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ORIGINAL ARTICLE

Cross-validation of ultrasound imaging in adolescent idiopathic scoliosis

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Abstract

Purpose Adolescent idiopathic scoliosis (AIS) patients are exposed to 9–10 times more radiation and a fivefold increased lifetime cancer risk. Radiation-free imaging alternatives are needed. Ultrasound imaging of spinal curvature was shown to be accurate, however, systematically underestimating the Cobb angle. The purpose of this study is to create and cross-validate an equation that calculates the expected Cobb angle using ultrasound spinal measurements of AIS patients.

Methods Seventy AIS patients with upright radiography and spinal ultrasound were split randomly in a 4:1 ratio to the equation creation ($n = 54$) or validation ($n = 16$) group. Ultrasound angles based on the spinous processes shadows were measured automatically by the ultrasound system (Scolioscan, Telefield, Hong Kong). For thoracic and lumbar curves separately, the equation: *expected Cobb angle = regression coefficient × ultrasound angle*, was created and subsequently cross-validated in the validation group.

Results Linear regression analysis between ultrasound angles and radiographic Cobb angles (thoracic: $R^2 = 0.968$, lumbar: $R^2 = 0.923$, $p < 0.001$) in the creation group resulted in the equations: *thoracic Cobb angle = 1.43 × ultrasound angle* and *lumbar Cobb angle = 1.23 × ultrasound angle*. With these equations, expected Cobb angles in the validation group were calculated and showed an excellent correlation with the radiographic Cobb angles (thoracic: $R^2 = 0.959$, lumbar: $R^2 = 0.936$, $p < 0.001$). The mean absolute differences were 6.5°–7.3°. Bland–Altman plots showed good accuracy and no proportional bias.

Conclusion The equations from ultrasound measurements to Cobb angles were valid and accurate. This supports the implementation of ultrasound imaging, possibly leading to less frequent radiography and reducing ionizing radiation in AIS patients.

Keywords Adolescent idiopathic scoliosis · Cobb angle · Ultrasound imaging · Radiation-free alternative · Validation

Introduction

Adolescent idiopathic scoliosis (AIS) is a complex three-dimensional (3D) deformity of the spine and trunk with severe consequences for young patients in terms of pain, possible cardiopulmonary compromise, psycho-social burden and disturbed self-image [1]. Patients with AIS are traditionally diagnosed and monitored with frequent upright anterior–posterior (AP) and lateral radiographs [2]. Additional imaging consists of magnetic resonance (MR) or computed tomography (CT) for surgical planning, to obtain in-depth 3D morphology or identification of spinal anomalies [1]. The major downside of radiography and CT is ionizing radiation: AIS patients are exposed to 9–10 times more radiation and have a lifetime relative risk of 4.8 for developing cancer as compared to the general population [3, 4]. MRI is not ionizing, but is mostly made in supine position,

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All authors contributed equally to this work by either writing, editing, brainstorming and/or supervising the current manuscript. Supporting data is available upon request.

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and is expensive and time-consuming, and cortical bone is poorly visible on standard MR imaging [5]. Low-dose biplanar radiography (EOS imaging, Paris, France) is performed upright, but is not widely available and still utilizes ionizing radiation [6]. Because of these difficulties, other radiation-free methods to create a 3D image of the spine in upright position have been developed, like ultrasound imaging. Several authors described the use of ultrasound landmarks such as the spinous process (SP) and transverse process (TP) to measure the severity of the AIS curve, and good-to-excellent correlations were shown between ultrasound angles and radiographic Cobb angles [7–11]. However, ultrasound angles were systematically smaller as compared to radiographic Cobb angles. The relationship between angles measured with ultrasound and radiography is described in earlier studies, but an equation to calculate the expected Cobb angle based on the ultrasound angle has not yet been properly cross-validated [9–11]. Therefore, the purpose of the current study is to create and cross-validate an equation to calculate the expected Cobb angle of thoracic and lumbar curves based on the ultrasound angle of AIS patients.

Methods

Study population

Patients suspected of AIS who had a conventional upright radiography of the complete spine planned were consecutively recruited between 2016 and 2019. Patients not between 10 and 18 years of age, with spinal pathology other than AIS, previous spinal surgery, neurological symptoms and/or syndromes associated with growth disorders were excluded. The patients were included in a tertiary spine clinic in the Netherlands, and the study was approved by the local Medical Research Ethics Committee. After informed consent was obtained from all patients and/or their parents, an ultrasound scan was made on the same day as the radiography. Patients could not receive the ultrasound investigation at the same visit as the radiograph or with a failed radiography and/or ultrasound investigation was excluded. In this validation study, the included patients were split randomly in a 4:1 ratio and put in the equation creation group and the validation group, respectively.

