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ORIGINAL ARTICLE

A comparative analysis of axial and appendicular skeletal maturity staging systems through assessment of longitudinal growth and curve modulation after VBT surgery

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Abstract

Purpose Appendicular skeleton markers are commonly used for maturity assessment for Adolescent Idiopathic Scoliosis (AIS) patients. Traditionally, Risser has been a standard skeletal maturity assessment method. More recently, Sanders classification (SSMS), as a more comprehensive system, became popular, especially in decision-making for Vertebral Body Tethering (VBT). Thumb-Ossification Composite Index (TOCI), using ossification of thumb epiphyses, has been claimed to more accurately stage patients around their peak height velocity. However, growth peaks may occur separately at lower limbs and trunk. Hence, Cervical Vertebral Maturity (CVM), using cervical spine morphology, possesses a potential to better estimate spinal growth as it uses axial skeleton markers instead of appendicular skeleton markers. The aim of the study was to compare various axial and appendicular skeletal maturity assessment methods for longitudinal growth and curve modulation after VBT.

Methods A retrospective analysis of prospectively collected data was conducted. Skeletal maturity was determined using Risser, SSMS, TOCI and CVM for each patient. Crosstabulations of axial vs. appendicular markers were formed to analyze their concordance and discordance. Logistic and logarithmic regression models were run to assess longitudinal growth (postoperative height gain and leg-length growth) and curve modulation (follow-up instrumented Cobb correction after index operation), respectively. Models were compared using Akaike information criterion (AIC).

Results 34 patients (32 F/2 M, mean age: 12.8 ± 1.5 years, mean follow-up: 47.7 (24–80) months) were included. The median preoperative maturity stages were: Risser: 1 (-1–4), SSMS: 4 (1–7), TOCI: 6 (1–8) and CVM: 4 (1–6). At latest follow-up, all patients reached skeletal maturity. Concordance and discordance were observed between axial vs. appendicular systems that demonstrated a range of possible distributions of CVM, where trunk peak height velocity occurred before, simultaneously with or after the standing height peak height velocity. R-squared values for Risser, SSMS, TOCI and CVM were 0.701, 0.783, 0.810 and 0.811, respectively, for prediction of final height; 0.759, 0.821, 0.831 and 0.775 for final leg-length, and 0.507, 0.588, 0.668 and 0.673 for curve modulation. Delta AIC values demonstrated that different skeletal maturity assessment methods provided distinctive information regarding follow-up height gain, leg-length growth and curve behavior.

Conclusions Risser score provided considerably less information for all three outcome variables. TOCI and SSMS provided substantial information regarding remaining leg-length assessments, while in terms of assessment of total height gain and curve modulation after surgery, CVM and TOCI offered substantial information and SSMS offered strong information. Mutual use of axial and appendicular markers may provide valuable insight concerning timing of surgery and magnitude of surgical correction.

Keywords Vertebral body tethering · Axial and appendicular skeletal markers · Sanders skeletal maturity staging · Thumb-ossification composite index · Cervical vertebral maturity

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Introduction

Vertebral Body Tethering (VBT) is a growth modulation technique working mainly according to the Hueter-Volkmann principle [1] aiming to redirect spinal growth to achieve correction. Determination of stages of growth and prediction of the remaining growth may have the potential to influence complications of under- and over-corrections, and reoperations performed in this regard [2–4].

Parameters such as Risser sign, menarche status and chronological age have been used; however, they were weakly associated with the timing of peak height velocity (PHV) and remaining growth [5–8]. Recently, to overcome the steep learning curve of using a score derived from the Tanner-Whitehouse atlas (TW3-RUS) [9], Sanders et al. [10] reduced the TW3-RUS into Simplified Skeletal Maturity Staging system (SSMS), which demonstrated correlation with curve progression. As a more comprehensive system, SSMS became popular, especially in decision-making for VBT. Although average follow-up curve behavior was demonstrated to be different in patients having different preoperative SSMS stages, the confidence intervals were wide with significant overlap among groups [11]. Hence, pursuit of a more precise system continues.

Thumb Ossification Composite Index (TOCI), is a more simplified marker as it only uses the ossification of thumb epiphyses from the same skeletal maturation continuum [12]. TOCI was shown to correlate with SSMS, was reported to be reliable and accurate in the prediction of skeletal maturity, and was claimed to more accurately stage patients around their peak growth [13].

Nevertheless, it is well-known that the standing height is oversimplified to provide an accurate insight into growth, as peak growth is a juxtaposition of three micro-peaks occurring at lower limbs, trunk and chest [14]. Therefore, Cervical Vertebral Maturation (CVM), which was introduced by Lamparski [15], and was modified by Baccetti et al. [16], possesses a potential to better estimate spinal growth as it uses axial skeleton markers. Numerous studies have demonstrated CVM's correlation with different appendicular markers [17, 18] and its effectiveness in determining skeletal maturation [19, 20]. Although CVM was almost exclusively used in orthodontics, a recent study reported the role of CVM in AIS patients [21].

All in all, various axial and appendicular skeletal maturity assessment methods might have different abilities in predicting longitudinal growth and post-VBT follow-up curve modulation. The purpose of this study was to perform a comparative analysis of four established assessment methods (CVM as an axial method, and Risser, SSMS and TOCI as appendicular methods) for the same patients, given the same setting of VBT surgery.

Materials and methods

Patients

A retrospective cohort study was conducted in an ethics board approved single-center prospectively recorded data set of consecutive patients. Patients who were (1) diagnosed with AIS where the major curve was the main thoracic curve, (2) had undergone single-row VBT solely for the major curve, (3) had completed growth at the latest follow-up and (4) had at least 24 months follow-up were included. Patients who (1) did not have a preoperative whole-body biplanar slot scanning image with a concomitant left-hand radiograph, and (2) had a continued growth after a tether breakage were excluded to assure consistent assessment of truncal height and curve behavior. Follow-up time points were 6 weeks, 3, 6, 12, 18 and 24 months; every 6 months until skeletal maturity and annually thereafter. Left hand-wrist radiographs were obtained every 6 months in accordance with the TW3 protocol [22].

