Quantitative Ultrasound Measurements of Bone Quality in Female Adolescents With Idiopathic Scoliosis Compared To Normal Controls

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Abstract

Objective: The aims of this study were to compare the speed-of-sound (SOS) between adolescent idiopathic scoliosis (AIS) patients and controls using quantitative ultrasound examination and to further analyze the relationship between the SOS and curve type, curve magnitude, maturation status and Risser’s sign in AIS patients compared to controls.

Methods: Seventy-eight female AIS patients and 58 healthy female controls 10 to 16 years of age were recruited to participate. Quantitative ultrasound measurements were performed at the non-dominant distal end of the radius. The standard method for estimating the SOS and z-score was used. Comparisons were made between the SOS values and z-score in AIS patients and age-matched Asian adolescents.

Results: The SOS values of the patients were significantly lower than the controls (P < .01). The percentage of cases with low bone quality was 25% in the entire AIS sample. The prevalence of low bone quality in AIS patients was 20.5%. However, there were no correlations between the SOS and types of scoliosis (P > .05). The SOS values among different severity groups were significant, particularly between the 10° to 19° and 20° to 39° groups as well as between 10° to 19° and ≥ 40° groups. However, there was no significant correlation between the SOS and Cobb angles. Significant correlations were also found between the pre- and post-menarchy status in patients. There was a significant difference in the SOS values for different Risser’s signs (P < .05).

Conclusions: Compared to nonscoliotic controls, subjects with AIS had a generally lower SOS, indicating lower bone quality. The age, Risser’s sign, or maturation status, may have an effect on the bone quality; however, the curve type and magnitude do not affect the bone quality. The results of this study indicate that slower bone maturation may affect the bone quality in adolescents with AIS. (J Manipulative Physiol Ther 2015;38:434-441)

Key Indexing Terms: Scoliosis; Bone; Ultrasonography; Adolescent; Female; Menstruation

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idiopathic scoliosis (IS) is a progressive spinal deformity. Curve progression is a common concern in patients during the growth spurt because it may lead to severe cosmetic distortion, vertebral malfunction, back pain, cardiopulmonary dysfunction, and most importantly, lowering the quality of life. Osteopenia may be an important risk factor in curve progression. Previous studies show low bone density or osteopenia in patients with adolescent idiopathic scoliosis (AIS). However, these studies applied different diagnostic criteria; some of the studies used either a z-score less than 2 SDs or less than 1 SD, whereas others used below the age and sex matched mean, or less than the estimated 95% CI of bone mineral density (BMD) as their study criteria. According to the International Society of Clinical Densitometry, low bone mineral content (BMC) or BMD is defined as a BMC or a real BMD that is less than or equal to −2.0, adjusted for age, sex, and body size. The term osteopenia is still used, but low bone density is preferred. Only 2 previously published studies applied a z-score below 2 SD as their study criteria. It is vital to apply standard criteria in the study of bone quality in patients with AIS.

Previous studies on bone density and IS have suggested that between 38% and 67% of IS patients have generalized osteopenia with low bone density on lumbar and proximal femur. Using dual-energy X-ray absorptiometry (DXA) scans of 49 adolescents with AIS, Szalay et al found that the BMD was most strongly correlated with the body mass index (BMI) and not the scoliotic curvature. However, studies from Cheng et al suggested a significant correlation between osteopenia and AIS. The measurement of the bone mineral status may help to identify patients who could be exposed to an increased risk for osteoporosis associated with scoliosis. This may be important for physicians as they choose the most appropriate intervention based on the bone quality.

Currently, the most valid methods for measuring bone quality and density are based on a biochemical evaluation of the serum alkaline phosphate and radiological evidence (such as DXA) of osteopenia. Although DXA is the standard diagnostic technique for bone density, which allows for the diagnosis of less severe forms of bone demineralization, DXA has not been extensively tested in spinal deformity patients who have a higher risk for developing further bone deformity. In addition, the cost and portability of DXA machines are not ideal for large sampled and community-based studies. As a result, a number of devices have been recently developed to measure the skeletal status. Quantitative ultrasound (QUS) measurement provides a safe, noninvasive method for obtaining information on the bone quality by measuring a peripheral site (such as the distal one-third of the radius and middle of the tibia) without using ionizing radiation. Importantly, the QUS scores are predictive of bone quality in both adults and children.

