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REVIEW ARTICLE

Scoliosis and Prognosis—a systematic review regarding patient-specific and radiological predictive factors for curve progression

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Abstract

Introduction Idiopathic scoliosis, defined as a > 10° curvature of the spine in the frontal plane, is one of the most common spinal deformities. Age, initial curve magnitude and other parameters define whether a scoliotic deformity will progress or not. Still, their interactions and amounts of individual contribution are not fully elaborated and were the aim of this systematic review.

Methods A systematic literature search was conducted in the common databases using MESH terms, searching for predictive factors of curve progression in adolescent idiopathic scoliosis ("adolescent idiopathic scoliosis" OR "ais" OR "idiopathic scoliosis") AND ("predictive factors" OR "progression" OR "curve progression" OR "prediction" OR "prognosis"). The identified and analysed factors of each study were rated to design a top five scale of the most relevant factors.

Results Twenty-eight investigations with 8255 patients were identified by literature search. Patient-specific risk factors for curve progression from initial curve were age (at diagnosis < 13 years), family history, bone mineral status (< 110 mg/cm^3 in quantitative CT) and height velocity (7–8 cm/year, peak 11.6 ± 1.4 years). Relevant radiological criteria indicating curve progression included skeletal maturity, marked by Risser stages (Risser < 1) or Sanders Maturity Scale (SMS < 5), the initial extent of the Cobb angle (> 25° progression) and curve location (thoracic single or double curve).

Discussion This systematic review summarised the current state of knowledge as the basis for creation of patient-specific algorithms regarding a risk calculation for a progressive scoliotic deformity. Curve magnitude is the most relevant predictive factor, followed by status of skeletal maturity and curve location.

Keywords Adolescent idiopathic scoliosis · Curve progression · Risk factors · Curve location · Skeletal maturity

Introduction

Idiopathic scoliosis, defined as a > 10° curvature of the spine in the frontal plane, is one of the most common spinal deformities. Ninety per cent of all idiopathic scoliosis occurs during adolescence with a prevalence of 1–2% [1, 2]. Most patients are female, at a ratio of 1.5:1 (female/male) in mild scoliosis and a ratio of up to 10:1 (f:m) in scoliosis, with a Cobb angle > 30° [1].

Risk factors for curve progression have been widely analysed with partially inconsistent findings [3–5]. Specifically, personal characteristics, such as sex, age, menarche status and bone mineral density (BMD), are still debated controversially. In a majority of studies, risk factors, such as initial magnitude of curve at first presentation and skeletal maturity status and curve presentation at peak height velocity (PHV), seem to show the highest correlation to curve progression [6, 7]. Nevertheless, most studies are limited due to certain factors, i.e., inclusion of only female patients, only skeletal immature patients, or treated patients without a control group. Moreover, many studies differ in the definition of progress, either as an increase in the analysed Cobb angle or until surgical treatment is

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obtained. In addition, the categorisation of patients along skeletal maturity scales (SMS, Risser sign), as well as determination of PHV are challenging.

Beyond the above-mentioned issues, the interactions of risk factors and amount of individual contribution to curve progression have not yet been fully elaborated. While age is obviously interacting with nearly every other risk factor, other factors seem to be independent, such as BMD or gender. In a previously published systematic review, Noshenkho et al. [8] identified 25 investigations yielding eight clinically assessable risk factors of curve severity or progression of adolescent idiopathic scoliosis (AIS). Furthermore, they reported nearly one-third of patients with brace treatment progressed and approximately 15% finally required surgical correction. However, they only found low evidence, due to limitations of the included studies and since no method for prediction of clinical use could be elaborated [8].

Therefore, the aim of this systematic review was to identify the most contributing patient-specific and radiological risk factors and their influence on curve progression. On the basis of the results, further investigations should be carried out with the overall aim to develop an artificial intelligence (AI) algorithm to predict progression of spinal curve at the time of initial clinical presentation.

