Aspects of *function* and *functioning* in patients with spinal deformity

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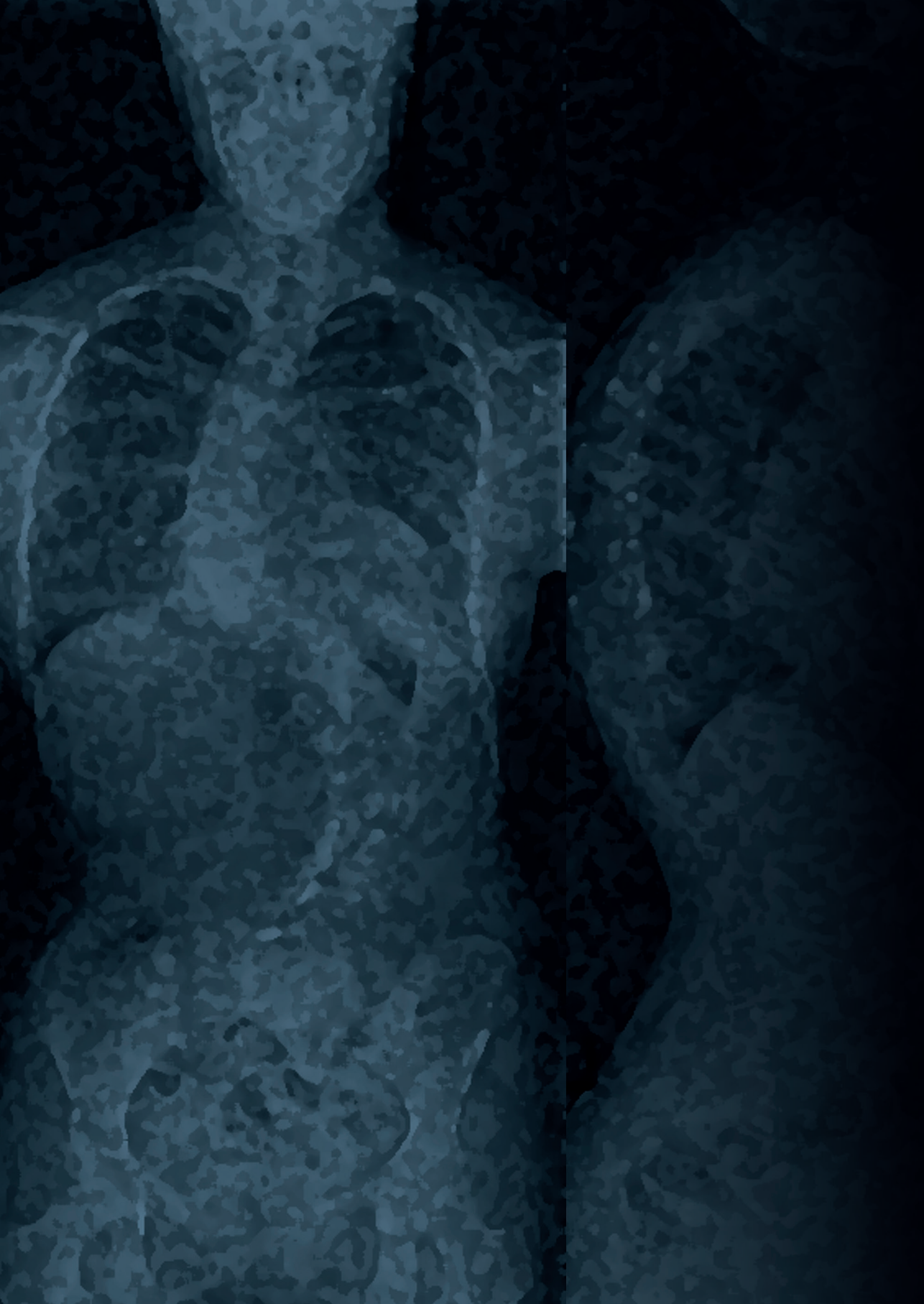


CHAPTER 1

GENERAL INTRODUCTION

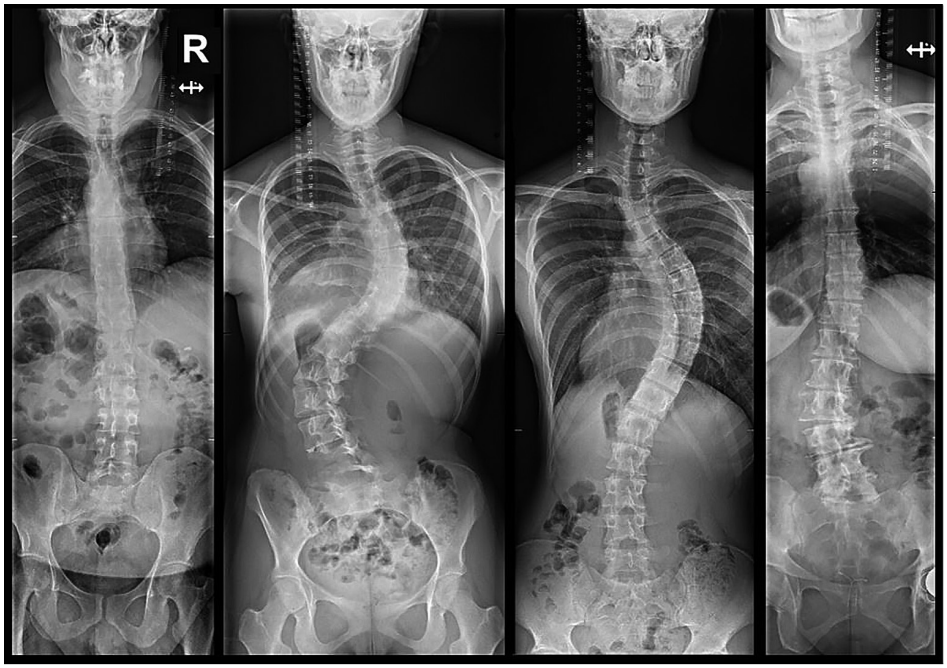
INTRODUCTION

SPINAL DEFORMITY

Spinal deformity refers to a broad spectrum of abnormalities from the typical structure and alignment of the spine.[1] The spine is a crucial part of the human skeletal system, providing support, stability, and protection for the spinal cord. When viewed from the front or back, normally the spine should have a straight and balanced alignment.[2] A spine deformity can manifest in various ways, including abnormal curvatures, rotations, or irregularities in the vertebral structure.[3] These deformities can occur in different regions of the spine, such as the neck (cervical), upper and mid-back (thoracic), and lower back (lumbar). Scoliosis is a common example of spinal deformity. This is a lateral and rotational curvature of the spine, where the spine deviates from the midline (see figure 1).

Spinal deformities can cause a wide range of symptoms, including back pain, increased fatigue, self-image and psychosocial challenges, neurological symptoms (such as spinal cord and nerve root compression) and pulmonary symptoms like breathlessness.[4,5–9] Management of spine deformities may involve observation, bracing, physical therapy, or, in more severe cases, surgical intervention to correct the alignment and stabilize the spine.[10,11] Early diagnosis and appropriate treatment are crucial for preventing complications and maintaining optimal spinal health. Scoliosis can occur at any age and may have various causes, including idiopathic (unknown etiology), congenital abnormalities of formation or segmentation (present at birth), neuromuscular (muscle weakness/imbalance), degenerative factors (due to aging) and some specific syndromes.[3,4] In the following paragraphs I will focus on the two most common spinal deformities in the otherwise healthy population, namely adolescent idiopathic scoliosis (AIS) and adult spinal deformity (ASD).[6,11–13]

FIGURE 1. Postero-anterior full spine radiographs of four patients demonstrating (1) normal coronal alignment, (2) idiopathic double major curve type scoliosis, (3) idiopathic single main thoracic curve type scoliosis and (4) lumbar, degenerative scoliosis (source: own database).



ADOLESCENT IDIOPATHIC SCOLIOSIS

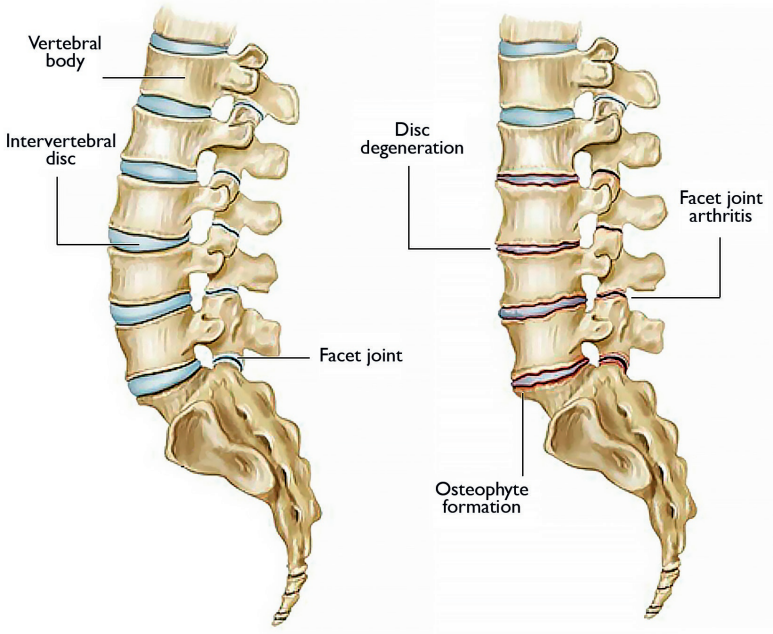
Adolescent idiopathic scoliosis (AIS) is a prevalent deformity of the spine and trunk that emerges during adolescence between the ages of 10 and 16 years and occurs in about 1–3% of the at-risk population.[14] It is characterized by an abnormal three-dimensional curvature of the spine, with lateral deviation and axial rotation of the vertebrae (back bones), which can cause asymmetry in the shoulders, hips, and waist. Notably, AIS lacks a discernible underlying cause, falling under the classification of idiopathic conditions.[13] Although the exact etiology remains unknown, there is evidence to suggest a familial, genetic predisposition to the condition. Furthermore, AIS displays a predilection for females (up to 66%) and the curvature is almost always to the right.[15] Patients with AIS can experience various symptoms such as back pain, particularly as the curvature progresses or if there is associated muscle strain. Significant back pain has been reported in up to 45%

of patients.[16] Patients may report increased fatigue, especially during prolonged periods of sitting or standing, as the spine's curvature can affect muscle efficiency and overall body alignment. Furthermore, adolescents may experience psychosocial challenges related to body image concerns, self-esteem issues, or coping with the emotional aspects of a visible spinal deformity.[5,6] Last but not least, pulmonary symptoms occur in patients with AIS.[7,8]

ADULT SPINAL DEFORMITY

Adult spinal deformity (ASD) encompasses a diverse range of conditions resulting in abnormal alignment or curvature of the spine in adults. These conditions include degenerative changes of the spine, neurodegenerative diseases such as Parkinson's, traumatic injuries to the spine or osteoporosis.[11,17] The degenerative processes involve structural changes in intervertebral discs, facet joint arthritis, and alterations in vertebral anatomy (figure 2). ASD can lead to significant medical, psychological, and social impairments due to symptoms like severe back pain, stiffness, postural changes and neurological issues such as leg weakness and numbness due to compression of the spinal cord or nerve roots.[9,18] The prevalence of ASD is notable, affecting 15% of the population with low back pain and 68% of asymptomatic adults over 60 years old.[12] The unpredictable nature of curve progression in ASD poses challenges for healthcare providers in informing patients about prognosis and intervention timing. One of the challenges in ASD is to understand the natural history, particularly the progression of spinal curvature in both coronal and sagittal planes among nonsurgical patients.[19] Recent years have witnessed more than a threefold increase in the prevalence and treatment of ASD, and further increases over the coming decades are expected with the growing elderly population worldwide.[12,20]

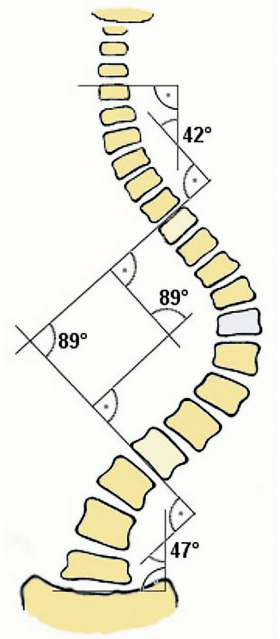
FIGURE 2. Schematic illustration of a spine without degenerative changes (left) and a spine exhibiting degenerative alterations characterized by a disc degeneration, the development of osteophytes and arthritis in the facet joints (right).



RADIOGRAPHIC FUNCTION

Radiographic assessment is an essential component in the evaluation and diagnosis of spinal deformities. X-rays are commonly used for the radiographic assessment of scoliosis to provide a detailed view of the spine's structure.[21] The Cobb angle is the primary measurement used to quantify the degree of scoliotic curvature. It is determined by drawing lines parallel to the endplates of the vertebrae that represent the maximum tilt in the curve. The angle formed by the intersection of these lines is measured and represents the severity of the scoliosis (figure 3).[22]

FIGURE 3. Measurement of Cobb angle (source: physiopedia.com)

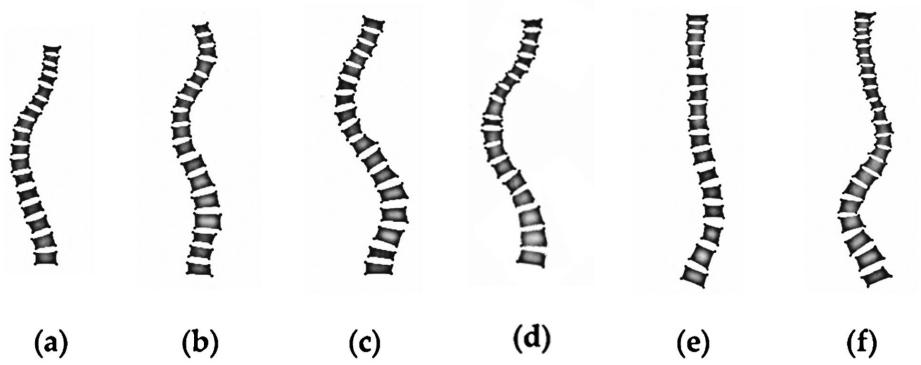


RADIOGRAPHIC CLASSIFICATIONS FOR AIS AND ASD

Scoliotic curves are categorized as either structural or nonstructural. Structural curves refer to the primary, typically larger curvatures that are generally rigid and inflexible. Nonstructural curves are more flexible and can correct to less than 25 degrees on bending radiographs.[23]

For AIS, the Lenke classification is widely used.[23] This classification aims to provide a standardized way to describe the three-dimensional characteristics of AIS curves. It considers both the location and flexibility of the curve, categorizing them into six main types, being: (1) *'main thoracic'*, (2) *'double thoracic'*, (3) *'double major'*, (4) *'triple major'*, (5) *'thoracolumbar/lumbar'* and (6) *'thoracolumbar/lumbar-main thoracic'* (see figure 4). Within each curve type, the system incorporates multiple modifiers to further refine the categorization of the curvatures. However, as this aspect is not relevant for this thesis I will not delve further into it.

FIGURE 4. Examples of the six Lenke types of scoliosis: (a) Lenke 1, 'Main thoracic'; (b) Lenke 2, 'Double thoracic'; (c) Lenke 3, 'Double major'; (d) Lenke 4, 'Triple major'; (e) Lenke 5, 'Thoracolumbar/Lumbar' and (f) Lenke 6, Thoracolumbar/Lumbar – Main thoracic'.[24]



Various classification systems exist for ASD, with one commonly used system proposed by Aebi et al.[11] This classification divides ASD into three etiological subcategories, being (1) primary (de novo) degenerative scoliosis, (2) adult idiopathic scoliosis (AdIS) and (3) secondary adult curvatures due to other factors such as neuromuscular or metabolic diseases. Primary degenerative scoliosis occurs in a normally aligned spine after the age of 50 and is caused by degenerative changes. This condition typically affects the lumbar region and is therefore often mentioned as 'de novo degenerative lumbar scoliosis' (DNDLS). AdIS is an idiopathic form that has persisted after adolescence and may progress further due to secondary degeneration in adult life.

Another often used classification is the Scoliosis Research Society-Schwab classification.[25] This morphological classification system divides the curves into (1) double curve type, (2) thoracic curve type (T), (3) thoracolumbar/lumbar type and (4) sagittal deformity without a coronal curve. It also includes multiple modifiers to further refine curvature categorization. However, since this aspect isn't relevant to this thesis, it won't be further discussed.

Generally, for ASD no classification system has achieved widespread or universal adoption at present.[26]

CURVE FLEXIBILITY ASSESSMENT

A crucial aspect in the treatment of spinal deformities is the assessment of the spinal curve function or flexibility, which can be performed using multiple techniques.[27] In assessing the curve flexibility, it helps understanding the dynamic behavior (function) of the deformity and aids in making therapeutic decisions. In surgical management, it helps in determining the number of vertebrae to be fused and the appropriate levels for fusion.[28]

Two commonly used techniques are side bending radiographs and traction radiographs. Side bending radiographs are often regarded as the current golden standard investigation.[28,29] However, some studies question the predictability of this technique[30,31] or found traction radiographs to better predict the post-operative curve correction.[32] This ongoing debate among spine surgeons highlights the lack of consensus on the preferred technique, underscoring the need for further research in this area.

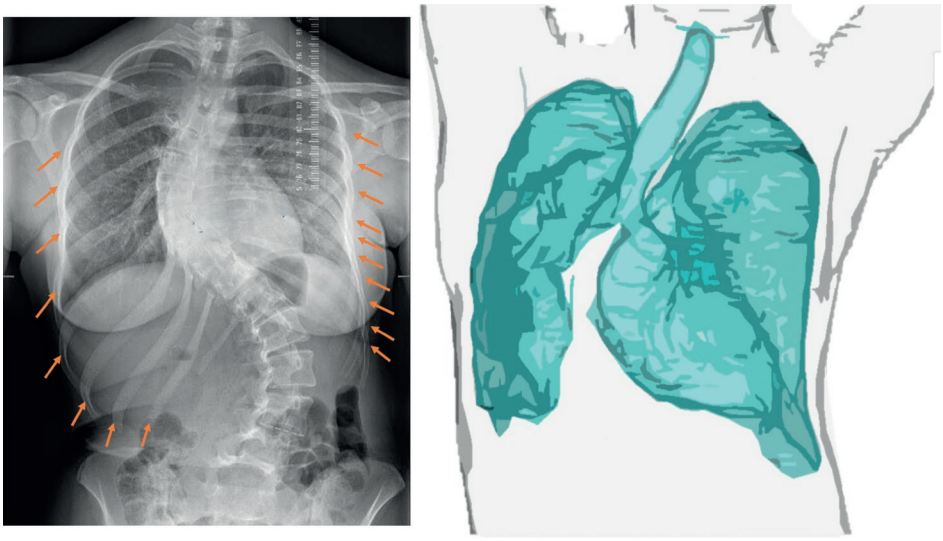
To obtain a traction radiograph a longitudinal force is applied to the cervical spine with the patient in supine position (face upwards) on a low-friction surface, while the ankles are fixated. Then, traction force is applied to maximum patient tolerance without anesthesia, which can be highly uncomfortable for patients. Conversely, for a side bending radiograph, patients are instructed to bend maximally to the right and to the left. While this technique is more patient friendly, it exposes patients to twice the amount of radiation.

PULMONARY FUNCTION

Scoliosis can potentially affect pulmonary function. The impact varies depending on the severity of the curve and its location along the spine.[6] Thoracic scoliosis, which affects the upper or mid-back region, can have a pronounced effect on pulmonary function as the ribcage is connected to the thoracic spine. Severe scoliosis can limit chest wall expansion, reducing the ability of the lungs to expand fully during breathing, leading to restrictive lung disease. The asymmetry caused by the curvature may result in decreased lung volumes and capacities (figure 5).[8,33,34] These decreased lung volumes correlate with the severity of the condition.[35] Besides this restrictive nature, recent investigations suggest an obstructive pattern originating from a right-sided bronchial constriction.[36,37] This is due to intrusion of the spine into the chest resulting from the endothoracic hump induced by the deformity. This can cause narrowing of the bronchial airways and increase the airway resistance, causing a mixed ventilatory defect.

Individuals with severe scoliosis may experience reduced exercise tolerance.[38] As physical activity increases, the demand for oxygen rises, and limitations in lung function may become more apparent. Scoliosis can sometimes lead to changes in the strength and endurance of respiratory muscles.[39] The altered mechanics of breathing in individuals with scoliosis may contribute to respiratory muscle fatigue. In some cases, particularly if scoliosis progresses, the negative impact on pulmonary function may also progress over time. Factors beyond the degree of lateral curvature, such as heightened thoracic lordosis, vertebral rotation, general muscle dysfunction, diminished respiratory muscle strength, and particularly decreased chest wall compliance, can potentially influence pulmonary function.[40,41]

FIGURE 5. Due to the vertebral rotation and thoracic curvature, the asymmetrical ribcage may result in decreased lung volumes and capacities



MANAGEMENT OF AIS AND ASD

CONSERVATIVE MANAGEMENT

The management of scoliosis depends on several factors, including symptoms, the severity of the curvature, the age of the individual, and the underlying cause of the scoliosis.[11,13] Treatment options may range from observation and monitoring to more active interventions. Mild cases of scoliosis may not require immediate intervention but are monitored regularly to track any progression. Observation is often recommended when the curvature is less than 25 degrees and is not associated with pain or other symptoms. Physical therapy may be recommended to improve muscle strength, flexibility, and overall spinal health. Specific exercises targeting the core muscles can help stabilize the spine and alleviate some symptoms associated with scoliosis.[42] Specific for AIS, when there is still remaining spinal growth, bracing is often considered for moderate scoliosis (25-40 degrees). The goal of bracing is to prevent further progression of the curvature. The type of brace, duration of wear, and specific guidelines depend on the individual case and local setting.

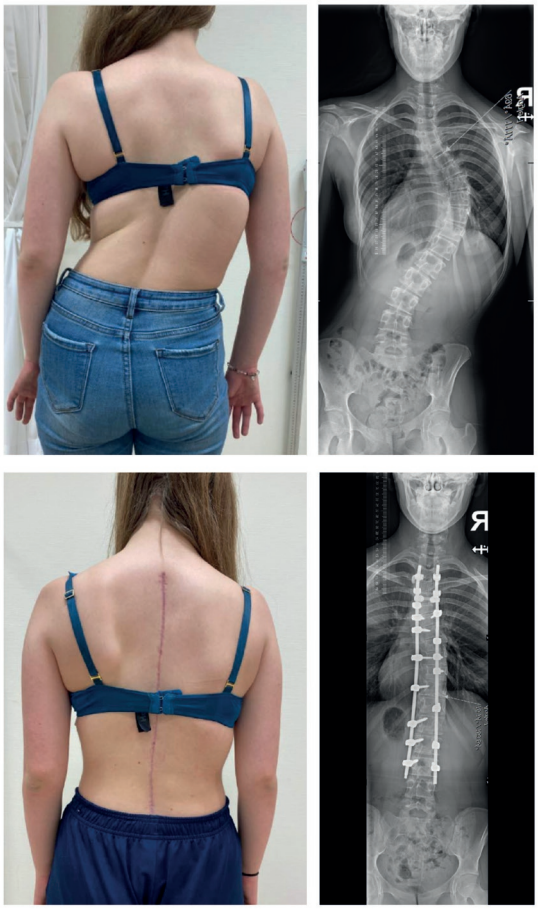
SURGERY

Surgery is considered for more severe cases of scoliosis, typically when the curvature exceeds 40-50 degrees, when the condition is causing significant pain and functional limitations, or when non-surgical methods have not been effective and the curvature poses a significant risk of progression. Spinal fusion is a common surgical procedure where the vertebrae are re-aligned and permanently fused together to correct the curvature. This is commonly performed by fixating the spine with instruments such as rods, screws and hooks to prevent any motion between the vertebrae. (see figure 6.) Subsequently, bone graft material is placed between and posterior to the vertebrae, which acts as a bridge that promotes the growth of new bone. Over time, the bone graft grows and merges with the existing bone, creating a single, solid bone mass. This process can take several months and is crucial for the success of the surgery.

Surgical management for both AIS and ASD aim to correct the spinal deformity. However, the approach differs based on factors such as growth potential, skeletal maturity, and the complexity of deformities associated with adulthood.[13,18] The selection of surgical techniques is individualized to each patient's specific needs and the goals of

treatment. In younger AIS patients for example, surgical interventions often consider the patient's growth potential. In rare cases, techniques such as growing rods or guided growth procedures may be employed to address the curvature while allowing for spinal growth. In ASD, as nerve compression is more common, a spinal fusion is regularly combined with lumbar decompression surgery, such as a laminectomy to expand the spinal canal (removal of the lamina, which is part of the vertebral arc).[43] The quality of life of patients with ASD can be significantly improved by surgical treatment.[44]

FIGURE 6. Preoperative picture and X-ray of a patient with AIS who underwent spinal fusion, illustrating the improvement of the standing posture and the correction of the curve. (source: own database, with kind permission of the patient).



KNOWLEDGE GAPS

CURVE PROGRESSION IN ADULT SPINAL DEFORMITY

Assessing the progression of the spinal curvature in adults with spinal deformities presents a significant challenge. The rate of curve progression has proven to be unpredictable.[19] In order to provide patients with accurate prognoses, determine the necessity of follow-up examinations, and ascertain the timing for potential interventions, it is essential to correctly estimate curve progression. A systematic review and meta-analysis conducted in 2016[19] identified several factors that could potentially influence the degree of curve progression. However, the available studies were limited in number, necessitating further research.

CURVE FLEXIBILITY

Assessing curve flexibility in patients with spinal deformities is crucial for planning the appropriate conservative or surgical treatment approach. In conservative management of growing children, it aids in estimating the likelihood of successful brace treatment, while in surgical management, it determines fusion levels and predicts operative correction potential. In numerous clinics, including ours, various techniques are used in most patients due to the limited number of studies comparing these methods. This leads to increased radiation exposure for patients and is more burdensome. There is ongoing debate and a lack of consensus among surgeons regarding the preferred method for assessing spinal deformity flexibility.

PULMONARY SYMPTOMS

Pulmonary symptoms are commonly observed in patients with spinal deformities and have been reported in the literature for many years.[6,8,33,34,38,39] Despite being frequently discussed in research, the focus on assessing pulmonary function has mainly relied on pulmonary function tests, which objectively measures pulmonary volumes and flow. However, the clinical significance of these findings for patients remains unclear, as does the underlying cause of these symptoms. Additionally, there is a lack of data regarding the frequency with which patients experience pulmonary symptoms.