Ultrasound and radiographic measurements

The ultrasound scans were obtained using the Scolioscan system (Model SCN801: Telefield Medical Imaging Ltd., Hong Kong), as described and tested for reliability in earlier studies on scoliosis (Fig. 1) [9–14]. This system uses a linear ultrasound probe (center frequency of 7.5 MHz and a width of 75 mm) for freehand scanning and a sensor to track the position and 3D orientation of the probe while scanning. The patients stand upright with their arms on the side and can breathe normally during the scanning, which takes approximately 1–2 min. After scanning from level S1 to level T1, the device creates a 2D coronal reconstruction of the spine and the system software automatically reconstructs a midline through the shadows of all SP, to calculate the thoracic and lumbar ultrasound angles (Fig. 2). The radiographs, which were part of the standard care of the included AIS patients and made on the same day as the ultrasound images, were manually measured using software in the local picture archiving and communication system (PACS) to determine the thoracic and lumbar Cobb angles, as described by the Scoliosis Research Society [15]. Two observers measured each curve, and the mean of both observers was used in this study as the radiographic Cobb angle.

Fig. 1 The ultrasound scans in this study were obtained using the Scolioscan system (Model SCN801: Telefield Medical Imaging Ltd., Hong Kong), containing a linear ultrasound probe for freehand scanning and a sensor to track the position and 3D orientation of the probe while scanning

Statistical analysis

Descriptive statistics were calculated for both groups (equation creation group and validation group): means, standard deviations and ranges for continues variables

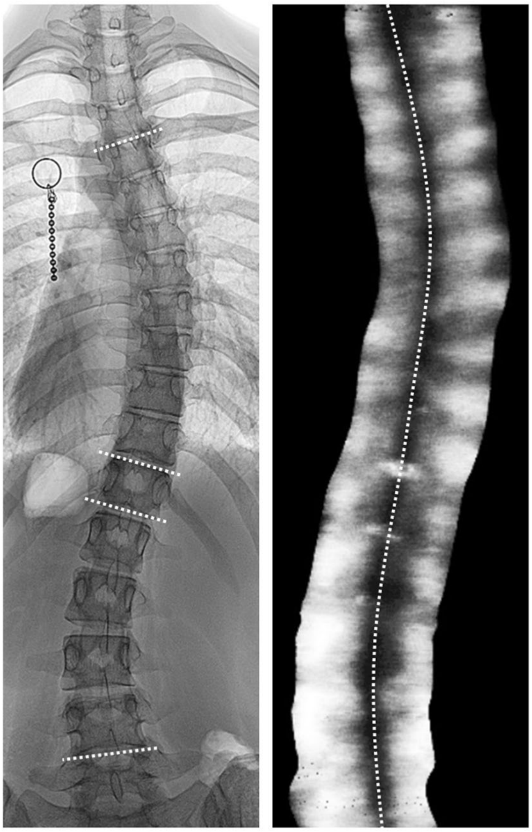

Fig. 2 On the left side, the measurement of the Cobb angle on anterior–posterior radiography of the complete spine in an AIS patient is shown. On the right side, a coronal ultrasound image of the same patient is shown. The system software automatically drew a line through the bone shadows of all spinous process, to calculate the thoracic and lumbar ultrasound angles

such as age and Cobb angle (tested with independent samples *t* tests), and numbers and percentages for categorical variables such as the number of girls in each group (tested with Pearson's Chi-squared tests). A simple linear regression analysis between the ultrasound and radiographic Cobb angles described the determination coefficients (R^2) and regression coefficients—without a constant in the equation—to create the equation: *expected Cobb angle = regression coefficient × ultrasound angle* for both thoracic and lumbar curves. Additionally, the R^2-values for the linear regression analyses with a constant in the equation were described. In the validation group, the equations were used to calculate expected Cobb angles and were compared to the radiographic Cobb angles to test the validity (linear regression) and accuracy (mean absolute difference [MAD], maximum error and Bland–Altman plot) of the equations. Post hoc linear regression analyses between the difference and the mean of expected and radiographic Cobb angles were done for both thoracic and lumbar curves to check for proportional bias, i.e., if curve severity influences the amount of variation between expected and radiographic Cobb angles. SPSS Statistics 25.0.0 for Windows (IBM, Armonk, NY, USA) was used for statistical analysis. The level of significance was set at 0.05.

