies or implants, sclerotic bone from degenerative changes, coronal or sagittal deformities, aortic calcifications, and obesity may confound measurements and overestimate BMD in the lumbar spine.[8,9]

Quantitative computed tomography (QCT) is a new imaging technique for volume BMD measurement, which can measure the bone density of cortical bone and pine bone respectively. Examinations are performed using an application-specific software package and a dedicated bone-equivalent calibration phantom imaged simultaneously with the patient to convert the CT numbers into bone-equivalent values.[10] However, the cumbersome operation and radiation dose problem limit its application in clinical applications. The present QCT application is expensive, the production factory is different, the corresponding postprocessing software is not unified, the material properties and the calibration standards are different, the precision and accuracy of the calibration phantom are not unified, and studies such as the practice of the QCT measured bone density, the rate of the menopause women's lumbar vertebral bone was 440%, while the correction rate of the hip was 18%, and the rate of the hip was lower than the low rate. Therefore, QCT is not available in clinical use.[11,12]

Quantitative ultrasound (QUS) uses the changes of the speed of sound (SOS, expressed as m/s) which means the necessary time to ultrasound waves go through a determined distance inside the calcaneus bone, and broadband ultrasound attenuation (BUA, expressed by dB/MHz) which is a measure of the ultrasound variation of attenuation with the incident frequency of wave sound, generating a rigidity index called stiffness of the bone or QUS index (expressed as a percentage of the result from young adults or the percentage of weight-matched references according to the manufacturer).[13] Estimated BMD is the result of the combination of BUA and SOS that gives a BMD value, but it is important to note that QUS BMD is inferred from a linear combination of BUA and SOS and it is not an actual measurement of calcaneal BMD.[14] Calcaneus is the preferred site for QUS measurement because it is mainly composed of cancellous bone, as well as has few soft tissues in this part and a large parallel plane for easy measurement.[15] Studies have shown that calcaneal QUS has been proved to be a useful means for early diagnosis and prescreening of osteoporosis, and its advantages of no-dose radiation, portability, and simple operation are suitable for extensive clinical use.[16]

The association between the DXA and QUS tests has been reported to present a margin of confidence of 90% in specificity and sensitivity suggesting that bone mass density and evaluation performed by QUS may be equally predictive of risk of future fractures, since 1 standard deviation decreased in BUA increases 2 times the risk of hip fractures.[17] However, it is a major problem in the clinical diagnosis of osteoporosis that the results were different when BMD values in different parts of the same patient were measured by QUS.[18,19] Therefore, this study aims to through the analysis of QUS in evaluation of the diagnostic value of senile osteoporosis, using DXA as gold standard, prevention, and treatment for senile osteoporosis to provide more theoretical reference.

2. Methods and materials

2.1. Participants

A total of 82 middle-aged and elderly patients treated in our hospital from October 2017 to November 2018 were selected. This study has obtained the ethics certification of the First Hospital Affiliated of Dalian Medical University (IRB approval: YJ-KY-FB-2017-114). All patients gave informed consent, including 70 females, with an average age of (63.9 ± 9.2) years. There were 12 males with an average age of (62.3 ± 11.6) years. Inclusion criteria: age ≥ 50 years old; calcaneal QUS T-score ≥ -4; no recent long-term bed rest history. Exclusion criteria: patients with recent lower limb fracture; related diseases affecting bone metabolism, such as hyperthyroidism and Cushing syndrome; complicated with rheumatic immune diseases; patients with malignant tumors and abnormal functions of the heart, brain, kidney, and other major organs; use or have used anti-osteoporosis drugs; recently, oral barium meals interfere with the examination results.

