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REVIEW ARTICLE

Current models to understand the onset and progression of scoliotic deformities in adolescent idiopathic scoliosis: a systematic review

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Abstract

Purpose To create an updated and comprehensive overview of the modeling studies that have been done to understand the mechanics underlying deformities of adolescent idiopathic scoliosis (AIS), to predict the risk of curve progression and thereby substantiate etiopathogenetic theories.

Methods In this systematic review, an online search in Scopus and PubMed together with an analysis in secondary references was done, which yielded 86 studies. The modeling types were extracted and the studies were categorized accordingly.

Results Animal modeling, together with machine learning modeling, forms the category of black box models. This category is perceived as the most clinically relevant. While animal models provide a tangible idea of the biomechanical effects in scoliotic deformities, machine learning modeling was found to be the best curve-progression predictor. The second category, that of artificial models, has, just as animal modeling, a tangible model as a result, but focusses more on the biomechanical process of the scoliotic deformity. The third category is formed by computational models, which are very popular in etiopathogenetic parameter-based studies. They are also the best in calculating stresses and strains on vertebrae, intervertebral discs, and other surrounding tissues.

Conclusion This study presents a comprehensive overview of the current modeling techniques to understand the mechanics of the scoliotic deformities, predict the risk of curve progression in AIS and thereby substantiate etiopathogenetic theories. Although AIS remains to be seen as a complex and multifactorial problem, the progression of its deformity can be predicted with good accuracy. Modeling of AIS develops rapidly and may lead to the identification of risk factors and mitigation strategies in the near future. The overview presented provides a basis to follow this development.

Keywords Adolescent idiopathic scoliosis · Modeling · Pathogenesis · Biomechanics · Curve progression

Introduction

SCOLIOSIS (literally: "twisted disease") is an abnormal rotation and curvature of the spine. There are four types of scoliosis: congenital scoliosis, neuromuscular scoliosis, adult de novo scoliosis, and adolescent idiopathic scoliosis (AIS) [1]. As the physical mechanism underlying AIS is unknown, many studies are carried out to create a better understanding of the etiopathogenesis and biomechanical effects of AIS.

A substantial number of these are modeling studies, in which representations of AIS are constructed and manipulated to investigate contributing factors and their possible effects. For some types of modeling, review studies have been carried out [2–5]. However, these reviews address only one type of modeling. There is no literature that provides an overview of all modeling on the onset and progression of the scoliotic deformities.

The aim of the current study is, therefore, to provide a structured overview of all modeling studies that have been done to (1) to understand the mechanics underlying scoliotic deformities, (2) predict the risk of curve progression in AIS, and (3) substantiate etiopathogenetic theories. The focus is

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not on genes and hormones per se, but rather on their phenotypic effects (e.g., bone structure or ligament stiffness [6]) in the initiation and progression of AIS. To achieve this, a systematic literature review was performed, in which publications were classified and subsequently discussed per modeling type.

Methods

Literature search

A literature search was done in two large electronic databases: Scopus and PubMed (Fig. 1). Only journal articles and reviews written in English were included. The search terms "Adolescent idiopathic scoliosis" AND "Model*" yielded 639 hits in Scopus and 515 in PubMed.

Evaluation criteria

Since the cause of AIS is unknown, it was determined that studies which induced scoliosis mechanically, e.g., by damaging tissues or the insertion of implants, are excluded as they essentially do not address the initiation and/or progression of idiopathic scoliosis. Also, the design of implants, braces, screws or other types of instrumentations were excluded. On the other hand, surgical strategies resulting in scoliotic deformities, but of which the exact cause-and-effect relationship is unknown (e.g., a pinealectomy) were included.

The term modeling refers to the construction and manipulation of representations of certain phenomena, in this case the onset and progression of scoliotic deformities. More specifically, studies that used reconstructions to drive a machine learning algorithm, for example to predict curve progression or assess Risser grade were included.

Searching results and categorization

At first, the results from Scopus were evaluated following the aforementioned evaluation criteria (Fig. 1). This evaluation of the 639 hits yielded 53 publications. Subsequently, the results from PubMed were evaluated and doubles were eliminated. This evaluation yielded 16 additional publications, bringing the total to 69 publications. The reference list of these 69 publications were then analyzed for additional publications. This resulted in a total of 86 publications.

The type of modeling was extracted by closely studying the Methods section of the papers and categorized in subgroups, with the use of the *ACRREx* method. ACRREx stands for Abstracting, Categorizing, Reflecting, Reformulating, and Extending [7]. It is a systematic method of mechanical design to categorize knowledge to find voids.