QUS uses sound waves to assess the bone quality with 2 parameters: (i) the ultrasound velocity or speed of sound (SOS/ms) to exploit the speed of the ultrasound wave to assess elasticity and bone density and (ii) broadband ultrasound attenuation (dB MHz) to exploit the frequency dependence of ultrasound attenuation to determine bone properties such as cortical thickness, elasticity, and microarchitecture, providing a more complete picture of the bone strength. Quantitative ultrasound BMD could be an indicator for vitamin D status in young children. The QUS measurement has also been used to assess osteopenia in children, and it has been reported that there is a significant correlation, on measuring BMD, between the QUS on the distal radius and DXA measurement on the lumbar spine. The advantages of using QUS include its being inexpensive, portable, and free of ionizing radiation, which is particularly ideal for conservative treatment.

QUS has been used to characterize bone material properties and its microarchitecture in a case-control study. However, the application of QUS in the studies on AIS is still sparse. In this study, we hypothesized that any abnormal bone quality in AIS patients could be detected with QUS technology, and if so, then QUS may become a useful tool in the diagnosis, management, and follow-up of osteopenia in patients with scoliosis.

The purposes of the present study were the following: (1) to measure the speed of sound (SOS) characteristics of the distal radius in a group of female patients with AIS and age-matched controls and compare these 2 groups and (2) to correlate the SOS measures with the curve type (as classified using the King method), curve magnitude (radiographically measured with the Cobb angle), maturation status (based on pre- or post-menarche at the time of evaluation), and Risser’s sign (based on radiography).

Methods

Subjects

Seventy-eight female Chinese AIS patients, 10 to 16 years of age, who visited our rehabilitation clinic from January 2010 to May 2013 were recruited. At the first presentation, all subjects underwent clinical and radiological evaluations to determine AIS status based on the Scoliosis Research Society criteria as well as to rule out other causes of spinal deformities. The excluded conditions included scoliosis related to congenital, neuromuscular, metabolic, and connective tissue etiologies; patients who lack information about height and weight; or patients whose curvature could not be classified by King-Moe classification. Patients with AIS who received any prior treatment, including the use of calcium supplements and other medication that might influence bone metabolism, were also excluded from the current study.

Fifty-eight age-matched healthy girls were also recruited as controls. Any medical condition that could potentially
The examination and measurement.

status (pre- and post-menarche); and (4) Risser sign.

The examination and measurement.

status was identified and recorded by the same rehabilita-

tion physician. The weight and height of AIS patients were

measured.26 For thoracic and lumbar double major curve

patients, the Cobb angle of the greater one was selected.

Curves that were less than 10° were excluded. 27 All

patients were significantly lower than for the controls (P < .05). Approximately 20.5% of the AIS patients

waves propagate faster through the bone than the soft tissue.

The device consists of a desktop main unit and a number of

small probes that were designed to measure SOS at different

sites. Each subject was seated and the patient’s non-
dominant arm rested on the surface of the exam table. The

forearm was set in pronation with the ulna parallel to the

surface of the table and the radius on the top. After

introducing the water-soluble coupling gel, the probe was

moved across the distal radius plane, searching for the site

with maximal reading. The measurement site was defined

as the distal one-third of the radius. The mean of 3

measurements of the radius SOS was selected for data

analysis. All measurements were performed by the same

trained personnel. The instrumental accuracy was 0.25% to

0.5%, and the precision was 0.4% to 0.8%, as reported by

the manufacturer.19

The z-score is given in terms of the standard deviation

from the average of population of same age and gender.

z-Scores were generated based on controls against the

Asian reference age-/sex-/race-matched population data-
based provided by the ultrasound manufacturer. The z-score

is defined as the difference between the raw score to be

standardized and the mean difference divided by the

standard deviation (a z-score less than or equal to −2.0

indicates low bone quality and a z-score greater than −2

indicates normal bone quality). Calibration was performed

on each scan day according to the manufacturer’s

instructions to ensure accurate measurement.