Demographic, perioperative and radiographic data

Retrospective chart review was conducted to obtain demographic, perioperative and radiographic data. Overcorrection was defined as the situation where a postoperative Cobb angle measurement decreases to zero and further changes that the laterality (direction of the apex) of the Cobb angle reverse, and a negative sign was assigned to an overcorrected curve. Mechanical and curve behavior complications and reoperations were noted. Broken tethers were indicated by $\geq 6°$ increase of angulation between adjacent screws between any two postoperative radiographs [3].

Outcome data

Standing height, leg length and instrumented Cobb were recorded at each visit and used to calculate three outcome variables.

Standing height was clinically measured without shoes. To eliminate the gain related to surgical correction, the increase from post-operative measurement onwards was defined as follow-up gain and "*Percentage Final Standing Height*" was calculated with the formula: Post-operative Standing Height / Latest Follow-up Standing Height * 100.

Leg length was measured radiographically on the whole-body biplanar slot scanning images as the average of right and left femorotibial lengths, to account for the bony leg length discrepancies [23]. As pre- and post-operative measurements are essentially the same, for consistency, the increase from post-operative measurement onwards was defined as follow-up growth and "*Percentage Final Leg*

Length" was calculated with the formula: Post-operative Leg Length / Latest Follow-up Leg Length * 100.

To analyze the curve behavior in the tethered segments, instrumented MT curve was measured. Follow-up correction was adjusted according to surgical correction to yield the "*Surgery-adjusted Follow-up Instrumented Cobb Correction*" using the formula: ((First Erect – Latest) / First Erect) / ((Preop – First Erect) / Preop). For patients who experienced a tether breakage after skeletal maturity, the last intact measurement was used as the latest instrumented Cobb.

Growth and skeletal maturity indicators

Modified Risser score, SSMS, TOCI and CVM were used to determine skeletal maturity. Measurements were independently performed by two senior spine surgeons who were blinded to the age and identity of the patients. Intraclass correlation coefficients (ICC) were calculated to range between 0.944 and 0.965, using preoperative measurements. In case of disagreement, the senior author acted as a third measurer.

Modified Risser score [24], in which open vs. closed triradiate cartilage constitutes two subgroups within Risser-0, was determined. Epiphyses of all hand digits, adductor sesamoid as well as radial and ulnar epiphyses were scored with the SSMS system on hand-wrist radiographs [10]. The same set of radiographs was scored with the TOCI system using the epiphyses of the thumb and adductor sesamoid [12] (Fig. 1a). CVM was determined from sagittal radiographs according to the Baccetti et al. definition [16] based on the development of concavities at the lower end-plates of C2, C3 and C4, and the change in the shape and size of the bodies of C3 and C4 (Fig. 1b).

Statistical analysis

SPSS 20.0 (Chicago, Illinois, USA) was used for analysis. A p value of < 0.05 was considered significant. Quantitative variables were expressed as mean and standard deviation or median and range, and categorical variables as percentages. Crosstabulations of axial vs. appendicular markers were formed to analyze their concordance and discordance.

Predictive abilities of the Modified Risser Score, SSMS, TOCI and CVM were compared for Percentage Final Standing Height, Percentage Final Leg Length and Surgery-adjusted Follow-up Instrumented Cobb Correction. Logistic and logarithmic regression models were run to assess longitudinal growth and curve modulation, respectively. As height and leg length have an expected end value, logistic regression models were issued an upper bound of 100%. "Group stages" of the skeletal maturity indicators (i.e. Risser-0, SSMS-3, TOCI-4 and CVM-5) were attributed "standardized group numbers" using duration of each stage in our cohort as follows: Stages of each classification were plotted at each visit for all patients. Timing of changes in stages (i.e. TOCI-4 to TOCI-5) were recorded. If a two-stage (i.e. TOCI-4 to TOCI-6) or three-stage (i.e. TOCI-4 to TOCI-7) change was observed, the time between the radiographs were equally distributed to each stage. The mean and median were calculated to attribute stage "durations" as precise as 3 months. Stages that were reported to coincide with the PHV, which were reported to be between − 1 and 0 for Risser [25], within 3 for SSMS [26], between 4 and 5 for TOCI [12] and at the mid of 3 for CVM [27, 28] were given the same standard group number. One year was assigned 1-integer change in the group number. Duration of each stage was used to calculate the "standardized group numbers".

Models were compared using Akaike information criterion (AIC). The model with the lowest AIC value denoted the preferred model. The models with delta AIC values of < 2, between 2 and 4 and between 4 and 7 were considered to have "substantial", "strong" and "considerably less" support, respectively [29].

Results

Our dataset comprised 129 VBT patients, 84 of whom were diagnosed with AIS with MT as the major curve and were operated ≥ 24 months before the data query. Fourteen patients underwent bilateral VBT and eleven had double-row VBT, while 14 patients had remaining growth potential at their latest follow-up, leaving 45 potentially eligible patients. Among these, 7 (15.6%) patients did not have a preoperative left-hand radiograph, 3 (6.7%) had a growth after a tether breakage, and 1 (2.2%) was lost to follow-up resulting in 34 (75.6%) patients operated between 2015 and 2019 being included for analysis. The mean follow-up duration was 47.7 (24–80) months.

The mean age at surgery was 12.8 ± 1.5 (9.8–15.9) years. Thirty-two (94.1%) patients were female, among whom, 17 (53.1%) were premenarchal, while the rest were, on average, 9.9 ± 6.9 (1–24) months postmenarchal. All patients were Caucasians. Spine and hand radiographs were evaluated in a total of 252 visits (mean: 7.4, range 4–10). Curve types, curve measurements, perioperative details and complications are given in Table 1. One patient was converted to fusion after reaching skeletal maturity.