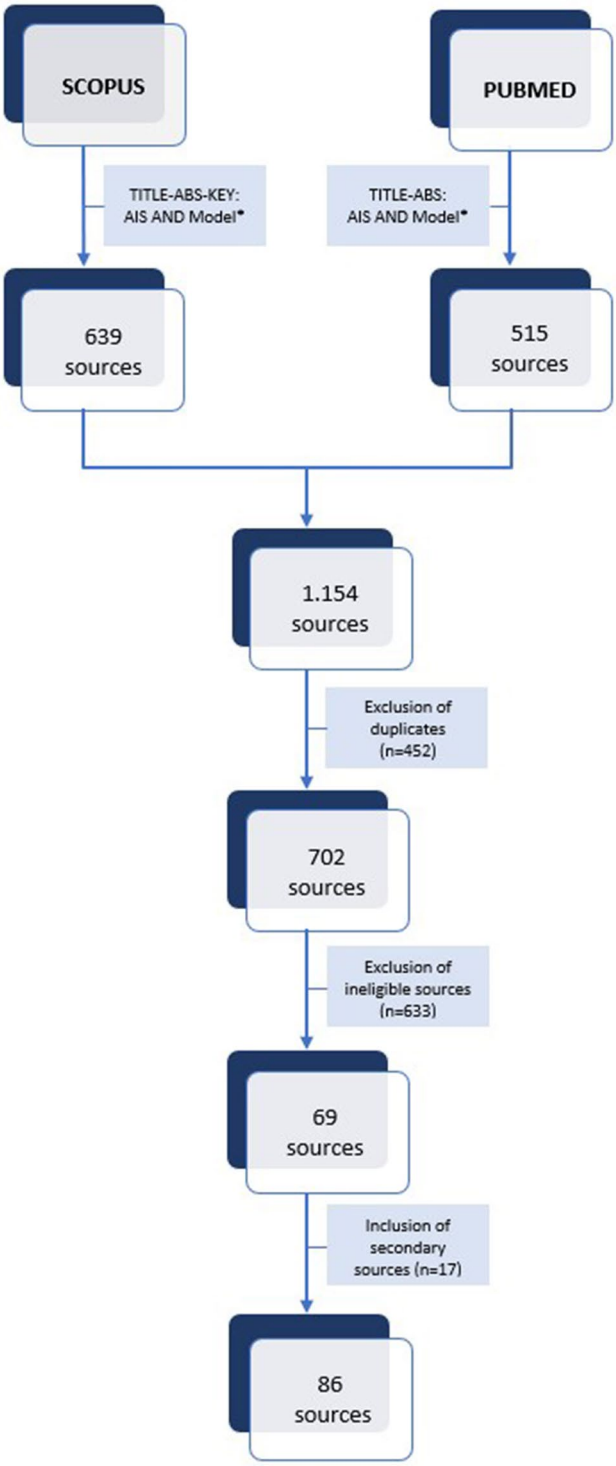

Fig. 1 Searching strategy

It was used in this review study to create an all-inclusive, mutually exclusive categorization of the modeling types (Fig. 2). We identified three subgroups: black box models, physical models, and computational models, that are expanded in more detail below.

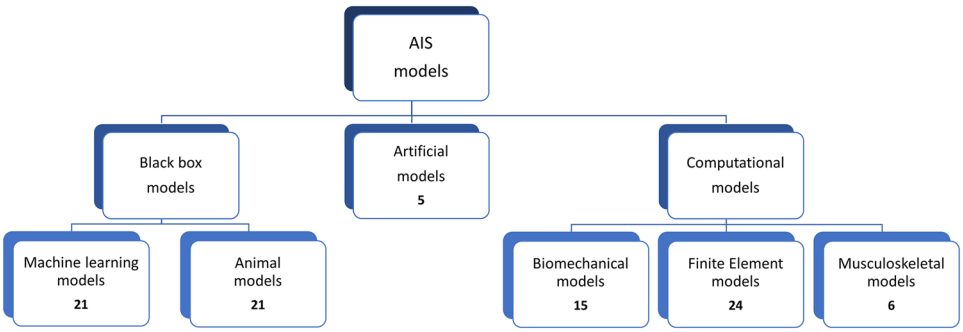

Fig. 2 ACRREx classification of modeling types, the number of studies in this category is shown. Note: hybrid studies are represented in both modeling types, yielding a higher number than the total of 86 studies

Modeling of adolescent idiopathic scoliosis

Black box models

Introduction

Black box models essentially focus on the relationship between input and output, to predict a pattern rather than the underlying mechanism. For machine learning models, the input can be clinically acquired images or other relevant data and for animal models the input is a non-spinal manipulation that results in a scoliosis. These types of models are particularly relevant for clinicians.

Machine learning models

Machine learning models are models that are driven by data and changes automatically when more data are provided. In medical applications of machine learning, the data often consist of radiographs or patient parameters, such as age or length. Machine earning models are subdivided in three paradigms: *unsupervised learning*, *supervised learning,* and *reinforcement learning* (Fig. 3). These paradigms differ in what is assessed and what part of the model (i.e., input, output, or both) can be adjusted. In unsupervised learning, only the input can be changed, for example by selecting a different radiograph. In supervised learning, the user changes the input, but is also able to provide the algorithm with feedback based on the output it was given. For example, the user can give the algorithm patient data from a follow-up appointment, so that the algorithm can improve its predictive capability. Finally, in reinforcement learning, an algorithm interacts with a certain environment to fulfill a goal. It does so by rewarding itself: the better the goal is achieved the more the algorithm is rewarded. Applications of reinforcement learning are, for example, in self-driving cars or in gaming. For the prediction or analysis of scoliotic deformities, there is not an environment with which the computer algorithm interacts. Therefore, reinforcement learning is not used for these applications.

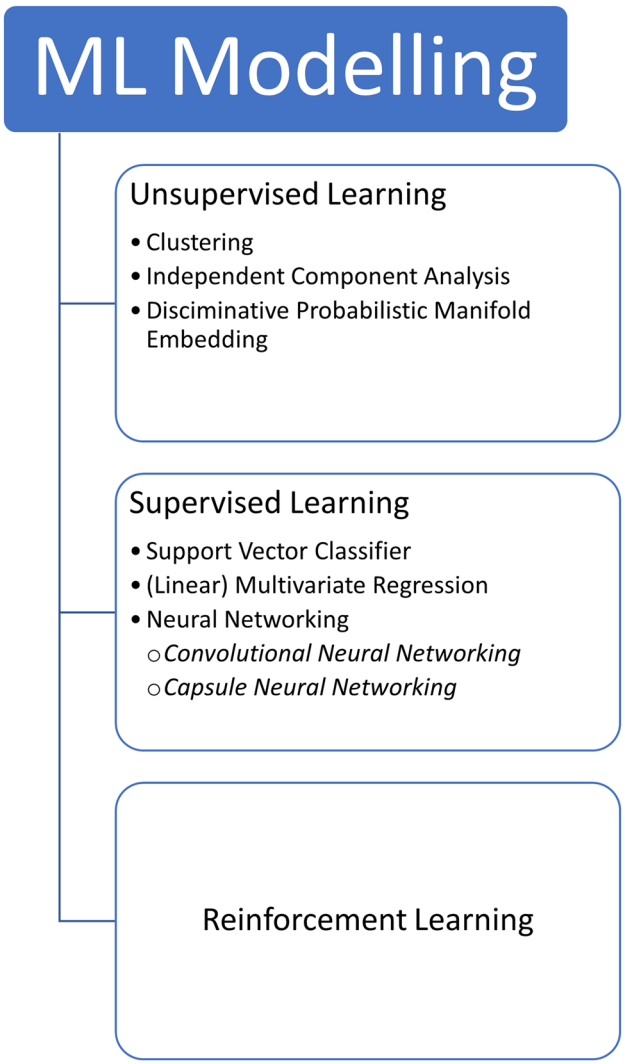

Fig. 3 Overview of the different types of machine learning modeling

Unsupervised learning covers many different modeling techniques, of which *clustering* is the most used. In this strategy, the data are clustered into groups that show similarities. Different types of clustering were used for the classification of spinal deformities [8–12] and for

the estimation of the torsion (i.e., the axial twist) of the spine [13]. These types of techniques provide a robust estimator to evaluate spinal parameters, which can be used for choosing a surgical strategy. Besides clustering, also *independent component analysis* [14] and *discriminative probabilistic manifold embedding* [15] have been used in machine learning models of AIS to predict the progression patterns of spinal deformities.

