3D prediction of curve progression in adolescent idiopathic scoliosis based on biplanar radiological reconstruction

a systematic review

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Aims
This systematic review aims to identify 3D predictors derived from biplanar reconstruction, and to describe current methods for improving curve prediction in patients with mild adolescent idiopathic scoliosis.

Methods
A comprehensive search was conducted by three independent investigators on MEDLINE, PubMed, Web of Science, and Cochrane Library. Search terms included "adolescent idiopathic scoliosis","3D", and "progression". The inclusion and exclusion criteria were carefully defined to include clinical studies. Risk of bias was assessed with the Quality in Prognostic Studies tool (QUIPS) and Appraisal tool for Cross-Sectional Studies (AXIS), and level of evidence for each predictor was rated with the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) approach. In all, 915 publications were identified, with 377 articles subjected to full-text screening; overall, 31 articles were included.

Results
Torsion index (TI) and apical vertebral rotation (AVR) were identified as accurate predictors of curve progression in early visits. Initial TI > 3.7° and AVR > 5.8° were predictive of curve progression. Thoracic hypokyphosis was inconsistently observed in progressive curves with weak evidence. While sagittal wedging was observed in mild curves, there is insufficient evidence for its correlation with curve progression. In curves with initial Cobb angle < 25°, Cobb angle was a poor predictor for future curve progression. Prediction accuracy was improved by incorporating serial reconstructions in stepwise layers. However, a lack of post-hoc analysis was identified in studies involving geometrical models.

Conclusion
For patients with mild curves, TI and AVR were identified as predictors of curve progression, with TI > 3.7° and AVR > 5.8° found to be important thresholds. Cobb angle acts as a poor predictor in mild curves, and more investigations are required to assess thoracic kyphosis and wedging as predictors. Cumulative reconstruction of radiographs improves prediction accuracy. Comprehensive analysis between progressive and non-progressive curves is recommended to extract meaningful thresholds for clinical prognostication.

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Take home message

- The torsion index and apical vertebral rotation are good 3D predictors of curve progression.
- 3D Cobb angle, thoracic kyphosis, and sagittal wedging are weaker predictors that require further investigation.
- Serial spinal reconstructions and inclusion of growth extrapolation are needed to provide better predictive model accuracy.

Introduction

Adolescent idiopathic scoliosis (AIS) is a complex condition that requires regular follow-up monitoring and casts significant psychosocial pressure on its patients.[1-6] Prediction of curve progression can reduce unnecessary consultations and bracing in non-progressive patients, while allowing earlier intervention and proper prognostication to progressive patients.[7,8]

As a 3D deformity, AIS is characterized by the lateral spinal curvature in the frontal plane, a disturbance of physiological spinal curvatures in the sagittal plane, and an axial rotation of the vertebrae in the transverse plane.[9-14] Despite hypokyphosis and axial rotation being recognized as important factors in curve development, patients undergoing conservative management are usually only assessed using 2D Cobb angle and bone age for prediction of curve progression. In the recent literature, more specialized centres have been characterizing spinal deformity in axial and sagittal planes to improve accuracy in predicting curve progression.[15-21]

To assess rotation in larger curves, the Nash-Moe[22] method has been extensively used, but it is limited by low accuracy and replicability.[23,24] Meanwhile, 3D reconstruction from CT scans are not routinely performed due to exposure to ionizing radiation.[25,26] In recent years, 3D reconstruction of biplanar radiographs has been increasingly validated for its accuracy and reproducibility.[27,28] It should be noted that 3D in the context of biplanar reconstruction also refers to the ability to derotate vertebral segments to obtain segmental kyphosis, wedging, and intervertebral rotation in the patient plane.[29–31] While providing extensive quantitative data, commercially available programs for biplanar reconstruction still require considerable manual effort in mapping spinal landmarks prior to the automated measurement sequence.[32] In recent years, we have also seen a rise in transdisciplinary studies using machine learning on clinical data to develop in-house programs for predicting curve progression,[7,16,33–36] which involves specialized terminology that may be challenging to digest.