Details of longitudinal growth and instrumented Cobb measurements, as well as preoperative and follow-up skeletal maturity indicators, are given in Table 2. Preoperatively, the mean Percentage Final Height was 96.4% ± 3.6% (84.9 – 99.9%), and the mean Percentage Final Leg Length was

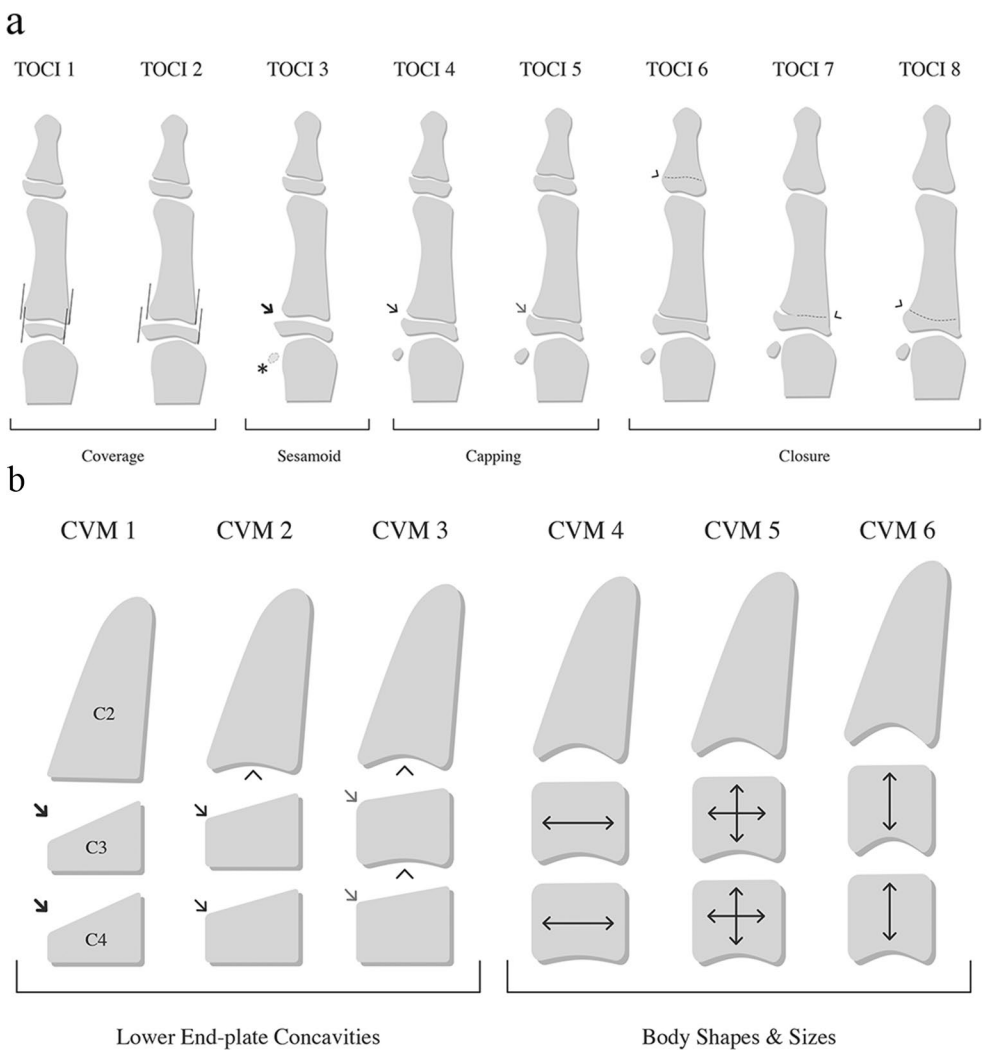

Fig. 1 **a** Stages of Thumb Ossification Composite Index. First two stages are defined by the coverage of the proximal phalangeal epiphyses (vertical lines). In TOCI 1 the proximal phalangeal epiphysis is uncovered, where the width of the epiphysis is not wider than that of the metaphysis. In TOCI 2 the proximal phalangeal epiphysis is covered, where the width of the epiphysis is wider than that of the metaphysis. TOCI 3 is defined by the ossification of the thumb adductor sesamoid (asterisk), where the epiphysis has not yet started capping (dark arrow). In TOCI 4, early capping is seen, where the spread of the epiphysis around the metaphysis is still below the imaginary line drawn over the physis (arrow). In TOCI 5, advanced capping is seen, where the spread of the epiphysis around the metaphysis is over the imaginary line drawn over the physis (light arrow). The last three stages are defined by the closure of the distal and proximal phalangeal epiphyses (arrowheads). In TOCI 6, the distal phalangeal epiphysis is fused, where the physeal scar may or may not be visible. In TOCI 7, the proximal phalangeal epiphysis is partly fused. In TOCI 8, the proximal phalangeal epiphysis is fused, where the physeal scar may or may not be visible
b Stages of Cervical Vertebral Maturation. First three stages are defined by the presence or otherwise of concavities at the lower end-plates of C2, C3 and C4. In CVM 1 all lower end-plates are flat. A concavity is seen at the lower end-plate of C2 in CVM 2, while both C2 and C3 end-plates develop concavities in CVM 3 (arrowheads). Simultaneously, the trapezoidal shape of C3 and C4 bodies transform into a more rectangular shape as the first three stages progress (bold arrows, arrows and light arrows, respectively). As a concavity is present in all three vertebrae after this stage, the last three stages are defined by the shape and size of the C3 and C4 vertebral bodies (double-sided arrows). In CVM 4, the bodies are rectangular in a horizontal fashion. In CVM 5, the bodies are nearly square in shape. In CVM 6, the bodies are rectangular in a vertical fashion

96.6% ± 4.0% (81.7 – 99.9%). The ratio of remaining leg growth to remaining standing height growth varied widely between 13% and 70% (mean 45.3%±15.0%). Conversely, at skeletal maturity, the ratio of leg length to the total standing height was relatively constant, and varied between 46% and 51% (mean 48.8%±1.3%). At the latest follow-up, the mean Surgery-adjusted Follow-up Instrumented Cobb Correction was 1.23 ± 1.16 (-0.20–4.79). At latest follow-up, all patients reached skeletal maturity, where 5 (14.7%) patients had CVM-5 as their final maturation stage and did not progress into CVM-6.