The first applied supervised learning technique for modeling of scoliotic deformities was a *support vector classifier*. This technique plots each data item as a point in space (its dimension being the number of data-features), followed by a classification that is driven by separating the data and drawing lines between the separated data groups. This technique can be used even if the data sets are small. This is the case for curve progressions, as patients are often diagnosed at later stages. Ajemba et al. [16] found an accuracy of up to 80% in predicting the risk of progression, concluding that this technique may be clinically relevant. Another supervised learning technique used in AIS modeling is *(linear) multivariate regression modeling*. Here, the linear relation between multiple independent variables is measured. This technique is used to predict the T2–T12 kyphosis [17], to show spinal deformations in 3D reconstructions [18] and to show the progression of vertebral and spinal deformations [19].

Recently, the most popular supervised learning technique for AIS purposes is *artificial neural networking*. Data are passed through a collection of connected units or nodes called "neurons" (based on biological brain neurons), allowing the user to classify and cluster data at a high velocity. Two classes of neural networking are used in the modeling of scoliotic deformities: *convolutional neural networking* and *capsule neural networking*.

Convolutional neural networking is known for its application in image analysis. It was used by Kaddioui et al. [20] to assess Risser stage automatically, by Kokabu et al. [21] to predict the Cobb angle, by Wu et al. [22] to predict curve progression and by Galbusera et al. [23] to assess a range of relevant parameters (T4–T12 kyphosis, L1–L5 lordosis, Cobb angle of scoliosis, pelvic incidence, sacral slope, and pelvic tilt). All of the studies showed promising results and concluded that convolutional neural networking has the potential to be the starting point for a fully automated radiological analysis and prediction of spinal deformities.

The main drawback of convolutional neural networking is that it has difficulties in recognizing certain structures in images when the image is orientated differently. This is why capsule neural networking was invented. Using capsules, which are collections of neurons, the technique can recognize structures regardless of the image orientation. Wang et al. [24] applied capsule neural networking on radiographs to predict curve progression and found that this technique performed better than convolutional neural networking or parameter-based regression models.

Machine learning techniques are also used in hybrid modeling studies, in combination with finite element analysis. This hybrid modeling was used to analyze trabecular configuration and bone mechanical properties [25], showing that the bone metabolism is abnormal in AIS patients. This hybrid modeling was also used to study patient-specific curve progression [26, 27], concluding that it has a great capability to capture spinal curvature progression for a specific patient.

Animal models

The underlying processes and mechanisms of the initiation and development of scoliosis in animals are unknown. However, animal models can be manipulated and give an idea of what scoliosis might look like in humans. How well the scoliosis resembles the scoliosis in humans, differs per animal. For the development of scoliosis in an animal, a certain impairment has to be induced. A well-known procedure to induce scoliosis is a *pinealectomy*, the surgical removal of the *pineal gland*. The pineal gland is a small gland in the brain that regulates a set of hormones, including melatonin. The surgical removal of the pineal gland leads to a deficit in melatonin and thereafter scoliosis. However, transplantation of the pineal gland into the body wall does not result in normal melatonin levels and, therefore, still leads to scoliosis [28]. Furthermore, a pinealectomy in non-human primates does not lead to the development of scoliosis, as was shown in a study done on monkeys [29].

In 1999, O'Kelly et al. [30] compared the production of scoliosis after a pinealectomy in chickens, rats and hamsters. The procedure was very similar but the scoliosis was only observed in chickens. No scoliosis development was found in rats or hamsters. Man et al. [3] showed the results of experiments done on mice, salmons and monkeys. This study concluded that scoliosis was only found in bipedal animals, so not in mice and, because the monkeys could not stand upright due to space limitation of the cages, also not in the monkeys. This result was backed up by Machida et al. [31], who found that scoliosis developed in pinealectomized rats that were forced to walk in a bipedal manner. On the other hand, most of the salmon did develop abnormal spinal curvatures. Evaluation of the vertebral bodies showed that they had a lower stiffness, yield limit, resilience, and total mineral content. This could, in combination with the mainly lateral flexion that is seen in fish, cause development of abnormal spinal curves.

Many other studies have used pinealectomized chickens as animal models for scoliosis. It was shown that the modeled scoliosis in chickens has a multifactorial etiology [32] and that different pinealectomy procedures lead to the same

incidence and characteristics of scoliosis [33]. Moreover, it was shown that the pinealectomy leads to an impaired endochondral ossification [34], osteoporosis [35], accelerated intervertebral disc degeneration [36], abnormalities in somatosensory evoked potentials [37], and that the primary curve in the chickens is at the thoracolumbar junction [38]. Rib length, on the other hand, was found to be unrelated to scoliosis in pinealectomized chickens [39].

Nette et al. [40] hypothesized that if a melatonin deficit leads to scoliosis, that any method of creating a melatonin deficit would suffice. They exposed chickens to intense, continuous light for 24 h each day to inhibit the production of melatonin. All chickens had low serum melatonin levels and scoliosis developed in 50% to 80% of the chickens, proving that their method worked and that low levels of melatonin has a significant effect on the development of scoliosis. Low melatonin levels can also be found when specific genes are knocked down. Machida et al. [41] knocked down the NAT gene in mice and found scoliosis in 29 out of 30 mice.

Not only a deficit in melatonin has been studied in animal studies. Machida et al. [42] also examined the effects of low serotonin levels on the development of scoliosis. While a melatonin deficit leads to scoliosis in every chicken, only 28 out of 40 chicken with a serotonin deficit developed scoliosis. Akel et al. [43] used melatonin deficit as the start of their research, but their goal was to evaluate the effect of giving calmodulin antagonists, called tamoxifen and trifluoperazine, to pinealectomized chickens. Although the overall incidence of scoliosis did not decrease, the group of chickens that were given tamoxifen had decreased curve magnitudes.

