Curve Progression in Adolescent Idiopathic Scoliosis Does Not Match Skeletal Growth

Running title: Curve Progression Patterns in AIS

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Abstract

Background Determining the peak growth velocity of a patient with adolescent idiopathic scoliosis (AIS) is important for timely treatment to prevent curve progression. It is important to be able to predict when the curve-progression risk is greatest to maximize the benefits of any intervention for AIS. The distal radius and ulna (DRU) classification has been shown to accurately predict skeletal growth. However, its utility in predicting curve progression and the rate of progression in AIS is unknown.

Questions/purposes (1) What is the relationship between radius and ulna grades to growth rate (body height and arm span) and curve progression rate? (2) When does peak curve progression occur in relation to peak growth rate as measured by months and by DRU grades? (3) How many months and how many DRU grades elapse between peak curve progression and plateau?

Methods This was a retrospective analysis of a longitudinally maintained dataset of growth and Cobb angle data of patients with AIS who presented with Risser Stages 0 to 3 and were followed to maturity at Risser Stage 5 at a single institute with territory-wide school screening service. From June 2014 to March 2016, a total of 513 patients with AIS fulfilled study inclusion criteria. Of these, 195 were treated with bracing at the initial presentation and were excluded. A total of 318 patients with AIS (74% girls) with a mean age of 12 ± 1.5 years were studied. For analysis, only data from initial presentation to commencement of intervention were recorded. Data for patients during the period of bracing or after surgery were not used for analysis to eliminate potential interventional confounders. Of these 318 patients, 192 were observed, 119 were braced, and seven underwent surgery. Therefore 192 patients (60.4%) who were observed were followed up until skeletal maturity at Risser Stage 5; no patients were lost to followup. The mean curve magnitude at baseline was $21.6^{o} \pm 4.8^{o}$. Mean followup before commencing intervention or skeletal maturity was 4.3 ± 2.3 years. Standing body height, arm span, curve magnitude, Risser stage, and DRU classification were studied. A subgroup analysis of 83 patients inclusive of acceleration, peak and deceleration progression phases for growth and curve progression was studied to determine any time lag between growth and curve progression. Results were described in mean ± SD.

Results There was positive correlation between growth rate and curve progression rate for body height ($r = 0.26$; $p < 0.001$) and arm span ($r = 0.26$; $p < 0.001$). Peak growth for body height occurred at radius grade (R) 6 (0.56 ± 0.29 cm/month) and ulna grade (U) 4 (0.65 ± 0.31 cm/month); peak change in arm span occurred at R5 (0.67 ± 0.33 cm/month) and U3 (0.67 ± 0.22 cm/month); and peak curve progression matched with R7 (0.80 ± 0.89 cm/month) and U5 (0.84 ± 0.78 cm/month). Subgroup analysis confirmed that peak curve progression lagged behind peak growth rate by approximately 7 months or 1 DRU grade. The mean time elapsed between the peak curve progression rate and the plateau phase at R9 U7 was approximately 16 months, corresponding to two DRU grades.

Conclusions By using a standard skeletal maturity parameter in the DRU classification, this study showed that the maximal curve progression occurs after the peak growth spurt, suggesting that the curve should be monitored closely even after peak growth. In addition, the period of potential curve continuing progression extends nearly 1.5 years beyond the peak growth phase until skeletal maturity. Future studies may evaluate whether by observing the trend of growth and curve progression rates, we can improve the outcomes of interventions like bracing for AIS.

Level of Evidence Level II, prognostic study.