Materials and methods

Study design

We conducted a comprehensive systematic review of the literature, according to PRISMA guidelines, including the PubMed and Google scholar databases [9]. The keywords used in the database search were ("adolescent idiopathic scoliosis" OR "ais" OR "idiopathic scoliosis") AND ("predictive factors" OR "progression" OR "curve progression" OR "prediction" OR "prognosis"), (english OR german).

Inclusion and study selection

All studies included were either in the English or German language. The period of analysis was set from 2010 to 2020 to gain new aspects in influencing factors. The authors limited the research to observational and interventional studies. Titles and abstracts were reviewed by two authors (ML and MJS), independently. Duplicates were removed and full texts were screened for suitability. Systematic reviews, meta-analyses as well as reviews, case reports and expert opinion articles were excluded from analysis. Moreover, studies analysing genetic or cellular risk factors were excluded.

Data analysis

Data regarding study design, year of publication, author names, number of patients, sex, age, hereditary, skeletal maturity, initial curve magnitude (as measured by the method of Cobb [10]), type of curve, growth velocity (body height velocity and spinal growth velocity) and progression of curve were extracted. Data were subdivided into (i) patient-specific factors and (ii) radiological parameters for interpretation. The level of evidence was defined based on the suggestions of evidence levels for orthopaedic journals by Slobogean et al. [11]. Where a level of evidence was already provided, it was either adopted or adjusted, if necessary.

Statistical analysis

After thorough discussion with a statistician following statistical measurements, further meta-analysis of the data was rejected due to the large heterogeneity of the studies and limited data provided in some investigations. We identified the top predictive factors of the included studies (if the study examined only one factor, it was regarded as the top factor) and generated a list of the five most relevant predictive factors in AIS.

Results

The initial research identified 1772 potentially eligible publications in both databases. After screening for titles and abstracts, 76 studies were left for analysis. After full text analysis, 28 studies were finally included in the systematic review. The further selection process is outlined by PRISMA flow chart in Fig. 1. In summary, 28 studies with 8.255 patients were identified, including patient-specific and radiological parameters. Twenty-one were retrospective investigations, five prospective and two biomedical simulation studies. Table 1 shows the studies included for analysis and their characteristics. The mean level of evidence of all studies was 3.08.

By analysing the studies' most examined factors and their individual contribution sorted within the studies, we generated a list of the top five factors that influence and predict curve progression in AIS. This Top 5-list of identified risk factors influencing curve progression included:

(1) Curve magnitude (initial presentation),
(2) Skeletal maturity (Risser, SMS, proximal humerus, distal radius/ulna),
(3) Curve location (thoracic or double-thoracic),