In human subjects, visual impairment has been shown to increase scoliosis incidence [44]. Therefore, Turhan et al. [44] investigated the effect of unilateral enucleation, the removal of one of the eye-balls, on the incidence and laterality of scoliotic curves in pinealectomized chickens. No effect on incidence and magnitude of scoliosis was found, but the unilateral enucleated chicken did show a significantly higher incidence of left thoracic curves. The side of the enucleation did not matter for this result.

Blecher et al. [45, 46] examined the role of proprioception in the development of scoliosis. In mice, specific genes were knocked-out to partially or fully eliminate the proprioception. Interestingly, the mice developed a progressive scoliosis about 40 days after birth, rather than a scoliosis at birth, similar to human AIS. This suggests that the proprioceptive system stabilizes the dynamic spine and when defect, spinal deformations may occur at adolescence. The malfunction of the proprioceptive system may also play a role in other musculoskeletal pathologies.

Finally, the model of the pinealectomized chicken has also been used as input to a finite element model to simulate early stages of scoliotic deformation process [47]. The results of this modeling study were seen as realistic and the model can be used to investigate different parameters influencing the progression of scoliosis.

Artificial models

Artificial models are models that represent scoliotic deformities by an assembly of materials. In comparison to black box models, the mechanism of an artificial model can be seen, felt and understood by adjustment of the model. Thus, these models give a tangible idea of the physical mechanism of the spinal deformation and thereby an insight in mechanical and kinematic consequences of specific theories.

The first artificial model dates back to 1952 [48]. Somerville built a model out of wooden blocks (vertebrae) and sponge rubber (intervertebral discs). Hooks on the back of the wooden blocks represented the posterior elements and were connected to each other. With this assembly, the results of combining lordosis with forward flexion and compression were shown. With this same assembly, another mechanism was shown which explains that anterior posterior differential growth leads to lordosis and diminished dorsal growth leads to rotation. This theory of "rotational lordosis" was long believed to be a key factor for the development and progression of scoliosis.

In 1996, an artificial model of AIS was published in which the spine was represented by a flexible plastic rod, the posterior vertebral elements by rigid struts and the supraspinous ligaments by a string [49]. They adjusted the length of the anterior and posterior elements. The authors showed that an anterior overgrowth of a mechanically normal symmetrical spine was enough to increase the deformation. Due to uncoupling of the anterior and posterior growth, the overgrowth kept increasing, resulting in progression of the deformity.

Yang et al. [50] used a spring and a string to simulate the spine and spinal cord, and a magnet under the board to simulate the restriction of muscles and ligaments. Free elongation of the spring was constrained resulting in a "S" shape deformity of the model. They concluded that the development of curvature of spine in the sagittal plane, the uncoupled spinal neuro-osseous growth, and the overgrowth of the spine in the puberty could be the crucial factors in the pathogenesis of AIS. This model was later used by Cheng et al. [51] to support their theory about the *uncoupled anterior and posterior spinal ligament tension*. This theory describes a difference in tension between anterior and posterior ligaments due to their anatomical differences.

The latest artificial model is a tensegrity model consisting of 17 vertebrae connected with ropes and springs representing the ligaments and muscles, made by Crijns et al. [52] (Fig. 4). It was used to test the hypothesis that AIS originates from restrained differential growth between the spine and the surrounding musculoligamentous structures. They found that

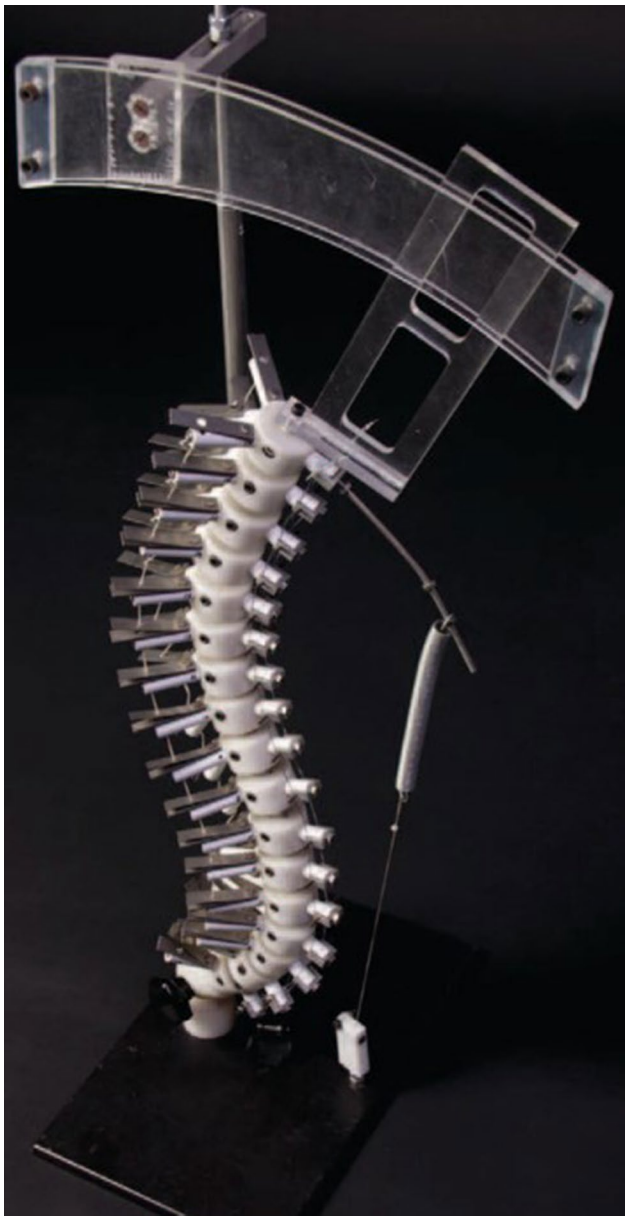

Fig. 4 Artificial tensegrity model. Adapted from Crijns et al. [34], with permission

the amount of pre-tension in the anterior band has a great effect on the onset and magnitude of scoliotic deformation. With that, they showed that AIS is not a phenomenon that only originates in the spine, but also in other structures of the vertebrate body.