Introduction

The main aim of treating patients with adolescent idiopathic scoliosis (AIS) who are skeletally immature is to prevent curve progression during growth [27]. Bracing is a commonly used treatment option initiated in adolescence to reduce the chances for adulthood curve progression [27-29]. Appropriate timing of bracing before the peak height velocity has been shown to prevent curves from reaching the surgical threshold, but only with good compliance [21, 22, 28]. In what is considered the “landmark” bracing study by Weinstein et al. [28], only 75% and 42% of patients experience treatment success with bracing and observation, respectively. This suggests that some patients with AIS experience deterioration even with bracing and some do not benefit from any treatment. However, there is limited information regarding the period of bracing and timing of weaning with success of curve control, particularly with reference to currently used growth parameters. The key parameter clinicians use to determine whether a patient with AIS may benefit from bracing is the remaining growth potential. To improve treatment outcomes, determining the peak height velocity is necessary to indicate when the risk for deformity progression is greatest and hence the period when brace treatment is most needed [9, 13, 28]. Many known radiographic parameters have been developed to aid in predicting peak height velocity of the long bones [4, 10, 17-19, 24]. A correlation between curve acceleration with timing of peak height velocity was identified by these studies but is highly variable and has limited utility for clinical decision-making. Thus, even with accurate prediction of growth rates, there are still difficulties in predicting when and how each patient might deteriorate regarding different growth phases.

The current limitations in knowledge of the relationship between growth and curve progression patterns in patients with AIS require attention. Epiphyseal capping as described by Sanders et al. [ ] tells us it is the time of peak height velocity but not necessarily the peak curve progression velocity. By predicting more accurately when the curve progression risk is greatest with reference to a patient's growth potential is necessary to maximize the benefits of any intervention. This can be determined by assessing how growth and curve progression rates match in patients with AIS. The distal radius and ulna (DRU) classification is a tested and validated maturity parameter, which has shown accuracy in predicting the peak growth and growth cessation [4-6]. It is simple to use and can encompass the entire period of adolescent growth necessary for AIS management. It has been compared and found superior to Risser staging and metacarpal and phalangeal complexes regarding peak height velocity prediction [4]. However, its utility for predicting curve progression is still unclear.

Therefore, we asked: (1) What is the relationship between radius and ulna grades to growth rate (body height and arm span) and curve progression rate? (2) When does peak curve progression occur in relation to peak growth rate, as measured by months and by DRU grades? (3) How many months and how many DRU grades elapse between peak curve progression and plateau?

Patients and Methods

We performed a retrospective study based on longitudinally maintained data collected since May 1998 from a tertiary scoliosis specialty clinic. This is one of two clinics receiving referrals from a territory-wide school screening service. All patients with AIS followed up in our clinic from June 2014 to March 2016 who presented with Risser stages of 0 to 3, less than 2 years postmenarche, and followed until skeletal maturity at Risser Stage 5 were included in this study.

Exclusion criteria were patients with nonidiopathic scoliosis and AIS who were treated with bracing or surgery before our initial assessment. The local institutional review board (Institutional Review Board of the University of Hong Kong/Hospital Authority Hong Kong West Cluster UW 14-613) approved this study.

A total of 513 patients with AIS fulfilled study inclusion criteria (Fig. 1). Of these, 195 were treated with bracing at the initial presentation and were excluded for analysis. A total of 318 patients remained for analysis (Table 1). This included 236 girls (74%) and 82 boys (26%) with a mean age of 12 ± 1.3 years (girls) and 13 ± 1.6 years (boys) at initial presentation. The baseline curve magnitude was 22° ± 5°. The mean duration of followup before commencing intervention or reaching skeletal maturity was 4.3 ± 2.3 years. For analysis, only data from initial presentation to commencement of intervention were recorded. Data for patients during the period of bracing or after surgery were not used for analysis to eliminate potential interventional confounders. Of these 318 patients, 192 were observed, 119 were braced, and seven underwent surgery at the end of followup. Therefore 192 patients (60.4%) who were observed without intervention had complete data until skeletal maturity at Risser Stage 5. None of the patients under study were lost to followup.

Subgroup Analyses

Of the original 318 patients, 83 who had data for acceleration, peak, and deceleration progression in growth and curve progression rates, underwent subgroup analysis to determine the variance in DRU grade and age for the peak growth by body height and arm span measurements and the peak curve progression (Table 2) in each individual. All of these individuals thus were Risser

Stage 0 and premenarchal at baseline. By this method, any time lag between peak growth and peak curve progression will be determined. For this group, 56.5% were observed only and the remaining patients were braced. The mean Cobb angle at baseline for this group was 21° ± 4°, similar to the main cohort as described above. There were no differences between girls (21° ± 4°) and boys (21° ± 5°) ($p > 0.05$).