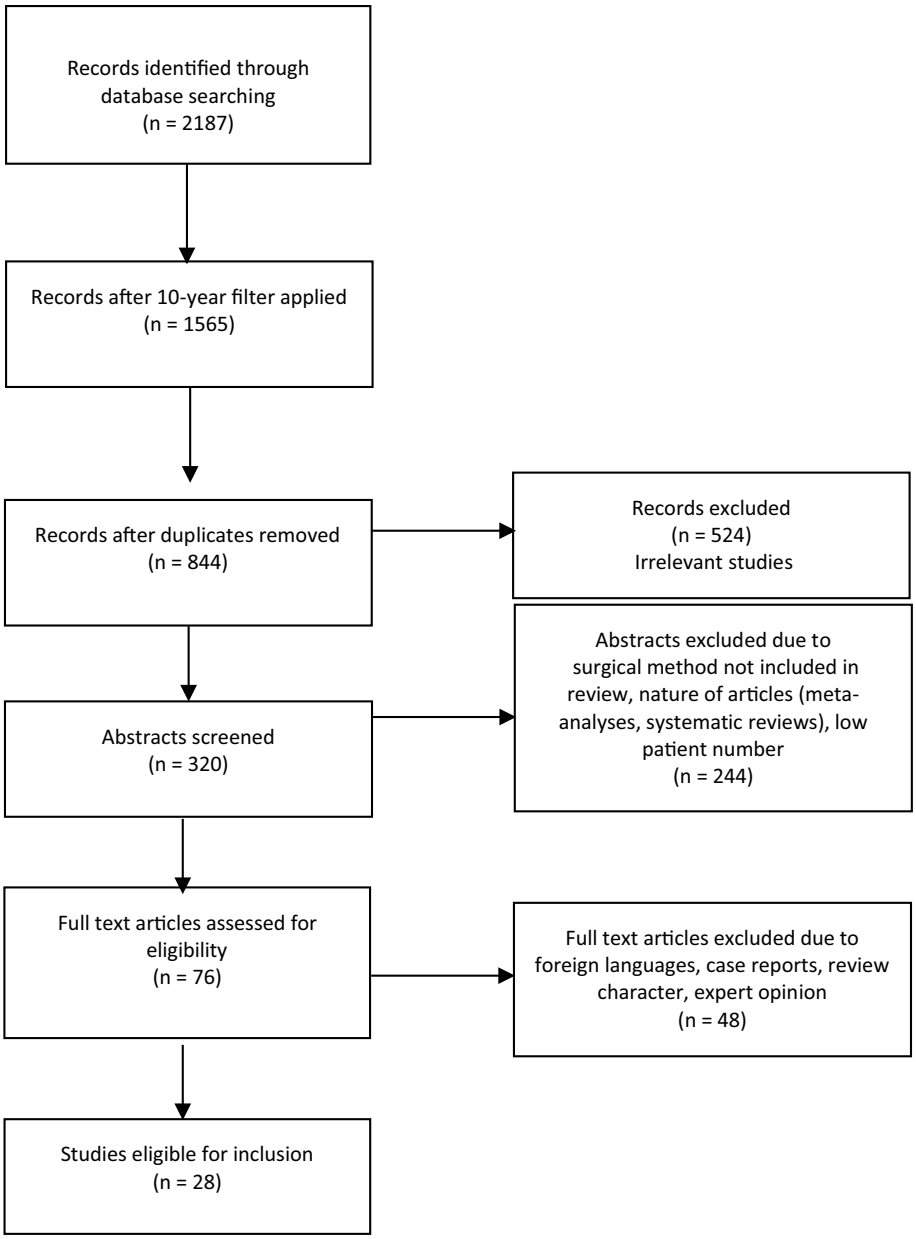

Fig. 1 Outline of literature research according to PRISMA guidelines

(4) Age,
(5) Status of menarche.

Patient-specific risk factors

Age

Age is one of the most important factors, as it is naturally linked to growth, skeletal maturity and consecutively to the onset of menarche in female patients. In their retrospective cohort study including 1464 patients, Lee et al. [6] stated that age was a relevant prognostic factor, with the age at risk of < 11.3 years. The impact of age decreased with age and height. Using Cox regression models, moderate effects between age and gender and age and initial curve were found.

PHV

Chazono et al. [13] published data of 56 skeletal immature patients reporting median PHV as 8.5 cm/year (non-surgical group [NS]) and 8.9 cm/year (surgical group [S]). A height velocity of > 7 cm/year suggested onset of PHV. Chronological age at PHV (APHV) was 11.9 and 11 years (NS vs. S group, respectively), narrowing PHV down to ages 11–12 years. Height at PHV (HPVH) was 152.9 and 149.3 (NS vs. S group, respectively).