Computational models

Introduction

Computational models comprehensively describe mechanical and kinematic processes by using advanced computational methods. These models are not straightforward to design and their results are not tangible. These numerical based models are especially relevant for engineers and scientists. Three types of computational models were identified for the modeling of the onset and progression of AIS: (1) biomechanical models that describe the structure, function and motion of the spine using mechanics, (2) finite element models that discretize the model in a finite number of elements, and (3) musculoskeletal models that use (pre-cooked) musculoskeletal templates.

Biomechanical models

As has been explained, rotational lordosis was long believed to be the key factor for the development and progression of scoliosis. Hefti [4], however, questioned whether this concept is the key factor, or whether asymmetrical growth and muscle activities should be taken into account. He concluded that the pathomechanism of AIS is multifactorial and that biomechanical modeling can contribute a lot to the understanding of this pathomechanism. The advantage of biomechanical modeling is that it has almost no limitations in the geometry or 3D model that is used, compared to the other types of computational modeling. Due to this freedom, biomechanical models can differ substantially from each other.

One of the simplest representations of the spine was made by Meade et al. [53]. They analyzed scoliotic deformities by describing the spine as a double curve and looking at the load-carrying capacity of each curve as a function of its magnitude, location, and flexibility. When the computing power of technology increased, the number of biomechanical studies increased as well. Wu et al. [54] described the spine as three-dimensional curves and looked at the deformity progressing by using a mathematical surface technique. Kiriyama et al. [55] used a roughly similar approach to quantify the spatial strain distribution of a scoliotic spine. Neelankatan et al. [56] reduced the model order of the scoliotic spine and determined deformation patterns and curve characteristics. All models closely mimic scoliotic curvatures in patients. Applying these techniques in the orthopedic field could reduce radiation exposure and aid physicians in deciding the proper treatment.

Another way of looking at the spine is by creating a multibody model. Most studies appoint the vertebrae as the modeling bodies. Veldhuizen and Scholten [57] used this to explain kinematical effects of spinal processes, Herzenberg et al. [58] to evaluate the relationship between the Cobb angle and the *spinous process angle* (measurement for posterior spinal deformity), Heidari et al. [59] to find the effect of collagenous fiber imbalance of intervertebral discs, and Brun-Cottan et al. [60] to apply an energy approach to describe spine equilibrium.

Guilbert et al. [61] assessed torques and forces in human gait between each vertebra by creating a multibody model which not only consisted of vertebrae, but also of lower-limb segments and a pelvis. This model was later used by Samadi et al. [62] to highlight the most relevant intervertebral effort indicators of individuals with scoliotic deformities during gait. The medio-lateral forces and antero-posterior forces and torques were found to be the most relevant intervertebral effort indicators.

Biomechanical models have also been personalized in recent years by using 3D medical imaging. Jalalian et al. [63] developed a patient-specific multibody kinematic model of the scoliotic spine to represent its movement in frontal plane of the human body. This method of creating patient- specific multibody models was later used to approximate nonlinear load–displacement relationships of spinal segments [64] and to find the line of action of the "erect spine"-force [65].

Pialasse et al. [66] looked at AIS from a completely different biomechanical view. Where the aforementioned Biomechanical models looked at the mechanics, they created a model that describes the neuromechanics and evaluated how AIS patients reacted when their vestibular system was stimulated using a *galvanic vestibular stimulation*. This is a non-invasive technique to stimulate the vestibular system. Their model showed that AIS patients reweigh their vestibular–sensory information differently, but that the severity of the scoliosis is not influential.

Finite element models

A finite element model is created by dividing the model into a large (finite) number of elements. After defining the mechanical parameters and applying forces and other boundary conditions, the computer will numerically evaluate the stresses, strains, deformations, and other mechanical parameters for each element. This method is, therefore, highly detailed and it allows for an accurate analysis of mechanical parameters, as these can be easily adjusted.

Wang et al. [5] reviewed the application of Finite Element models in AIS research and discussed it to be fourfold: understanding the etiology, improvement of surgical and non-surgical treatment and to improve the accuracy of finite element models. They presented finite element studies that describe scoliotic deformities as a buckling phenomenon as well as a product of asymmetrical growth of vertebral growth plate and thorax. The review concludes that finite element simulations allow for evaluation of different theories of scoliosis etiology.

The model that is meshed in a finite element study does not necessarily have a complex geometry. Vanderby et al. [67] estimated the stiffness of spinal segments by representing them as three-dimensional beams. Their systematic procedure was compared with an instrumented spine and was shown to work well and yield useful information. Pasha [68] used a slightly different approach: scoliotic spines were subdivided in one of five sagittal subtypes after which finite element models were made representing the subtypes as 2D-elastic rods. It was shown that deformation patterns change as a function of the rod's curvature. Pasha et al. [69] continued on this study by applying the method to investigate the development of pediatric spinal deformity.

Most studies, however, did use a complex geometry as basis of the model. Meijer et al. [70] did not look at the entire spine, but created a finite element model of a spinal segment. By changing the geometry based on changes in adolescent growth, they found that the stiffness of a lumbar spinal segment increases about 40%. Pasha et al. [71] did use the spine as their geometry and they estimated mechanical loading of the sacrum, showing that the (thoraco)lumbar scoliotic curve has an increased influence on sacral loads. Zhang et al. [72] also investigated mechanical loading, but did this for the five lumbar vertebrae and for different types of loading. Detailed displacement profiles and stress distributions were depicted for different loading types and different physiological shapes.

Villemure et al. [73, 74] incorporated vertebral growth and growth modulation and extended the model by looking at five different linear/rotational shifts of the spine, showing the effects of each of the shifts. Shi et al. [75] also looked at (accelerated) vertebral growth and showed that this could indeed lead to progression of scoliosis. Other possible causes that were tested on their effect on spine mechanics or scoliosis initiation/progression are: pedicle growth asymmetry [76], soft tissue parameters [77], low bone mineral status [78], hypokyphosis of the T5–T10 segment [79], presence of a rib cage [80], unilateral postponement in growth of ligaments of the spine [81] and asymmetrical intrapleural pressure distribution [82]. Pedicle growth asymmetry was found not to be an independent cause, but the other causes could have a (conditional) influence on the initiation and progression of scoliosis. Furthermore, ligament and collagen fiber stiffness seem to have very little effect on scoliotic curve fulcrum flexibility.