To extract useful clinical points from the diverse range of existing studies, this systematic review aims to identify and investigate 3D parameters derived from biplanar reconstruction as predictors of curve progression. The focus is on nonoperative AIS patients, especially to stratify risk of progression at early visits. In addition, the review aims to summarize current techniques to improve predictive accuracy using machine learning.

Methods

Search strategy and selection criteria

The literature search and reporting of study results were conducted according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement.[37] Three independent investigators (HTSW, DLLW, CHST) performed an extensive search on the following databases: PubMed, Web of Science, MEDLINE, and Cochrane Library. All fields were searched in the databases using the following keywords: (adolescent idiopathic scoliosis) AND ((biplanar) OR (3D) OR (three-dimensional)) AND ((progression) OR (alignment) OR (prognosis)). The search was limited to publications from 1 January 1996 to 31 December 2023 to exclude obsolete techniques in generating 3D spinal models. The full search strategy can be seen in Supplementary Table i. Potentially relevant abstracts were screened based on the inclusion and exclusion criteria (Table I), and full-text articles were obtained for eligible results. The references of each included article were screened for any other pertinent articles (see Supplementary Table ii). Any discrepancies in the final decision of inclusion were settled through discussion with all authors.

Data extraction and critical appraisal

The primary outcome of this systematic review was the efficacy of 3D parameters derived from biplanar radiographs as predictors of curve progression in nonoperative AIS, which was reported using statistical measures including sensitivity and specificity, positive predictive value (PPV), negative predictive value (NPV), area under the curve (AUC), root mean square error (RMSE), and R-squared (r^2). The secondary outcome was to summarize methods to improve prediction analysis involving geometrical models.

The 3D parameters derived from biplanar radiographs include Cobb angle, coronal tilt, thoracic kyphosis (TK), lumbar lordosis (LL), apical vertebral rotation (AVR), intervertebral rotation at the upper junctional zone (upper IAR), intervertebral rotation at the lower junctional zone (lower IAR), angle of the plane of the maximum curvature (POMC), torsion index (TI), hypokyphosis index, and vertebral and/or disc wedging in the frontal and sagittal planes. Detailed descriptions of the included parameters are shown in Supplementary Tables iv to vi.

Other information regarding the study design, sample size, patient population, predictors identified, risk of bias, and level of evidence can also be viewed in the Supplementary Material.

Risk of bias

Three independent reviewers (HTSW, DLLW, CHST) assessed the risk of bias for the included longitudinal studies using the six domains of the Quality in Prognostic Studies (QUIPS).[38] For retrospective studies, bias due to attrition is not applicable and therefore not assessed. The QUIPS risk of bias for these studies is detailed in the Supplementary Table iii. Cross-sectional studies were assessed using the Appraisal tool for Cross-Sectional Studies (AXIS).[39] Due to lack of a scoring system, overall results will be described using mean number of items achieved and any notable underperformance in particular items will be reported. Any discrepancy was discussed with all authors until a consensus was reached.

Grading of evidence

The three reviewers assessed the quality of evidence of the outcomes according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.[40] All included studies in this review were

Table I. Inclusion and exclusion criteria.

Inclusion criteria	Exclusion criteria
• Patients with nonoperative adolescent idiopathic scoliosis • Studies reporting 3D parameters derived from 2D and biplanar radiographs as predictors of curve progression	• Biomechanical or cadaveric studies • Case reports, conference summaries, unpublished literature, commentaries, and reviews • Sample size fewer than 10 • Studies including patients with idiopathic scoliosis of non-adolescent type, or non-idiopathic scoliosis caused by known pathologies such as trauma, congenital conditions, or infections

observational studies and were thus initially assigned as having a low level of evidence, according to GRADE guidelines.[40] Downgrading of quality of evidence was done according to the five domains in the GRADE guidelines: risk of bias,[41] imprecision,[41,42] indirectness,[43] inconsistency,[41] and publication bias.[44] Meanwhile, the quality of evidence was upgraded based on large magnitude of effect, dose-response gradient, and plausible confounding that can increase confidence in estimated effects.[45] The overall quality of evidence is detailed in the Supplementary Tables vii to viii.