STATISTICS

An unpaired Student’s t-test was used to compare the

SOS data between female patients with AIS and gender

and age-matched controls. One-way analysis of variance

(ANOVA) and Pearson and Spearman correlation analysis

were used to determine the relative contribution of these

variables (classifications, Cobb’s angle, menarche, family

history, and Risser’s sign). Data were processed using the

statistical program SPSS17.0 (SPSS Inc, Chicago, IL) and

presented as the mean and SD. Statistical significance was

considered at P < .05.

RESULTS

In total, we reported data from 78 radius scans from AIS

patients and 58 scans from the controls. The general

physical characteristics of AIS patients and controls are

shown in Table 1. The average Cobb angle for AIS patients

was 27.4° ± 10.4°. There was no significant difference for

age, height, and menarchal status between AIS patients and

controls (P > .05). However, the weight and BMI of AIS

patients were significantly lower than for the controls (P < .05). Approximately 20.5% of the AIS patients’ z-scores

affect bone metabolism was excluded. The Adam’s forward-
bending test was performed, and the angle of trunk rotation was

measured with a scoliometer. Girls with an angle of trunk

rotation of 5° or more were excluded from the control group as

well as to rule out the existence of scoliosis.

The AIS patients were further divided into five

subgroups based on the following: (1) King-Moe classifi-
cation24 of curvature; (2) degrees of Cobb angle (group 1:
10–19°; group 2: 20–39°; and group 3: ≥ 40°); 3) menarche
status (pre- and post-menarche); and (4) Risser sign.

This study protocol was approved by the Clinical

Research Ethics Committee of XinHua Hospital affiliated

to Shanghai Jiao Tong University School of Medicine,

China. All subjects’ parents signed informed consent before

the examination and measurement.

Radiographic Assessment

Radiographic assessment was performed during the

patients’ first visit to the clinic. The radiographic classifi-
cation of curvature (based on the King-Moe method), Cobb
angle and Risser’s sign25 were assessed in these patients.

Radiographs included posterior-anterior and lateral whole

spines. The same rehabilitation physician, who specialized

in spine rehabilitation, was assigned to determine the curve

type, magnitude of the Cobb angle and Risser’s sign. A

standard protocol was used to measure and record the Cobb

angle. Briefly, the vertebrae at the upper and lower limits of

the curve deformity were identified. One parallel line to the

endplate of the superior end vertebra and the other line

parallel to the endplate of the inferior end vertebra were
drawn. Then, two lines that were vertical to these lines were
drawn. The angle of these two lines was manually

measured.26 For thoracic and lumbar double major curve

patients, the Cobb angle of the greater one was selected.

Curves that were less than 10° were excluded.27 All

numerical data are reported as the mean and SD.

Clinical Assessment

Clinical assessment of maturity based on menarche

status was identified and recorded by the same rehabilita-

tion physician. The weight and height of AIS patients were

also measured and recorded. The BMI was calculated using

the formula BMI = weight/height.2

QUS Bone Measurement

The left distal radius bone was used for performing

forearm QUS measurements by a QUS machine (Omnis-

ense 7000P, Sunlight Medical Inc, Israel); a quantitative

ultrasound method was designed to measure the SOS (m/s)
at multiple skeletal sites by axial transmission. The

technique was developed for non-harmful testing, and it

was validated in several models, including animal bones.28

The SOS measurement is based on the fact that ultrasound

waves propagate faster through the bone than the soft tissue.
Table 1. General Physical Characteristics of AIS Patients and Controls