Grünwald et al. [83] personalized finite element modeling with the use of a CAD-model of a ribcage and vertebral column. They adjusted it with the use of subject-specific deformations that were retrieved from non-invasive body scanning. With this method, they recreated patient-specific spine configurations and compared this with X-ray images (Fig. 5). The results showed reasonably good matchings, therefore setting a preliminary step towards faster personalization of finite element models.

There are six studies that have either successfully applied a finite element analysis to an animal study or combined a finite element analysis with a machine learning modeling

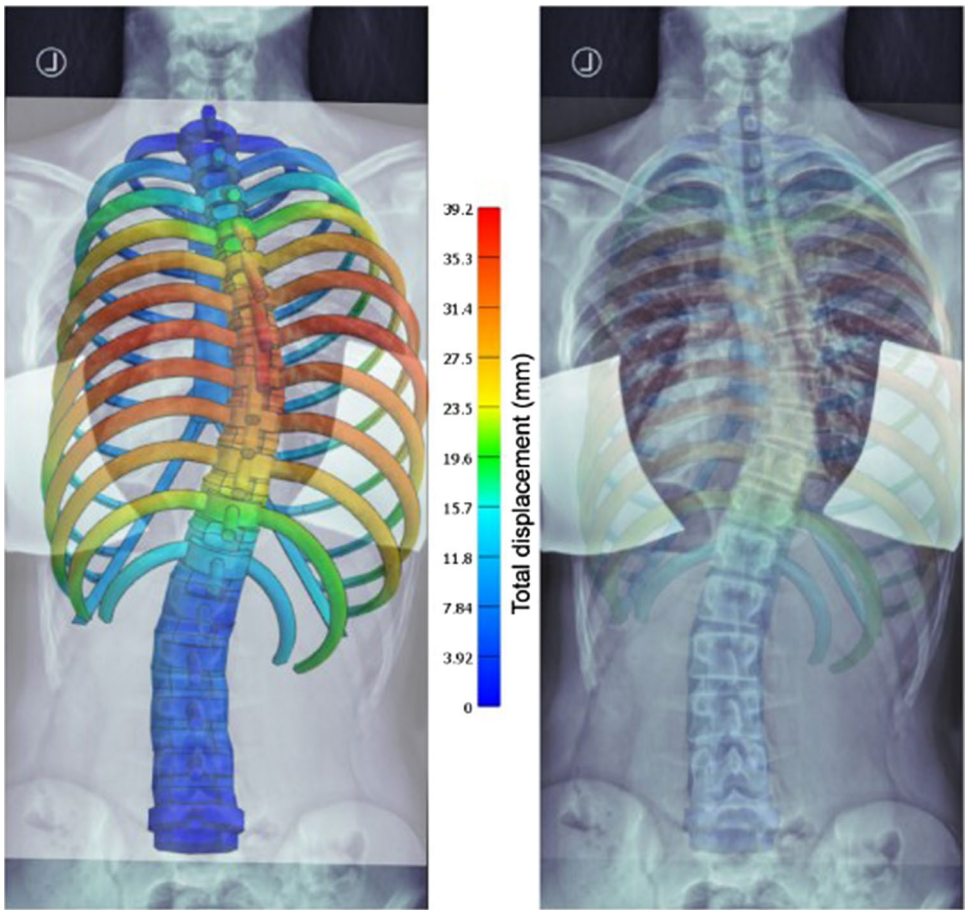

Fig. 5 Comparison of personalized Finite Element model with X-ray. The colors correspond to the displacement profile. Adapted from Grünwald et al. [62], permission requested

study or musculoskeletal modeling study. These studies have been or will be discussed at the corresponding subsection.

Musculoskeletal models

The third type of computational modeling is musculoskeletal modeling, which is gaining popularity for biomechanical applications. This type of modeling is only recently used for AIS research, because it requires high computing power and is often created in specific software environments (e.g., *AnyBody™ Modeling System (AnyBody Technology, Aalborg, Denmark)* or *OpenSIM*). Both software packages contain a "pre-cooked" musculoskeletal model that can quantify forces and motions through data-driven simulations. However, it is not absolutely necessary to work with one of these systems.

The first musculoskeletal modeling study about AIS was a hybrid study of musculoskeletal modeling and finite element modeling, in which the musculoskeletal modeling part was done in MATLAB scripting (MATLAB® R2014b, Mathworks Inc., Natick, MA, US) [84]. With the combination of techniques, stability-based muscle forces were evaluated and the effects of stress distribution within growth plates could be determined. The results showed the compatibility of the novel trunk model to estimate muscle forces and reaction moments of a scoliotic spine, while integrating vertebral growth and growth modulation. The authors used their hybrid approach one year later to examine the stress distribution changes in growth plates with AIS following unilateral muscle paralysis [85]. By reducing the strength of the concave-side muscles, and thus decreasing the compressive stress on the concave side of the spine, the authors showed a reduction in scoliosis progression.

Other musculoskeletal modeling studies for AIS did use either *AnyBody* or *OpenSIM*. The goals of these studies differed slightly: Shayestehpour et al. [86] used dependent kinematic variables to reproduce deformation patterns, Schmid et al. [87] estimated segmental compressive forces around the curve apex in patients that were carrying weights and Barba et al. [88] (Fig. 6) assessed both intervertebral loads as well as trunk muscle activation.

The most recent Musculoskeletal modeling study tried to predict curve progression. Bassani et al. [89] hypothesized that prediction can be improved if not only geometrical, but also biomechanical measurements were included, such as trunk muscle activation and intervertebral loading. Therefore, they quantified biomechanical parameters using *AnyBody* and used these as input into their prediction algorithm.