Search results

The search results are illustrated in the PRISMA flowchart (Figure 1). A total of 915 articles were yielded from the initial search, of which 183 articles were from MEDLINE, 299 articles from Web of Science, 37 articles from Cochrane library, and 396 articles from PubMed. Of the 915 articles, there were 538 duplicated articles, and 377 unique articles were screened for the inclusion and exclusion criteria. As a result, a total of 31 articles were included in the final study for further analysis.

Among the 31 articles included, 16 were cross-sectional studies, 13 were retrospective cohort studies, one was a prospective cohort study, and another a prospective case-control study. Sample sizes ranged from ten to 321 AIS subjects. Overall, nine studies included patients with mild curves (< 20°) exclusively, while the remaining studies included moderate (20° to 40°) or severe curves (> 40°). The mean age of subjects across studies was 13.3 years (10 to 18) and the length of follow-up ranged from three months to eight years. Progression was defined by most studies as interval increase in Cobb angle > 5°, or the initiation of brace treatment as determined by an orthopaedic specialist. The overall risk of bias for included studies was low. For cross-sectional studies, the mean number of AXIS items accomplished was 19.2 (standard deviation (SD) 1.0; 17 to 20), with cohort base being the most frequently violated item, followed by eligibility criteria.

Results

Coronal plane

For patients with mild curves, there is moderate evidence from five studies supporting 3D Cobb angle as a weak predictor for differentiating the risk of curve progression. Wang et al[19] and Nault et al[46] reported no significant difference in initial 3D Cobb angle comparing progressive and non-progressive groups. The two studies each had considerable sample sizes compared to 3D reconstruction studies in the literature, with 490 subjects and 172 subjects, respectively. Vergari et al[16,17] also found initial 3D Cobb angle to be similar (mean difference < 3°) between progressive and non-progressive groups, but did not present results of statistical comparison. Aside from 3D Cobb angle, Nault et al[47] also reported coronal apical disc wedging as a statistically significant predictor of final Cobb angle (β = 0.820; p = 0.016). However, the effect is small, and prior study by the same group of authors found no difference in initial coronal apical disc wedging between progressive and non-progressive groups.[46] Almansour et al[48] used coronal tilt to characterize segmental lateral displacement in the frontal plane. However, changes in coronal tilt after bracing largely reflected reduction in Cobb angle and provided little additional information.

Sagittal plane

In our included studies, 3D thoracic kyphosis (3D TK) and sagittal wedging were the most frequently reported sagittal parameters. There is weak evidence supporting 3D TK as a predictor of curve progression from three studies.[18,46,49] In a study of 172 patients, Nault et al[18] reported weak correlation between 3D T4-T12 TK at first visit and final 3D Cobb angle (r = –0.288, p = 0.01). Another study by the same group of authors[46] reported that patients with progressive curves had lower initial 3D T4-T12 TK compared to the non-progressive group (mean 20.6° vs 25.0°; p = 0.02). Conversely, Wang et al[19] reported no significant difference in initial 3D T4-T12 TK between two groups (22.3 (SD 8.5) vs 21.4 (SD 9.2), p = 0.635).

Sagittal vertebral wedging was reported in five studies.[49–53] Begon et al[50] reported that sagittal vertebral wedging is present in mild curves. Scherrer et al[51] reported that vertebral wedging at thoracic apices was associated with increase in Cobb angle. However, statistical evidence supporting its use in predicting curve progression is lacking. A 'hypokyphosis index' was mentioned in two studies,[49,53] which was a function of wedging of the apical vertebra compared to normal controls. While its replicability is low, the hypokyphosis index was reported to increase predictive accuracy for curve progression. Lastly, none of our included studies reported spinopelvic parameters as curve predictors of significance.