2.2. Measurements

2.2.1. DXA measurement. The lumbar spine (L1–L4) and left hip were detected by DXA (Discovery A, Hologic, machine accuracy $\leq 1.0\%$), and BMD values with T-scores of these 2 parts were evaluated. The output parameters of DXA include the actual measured and the calculated values. The actual measured value is BMD value, which is compared with the reference database through the calculation software, so as to get the calculated score, T-score. The T-score represents the results of the normal reference database for normal young people of the same race and sex. The presence of osteoporosis at any region of interest was defined as a T-score ≤ 2.5. A T-score between –1 and –2.5 was classified as low bone mass/osteopenia and a T-score ≥ -1 was classified as normal.[20]

2.2.2. QUS measurement. SONOST 3000 (Osteosys, Korea) calcaneal QUS was used to determine BQI and QUS T-score of bilateral calcaneum. BQI is the result obtained by integrating SOS and BUA, which is more representative to reflect bone strength, and its accuracy error is less than 1.5%. Among them, SOS can reflect the bone structure, which is related to BMD. If BMD is reduced, SOS decreases. BUA can reflect the characteristics of bone. If BMD is reduced, the attenuation is small; the QUS T-score is the same as the DXA T-score.[21]

2.3. Parameters and statistical analysis

The distribution of osteoporosis degrees in different ages was analyzed. The QUS parameters of both calcanei were taken to obtain a mean value, and then the correlation between QUS T-score and BQI of calcaneum and DXA parameters of lumbar spine and proximal femur was analyzed for male and female, respectively. Using DXA parameters as standard, the accuracy, sensitivity, specificity, positive predictive value, and negative predictive value of calcaneal QUS in the diagnosis of osteoporosis were calculated. Using specificity as the abscissa and sensitivity as the ordinate, the receiver operating characteristic (ROC) curve was drawn and the maximum point of Youden index was taken as the cut-off value to evaluate the efficacy of calcaneal QUS in the diagnosis of osteoporosis.

SPSS20.0 statistical software was used and all measurement data were expressed as (mean $\pm$ standard deviation). The

distribution of osteoporosis degree in different ages was compared by trend chi-square test, and the correlation between calcaneal QUS and DXA parameters of lumbar spine and proximal femur was analyzed by Pearson correlation analysis. The diagnostic efficacy of QUS for osteoporosis was analyzed by ROC curve. Test standard: $P < .05$, the difference was statistically significant.

3. Results

3.1. Comparison of distribution of osteoporosis degree in different ages

Among the 82 middle-aged and elderly subjects, 8 cases (9.76%) had normal bone mass, 24 cases (29.27%) had reduced bone mass, and 50 cases (60.98%) had osteoporosis. With the increase of age, the percentage of normal bone mass and loss of bone mass decreased gradually. However, the incidence of osteoporosis was significantly increased, and the results were statistically significant ($\chi^2_{trend} = 5.436$, $P = .02$). See Table 1 and Figure 1.

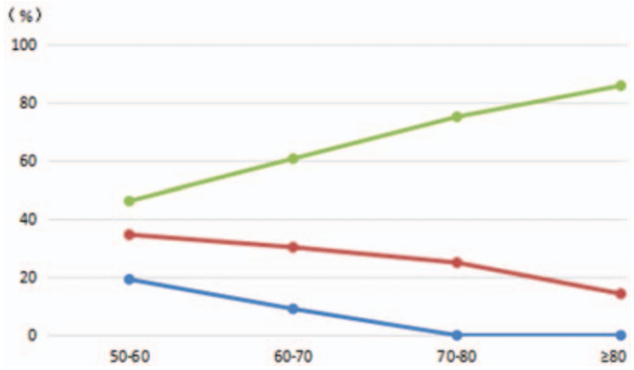

Figure 1. Comparison of the distribution of osteoporosis at different ages. The green line: normal. The green line: osteopenia. The green line: osteoporosis.

3.2. Correlation analysis of calcaneal QUS with DXA parameters of lumbar spine and proximal femur

3.2.1. Correlation analysis of calcaneal QUS and DXA parameters of lumbar spine and proximal femur in males. For middle-aged and elderly men, the correlation between calcaneal QUS and femoral neck, trochanter, and left hip T-score measured by DXA was 0.683, 0.645, and 0.612 ($P < .05$), while the correlation with L1–L4 T-score measured by DXA was 0.426 ($P > .05$). The correlation between QUS-BQI and femoral neck, trochanter, left hip BMD values measured by DXA was 0.650, 0.664, 0.600 ($P < .05$), and the correlation between QUS-BQI and L1–L4 BMD values measured by DXA was 0.252 ($P > .05$). Therefore, in men, calcaneal QUS were moderately correlated with proximal femoral BMD ($P < .05$), but not with lumbar BMD ($P > .05$). See Table 2.