Table 1 Characteristics of analysed studies

Author	Year	Number of subjects	Study design	Evidence level	Country	Relevant factors
Aulisa et al. [12]	2017	134	Prospective study	3	Italy	(1) Hump dimension (2) Curve magnitude
Chazono et al. [13]	2015	56	Retrospective study	3	Japan	(1) Curve magnitude at PHV
Chen et al. [14]	2011	217	Retrospective case review	3	China	(1) Curve flexibility
Cheung et al. [15]	2018	513	Prospective study	2	China	(1) Skeletal maturity (2) Curve magnitude
Dolan et al. [16]	2019	115	Prognostic validation study	3	USA	(1) Curve magnitude (2) Curve location (3) Skeletal maturity
Drevelle et al. [17]	2010	12	Biomedical simulation	4	France	(1) Anterior spinal growth (2) Decrease of disc's mechanical stiffness
Grauers et al. [18]	2013	1463	Retrospective case study	3	Sweden	(1) Family history (2) Curve magnitude
Grothaus et al. [19]	2019	89	Retrospective research study	3	USA	(1) Curve magnitude (2) Skeletal maturity
Guo et al. [20]	2012	60	Pprospective study	2	China	(1) Skeletal maturity (2) Pelvic tilt and T1-spinopelvic inclination
Lara et al. [21]	2017	738	Retrospective study	3	USA	(1) Curve magnitude (2) Age
Lee et al. [6]	2012	1464	Retrospective cohort study	3	China	(1) Curve magnitude (2) Age (3) Menarche status
Li et al. [22]	2017	36	Retrospective study	4	China	(1) Curve magnitude (2) RAV + L5 TA
Li et al. [23]	2019	216	Retrospective case review	4	USA	(1) Skeletal maturity
Li et al. [24]	2020	40	Retrospective consecutive longitudinal study	3	China	(1) Skeletal maturity (2) Spinal growth velocity
Morrison et al. [25]	2015	84	Retrospective case review	4	Canada	(1) SPA (2) AVR
Nault et al. [26]	2010	100	Retrospective cross sectional descriptive study	4	France	(1) Skeletal maturity
Nault et al. [27]	2013	37	Biomedical simulation	4	France	(1) 3D Spine morphologic parameters
Neal et al. [28]	2018	452	Retrospective review	3	USA	(1) Skeletal maturity
Ohashi et al. [29]	2018	56	Retrospective study	4	Japan	(1) L3/4 Tilt significant (2) Curve location
Ramo et al. [30]	2019	143	Retrospective study	3	USA	(1) Skeletal maturity (2) Menarche Status
Shi et al. [31]	2016	62	Retrospective study	3	China	(1) PHV + PSGV (2) Curve magnitude
Sitoula et al. [32]	2015	161	Retrospective case review	3	USA	(1) Curve magnitude (2) Skeletal maturity
Smorgick et al. [33]	2019	163	Retrospective study	3	Israel	(1) Curve location
Song et al. [38]	2018	1	Biomedical simulation	5	China	(1) Bone mineral status
Wang et al. [34]	2010	290	Retrospective study	3	China	(1) Radius dimension ratio (RD/RL) + skeletal growth
Ward et al. [35]	2020	738	Prospective cohort study	2	USA	(1) Curve magnitude (2) Skeletal maturity
Yip et al. [36]	2016	513	Prospective consecutive longitudinal study	2	China	(1) BMD (2) Curve magnitude
Zapata et al. [37]	2019	302	Retrospective case review	3	USA	(1) Curve magnitude (2) Skeletal maturity

RAV rotation of apical vertebrae, *TA* tilt angle, *SPA* spinous process angle, *AVR* apical vertebrae rotation, *PHV* peak height velocity, *PSGV* peak spinal growth velocity, *RD* radius diameter, *RL* radius length, *BMD* bone mineral density

Family history

With numerous findings regarding hereditary aspects in AIS, the cause of scoliosis seems to rely on several genetic aspects. Grauers et al. [18] published data of 1463 patients revealing a significant difference in maximum curve size between patients with one or more relative (any kind) with scoliosis (median = 35°, interquartile range = 25) and patients without any relative with scoliosis (median = 32°, interquartile range = 23) ($p = 0.022$). Moreover, the odds ratio (OR; 95% confidence interval [CI]) for having a Cobb angle of > 40° or more was 1.30 (1.05–1.6) if the patient had a family history of scoliosis [18].