<table>
<thead>
<tr>
<th>Age (y)</th>
<th>AIS</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>12.3 ± 1.6</td>
<td>12.6 ± 1.9</td>
<td></td>
</tr>
<tr>
<td>Body height (cm)</td>
<td>157.4 ± 7.5</td>
<td>157.6 ± 12.5</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>41.6 ± 6.7</td>
<td>47.8 ± 12.3</td>
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<tr>
<td>BMI (kg/m²)</td>
<td>16.7 ± 2.0</td>
<td>19.0 ± 3.5</td>
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</table>

Table 2. z-Score by Age and Group

<table>
<thead>
<tr>
<th>Age (y)</th>
<th>z-Score of AIS SD</th>
<th>z-Score of Controls SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>-0.533 ± 1.59</td>
<td>1.244 ± 0.60</td>
</tr>
<tr>
<td>11</td>
<td>-1.444 ± 1.22</td>
<td>1.770 ± 0.39</td>
</tr>
<tr>
<td>12</td>
<td>-0.553 ± 1.47</td>
<td>1.190 ± 0.30</td>
</tr>
<tr>
<td>13</td>
<td>-0.967 ± 1.41</td>
<td>1.600 ± 0.49</td>
</tr>
<tr>
<td>14</td>
<td>-0.567 ± 0.59</td>
<td>1.922 ± 0.99</td>
</tr>
<tr>
<td>15</td>
<td>0.740 ± 1.20</td>
<td>1.780 ± 0.18</td>
</tr>
<tr>
<td>16</td>
<td>-0.075 ± 1.96</td>
<td>1.160 ± 0.09</td>
</tr>
<tr>
<td>Average</td>
<td>-0.722 ± 1.44</td>
<td>1.531 ± 0.60</td>
</tr>
</tbody>
</table>

Table 3. SOS Values by Age and Group

<table>
<thead>
<tr>
<th>Age</th>
<th>SOS of AIS (m/s)</th>
<th>SD</th>
<th>SOS of Controls (m/s)</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>3651.67 a</td>
<td></td>
<td>170.803</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>3568.06 b</td>
<td></td>
<td>132.399</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>3679.35 c</td>
<td></td>
<td>156.646</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>3659.72 b</td>
<td></td>
<td>150.217</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>3721.00 b</td>
<td></td>
<td>69.874</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>3906.80</td>
<td></td>
<td>120.581</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>3861.00</td>
<td></td>
<td>218.853</td>
<td></td>
</tr>
<tr>
<td>Average</td>
<td>3674.83 b</td>
<td></td>
<td>169.034</td>
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</table>

DISCUSSION

We found the mean SOS value in group 1 (10°-19°) was significantly lower than that in groups 2 (20°-39°) and 3 (≥40°). There was no significant difference between groups 2 and 3. However, there was no significant correlation between the radial SOS and Cobb angles (r = 0.145, P > 0.05). There was no significant difference in the average age, menarchal status or Risser sign among 3 different Cobb angle groups. The mean value of the SOS in the pre-menarche group was significantly lower than that of the post-menarche group (3624.39 vs 3711.82, P = .023).

Table 4 summarizes the number of patients with different Risser stages and SOS values. There are significant differences among the different Risser stages. Pearson correlation also suggested a significant correlation between Risser stages and radial SOS values (r = 0.318, P = .005). AIS patients with a lower Risser stage had lower radial SOS values. Patients who were more skeletally immature patients were more osteopenic.