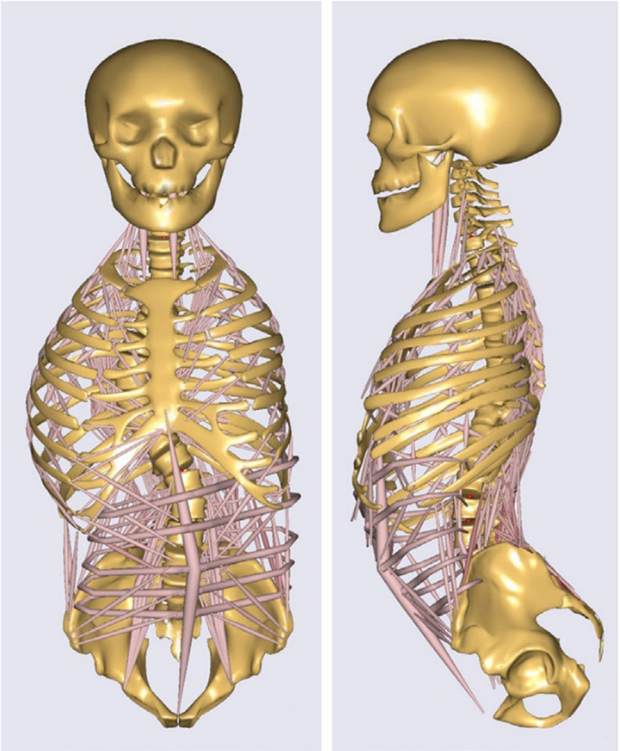

Fig. 6 Musculoskeletal model. Adapted from Barba et al. [67], permission requested

Using biomechanical measurements did not improve the performance of the model, which shows that the method is not yet beneficial for clinical applications.

Discussion

General insights

An overview of AIS models is presented in which the models were divided in six different categories. The first model made dates back to 1952, but the popularity increased much later (Fig. 7). The figure shows that animal models are more popular than artificial models, but it also shows that the popularity of Animal modeling is decreasing in recent years. This could be a result of stricter regulations on animal testing. Computational modeling, on the other hand, gains popularity, as technology keeps improving computation power and software environments.

While clinicians are mostly interested in the prediction of deformities and the effect of treatments, scientists are rather interested in the mechanism underlying scoliotic deformations of the spine. Their collaboration is essential to understand the progression of this spinal deformation and the optimal way to prevent and treat it. Model driving data are in many cases provided by clinicians. Scientists can use these data to manipulate models and run tests. The personalization of these models makes the results increasingly relevant for clinicians. By providing an overview of the many different modeling strategies, this study helps in reducing the gap between clinicians and technicians.

Modeling of biomechanics underlying scoliotic deformities

The biomechanics underlying scoliotic deformities were analyzed most efficiently by using Computational modeling (Fig. 8a). Effects on the muscle and bone tissue are more and more tested with the use of Musculoskeletal modeling. This is due to the fact that individual bones and muscles can be analyzed easily. It was shown, for example, that compressive forces in the curve apex of a scoliotic spine are higher than in a normal spine.

For testing of biomechanical effects on other types of tissue, for example on cartilage, Finite Element and Biomechanical modeling can be used. Spatial strain of the spine and surrounding tissue was quantified which can be used for surgical planning. Furthermore, it was shown that loads on intervertebral discs change with a changing spinal deformation. This suggests that a substantial part of the vicious cycle theory of Stokes et al. [90] applies to AIS.

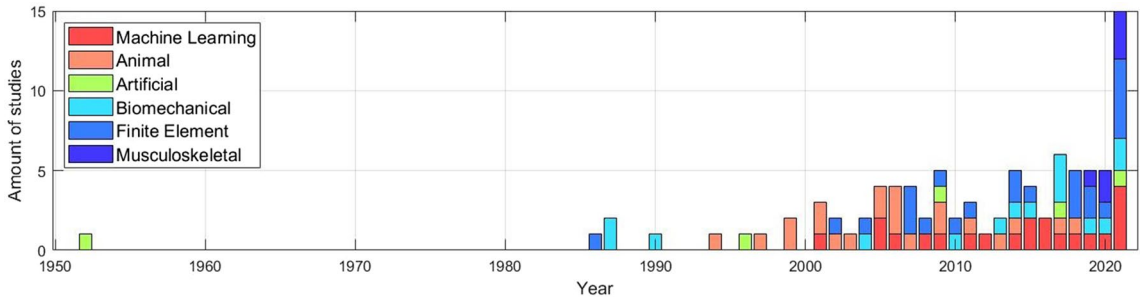

Fig. 7 Number of articles per year. Note: hybrid studies are represented in both modeling types, yielding a higher number than the total of 86 studies