Axial plane

There is moderate evidence from five studies supporting axial rotation and/or TI as good predictors of curve progression (Table II). Among our included studies, AVR, intervertebral axial rotation (IAR), and TI were the most reported parameters representing axial rotation. In sterEOS 3D (EOS Imaging, France), axial rotation is calculated for each vertebra after adjusting for pelvic rotation.[49,54–58] IAR was typically reported for both upper and lower junctions.[59,60] The TI was generally defined as the mean of the two sums of IAR from the lower junction to the apex, and from the apex to the upper junction, as described by Steib et al.[18,46,61,62] Several studies used geometrical modelling to obtain torsion,[16,49,63,64] and Skalli et al[49] incorporated torsion into the 'severity index' for predicting progression.

Among the transverse parameters, Courvoisier et al[65] reported that TI had the highest predictive value (Figure 2) for progression compared to AVR and IAR. When a TI of 3.7 was used as a cut-off, prediction of progression had a sensitivity and specificity of 81% (AUC 0.85 (0.77 to 0.94)). Wang et al[19] analyzed radiographs of patients at the first visit, and reported that while the progressive group had similar Cobb angle, TK, and LL with the non-progressive group, the progressive group had higher AVR and torsion.

Several cross-sectional studies that were included also analyzed differences between Lenke curve types. Despite the lack of serial data, the differences in 3D spinal deformity between curve types may offer insights into the pathomechanism of curve progression. Karam et al[53] reported that thoracic curves, which typically have larger Cobb angles, had the highest TI, while TL curves had the highest AVR. Conversely, Courvoisier et al[65] found that TI was comparable for T and L curves.

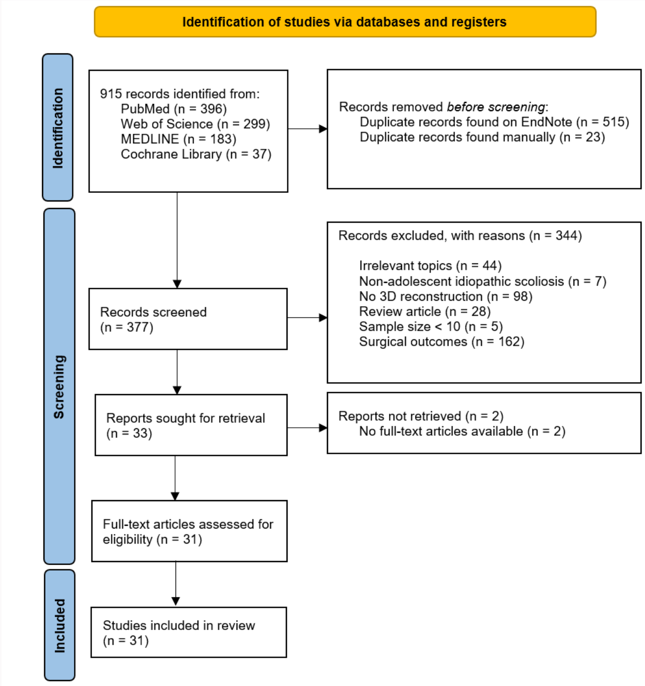

Fig. 1
PRISMA (preferred reporting items for systematic reviews and meta-analyses) flowchart illustrating selection process of articles.

Table II. Comparison of axial parameters between progressive and non-progressive groups.

	Mean Torsion index, ° (SD)			Mean apical vertebral rotation, ° (SD)		
Author	**Progressive**	**Non-progressive**	**p-value**	**Progressive**	**Non-progressive**	**p-value**
Courvoisier et al[65]	7 (2)	3 (1)	< 0.001†	9 (3)	4 (2)	< 0.001†
Wang et al[19]	6 (3)	3 (2)	0.020‡	7 (5)	4 (3)	0.006‡
Nault et al[46]	4.5*	3.1*	0.02‡	8.1*	5.7*	0.006‡
Vergari et al[16]	4.1 (2.1)	5.6 (2.8)	N/A	7.6 (4.1)	6.1 (3.6)	N/A
Skalli et al[49]	6 (3	4 ± 2	< 0.05‡	7 (4)	6 (4)	N/A

Different authors reported the means and standard deviations in different decimal places.
*Nault et al did not report SDs.
†< 0.001.
‡< 0.05.
N/A, not available; SD, standard deviation.