3.2.2. Correlation analysis of calcaneal QUS and DXA parameters of lumbar spine and proximal femur in women. For middle-aged and elderly women, the correlation between QUS and femoral neck, trochanter, left hip, and L1–L4 T-score measured by DXA was 0.746, 0.731, 0.757, and 0.663 ($P < .05$). The correlation between QUS-BQI and femoral neck, trochanter, left hip, and L1–L4 BMD values measured by DXA was 0.628, 0.687, 0.728, 0.655 ($P < .05$). Therefore, in women, calcaneal QUS were moderately correlated with lumbar and proximal femoral BMD ($P < .05$). See Table 3.

3.3. Evaluation of the diagnostic efficacy of calcaneal QUS for osteoporosis

Using DXA parameters as the gold standard, the accuracy, sensitivity, specificity, positive predictive value, and negative predictive value of calcaneal QUS in the diagnosis of abnormal BMD were 90.24%, 89.20%, 100%, 100%, and 50.00%. See Table 4.

Table 1

Comparison of the distribution of osteoporosis at different ages.

Age range (yrs)	Number	Normal (n, %)	Osteopenia (n, %)	Osteoporosis (n, %)
50–60	26	5 (19.23)	9 (34.62)	14 (46.15)
60–70	33	3 (9.09)	10 (30.30)	22 (60.60)
70–80	16	0 (0)	4 (25.00)	13 (75.00)
≥80	7	0 (0)	1 (14.29)	6 (85.71)
Total	82	8 (9.76)	24 (29.27)	50 (60.98)
χ^2_{trend}		5.436		
P value		.02		

Table 2

Comparison of DXA parameters between calcaneal QUS and lumbar and proximal femur in men.

	QUS T-score/lumbar spine and proximal femoral T-score			QUS-BQI/lumbar spine and proximal femoral BMD		
Site	Number	Correlation coefficient (r)	*P* value	Number	Correlation coefficient (r)	*P* value
Femoral neck	12	0.683	.014	12	0.650	.022
Femoral trochanter	12	0.645	.024	12	0.664	.018
Left hip	12	0.612	.034	12	0.600	.039
L1–L4	12	0.426	.168	12	0.252	.430

BMD = bone mineral density, DXA = dual-energy X-ray absorptiometry, QUS = quantitative ultrasound.

Table 3

Comparison of DXA parameters between calcaneal QUS and lumbar and proximal femur in women.

	QUS T-score/lumbar spine and proximal femoral T-score			QUS-BQI/lumbar spine and proximal femoral BMD		
Site	Number	Correlation coefficient (r)	*P* value	Number	Correlation coefficient (r)	*P* value
Femoral neck	70	0.746	.000	12	0.628	.000
Femoral trochanter	70	0.731	.000	12	0.687	.000
Total hip	70	0.757	.000	12	0.728	.000
L1–L4	70	0.663	.000	12	0.655	.000

BMD = bone mineral density, DXA = dual-energy X-ray absorptiometry, QUS = quantitative ultrasound.

Table 4

Comparison of diagnosis results of calcaneal QUS and DXA.

	DXA			
Calcaneal QUS	Normal	Osteopenia	Osteoporosis	Total
Normal	8	6	2	16
Osteopenia	0	18	32	50
Osteoporosis	0	0	16	16
Total	8	24	50	82

DXA = dual-energy X-ray absorptiometry, QUS = quantitative ultrasound.

3.4. The optimal cut-off value of calcaneal QUS in the diagnosis of osteoporosis

The ROC curve was drawn based on the measured QUS T-scores of 82 middle-aged and elderly subjects as the test variable and disease diagnosis as the state variable. Youden index (sensitivity + specificity − 1) was calculated. The maximum value was taken as the best cut-off value of QUS T-score of calcaneal bone for diagnosis of osteoporosis. The corresponding sensitivity and specificity were obtained. When calcaneal QUS T-score was −1.8, the area under the curve was 0.888, and the 95% confidence interval was 0.799 to 0.947. The sensitivity and specificity for the diagnosis of middle-aged and elderly osteoporosis were 73.21% and 92.31% ($P < .05$). When QUS T-score calcaneus was −2.35, the sensitivity and specificity for the diagnosis of osteoporosis were 37.2% and 100%. See Figure 2.