Table 1 Patients characteristics

	Creation group *n* = 54	Validation group *n* = 16	*p*
Age (years)			
Mean (SD)	14.7 (2.0)	13.9 (2.1)	0.195
Range	10.1–17.5	10.6–17.2	
Girls			
n (%)	43 (80%)	13 (81%)	0.887
Ultrasound angle (°)			
Main thoracic curve			
Mean (SD)	26.5 (14.1)	23.1 (11.8)	0.387
Range	5.5–73.6	6.5–43.2	
Main lumbar curve			
Mean (SD)	20.4 (10.5)	22.2 (10.4)	0.566
Range	1.5–50.7	3.4–44.9	
Radiographic Cobb angle (°)			
Main thoracic curve			
Mean (SD)	38.4 (20.5)	31.4 (19.1)	0.226
Range	6.6–89.6	2.8–56.1	
Main lumbar curve			
Mean (SD)	26.3 (13.0)	29.4 (15.6)	0.428
Range	1.5–61.9	10.8–80.0	

SD standard deviation

Results

Study population

From 86 initially recruited patients, five were excluded for being under the age of 10, one had a congenital spinal malformation, three could not be planned for ultrasound investigation on the same day as the radiograph, five had insufficient ultrasound investigations (two had their scapula excessively overlapping the thoracic spine, and three had loss of proper probe contact in the lumbar region) and two had insufficient radiography investigations. (One had only forward/lateral bending images, and one was taken seated.) Thereafter, a total of 70 patients were included, 54 in the equation creation group and 16 in the validation group. There were no significant differences in age, sex, ultrasound angles and radiographic Cobb angles (Table 1).

Equation creation

Significant correlations were observed between ultrasound angles and radiographic Cobb angles of thoracic ($R^2 = 0.968$ with no constant and $R^2 = 0.859$ with constant in equation, $p < 0.001$) and lumbar ($R^2 = 0.923$ with no constant and $R^2 = 0.647$ with constant in equation, $p < 0.001$) curves. The linear regression coefficient for thoracic curves was 1.43 (95%CI:1.36–1.50) and for lumbar curves was 1.23 (95%CI:1.13–1.32). So, the equations to calculate the expected Cobb angle based on the ultrasound angle were *thoracic Cobb angle = 1.43 × ultrasound angle* and *lumbar Cobb angle = 1.23 × ultrasound angle* (Fig. 3).

Equation validation

The expected Cobb angles (calculated with the created equation, based on ultrasound angles) correlated with the radiographic Cobb angles of thoracic ($R^2 = 0.959$ with no constant and $R^2 = 0.844$ with constant in equation, $p < 0.001$) and lumbar ($R^2 = 0.936$ with no constant and $R^2 = 0.695$ with constant in equation, $p < 0.001$) curves. The mean expected Cobb angle of the thoracic curves was 33.0° ± 16.9° and the radiographic Cobb angle was 31.4° ± 19.1° ($p = 0.406$); the MAD was 6.5° ± 3.9° and the maximum error was 14.3°. For lumbar curves, the mean expected Cobb angle was 27.2° ± 12.7° and the mean radiographic Cobb angle was 29.4° ± 15.6° ($p = 0.328$); the MAD was 7.3° ± 4.7° and the maximum error was 18.9°. Bland–Altman plots between expected Cobb angles and radiographic Cobb angles are shown in Fig. 4. There was no significant correlation between the difference and mean of expected and radiographic Cobb angles for thoracic ($p = 0.838$) and lumbar ($p = 0.140$) curves, indicating that there was no proportional bias, i.e., curve severity did not influence the amount of variation.

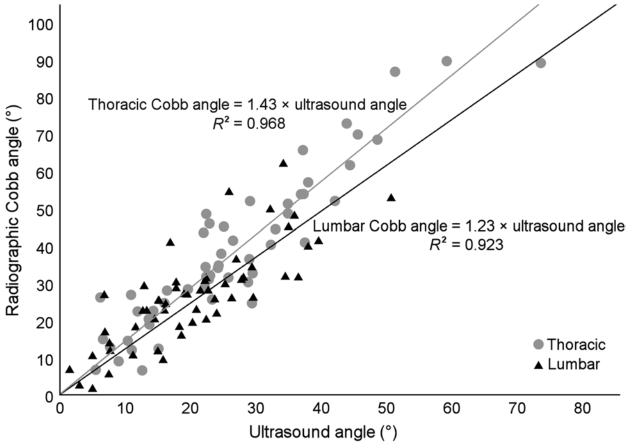

Fig. 3 To create the equations, a linear regression analysis between ultrasound angles and radiographic Cobb angles in 54 AIS patients was done for thoracic and lumbar curves. The scatter plot, linear regression and equation: *Cobb angle = regression coefficient × ultrasound angle*, are shown. The linear regression coefficient for thoracic curves was 1.43 (95% CI:1.36–1.50) and for lumbar curves was 1.23 (95% CI:1.13–1.32). Also, the coefficients of determination (R^2, with no constant in the equation) are shown for both linear regressions