In both AIS and ASD, a core outcome set was developed in 2017 and 2019.[45,46] Expert clinicians worldwide recognized the importance of somehow routinely assessing pulmonary function in both conditions. However, a patient-relevant measure for this assessment is currently unavailable and thus not routinely monitored. Consequently, there is a pressing need for a new measurement instrument to routinely evaluate pulmonary symptoms and function in patients with spinal deformities.

OUTLINE OF THIS THESIS

AIMS OF THIS THESIS

The aim of this thesis is to assess multiple aspects of function and functioning in patients with spinal deformity, being: the radiographic measurements in patients with scoliosis, to provide further insight into the encountered pulmonary problems and to lay the groundwork for the development of a new measurement tool for routinely evaluating the pulmonary challenges faced by scoliosis patients.

This thesis developed through an iterative process of discovery, reflection and refinement, with each phase building upon the last to expand its scope. Throughout its progression, every step offered deeper insights, ultimately shaping the work into three distinctive parts and emphasizing the critical distinction between function and functioning.

The following aims are addressed in this thesis:

PART 1: RADIOGRAPHIC FUNCTION

1. To evaluate radiographic factors for predicting curve progression in adult spinal deformity patients (**chapter 2**).
2. To identify the superior radiographic technique for assessing the spinal curve flexibility; supine traction radiographs or prone side bending radiographs (**chapter 3**).

PART 2: PULMONARY FUNCTION

3. To perform an exploratory survey of pulmonary symptoms in patients with spinal deformities (**chapter 4**).
4. To perform a systematic review of the literature to identify patient-reported and clinical measurement tools used for assessing pulmonary function in patients with AIS (**chapter 5**).

PART 3: PULMONARY FUNCTIONING

5. To assess the feasibility of utilizing a wearable 'smart shirt' for continuous monitoring of lung volumes and heart rate, during routine activities in patients with AIS (**chapter 6**).
6. To build a theoretical framework and identify relevant patient experienced outcomes for symptoms related to breathing and exercise tolerance in patients with idiopathic and adult scoliosis (**chapter 7**).

SHORT DESCRIPTION OF CHAPTERS

In **chapter 1**, a general introduction and the background of this work is described. In **chapter 2**, the natural history of a unique retrospective cohort of patients with ASD who had not been operated was evaluated. It focusses on three key factors: the direction of scoliosis, curve magnitude, and the position of the intercrest line. The prognostic value of these factors and their predictive capacity for curve progression is analyzed.

In **chapter 3**, a comparative analysis is performed of radiographic techniques used in evaluating the flexibility function of spinal deformities. The efficacy of supine traction radiographs versus prone side bending radiographs is assessed, aiming to identify the superior technique which enhances the clinical decision-making and optimize radiographic protocols in spinal deformity assessment.

In **chapter 4**, the prevalence and severity of pulmonary problems are assessed for the first time in patients with AIS and ASD through an anonymous survey (n=58). **Chapter 5** undertakes a thorough review and analysis of existing literature to identify clinical and patient-reported measurement instruments utilized for assessing pulmonary function and symptoms in adolescent idiopathic scoliosis patients.

Chapter 6 delves into the evaluation of a novel smart shirt equipped with respiratory, cardiac, and activity sensors, for continuous measurement of lung volumes and heart rate in adolescent idiopathic scoliosis patients for a better understanding of the pulmonary problems patients with AIS experience.

In **chapter 7**, a theoretical framework was built for the symptoms related to breathing and exercise tolerance in patients with idiopathic and adult scoliosis. This is done by identifying the most relevant patient experienced outcomes, using structured interviews performed in an international multicenter qualitative study. This chapter aims to enrich our understanding of patient perspectives on pulmonary functioning.

Chapter 8 includes the general discussion and conclusion.

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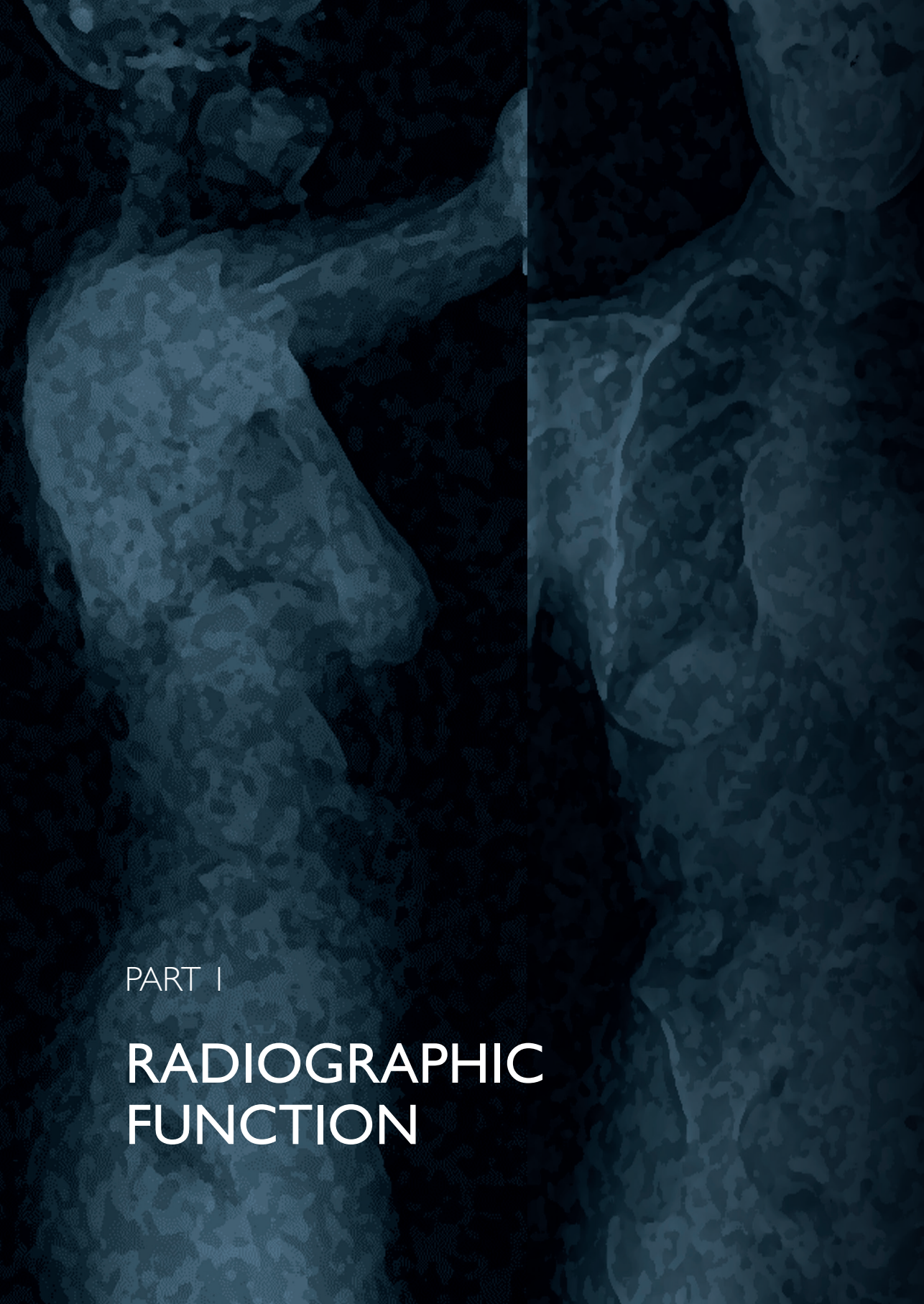

PART I

RADIOGRAPHIC FUNCTION

CHAPTER 2

THE NATURAL HISTORY OF PROGRESSION IN ADULT SPINAL DEFORMITY: A RADIOGRAPHIC ANALYSIS

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ABSTRACT

Study Design: Historical cohort study.

Objective: To evaluate progression in the coronal and sagittal planes in nonsurgical patients with adult spinal deformity (ASD).

Methods: A retrospective analysis of nonsurgical ASD patients between 2005 and 2017 was performed. Magnitude of the coronal and sagittal planes were compared on the day of presentation and at most recent follow-up. Previous reported prognostic factors for progression in the coronal plane, including the direction of scoliosis, curve magnitude, and the position of the intercrest line (passing through L4 or L5 vertebra), were studied.

Results: Fifty-eight patients were included with a mean follow-up of 59.8 ± 34.5 months. Progression in the coronal plane was seen in 72% of patients. Mean Cobb angle on the day of presentation and most recent follow-up was 37.2 ± 14.6° and 40.8° ± 16.5°, respectively. No significant differences were found in curve progression in left- versus right-sided scoliosis (3.3 ± 7.1 vs 3.7 ± 5.4, P = .81), Cobb angle <30° versus ≥30° (2.6 ± 5.0 vs 4.3 ± 6.5, P = .30), or when the intercrest line passed through L4 rather than L5 vertebra (3.4 ± 5.0° vs 3.8 ± 7.1°, P = .79). No significant differences were found in the sagittal plane between presentation and most recent follow-up.

Conclusions: This is the first study that describes progression in the coronal and sagittal planes in nonsurgical patients with ASD. Previous reported prognostic factors were not confirmed as truly relevant. Although progression appears to occur, large variation exists and these results may not be directly applicable to the individual patient.

Keywords: adult spinal deformity, scoliosis, progression, natural history

INTRODUCTION

Adult spinal deformity (ASD) comprises a wide range of conditions that result in an abnormality in the alignment, formation, or curvature of the spine. This diverse group of spine deformities seen in adults can result in strong medical, psychological, and social impairments due to severe back pain and neurological symptoms including leg weakness and numbness.[1] Nonsurgical management of ASD has been reported to be insufficient in providing relief of symptoms. Still, a large subset of patients ultimately may reach the point of undergoing reconstructive spinal surgery, a decision that depends on patient-surgeon preferences, functional limitations, neurological symptoms, or curve progression. The prevalence of ASD in the low back pain population has been reported to be 15%, and 68% in asymptomatic adults over the age of 60 years.[2] In light of the ageing population, the prevalence of ASD will continue to increase and will undoubtedly lead to increased surgical interventions for ASD. For this reason, the matter of evaluating the natural history of ASD, is becoming even more urgent.

In ASD, curve progression differs markedly between patients.[3] This unpredictable rate of curve progression subsequently makes it challenging for health care providers to accurately inform patients about their prognosis, the need for follow-up examinations, and the subsequent timing of possible interventions.[4] In the current literature, there are a limited number of studies that evaluated curve progression in ASD. These studies found several prognostic factors that may influence the degree of curve progression in the coronal plane, including the direction of scoliosis, curve magnitude, and the position of the intercrest line (passing through L4 or L5 vertebra).[5-10] However, best to our knowledge, no studies have evaluated curve progression in the sagittal plane, albeit that restoration of sagittal spinopelvic malalignment has become a focal target in ASD when planning surgical correction in providing relief of symptoms and improving health-related quality of life.[11]

The primary aim of this study was to evaluate the natural history of ASD, hence curve progression in the coronal and sagittal planes in a cohort of nonsurgical patients. This may provide more insight in the natural history of progression in ASD, including its complex pathophysiology, and may aid health care providers to inform patients about their prognosis and need for clinical follow-up examination.

MATERIALS AND METHODS

This is a single-center historical cohort of ASD patients who consulted the outpatient clinic between 2005 and 2017. Patients had complete series of standing anteroposterior (AP) and lateral (L) full-length spine radiographs. All full-spine radiographs were retrieved in order to adequately evaluate curve progression in the coronal and sagittal planes. Inclusion criteria were the following: (1) age ≥40 years; (2) diagnosed with ASD (de novo degenerative lumbar scoliosis [DNDLS] and adult idiopathic scoliosis [AIS])[12]; (3) patients that had undergone conservative treatments, which included (but was not limited to) exercise therapy if possible, steroid injections, and/or pharmacological treatments; (4) no history of spine surgery; and (5) a follow-up ≥2 years between initial and final radiographs. Patients with a follow-up of less than 2 years and a history of juvenile or neuromuscular spinal abnormalities, metabolic spinal pathology, or surgical treatment were excluded. The hospital's Institutional Review Board approved the study protocol (SMK713).

DATA COLLECTION

Demographic data including age, follow-up time, and gender were retrieved from electronical medical records. Radiographic measures were obtained using a dedicated spine measurement software (Surgimap, Nemaris Inc) and included the following: Cobb angle (CA), position of the intercrest line through L4 or L5, direction of scoliosis, thoracic kyphosis (TK), lumbar lordosis (LL), pelvic tilt (PT), pelvic incidence (PI), sacral slope (SS), and pelvic incidence minus lumbar lordosis (PI – LL). Finally, recently proposed T1-pelvic angle (TPA; T1 sagittal tilt + pelvic tilt)[13] was measured, which accounts for pelvis motion and is least affected by the patient's position during radiographic examination. All radiographic measures were independently measured by 2 authors (interrater reliability: intra-class correlation [ICC] = 0.96).

CURVE PROGRESSION IN THE CORONAL PLANE

In ASD patients with complete standing AP full-length spine radiographs at initial presentation and final follow-up, curve progression was evaluated in the coronal plane. Previous reported prognostic factors for curve progression were evaluated (direction

of scoliosis, curve magnitude [Cobb angle <30° or ≥30°], and position of the intercrest line).[3] Finally, patients were stratified into 3 groups according to the amount of curve progression in Cobb angle: no progression (group 1), 0° to 1° progression per year (group 2), and ≥1° progression per year (group 3).

CURVE PROGRESSION IN THE SAGITTAL PLANE

In ASD patients with complete L full-length spine radiographs, curve progression in sagittal spinopelvic parameters were evaluated between initial presentation and final follow-up.

STATISTICAL ANALYSIS

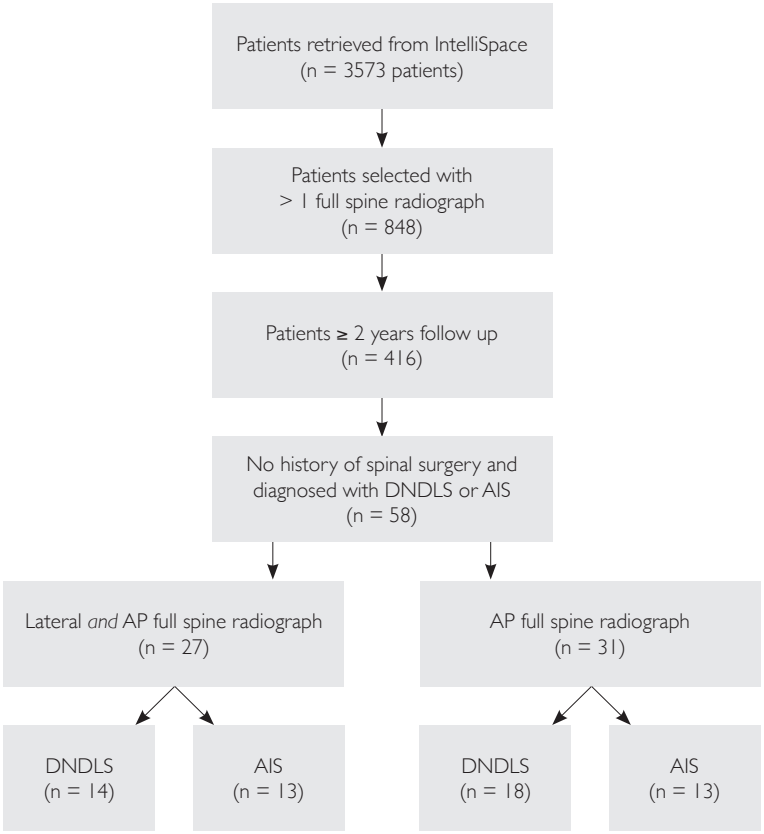
Data collection was tested for normal distribution (Shapiro-Wilk test). Descriptive analysis was used to calculate demographic and radiology data. Baseline demographic and radiographic values were compared between both groups using independent Student's t test. Frequency analysis of categorical variables (direction of scoliosis, curve magnitude, and position of the intercrest line) was performed using a Fisher exact test. Finally, patients were stratified according to the amount of curve progression in Cobb angle in 3 groups: no progression (group 1), >0° to 1° progression per year (group 2), and ≥1° progression per year (group 3). Mean values of demographic and radiographic parameters were compared between groups using a one-way ANOVA test for continuous variables and a $\chi 2$ test for categorical variables. All statistical tests were performed with SPSS 25.0 IBM. Statistical significance was set at $P < .05$.

RESULTS

STUDY POPULATION

A total of 5407 complete standing full-length spine radiographs of 3573 patients were retrieved between 2005 and 2017. Based on the study criteria, a total of 58 patients were included: 31 (53%) patients underwent AP full-length spine radiograph, whereas 27 (47%) patients underwent AP and L full-length spine radiographs at baseline and final follow-up (Figure 1).

FIGURE 1. Patient selection.



In this group of 58 patients, comprising 31 (53%) DNDLS and 27 (47%) AIS patients, the mean patient age was 56.0 ± 10.1 years with a mean follow-up of 59.8 ± 34.5 months (Table 1). A significant difference in age was shown between patients diagnosed with DNDLS and AIS (*P* = .03; 58.9 ± 10.6 vs 53.3 ± 8.7, respectively).

TABLE 1. Demographics

	Number of Patients, n (%)	F:M, n	Age at Baseline (Years), Mean ± SD	Follow-up Time (Months), Mean ± SD
ASD	58 (100%)	51:7	56.3 ± 10.1	59.8 ± 34.5
DNDLS	31 (53%)	24:7	58.9 ± 10.6	63.6 ± 37.8
AIS	27 (47%)	27:0	53.3 ± 8.7	55.3 ± 30.3
P value [a]			**.03**	.37

Abbreviations: *ASD, adult spinal deformity; DNDLS, de novo degenerative lumbar scoliosis; AIS, adult idiopathic scoliosis; F, female; M, male.*

[a] *P values are given between subgroups DNDLS and AIS. Boldface indicates statistical significance (P < .05)*

CURVE PROGRESSION IN THE CORONAL PLANE

ASD patients demonstrated a mean coronal curve progression of 0.83 ± 1.1° per year, concomitant to an increase of 3.6° in Cobb angle between initial presentation and final follow-up (Table 2). No significant difference was shown in mean coronal curve progression per year between patients subdiagnosed with DNDLS and AIS (P = .07; 0.98 ± 1.1 vs 0.37 ± 1.4, respectively). Figure 2 present the gradual curve progression in the coronal plane of both subgroups.

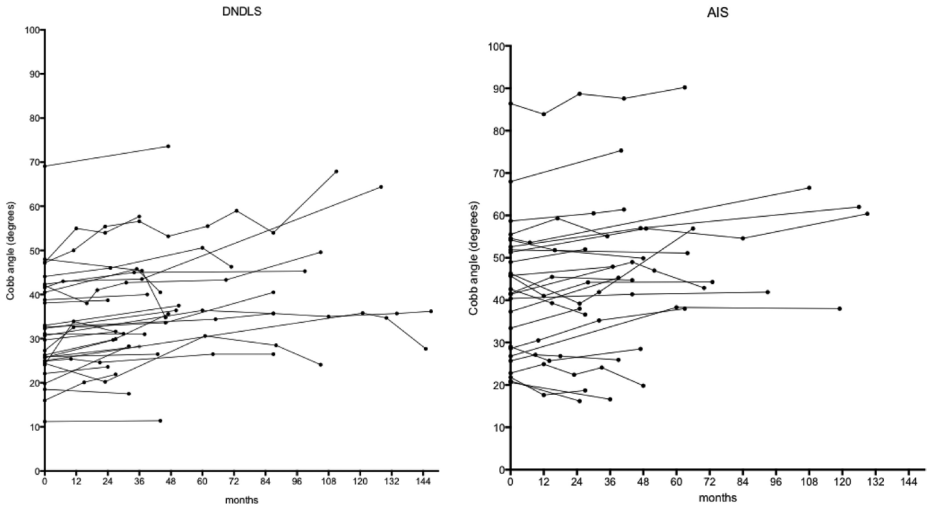
TABLE 2. Progression in the Coronal Plane After a Mean Follow-up of 5 Years.

	Initial Presentation Cobb Angle (°), Mean ± SD	Final Follow-up Cobb Angle (°), Mean ±SD	Curve Progression Cobb Angle/Year (°), Mean ± SD
ASD (n = 58)	37.2 ± 14.6	40.8 ± 16.5	0.83 ± 1.1
DNDLS (n = 31)	32.4 ± 11.8	36.9 ± 14.2	0.98 ± 1.1
AIS (n = 27)	42.7 ± 15.7	45.3 ± 18,0	0.37 ± 1.4
P value [a]	**.01**	.05	.07

Abbreviations: *ASD, adult spinal deformity; DNDLS, de novo degenerative lumbar scoliosis; AIS, adult idiopathic scoliosis.*

[a] *P values are given between subgroups DNDLS and AIS. Boldface indicates statistical significance (P < .05).*

FIGURE 2. Curve progression in Cobb angle in de novo degenerative lumbar scoliosis (DNDLS; n = 31) and adult idiopathic scoliosis (AIS; n = 27) patients over a mean follow-up of 5 years.



PREVIOUS REPORTED PROGNOSTIC FACTORS FOR CURVE PROGRESSION IN THE CORONAL PLANE

No significant differences were found in mean curve progression per year with regard to direction of scoliosis, curve magnitude, and position of the intercrest line (Table 3).

TABLE 3. Previous Reported Prognostic Factors for Curve Progression in the Coronal Plane in ASD (n=58)[a]

Parameter	Cobb Angle baseline (°)	Cobb Angle Final Follow-up (°)	Mean Curve Progression/Year (°)
Direction of scoliosis			
Right	37.2 ± 14.8	40.9 ± 16.9	0.65 ± 1.21
Left	37.2 ± 14.5	40.5 ± 15.9	0.81 ± 1.42
P value			.655
Position of the intercrest line			
L4 vertebra	35.6 ± 16.4	39.0 ± 17.6	0.79 ± 1.21
L5 vertebra	39.5 ± 11.6	43.3 ± 14.8	0.56 ± 1.35
P value			.504
Curve magnitude at baseline			
Cobb angle <30°	24.2 ± 5,2	26.8 ± 7.8	0.60 ± 1.39
Cobb angle ≥30°	46.4 ± 11.8	50.7 ± 13.6	0.76 ± 1.18
P value			.635

Abbreviation: *ASD, adult spinal deformity.*

[a] *Data shown are mean ± standard deviation.*

GROUP STRATIFICATION ACCORDING TO SEVERITY OF CURVE PROGRESSION

Progression in the coronal plane was seen in 42/58 (72%) of patients with ASD (Table 4). Stratification into 3 groups according to the amount of curve progression demonstrated no significant difference in age, follow-up time, direction of scoliosis, position of the intercrest line, and curve magnitude at baseline ($P < .05$).

TABLE 4. Group Stratification According to Severity of Curve Progression in ASD (n = 58).

Baseline	Group 1 (No Progression)	Group 2 (0° to 1° Progression/Year)	Group 3 (≥1° Progression/ Year)	P Value
Number of patients, n (%)	16 (28%)	23 (40%)	19 (32%)	
Age at baseline (years), mean ± SD	55.9 ± 9.1	54.4 ± 10.5	58.8 ± 10.4	.382
Follow-up time (months), mean ± SD	48.4 ± 25.1	70.9 ± 39.3	55.8 ± 32.6	.111
Cobb angle (°), mean ± SD	34.6 ± 13.4	38.4 ± 15.2	38.0 ± 15.2	.700
Direction of scoliosis				
Right (n)	10	19	7	
Left (n)	6	4	12	.270
Position of the intercrest line				
L4 vertebra (n)	9	13	12	
L5 vertebra (n)	7	10	7	.887
Curve magnitude at initial presentation				
Cobb angle <30° (n)	8	8	8	
Cobb angle ≥30° (n)	8	15	11	.635

Abbreviation: *ASD, adult spinal deformity.*

CURVE PROGRESSION IN THE SAGITTAL PLANE

In the cohort of 58 ASD patients, a total of 27 were identified with complete standing AP and L full-length spine radiographs, comprising 14 (52%) DNDLS and 13 (48%) AIS patients. The mean patient age was 56.7 ± 10.6 years with a mean follow-up of 58.2 ± 33.7 months. No significant differences were found with regard to sagittal radiographic parameters at baseline between DNDLS and AIS (Table 5). No significant differences were found with regard to progression in the sagittal spinopelvic parameters between initial presentation and final follow-up (Table 6).

TABLE 5. Demographic Parameters of ASD Patients Who Underwent Complete AP and L Full-Length Spine Radiographs (n = 27).

	ASD	DNDLS	AIS	P Value [a]
Number of patients, (n)	27	14	13	
Female–male (n)	23:4	10:4	13:0	
Age at baseline (years), mean ± SD	56.7 ± 10.6	59.4 ± 11.5	53.8 ± 8.9	.168
Follow-up time (years), mean ± SD	58.2 ± 33.7	62.0 ± 38.8	54.2 ± 28.2	.556
Coronal parameters				
Cobb angle (°), mean ± SD	37.2 ± 14.7	29.3 ± 11.5	45.8 ± 13.2	.002
Intercrest line (L4 or L5) (n), mean ± SD	16:11	11:3	5:8	
Direction of scoliosis (R or L) (n), mean ± SD	15:12	8:6	7:6	
Sagittal parameters				
T1 pelvic angle (TPA) (°), mean ± SD	19.0 ± 11.7	21.4 ± 13.2	16.3 ± 9.7	.268
Thoracic kyphosis (TK) (°), mean ± SD	31.0 ± 17.0	31.8 ± 21.8	30.2 ± 10.4	.818
Lumbar lordosis (LL)(°), mean ± SD	−39.0 ± 14.1	−37.1 ± 18.0	-41.1 ± 8.3	.469
Pelvic tilt (PT)(°), mean ± SD	22.2 ± 10.7	23.8 ± 11.0	20.5 ± 10.5	.432
Pelvic incidence (PI) (°), mean ± SD	49.2 ± 10.8	49.8 ± 9.4	48.5 ± 12.4	.749
Sacral slope (SS) (°), mean ± SD	26.9 ± 6.3	25.7 ± 7.3	28.1 ± 5.1	.337
PI − LL (°), mean ± SD	10.6 ± 16.8	12.8 ± 20.4	7.4 ± 12.1	.417

Abbreviations: *ASD, adult spinal deformity; DNDLS, de novo degenerative lumbar scoliosis; AIS, adult idiopathic scoliosis; R, right; L, left; PI − LL, pelvic incidence minus lumbar lordosis.*

TABLE 6. Curve Progression in the Sagittal Plane in ASD Patients Between Initial Presentation and Final Follow-up (n = 27).