Prediction analysis

Inclusion of cumulative reconstructions was reported to improve prediction accuracy, when compared to only using the spinal reconstruction from the most recent visit (i.e. sequential layering). García-Cano et al[66] reported that the average root mean square error (RMSE) of the spinal model was improved from 10.36 mm to 8.78 mm after considering all reconstructions from prior visits. Regarding the type of prediction model, García-Cano et al[66] reported using a random forest model to directly predict spinal morphology, while Kadoury et al[67] used probabilistic classification model to identify progressive curves, in which the model was reported to be superior to using a support vector machine model.

Five studies used geometrical spinal models instead of conventional 3D parameters, thus the predictors were presented as clusters of 3D morphology,[66] or composite 'black-box' models, in which relative importance of spinal parameters was not specified.[16,49,67,68] Despite the lack of detailed analysis, these studies on a whole demonstrated accurate predictions, with sensitivity ranging from 88% to 92% and specificity ranging from 74% to 84%.

Discussion

3D reconstruction of biplanar radiographs allows comprehensive evaluation of the scoliotic spine and offers robust data for accurately predicting curve prediction. In this review, we have collected and summarized the key predictors of

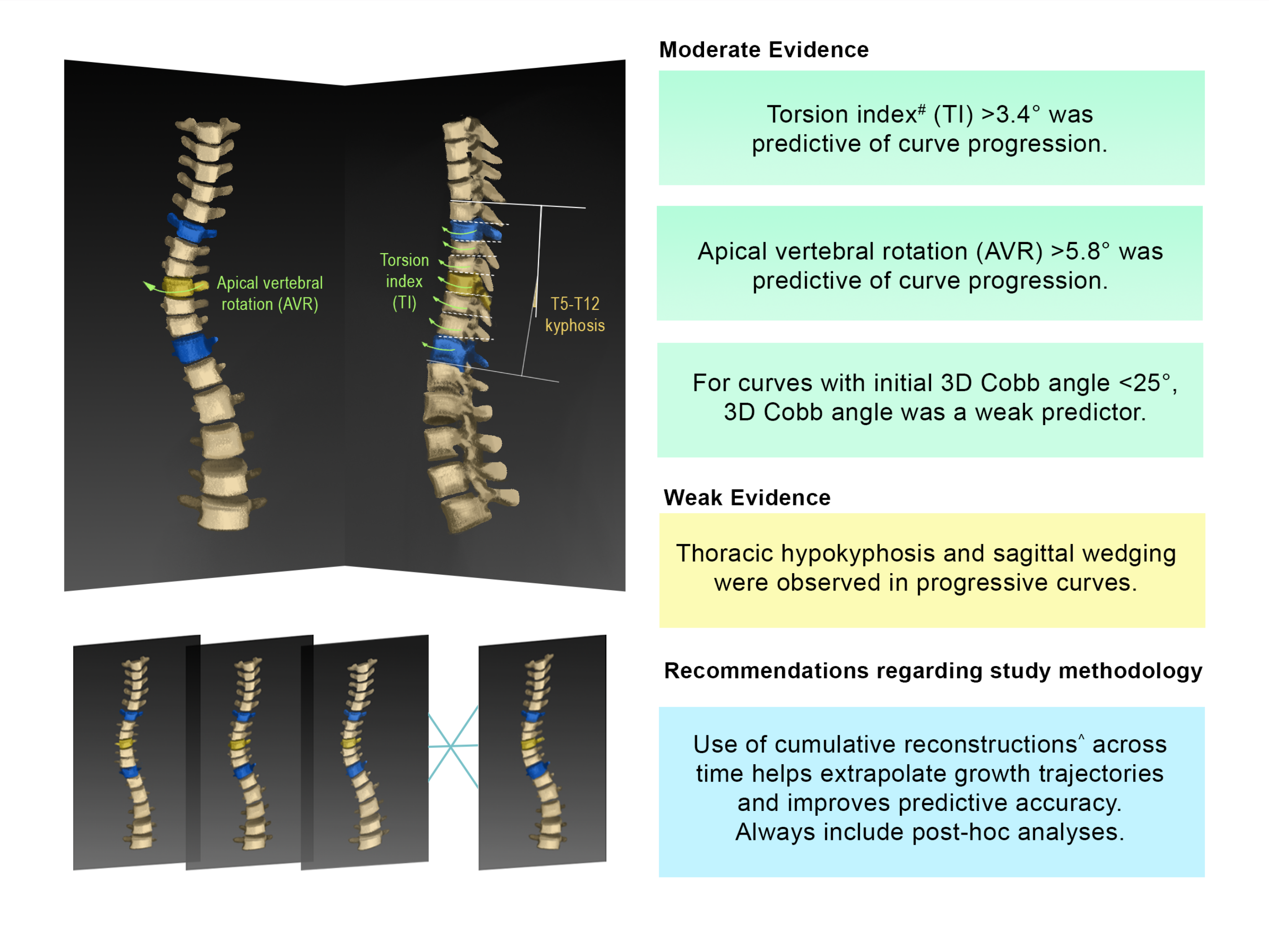

Fig. 2

Summary of important outcomes from the current review. #Torsion index refers to the mean intervertebral rotation within the scoliotic segment. *Hypokyphosis was quantified by 3D T5-T12 thoracic kyphosis as well as sagittal wedging of the vertebra and intervertebral disc, respectively. ^Cumulative reconstruction refers to including all past reconstructions and intermediate output layers in every input layer of the predictive model, as opposed to sequential layering, in which only the most recent spinal reconstruction is included in the input layer.

curve progression in mild curves. TI and AVR, both transverse parameters, were identified as accurate predictors with moderate evidence, while 3D TK and sagittal wedging was identified as predictors with weak evidence (Figure 2). In patients with mild curves, 3D Cobb angle was found to be a weak predictor with moderate evidence. In terms of predictive modelling, using cumulative layering of past reconstructions increases predictive accuracy.