Table 1 Curve types, pre-operative and latest follow-up maximum Cobb angle measurements, perioperative details and complications

	Patient cohort (*n*=34)
Lenke classification, *n* (%)	
1 A	13 (38.2%)
1Ar	9 (26.6%)
1B	8 (23.5%)
1 C	3 (8.8%)
2B	1 (2.9%)
Pre-operative measurements, degree, mean ± SD (Range)	
Proximal Thoracic	28.9 ± 6.9 (17 – 45)
Main Thoracic	48.2 ± 7.6 (38 – 68)
Thoracolumbar/Lumbar	29.6 ± 6.3 (19 – 43)
Kyphosis	30.3 ± 10.7 (12 – 59)
Lordosis	61.6 ± 10.8 (37 – 91)
Approach, n (%)	
Thoracoscopic	31 (91.2%)
Thoracoscopic + Retroperitoneal	3 (8.8%)
UIV Location, n (%)	
T5	18 (52.9%)
T6	14 (41.2%)
T7	2 (5.9%)
LIV Location, n (%)	
T11	14 (41.2%)
T12	12 (35.3%)
L1	5 (14.7%)
L2	1 (2.9%)
L3	2 (5.9%)
Levels tethered, median (Range)	7 (6 - 9)
Surgical Time, min, Mean ± SD (Range)	243 ± 79 (125 - 420)
EBL, ml, Mean ± SD (Range)	77 ± 43 (40 - 250)
LoS, days, Mean ± SD (Range)	4.3 ± 1.2 (3 - 9)
Latest follow-up measurements, degree, mean ± SD (Range)	
Proximal Thoracic	16.7 ± 7.9 (4 – 38)
Main Thoracic	19.7 ± 11.0 (-11 – 43)
Thoracolumbar/Lumbar	10.0 ± 14.2 (-33 – 46)
Kyphosis	30.4 ± 10.5 (6 – 50)
Lordosis	57.0 ± 7.7 (38 – 70)
Mechanical Complications	
Tether Breakage, n (%)	6 (17.6%)
UIV loosening and/or migration, n (%)	3 (8.8%)
LIV loosening and/or migration, n (%)	1 (2.9%)
Curve behavior complication	
Overcorrection, n (%)	6 (17.6%)
Distal adding on, n (%)	2 (5.9%)
Worsening of the compensatory curve, n (%)	1 (2.9%)

n: number; min: minutes; ml: milliliters; SD: Standard Deviation; EBL: Estimated Blood Loss; LoS: Length of hospital stay; UIV: Upper Instrumented Vertebra; LIV: Lower Instrumented Vertebra

Crosstabulations of preoperative CVM vs. Risser, SSMS and TOCI demonstrated that trunk PHV can occur before, simultaneously with or after the standing height PHV (Table 3). Given these observations of concordance and discordance between axial vs. appendicular skeletal markers, Fig. 2 depicts the range of possible scenarios and the distribution of CVM. Figure 3a depicts a patient with documented trunk growth despite being in later stages of growth according to appendicular markers while Fig. 3b represents a patient who didn't experience overcorrection albeit being in earlier stages of growth according to appendicular markers.

Table 4 summarizes the timing of observed changes in stages, as well as the "duration" attributed to each stage for this cohort, which was used for the calculation of standardized group numbers. Plots of observed cases, graphical representations of logistic and logarithmic regression models as well as their relevant adjusted R-squared and standard error values are given in Fig. 4, and details of model comparisons in Table 5. SSMS, TOCI consistently provided substantial or strong information, while CVM provided substantial information for standing height and curve correction, but not for leg length prediction. Risser score provided considerably less information for all three outcome variables.

Discussion

Skeletal maturation is an ongoing process and estimation of remaining growth is essential to form a well-balanced treatment strategy. Since surgical growth modulation methods are gaining popularity, a need for a detailed and effective growth predictor emerged. The current study assessed different skeletal maturity staging systems revealing separate distinctive abilities of axial and appendicular systems for different phases of growth.

Appendicular markers

Modified Risser Score [24] demonstrated the lowest predictive ability for all three outcome measures investigated. Previous reports [9, 30, 31] also revealed poor correlation between Risser and rapid curve progression phase. Moreover, high variability of progression from Risser-1 to Risser-5, together with short durations attributed to each stage, makes the prediction of cessation of growth unreliable [32, 33].

Sanders et al. [10] reported that SSMS has a high correlation with curve behavior. Our results both confirmed and refuted their findings. While SMSS had substantial predictive ability for remaining leg growth, its delta AIC value for prediction of remaining standing height was inferior

Table 2 Standing height, leg length and instrumented Cobb angle measurements and skeletal maturity indicators pre-operatively and at each follow-up time point