Body height and arm span measured in centimeters, coronal Cobb angle magnitude, Risser stage, and DRU grades were recorded at each visit. DRU grades were based on the simplified DRU classification, which was tested and validated [5, 6] and was shown to be accurate in predicting peak growth by radius grade 6 (R6) and ulna grade 5 (U5), and growth cessation by radius grade 9 (R9) and ulna grade 7 (U7) [4]. All data were recorded by two independent readers (JC and PC) blinded to the patient details. An average score of the Cobb angle was recorded if the measured degrees were within 5°. Any deviation beyond this and discrepancies with other measurements were decided by consensus between JC and PC. Age of menarche was listed for girls. For patients who were only observed and did not receive any treatment, the data were recorded every 4 to 5 months until skeletal maturity. For patients who ultimately were treated with bracing or surgery, only data before the intervention were recorded for analysis to keep the natural history data clean. All Cobb angles were measured on a standing posteroanterior whole-spine radiograph. The major curve Cobb angle was used for progression analysis. The same radiograph was used for grading the Risser stage (United States version) [1]. All radiographic measurements were performed by spine surgeons as part of routine consultations and independent of the clinical parameters.

Statistical Analysis

Descriptive statistics including the mean and SD of the growth rate (based on body height and arm span) and the curve progression rate then were calculated for each DRU grade. Based on DRU grades, the growth and curve progression rates were studied. The growth rate was calculated by the change in body height and arm span with time (months) between appointments. The DRU was assessed at the preceding visit and the change to the subsequent visit was calculated. At the same visits, curve progression rate was calculated by the change in Cobb angle with time (months). Shapiro-Wilk analysis revealed that age parameters were normally distributed but DRU grades were not. Therefore, a comparison was performed using a paired t-test for age and the Wilcoxon signed-rank test for DRU grades. Spearman's correlation coefficient was used to analyze the strength and direction of any association between the growth rate and the rate of curve progression. Data analyses were conducted using SPSS for Windows Version 23.0 (IBM SPSS Inc, Armonk, NY, USA). A p value less than 0.05 was considered statistically significant. Ninety-five percent confidence intervals were listed when appropriate to assess precision.

Results

Based on the overall cohort, there was correlation between growth rate and curve progression rate for body height ($r = 0.26$; $p < 0.001$) and arm span ($r = 0.26$; $p < 0.001$). Peak growth for body height occurred at R6 (0.56 ± 0.29 cm/month) and U4 (0.65 ± 0.31 cm/month); peak change in arm span occurred at R5 (0.67 ± 0.33 cm/month) and U3 (0.67 ± 0.22 cm/month); and peak curve progression matched with R7 (0.80 ± 0.89 cm/month) and U5 (0.84 ± 0.78 cm/month) (Table 3).

There was a lag in curve progression as compared with the growth rate (Table 2). The peak curve progression was one DRU grade behind peak growth by body height and arm span, consistent for both girls and boys. This amounted to a lag of an average 7.2 months (girls: 8 months, boys: 6.8 months) for body height and 7 months (girls: 8 months, boys: 6.4 months) for arm span. Looking at the overall cohort (Fig. 2), a similar lag was observed regarding the peak growth and curve progression rates. At the peak curve progression, the growth rates are already in the deceleration phase for R7 (0.31 ± 0.21 cm/month for body height and 0.39 ± 0.24 cm/month for arm span) and U5 (0.53 ± 0.27 cm/month for body height and 0.58 ± 0.36 cm/month for arm span). Similarly, the curve progression rates were lower than at its peak for the peak growth rate for body height (0.71° ± 0.69°/month for R6 and 0.44° ± 0.42°/month for U4) and arm span (0.51° ± 0.58°/month for R5 and 0.39° ± 0.50°/month for U3).

The mean time elapsed between the peak curve progression rate and the plateau phase at R9 U7 was 16 ± 8 months based on body height and 17 ± 8 months based on arm span. This corresponded to two DRU grades. The curve progression rates appeared to be similarly reduced to the growth rate at R9 and U7 where all rates began to plateau. These findings were similar for both body height and arm span.