Parameters	Initial Presentation	Final Follow-up	P Value
Cobb angle (CA) (°), mean ± SD	37.2 ± 14.7	41.1 ± 16.1	.356
T1 pelvic angle (TPA) (°), mean ± SD	19.0 ± 11.7	20.9 ± 13.4	.583
Thoracic kyphosis (TK) (°), mean ± SD	31.0 ± 17.0	29.7 ± 18.8	.787
Lumbar lordosis (LL) (°), mean ± SD	−39.0 ± 14.1	−31.6 ± 20.3	.127
Pelvic tilt (PT) (°), mean ± SD	22.2 ± 10.7	23.5 ± 11.2	.667
Pelvic incidence (PI) (°), mean ± SD	49.2 ± 10.8	47.4 ± 12.4	.571
Sacral slope (SS) (°), mean ± SD	26.9 ± 6.3	24.1 ± 11.3	.268
PI-LL (°), mean ± SD	10.6 ± 16.8	15.7 ± 20.4	.278

Abbreviation: *PI − LL, pelvic incidence minus lumbar lordosis.*

DISCUSSION

This study provides the first long-term evaluation of progression in the coronal and sagittal planes in a cohort of nonsurgical ASD patients. Although nonsignificant, the results of the present study demonstrate that progression in the coronal and sagittal planes occurs over a mean follow-up of 5 years. Progression in the coronal plane was seen in 72% of patients with ASD, and previous reported radiographic risk factors for curve progression were not confirmed as truly relevant (direction of scoliosis, curve magnitude, and position of the intercrest line).

The findings of the present study seem contradictory compared with previous studies that have suggested that there is a strong relationship between the direction of scoliosis and the likelihood of curve progression. In a retrospective analyzed case series, Chin et al[7] described the natural course of curve progression in 24 ASD patients with a mean follow-up of 4.85 years. Chin and colleagues found a significant difference in curve progression between the direction of scoliosis: patients with left-sided scoliosis progressed 3° per year, whereas patients with a right-sided scoliosis 1° per year.[7] These

results differ from the present study in which we found that the direction of scoliosis should not be considered as a relevant risk factor for curve progression (Tables 3 and 4). These contradicting findings may be explained by the difference between the 2 groups. The study by Chin and colleagues[7] included patients with curves of no more than 30°, while the present study included all ASD patients with curves of more than 10°. It is possible that the direction of scoliosis may be a risk factor for rapid curve progression in the early phase of ASD and not in the later phase. Additionally, in the current study, we were not unable to demonstrate that curve magnitude at initial presentation should be considered a risk factor for curve progression (Table 3 and 4). This is contrary to previous studies.[6,10] In a retrospective study, Sapkas et al[6] evaluated the risk of curve progression in 162 ASD patients (all women) with a mean follow-up of 8 years. Sapkas and colleagues reported that patients with a Cobb angle ≥30° were more likely to progress, while in the present study we found no significant difference in mean curve progression per year between patients with a Cobb angle <30° and ≥30° (Table 3). The relatively short follow-up time of the present study, including the nonlinear tendency of curve progression in particularly women,[7] might account for this discrepancy.

We found that adult patients with AIS appear to demonstrate less progression than DNDLS (Table 2). We postulate that a possible explanation for this variation is caused by the difference in etiology. Adult idiopathic (nondegenerative) scoliosis is a pediatric deformity. Over time, the pediatric curve may progress, leading to a compensatory curve, or in some instances it may be affected by secondary degeneration as patients get older.[14] This is very different from DNDLS, which is caused by primary mono- and multilevel disc degeneration located in the lumbar region, and typically develops after the sixth decade of life.[12] As such, adult patients with DNDLS are unlikely to suffer from the same distribution, localization, and intensity of degenerated areas as patients with AIS, as argued before.[12,15] Moreover, in a landmark study by Weinstein et al[16] (including the Iowa series[17-19]), it was demonstrated that these entities have their own natural histories based on curve type and magnitude, including associated problems that may significantly affect daily functioning. It is, therefore, most likely that a distinction between subtypes of ASD should be made in determining the clinical course.

Previous multicenter studies demonstrated that in ASD, sagittal spinopelvic malalignment is associated with pain and poor health-related quality of life scores.[11] As a result, Schwab et al[20] developed a classification system for ASD based on the

most clinically relevant sagittal spinopelvic modifiers that are associated with pain and health-related quality of life scores: sagittal vertical axis (SVA), PT, and PI – LL mismatch. Consequently, it is of paramount importance to evaluate progression in these sagittal spinopelvic parameters. Notable, the present study did not include the SVA as measurement to evaluate progression in the sagittal plane. Previous studies have demonstrated that the SVA is dependent of positional changes during radiographic examination,[21,22] and was therefore deemed not appropriate to evaluate progression in the sagittal plane. Consequently, we included the recently proposed T1-pelvic angle to evaluate progression in the sagittal plane, which accounts for pelvis motion and is least affected by the patient's position during radiographic examination.[13] Although we did not find any significant changes over a mean follow-up of 5 years, our results seem to indicate that PI remains relatively stable (+1.8°) and that there is a nonsignificant tendency toward loss of LL (–7.4°; Table 6). As a result, we observed a concomitant nonsignificant increase in PI – LL mismatch (+4.9°). Notable, PI – LL mismatch has become a focal target when planning surgical correction in ASD in order to achieve global sagittal balance and improve health-related quality of life scores. Lafage et al.[23] demonstrated that ideal sagittal spinopelvic values varies with age, and that elderly ASD patients may tolerate PI – LL mismatch (i.e., sagittal malalignment) better than relatively young patients, which could be related to the natural human aging process. As humans age, a loss of lumbar lordosis occurs that induces an anterior displacement of the trunk, a so-called "stooped posture."[24] Although our findings seem to indicate that patients with ASD show a tendency toward an increase in sagittal malalignment over time, it is not clear whether this is part of a normal aging process or not.

LIMITATIONS

First, although the Cobb angle is considered the gold standard in evaluating the coronal plane, a measurement error of 3° to 5° is known.[25] This subsequently increases the chance of obtaining a nonsignificant result.[26] Second, selection bias might have been introduced. Nonsurgically treated ASD patients were included with a minimal follow-up of 2 years. As such, we may have excluded patients with more rapid curve progression who underwent surgical management. Subsequently, this may not accurately reflect the rate of curve progression in clinical practice and these results may not be directly applicable to the individual patient. Third, there is an absence of data related

to nonsurgical management (e.g., physiotherapy, bracing) between initial presentation and final follow-up that patients may have tried. Fourth, there is a small sample size. A larger number of patients could render the trend of an association between prognostic factors with progression more statistically significant. Finally, clinical factors such as osteoporosis, cigarette smoking, and body mass index were not reported. It is possible that these clinical factors may influence the degree of progression in ASD and future studies are warranted. To date, patient data (including clinical and radiographic data) on the surgical management of ASD are collected in multiple multicenter, regional, and national spine registries worldwide.[27] Unfortunately, there is a lack of comprehensive data on the nonoperative course of ASD. For this reason, we recommend that nonsurgically treated ASD patients should be included in current spine registries and as part of future long-term follow-up studies. This will provide more insight in the manifestation and natural history of ASD and provide the opportunity to evaluate prognostic (clinical and radiographic) factors associated with the variance found in curve progression.

CONCLUSION

This is the first study that evaluates curve progression in both the coronal and sagittal planes in a nonsurgical cohort of patients with ASD. Our results appear to indicate that curve progression occurs over a mean follow-up of 5 years in both the coronal and sagittal planes. In contrast to previous studies, the direction of scoliosis, curve magnitude, and position of the intercrest line were found not to be risk factors for coronal curve progression. On average adult patients with AIS appear to demonstrates less progression than DNDLS. Large variations exist, and individual guidance is very difficult to give, even with the current data. Until then perhaps the best advice is to perform a new radiograph after 3 to 5 years to be able to identify those patients whose curve progresses, in order to provide patients with personalized advice. Moreover, sagittal malalignment in ASD appears to increase with age; however, we do not know whether this is part of a normal aging process or not.

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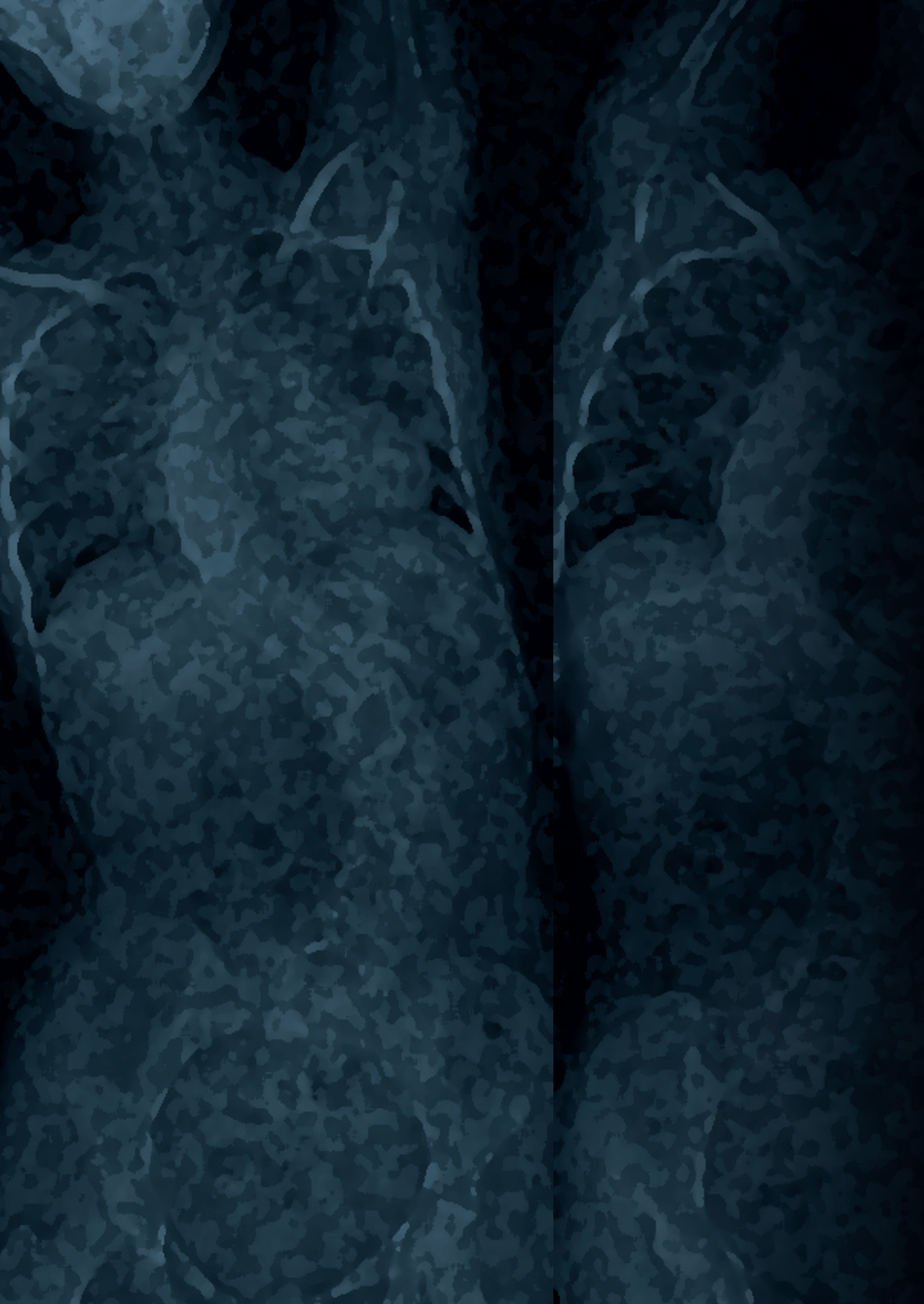

CHAPTER 3

SUPINE TRACTION VERSUS PRONE BENDING RADIOGRAPHS FOR ASSESSING THE CURVE FLEXIBILITY IN SPINAL DEFORMITY

Niek te Hennepe
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Global Spine Journal, 2022 Sep;12(7):1345-1351

ABSTRACT

Study design: Retrospective cohort study.

Objectives: No consensus exists among surgeons on which radiologic method to prefer for the assessment of curve flexibility in spinal deformity. The objective of this study was to evaluate the difference in curve correction on supine traction radiographs versus prone side bending radiographs.

Methods: A retrospective analysis of idiopathic scoliosis (IS), degenerative idiopathic scoliosis (DIS) and de novo degenerative lumbar scoliosis (DNDLS) patients was performed on supine traction as well as prone bending films (when available). Age, weight, traction force, diagnosis and Cobb angles of the primary and secondary curves were extracted. Differences in curve correction (percentages) on traction versus prone bending radiographs were analyzed for the primary and secondary curve. Subgroup analyses were performed for the 3 different diagnoses.

Results: In total, 170 patients were eligible for inclusion. 43 were diagnosed with IS, 58 with DIS and 69 with DNDLS. For the primary curve, greater curve correction was obtained with bending in the DNDLS group ($P < 0.001$). In the DIS group, there was a trend toward more correction on bending ($P = 0.054$). In de IS group no difference was found. For the secondary curve, bending showed more curve correction in the IS and DIS group ($P = 0.002$ and $P < 0.001$). No difference was found in the DNDLS group.

Conclusion: Compared to traction radiographs, bending radiographs better serve the purpose of curve flexibility assessment of IS, DIS and DNDLS spinal deformity, despite the fact that patients are exposed to more radiation.

Keywords: bending; flexibility assessment; scoliosis; traction.

INTRODUCTION

The most common form of spinal deformity is idiopathic scoliosis (IS), which has an unknown etiology.[1] In the adult, spinal deformity can occur due to degenerative changes of the spine. The Aebi classification has divided adult spinal deformity into: (1) primary degenerative scoliosis, which typically occurs in the lumbar spine, hence "de novo degenerative lumbar scoliosis" (DNDLS) and (2) degenerative idiopathic scoliosis (DIS) that has progressed in adult life, which is usually combined with secondary degeneration and/or imbalance.[2]

In the assessment of spinal deformity for conservative care (for instance bracing in adolescent idiopathic scoliosis (AIS) patients) or as preoperative work-up, curve flexibility or stiffness are essential; for surgical strategy it will help to determine fusion levels and estimate operative correction potential.[3] Many different radiographic techniques exist for obtaining information on the flexibility of spinal deformity such as side bending, fulcrum bending, push-prone, suspension, push traction and traction.[4] However, obtaining traction radiographs is more labor intensive than a bending radiograph as it requires careful preparation, 2 employees instead of 1, clear instructions, and guidance of patients. Side bending radiographs are considered the current gold standard investigation as it only requires patients to voluntarily bend to their maximum in prone position.[3,5] Still, some studies doubt the predictability of this technique.[6,7] In a review by Khodaei et al.,[8] side bending was the most used method, but traction appeared to be a better method in predicting the post-operative curve correction. Khodaei et al. did note that there was a limited number of studies reporting the traction method and the quality of evidence was very low. Overall and in everyday practice, there is ongoing debate and there is no agreement among surgeons about the preferred method to assess spinal deformity flexibility.

Currently, very few studies exist assessing the curve flexibility of patients with spinal deformity. Furthermore, to our knowledge, no studies exist comparing the flexibility in IS versus DNDLS or DIS. Therefore, the main objective of our research is to assess which radiographic method displays the best method to demonstrate curve correction and potential flexibility in IS, DIS, and DNDLS patients.

METHODS

STUDY DESIGN AND PATIENT POPULATION

This study describes a single-center retrospective database of traction and posterior-anterior (PA) full spine radiographs of IS, DIS and DNDLS patients. Inclusion criteria for selection in our study database were: (1) diagnosis IS, DIS, or DNDLS, (2) at least 1 traction radiograph, (3) at least 1 standing PA full spine (StFS) radiograph and (4) bending radiographs when available. Bending radiographs of the selected patients were also included upon availability (not routinely performed in all cases, but at the discretion of the surgeon). Exclusion criteria were: (1) prior juvenile, infantile, associated congenital, developmental or neuromuscular spine abnormalities and (2) time between traction and StFS radiographs > 3 months. In case of IS, the age of 25 was chosen for the division between adolescents and adults. The hospital review board approved the study protocol (SMK879), according to the Dutch law no additional ethical review was required.

DATA COLLECTION

All traction radiographs between 01-09-2014 and 31-08-2019 were retrieved from IntelliSpace® PACS Enterprise V4.4.532.10, Philips), the database of the Sint Maartenskliniek in Nijmegen, the Netherlands. This time frame was chosen as this supine traction imaging technique started in a standardized way from September 2014. Age, weight, traction force, diagnosis, and Cobb angles of the primary (major) and secondary (minor) curves were extracted from the electronical medical records. As defined by The Scoliosis Research Society (SRS), the primary curve has the biggest Cobb angle and the secondary curve the smallest. The Cobb angles of the traction, bending or StFS radiographs were already measured by experienced radiology workers for standard care purposes. The diagnosis was retrieved from the medical history. If this was not mentioned explicitly, the radiographs and medical history were assessed by 2 experienced spinal surgeons (MP and MS) to clarify the diagnosis. To differentiate between DIS and DNDLS the classification of Aebi was used.[2]

TRACTION AND BENDING

Traction radiographs and bending radiographs were performed to assess spinal deformity curve flexibility. For a traction radiograph a longitudinal force was applied to the cervical spine on a low-friction surface, while the ankles were fixated with the patient in supine position (Figure 1). The traction force was applied to maximum patient tolerance, and was indicated on the dynamometer (in kilograms). Traction radiographs were not obtained with any form of anesthesia. For the bending radiographs, the patient was asked to bend maximally (left and right) in prone position (Figure 2).

FIGURE 1. Traction technique in supine position, with ankles fixated and a dynamometer attached to the head halter. One employee applies traction force.

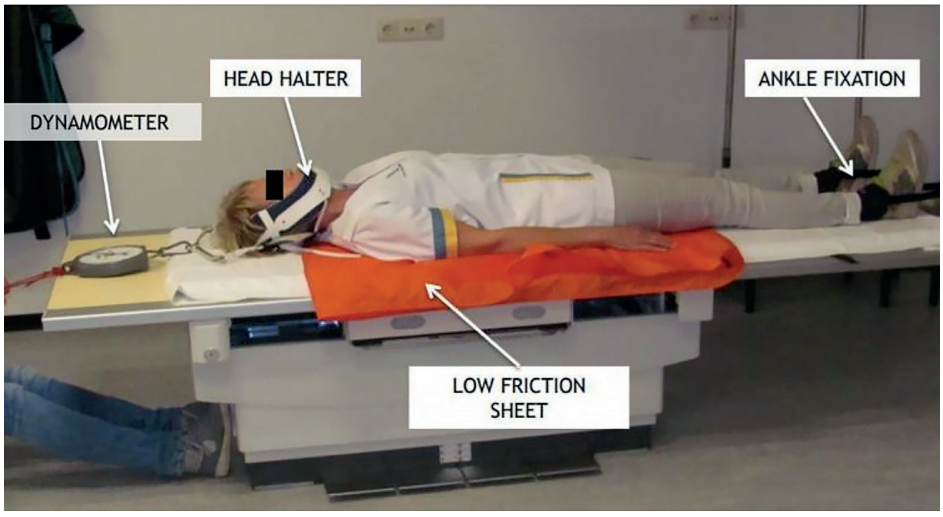
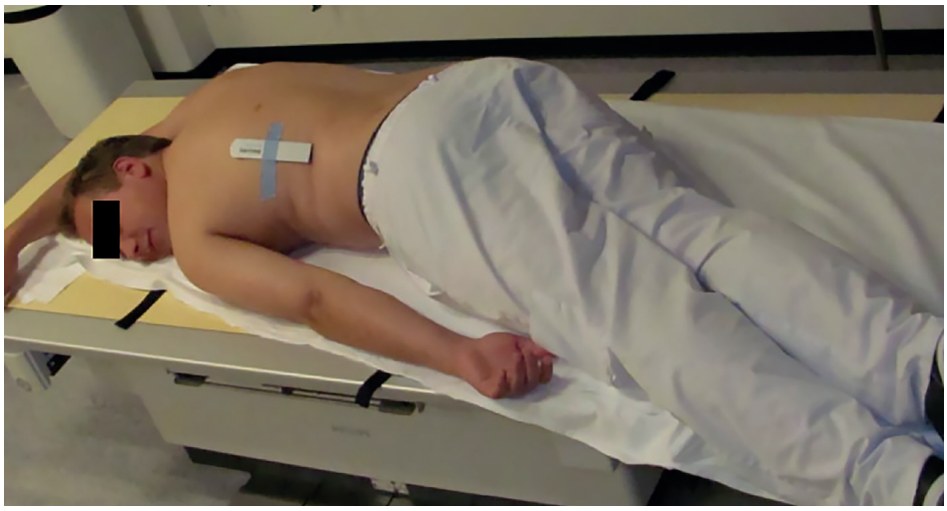


FIGURE 2. Bending technique in prone position. The patient is asked to bend in maximally both sides.



When traction force is applied, or when a patient bends maximally (left and right), the Cobb angle may change. The curve correction, in percentages, is defined as follows:

$$Curve\ correction = \frac{Cobb\ angle\ on\ StFS - Cobb\ angle\ on\ TR\ or\ BE}{Cobb\ angle\ on\ StFS}\ X\ 100\%$$

Differences in this curve correction obtained with traction and bending were analyzed for the primary and secondary curve. Subgroup analyses were performed for the 3 different diagnoses.

STATISTICAL ANALYSIS

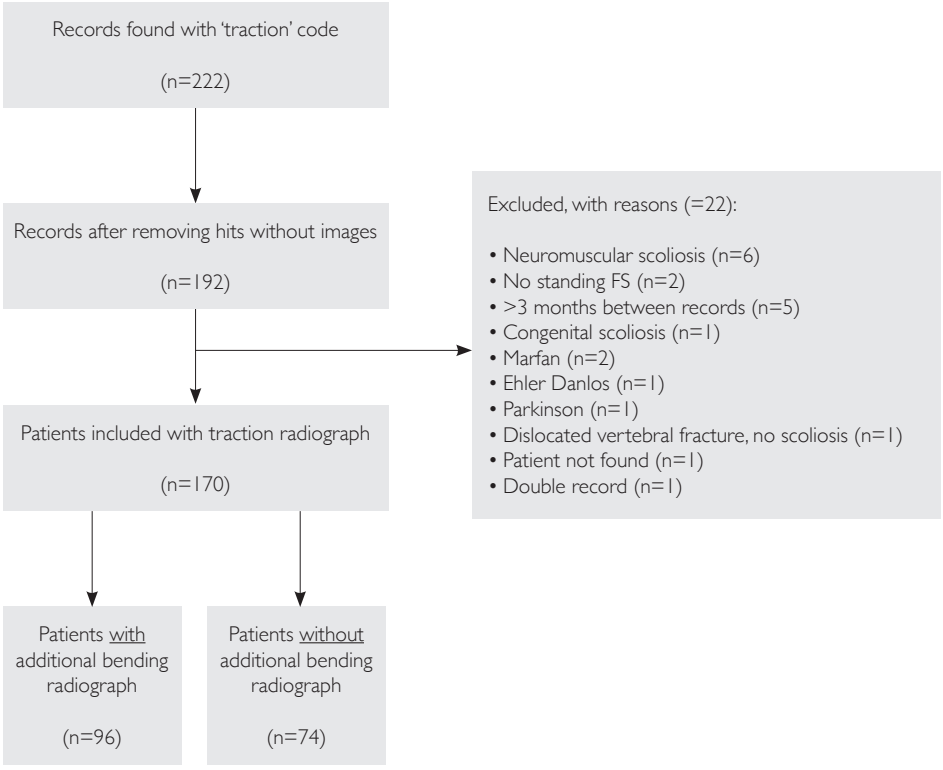
Data was tested for normal distribution (Sharpiro Wilk test). Descriptive analyses were used to describe demographics and Cobb angles. Differences in Cobb angles and curve correction between the 3 subgroups were analyzed with the 1-way ANOVA test. Differences in curve correction on traction and bending radiographs within the subgroups (paired data) were analyzed with the Wilcoxon signed rank test. All statistical tests were performed with Stata (version 13.1, StataCorp LP, USA). Statistical significance was set at $P < 0.05$.

RESULTS

STUDY POPULATION

A total of 222 radiographs were retrieved from the database. 30 radiographs had no images attached to the file. Based on the study criteria, a total of 170 patients were eligible for inclusion (Figure 3).

FIGURE 3. Flowchart of the inclusion and exclusion of radiographs.



PATIENT CHARACTERISTICS

Table 1 provides information on the patient characteristics. Of the 170 patients, 43 were diagnosed with IS (25.3%), 58 with DIS (34.1%) and 69 with DNDLS (40.6%). The age and weight differed between IS and DIS, and between DIS and DNDLS, $p < 0.001$. Corrected for their weight, IS patients tolerated the most traction force (53.1%), while DIS and DNDLS patients tolerated an equal percentage (respectively 46.1% and 46.7%).

TABLE 1. Characteristics of included patients

	IS (n = 43)	DIS (n = 58)	DNDLS (n = 69)	Total (n = 170)
Age (yrs) *§	17.8 ± 3.8	46.4 ± 12.2	59.8 ± 8.4	44.6 ± 19.0
Weight (kg)**	55 [16]	65 [19.5]	71 [16]	65 [18]
	(n = 38)	(n = 44)	(n = 53)	(n = 135)
Traction force (N)**	32.5 [14]	30 [10]	35 [10]	33 [12]
	(n = 40)	(n = 45)	(n = 55)	(n = 140)

*: *Normal distribution. The mean and the standard deviation (SD) are shown. P-value was calculated with the ANOVA test.*
**: *Non-normal distribution. The median and the interquartile range [IQR] are shown. P-value was calculated with the Kruskal-Wallis test.*
§: *n = all patients in that group.*

PRIMARY CURVE (TABLE 2)

The differences between Cobb angles on StFS between the 3 subgroups were statistically significant ($P < 0.001$).

The percentage curve correction on a traction radiograph between IS, DIS and DNDLS was not statistically significant ($P = 0.30$), whereas the percentage curve correction on a bending radiograph was different between the different groups ($P = 0.014$). The greatest curve correction with bending was obtained in the DNDLS group; 44.5% vs. 38.6% (IS) and 34.9% (DIS).

In the DNDLS group, bending showed statistically significant more curve correction compared to traction (44.5% vs. 30.7%; $P < 0.001$). In the DIS group, the difference showed a trend toward more curve correction with bending (34.9% vs. 27.9%; $P = 0.054$). In the IS group, no difference in curve correction was found between bending and traction (38.6% vs. 33.6%; $P = 0.18$).

TABLE 2. Primary Curve Analysis.