	Pre-operative	Post-operative*	6 months	12 months	24 months	Latest follow-up
Standing height, cm						
Mean ± SD	155.7 ± 8.3	157.1 ± 8.1	159.1 ± 7.4	160.3 ± 6.9	161.7 ± 6.3	162.9 ± 6.1
Range	130 – 171	133 – 173	140 – 175	143 – 177	147 – 177	151 – 177
Leg Length, cm						
Mean ± SD	76.9 ± 4.3	76.9 ± 4.3	77.9 ± 4.3	78.4 ± 4.1	79.2 ± 4.0	79.6 ± 4.1
Range	67.0 – 86.6	67.0 – 86.6	69.5 – 87.7	71.5 – 88.1	73.1 – 88.3	73.1 – 88.3
Remaining standing height, cm						
Mean ± SD	7.1 ± 6.2	5.8 ± 5.9	3.8 ± 4.8	2.6 ± 4.0	1.2 ± 2.3	0.0 ± 0.0
Range	0.5 - 26	0.5 – 25.0	0.0 – 22.0	0.0 – 20.0	0.0 – 12.0	0.0 – 0.0
Remaining leg length, cm						
Mean ± SD	2.8 ± 3.3	2.8 ± 3.3	1.6 ± 2.6	1.1 ± 2.1	0.5 ± 1.3	0.0 ± 0.0
Range	0.1 – 15.0	0.1 – 15.0	0.0 – 12.5	0.0 – 10.5	0.0 – 7.1	0.0 – 0.0
Instrumented Cobb, degree						
Mean ± SD	45.0 ± 7.3	20.7 ± 6.1	18.4 ± 7.0	14.9 ± 7.8	11.4 ± 10.9	8.4 ± 13.3
Range	35 – 65	6 – 30	-2 – 28	-4 – 30	-19 – 30	-35 – 26
Modified Risser score						
Median	1	n/a	3	4	5	5
Range	-1 – 4		-1 – 5	-1 – 5	-1 – 5	5 – 5
SSMS						
Median	4	n/a	6	7	7	8
Range	1 – 7		2 – 8	2 – 8	2 – 8	8 – 8
TOCI						
Median	6	n/a	7	8	8	8
Range	1 – 8		2 – 8	2 – 8	3 – 8	8 – 8
CVM						
Median	4	n/a	4	5	5	6
Range	1 – 6		1 – 6	2 – 6	2 – 6	5 – 6

*First-erect radiographs taken before discharge

SD: Standard Deviation; n/a: not applicable; SSMS: Sanders Simplified Skeletal Maturity Staging System, TOCI: Thumb Ossification Composite Index, CVM: Cervical Vertebral Maturation

compared to TOCI and CVM. These results comply with the findings of a previous report on follow-up curve behavior after VBT in different Sanders stages [11]. In that study, although the mean anticipated curve modulation was different for each stage, there was a significant overlap between their ranges. Interpretation of the results of both studies together indicate that the correlation of SMSS with trunk growth is lower than its correlation with leg growth, which reflects into a lower predictive ability for instrumented Cobb correction.

As they belong to the same skeletal maturation continuum, high interchangeability with overlapping time periods between SSMS and TOCI have been reported. Nonetheless, in the current study, TOCI was the best predictor of leg growth, and a close second for both standing height and curve modulation predictions. This might be due to its ability to classify skeletal maturity more precisely around pre-peak period, to easily identify the timing of PHV, and its high sensitivity in the prediction of late descending phase [13].

Axial markers

Dimeglio et al. [7, 14] have shown that the peak of growth is a combination of three small peaks that occur in lower limbs, trunk and thorax. The current study validated their results. The increase in leg lengths, and standing heights varied between 0.1 cm and 15 cm, and 0.5 cm to 25 cm, respectively. However, such increases were not evenly distributed in all cases. The ratio of remaining growth (i.e. legs vs. rest of the body) varied widely, where the leg growth constituted 13–70% of the remaining total growth. Accordingly, the patients displayed different leg vs. trunk growth patterns during follow-up. Yet, they ended up having similar body proportions, where the leg length to standing height ratio at skeletal maturity showed a narrow variability (Fig. 4). Subsequently, our results suggest that although the estimation of remaining growth is essential, it is not solely sufficient, and that using different skeletal markers for different body regions might be necessary.

Table 3 Crosstabulations of preoperative CVM stages vs. preoperative Risser, SSMS and TOCI stages

	CVM※						Total
	1	2	3	4	5	6	
Risser※							
-1	1	3	1 †	-	-	-	5
0	-	-	4 *	3	2	-	9
1	-	-	1 §	5	1	-	7
2	-	-	-	1	2	-	3
3	-	-	-	1	1	-	2
4	-	-	-	2	4	2	8
SSMS※							
1	1	1	-	-	-	-	2
2	-	2	2 †	-	-	-	4
3	-	-	3 *	4	1	-	8
4	-	-	-	5	2	-	7
5	-	-	1 §	-	1	-	2
6	-	-	-	3	1	-	4
7	-	-	-	-	5	2	7
TOCI※							
1	1	-	-	-	-	-	1
2	-	1	-	-	-	-	1
3	-	1	-	-	-	-	1
4	-	1	3 †	-	-	-	4
5	-	-	2 *	4	1	-	7
6	-	-	1 §	7	3	-	11
7	-	-	-	1	1	-	2
8	-	-	-	-	5	2	7
Total	1	3	6	12	10	2	34

※ Reported stages that coincide with the peak height velocity is between − 1 and 0 for Risser [25], within 3 for SSMS [26], between 4 and 5 for TOCI [12] and at the mid of 3 for CVM [27, 28]

* Denotes patients with simultaneous trunk and standing height peak height velocity

† Denotes patients who reached trunk peak height velocity earlier than that of the standing height

§ Denotes patients who reached trunk peak height velocity later than that of the standing height