Gender

Gender as a risk factor continues to be debated, in regards to curve progression. Smorgick et al. [33] presented data of 163 patients with indications for surgical correction and could not find significant differences in curve severity or progression of curve.

BMD

Regarding BMD, two studies were found for analysis. Yip et al. [36] published data of 513 patients, with 169 subjects displaying osteopenia with a mean follow-up of 4.6 years. Osteopenic AIS patients had a significantly later menarche age (12.2 vs. 13.1 years) and taller standing heights (155.7 cm vs. 152.7 cm). Following univariate and multivariate analysis, the risk of progression decreased with maturity (age and menarche status), but increased with initial curve magnitude. With significant difference, osteopenic AIS patients have a twofold higher risk of progressing to surgical level (hazard ratio [HR] = 2.25, 95% CI = 1.2–4.2). In 90 patients receiving high-resolution peripheral quantitative computed tomography (HR-pQCT) of distal radius, cut-off values of Cobb angle > 24° and D_{cort} (volumetric density of cortical bone measured at distal radius) less than 570 mg HA/cm^3 were found to showing curve progression. A biomedical simulation study supporting the role of BMD in AIS was published by Song et al. [38]. Their finite element model, based on a 14-year-old male patient with Lenke Type 1 curve and Cobb angle of 31°, showed curve progression when grading the bone mineral status in normal, osteopenia and middle-grade osteoporosis (200, 110 and 50 mg/cm^3 in quantitative CT, respectively).

Hump dimensions

Aulisa et al. [12] found a significant correlation of hump dimensions and curve severity at the beginning and end of brace treatment in an investigation of 134 patients, except of lumbar curves at baseline. The change of hump dimensions was more evident than the change of curve correction.

Radiological parameters

Initial curve magnitude, curve location and form of curve

In a risk classification study, Lee et al. [6] found initial curve magnitude to be the most important factor for risk of progression in a set of 1464 subjects. At highest risk were patients with Cobb angle > 26° (HR = 8.8), while lowest risk patients were recorded with an initial Cobb angle < 18° (HR = 1) [6]. Initial curve magnitude was seen as a relevant predictive factor by Sitoula et al. [32]. They found that in Sanders Stage 2 (SS), patients with an initial Cobb angle > 25° progressed, and SS1 and SS3 patients with initial Cobb angles > 35° also progressed [32]. All patients with initial Cobb angles > 40° progressed, however, none of the patients with initial Cobb angles < 30° in SS 5–7 showed progression [32]. Lara et al. [21] published retrospective data of 72 patients of African-American background who were assessed for curve progression in AIS. Higher curve magnitude at presentation was significantly associated with further curve progression [21]. This finding was also supported by Cheung et al. [15]. Performing receiver operating characteristics (ROC) analysis for PHV and curve magnitude and form, Chazono et al. [13] report an initial Cobb angle of 31.5° at PHV as the cut-off for progression in single curve and 30° in double curves. Zapata et al. [37] found similar progression rates (> 5° Cobb angle) in skeletal immature patients (Risser 0 and 1) and mild forms of scoliosis. Patients with curves 20–24° did not progress significantly more than patients with curves 15–19° (mean progression of 10° vs. 9°).

Dolan et al. [16] found a higher risk of progression when one or more thoracic curves was found at initial presentation. Morrison et al. [25] demonstrated a significant correlation of spinous process angle (SPA) with Cobb angle, as well as apical vertebrae rotation (AVR). Therefore, SPA and AVR represent further radiological parameter that predict Cobb angle. Ohashi et al. [29] found significant curve progression in patients with higher L3 and L4 tilt (> 16°) in skeletal maturity. Guo et al. [20] published data regarding 60 patients with bracing showing that mean pelvic tilt, T1-spinopelvic inclination and T9-spinopelvic inclination angles were independent predictors for curve progression. Pre-bracing pelvic tilt ≤ −0.5° was strongly predictive and T1-spinopelvic inclination ≤ 3.5° was moderately predictive in curve progression during brace treatment. Regarding curve flexibility in bending x-rays, Chen et al. [14] demonstrated that in patients with Risser < 5, Cobb angle and