	IS (n=43)	DIS (n = 58)	DNDLS (n = 69)	Total (n = 170)	p value
Cobb on StFS (°)*§	58.5 [10.3]	55.7 [17]	36 [19.4]	50.5 [25]	<0.001
Cobb on TR (°)§	37.9 [14]	37.7 [17.3]	25.5 [13.2]	32.7 [17.6]	-
Cobb on BE (°)	37 [20.7] *(n = 30)*	35.0 [24.3] *(n=34)*	21.4 [19] *(n = 32)*	30.8 [26.1] *(n = 96)*	-
CC on TR vs. StFS (%)*§	33.6 [18.0]	27.9 [17.8]	30.7 [21.1]	30.8 [18.6]	0.30
CC on BE vs. StFS (%)*§	38.6 [22.8] *(n = 30)*	34.9 [24.8] *(n = 33)*	44.5 [27.4] *(n = 32)*	37.7 [25.5] *(n = 95)*	0.014
p-value CC TR vs. CC BE**	0.18	0.054	<0.001	-	

**: Non-normal distribution. The median and the interquartile range [IQR] are shown. P-value was calculated with the Kruskal-Wallis test.*
§: n = all patients in that group.
***: Non-normal distribution. The median and the interquartile range [IQR] are shown. P-values were calculated with the Wilcoxon signed-rank test.*
StFS = Standing Full Spine radiograph; TR = traction radiograph; BE = bending radiograph; CC = curve correction.

SECONDARY CURVE (TABLE 3)

Also the Cobb angles of the secondary curve on StFS differed between the groups (P < 0.001).

In contrast to the results for the primary curve, there was a statistically significant difference between curve correction on the traction radiograph between IS, DIS and DNDLS (respectively 34.8% vs. 23.2% vs. 36.1%; P = 0.002). No difference in curve correction on a bending radiograph was seen between the subgroups. (55.0% vs. 41.9% vs. 52.4% for IS, DIS and DNDLS, respectively; P = 0.16).

In the IS and DIS group, bending showed more curve correction compared to traction (55.0% vs. 34.8%; P = 0.002 for IS and 41.9% vs. 23.2%; P < 0.001 for DIS).

TABLE 3. Secondary Curve Analysis.

	IS (n=43)	DIS (n = 58)	DNDLS (n = 69)	Total (n = 170)	p value
Cobb on StFS (°)*§	46.6 [8.9] *(n = 24)*	45.7 [17.9] *(n = 39)*	23 [10.9] *(n = 19)*	41.3 [21.9] *(n = 82)*	<0.001
Cobb on TR (°)§	29.3 [10.6] *(n = 24)*	35.8 [18.7] *(n = 39)*	12.3 [10.1] *(n = 19)*	25.7 [16.5] *(n = 82)*	
Cobb on BE (°)	20.1 [16.3] *(n = 16)*	25.5 [20.1] *(n = 26)*	10.2 [8.1] *(n = 10)*	20.8 [18.6] *(n = 52)*	-
CC on TR vs. StFS (%)*§	34.8 [18.9] *(n = 24)*	23.2 [12.1] *(n = 37)*	36.1 [24.0] *(n = 18)*	28.0 [22.2] *(n = 79)*	0.002
CC on BE vs. StFS (%)*§	55.0 [31.1] *(n = 16)*	41.9 [28.4] *(n = 25)*	52.4 [39.4] *(n = 10)*	49.3 [32.7] *(n = 51)*	0.16
p-value CC TR vs. CC BE**	0.002	<0.001	0.185	-	

**: Non-normal distribution. The median and the interquartile range [IQR] are shown. P-value was calculated with the Kruskal-Wallis test.*
§: n = all patients in that group.
***: Non-normal distribution. The median and the interquartile range [IQR] are shown. P-values were calculated with the Wilcoxon signed-rank test.*
StFS = Standing Full Spine radiograph; TR = traction radiograph; BE = bending radiograph; CC = curve correction.

DISCUSSION

This study demonstrated that prone bending radiographs showed a greater curve correction compared to traction radiographs in DNDLS patients for the primary curve and in IS and DIS patients for the secondary curve. Bending radiographs are considered the current golden standard for assessing the flexibility of the spine in patients with spinal deformity,[3,5] and it is the most used and most investigated method.[8] In an addition to the existing research on spinal deformity assessment techniques, we performed an analysis on traction versus bending radiographs in a cohort of IS, DIS and DNDLS patients. To our knowledge, this is the first study that compares traction and bending radiographs in IS as well as adult spinal deformity.

Our study provides detailed information on the curve correction between traction and bending in 3 different subgroups of scoliosis, including the traction force needed

to obtain supine traction films. The analysis showed that for the primary curve, bending showed a greater correction than traction in the DNDLS and DIS group (trend for the DIS group, P = 0.054). As for the secondary curve, the analysis showed that the most curve correction was obtained by bending radiographs in IS and DIS patients. In the DNDLS group, bending obtained a considerably greater curve correction but this was not statistically significant (P = 0.185). Probably, due to the small number of patients ($n_{traction}$ = 18 and $n_{bending}$ = 10) in this group.

In the literature, only few studies exist evaluating traction versus bending radiographs. All of these studies analyzed the IS population.[4,9-12] Our analysis showed similar results as reported by Hamzaoglu et al.[9] They studied 34 IS patients and found that supine bending had an overall greater curve correction than traction, although no statistical significance was reported. In contrast, O'Neill et al.[4] showed an overall greater correction on the traction radiograph. However, the traction force was applied to the axillae instead of the cervical spine, only 15 patients were analyzed and most patients had thoracic curves (10/15). Although they showed that a greater curve correction was achieved on traction, our data showed a greater correction on bending. A possible explanation for our different conclusion is the increased stability/stiffness of the thoracic spine due to the rib cage and the number of thoracic curves in their population. A computer-simulated mathematical model on the flexibility of the thoracic spine[13] which suggested that the rib cage enhances the stability of the normal thoracic spine during lateral bending. In addition, Watanabe et al.,[12] who studied 229 IS patients, suggested that more curve correction is seen on traction radiographs when the curve apex is located more cranially than T9, which can also be attributed to the rib cage.

The procedure to obtain a traction radiograph is more labor intensive compared to a bending radiograph. As it requires 2 radiology workers; 1 to obtain the radiograph, and 1 to provide the traction force. Also, a traction radiograph is very uncomfortable for patients, compared to side bending radiographs, as the cervical traction is applied to maximum patient tolerance. On the other hand, making side bending radiographs requires 2 radiographs instead of 1. This exposes the patients to twice the amount of radiation. Taking these 3 factors into account when choosing a method for flexibility assessment, in combination with the results of our analysis (greater correction on bending, or no difference between traction or bending), bending radiographs seem the preferable method for everyday clinical care of the spinal deformity patients. Based on the results of

the present study, we abandoned the traction radiographs for curve flexibility assessment in IS, DIS and DNDLS patients in our practice.

LIMITATIONS

Several limitations should be mentioned. First, this is a retrospective cohort study and therefore we could not influence the decision-making process for obtaining which radiographs. The type of radiographs obtained in each case was at the surgeon's discretion. The available radiograph sets, including bending radiographs, were less frequently available in the DNDLS group (32/69; 46%) compared to the IS (30/43; 70%) and DIS (34/58; 59%) group. Second, although the Cobb angle is considered the gold standard in evaluating the coronal plane, a measurement error of 3 to 5 is known.[14] This subsequently increases the chance of obtaining a nonsignificant result.[15] Third, no distinction in curve severity or Lenke classification was made for IS curves. Our subgroups would become too small and the analysis would lose its power. Fourth, our research only included the flexibility assessment in the coronal plane for the bending and traction radiographs. Fifth, the surgical implications (planning, surgical approach and determining osteotomy or fusion levels) and the sagittal parameters were not included in the scope of our research.

CONCLUSION

In conclusion, prone bending radiographs compared to supine traction radiographs better serve the purpose of curve flexibility assessment of (IS, DIS and DNDLS) spinal deformity, despite the fact that patients are exposed to more radiation.

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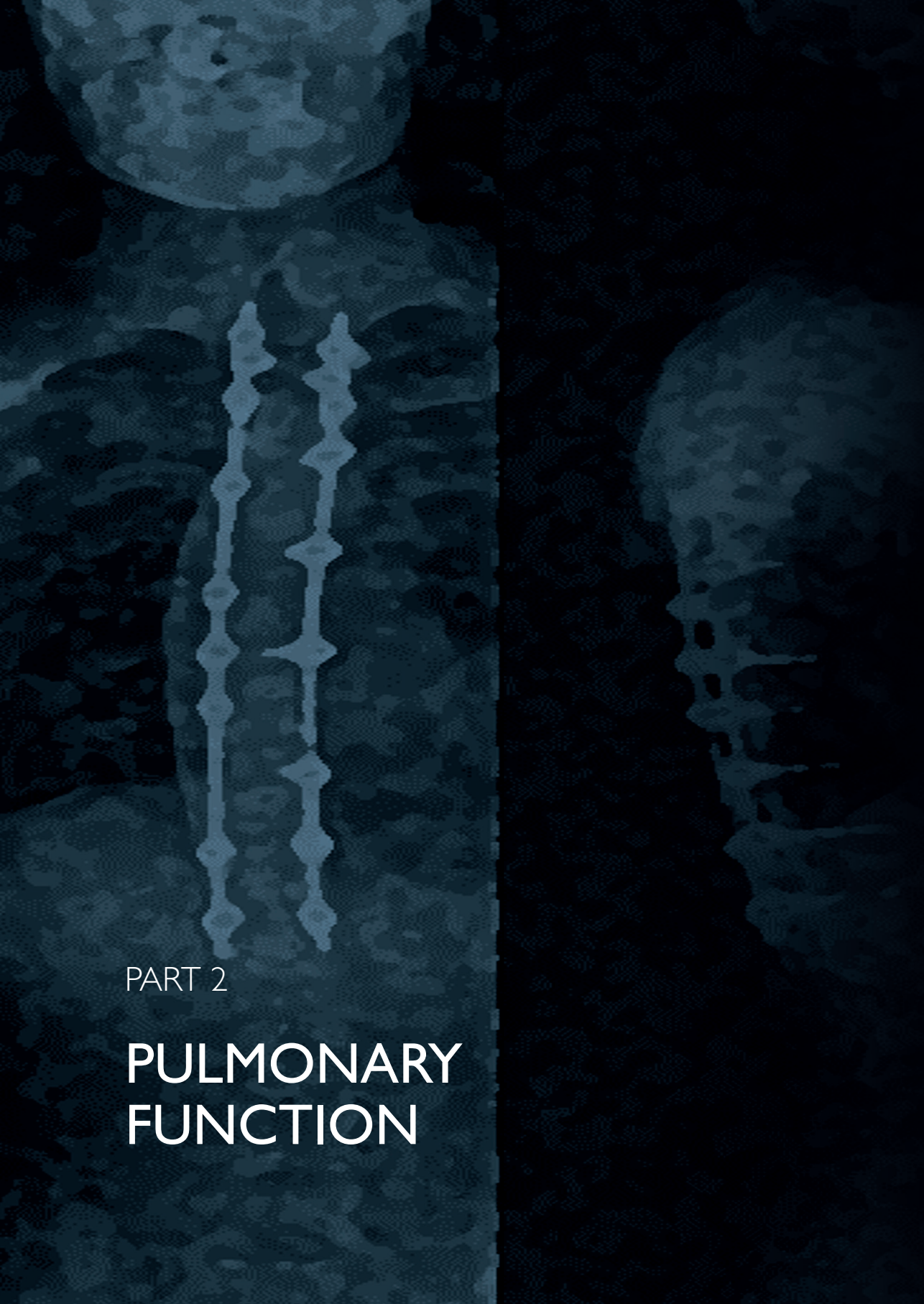

PART 2

PULMONARY FUNCTION

CHAPTER 4

PULMONARY FUNCTION IN PATIENTS WITH SPINAL DEFORMITY: HAVE WE BEEN IGNORANT?

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Niek te Hennepe
Marinus de Kleuver

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PULMONARY FUNCTION IN PATIENTS WITH SPINAL DEFORMITY: HAVE WE BEEN IGNORANT?

Spine deformity refers to a broad spectrum of abnormal spinal curvatures, which are prevalent in all ages, and are seen by family physicians, orthopedists, and spine specialists. Pulmonary symptoms such as shortness of breath with exertion and reduced exercise tolerance are commonly experienced in both adolescents and adults with a spinal deformity. As yet, these clinically relevant pulmonary symptoms are not routinely monitored and may have health implications later in the patient's life as pulmonary function gradually deteriorates with age. This Perspective aims to create awareness among care providers and researchers: attention should be paid to this underexposed domain when consulting with patients who have a spinal deformity, and adequate measurement instruments need to be developed to ultimately enhance the quality of care delivered to these patients.

ADOLESCENT IDIOPATHIC SCOLIOSIS (AIS)

In adolescence, idiopathic scoliosis is the most common type of scoliosis, occurring in about 2–3% of adolescents aged 16 years or younger.[1] Various symptoms, such as back pain, reduced self-image, physical disability, and cardiopulmonary compromise, are well reported in AIS.[1,2] The effect of AIS on pulmonary function has been recognized and could lead, when untreated, to disability secondary to pulmonary symptoms, such as shortness of breath during daily functioning or exercise intolerance.[3–5] Furthermore, it seems an important contributing factor to avoidance of activities and exercise training in patients with AIS.[6] Surprisingly, however, it is not routinely quantified/measured, and in all scientific publications this domain is rarely reported and extremely underexposed. Have we been ignorant?

In research, attempts have been made to objectively quantify pulmonary function in patients with AIS using clinical pulmonary function tests (PFTs). Even though a decrease in values of total lung capacity may be seen, dissociation exists between the measured pulmonary deficits and symptoms experienced by the patients.[4] Although PFTs are valuable to investigate and monitor patients with suspected or known respiratory pathology and to evaluate patients prior to major surgery[7], conflicting evidence exists regarding their clinical value for both clinicians and patients in routine care for AIS

patients. As such, obtaining routine PFTs for long-term patient surveillance and/or quantifying treatment effects is not standard practice as they lack clinical relevance, and are time consuming and costly to obtain.

ADULT SPINAL DEFORMITY (ASD)

Symptomatic ASD refers to various degenerative, progressive conditions and affects the thoracic or thoracolumbar spine throughout the aging process.[8] In younger adults the most common spinal deformity is persistent idiopathic scoliosis, whereas in middle-aged and older adults de novo degenerative lumbar scoliosis or adult degenerative scoliosis are more common.[8,9] Given its prevalence, with rapid increases expected over the coming decades, the disorder is of growing interest in health care. Global disparities in both assessment and treatment of ASD exist, resulting in high costs for society.[8]

Despite the (limited) knowledge regarding pulmonary function in adolescents, even less evidence is available regarding the effects of ASD on pulmonary function and the impact of (surgical) interventions for ASD on pulmonary function.[10] A natural decline in pulmonary function is seen with aging but seems more pronounced in patients with untreated spinal deformity.[3] Surgery in ASD patients has been reported to result in a significant deterioration in (clinical) PFTs two years following surgical correction.[10] However, here too it is not routinely quantified/measured, and in scientific publications this domain is rarely reported and extremely underexposed.

PULMONARY FUNCTION: CLINICIANS' AND PATIENTS' PERSPECTIVE

CLINICIANS' PERSPECTIVE

Recently, for both AIS[11] and ASD[12] a standard outcome set was developed. The relevance of routinely assessing pulmonary function in both AIS and ASD was recognized by a worldwide group of expert clinicians, but such a patient-relevant measure is not currently available.

PATIENTS' PERSPECTIVE

To obtain a first impression of pulmonary problems as experienced by patients with AIS and ASD, an anonymous exploratory survey was performed during an information

day for adolescents and adults with scoliosis in the Netherlands. Questions were related to pulmonary symptoms (including description in own words); limitations in daily functioning due to pulmonary symptoms; worsening of symptoms with increased fatigue; differences during the course of the day (answer options yes/no). Patient characteristics included age, concomitant respiratory disease, and previous surgical treatment for AIS or ASD. When previous spine surgery had been performed it was asked whether symptoms were different after surgery (relevant difference in terms of improvement and worsening, or no difference). After brief instruction, in total 58 patients completed the survey, aged 43 years (SD 12; categorized 10–17 years [n = 9]; 18–24 years [n = 10]; 25–40 years [n = 6], and ≥ 40 years [n = 33]). 3 patients reported having a respiratory disease (COPD [n = 1]; asthma [n = 2]). Among the 58 patients, 26 experienced pulmonary symptoms (age < 40 years [8/25]; ≥ 40 years [15/33]). Most patients described their symptoms as "breathlessness" (10/26) or "fatigue"/"fatigue due to limited endurance" (5/26). Daily functioning of 19/26 patients was limited due to the pulmonary problems and 18/26 patients reported worsening of symptoms with increased fatigue. Fourteen patients underwent scoliosis surgery and four of them experienced a relevant difference before and after the surgery. Although this survey undoubtedly has selection bias, these preliminary results indicate that pulmonary symptoms are prevalent and were commonly experienced in about half of both adolescent and adult patients.

CONTINUOUS OUTCOME MONITORING: PULMONARY FUNCTION

In the era of value-based healthcare, to monitor the quality of the full cycle of care for patients with spinal disorders, routine outcome monitoring through outcome registries is valuable.[13] These outcome registries are based on a standard set of patient-relevant outcomes, i.e. patient-reported and clinician-based outcomes that matter to patients.[13] Based on the above, an outcome measure that includes patients' experience regarding pulmonary function is clearly needed.

RELEVANCE OF PATIENT-REPORTED OUTCOME MEASURE (PROMS): THE WAY FORWARD?

As yet, the theoretical construct of pulmonary function in both AIS and ASD, in terms of for example shortness of breath, and/or reduced exercise tolerance and/or respiratory fatigue, is not clearly understood. As such, no adequate methods are available that take patients' perspective into account to quantify this in routine clinical practice. Clinical PFTs lack clinical relevance, as they do not cover the patients' perspective, are time consuming, and are expensive to obtain in routine clinical daily practice. An adequate PROM might be a good alternative to assess pulmonary function in patients with spinal deformity. However, when following guidelines for the development of PROMs it takes several years to develop an adequate PROM in different languages and in terms of validity, reliability, and responsiveness (measurement properties). A general PROM development process, in which both clinicians and patients are involved, consists of several iterative steps that require mixed qualitative and quantitative (longitudinal) study designs[14,15]: definition of the theoretical construct to be measured, item generation, generating and selecting items, development of scales and scoring methods, initial pilot testing (feasibility and usability), and clinical field testing to evaluate its validity, reliability, and responsiveness (measurement properties). Our patient survey has demonstrated that we may indeed have been ignorant of an important aspect of adolescent and adult spinal deformity patients' lives, and that we need to explore this further. Meanwhile, whilst work is performed to develop an adequate PROM, we recommend that care providers who see adolescents and adults with a spinal deformity should be aware of, pay attention to, and address pulmonary symptoms experienced, such as shortness of breath or reduced exercise tolerance.

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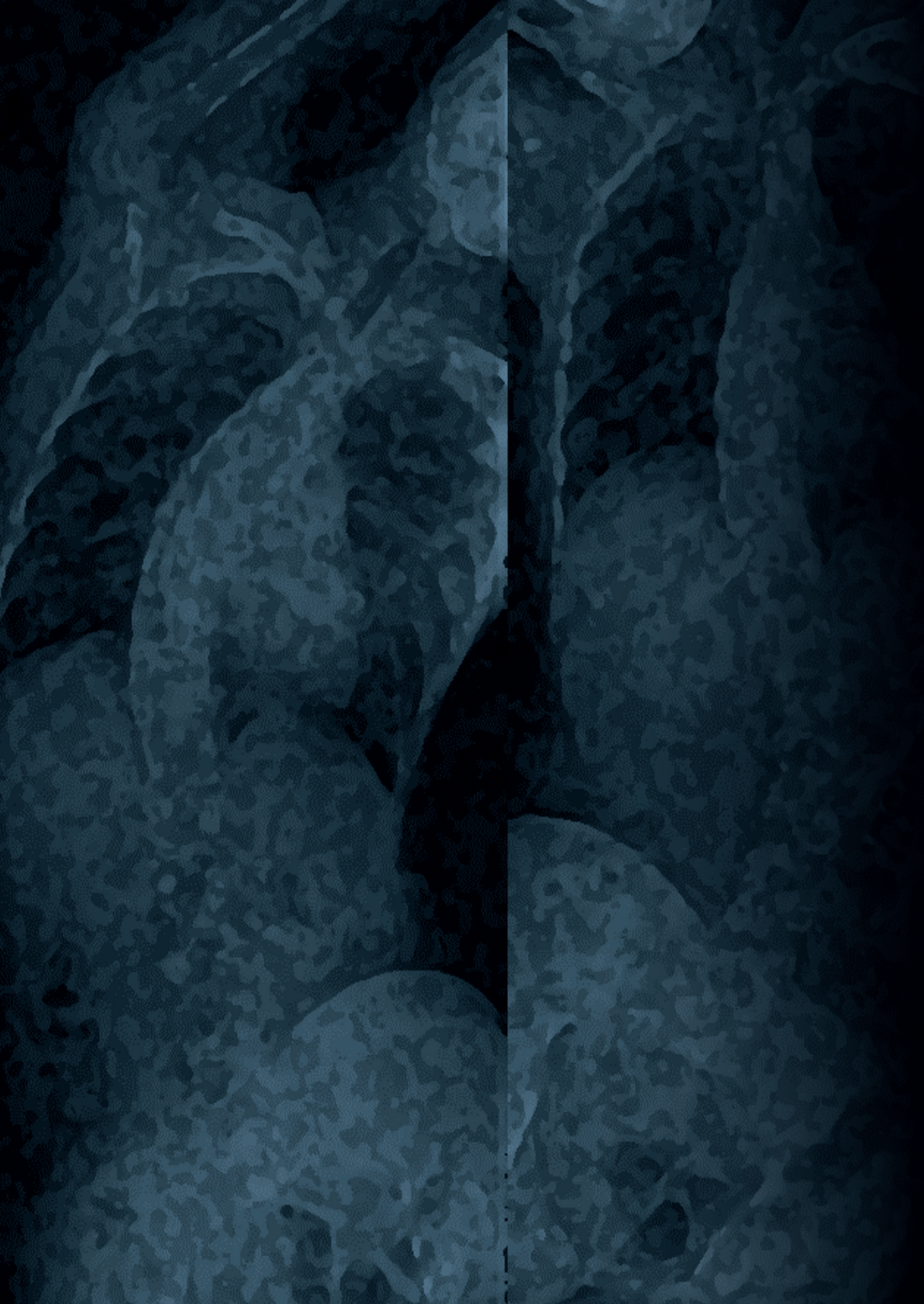

CHAPTER 5

PULMONARY SYMPTOMS IN ADOLESCENT IDIOPATHIC SCOLIOSIS: A SYSTEMATIC REVIEW TO IDENTIFY PATIENT-REPORTED AND CLINICAL MEASUREMENT INSTRUMENTS

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ABSTRACT

Study design: Systematic review.

Purpose: Adolescent idiopathic scoliosis (AIS) is a deformity of the trunk and chest and can cause a spectrum of pulmonary symptoms. However, no standardized measurement instrument exists. The aim of this systematic review is to identify and describe patient-reported and clinical measurement instruments used to evaluate pulmonary symptoms in patients with AIS.

Methods: Studies published after 01.01.2000 were included in a systematic search. Patient-reported outcome measures (PROMs) and clinical measurement instruments for pulmonary symptoms were extracted as well as their measurement properties (floor-ceiling effects, validity, reliability, responsivity and interpretability). The Risk of Bias (RoB) was evaluated.

Results: Out of 3146 studies, 122 were eligible for inclusion. Seven clinical measurement instruments, measuring 50 measurement parameters, were identified. Five PROMs for pulmonary symptoms were identified. Studies assessing the quality of measurement properties in the AIS population were not identified. As such, the RoB could not be determined.

Conclusion: No available adequate patent centric instruments were identified that measure pulmonary functioning and symptoms. Although clinical measurement instruments are regularly used, their use in routine practice does not seem feasible. The measurement properties of some identified PROMs seem promising; however, they have not been validated in an AIS population. As pulmonary symptoms in patients with AIS are still poorly understood, the development of such a construct and potentially a subsequent PROM to routinely measure pulmonary functioning and patient experience is recommended.

Keywords: Adolescent idiopathic scoliosis; Clinimetric; Measurement properties; PROM; Pulmonary function; Pulmonary symptoms.

INTRODUCTION

Adolescent idiopathic scoliosis (AIS) is a complex, three-dimensional deformity of the spine and chest wall and is defined as a curvature of the spine ≥10 degrees in the coronal plane.[1,2] AIS can cause a wide range of symptoms, e.g. impaired mobility, reduced strength, function loss and back pain.[3,4] Depending on the location and severity of the curvature, pulmonary symptoms such as shortness of breath and reduced exercise tolerance may occur.[5] As pulmonary functioning and symptoms change over time with aging, this potentially has negative consequences for quality of life and exercise tolerance for adult patients with an adolescent onset idiopathic scoliosis.

Despite the above, pulmonary functioning and symptoms are not routinely monitored and in scientific publications this domain is rarely reported and extremely underexposed.[6] The need for routine assessment of pulmonary function in patients with spinal deformities has been identified in a recent patient survey.[6] Furthermore, international consensus studies revealed that "pulmonary fatigue" should be included as an outcome domain in a standard outcome set for adolescents and young adults (AYA)[7] as well as for adults[8] with a spinal deformity undergoing surgical treatment. Although determined as a standard outcome, the authors concluded in both studies that as yet an adequate patient-relevant measure is not available.[7,8]

In AIS clinical measurement instruments (e.g. spirometry) to assess pulmonary functioning and symptoms, have been frequently used. Out of many available clinical tests, spirometry is the most frequently used modality to assess key parameters of pulmonary function, in particular forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV_1). Classic patterns deriving from spirometry are so-called obstructive and restrictive patterns.[9] Obstruction, i.e. decreased FEV_1/FVC ratio, is seen in lung diseases such as chronic obstructive pulmonary disease (COPD), asthma, or cystic fibrosis.[9] Restrictive patterns, i.e. normal FEV_1/FVC ratio but decreased FVC, are seen in various parenchymatous fibrotic lung diseases as well as in patient with thoracic deformities.[9] Of importance, spirometry has proven a reproducible diagnostic tool allowing for long-term repeated measurements as well as for evaluating the effect of interventions that may have altered pulmonary function.[9] AIS can cause a restrictive spirometric pattern due to decreased chest wall compliance that prevents normal inflation of the lungs.[10,11] A

negative association between the severity of the thoracic curvature and FVC and FEV_1 has been reported.[12]

Although clinical measurement instruments such as spirometry are frequently used, these instruments seem to lack clinical relevance, as they do not represent the patients experience (i.e. objective values that may not correlate with the patients symptoms), they are time consuming, and they are expensive to obtain in routine clinical daily practice.[6] Additionally, the focus of routine outcome measurement has broadened toward including outcome assessment from the patient's perspective which can easily be monitored over time (e.g. patient-reported outcome measures (PROMs)).[13,14]

The objective of this systematic review is to identify currently available patient-reported and clinical measurement instruments that assess pulmonary functioning and symptoms in AIS.