Discussion

Conventional upright radiography is the most used imaging method for the scoliotic spine, resulting in more radiation exposure and an increased incidence of cancer as compared to the general population [3, 4]. To reduce the potential radiation, alternatives have been sought. Ultrasound imaging is a potential alternative, and good-to-excellent correlations were described previously between ultrasound angles and radiographic Cobb angles [7–11]. However, the ultrasound imaging systematically underestimates the radiographic Cobb angle, and therefore, to implement ultrasound in AIS clinics, a properly developed and validated equation is essential. The purpose of this study was to create and cross-validate an equation to calculate the expected Cobb angle using ultrasound measurements of the AIS spine. Excellent correlations between ultrasound angles and radiographic Cobb angles were observed for both thoracic ($R^2 = 0.968$) and lumbar ($R^2 = 0.923$) curves. The equations as derived from the data were *thoracic Cobb angle = 1.43 × ultrasound angle* and *lumbar Cobb angle = 1.23 × ultrasound angle*. The expected Cobb angles calculated by the equations were valid (excellent correlations with radiographic Cobb angles, thoracic: $R^2 = 0.959$ and lumbar: $R^2 = 0.936$) and accurate (Fig. 4).

The correlations between the ultrasound and radiographic coronal spinal angles of AIS patients, as described in this study, are comparable to previous studies ($R^2 = 0.722$–0.991) [9–11]. Also, the regression coefficient between ultrasound angles and radiographic Cobb angle of 1.43 for thoracic curves and 1.23 for lumbar curves found in this study is in the range of previous studies (thoracic: 1.20–1.55 and lumbar: 1.15–1.34) [9, 10].

The concept of one spinal anatomical parameter strongly correlating with the Cobb angle and creating an equation to translate between these two is demonstrated before by Korovessis et al. in 1996 for the scoliometer used in physical examination of scoliosis patients [16]. The current study is the first to create and cross-validate an equation to calculate the expected Cobb angle using ultrasound measurements of the spine in AIS patients. The expected Cobb angles calculated by the equations were valid and accurate. Also, the MAD was 6.5° to 7.3° and the Bland–Altman plots show that the expected Cobb angle is in 23 out of 28 cases within 10° of the radiographic Cobb angle (Fig. 4). This is comparable to the intra- and interobserver variability of around 5°