Coronal curvature

It is well established that a larger Cobb angle predisposes to curve progression.[1,7,18] A systematic review by Wong et al[1] found that initial 2D Cobb angle > 25° and thoracic curves were predictive of curve progression. However, most of our included longitudinal studies involves the first radiograph at early visits, when patients are skeletally immature and have mild curves. Nault et al[46] and Wang et al[19] reported no significant differences when comparing initial 3D Cobb angle between progressive and non-progressive groups. The evidence supports the theory that coronal curvature is not the initial trigger of curve progression, which will be elaborated in the following sections. Nevertheless, as Cobb angle acts as a poor predictor at mild stages, the coronal curvature eventually evolves along with wedging and rotation in other planes, which adds predictive value. To evaluate the predictive power of increasing Cobb angle on growing patients, Parent et al[7] compared the accuracy of predictive models based on 2D Cobb angle assessed at different consultations. Relative skeletal immaturity with larger initial 2D Cobb angle and longer duration of observation were associated with curve progression, though the cohort had a larger range of baseline Cobb angle (20° (SD 10°)). The longitudinal study design and clinically oriented reporting present as a strong framework for potential studies using 3D spinal parameters, and can pave the way for accurate predictions at first visits.

Sagittal deformity

While there is no universally accepted theory explaining the pathogenesis of AIS, anterior column overgrowth is a frequently studied phenomenon,[69–75] with ongoing debate surrounding the cause-effect relationship with wedging and rotation.[76,77] Our included studies also reported sagittal wedging in lower junctional vertebrae and discs, which was associated with increases in Cobb angle.[49,51] Among thoracic, thoracolumbar, and lumbar curves, thoracic hypokyphosis was consistently observed in 3D studies.[53,78–80] Using CT reconstruction, Schlösser et al[81] reported that anterior overgrowth was observed in primary and compensatory curves, but not at junctional segments. In contrast, 2D studies have either identified hypokyphosis in thoracic curves only,[82,83] or found that TK in AIS patients was equivocal to controls.[84]