METHODS

A systematic review of the literature was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.[15] The protocol of this review was registered in PROSPERO (ID 129174), an international prospective registry of systematic reviews.[16]

SEARCH STRATEGY AND ELIGIBILITY CRITERIA

A literature search was conducted on 18.06.2020 in the databases of PubMed, EMBASE and The Cochrane Library (Appendix 1). Keywords used to identify relevant papers were "spinal curvatures"(MeSH), "patient reported outcome measures"(MeSH), "respiratory function test"(MeSH), "scoliosis", "pulmonary function", "respiratory function", "lung function", "cardiopulmonary", "lung volume", "respiratory test", and "ventilation test" in the title or abstract. Duplicates were removed. An online web application (Rayyan[17]) was used for the title, abstract, and full text screening. The titles and abstracts were independently screened by two authors (NtH and SSAF). Full texts were retrieved from all publications which passed the title and abstract screening and were independently reviewed for inclusion by the same two authors according to the following inclusion

criteria: (1) diagnosis AIS, (2) minimal use of one measurement instrument for pulmonary function (patient-reported or clinician based), (3) all forms of treatment (surgical and non-operative), and (4) retrospective and prospective cohort studies, randomized controlled trials, case-control studies and case-reports. Exclusion criteria were (1) reviews, (2) non-English language, (3) publication prior to 01.01.2000, and (4) other diagnosis than AIS (i.e. infantile, juvenile idiopathic scoliosis, early onset scoliosis, congenital scoliosis or neuromuscular scoliosis). In case of disagreement regarding the inclusion or exclusion of studies, the authors arranged a consensus meeting. When disagreement persisted, a third independent reviewer (MP) made the final decision.

DATA EXTRACTION

The following data were extracted from the included studies: first author, region of origin, year of publication, number of AIS patients, mean age of patients, given treatment, mean follow up, used measurement instruments, and measured parameters to evaluate pulmonary symptoms.

MEASUREMENT PROPERTIES

To determine the adequacy of the identified measurement instruments, in terms of measurement properties, an additional literature search was performed in PubMed, EMBASE and The Cochrane Library. The additional search was performed to find relevant studies that assessed the measurement properties of PROMs and the four most-used clinical measurement instruments identified in the systematic review (Appendix 2). Additionally, studies were searched through backwards citation (Appendix 3).

Assessment of the measurement properties of identified PROMs was based on the quality criteria as developed by Terwee et al[18]. The following measurement properties were evaluated: (1) content validity, (2) internal consistency, (3) criterion validity, (4) construct validity, (5) reproducibility (5a agreement and 5b reliability), (6) responsiveness, (7) floor and ceiling effects and (8) interpretability.

QUALITY ASSESSMENT

The COSMIN Risk of Bias (RoB) checklist[19,20,21] was used to assess the quality of the included publications in which the measurement properties were determined.

RESULTS

SEARCH RESULTS

The systematic search generated a total of 3,146 papers (Fig. 1). After removing duplicates, 2,388 studies remained, which were screened on title and abstract. Of these 2,388 studies, 335 were potentially eligible and the full texts were retrieved and screened. 213 papers were excluded after full text screening, and 122 were eligible for inclusion.

FIGURE 1. PRISMA flow diagram of identification, screening and inclusion of papers.

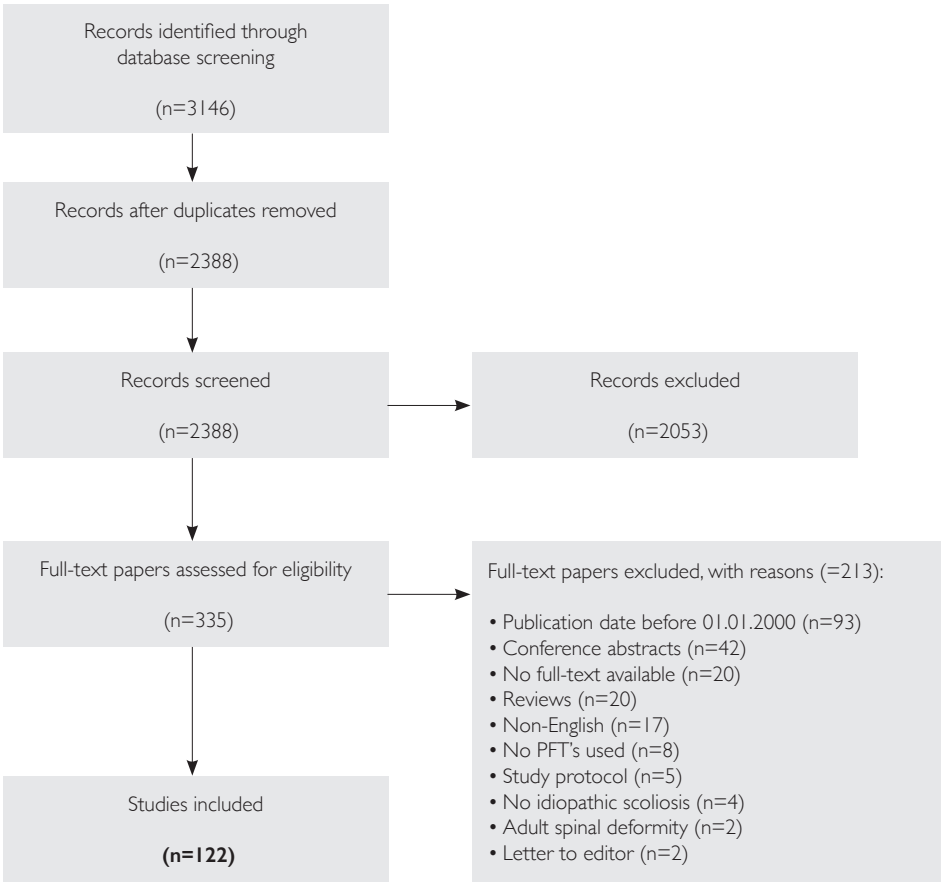

TABLE 1. Characteristics of included studies

Variables	Total n = 122	N	%
World region	Asia	46	38
	North America	41	34
	Europe	29	24
	South America	5	4
	Australia	1	0.8
Year	2016–2020	42	34
	2011–2015	33	27
	2006–2010	28	23
	2000–2005	19	16
No patients	> 200	9	7
(Mean = 77.6)	100–199	15	12
	50–99	33	27
	10–49	57	47
	2–9	5	4
	1	3	2
Mean age	> 20 years	7	6
(Mean = 15.8)	15–19 years	30	25
	10–15 years	82	67
	Not reported	3	2
Treatment	Surgical	83	68
	Brace	6	5
	Surgical vs. brace	1	0.8
	Traction (Halo-gravity or halo-femoral)	2	2
	Exercise therapy	6	5
	No treatment reported	24	20
Follow-up	> 10 years	10	8
	5–10 years	8	7
	2–5 years	14	11
	0–2 years	51	42
	No follow-up	39	32

CHARACTERISTICS OF INCLUDED STUDIES

Table 1 provides the main characteristics of all the included studies. Of the included studies, most were conducted in Asia (46/122; 38%) or North America (41/122; 34%). The vast majority of the studies (82/122; 67%) described a population between 10-15 years of age and the greater proportion had surgical treatment (83/122; 68%). In 39/122 (32%) studies no follow up was reported and in 24/122 (20%) treatment modality was not described.

EXTRACTED DATA

CLINICAL MEASUREMENT INSTRUMENTS

50 pulmonary parameters were identified, measured by seven different clinical measurement instruments (spirometry, plethysmography, 3D-reconstruction (by MRI, CT or radiographs), manometer, gas analyzer, arterial blood analysis and physical examination). Parameters that were used in 10% or more of the studies (≥12/122) are presented in Table 2, categorized by used method or instrument. In Appendix 4 the parameters used in less than 10% of the studies are presented.

Forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), the Tiffeneau index (FEV_1/FVC) and total lung capacity (TLC) measured by spirometry or plethysmography are most frequently used (respectively 99/122; 81%, 97/122; 80%, 31/122; 25% and 29/122; 24%). Three-dimensional reconstruction (of the lungs or chest wall) by MRI, CT or radiographs was also commonly used (total 15/122; 12%). Exercise capacity (VO_2max) and maximal ventilation ($V_E$max) was used in 11% of the included studies.

PATIENT-REPORTED OUTCOME MEASURES (PROMS)

9% of the studies (11/122) used a PROM (Table 3). A total of five different PROMs were identified, being the Borg dyspnea scale, the Borg ratings of perceived exertion (RPE) scale, the MRC Breathlessness scale, the University of California at San Diego Shortness of Breath questionnaire (UCSD SOBQ) and a breathing effort scale. The most commonly used PROM is the Borg dyspnea scale (6/11; 55%). The Breathing effort scale was a scale improvised by the authors of the paper, not officially developed in original research.

TABLE 2. Identified clinician based measurement instruments

Measurement instrument	Explanation [1-6]	N	%
Spirometry		110	90
FVC	Forced vital capacity. The amount of air that can be forcibly exhaled after maximal inspiration	99	81
FEV_1	Forced expiratory volume in one second. The amount of air that can be forcibly exhaled after maximal inspiration during the first second	97	80
FEV_1/FVC	Ratio of the volume of air exhaled during the first Second of a forced expiratory effort to the total Volume of air exhaled during the FVC	31	25
VC	Maximum volume of air exhaled from a point of full inspiration	20	16
Plethysmography		32	26
TLC/TLV	Total air capacity of the lungs after a full inspiration (including lung residual volume), measured during a full pulmonary function test	29	24
Imaging techniques			
3D reconstruction	Using different kinds of imaging techniques to analyze and measure the volume of the lungs or the thorax. Techniques used are:	15	12
	Dynamic breathing MRI; inspiratory and expiratory lung volumes	2	2
	CT; reconstruction of lung volumes using computed-tomography	8	7
	Radiographs; reconstruction of the rib cage using AP and lateral radiographs	4	3
	Ventilation/perfusion scan with SPECT/CT and radiolabeled macroaggregates of human albumin	1	0.8
	Kinematic analysis of the trunk; using 41 reflective markers recording volume changes for upper chest, lower chest and abdomen using a motion analysis system	1	0.8
Gas analyzer	*(During exercise, often ISWT*, 6MWT** or cycle ergometer)*		
VO_2max	Maximum volume of oxygen consumption per minute	14	11
$V_E$max	Ventilation (based on tidal volume and respiratory rate) during exercise. Peak VE can be assessed relative it can help determine if exercise intolerance or dyspnea relate to a pulmonary limitation	13	11

** = incremental shuttle walk test. ** = 6 min walk test*

TABLE 3. Identified patient reported outcome measures

Measurement instrument	Explanation	N	%
Borg dyspnea scale	A scale from 0 to 10 that rates the difficulty of breathing experienced by patients at a given point	6	5
Borg rating of perceived exertion scale	A scale from 6 to 20 that rates the perceived exertion experienced by patients at a given point	1	0.8
MRC breathlessness scale	A scale from 1 to 5 that rates the degree of breathlessness related to activities	2	2
UCSD SOBQ	University of California at San Diego Shortness of Breath questionnaire. A 24-item measure that assesses self-reported shortness of breath while performing a variety of activities of daily living	1	0.8
Breathing effort scale	Unofficial score of breathing effort. Scale from 1 to 9 with ascending order of effort	1	0.8

The Borg RPE scale[22] was originally defined by Borg in 1970, assessing the amount of exertion during exercise, ranging from 6-20, with 7 being "very, very light" and 19 being "very, very hard" and assesses the exertion during physical exercise, which is not only affected by the pulmonary function, but also by the cardiac function, vascular function and overall fitness. The Borg dyspnea scale[23] was created in 1982, as a modification on the originally defined RPE scale, therefore it is also known as the modified Borg scale (*m*Borg scale). It rates the breathlessness from 0 (nothing) to 10 (maximal) during exercise. This only represents the dyspnea experienced by a patient at a certain point in time, not taking fatigue or weariness during the day into account which is deemed important in AIS. Moreover, the mBorg scale is assessed during exercise.

The MRC Breathlessness scale quantifies the disability associated with breathlessness with one question by identifying when breathlessness and restrictions occur during daily activities.[24] It was defined by Fletcher et al.[25] in 1959. This single question originally comprised a 1 to 5 points scale with 1 being "I only get breathless with strenuous exercise" and 5 being "I am too breathless to leave the house" or "I am breathless when dressing". This was later modified to a 0 to 4 scale, with the same items.

The UCSD SOBQ was originally developed 1987.[26] It is a 24 item questionnaire that assesses the shortness of breath while performing a variety of activities of daily living, thereby evaluating the functional limitations. The questionnaire consists of 21 activity-

based items and three questions about limitations due to shortness of breath, fear of harm from overexertion and fear of shortness of breath. The activity based items are scored on a 6 point scale, with 0 indicating no shortness of breath and 5 indicating "worst" or "unable to do due to shortness of breath". [27,28]

MEASUREMENT PROPERTIES

No studies were identified assessing the measurement properties of the Borg dyspnea scale, Borg RPE scale, MRC Breathlessness scale, UCSD SOBQ, FVC, FEV_1, FEV_1/FVC or TLC in an AIS population (Appendix 2).

QUALITY ASSESSMENT – RISK OF BIAS

The Risk of Bias could not be determined, as no studies were identified that evaluate the measurement properties of these measurement instruments in AIS.

DISCUSSION

AIS can significantly affect pulmonary function[5,10–12], which is recognized by both clinicians[7] and patients.[6] Currently, no consensus exists on how to measure pulmonary functioning and symptoms in this group of patients, and a plethora of measurement instruments are being used.[6] This systematic review identified a total of seven clinical measurement instruments and five patient-reported outcome measures (PROMs) that have been used in studies of AIS patients from 2000 to 2020. No studies were identified on concomitant measurement properties to determine the adequacy of the identified measurement instruments. As such, floor-ceiling effects, validity, reliability, responsivity and interpretability of identified PROMs could not be evaluated in an AIS population. This study has not been able to identify any currently available adequate patient centric instrument to measure pulmonary outcomes following treatment for AIS in routine daily practice.

CLINICAL MEASUREMENT INSTRUMENTS

A total of seven clinical measurement instruments were identified, measuring 50 pulmonary parameters such as FVC, FEV_1, FEV_1/FVC and TLC (Table 2 and Appendix 4). Spirometry and plethysmography are the most frequently used clinical based measurement instruments and generally provide an adequate assessment of the volume and flow functions of the lungs.[29] Although both are reliable measurement instruments for the diagnosis of restrictive lung defects[9,30,31], as yet, no evidence exists for the adequacy of these instruments as outcomes measurement instruments in patients with AIS.

Even though many clinical measurement instruments are frequently used in the literature, they are not suited for routine outcome measurement for patient-centered care reporting in an AIS population. They lack clinical relevance as they do not cover the patients' perspective, are time consuming, and are expensive to obtain in routine clinical daily practice.[6]

PATIENT-REPORTED OUTCOME MEASUREMENTS (PROMS)

Five PROMs were identified that have been used to assess pulmonary symptoms in AIS (Table 3). As yet, the quality of these PROMs, in terms of measurement properties as described by Terwee et. al[18], have not been evaluated in the AIS population. The Borg dyspnea scale, Borg RPE scale, MRC Breathlessness scale and the breathing effort scale evaluate the amount of breathlessness/dyspnea in a single point in time, scoring it from 6-20 (Borg RPE), 0-10 (Borg dyspnea), 1-5 (MRC) or 1-9 (breathing effort). The 24 item UCSD SOBQ is the only scale that includes the experienced limitations during daily activities. It consists of 21 items covering the amount of breathlessness (0-5) during daily activities and 3 items concerning shortness of breath, fear of hurting themselves by overexerting, and fear of shortness of breath limiting daily lives.

No evidence was found regarding the measurement properties of any of the identified PROMs in an AIS population. This does not mean that the evidence is absent. To evaluate which PROM might be eligible for future use a post-hoc literature search was performed to find studies that assessed the measurement properties of the identified PROMs in populations other than AIS (Appendix 5). Twenty studies were found and the quality these studies was good ('very good' (13/20; 65%), 'adequate' (6/20; 30%), 'doubtful' (1/20; 5%) [Appendix 6 and 7]). For substantiation of the COSMIN checklist, see appendix

8. None of these studies evaluated all measurement properties as described by Terwee et. al.[18] Overall, the UCSD SOBQ seems adequate: 6/9 measurement properties, being content validity, internal consistency, criterion validity, construct validity, agreement and responsiveness were evaluated and were scored 'positive' (Appendix 7). The UCSD SOBQ has been studied in populations with lung disease; obstructive lung disease (OLD)[27], chronic obstructive pulmonary disease (COPD)[32,33] or asthma and idiopathic pulmonary fibrosis (IPF)[28,34]. Although the UCSD SOBQ has good measurement properties and seems promising, patients with lung diseases cannot be directly compared to patients with AIS as patients with AIS have restricted, but overall healthy lungs. Research regarding the measurement properties in an AIS population is needed to demonstrate the adequacy and the clinical usefulness of this PROM.

Besides the UCSD SOBQ, the only other PROM with promising measurement properties was the Borg RPE scale (3/9 properties evaluated), and it appeared to have a good criterion validity, meaning that it relates to the gold standard.[18] The populations studied have been more variable, including patients without primary pulmonary disease, ranging from children to healthy adults and Parkinson patients to patients recovering from a stroke.

Overall, the UCSD SOBQ seems promising as it has good measurement properties and includes the limitations of daily activities, which are important in an AIS population.[6] However, these measurement properties have not been assessed in an AIS population and the questionnaire seems too comprehensive for routine outcome assessment when for example it is compared to the frequently used SRS 22 questionnaire. This questionnaire comprises 22 questions for *five* different outcome domains, versus 24 questions for *one* outcome domain in the UCSD SOBQ. Where the UCSD SOBQ seems too comprehensive for routine use, the Borg RPE scale seems too concise for assessing the pulmonary problems in AIS, even though it has good criterion validity (also not evaluated in an AIS population). The Borg RPE scale only assesses the amount of breathlessness in a single point in time, mostly used during or directly after exercise. It does not include any other information on pulmonary symptoms such as an increased fatigue, which is a regularly reported symptom in AIS patients.[6]

FUTURE PERSPECTIVE

Patients experience a large variety of pulmonary signs and symptoms such as shortness of breath, reduced exercise tolerance, respiratory fatigue, and perceive limited daily functioning due to these pulmonary symptoms.[6] However, as yet, the underlying cause and theoretical construct is not understood. Are the experienced limitations based on the dysfunction of the lungs themselves (e.g. limited inflation of the lungs) or is the fatigue due to increased energy consumption by the musculoskeletal system the main problem? Could the symptoms have a cardiovascular origin? A recent study showed that a proportion of AIS patients seem to have impaired right cardiac function, with pulmonary hypertension. This dysfunction normalized after scoliosis surgery, indicating the benefits of spine surgery on cardiac function, possible due to re-alignment of the spine, cardiovascular structures, or rib cage.[35] Insight in the pulmonary symptoms that are experienced by patients with AIS will support the process of the development of an adequate PROM that might be implemented for outcome measurement in routine daily use. This will also aid the evaluation of aging, progression of the curve or different treatment strategies on the pulmonary function and symptoms in patients with scoliosis. We therefore recommend to explore further with patients what limitations they experience, and with which questions / items this might be measured. This will help create a theoretical construct for the pulmonary problems experienced by patients with AIS, ultimately leading to the identification and validation of an existing PROM, such as the UCSD SOBQ or the development of a new disease specific PROM.

LIMITATIONS

Several limitations of this study should be mentioned. First, selection bias might have occurred, as articles prior to 01.01.2000 and non-English articles were excluded to acquire the most relevant literature. Second, measurement properties of only the four most used clinical measurement properties (FVC, FEV_1, FEV_1/FVC and TLC) were assessed. However unlikely, it is possible that measurement properties of other clinical measurement instruments have been missed. Third, common language is lacking. A clear

definition of the pulmonary problems in AIS does not (yet) exist, which subsequently makes it challenging performing research in this subject. Pulmonologists and physicians treating scoliosis patients have different perspectives on the matter. Pulmonary fatigue, for instance, is a definition unheard of in the pulmonary department but has been included in a core outcome set for adults and young adolescents with spinal deformity.[7]

CONCLUSION

Both clinicians and patients recognize pulmonary symptoms and patient experienced limitations in routine daily practice as an important outcome domain in the treatment of patients with idiopathic scoliosis. Despite not being routinely reported or studies, we speculate that this domain is clinically very relevant for patients during adolescence, and also in later adult life, with implications on Quality of Life. In this study no currently available adequate patient centric instruments were identified to measure this domain in patients with idiopathic scoliosis. Although clinical measurement instruments such as spirometry has been reported regularly in research papers, their use in routine practice is not patient centric and does not seem feasible. Several available PROM's may potentially be used, most notably the UCSD SOBQ and the Borg RPE scale. Their measurement properties in this specific patient population are still unknown, and both have limitations in feasibility for use in routine clinical practice. Furthermore, a major hurdle in identifying the right instrument is that the underlying theoretical construct and common language of pulmonary functioning and symptoms in these patients is still elusive. The development of such a construct and potentially a subsequent PROM to routinely measure pulmonary functioning and patient experience is recommended.

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APPENDICES

APPENDIX 4. Identified clinician based measurement instruments used in < 10%

Measurement instrument	Explanation[1–11]	N	%
Spirometry			
SlowVC	Maximum volume of air slowly exhaled from a point of full inspiration.	2	1.6
FEV_1/VC	Ratio of the volume of air exhaled during the first second of a expiratory effort to the total volume of air exhaled during the VC.	3	2.5
$FEF_{25-75\%}$	Forced expiratory flow 25-75%. Mean forced expiratory flow during the middle half of the FVC.	6	4.9
FEF_{25}	Forced expiratory flow at 25% of the FVC	2	1.0
FEF_{75}	Forced expiratory flow at 75% of the FVC	2	1.0
PEF	Peak expiratory flow. Maximum speed of expiration, as measured with a peak flow meter.	11	9.0
PCF	Peak cough flow. Maximal expiratory flow during a cough maneuver.	1	0.8
MVV	Maximum voluntary ventilation. A measure of the maximum amount of air that can be inhaled and exhaled within one minute. The FEV1*40 is sometimes used as another estimate of this value.	5	4.1
IC	Inspiratory capacity. The maximum volume of air that can be inspired after reaching the end of a normal expiration.	3	2.5
IRV	Inspiratory reserve volume. The maximal amount of additional air that can be drawn into the lungs by determined effort after normal inspiration.	1	0.8
TV	Tidal volume. The normal volume of air displaced between normal inhalation and exhalation when extra effort is not applied.	5	4.1
Phlethysmography			
Airway resistance	Total, inhaled or exhaled airway resistance. The ratio of driving pressure to the rate of the airflow in the airways.	3	2.5
FRC	Functional residual capacity. The volume of air present in the lungs at the end of passive expiration.	4	3.3
RV	Residual volume. The volume of air that remains in the lungs after maximum forceful expiration.	7	5.7
RV/TLC	The RV/TLC ratio is used as a measure of resting pulmonary hyperinflation.	2	1.6
Manometer			
MIP	Maximum inspiratory pressure. Measurement of the highest sub-atmospheric pressure and thereby the inspiratory muscle strength.	7	5.7

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MEP	Maximum expiratory pressure. Measurement of a supra-atmospheric pressure which can be developed in an effort of the abdominal and intercostal muscles.	5	4.1
Respiratory rate	Number of breaths per minute.	4	3.3
Gas analyzer	*(During exercise, often ISWT*, 6MWT** or cycle ergometer)*		
VCO_2max	Maximum volume of carbon dioxide production per minute.	6	4.9
VCO_2/VO_2	Respiratory exchange ratio. Amount of CO_2 produced and O_2 used.	8	6.6
V_E/VO_2	Ventilatory equivalent of O_2. Number of liters of ventilation per liter of oxygen consumed.	6	4.9
V_E/VCO_2	Ventilatory equivalent of CO_2. Number of liters of ventilation per liter of CO_2 output.	4	3.3
$\Delta VO_2/\Delta logV_E$	Oxygen uptake efficiency slope (OUES). Quantifies the efficiency which oxygen is extracted from the lungs and used in the periphery.	1	0.8
V_d/V_t	Physiologic dead space (volume of air which is inhaled that does not take part in the gas exchange) over tidal volume.	1	0.8
D_{LCO}	Diffusing capacity for CO_2.	2	1.6
D_{LCL} VA	Diffusing capacity/alveolar volume ratio, the carbon monoxide diffusing capacity per liter of alveolar volume as determined by the dilution of helium).	1	0.8
BR	Breathing reserve, V_E/FEV1*40 or VE/MVV.	6	4.9
Single breath oxygen	Measuring the nitrogen in the exhaled air after one single breath of pure oxygen.	1	0.8
Anaerobic threshold	The point in a progressive work exercise test where lactic acidosis begins to develop.	1	0.8
Arterial blood analysis			
pH	Specifies acidity or basicity.	1	0.8
PaO_2	O_2 tension	2	1.6
$PaCO_2$	CO_2 tension	2	1.6
HCO_3^-	Concentration of bicarbonate	2	1.6
Total CO_2		1	0.8
Base excess	Excess in the amount of base present in the blood.	1	0.8
Physical examination			
Chest expansion (mm)	Manually, in millimeters. Using a tape measure at junction between xiphoid process and the body of the sternum.	2	1.6
V/Q Lung scan	Ventilation/perfusion scan, with krypton-81m.	1	0.8
SpO_2	Blood oxygen saturation with a pulse oximeter.	4	3.3
Remaining			
Thoracic volume calculation	Based on radiographs, using the formula of Stolle et. al.[11]	1	0.8

** = incremental shuttle walk test. ** = 6 minute walk test*

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APPENDIX 6. PRISMA flow diagram of identification, screening and inclusion of papers regarding clinimetric qualities