Discussion

The ability to predict which patients with AIS undergo curve progression and how curve progression can be predicted by growth is still limited. Decision-making is based on the clinician’s experience, the patient’s growth rate, and Cobb angle on presentation [11, 22]. Accurate prediction of a patient’s growth rate and risk of curve progression are crucial in determining the best time to intervene. Indiscriminate or prolonged bracing, for example, may be associated with deleterious effects including reduced spinal mobility, poor body image and self-esteem, and worse quality of life [7, 8, 15, 16, 25, 26]. Once bracing is initiated, it is continued until skeletal maturity because there is no way of knowing whether the scoliosis is nonprogressive or that the brace is actually preventing curve progression. It therefore is necessary to correlate the curve progression of AIS with natural growth to refine our understanding of the period of actual curve progression risk so that interventions can be provided in a timely manner and only for patients who really need it. As such, in this study we used a consistent and reproducible skeletal growth parameter to identify the relationship between the growth rate with the curve progression rate at its peak and plateau for our patients with scoliosis. Using standardized skeletal maturity parameters is necessary for this analysis because chronologic age has been shown to be inconsistent, with large interethnic variations and timing of the growth spurt. Variation of up to 4 years has been reported with chronologic age [17]. Our study results suggest that the DRU grades have a strong relationship with growth and curve progression rates. The peak curve progression rate was found to lag behind peak growth by approximately 7 months and the period of curve progression risk can extend to approximately 1.5 years after peak growth. Therefore, we have identified a mismatch between growth and curve progression rates.

There are several inherent limitations to this study. As discussed earlier, body height and arm span were used as growth parameters. Specific vertebral body height measures should be studied to provide the most accurate growth indicator. Nevertheless, body height and arm span are still valuable as indirect growth parameters and are easily obtained even in a busy clinic. In addition, this study is devoid of in-brace data for patients undergoing bracing. Although this methodology of excluding data from patients who underwent bracing or surgery eliminates potential interventional confounders, we cannot determine whether the effective bracing period coincides with our determined curve progression risk period. An additional focus study is required to address this gap. This study also is based on a homogenous southern Chinese population. These findings should be validated in other ethnicities. However, the homogeneous nature of the population further decreases any potential for ethnic-specific confounding that can further affect the interpretation of the findings. Finally, even with our relatively closely spaced DRU measurements every 4 to 5 months, it still might not capture the absolute peak. However, the value of this study is to identify a mismatch between growth and curve progression rates which has been achieved.

Our subgroup analysis showed a relationship between the DRU grades and the growth and curve progression rates (Table 2). Having a validated and standardized maturity scale is crucial for determining which patients have remaining growth potential and may benefit from bracing. Many parameters like the Risser sign have been used to predict peak height velocity focused on long bone growth [4, 10, 17, 18, 19, 24]. However, the correlations between these growth parameters with curve progression risk are variable. The limited utility can be explained by inaccuracies with height measurements, the retrospective nature of determining peak height velocity, lack of ease of use and standardized growth measurements, and interpretation difficulties and inaccuracies with the Tanner-Whitehouse III maturity parameter and Risser stage. The DRU grades have been shown to be superior to the Risser stage, age of menarche, and metacarpal and phalangeal complexes in terms of growth prediction [4]. In the current study, we determined its utility in measuring curve progression risk as well.