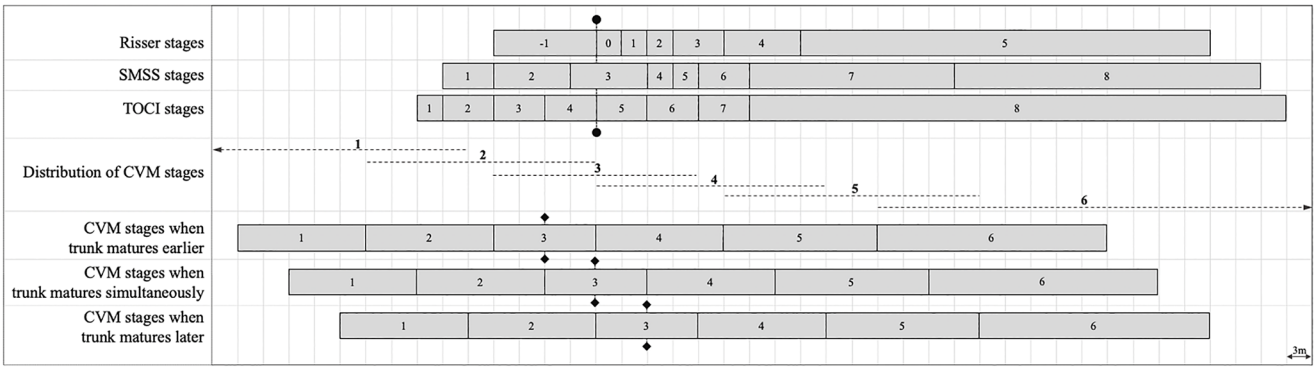

Fig. 2 The diagram of attributed durations of different skeletal maturity staging systems in our cohort demonstrating concordance and discordance between axial vs. appendicular skeletal markers in regards to the peak height velocity (PHV) of the standing height and the range of possible scenarios of the distribution of CVM for early, simultaneous and late maturation of the trunk in comparison to the leg growth. ● depicts PHV of standing height. ◆ depicts range of possible peaks of trunk growth. 3 m stands for 3 months, acting as a legend for stage durations

CVM displayed the highest predictive ability for curve modulation after VBT, possibly because it is a marker originating from the spine. Crosstabulations of axial vs. appendicular systems revealed concordance and discordance that demonstrated a range of possible scenarios, in which Trunk-PHV occurred before, simultaneously with or after Height-PHV. As such, growth and curve modulation were not always simultaneous. These different maturation patterns were

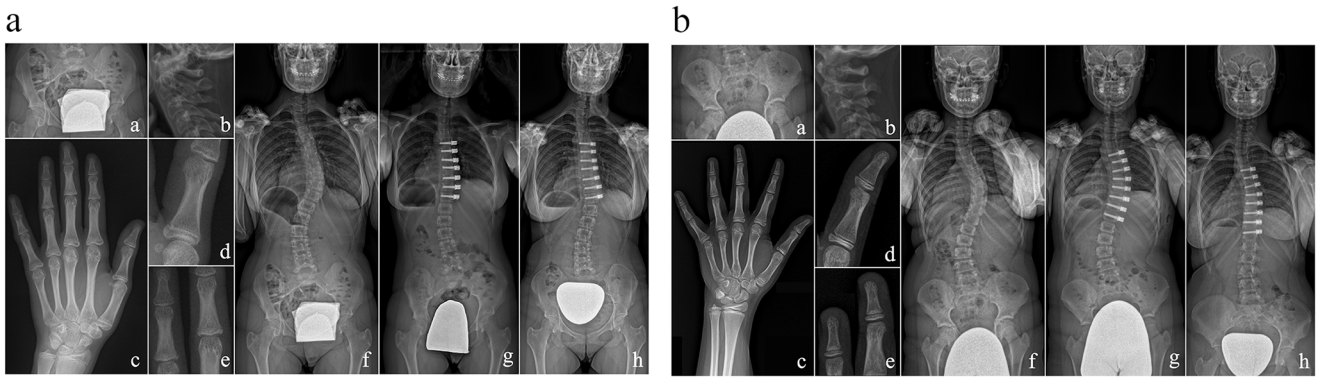

Fig. 3 **a** A 14-years-and-6-months-old female patient, who was 12 months postmenarchal, displayed (**a**) Risser 4, (**b**) CVM 4, (**c**, **d**, **e**) SSMS 6 and TOCI 7 characteristics preoperatively. Her pre-discharge standing height of 157 cm increased to 161 at the latest follow-up demonstrating a percentage final standing height of 2.5%. On the other hand, her leg length increased from 78.10 to 78.85 demonstrating a percentage final leg length of 1.0%. As such, the ratio of her follow-up leg growth to follow-up standing height growth was 19% indicating that her axial skeleton maturation occurred later than her appendicular skeleton maturation. Accordingly, her instrumented Cobb that measured (**f**) 43° preoperatively and (**g**) 12° at first-erect (**h**) was measured to be 0° at the latest follow-up, demonstrating a surgery-adjusted follow-up instrumented Cobb correction of 1.39. A significant curve modulation was noted, where the angle between the horizontal reference line and the UIV screw changed, and 3 vertebrae from the compensatory curve added-on to the tethered curve
b A 10-years-and-10-months-old female patient, who was premenarchal, displayed (**a**) triradiate open Risser − 1, (**b**) CVM 3, (**c**, **d**, **e**) SSMS 2 and TOCI 4 characteristics preoperatively. Her pre-discharge standing height of 144 cm increased to 157.5 at the latest follow-up demonstrating a percentage final standing height of 8.6%. On the other hand, her leg length increased from 72.40 to 78.20 demonstrating a percentage final leg length of 7.4%. The ratio of her follow-up leg growth to follow-up standing height growth was 43%. Combined information of SSMS and TOCI indicated that she had less growth potential compared to patients in the same SMSS and Risser, but earlier TOCI stages. Additional information on CVM indicated that her axial skeleton maturation occurred earlier than her appendicular skeleton maturation. Accordingly, her instrumented Cobb that measured (**f**) 49° preoperatively and (**g**) 30° at first-erect (**h**) was measured to be 7° at the latest follow-up, demonstrating a surgery-adjusted follow-up instrumented Cobb correction of 1.98. Although, the tethered curve was significantly modulated, no overcorrection was noted

reflected into radiographic outcomes (Fig. 3a) in the clinical setup, where curve modulation was more closely linked to the trunk height gain compared to the total standing height gain. As more data is gathered regarding the use of CVM in AIS, the need for frequent hand-wrist radiographs may be reduced. Nevertheless, for all staging systems, growth-related predictions were more successful than that of curve modulation, despite using a standardized outcome variable instead of absolute Cobb angle measurements. This is an expected finding, since this study did not aim to ameliorate curve behavior predictions with potential covariates, such as patient demographics, body measurements or curve characteristics, flexibility and compression applied at each level. Instead, various staging systems were compared under the same circumstances.