According to the official position statement of the International Society of Clinical Densitometry in 2007, the diagnosis of osteoporosis in children and adolescents requires the presence of both a clinically significant fracture history and low BMC or BMD and is defined as a BMC or a real BMD z-score that is less than or equal to −2.0, adjusted for the age, sex, and body size. In this study we compared the z-scores of 58 female controls with 78 female AIS patients whose ages range from 10–16 years old in seven different groups. We found that female AIS patients had significantly lower z-scores than control females, and 20.5% of AIS patients’ z-scores were less than or equal to −2.0, indicating low BMC. Ultrasound speed has a positive correlation with the bone specific gravity of cortical bone and an inverse correlation with porosity. Therefore, the lower z-score of AIS patients in this study may indicate poorer bone quality at the microstructural level.
Some studies have revealed that the presence of low BMD in the pre- and early menarche girls with AIS which is a systemic and generalized phenomenon that corresponds to mild scoliosis. However, few studies have evaluated the micro-architectural changes in the bone that are associated with the spinal deformity using histological methods. In the past, several studies have shown that a reduced value of the QUS variables, both velocity- and attenuation-based, is associated with reduced bone quality in younger individuals and that rheumatologic disorders affect bone health. QUS and DXA parameters, measured at different skeletal sites, showed similar results, suggesting that both methods can identify a reduced bone mineral status. These results suggest that QUS devices could be used to a similar extent as DXA measurements to estimate bone status in younger patients. It should be considered that QUS parameters are influenced by bone density, as is the case for DXA, as well as by bone structure and composition, which is an aspect of bone quality. One of the characteristics of bone qualities, especially measured by QUS, is bone microarchitecture, including porosity, connectivity, and anisotropy. In fact, some QUS parameters can detect collagen and organic matrix abnormalities in vitro and in vivo, providing information on the organic components of bone material. SOS measurements at the distal radius could also be used to measure bone organic components and bone density; therefore, the low BMC in 20.5% of AIS patients in the current study could be considered a low bone quality, both BMD and microstructures, in this group of patients. Multiple studies have now shown that QUS at peripheral sites can be used as a screening tool to assess bone quality.

QUS has a positive correlation with age in healthy children who are 5 to 19 years old, and there is a negative correlation with age in adults who are 22 to 76 years old. The results of our study are in agreement with the conclusion of a previously published study that there is a positive correlation between the QUS measurements and age among study subjects whose age range from 10 to 16 years old. However, this correlation is weaker in AIS patients. The age-related radial SOS in the current study suggests that although the generalized bone quality in AIS is lower than that in the healthy population, bone microarchitecture may still improve, which is associated with growth; however, this improvement in the bone quality (BMD and microstructures) in AIS patients is slower than that in healthy children. Future studies need to be performed to determine whether a weaker correlation persists throughout the adolescent period and whether the negative correlation in AIS accelerates in adult life.

![Fig 1. The mean of SOS in each control and AIS patient age group. SOS, speed of sound.](image1)

![Fig 2. Correlation between the SOS values and scoliosis type according to King-Moe. SOS, speed of sound.](image2)

<table>
<thead>
<tr>
<th>Table 4. SOS Values by Risser Stage</th>
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<tbody>
<tr>
<td>Risser Stage</td>
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<tr>
<td>-------------</td>
</tr>
<tr>
<td>0</td>
</tr>
<tr>
<td>I</td>
</tr>
<tr>
<td>II</td>
</tr>
<tr>
<td>III</td>
</tr>
<tr>
<td>IV</td>
</tr>
<tr>
<td>V</td>
</tr>
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</table>

SD, standard deviation; SOS, speed of sound.

- a P = .020 Risser 0 vs Risser III
- b P = .004, Risser 0 vs Risser V.
- c P = .007, Risser II vs Risser V.
- d P = .033, Risser IV vs Risser V.
In addition to the significant correlation between the QUS data and ages, this study also reports the significant correlation between the radial SOS and menarche status and Risser sign. Age, menarche status, and Risser sign are also indicators of bone maturity. This study agrees with the findings of Cheng et al in which the BMD correlated with the chronological age and years since menarche in 12- to 14-year-old AIS patients. The exact underlying mechanisms for such a correlation are unknown. It seems that even with AIS, the patients’ bone strength still improves. The positive correlation between the radial SOS value and Risser sign could be another piece of evidence that maturation could play a role in improved radial SOS value. It is interesting to note that previous studies have shown that AIS patients have disproportional but faster growth rates, and growth hormones might be one of the possible etiologies. Therefore, the improved radial SOS value could also be contributed by the abnormal level of growth hormone.