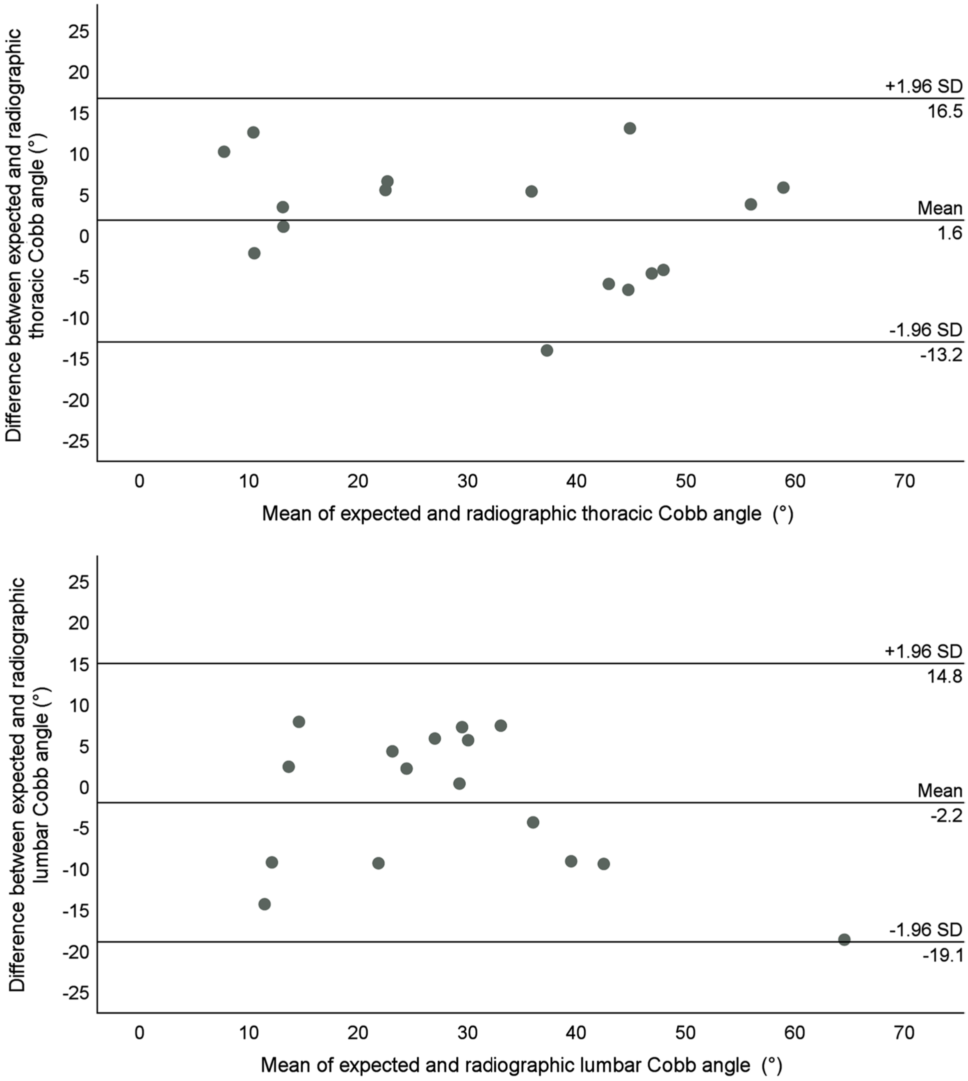

Fig. 4 To show accuracy of the equations, the agreement between expected Cobb angle (calculated with *thoracic Cobb angle* = *1.43* × *ultrasound angle* and *lumbar Cobb angle* = *1.23* × *ultrasound angle*) and radiographic Cobb angle is shown in Bland–Altman plots, separately for thoracic (figure above) and lumbar curves (figure below)

reported for radiographic Cobb angle measurements of the same curve [17, 18]. The automatic software method used in this study to determine ultrasound angles has ICCs for intra- and interobserver reliabilities of 1.00 and 1.00 for the same ultrasound image analyzed again and 0.97 and 0.94 for different ultrasound images of the same curve [10]. This is better than or at least similar to the ICCs of the conventional Cobb angle, ranging from 0.83 to 0.99 as determined on radiographs [19].

The results of this study suggest that ultrasound measurements of curve severity in AIS are valid and accurate as conventional radiography. However, three important questions remain unanswered so far. First, despite demonstrating a similar variability in spinal curvature determination by ultrasound versus radiography, for ultrasound to replace radiography in AIS clinics, the level of accuracy and safety in determining clinically relevant cutoff points has to be studied, i.e., the sensitivity and specificity of the ultrasound system for indicating observation, exercise therapy, brace therapy and/or spinal surgery. Second, the cross-sectional design of this study makes it impossible to test validity and accuracy of monitoring curve progression, which can be tested when ultrasound and radiography data are gathered on multiple time points within the same AIS patient. Third, this study was conducted in AIS patients seen in a tertiary spine center in the Netherlands, and it remains unclear whether the equation can be used for other populations as well.

Conclusions

The spinal curvature in AIS measured by ultrasound can be accurately calculated to the expected Cobb angle with simple equations: *thoracic Cobb angle* = *1.43* × *ultrasound angle* and *lumbar Cobb angle* = *1.23* × *ultrasound angle*. This finding supports the possible implementation of ultrasound in AIS clinics, which can lead to less frequent radiography, lowering the cumulative ionizing radiation dose and subsequently the cancer risk in young AIS patients.

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Compliance with ethical standards

Conflict of interest Steven de Reuver: Annafonds – NOREF research grant. Rob Brink: Alexandre Suerman grant UMC Utrecht. Timothy Lee: nothing to declare. Yong-Ping Zheng: Research Grant Council of Hong Kong (PolyU5332/07E, PolyU152220/14E) and the Hong Kong Innovation and Technology Fund (UIM213). Conflict of interest: inventor of a number of patents related to the ultrasound device called Scolioscan, which has been licensed to Telefield Medical Imaging Limited through the Hong Kong Polytechnic University. Also served as consultant for this company for enhancing functions of the system via the university. Frederik Beek: nothing to declare. René Castelein: Stryker Spine Research Grant.

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