curve location were significantly related to curve flexibility, whereas in Risser = 5, the reduction in flexibility increased. Drevelle et al. [17] presented a biomedical simulation study evaluation 12 patients with mild scoliosis and six asymptomatic ones. After 3D reconstruction of the spine, a patient-specific finite element model was used. They found that in pre-existing scoliosis, anterior spinal growth with a decrease of disc mechanical stiffness could lead to progression of scoliosis [17]. Further spinal parameters were assessed by Nault et al. [27], who analysed the spinal morphology data of 37 patients using 2D and 3D computerised measurements. They stated that disc wedging is followed by the vertebral body.

Annual curve progression (ACP)

Several studies analysed an ACP defining the growth of the Cobb angle over one year. In a prospective cohort study, Ward et al. [35] found ACP was not linear over time in curves > 40° Cobb angles in 738 patients. Mean ACP was 6.3 ± 10.4°, yet, in the first year of follow-up, ACP was 11.5. After 1–2 years of follow-up, ACP was 8.2 ± 8.8° and at 2–5 years, ACP was 3.7 ± 4.1°, with average follow-up of 3.2 years. The ACP is supposed to be at its maximum immediately after the Cobb angle reaches 40°. In the literature, a progression rate of > 1° of the Cobb angle in cases of severe scoliosis (Cobb > 40°) is widely accepted [4, 39, 40]. Ohashi et al. [29] presented a general ACP of 0.41°/year in cases of > 40° Cobb angle and skeletal maturity with a follow-up of 25 years (± 6.9 years). Grothaus et al. [19] published an ACP of 2.3°/year in a follow-up of 2 years in patients with > SS7 and < 50° at initial examination. Ramo et al. [30] presented the data of skeletal immature patients with a delay for surgical correction of severe scoliosis, which, in 6 months' progression in Risser 0 was 1.6°/month, while in Risser 1–5, it was only 0.4°/month.

Skeletal maturity

In a validation study, Sitoula et al. [32] found a strong predictive correlation between SS and initial Cobb angle in prediction of curve progression in AIS. In 161 patients, curve progression > 50° was found in 58 patients. Curve progression in SS2 patients with initial Cobb angles > 25° progressed, while in SS1 and SS3 patients with initial Cobb angles > 35° progressed. All patients, regardless of SS with initial Cobb angles > 40°, progressed. In their prospective study, Cheung et al. [15] found Risser 0 as significant predictor of surgical threshold, but the classification up to Risser 3 are still at risk for progression, despite inability to set up a significant prediction model for Risser stages. In 2010, Nault et al. [26] published matching European and US Risser stages in 100 female patients. Although moderate agreement between the US and European grading systems was seen, Risser stages were not good predictors of the curve acceleration phase. They introduced a new group, Risser 0 with closed triradiate cartilage, and Risser 1, which were the best predictors of the beginning of the acceleration phase. Triradiate cartilage was considered to be another sign classifying skeletal maturity, however, triradiate cartilage cannot be graded in to steps.

Cheung et al. [15] analysed prediction of curve progression using the distal radius and ulna (DRU) classification, displaying that at stage R6/U5, curves are likely to progress > 40° in Cobb angle when initial Cobb angle was approximately 25°. In initial curves of ≥ 35°, regardless of skeletal maturity, progression was found. In the case–control study of Dolan et al. [16] with 115 patients validating the SMS scale for skeletal maturity, it was demonstrated that untreated patients were much more likely to progress to severe scoliosis. At high risk of progression were patients with an SMS of 1–2 and Cobb angles of > 16°. Differentiation in SMS2 and SMS3 patients, however, seems to be essential, due to timing of PHV.