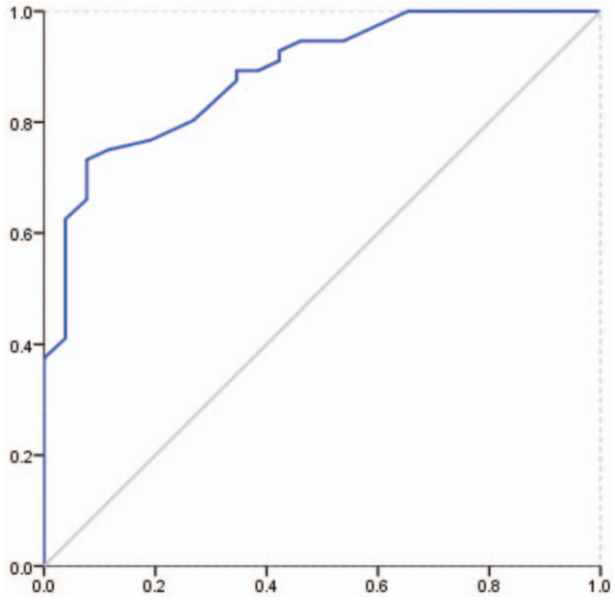

Figure 2. ROC curve of QUS diagnosis of osteoporosis. QUS = quantitative ultrasound, ROC = receiver operating characteristic.

4. Discussions

The incidence of hip fractures is higher in people 50 years of age and older, especially in people 85 years of age and older where osteoporosis is not adequately assessed and the prevalence of osteoporosis is higher than recorded diagnoses.[22] The results of this study showed that the percentage of normal bone mass and loss of bone mass decreased gradually with age, while the incidence of osteoporosis increased significantly. Osteoporosis often has a relatively insidious onset with relatively few conscious symptoms, and is difficult to differentiate from related diseases leading to back and leg pain. Therefore, more patients are found to have osteoporosis only after a fracture occurs.[23] Many countries recommend screening for osteoporosis in older men aged 70 years or older, regardless of the presence of risk factors.[24] The International Osteoporosis Foundation also advocates screening for osteoporosis for all women over 65 years of age and for men at risk of fracture.[25] The best way to evaluate osteoporosis is to measure bone strength, but there is no mature technique for non-invasive detection of bone strength. In the clinical diagnosis of osteoporosis and related studies, BMD is an important indicator to detect bone mass and reflect bone condition, contributing about 58% to 70% to the factors of human bone strength.[26] Kanis et al[27] reported that every reduction of BMD value by 1 standard deviation will increase the risk of fracture by 1.4 to 2.6 times. DXA is most commonly used in patients who have already developed a brittle fracture for the first time to trigger treatment for osteoporosis. However, extensive DXA screening for osteoporosis in the entire population is neither recommended nor accomplished.

Improved ultrasound imaging quality has allowed for its expanded use in diagnosis of musculoskeletal ultrasound conditions. As musculoskeletal ultrasound is used more in clinical practice, there has been increased desire to further innovate its use.[28] Combining the benefits of high-resolution imaging, portability, and cost-effectiveness, ultrasound is gaining popularity in the evaluation of ligaments, tendons, and nerves in the extremities.[29] Han et al[30] have shown that patients with sarcopenia have a higher risk of shoulder pain and a consistent tendinopathic change develops in the supraspinatus tendons in sarcopenic patients. Chang et al[31] have studied acceptable reliability of ultrasound in the evaluation of superficial and deep masticatory muscle thickness. In this study, calcaneal QUS was proved to be a method of osteoporosis pre-screening that could be widely promoted in the general population, especially the middle-aged and elderly, due to its portability, low cost, and ease of use.