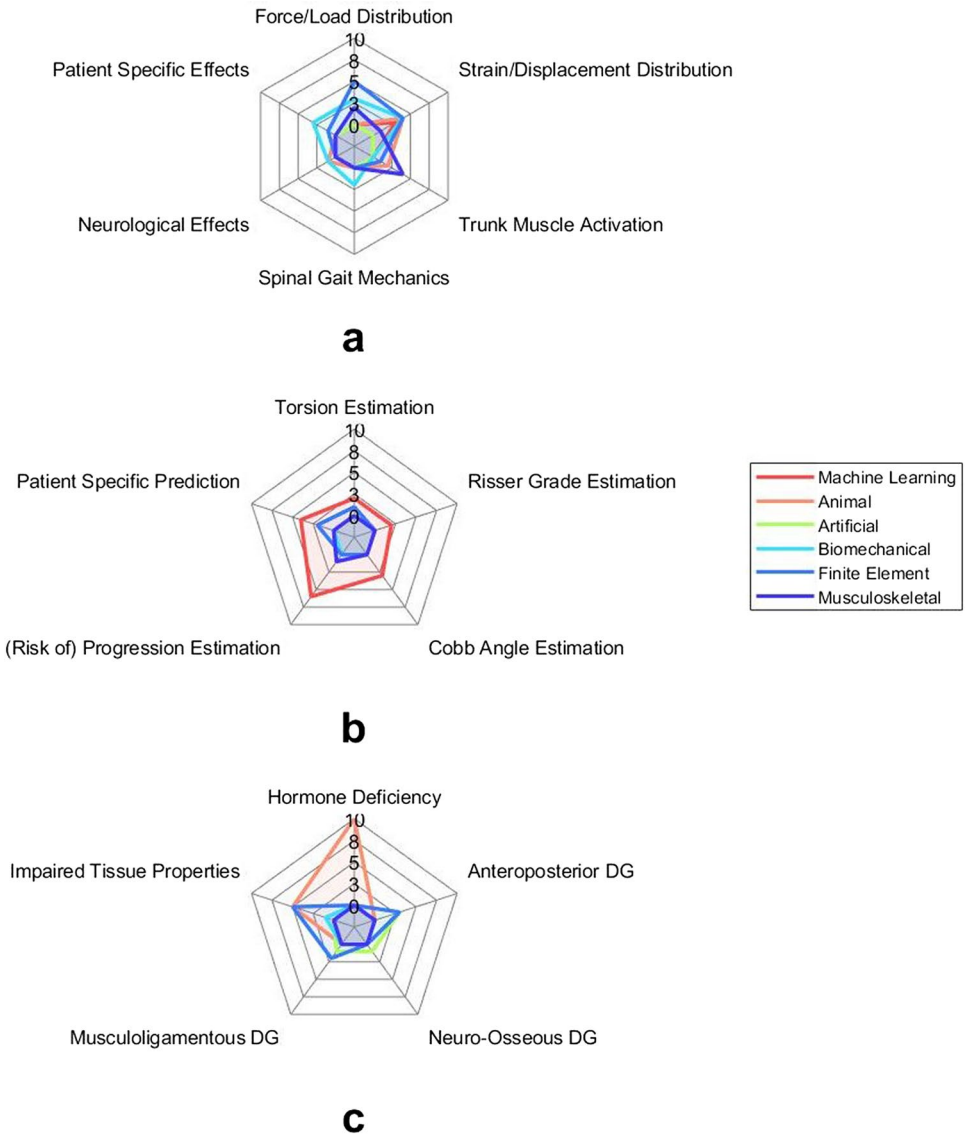

Fig. 8 Radar plots showing the number of times a modeling type has been used for a specific goal. *DG* Differential growth

Compared to computational modeling, artificial and animal modeling offer easier understanding of the results, because these types of models are more straightforward and can be handheld. This is especially relevant for clinicians and, if artificial models will be of educative value, for patients.

Modeling of curve-progression prediction

Predicting the progression of a scoliotic curve is of essential value for clinicians and patients. It helps to determine if treatment is necessary and, if so, which treatment is best to apply. The biggest problem for curve-progression prediction is that patients are often diagnosed at very late stages, when the scoliotic curve is already substantially progressed.

Spinal curves that can be analyzed, are in most cases used as input to a machine learning algorithm, which can also be seen in the number of times machine learning modeling has been used for curve-progression prediction (Fig. 8b). Machine learning modeling has been shown to be the best predictor of curve progression. Neural networking is found to be the most popular machine learning technique, with capsule neural networking having the highest sensitivity and specificity.

The prediction is mostly driven by geometrical parameters. These parameters include, but are not limited to: curve magnitude (Cobb angle), skeletal maturation (Risser grade), chronological age and current 3D spinal shape. It was shown that including biomechanical measures in the input did as yet not enhance the prediction of curve progression.

Modeling of etiopathogenetic theories

Many different etiopathogenetic theories and hypotheses are tested by modeling AIS. Almost every theory was found able to explain the initiation or progression, which unfortunately means that the initiation and progression of AIS remains not fully understood. Asymmetrical pedicle growth was one of the only potential causes that can be disregarded because it is now seen as a consequence rather than a cause of scoliotic deformities. Figure 8c shows how many times specific modeling types have been used to substantiate an etiopathogenetic theory.

Of all the modeling types, computational modeling types are the most efficient tools to test current etiopathogenetic theories and hypotheses. In view of the fact that users test parameters that are assumed or known a priori, it is inherent that computational models are an appropriate tool for testing hypotheses, especially finite element modeling. On the other hand, Animal models allow for a good examination of the effect of melatonin and other hormone deficiencies. This aspect is, as yet, not included in computational or artificial models.

Finally, artificial models allow for a cheap, easy and tangible representation of a scoliotic spine. Although the number of studies was low, they all implicate that differential growth can cause and progress scoliosis. What the type of differential growth is, remains a question. Tested types are spinal cord vs. vertebral column, anterior column vs. posterior column and vertebral column vs. ligaments. For all of these types of differential growth it was shown that they are able to either develop or progress spinal deformations, which means that the models are inconclusive.

Future research

The scope of the study has been set out to focus on creating an overview and thereby finding answers in the biomechanics underlying the deformities seen in adolescent idiopathic scoliosis. However, by doing so, many other types of modeling have been excluded. The modeling of surgical planning, effects of surgical treatment, effects of bracing or direct effects of genes/hormones have been omitted, but they all offer important information for clinicians and basic scientists. It is recommended that they are also included in a future study.

In this study only the databases Scopus and PubMed were used by searching with specific search terms. This was knowingly chosen to support a high reproducibility of this study. However, this does cause a more narrow search of scientific articles. To increase the number of scientific articles that are related to this subject, other electronic databases can be consulted and snowballing (identifying new studies from the references of selected articles) can be applied more rigorously.

It is expected that the modeling will keep developing over the coming years. This will especially be the case for computational models, as computing power increases and new software is developed. This can directly cause a more comprehensive understanding of the processes involved in the initiation and progression of the spinal deformity. One can, therefore, imagine that finding the exact causes and effects of AIS can happen in the near future. This review has laid a basis for the essential monitoring of the development of AIS modeling including the underlying biomechanics, the prediction of curve progression and etiopathogenetic theories.

Conclusion

This literature review provides an overview and classification of modeling studies for AIS research. Differential growth, impaired tissue properties, buckling of the spine and melatonin deficiencies have all been shown to (indirectly) initiate and/or progress the spinal deformity. Furthermore, it has been shown that curve-progression prediction is appropriately accurate and has high clinical potential. As computer power increases and more software is created, modeling and predicting of scoliotic deformities will improve. Therefore, finding the exact causes and effects of AIS should be feasible in the near future. It is therefore vital to monitor this development. The presented overview of the currently available modeling techniques for AIS can help to get a clear view of all the possibilities that modeling has to offer.

Author contributions ARM: conception of the work, drafting the work, final approval, accountability agreement. EK: conception of the work, revising the work, final approval, accountability agreement. AS: interpretation of the work, revising the work, final approval, accountability agreement. BJR: interpretation of the work, revising the work, final approval, accountability agreement. PB: analysis of the work, revising the work, final approval, accountability agreement. THS: analysis of the work, revising the work, final approval, accountability agreement.

Declarations

Conflict of interest The authors have no relevant financial or non-financial interests to disclose.

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