In addition to Risser's sign and SMS, the status of the triradiate cartilage is another marker of skeletal maturity. Ramo et al. [30] marked open triradiate cartilage as a significant risk factor for severe curve progression. Wang et al. [34] presented the radius dimension ratio (Radius Diameter/Radius Lenght), showing significantly lower ratios in patients with severe AIS and a ratio that correlated with curve severity ($r = -0.120$; $p = 0.039$). In 2019, Li et al. [23] published data of 216 patients, presenting a new classification in skeletal maturity according to the stages of humeral head ossification. They found significant reliability in intra-observer and inter-observer correlation coefficients of 0.97 and 0.92, respectively, among eight investigators. The combination of the proximal humeral ossification system and Sanders Hand System was capable of predicting PHV more accurately, compared to a combination of Risser and triradiate closure. In 2020, Li et al. [24] presented the DRU scoring system analysing ossification. They demonstrated a significant correlation combining radius and ulna scores in 40 patients, predicting PHV with an intra-observer score of 0.94 and inter-observer reliability of 0.93.

Discussion

Idiopathic scoliosis is the most common spinal deformity seen in adolescence with severe sequelae, and if curve progression is not stopped, the need for surgical correction is often inevitable. At a patient's initial presentation, prediction of further curve progression is key in managing therapy. An algorithm for risk analysis of curve progression would serve as a great support for patients and their families. In our systematic review, we found several predictive factors

that were correlated with a higher risk of curve progression. In particular, initial curve magnitude and status of skeletal maturity were the most relevant factors to predict curve progression, followed by curve location, age and status of menarche. However, these factors are still considered independently and their interactions have not yet been further investigated. When developing an algorithm for risk analysis in curve progression of AIS, the focus should be on radiological parameter accessible during clinic visits requiring the least radiation as possible.

Focusing on radiological parameters, the initial curve magnitude at presentation seems to be one of the most important risk factors for curve progression (Table 2). With several studies highlighting the significant correlation of initial curve magnitude with risk for progression, initial curve magnitude is a radiological parameter that is easy to diagnose in standard radiographs. In the studies dealing with initial curve magnitude that were included in this analysis, a Cobb angle > 25–28° at initial presentation was mainly correlated to curve progression to > 50° of Cobb or to surgical intervention. Certainly, as the patients in adolescence are still in the growth phase, the actual curve progression also depends on skeletal maturity.

Interestingly, the curve location, which is also easily diagnosed, was found significant in the investigation of Dolan et al. [16]. In their Akaike information criterion (AIC) model, they presented that thoracic curves were more likely to progress than lumbar or thoracolumbar curves (OR = 4.09). However, two other studies did not find any significance in curve location [32, 21].

Skeletal maturity is another major risk factor in terms of progression [13, 32, 15, 16, 23, 24]. Controversial findings exist regarding the actual categorisation mechanism, with numerous studies highlighting inadequate predictability of further growth by Risser stages, and Risser classification being dependent on descent or bone mineral status [26]. Tanner and Whitehouse used DRU scores to establish a different method for determining skeletal maturity in adolescence [41]. Sanders, however, reported the lowest correlation of radius/ulna scores to curve acceleration phase [42], and DRU scores were modified by Luk et al. [43]. Neal et al. [28] documented a higher correlation to skeletal ossification based on SMS rather than Risser, but Risser is still significant, as confirmed by Sitoula et al. [32], who reported significant predictive probability for SMS and Risser stages. Moreover, recently published additional classification systems, such as the distal radius and ulna score, as well as the proximal humerus ossification scale, may allow for even further evaluation of stages at risk, as demonstrated by Li et al. [23, 24].

With regard to additional radiological parameters, specifically sagittal parameters, such as L3/4 tilt, pelvic tilt, T1 and T9 spinopelvic inclination, SPA and apical vertebrae angle, are parameters easily to analyse in standard radiographs and do not require additional radiation. These new parameters should be evaluated further in prospective studies.