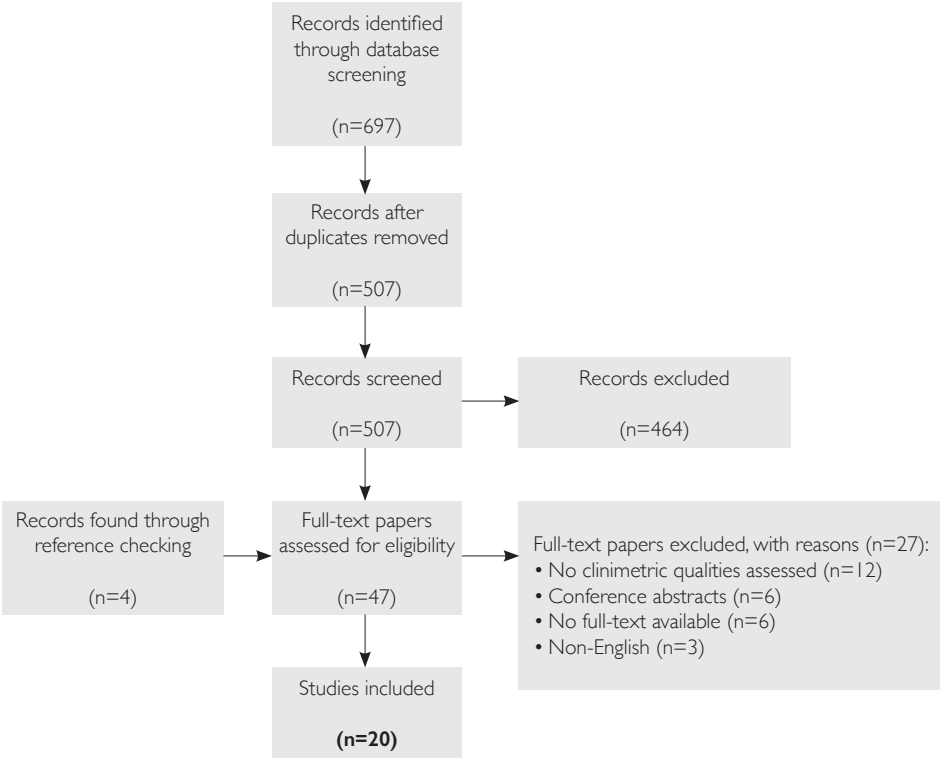

TABLE 1 OF APPENDIX 7. Dlinimetric properties of PROMs in other populations

PROM	Population	Content validity	Internal consistancy	Criterion validity	Construct validity	Agreement (test/retest)	Reliability	Respon-siveness	Floor or ceiling effect	Inter-pretability
Borg dyspnea scale	OLD[1]		N/A		±	-				
MRC Breathlessness	OLD[1]			+	±		+			
	COPD[2]			-			+			
	Asthma, COPD, ILD[3]			±						
UCSD SOBQ	OLD[1]		+		±	+				
	SSc with PH[4]			+	+	+		+		
	COPD, CF, PLT[5]		+	±						
	IPF[6]	+								
	IPF[7]				+					
Borg RPE scale	Children[8]					±				
	MS[9]			±			±			
	Children with SHD[10]			+						
	Swimming training[11] proposed by Borg (1962)			±						
	Spinning[12]			-						
	Parkinson[13]			±						
	Adolescent girls[14]			-			+			
	Active video gameplay[15]			±						
	Ergometry in water[16]			±						
	Stroke recovery[17]			±						
	Youth football players[18]			+						
	Professional ballet dancers[19]			+						
	Aquatic cycling for young men[20]			+						

COPD = chronic obstructive pulmonary disease; RLD = restrictive lung disease; OLD = obstructive lung disease; ILD = interstitial lung disease; SSc = systemic sclerosis; PH = pulmonary hypertension; CF = cystic fibrosis; PLT = postlung transplants; IPF = idiopathic pulmonary fibrosis; MS = multiple sclerosis; SHD = structural heart defects
+ = positive; ± = doubtful; - = poor; N/A = not applicable; blank = no information available

TABLE 2 OF APPENDIX 7. Methodological quality according to the COSMIN Risk of Bias checklist

Score	Nº	Papers
Very good	13	Asthma, COPD and ILD[3], COPD, CF and PLT[5], IPF[7], Children with SHD [10], Swimming training[11]proposed by Borg (1962, Spinning[12], Parkinson[13], Active video gameplay[15], Ergometry in water[16], Stroke recovery[17], Youth football players[18], Professional ballet dancers[19], Aquatic cycling for young men[20]
Adequate	6	OLD[1], COPD[2], SSc with PH[4], Children[8], MS[9], Adolescent girls[14],
Doubtful	1	IPF[6]
Inadequate	0	

COPD = chronic obstructive pulmonary disease; RLD = restrictive lung disease; OLD = obstructive lung disease; ILD = interstitial lung disease; SSc = systemic sclerosis; PH = pulmonary hypertension; CF = cystic fibrosis; PLT = postlung transplants; IPF = idiopathic pulmonary fibrosis; MS = multiple sclerosis; SHD = structural heart defects

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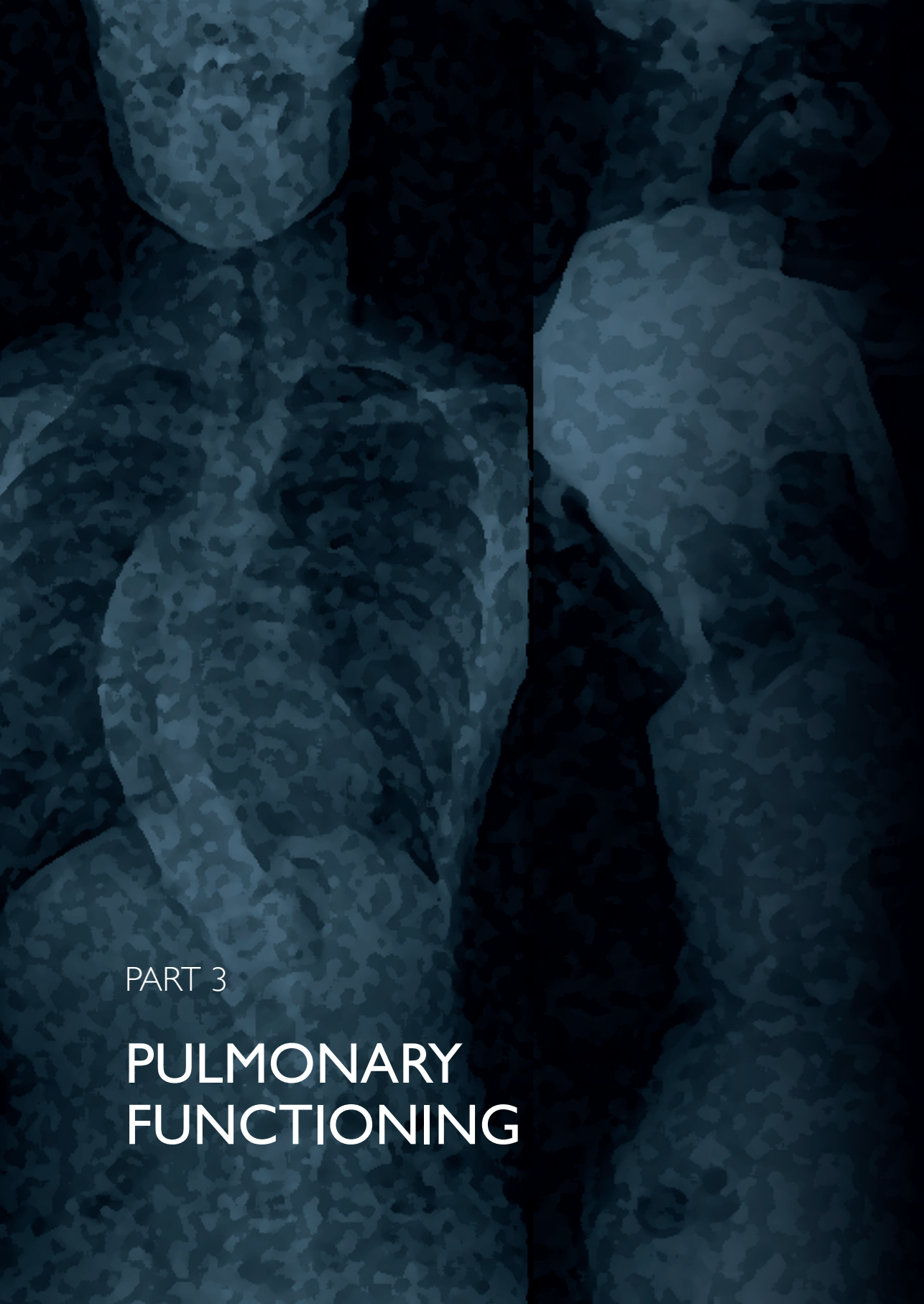

PART 3

PULMONARY FUNCTIONING

CHAPTER 6

PULMONARY FUNCTION IN PATIENTS WITH ADOLESCENT IDIOPATHIC SCOLIOSIS: AN EXPLORATIVE STUDY OF A WEARABLE SMART SHIRT AS A MEASUREMENT INSTRUMENT

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ABSTRACT

Purpose: Adolescent idiopathic scoliosis (AIS) presents various challenges, including respiratory symptoms that impact pulmonary function. This study aims to explore the feasibility of using a smart shirt for continuous monitoring of lung volumes and heart rate during routine activities in AIS patients.

Methods: A single-center exploratory feasibility study was conducted with AIS patients aged 16-35 years with a thoracic curvature of ≥30 degrees and absence of respiratory comorbidities. A smart shirt was utilized to continuously monitor cardiopulmonary parameters during mild exercise, which included a standardized walking route with the ascent of multiple stairs.

Results: Five participants completed the study. Baseline spirometry measurements showed a range of values for forced vital capacity (FVC), forced expiratory volume in 1 s (FEV_1), and FEV_1/FVC ratio. During mild exercise, participants exhibited variability in tidal volume, heart rate, breathing rate, and minute ventilation, with increases observed during stair climbing. Breathlessness levels also varied throughout the activity but did not correlate with the measured lung volumes. Overall, the use of the smart shirt for assessing pulmonary function in AIS patients was deemed feasible and well tolerated by participants during the test activities.

Conclusion: The study confirms the feasibility of using a smart shirt for continuous measurement of cardiopulmonary parameters in AIS patients during daily activities. Incongruities between spirometry results and perceived dyspnea exists, which questions the nature of the perceived dyspnea. Further research is needed to validate these findings and explore the impact of AIS characteristics on measurement accuracy.

INTRODUCTION

Adolescent idiopathic scoliosis (AIS) is associated with various symptoms, including back pain, diminished self-image, physical limitations, and cardiopulmonary compromise.[1,2] The impact of AIS on pulmonary function has been identified as a significant area of concern.[3] As the scoliosis progresses and the curvature of the spine and trunk deformity become more pronounced, individuals often experience respiratory symptoms such as breathlessness during routine activities. Respiratory problems and a reduced ability to tolerate exercise are commonly observed. Decreased lung volumes correlate with the severity of the scoliosis.[4] Factors beyond the magnitude of the coronal curvature, such as reduced thoracic kyphosis, vertebral rotation, general muscle dysfunction, diminished respiratory muscle strength, and particularly decreased chest wall compliance, can all potentially influence pulmonary function.[1,5,6.]

Recent studies have also indicated that spinal-thoracic deformities can lead to malformations in the bronchial airways, resulting in increased airway resistance.[7] Limitations in ventilation can lead to disability, which in turn may contribute to the avoidance of activities and exercise among AIS patients.[8]

Both physicians and patients have recognized the impact of pulmonary problems and exercise intolerance. In 2017, a standardized set of outcomes for AIS was developed using the Delphi method.[3] Initially encompassing "pulmonary function" as a pertinent outcome domain, it was subsequently redefined as "pulmonary fatigue" to better encapsulate patients' perspectives on pulmonary well-being. An underlying theoretical framework for this domain is imperative for future accurate assessment. The significance of pulmonary function in AIS has been acknowledged not only by physicians but has also been explored in patients with spinal deformities. Many patients encounter pulmonary symptoms, such as breathlessness during exertion and reduced exercise tolerance, which often curtail their daily activities.[9]

How to measure pulmonary function in AIS remains unclear. It is commonly assessed using spirometry, involving a single-timed, forced measurement that does not accurately represent respiratory function during typical daily activities or exercise.[10] Multiple studies have demonstrated that lung volumes measured using CT scans correlate significantly with those measured by standard pulmonary function tests.[11–13] These findings suggest that

externally measured lung volumes can be directly related to measured airflow. Recently, a novel 'smart shirt'[14] has been developed to continuously monitor cardiopulmonary function by measuring chest circumference at two levels. By employing this shirt, it may potentially also be possible to continuously monitor the lung volume of AIS patients, offering insights into pulmonary capacities during everyday activities and potentially shedding light on the relation between fatigue and pulmonary function.

Hence, the aim of the current study is to explore the feasibility of wearing a smart shirt to gauge lung volumes as an outcome measure during routine activities in patients with AIS.

METHODS

STUDY DESIGN AND PATIENTS:

This study is a single center explorative pilot feasibility study to investigate the feasibility of using a 'smart shirt' as a novel measurement instrument for assessing pulmonary function in a population of adolescents and young adults diagnosed with adolescent idiopathic scoliosis (AIS). Patients were included when they met the following criteria: age between 16-35 years, diagnosed with AIS with a thoracic coronal curvature of ≥30 degrees, ability to walk for thirty minutes and willingness to participate. Exclusion criteria were (a history of) smoking, having any respiratory comorbidity, active use of pulmonary medication, previous spinal surgery, or current brace treatment.

SMART SHIRT DESCRIPTION

The smart shirt (Hexoskin® Pro Shirt) is an novel wearable technology designed to monitor and analyze various physiological parameters real-time. To analyze the cardiorespiratory function, the shirt continuously monitors chest circumference at two specific levels: upper chest (at the lower end of the sternum) and the abdomen (approximately at the level of the umbilicus). Depending on the sex, height and age of the patient, it calculates the lung volumes. Furthermore, it has three electrocardiographic leads to continuously produce a 1-lead electrocardiogram (ECG, 256 Hz) and a 3-axis accelerometer. The shirt assesses breathing rate (2 to 60/min), heart rate (30 to 220 beats/min), minute ventilation (L/min) and tidal volumes (ml).

MEASUREMENT PROCEDURE:

Participants were fitted with the appropriate size of the smart shirt, ensuring good fit. Next, participants underwent pulmonary function testing (PFT) by spirometry using a calibrated spirometer (Vyntus ONE (2020), Vyaire Medical GmbH). PFT's were conducted by a trained pulmonary function technician according to ATS/ERS criteria.[15,16] This was performed to assess the participants' pulmonary status. The smart shirt was not calibrated against the spirometric measurements. Following spirometry, participants embarked on a 2.8-kilometer walk along a standardized route, including the ascent of four flights of stairs at the end of the route. Smart shirt measurements began after 2-3 minutes of walking (distance from spirometer to starting point). Participants were instructed to walk and climb the stairs at a normal walking speed. First the ascent of two flights of stairs, followed by 2-3 minutes walking, then one flight of stairs, followed by 2-3 minutes walking and lastly again one flight of stairs which was concluded with another 2-3 minutes walking.

The level of breathlessness, as experienced by the participant, was evaluated both prior to and at various standardized points during the activity, i.e. after 10 minutes, after 20 minutes, and at the end of climbing the stairs, as well at conclusion of the walk. Breathlessness was assessed using a Dutch version of the Modified Borg dyspnea scale (*m*Borg scale). The *m*Borg scale is a subjective rating scale used to assess a person's level of breathlessness or dyspnea during physical activity or exercise. It is a numerical scale ranging from 0 to 10, where 0 represents "no breathlessness at all" or "no effort," and 10 indicates "maximum breathlessness" or "maximal effort". [17,18] The walking test was conducted partly outdoors and partly indoors. To assess the comfort of the shirt, participants were asked to score the comfortability after the walk concluded, ranging from 0 ("very uncomfortable") to 10 ("very comfortable").

DESCRIPTION OF MEASURED PARAMETERS:[19,20]

The forced vital capacity (FVC), Forced Expiratory Volume in One Second (FEV_1), and the FEV_1/FVC ratio were assessed with spirometry at baseline. The smart shirt continuously measured tidal volume, breathing rate, heart rate, and minute ventilation.

FVC

FVC refers to the maximum amount of air that can be forcefully exhaled following a single, deep inhalation.

FEV_1

FEV_1 refers to the volume of air that can be forcibly exhaled during the initial second after taking a deep breath.

FEV_1/FVC RATIO

FEV_1/FVC represents the ratio of the air volume exhaled within the first second of a forced exhalation effort to the total air volume exhaled during the FVC test. This parameter is used to identify two classic patterns in spirometry results: obstructive and restrictive patterns.

TIDAL VOLUME

Tidal volume refers to the amount of air a person inhales or exhales during a normal, quiet breath, typically in a single breath cycle. It represents the volume of air that moves in and out of the lungs with each breath when a person is at rest and not exerting themselves.

MINUTE VENTILATION

Minute ventilation describes the total volume of air a person inhales and exhales in one minute. It is calculated by multiplying the tidal volume by the respiratory rate (the number of breaths taken per minute).

DATA ANALYSIS:

Since this study was exploratory and represents a pilot case series, only descriptive statistics were used. Characteristics were described per participant, including age, sex, BMI (length weight), Cobb angle (thoracic curve), and Lenke type. The baseline spirometry values are presented per participant. Although 'normal' FVC and FEV_1 are dependent on multiple factors (e.g. age, sex, length, ethnicity), the lower level of normal was roughly 80%, meaning that a measured FVC or FEV_1 of at least 80% of the predicted value was considered as normal.[21] The FEV_1 /FVC ratio was described as 'normal' when it was within 10.4% of the predicted ratio.[21] The data acquired from smart shirt measurements were described over time. The raw data was downloaded from an online database and exported in Excel for descriptive analysis. No further statistical analyses were performed. The amount of breathlessness was described across the recorded timeframe.

ETHICAL CONSIDERATIONS:

The study was conducted in compliance with the regulations and guidelines set forth by our institutional review board (IRB). The study protocol was reviewed and approved by the regional medical ethical review board (METC-Oost Nederland; 2022-13282). Prior to participation, all study participants were provided with information about the study's objectives, procedures, and potential risks and benefits. Informed consent was obtained from all participants.

RESULTS

PARTICIPANT CHARACTERISTICS (TABLE 1)

A total of six participants were initially enrolled in the study. Data from the final participant were lost due to technical issues. The saved file could not be located by the software, rendering it impossible to upload. Consequently, the data from this participant were excluded from the analysis. As it was a single time measurement, no patients were lost in follow up. Therefore in total, five patients were included. The ages of the remaining five participants ranged from 16 to 22 years. Among these participants, there were three females and two males. The length of the participants varied from 148 to 180 cm, and the mean body mass index (BMI) ranged from 18.5 to 23.7 kg/m2. The Cobb angle ranged from 35 to 65 degrees. Three participants were classified as Lenke 1A, one participant as Lenke 2A, and one participant as Lenke 3C.

BASELINE PULMONARY FUNCTION TEST (TABLE 1)

The FVC ranged from 3.09 to 3.75 liters, and the predicted values from 66 to 104% (based on age, height, and gender). The FEV_1 ranged from 2.70 to 3.37 liters, and the predicted values from 58 to 101%. The FEV_1/FVC ratio ranged from 72.4 to 87.4%, and the predicted values from 85 to 102%.

TABLE 1. Characteristics of included patients

Patient:	1	2	3	4	5
Characteristics participants					
Age (y), sex	20, F	16, F	20, M	16, M	22, F
Length (cm)	170	148	180	170	169
Weight (kg)	61	52	60	64	63
BMI (kg/m^2)	21.2	23.7	18.5	22.1	22.1
Thoracic coronal Cobb angle (º)	45	63	63	35	65
Lenke Classification	1A	3C	1A	1A	2A
Pulmonary function parameters (spirometry)					
FVC (L)	3,74	3,09	3,75	3,77	3,52
FVC (%)*	89	104	66	83	85
FEV_1(L)	3,24	2,7	2,78	3,37	3,12
FEV_1 (%)*	89	101	58	86	87
FEV_1/FVC(%)	86,8	87,4	72,4	88	88,5
FEV_1/FVC (%)*	99	97	85	102	102

*F= female; M= male; * = percentage of the predicted value (based on age, height and weight); L = absolute values, in liters; FVC= forced vital capacity; FEV_1 = forced expiratory volume in one second*

DESCRIPTIVES OF WALKING ROUTE (TABLE 2)

The total duration, instances of climbing the stairs and average walking speed is shown in Table 2. The average walking speed varied from 4.8 to 5.4 km/h. Each participant covered a walking route of 2.8 km, resulting in a total walking duration of 31 to 35 minutes.

TABLE 2. Descriptives of the walking route (2.8 km)

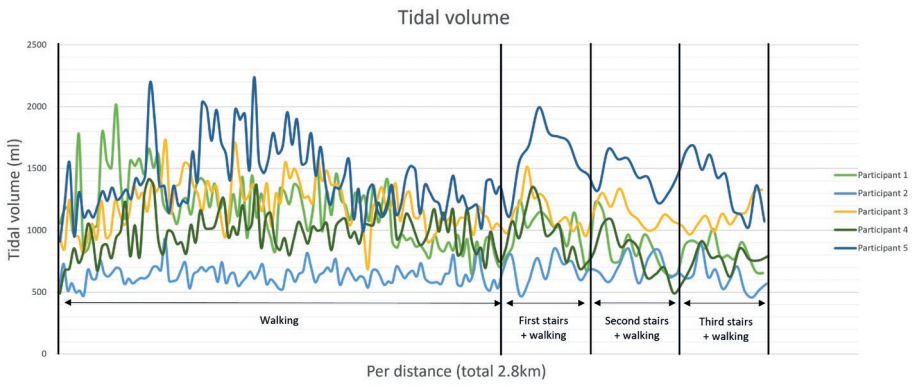
Patient:	1	2	3	4	5
Total duration (min)	32:58	35:20	32:58	32:01	30:54
Start first flight of stairs (min)	23:50	27:28	24:16	23:51	23:33
Start second flight of stairs (min)	27:07	30:03	27:41	27:10	25:49
Start third flight of stairs (min)	29:51	32:17	30:11	29:41	28:03
Mean walking speed (km/h)	5.1	4.8	5.1	5.3	5.4

SMART SHIRT MEASUREMENTS

TIDAL VOLUME (TV; FIGURE 1)

The TV measurements collected using the smart shirt revealed large variability among participants. It ranged from approximately 500 mL to 2000 mL. Participant 1, 3, 4 and 5 showed an increase in tidal volumes after one to three minutes of walking and a significant rise during walking the stairs. Participant two showed a minimal increase during walking and a modest increase during climbing the stairs.

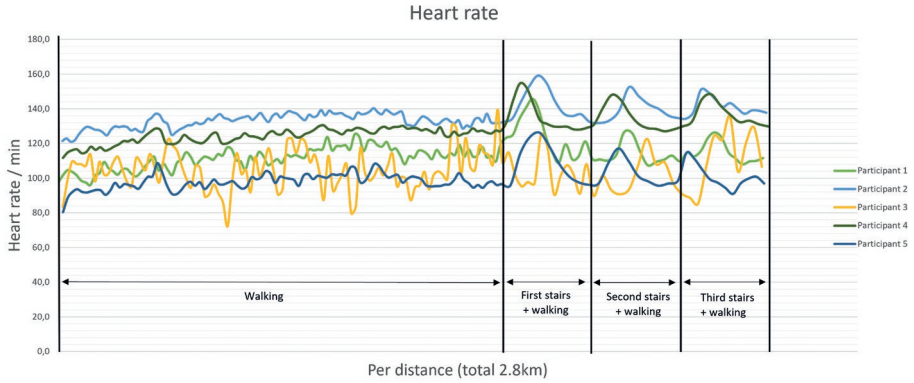
FIGURE 1. Graph demonstrating the tidal volume per distance, as generated by the smart shirt, for 5 patients with AIS.



HEART RATE (HR; FIGURE 2)

The HR measurements also varied greatly between participants, from approximately 80 to 120 beats per minute. The heart rate showed a slight increase during walking, and a greater increase during climbing the stairs.

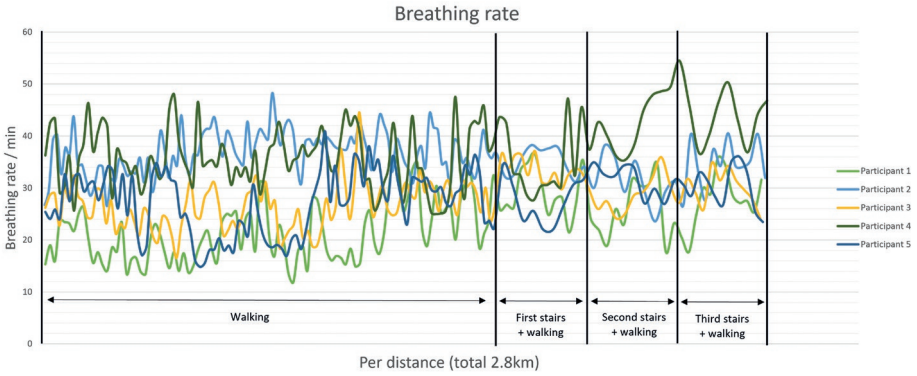
FIGURE 2. Graph demonstrating the heart rate per distance, as generated by the smart shirt, for 5 patients with AIS.



BREATHING RATE (BR; FIGURE 3)

The BR ranged from approximately 15 to 40 per minute. Over time, no evident increase is seen during walking, and only participant 4 showed an increase during climbing the stairs. Participant 4 showed a significant increase in breathing rate during climbing the stairs.

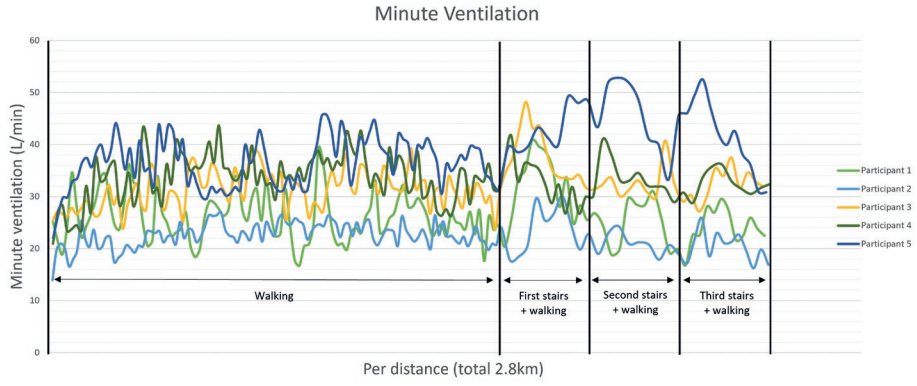
FIGURE 3. Graph demonstrating the breathing rate per distance, as generated by the smart shirt, for 5 patients with AIS.