Peak curve progression occurs approximately 7 months after the peak growth rate for body height and arm span measurements, based on our subgroup analysis. This suggests that peak height velocity occurs during the curve acceleration phase “just before” rather than “at” the peak curve progression period. The relationship between peak curve progression and peak height velocity is particularly important. A disjunction between growth and curve progression rates was suggested in previous studies [20, 22], but not fully quantified or put into clinical relevance. The peak height velocity noted in our study was slightly earlier (approximately one DRU grade) than what has been reported [4]. However, the findings were not confounded or influenced by interventions such as bracing, because data regarding such modalities initially were excluded from our study. Therefore, it was possible for these patients to have even more rapid height gain during treatment, which was not included in our analysis because we only included data up to the point of initiating intervention. Nevertheless, we were able to capture summits (inclusive of an acceleration and deceleration phase) for growth and curve progression indicating that the data were near if not at the peak. This study shows the timing of peak curve progression does not match the peak height velocity and in fact the maximal curve progression occurs after the peak growth spurt, suggesting that any treatment such as bracing is still relevant after peak height velocity owing to this mismatch. This may be explained by the distal-to-proximal growth gradient which has been established, suggesting that more distal body parts like the foot reach the pubertal growth spurt earlier [23]. Busscher et al. [2] echoed this finding, showing that the timing of peak growth velocities differs with foot length occurring earliest at approximately 11 years of age for girls, followed by the subischial leg length, total body height, and finally sitting height at 12 years of age. For scoliosis management, standing height is a useful representation of overall growth, but because it incorporates the lower limbs, pelvis, and the skull, it may not be as sensitive for monitoring spine growth in managing deformity as the sitting height, which eliminates the contribution of the lower limbs. In this study, with our use of body height with arm span for measuring growth rate, the growth data may be more representative of long bone growth rather than spine growth. Arm span is useful in patients with scoliosis because curve deterioration may cause a reduction in overall height and thus mask the actual spine growth achieved [4]. Nevertheless, the correlation between these two measurements is near identical so body height and arm span changes are representative [3]. As such, it can be deduced that the earlier finding of peak growth can be contributed by our use of standing body height and arm span rather than sitting height because the lower limbs reach peak height velocity earlier than the spine. However, sitting height is still an indirect measure of spine growth and actual measurements of individual vertebral height gains, especially areas not affected by scoliosis, may be more accurate for this purpose. Standing body height and sitting height may be affected by increased curve magnitude. Data regarding the pattern of vertebral growth are lacking and should be addressed in a future study. Another potential reason for the mismatch between growth and curve progression may be related to variable responses of a spinal deformity to growth. Skeletal growth may not be the sole determinant of curve progression because up to 42% of patients during the adolescent growth spurt do not experience substantial curve progression [28]. The curve magnitude also may be related to the rate of curve progression. Larger curve magnitudes may behave differently than smaller curves. Moreover, several morphologic characteristics like rotational deformity or vertebral wedging have been studied to differentiate the patients with AIS who are progressive [14]. Therefore, it is possible that despite a close relationship between growth and curve progression peak rates, some spine deformities do not deteriorate with growth and may be attributed to genetic or environmental influences.

Based on the patients followed until skeletal maturity, the period of curve progression risk extends to nearly 1.5 years, even after peak growth has been achieved. This was determined as the relevant curve progression period because no additional progression was observed once patients reached a maturity status of R9 and U7. This finding correlates closely with growth as indicated by the matching troughs of growth and progression rates. Taking our findings into consideration, clinicians can decide when is the best time to wean bracing. However, as this is not a bracing intervention study, whether this relationship is true requires a dedicated study regarding brace weaning. The period between the peak curve progression at R7 and U5 to the beginning of a plateau phase seen for growth and curve progression at R9 and U7 was approximately 16 to 17 months. This information may provide clinicians with valuable information for counseling patients and their families, which is also an important component to reduce anxiety and even improve compliance [12].

Understanding the relationship between growth and curve progression rates based on a standardized maturity scale such as the DRU is a novel concept highlighted in this study. There is consistent mismatch between growth and curve progression rates when assessed by body height or arm span, and peak curve progression lags approximately 7 months behind peak growth. Therefore the curve should be monitored closely even after peak growth, and effective bracing does not only pertain to the period at or before the peak height velocity but even after. Furthermore, the period of actual curve progression risk has been determined to be approximately 1.5 years; thereby, growth and curve progression rates simultaneously reduce to a plateau phase. This study has great value in providing practitioners who treat patients with scoliosis with better understanding of the relationship between curve progression risk and growth rate. This new information provides us with better tools to design more appropriate bracing protocols for patients with AIS.

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Legend

Fig. 1 The diagram shows how patients were included for the main cohort and subgroup analyses.

Fig. 2A-B The graphs show the relationship between curve progression rate and growth rate (body height and arm span) plotted with **(A)** radius and **(B)** ulna grades. They indicate that the peak curve progression rate occurs after the peak growth rate. Curve progression and growth rates reduced to a plateau at R9 and U7.