Table 2 Radiological parameters regarding risk of progression

Author	Level of evidence	Initial curve magnitude	Skeletal maturity	Curve location	Additional radiological signs
Chazono et al. [13]	3	Significant	–	–	–
Cheung et al. [15]	2	–	Significant°	–	–
Dolan et al. [16]	3	–	Significant*	Significant	–
Guo et al. [20]	2	–	–	–	Pelvic tilt, T1- and T9-spinopelvic inclination
Lara et al.[21]	3	Significant	–	Not significant	–
Li D. et al. [23]	4	–	Significant^{+}	–	–
Li Y. et al. [24]	3	–	Significant°	–	–
Li Z. et al. [22]	4	Significant	–	–	AVR, L5 tilt angle
Morrison et al.[25]	4	–	–	–	SPA AVR
Ohashi et al. [29]	4	–	–	–	L3/4 tilt significant
Sitoula et al. [32]	3	Significant	Significant*	Not significant	–
Wang et al. [34]	3	–	–	–	Radius dimension ratio (RD/RL)

RAV rotation of apical vertebrae, *SPA* spinous process angle, *AVR* apical vertebrae rotation, *RD* radius diameter, *RL* radius length

*measured by either Risser stage or SMS

°measured by distal radius and ulna ossification stage

$^{+}$measured by proximal humerus ossification stage

Patient-specific risk factors

Identified patient-specific risk factors included age (age at diagnosis < 13 years), positive family history, bone quality and mineral status. The trend regarding female patients exhibiting earlier onset of scoliosis and higher prevalence of greater curve magnitude may be in contrast to the actual risk of curve progression, which seems not to be gender dependent. Smorgick et al. [33] could not demonstrate a significant difference in gender regarding curve severity or progression. The authors did, however, postulate a male trend of lower thoracic flexibility, compared to female patients, assumingly increasing the failure rate of brace treatment and less effective surgical correction [44]. These findings are consistent with previous studies on gender regarding scoliosis severity [45, 46]. Therefore, gender cannot be seen as significant risk factor for severe curve progression. Regarding bone quality, based on the clinical data of Yip et al. [36] and the simulation data of Song et al. [38], BMD seems to be a consistent risk factor for curve progression in AIS. However, both studies have limitations, as activity levels and nutrition levels were not analysed. As a result, the concern of BMD causing AIS or scoliosis and back pain, leading to decreased activity resulting in lower BMD, remains elusive. In patients with positive family history, more severe curves are seen in patients with one family member. With regard to the top five predictive factors, age is the one factor that influences status of skeletal maturity and menarche. Patient-specific risk factors, however, seem to be more of a yes–no scheme in terms of risk, although radiological factors present a more significant risk.

Limitations

This systematic review should identify all radiological parameters associated to the risk of curve progression and may be used as clinical markers on standardised radiographs. The mean level of evidence of the included studies is 3.08. As recently published by Noshenkho et al., the study's characteristics show high heterogeneity and level of evidence remains low in observational studies. The paucity of good, randomised controlled clinical studies reveals the necessity to increase research in this field and additional studies should mainly include the predictive factors found by our systematic review.

Conclusion

In summary, several risk factors of curve progression in AIS have been identified in recent years. Especially, radiological parameters, which are more objective, seem to have highest value in predicting risk of curve progression. Summarising the majority of parameters showing significance, the most relevant factors found are the initial curve magnitude and status of skeletal maturity. These two factors may successfully predict the risk of progression of AIS. Factors such as age, status of menarche, BMD and other radiographic parameters might influence the amount of curve progression and should be reflected as well. Unfortunately, no further meta-analysis was possible due to high heterogeneity and lack of evidence within the included studies. Hence, new investigations regarding this topic should analyse the main factors identified thus far. Finally, designing an AI model based on patient-specific factors and radiological parameters calculating individual risk of progression would be desirable.

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Declarations

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