QUS is often used to measure BMD of the peripheral bone. Roldan et al[32] used DXA to measure lumbar spine, proximal femur and QUS to measure calcaneal BMD in 73 patients, and the results showed a moderate correlation between DXA T-scores and QUS T-scores. In this study, on the one hand, the correlation analysis of calcaneal QUS and DXA parameters showed that the correlation coefficient of QUS T-score and QUS-BQI of female calcaneus and DXA parameters of lumbar spine and proximal femur was 0.628 to 0.757 ($P < .05$), indicating that calcaneal BMD of middle-aged and elderly women was moderately positively correlated with lumbar spine and proximal femur BMD. As a result, calcaneal QUS can be used to predict BMD of the lumbar spine and proximal femur in women. On the other hand, the correlation coefficients of QUS T-score and QUS-BQI of male calcaneus and DXA parameters of proximal femur were 0.600 to 0.683 ($P < .05$), however, the correlation coefficients with DXA parameters of lumbar spine were 0.426 and 0.252 ($P > .05$). These indicate that calcaneal BMD is moderately positively correlated with proximal femoral BMD in middle-aged and elderly men but not with lumbar BMD, suggesting that calcaneal QUS can only be used to predict proximal femoral BMD in men, rather than to evaluate lumbar BMD. Reasons may be lumbar BMD is affected by abdominal aortic calcification, hyperostosis, kyphosis, and intervertebral disc calcification when measured by DXA method, and its bone density may not decrease with age.[33,34]

In this study, the diagnostic efficiency analysis of calcaneal QUS for osteoporosis showed that the accuracy, sensitivity, specificity, positive predictive value, and negative predictive value of calcaneal QUS T-score in the diagnosis of osteoporosis were 90.24%, 89.20%, 100%, 100%, and 50.00% using DXA parameters as the gold standard. Calcaneal QUS showed strong specificity in the diagnosis of osteoporosis. In addition, we drew ROC curve with 82 middle-aged and elderly participants measured calcaneal QUS T-score as the test variable and disease diagnosis as the state variable. The results showed that when the calcaneal QUS T-score was –1.8, the area under the curve was 0.888, the sensitivity was 73.21%, and the specificity was 92.31% ($P < .05$). It indicates that when the calcaneal QUS T-score is –1.8, the diagnosis of osteoporosis has the maximum efficacy and high specificity. Therefore, calcaneal QUS has a very high value in the screening of osteoporosis. In addition, when calcaneal QUS T-score was –2.35, the sensitivity and specificity for the diagnosis of osteoporosis were 37.2% and 100%, that is when calcaneal QUS T-score was $\leq$–2.35, osteoporosis could be diagnosed. Although QUS has not been able to directly measure BMD at common sites of osteoporotic fractures, such as the lumbar spine and the proximal femur, Chan et al[35] used QUS to measure calcaneus in 454 women and 445 men, and conducted a 20-year prospective study, which confirmed that calcaneal QUS is a predictor of the risk of lumbar and hip fractures. Olszynski et al[36] used QUS to measure multiple sites (distal radius, tibia, and phalanx) of volunteers in a multicenter in Canada and followed up for 5 years to observe their fracture conditions. They also concluded that QUS could be used for fracture risk assessment. So QUS could play an important role in the screening, diagnosis, and prevention of osteoporosis.[37,38]

5. Conclusions

To sum up, this study assessed calcaneal QUS and DXA in senile osteoporosis diagnosis performance, as osteoporosis screening not only has good specific degrees, and with the lumbar spine and proximal femur DXA has good correlation, in screening for large-scale people play the role of more convenient, economic, Therefore, calcaneal QUS can be recommended as a pre-screening tool to determine whether DXA screening should be performed and timely treatment should be performed in patients with pre-existing risk of osteoporosis and patients with mild osteoporosis to reduce the risk of fracture. Of course, the screening and diagnosis of abnormal bone mass should also refer to the patient's clinical symptoms, biochemical indicators and bone metabolism indicators, and other indicators for comprehensive judgment, in order to reduce the rate of misdiagnosis and missed diagnosis. The limitation of this study is that the sample size is small, so it is necessary to expand the sample size to continue the study.

Acknowledgments

We would like to thank all our colleagues working in the Ultrasound Department of the First Affiliated Hospital to Dalian Medical University.

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Conceptualization: Li Yu.
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Validation: Jifeng Sun.
Visualization: Jifeng Sun.
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Writing – review & editing: Changzhou Li, Jifeng Sun, Li Yu.

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