MINUTE VENTILATION (MV; FIGURE 4)

The smart shirt facilitated the calculation of MV by multiplying TV and BR. Due to the increase in TV and a slight increase in BR, the MV increased in every participant during walking and increased further during climbing the stairs. Participant 5 showed a substantial increase during climbing the stairs.

FIGURE 4. Graph demonstrating the minute ventilation per distance, as generated by the smart shirt, for 5 patients with AIS.



BREATHLESSNESS (mBORG SCALE; TABLE 3)

The initial level of breathlessness ranged from 0 to 3 (out of 10) and showed an increase after 10 minutes which ranged from 1 to 7. At the 20-minute mark, the level of breathlessness decreased for participant one from 7 to 5, whilst for participant two to five it increased or stayed the same (range 2-5). After climbing the first flight of stairs, participants reported a notable escalation in breathlessness, ranging from 3 to 8. As the walk concluded, the level of breathlessness ranged from 2 to 7. The amount of breathlessness at the finish from participant one was lost.

FEASIBILITY AND COMPLIANCE (TABLE 3)

The utilization of the smart shirt as a tool for assessing pulmonary function in AIS participants was determined to be both "feasible" and "well-tolerated". Nearly all participants reported a high level of comfort with the shirt, giving it scores of 9, 8, 8, 6, and 8 out of 10.

TABLE 3. Breathlessness (modified Borg dyspnea scale) and comfortability (0-10)

Patient:	**1**	**2**	**3**	**4**	**5**
Start	3	1	1	0	2
After 10 minutes	7	2	1	2	2
After 20 minutes	5	5	2	3	2
After first flight of stairs	8	8	4	5	3
At finish	N/A	7	2	6	2
Comfort score	9	8	8	6	8

DISCUSSION

This study has shown that measurement of cardiopulmonary parameters in adolescent idiopathic scoliosis (AIS) patients with a smart shirt is feasible. The smart shirt has been clinically validated in various studies predominantly in a healthy population[22–28], with additional assessments extending to patients with COPD.[29] Tidal volume[22,26,28,29], heart rate[22–26], breathing rate[22,23,25–27,29] and minute ventilation[22,25,26,29] seem to be accurately measured by the smart shirt. The measurements in these studies encompassed diverse physiological conditions, including running[27], periods of rest, submaximal exercise and maximal exercise[26], routine activities of daily living[22,28,29], running[27], (high-intensity) cycling[24,25] and walking.[22,23] The studies validating heart rate[22–26] consistently reported high interclass correlation coefficients (ICCs), with Pearson's correlation coefficients across different exercise loads all exceeding 0.90. These measurements were conducted using widely validated clinical tools, including 3 or 12 lead ECG measurements and metabolic cart systems. Similarly, the studies validating breathing rate[22,23,25–27] also demonstrated high ICCs, with values often exceeding 0.96 and consistently above 0.84. These assessments were performed using breath-by-breath measurement systems or metabolic cart systems. One study was an abstract, so detailed information was not found.[29] For tidal volume assessments[22,26,28], good accuracy was reported[22], with ICCs ranging from 0.69 to 0.82 when compared with breath-by-breath measurement systems at different exercise loads[26], and a mean bias of 0.6% compared to a spirometer.[28] Finally, studies evaluating minute ventilation[22,25,26] reported good correlations, with ICCs greater than 0.8126, ranging from 0.69 to 0.8425, or described as very comparable.[22] These measurements were validated using widely used breath-by-breath flow sensors. Beyond tidal volumes, heart- and breathing rate and minute ventilation, prior studies regarding the smart shirt have not addressed other pulmonary parameters.

The findings of this feasibility study offer insights into the potential applications of wearable technology in monitoring respiratory parameters among individuals with AIS. The utilization of this smart shirt as a measurement instrument for pulmonary function assessment was found to be well-tolerated and accepted by AIS patients during the test activities. Moreover, it offers preliminary insights into the real-time pulmonary performance of AIS patients, contributing to a deeper understanding of the theory underlying their pulmonary complaints.

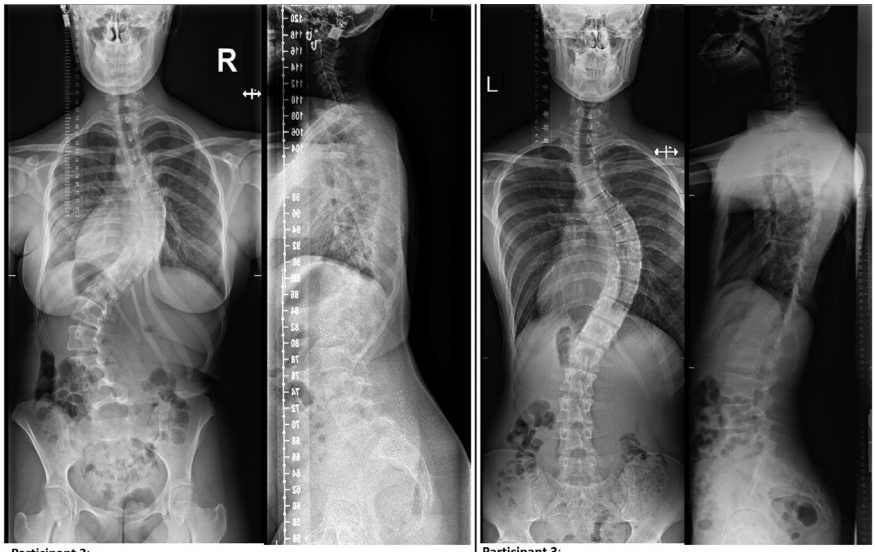
Pulmonary complaints, as observed in patients with AIS, have conventionally been believed to be the result of a restrictive nature. This implies a limitation in the total lung air volume attributed to deformities in the thoracic cage, thoracic spine shortening, diminished chest wall compliance, decreased respiratory muscle effectiveness and increased stiffness.[30,31] Notably, an inverse relationship appears to exist between the Cobb angle and diminished lung volumes, extending even to smaller curvatures.[4] The potential involvement of respiratory muscle dysfunction is mentioned as well.[6,32] Contrary to conventional understanding, recent investigations propose an obstructive pattern originating from a right-sided bronchial constriction.[33,34] This is due to intrusion of the spine into the chest resulting from the endothoracic hump induced by the deformity and is seen more in patients with loss of kyphosis. Furthermore, emerging evidence suggests a potential cardiac etiology for the perceived breathlessness, attributed to compression of the pulmonary artery leading to (mild) pulmonary hypertension.[35,36]

In a healthy individual, during mild to moderate exercise, the tidal volume and breathing rate typically increase which can result in a 12-fold increase of minute ventilation.[37,38] In the majority of the study participants, tidal volumes exhibited an initial increase ranging from a factor of two to three (participant 1, 3, 4, and 5; Figure 1), followed by a gradual decline over time, only to re-elevate during stair climbing. One participant (P2) displayed marginal increase in tidal volume. The overall breathing rate remained relatively constant, demonstrating only modest increases, except during stair ascent. While the heart rate exhibited minimal increments over time, a considerable rise was observed during stair climbing. The minute ventilation, calculated as the product of respiratory rate and tidal volume, displayed an overall increase, reached a plateau, and experienced a significant surge during stair climbing. The maximal increase in minute ventilation was noted to be a factor of 2.5.

Surprisingly, the degree of perceived dyspnea as measured with the modified Borg scale did not demonstrate a discernible association with spirometry outcome or data obtained from the smart shirt. Notably, participants 2 and 3 exhibited comparable thoracic Cobb angles (63^0; Table 1), yet their spirometric results varied greatly (figure 5). Participant 2, despite displaying good spirometry values, reflected by forced vital capacity (FVC) and forced expiratory volume in one second (FEV_1) exceeding 100% of predicted values (Table 2), reported substantial breathlessness (modified Borg dyspnea scale [mBorg], maximum score of 8/10; Table 4). Conversely, participant 3 exhibited

decreased FVC (58%/predicted) and FEV_1 (66%/predicted), yet reported a lower intensity of breathlessness (mBorg maximum score of 4/10). This incongruity suggests that spirometry in AIS patients may not offer the necessary insights into pulmonary symptoms as perceived by the patients.

FIGURE 5. Posteroanterior (PA) and lateral full spine radiographs of participant 2 and 3 with similar curve magnitude and hypokyphosis , demonstrating markedly different spirometry and breathlessness measurements. Participant 2 has normal spirometry yet experiences significant breathlessness during exercise, whereas participant 3 demonstrates markedly reduced spirometry results but very little breathlessness during exercise.



Participant 2:
Spirometry: FVC 3.09L (104% of predicted), FEV_1 2.7L (101% of predicted), FEV_1/FVC 87.4% (97% of predicted)
Breathlessness: At start 1/10, after 10 minutes 2/10, after 20 minutes 5/10, after stairs 8/10, at end 7/10.

Participant 3:
Spirometry: FVC 3.75L (66% of predicted), FEV_1 2.78L (58% of predicted), FEV_1/FVC 72.4% (85% of predicted)
Breathlessness: At start 1/10, after 10 minutes 1/10, after 20 minutes 2/10, after stairs 4/10, at end 2/10.

Analysis of smart shirt data revealed that participant 2, despite experiencing severe breathlessness, did not manifest an elevation in tidal volumes, only a marginal increase in heart rate (more pronounced during stair climbing), no conspicuous escalation in breathing rate, and a modest rise in minute ventilation. We assume that this caused by the inability of the participant to augment chest volume due to chest wall stiffness

and reduced compliance or the potential presence of respiratory muscle dysfunction, as mentioned in prior literature.[6,32] Additionally, cardiovascular factors should be considered a cause for dyspnea.[35,36] In contrast, participant 1, who similarly reported intense breathlessness, exhibited an initial increase in tidal volume, a slight elevation in heart rate (more pronounced during stair climbing), a modest rise in breathing rate, and a more pronounced increase in minute ventilation. She also had a normal spirometry but her Cobb angle was smaller (45 degrees). These measurements from spirometry and the smart shirt both have a poor correlation with self-reported pulmonary symptoms. This suggests a multifactorial nature of perceived dyspnea, or it could potentially be purely cardiac. These findings questions the clinical relevance of further prioritizing objectively measured lung volumes, such as those obtained through the use of a smart shirt.

STRENGTHS & LIMITATIONS

To our knowledge this is the first study in which lung volumes are continuously evaluated while performing activities. While this study provides valuable insights into the feasibility of employing the smart shirt to assess pulmonary function when performing daily activities in AIS patients, it is essential to acknowledge several limitations that should be considered in the interpretation of the findings. First, the smart shirt was not calibrated using spirometry. This means that the accuracy of the tidal volumes and minute ventilation cannot be established. Only the relative changes can be interpreted. Second, the sample size in this feasibility study was small. As a result, the findings may not be representative of the entire AIS population and may not account for potential variations in pulmonary function associated with different AIS characteristics, such as curve severity or patient age. However, the primary aim of this study was not to describe a representative AIS population but to outline a small case series to assess its feasibility. Third, wearable technology, such as the smart shirt, can be influenced by inherent technological limitations. For example, the fit of the shirt and signal interference have the potential to impact measurements accuracy. To prevent this, a glycerin-based ointment was applied to the sensors, as per the manufacturer's recommendation. However, this may have contributed to the variable measurements in participant three compared to others. In future research endeavors, repeated measurements in the same patients would need to be performed to test the reproducibility of the measurements. Fourth, this feasibility

study did not include a healthy control group without AIS and we cannot compare our data with the normal population. This would be interesting for a follow up study.

CONCLUSION

In conclusion, this feasibility study demonstrates the promise of a smart shirt as a well-tolerated tool for the continuous monitoring of cardiopulmonary parameters in adolescent idiopathic scoliosis (AIS) patients. It offers valuable insights into cardiopulmonary changes during mild exercise in this patient population. However, in this small exploratory study we could not identify any relation between spirometry findings, smart shirt measurements or perceived dyspnea. To delve deeper into the alterations in lung volumes during activities in patients with AIS, further research is necessary. We recommend further evaluation of the smart shirt in AIS patients, as the chest mobility and, consequently, measurement accuracy may be affected by the thoracic deformity.

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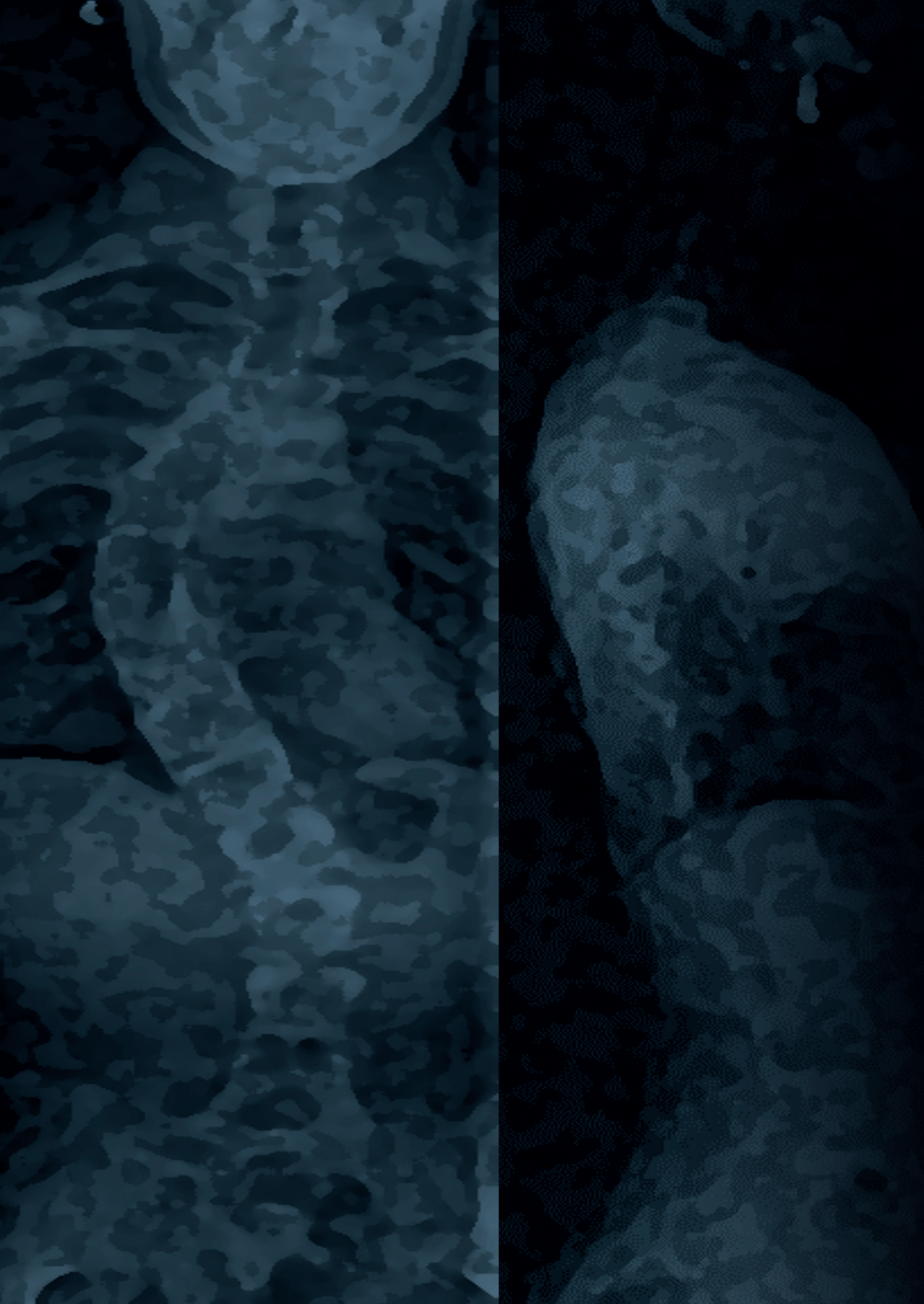

CHAPTER 7

DEVELOPMENT OF A THEORETICAL FRAMEWORK FOR PATIENT-EXPERIENCED SYMPTOMS RELATED TO BREATHING AND EXERCISE TOLERANCE IN ADOLESCENT AND ADULT SCOLIOSIS: AN EXPLORATIVE STUDY BASED ON STRUCTURED INTERVIEWS

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ABSTRACT

Purpose: To explore symptoms related to breathing and exercise tolerance that are experienced by patients with adolescent and adult scoliosis and to develop a theoretical framework in alignment with the International Classification of Functioning, Disability and Health (ICF) framework for global applicability and standards compliance.

Methods: An international multicenter study using qualitative methods and in-depth semi-structured interviews with 15 spinal deformity patients with complaints related to breathing and exercise tolerance was conducted using a preliminary theoretical construct. Transcripts were coded and analyzed iteratively, following a framework approach.

Results: Six adolescents and six adults with scoliosis from the Netherlands, and three adults with scoliosis from the USA were included. Patients reported 'shortness of breath' (15/15), 'breathlessness' (11/15), 'pulmonary fatigue' (10/15), and 'reduced exercise tolerance' (13/15). Additional symptoms, such as 'wheezing' and 'exercise-induced chest pains', were observed in specific cases (3/15 and 4/15, respectively). These can be captured by the ICF categories 'symptoms related to sensations associated with cardiovascular and respiratory functions' (b. 460) and 'symptoms related to exercise tolerance functions' (b. 455).

Conclusion: This study identified two main categories within the ICF framework: symptoms related to sensations associated with cardiovascular and respiratory functions (b. 460) and symptoms related to exercise tolerance functions (b.455).

INTRODUCTION

Pulmonary symptoms are a known, but less evaluated, problem in patients with spinal deformities. Multiple different types of spinal deformities can occur or become symptomatic at all age groups.[1,2] Most research into the natural history and treatment outcomes focus on radiologic parameters, and to a lesser degree clinical outcomes, with a focus on back pain and quality of life. However, all spinal deformities cause a change in shape and function of the trunk and potentially the enclosed organs.[3]

Little is known of the incidence, prevalence, and severity of symptoms related to the change in trunk shape. Most focus in this area has been on pulmonary function. In a meta regression analysis, increasing thoracic curve severity correlated with decreased lung volumes and function in adolescent patients.[4] It is known that there is a restrictive component, due to restricted rib movement, and stiffness of the chest wall.[5] Furthermore loss of physiological thoracic kyphosis and intrusion of the spine into the chest can lead to right bronchus constriction and an obstructive pattern in function tests.[6-8] And finally, the function of the diaphragm for breathing in relation to spine and trunk deformity has not been clarified, but probably plays a significant role.

The experienced pulmonary symptoms could potentially lead to (significant) disabilities and impairment in daily and social life, including exercise intolerance and activity avoidance. However, these aspects are often not addressed in research and clinical practice.[9]

Pulmonary function tests (PFTs) have been used to quantify symptoms related to breathing and exercise tolerance in patients with scoliosis, but a discrepancy exists between the outcome of quantitative measurements and patient-experienced symptoms.[10] To quantify patient-experienced symptoms related to breathing and exercise tolerance, patient-reported outcome measures (PROMs) may be valuable. However, commonly used PROMs for adolescents and adults with scoliosis, such as the Scoliosis Research Society-22r (SRS-22r) and the EuroQol five dimensions; health-related QoL (EQ-5D), lack a patient-reported outcome (PRO) domain specifically addressing patient-experienced symptoms related to breathing and exercise tolerance.[11, 12]

No other measurement tools are available that adequately measure 1 these symptoms in terms of measurement properties.[13-15] Also, no theoretical framework of pulmonary

function in both adolescent and adult spine deformity patients currently exists.[9] The aim of this study is to develop a theoretical framework (patient-reported outcome) for patient-experienced symptoms related to breathing and exercise tolerance in adolescents and adults with scoliosis. Ultimately, this would pave the way for the development of a PROM to adequately evaluate these symptoms over time. The theoretical framework will be in harmony with the International Classification of Functioning, Disability, and Health (ICF) framework to ensure its cross-cultural applicability and alignment with global standards, and will be available in two languages (English and Dutch).[16-17]

METHODS

DESIGN

An international multicenter study using qualitative methods was conducted. Semi-structured in depth interviews were held with patients with adolescent and adult scoliosis. The Standards for Reporting Qualitative Research were used as a reporting guideline for the qualitative research.[18]

SETTING

The study was conducted in both the United States of America and the Netherlands and is part of the *'Development And Measurement Properties Of A Patient-reported Outcome Measure Of Pulmonary Function In Patients With Spinal Deformity'* project, as funded by the Scoliosis Research Society. The ultimate aim of this project is to create a PROM that covers a new to be developed patient-experienced theoretical framework of symptoms related to breathing and exercise tolerance in patients with scoliosis.

ETHICAL STATEMENT

Local Approval was obtained by the local Medical Ethics Committees (2021-7428 and WO21.178) in both the Netherlands and USA. While the medical ethics committee confirmed that this study is not WMO-compulsory by Dutch law, it was ensured that it adheres to the Medical Treatment Agreement Act (WGBO) and General Data Protection Regulation (AVG). Written informed consent was obtained from all participants. Patient

data was pseudonymized using numerical identifiers and linked to interview quotes, ensuring confidentiality and maintaining data integrity.

STUDY PARTICIPANTS

The study participants were recruited from four centers in the Netherlands (Radboud University Medical Center Nijmegen, OLVG Amsterdam, Sint Maartenskliniek Nijmegen, University Medical Center Utrecht in the Netherlands) and one center in the USA (Columbia University Medical Center New York) between 2021 and 2023. Patients with scoliosis with symptoms related to breathing or exercise tolerance at the outpatient clinic were approached and invited to 1 participate in the study by their treating physician. It is important to keep in mind that the goal of the study was not to determine the epidemiology of symptoms related to breathing or exercise tolerance, but to determine the nature of the symptoms as experienced by patients with scoliosis. Inclusion criteria were age ≥14 years, a physician's diagnosis of scoliosis and symptoms related to breathing or exercise tolerance currently or in the past. Patients were excluded from study participation if they insufficiently mastered written and oral Dutch or English language and/or suffered from diseases likely to interfere with the patients' experience of their symptoms related to breathing and exercise tolerance.

DATA COLLECTION

In-depth interviews were held online using Microsoft Teams. The audio of the meetings was recorded, transcribed verbatim and pseudonymized after completion. A semi-structured interview guide was used, which was based on a previous study that explored pulmonary symptoms in an adolescent population.9 The main topics and questions are shown in Table 1. Before the interviews were performed, patient and curve characteristics were collected. These characteristics included information on the patient's gender, age, employment status, sports participation, duration of the condition, history of corrective surgery, the presence of minor lung diseases and Cobb angles. Interviews were divided and performed by a researcher experienced in qualitative research (IA) and two researchers (IK & FH) who received training to conduct and analyze interviews.

TABLE 1. Interview guide

Question	What does this* feel like for you? How do you experience this*? Can you describe it?
	When do you experience this* complaint? (Continuously? Only after certain activities?)
	How long does the complaint last when you experience it*?
	Is it* worse in some situations than in others?
	To what extent does this* complaint impact your daily life? How do you notice this?
	When you feel tired, do you also feel this* specifically in your breath? How?

** Symptoms related to breathing and exercise tolerance*

DATA ANALYSIS

Interviews and analysis were conducted iteratively using ATLAS.ti 22.0.11 for data analysis and by using a framework approach.

An initial codebook was formulated using a deductive approach based from the same study as the interview questions, providing a structured foundation for the initial coding process.[9] Inductive modification was used to add codes as new themes and patterns emerged from the data. This iterative refinement enhanced the depth and accuracy of the codebook, ensuring a comprehensive analysis that incorporated both established concepts and novel findings. Two researchers (IK and MvH) independently analyzed the first individual interview and then compared codes to reach consensus. Due to the expected small scope of the theoretical framework, a pragmatic approach was used, with one researcher (IK) coding the remaining transcripts. Intercoder reliability was improved by the second researcher (MvH) randomly coding two transcripts, ensuring consistency and reducing individual bias in the interpretation of qualitative data. More consensus meetings were held to discuss codes, with new codes added to the codebook and previous interviews reviewed. When no new codes emerged data saturation was considered reached. The project team discussed and interpreted the results, which led to the final construct of the theoretical framework.

ICF CLASSIFICATION

The International Classification of Functioning, Disability and Health (ICF) serves as a universally accepted standard for health-related domains.[16,17] In this study, the codes of the final codebook were matched to items from the ICF classification to ensure its applicability across different cultures and to harmonize between languages (Dutch and English).

RESULTS

STUDY PARTICIPANTS

All 15 approached patients with symptoms related to breathing and/or exercise tolerance consented to participation. Six adolescents (four females; median age 16.5 years [IQR 14-20]) and nine adults with scoliosis (six females; median age 51 [IQR 25-74]) were included. One included participant reported a history of mild asthma with no current use of medication, who was therefore not excluded. A complete overview of participant characteristics is displayed in Table 2.

TABLE 2. Characteristics study participants

Characteristics	Adolescents n=6		Adults n=9	
	Number (%)	Median (IQR)	Number (%)	Median (IQR)
Nationality, Dutch	6 (100)		6 (67)	
Gender, female	4 (67)		6 (67)	
Age in years		16.5 (14-20)		51 (25-74)
Employment status				
Scholar / student	5 (83)			
Employed			3 (33)	
Self-employed	1 (17)		1 (11)	
Retired			3 (33)	
Unemployed			1 (11)	
Unknown			1 (11)	
Sports				
Yes	3 (50)		6 (66)	
Hours physical exercise a week		4.5 (4-7)		3 (1-4)
Years since scoliosis diagnosis		4 (2-8)		40 (19-61)
Main Cobb angle		62 (52-80)		73 (50-114)
Scoliosis surgery, yes	5 (80)		4 (44)	
N months since surgery		6 (2-12)		18 (2.5 - 480)
Lung disease				
No	6 (100)		8 (89)	
Mild asthma			1 (11)	

An overview of quotes by participants is given in Table 3. Table 4 shows an overview of terminology as used by participants and how the terminology was coded.