Although further investigations are needed, the current evidence from 3D studies supports thoracic hypokyphosis and sagittal wedging as potential predictors present even in mild curves.[18,49,72] This may be explained by the shift of plane of maximum curvature towards the frontal plane in hypokyphotic patients. The asymmetrical loading on the vertebral bodies due to gravity-induced torque may result in frontal wedging and progressive intervertebral rotation.[75,85,86] While accurate estimation of TK in the patient plane remains challenging on plain radiography,[87,88] algorithms to predict 3D TK based on 2D Cobb and 2D TK present as promising, accessible tools for clinical practice.[89]

Rotation and torsion

Our included studies indicated that axial rotation and TI improved overall accuracy of predicting curve progression. TI > 3.4° was strongly predictive of progression, which was likely because TI is a summative parameter taking in account of all intervertebral rotations across the scoliotic segment, and thus also captures curve types by location. Interestingly, Wang et al[19] reported increase in AVR ahead of TK increase, which remains to be further investigated as the cohort only included 162 subjects. Among curve types, thoracic curves had the highest TI while thoracolumbar curves had the highest AVR, and both had significantly larger Cobb angle than lumbar curves.[53] While a systematic review of 2D predictors by Wong et al[1] has also found that thoracic curves and high AVR were associated with curve progression, characterizing rotation of the whole curve may improve prediction of curve progression.[19,49]

While conventional methods of estimating rotation in daily practice, such as Nash-Moe grading, are limited by low reproducibility,[24] estimation of AVR using 2D Cobb angle and 2D TK,[90] as well as fully automated measurement programmes,[91] both exist as efficient solutions. Digital surface topography devices to quantify spinal and trunk rotation have also become more widely used in place of scoliometers, allowing whole-spine assessment.[92–94]

Prediction analysis

Machine-learning algorithms are capable of processing complex data and generating more accurate predictions compared to traditional regression models. Serial reconstructions arranged in stepwise layers were found to strongly improve prediction accuracy,[7,66] as this allows better extrapolation of growth trajectories. While random forest model and probabilistic classification model were reported as useful prognostication models,[66,67] more complex models, such artificial neural network models,[19,34] have yet to be explored in 3D analysis. Regardless of reconstruction technique, most machine-learning programs can generate a vast amount of quantitative data. While dimensionality reduction tools aids in the extraction and refinement of statistically significant parameters, these often result in complex clusters involving combinations of coronal, sagittal, and axial deformities that are difficult to translate into clinical prognostication. Despite the ability to capture complex deformities, generalizable nomenclature is still necessary for meaningful interpretation. Comprehensive post-hoc analysis is also integral for generating cut-offs and analyzing interactions between spinal parameters, and thus should always be incorporated.

This is the first review to evaluate predictors of curve progression based on 3D reconstruction of biplanar radiographs. There were several limitations in this review. First, due to different methodologies in our included studies in terms of timeframe and reconstruction technique, a meta-analysis could not be performed. For studies using semi-automated methods for variable extraction, more comprehensive characterization of synthesized features would allow better interpretation. Second, publication bias could not be assessed, as most studies did not report effect sizes and confidence intervals. Third, no randomized controlled trials were identified during our search. Nevertheless, the predictors extracted from included studies were rigorously examined for quality of evidence.

In conclusion, TI and AVR were good predictors of curve progression, while more investigations are needed to validate 3D thoracic kyphosis and sagittal wedging as predictors; 3D Cobb angle was found to be a weak predictor. To improve predictive accuracy, machine-learning models based on serial spinal reconstructions can be used to capture the complex interactions between spinal parameters and extrapolate growth trajectories. Future research should include more comprehensive post-hoc analysis with comparison of relative importance among various parameters to facilitate interpretation. In daily practice, algorithms to predict 3D TK and AVR based on 2D parameters, as well as surface topography, can be applied to quickly assess curve morphology.

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Supplementary material

Tables showing the search strategy; details of included studies; risk of bias assessed using Quality in Prognostic Studies (QUIPS); coronal, sagittal, and axial parameters; machine-learning methods; and details of the included 3D parameters.

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