Previous studies reported that there is no significant correlation between the BMD and Cobb angle, pattern of scoliosis and progression using dual-photon absorptiometry. Similarly, our data also indicate that there is no significant correlation between the SOS values and degree of the Cobb angle and type of scoliosis. This phenomenon may indicate that low bone quality is not transient and appears to be characteristic of idiopathic scoliosis. However, two relatively recent published studies have suggested the significant effects of the degree of Cobb angle on the BMD value in AIS patients. The same group carried out these studies with the aim of studying the predictors of progression of scoliosis using different methods. The disparity between our study and the studies from that group warrants further study in this area to define the bone quality and its roles in the pathogenesis of AIS.

The results of the current study indicate that there are important potential clinical implications for QUS in assessing AIS. Both cross-sectional and prospective studies have demonstrated a close association between the QUS parameters and BMD status, such as correlations in AIS patients. Low BMD can be an indicator for curve progression in AIS. Therefore, improvement of low BMD should be considered as part of the clinical strategy in managing curve progression, and a QUS measurement may serve as a useful indicator in monitoring the clinical management of curve progression. The advantages of the QUS technique can be summarized as follows: it allows for non-harmful testing; 2) can be performed noninvasively; 3) is portable and less expensive; and 4) is less demanding for regulation and space. Because of these advantages, QUS could be used as an alternative for other densitometric techniques in AIS patients who are relatively young. Further studies are necessary to gather more information between the QUS parameters and bone structure in AIS.

LIMITATIONS

There are some limitations in this study. First, the weight and BMI in the controls were significantly greater than in AIS patients. While the BMI could be part of the pathologies of AIS, it might also be a factor impacting the bone quality. Second, in this study, the menarchal status was briefly divided as pre- and post-menarche. There was no other information about the age of first menarche for all AIS patients. The length of time since menarche might also have an impact on the BMD and SOS value. Finally, we applied the King-Moe classification because most of the existing classifications were designed for surgical purposes. King-Moe classification was the best fit for our study. However, owing to the limitation in the patient sample size, there were no type V or lumbar, double major, and triple major patients in this study. All of the above factors might also impact the results of this study. Based on the results, a prospective follow-up study may be needed to further study bone quality in terms of the QUS measurements.

FUTURES STUDIES AND CONSIDERATIONS

Radial QUS measurements should be considered in the evaluation of younger female AIS patients. Younger female AIS patients should be counseled on interventions to improve their bone quality. Further studies should include the predictive and longitudinal validity of QUS techniques in AIS.

CONCLUSION

The successful performance of radial QUS measurements in female AIS patients in this study suggests that patients with AIS may have lower bone quality than controls. The bone quality in AIS patients is correlated with the age and maturation but not to the type and severity of curvature. The results of this study may shed light on further studies on the use of QUS techniques for AIS bone quality assessment and treatment planning.

FUNDING SOURCES AND POTENTIAL CONFLICTS OF INTEREST

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No conflicts of interest were reported for this study.

CONTRIBUTORSHIP INFORMATION

Concept development (provided idea for the research): P.J.C., Q.D., J.A.L., X.Z., L.Z.
Design (planned the methods to generate the results): P.J.C., Q.D., J.A.L.
Supervision (provided oversight, responsible for organization and implementation, writing of the manuscript): P.J.C., Q.D., J.A.L., X.Z., X.H.H.
Analysis/interpretation (responsible for statistical analysis, evaluation, and presentation of the results): P.J.C., Q.D., J.A.L., X.Z., X.H.H.
Writing (responsible for writing a substantive part of the manuscript): P.J.C., Q.D., J.A.L., X.Z., X.H.H.
Critical review (revised manuscript for intellectual content, this does not relate to spelling and grammar checking): P.J.C., Q.D., J.A.L., X.H.H.

Practical Applications
• Comparing to non-scoliotic controls, female AIS patients have generally lower bone quality measurement by quantitative ultrasound.
• The bone quality in AIS patients is correlated with the age and maturation.
• The bone quality in AIS patients is not correlated with the type and severity of curvature.

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