Despite its aforementioned advantages, our results do not indicate that CVM should be used in isolation as the sole skeletal maturity indicator. Firstly, durations of CVM stages are longer compared to those of appendicular markers. Thus, identifying a stage would not indicate whether the patient is near the beginning, middle or end of that stage. Therefore, follow-up radiographs would be necessary to judge the continuation or cessation of stages. Using CVM distributions depicted in Fig. 2, appendicular systems can help in this aspect. Additionally, SSMS and TOCI demonstrated separate distinctive abilities at different phases of growth although their stages have several overlapping thresholds (Fig. 3b). Furthermore, previous studies have shown that approximately 17% of females never reach CVM-6 [34]. Similarly, in our study, 14.7% of the patients were observed to demonstrate stage 5 features albeit having longer follow-up than the attributed duration of that stage. Overall, the accurate estimation of skeletal maturity and remaining growth potential, and curve modulation after VBT is still a challenge.

Limitations of the study

There are several limitations to this study including its retrospective nature. The cohort is relatively small due to strict inclusion and exclusion criteria. Yet, this cohort is a near-ideal one in regards to our study question with a long follow-up duration. In addition, the analyses were based on durations attributed to each stage, while in reality, patients in each stage show variable durations. Another limitation is that the hand-wrist radiographs were obtained on 6-months intervals, and that whenever two or more stage progressions were observed, the time between the two radiographs were evenly distributed. However, more frequent follow-up may not be feasible and/or desirable. Lastly, patients in our

Table 4 Timing of changes in skeletal maturity classification stages observed in this cohort

	Age *	Duration & number of patients observed to change stages										Timing of observed changes		Attributed duration, months
	Mean ± SD, years	2 m, n	3 m, n	6 m, n	12 m, n	15 m, n	18 m, n	24 m, n	30 m, n	36 m, n	Total,	Mean ± SD, months	Median (Range), months	
Risser														
-1 to 0	10.8 ± 0.6	-	-	2	2	-	-	-	1	-	5	13.2 ± 9.9	12 (6 – 30)	12
0 to 1	12.7 ± 3.6	1	7	4	-	-	-	-	-	-	12	3.9 ± 1.6	3 (2 – 6)	3
1 to 2	13.1 ± 1.1	4	13	1	-	-	-	-	-	-	18	2.9 ± 0.9	3 (2 – 6)	3
2 to 3	13.3 ± 1.1	3	13	4	-	-	-	-	-	-	20	3.5 ± 1.4	3 (2 – 6)	3
3 to 4	13.6 ± 0.9	3	7	12	-	-	-	-	-	-	22	4.5 ± 1.7	6 (2 – 6)	6
4 to 5	13.9 ± 1.1	-	-	16	13	-	3	-	-	-	32	9.6 ± 4.0	9 (6 – 18)	9
SSMS														
1 to 2	9.8 ± 0.0	-	-	1	-	-	-	-	-	-	1	6.0 ± 0.0	6 (6 – 6)	6
2 to 3	11.1 ± 0.3	-	-	3	1	-	1	-	-	-	5	9.6 ± 5.4	6 (6 – 18)	9
3 to 4	12.3 ± 0.7	2	1	4	5	-	-	-	-	-	11	7.6 ± 4.2	6 (2 – 12)	9
4 to 5	12.7 ± 1.2	3	8	2	-	-	-	-	-	-	13	3.2 ± 1.3	3 (2 – 6)	3
5 to 6	12.8 ±1.3	3	9	1	-	-	-	-	-	-	13	3.0 ± 1.0	3 (2 – 6)	3
6 to 7	13.5 ± 1.2	-	1	11	4	-	-	-	-	-	16	7.3 ± 2.9	6 (3 – 12)	6
7 to 8	14.0 ± 1.2	-	-	1	5	-	4	8	5	-	23	20.9 ± 7.2	24 (3 – 30)	24
TOCI														
1 to 2	9.8 ± 0.0	-	1	-	-	-	-	-	-	-	1	3.0 ± 0.0	3 (3 – 3)	3
2 to 3	10.8 ± 0.0	-	-	1	-	-	-	-	-	-	1	6.0 ± 0.0	6 (6 – 6)	6
3 to 4	11.6 ± 0.4	-	-	2	-	-	-	-	-	-	2	6.0 ± 0.0	6 (6 – 6)	6
4 to 5	11.4 ± 0.5	-	1	5	-	-	-	-	-	-	6	5.5 ± 1.2	6 (3 – 6)	6
5 to 6	12.1 ± 0.8	-	4	2	4	-	-	-	-	-	10	7.2 ± 4.3	6 (3 – 12)	6
6 to 7	12.9 ± 1.1	-	6	7	2	-	-	-	-	-	15	5.6 ± 3.0	6 (3 – 12)	6
7 to 8	13.5 ± 1.1	-	2	13	1	-	-	-	-	-	16	6.0 ± 1.9	6 (3 – 12)	6
CVM														
1 to 2	9.8 ± 0.0	-	-	-	-	1	-	-	-	-	1	15.0 ± 0.0	15 (15 – 15)	15
2 to 3	11.1 ± 0.4	-	-	-	1	-	1	-	-	-	2	15.0 ± 4.2	15 (12 – 18)	15
3 to 4	12.0 ± 0.9	-	-	3	3	-	4	-	-	-	10	12.6 ± 5.3	12 (6 – 18)	12
4 to 5	12.9 ± 1.1	-	-	4	7	-	5	2	-	-	18	13.7 ± 5.7	12 (6 – 24)	15
5 to 6	13.6 ± 1.2	-	-	-	5	-	11	4	-	1	21	18.6 ± 5.7	18 (12 – 36)	18

* Age at the visit where a given stage is observed for the first time

n: number, m: months, SD: Standard Deviation, Risser: Modified Risser Score, SSMS: Sanders Simplified Skeletal Maturity Staging System, TOCI: Thumb Ossification Composite Index, CVM: Cervical Vertebral Maturation

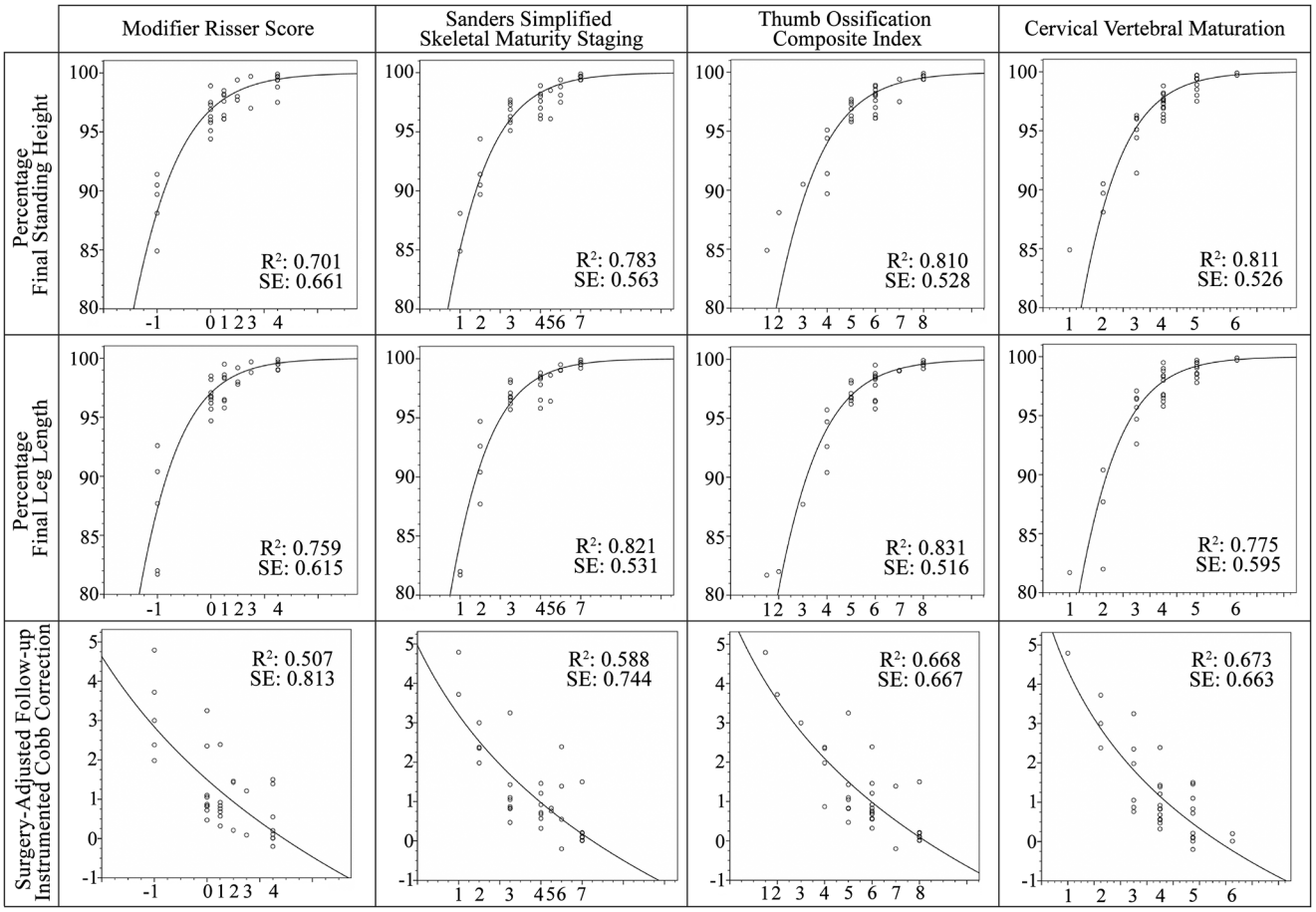

Fig. 4 Observed cases and estimated curves of logistic and logarithmic regression models for percentage of final standing height, percentage of final leg length and surgery-adjusted instrumented curve correction during follow-up. Analysis was made using "normalized group numbers", while "group names" were depicted in the image for ease of interpretation. Uneven distances between "group names" refer to the attributed stage durations. R^2: Adjusted R-squared, SE: Standard Error of the Estimate

cohort were unevenly distributed into classification stages. Yet, this is due to the treatment method in question and the most relevant subset of patients are sufficiently represented.

Conclusions

As appendicular assessment systems, TOCI and SSMS provided substantial information regarding leg length predictions, while CVM, which uses axial markers, provided strong information. Contrarily, CVM and TOCI were found to offer more information regarding total height gain and curve modulation after VBT. As each system demonstrated separate distinctive abilities for different phases of trunk and limb growth, mutual use of axial and appendicular markers may result in more reliable assessment providing valuable insight concerning timing of surgery and magnitude of surgical correction.

Table 5 Results of model comparisons and their interpretation based on delta AIC values

	Adjusted R^2	AIC	Delta AIC	Interpretation
Percentage final standing height				
Risser	0.701	-7.10193	6.772	Considerably Less
SSMS	0.783	-11.8475	2.027	Strong*
TOCI	0.81	13.7744	0.1	Substantial
CVM	0.811	-13.8742	AIC_{min}	Substantial
Percentage Final Leg Length				
Risser	0.759	-10.1887	5.193	Considerably Less
SSMS	0.821	-14.5432	0.839	Substantial
TOCI	0.831	-15.3818	AIC_{min}	Substantial
CVM	0.775	-11.22043	4.177	Considerably Less
Surgery-adjusted follow-up instrumented cobb correction				
Risser	0.507	-1.00205	6.045	Considerably Less
SSMS	0.588	-3.62918	3.418	Strong
TOCI	0.668	-6.81573	0.231	Substantial
CVM	0.673	-7.04719	AIC_{min}	Substantial

* Delta AIC value very close to the threshold that separates the Substantial and Strong categories

R^2: R-squared; AIC: Akaike Information Criterion; AIC_{min}: The model with the lowest AIC value; Risser: Modified Risser Score, SSMS: Sanders Simplified Skeletal Maturity Staging System, TOCI: Thumb Ossification Composite Index, CVM: Cervical Vertebral Maturation

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