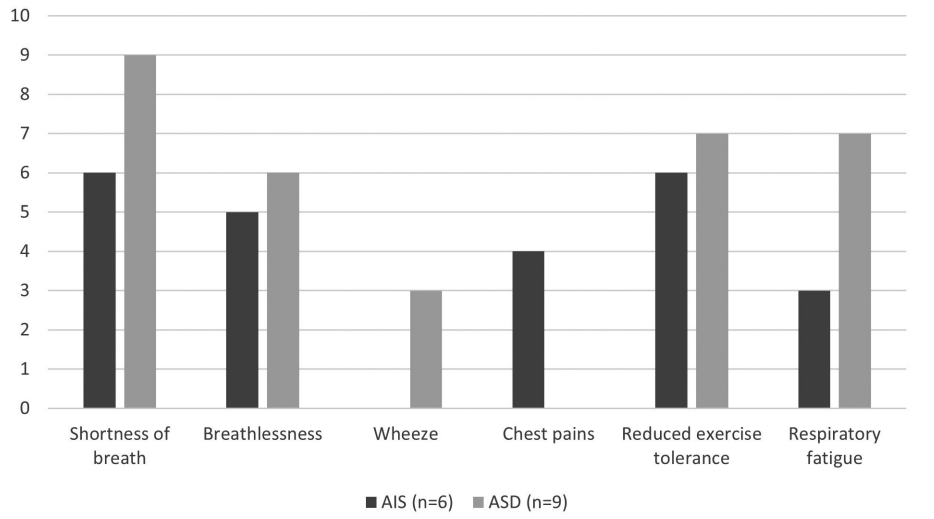
TABLE 3. Overview of quotes given by study participants

Symptom	Quote	Patient
Shortness of breath / Breathlessness	"… so my lungs can't actually fully extend and I can't take a full breath."	USPF3 adult
	"It feels like there's suddenly less space or breath in my lungs, as if it has disappeared all of a sudden."	NLPF6 adolescent
	"I can walk a small distance and then I get totally breathless. I'm fighting for my breath, trying to get air."	NLPF6 adult
	"When I try to walk, just walking a short distance, a very short distance, just gave me acute shortness of breath."	USPF1 adult
	"It just felt like you couldn't... I couldn't take a deep breath, mostly that."	NLPF5 adolescent
	"Occasionally, when I had the shower really hot and there was a lot of steam, I would quickly feel short of breath."	NLPF3 adolescent
Wheeze	"... breathing problems that are similar to asthma if I compare them, with something like a wheeze."	NLPF3 adult
Chest pain	"If I didn't consciously think about breathing, I simply wouldn't breathe because it just hurt to breathe at that moment, if I was moving."	NLPF2 adolescent
Reduced exercise tolerance	"Up to a certain point everything is fine and that point is a bit sooner than for peers of the same age."	NLPF4 adult
	"When we go cycling, I want to be able to keep up and it sucks when I fall far behind and feel like I'm not making progress. It can be really frustrating."	NLPF4 adult
	"If, as a boy, you have worse stamina than certain girls who are actually much heavier or have a much harder time … then that can feel really below…, maybe even severely below average."	NLPF2 adolescent
	"I had a relatively good stamina, and then suddenly it became very bad very quickly."	NLPF3 adolescent
	"At first, I was able to do everything I wanted, but over the last 9 months to a year, that became increasingly limiting."	NLPF1 adolescent
Respiratory fatigue	"When I'm doing (things) in the house, like making the bed, I lift up the duvet to shake it and then I'm completely out of breath from doing that."	NLPF6 adult
	"… it kind of affects everything, and I'm pretty much always tired…"	USPF3 adult

USPF: United States pulmonary function. NLPF: Netherlands pulmonary function

All participants experienced insufficient lung capacity, reporting that 'air suddenly appeared to be gone from the lungs'. Participants utilized multiple methods to maximize chest expansion, such as yoga and breathing techniques. These efforts aimed to subjectively increase usable lung capacity. All participants reported symptoms that are considered to fall under the umbrella term 'shortness of breath' or 'breathlessness' (Figure 1). Participants described experiencing these symptoms especially during physical activity. Some described the sensation of their breath being caught in their throat or pressure on their chest, making it difficult to breathe adequately to their needs. Participants also mentioned these complaints in certain specific situations. Walking up an incline or a flight of stairs, for instance, often left participants feeling 'out of breath' or 'huffing and puffing' on the way up or when reaching the top. Participants described a feeling of restriction in their ability to breathe freely. They reported being unable to take air in, sometimes causing dizziness and fear of fainting. This was mostly related to physical activity, but might also occur in a steamy shower or crowded room.

FIGURE 1. Codes and in how many participants they were present *(total number of participants = 15)*



Interestingly, three adult participants mentioned 'feeling a clearly distinguishable difference in complaints between the left and right side of their chest'.

Three adult participants experienced a 'wheeze', mostly related to increased 1 physical activity. None of the adolescent participants reported this symptom.

Four out of six adolescent participants described a feeling of 'stabbing' or 'burning' exercise-induced respiratory-related 'chest pains', in contrast to none of the adult participants (Figure 1). Participants also mentioned a decrease in physical ability and limitations in their physical activities. As a consequence, they reported experiencing disappointment, isolation, and an avoidance of these physical activities. Participants felt frustrated with their inability to keep up. Some have noticed a severe disability in their daily life, including difficulty walking or standing for extended periods of time, difficulty climbing stairs or performing household chores.

Others found their functioning in daily life to be intact, but when comparing themselves to their peers they noticed that they were limited in their functioning. For instance, they may have noticed that they were unable to keep up with their friends during physical activities, and had to take more frequent breaks or rest periods in between (Table 4). Furthermore, this limitation appeared to progress over time. Both adult and adolescent participants who previously considered themselves in good shape noticed a steep decline in their stamina.

TABLE 4. Overview of terminology as used by participants

Category	Terminology in English	Terminology in Dutch
Shortness of breath / breathlessness	short of breath	korte / hoge ademhaling
	out of breath	buiten adem
	breathless	kortademig
	tightness in the chest	druk op de borst
	suffocating	benauwdheid / beklemming
	shallow breathing	oppervlakkige ademhaling
	limited lung capacity	niet veel longinhoud
	constricted breathing	geblokkeerde ademhaling
	huffing and puffing	hijgen en puffen
	air gone from the lungs	lucht verdwenen uit de longen
Wheezing	wheeze	piepende ademhaling
Chest pains	painful breathing	pijn bij de ademhaling
	sharp pains	scherpe pijn
	stitching in the chest	steken op de borst
Reduced exercise tolerance	no / reduced stamina / endurance	geen / verminderd uithoudingsvermogen
	increased limitations	steeds beperkter
	reduced physical condition (compared to others)	onder gemiddelde conditie
Respiratory fatigue	sudden exhaustion	in één keer uitgeput
	tiredness	vermoeidheid
	tiring	vermoeiend

PROJECT TEAM DISCUSSIONS

A discussion was held on whether or not to distinguish between "shortness of breath" and "breathlessness". Because, based on experience, these symptoms have the same meaning in clinical practice it was decided to merge these items to ensure a comprehensive and practical framework.

ICF CLASSIFICATION

Based on the data analysis, two categories within the ICF were identified. The first category encompassed symptoms related to sensations associated with cardiovascular and respiratory functions (ICF b.460), and includes shortness of breath, breathlessness, wheezing and chest pains. The second category encompassed symptoms related to exercise tolerance functions (ICF b.455), and includes reduced exercise tolerance and respiratory fatigue. The final codebook, and with that the final theoretical framework, is displayed in Table 5.

TABLE 5. Final theoretical framework for PRO: patient-experienced symptoms related to breathing and exercise tolerance

English terminology Category	Dutch terminology Categorie	ICF code
Symptoms related to sensations associated with cardiovascular and respiratory functions	**Symptomen gerelateerd aan gewaarwordingen gepaard gaande met cardiovasculaire en respiratoire functies**	**b.460**
Shortness of breath / breathlessness	Kortademigheid / Benauwdheid	
Wheezing	Piepende ademhaling	
Chest pains	Pijn aan de borstkas	
Symptoms related to exercise tolerance functions	**Symptomen gerelateerd aan inspanningstolerantie**	**b.455**
Reduced exercise tolerance	Verminderde inspanningstolerantie	
Respiratory fatigue	Ademhalingsvermoeidheid	

DISCUSSION

FRAMEWORK: 1. SYMPTOMS RELATED TO SENSATIONS ASSOCIATED WITH CARDIOVASCULAR AND RESPIRATORY FUNCTIONS (ICF B.460)

In this study, all participants (100%, 15/15) reported symptoms that can be covered by the terms 'shortness of breath' and/or 'breathlessness'. This indicates that this is the predominant symptom experienced by adolescents and adults with scoliosis that presented with symptoms related to breathing and exercise function. In a previous study conducted with adolescents and adults with scoliosis in the Netherlands, an anonymous survey also revealed breathlessness as the primary symptom reported.[9] This could explain why evaluation and monitoring of symptoms related to breathing and exercise tolerance is a challenge in this population as these are patient-experienced symptoms, rendering them inherently subjective. In the current study this is further emphasized by the variety of terminologies patients used to describe these sensations in this study (Table 5).

A 'wheeze' was reported by adult patients, but no adolescent patients reported this. In contrast, exertion-induced respiratory-related 'chest pains' were only reported by adolescent patients. Notably, in a previous anonymous survey, based on which the current interview guide was made, no significant differences were reported in symptoms between adolescents and adults with scoliosis. As yet, to our knowledge, no other literature exists on the difference in experienced symptoms between patients of different age groups.

FRAMEWORK: 2. SYMPTOMS RELATED TO EXERCISE TOLERANCE FUNCTIONS (ICF B.455)

With regard to the second category of complaints, patients commonly reported reduced exercise tolerance and limitations in physical activities, leading to frustration, isolation, and decreased overall well-being. These findings could explain the observation of avoidance of aerobic exercise in patients with scoliosis reported by Lenke et al.[20] Some patients reported experiencing difficulties with performing daily tasks. Others did not experience this, but still reported a difference in ability compared to their healthy peers. The limitations appeared to be progressive over time in most patients, impacting both physical and social aspects of patients' lives, leading to isolation and disappointment. This

is further emphasized by previous research on the negative impact of perceived difference in physical ability on self-esteem and confidence.[21]

STRENGTHS & LIMITATIONS

A strength of this study is the use of systematic qualitative methods with a deductive approach, in which patients were consulted, thereby ensuring a more detailed understanding of the theoretical framework. A study-specific semi-structured interview guide was prepared to perform the interviews. This allowed interviews to be structured, standardized, and comparable, whilst also allowing flexibility for interview-specific follow-up questions. Second, the inclusion process was terminated after data saturation was expected to have been reached and no new categories or items were identified.[22] This indicates that sufficient data had been collected to explore categories related symptoms related to breathing and exercise tolerance in adolescents and adults with scoliosis. Third, by using the ICF classification the definitions in the developed framework are harmonized for the languages and the applicability across different cultures is ensured.[16,17]

This study also has its limitations. First, qualitative research methods pose a risk for researcher and/or interviewer bias.[23] The results of the study may have been influenced by the researchers' personal beliefs. On the other hand, these personal beliefs can also provide valuable insights and interpretations. They could also encourage patients to open up about their experiences. As recommended to increase intercoder reliability, a second coder was included to objectify the results.[24] Second, no triangulation was used in this study, meaning that the data in this study was collected using a single method. Using multiple qualitative methods (e.g. journal keeping) to collect data potentially increases the credibility and reliability of the results.[25] This limitation was mitigated by thorough literature review and consultation with qualitative experts. Another limitation of the study is the lack of purposive sampling based on the level of scoliosis (cervical, thoracic, lumbar), a characteristic which could have an impact on symptoms such as wheezing, particularly if this symptom is caused by obstruction of the airway. Future research could address this by investigating the association between scoliosis level and specific symptoms related to breathing and exercise tolerance, providing a more nuanced understanding of their prevalence and management in different scoliosis subtypes. This was however not the purpose of this study. Lastly, while this study's goal was not to develop a screening instrument, it is important to note that the focus on patients presenting with symptoms

related to breathing or exercise tolerance may introduce selection bias, potentially limiting the applicability of these findings to those with subclinical symptoms not typically addressed in a clinical setting.

CONCLUSION

The study identified two key categories within the ICF framework: symptoms related to sensations associated with cardiovascular and respiratory functions (ICF b.460) and symptoms related to exercise tolerance functions (ICF b.455). These findings provide a structured theoretical framework for understanding patient-reported symptoms in adolescents and adults with scoliosis.

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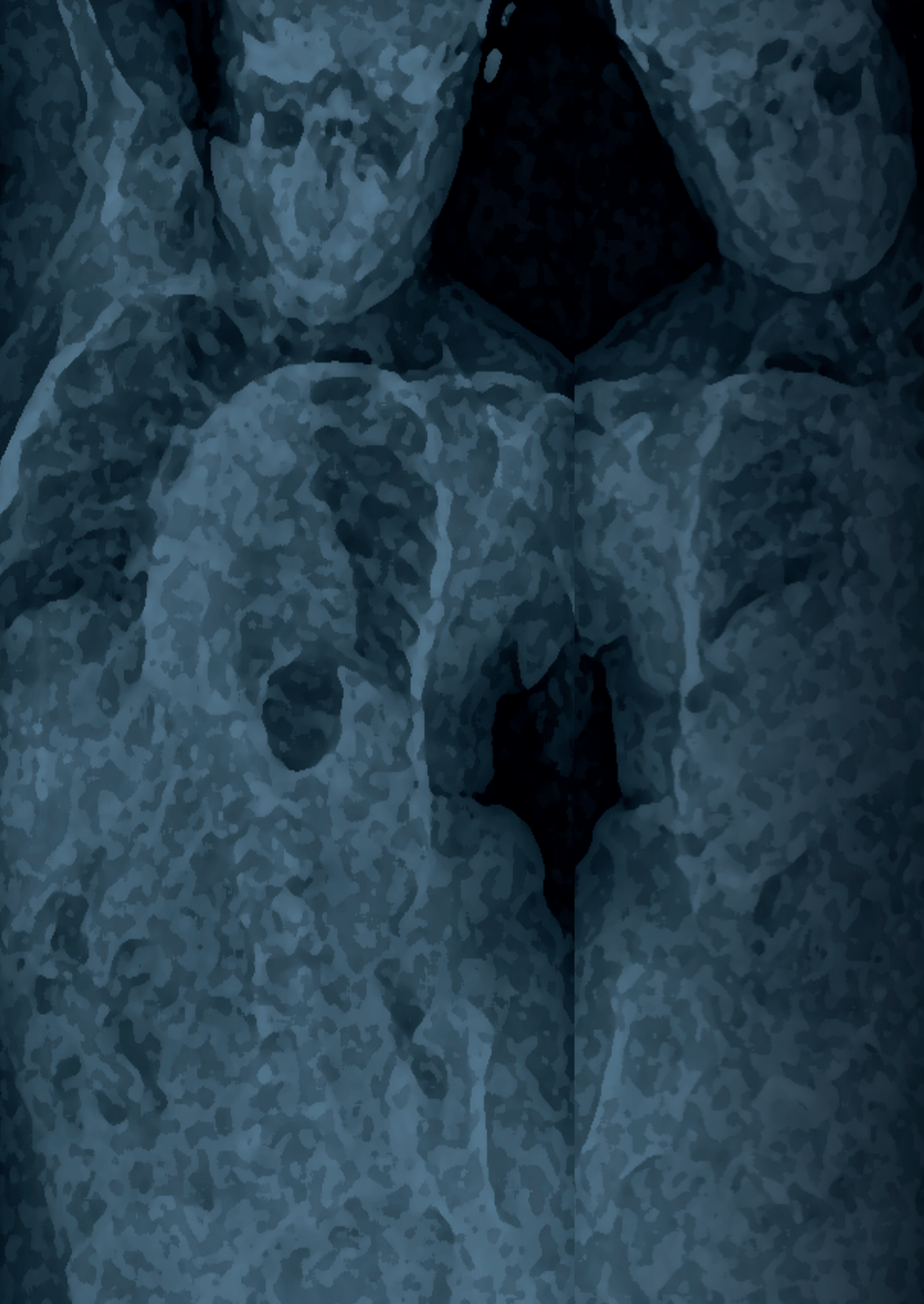

CHAPTER 8

GENERAL DISCUSSION & SUMMARY

8

GENERAL DISCUSSION & SUMMARY

The aim of this thesis is to assess multiple aspects of function and functioning in patients with spinal deformity, being: the radiographic measurements in patients with scoliosis, to provide further insight into the encountered pulmonary problems and to lay the groundwork for the development of a new measurement tool for routinely evaluating the pulmonary challenges faced by patients with scoliosis. Specific aims were formulated and outlined in chapter 1. This chapter discusses the main findings, conclusions, and key limitations for each aim. A summary is provided at the end. A more detailed discussion of strengths and limitations can be found in the respective chapters.

As outlined in the introduction, this thesis evolved over time, ultimately shaping the work into three distinctive parts and emphasizing the critical distinction between function and functioning.

Function[1,2] refers to the physiological or anatomical capacity of the body's systems to perform specific tasks. It is an objective measure of what the body is capable of under ideal or controlled conditions. In clinical practice, function is typically assessed through standardized tests or imaging, such as measuring spinal curvature angles or evaluating pulmonary volumes using spirometry. These metrics offer valuable insights into the physical capacity of specific body systems but do not capture how these capacities—or their limitations—manifest in real-world contexts.

In contrast, **functioning** reflects the holistic integration of physical, mental, and social health within an individual's life.[1,2] It encompasses how a person applies their physiological capabilities to perform daily activities and fulfill social roles, taking into account environmental and personal factors. While function focuses on the potential capacity of a body part or system, functioning considers the actual realization of that potential in the context of an individual's life. Assessments of function and functioning are guided by the International Classification of Functioning, Disability and Health (ICF) framework, which evaluates not only physical health but also the interaction of environmental and personal influences.

Although function and functioning are interconnected, they are not always directly proportional and healthcare professionals tend to use these terms interchangeably. Good function does not necessarily ensure good functioning, and poor function does not

always result in poor functioning. Medical treatments may enhance function but may not lead to improved functioning unless they address barriers that individuals face in real-world scenarios. Throughout this process, we often faced a challenge with the nuances of the correct terminology. This challenge arose because an adequate term has yet to be established to describe the symptoms patients experience in relation to pulmonary function.

PART 1: RADIOGRAPHIC FUNCTION

AIM 1: TO EVALUATE RADIOGRAPHIC FACTORS FOR PREDICTING CURVE PROGRESSION IN ADULT SPINAL DEFORMITY PATIENTS (CHAPTER 2).

In chapter 2, we performed a long-term evaluation of curve progression in both coronal and sagittal planes among non-surgically treated patients with adult spinal deformity (ASD). Thus, radiographic assessment over time of the function, stability of the spine, in patients with ASD. The group of patients with ASD was categorized into two subgroups: (1) de novo degenerative lumbar scoliosis (DNDLS) and (2) adult idiopathic scoliosis (AdIS). The results show progression in the coronal plane occurring in the large majority of patients (42/58, 72%) over an average 5-year follow-up period (*chapter 2, table 4*). Among all 58 ASD patients, there was a mean increase in coronal Cobb angle of approximately 1^0 per year ($0.83^0 \pm 1.1^0$, *chapter 2, table 2*). No significant difference was seen in curve progression between patients with DNDLS and AdIS (0.98 ± 1.1 vs. 0.37 ± 1.4, p = 0.07; *chapter 2, table 2*).

Contradicting previous studies,[3–5] we found no significant differences in curve progression per year in left- versus right-sided scoliosis (0.81° ± 1.42 vs. 0.65° ± 1.21, p = .655), Cobb angle <30° versus ≥30° (0.60° ± 1.39 vs. 0.76° ± 1.18, p = .635), or when the intercrest line passed through L4 rather than the L5 vertebra (0.79° ± 1.21 vs. 0.56° ± 1.35, p = .504; *chapter 2, table 3*). Similarly, sagittal spinopelvic parameters did not significantly change over the follow-up period. However, there was a trend towards a decrease in lumbar lordosis (–39.0 ± 14.1 to –31.6 ± 20.3, p = .127; *chapter 2, table 6*). Although our findings imply a tendency towards increased sagittal malalignment over

time in ASD patients, it remains unclear whether this is due to the normal aging process. This ambiguity arises from the fact that with advancing age, there is a natural decrease in lumbar lordosis, leading to anterior trunk displacement, commonly referred to as a "stooped posture".[6]

These conflicting results of our study and previous studies[3–5] could originate from variations between the two groups. One study, reporting the curve direction as a risk factor[4], included patients with primary curves not exceeding 30°. Whereas our current study involved all ASD patients with primary curves greater than 10°. Another study reporting the curve magnitude as a risk factor[5], involving 162 ASD patients (all female), with an average follow-up of 8 years. The shorter follow-up duration in our study (5 years), combined with the nonlinear nature of curve progression, may contribute to this inconsistency.

Due to the large variations in the rate of curve progression it is challenging to give guidance to individual patients with ASD. We recommend that non-surgically treated ASD patients are included in spine registries for better understanding of the condition's natural history and prognostic factors. Overall, our findings suggest a need for personalized follow-up strategies for ASD patients and raise questions regarding sagittal malalignment and its relation to aging.

AIM 2: TO IDENTIFY THE SUPERIOR RADIOGRAPHIC TECHNIQUE FOR ASSESSING THE SPINAL CURVE FLEXIBILITY; SUPINE TRACTION RADIOGRAPHS OR PRONE SIDE BENDING RADIOGRAPHS.

In chapter 3, we compared the efficacy of prone side bending radiographs versus supine traction radiographs in assessing the curve flexibility function in patients with different types of spinal deformities, including adolescents with idiopathic scoliosis (AIS), and adults with spinal deformity (ASD), i.e. adult (or degenerative) idiopathic scoliosis (AdIS), and 'de novo degenerative lumbar scoliosis' (DNDLS). The assessment of the curve flexibility is essential for surgical planning. The greater the flexibility, the more curve correction can be obtained with spinal fusion. To our knowledge, this is the first study that compares traction and bending radiographs in AIS *as well* as ASD. Results revealed that for the primary curve, prone bending radiographs showed a greater curve correction compared to traction radiographs in DNDLS patients (44,5% vs. 30.7%, $p <$

0.001) and a trend for AdIS patients (44,% vs. 27.9% , p = 0.054; *chapter 3, table 2*). In AIS, no difference was found (38.6% vs. 33.6%, p = 0.18). For the secondary curve bending showed a greater curve correction in AIS and AdIS patients (AIS: 55% vs. 34.8%, p = 0.002; AdIS: 41.9% vs. 23.2%, p <0.001; *chapter 3, table 3*). In the DNDLS group, bending obtained a considerably greater curve correction but this was not statistically significant (52.4% vs. 36.1%, p = 0.185; *chapter 3, table 3*). This is probably due to the small number of patients ($n_{traction}$ = 18 and $n_{bending}$ = 10) in this group. Although we did not define any minimal clinically important difference (MCID) for the difference in curve correction, we consider the greater curve correction on bending as clinically relevant.

In the existing literature, only a limited number of studies have explored the comparison between traction and bending radiographs. Notably, these studies have primarily focused on the AIS population.[7–11] Our analysis yielded results consistent with those reported by Hamzaoglu et al.,[8] who investigated 34 AIS patients and observed a generally greater curve correction with supine bending compared to traction, although statistical significance was not reported. Conversely, O'Neill et al.[7] documented an overall greater correction on traction radiographs. However, their study applied traction force to the axillae rather than the cervical spine, analyzed only 15 patients and predominantly included thoracic curves (10 out of 15). Despite their demonstration of greater curve correction with traction, our data showed greater curve correction on bending. One plausible explanation for this discrepancy could be the heightened stability or stiffness of the thoracic spine due to the presence of the rib cage, along with the prevalence of thoracic curves in their patient cohort. This interpretation aligns with a computer-simulated mathematical model on thoracic spine flexibility,[12] suggesting that the rib cage enhances stability during lateral bending. Furthermore, Watanabe et al.[11] studied 229 AIS patients, suggesting that traction radiographs exhibit more curve correction when the curve apex is positioned more cranially than T9, a phenomenon that may also be influenced by the rib cage. The study population in both studies[7,8] had comparable curve severity and the definition of curve correction was the same (amount of reduction of Cobb angle in degrees).

In practice, obtaining a traction radiograph entails greater labor intensity for the radiology team compared to a bending radiograph, as it necessitates the involvement of two radiology technologists: one for obtaining the radiograph and at least one other for providing the traction force. Additionally, traction radiographs tend to be less comfortable

for patients, as cervical traction is applied up to their maximum tolerance. Conversely, generating side bending radiographs requires two radiographs, thereby subjecting patients to twice the amount of radiation. Considering these three factors and the outcomes of our analysis (which indicate greater correction on bending or no significant difference between traction and bending) for assessing flexibility in routine clinical pre-operative work up of patients with degenerative and/or idiopathic scoliosis, we feel the benefits of bending radiographs outweigh the risk of the double radiation exposure.

Consequently, based on the findings of our study, we have discontinued the use of traction radiographs for assessing curve flexibility in patients with AIS, AdIS, and DNDLS in our pre-operative work-up. There may continue to be an indication for traction films for other patients, e.g. those with spinal deformities as a result of other underlying pathology, such as patients with cerebral palsy or patients who are not able to perform the active bending motion required.

Building upon the findings regarding radiographic techniques for assessing spinal curve flexibility, our focus in chapter 4 shifts to another key aspect of clinical outcomes for patients with spinal deformities, being pulmonary function. While curve flexibility assessments are critical for surgical planning, pulmonary health is equally essential to consider in the comprehensive management of these patients.

PART 2: PULMONARY FUNCTION

AIM 3: TO PERFORM AN EXPLORATORY SURVEY OF PULMONARY SYMPTOMS IN PATIENTS WITH SPINAL DEFORMITIES.

In chapter 4, we confront the challenge of distinguishing between the terms function and functioning for the first time. Clinicians often focus on function, typically assessing measurable physical abilities, while overlooking the broader concept of functioning, which involves how these abilities are applied in real-life situations. We highlight the impact of adolescent idiopathic scoliosis (AIS) and adult spinal deformity (ASD) on pulmonary function and the lack of routine assessment and consideration of this aspect in clinical practice. The effect of AIS and ASD on pulmonary function has been reported in the literature for many years and could lead to disability secondary to pulmonary symptoms,

such as shortness of breath during daily functioning or exercise intolerance.[13–21] However, pulmonary function is rarely assessed in AIS patients during routine clinical practice. Due to their doubtful clinical relevance and high cost, clinical pulmonary function tests (PFTs) are not routinely performed.

We highlight the perspective of both clinicians and patients in chapter 4. Clinicians recognize the importance of assessing pulmonary function in both AIS and ASD but lack a patient-relevant measure for routine use.[22,23] We performed an exploratory survey in which patients reveal to experience pulmonary symptoms commonly. Among the 58 patients, 26 experienced pulmonary symptoms (45%). Most patients described their symptoms as "breathlessness" (10/26, 38%) or "fatigue"/"fatigue due to limited endurance" (5/26, 19%). Daily functioning of 19/26 (73%) patients was limited due to the pulmonary problems and 18/26 (69%) patients reported worsening of symptoms with increased fatigue. Despite the selection bias in this survey, it underscores the necessity for improved assessment and management strategies. Utilizing patient-reported outcome measures (PROMs) could serve as a valuable tool for capturing the patient's perspective. However, it remains unexplored whether such a tool is currently available.

AIM 4: TO PERFORM A SYSTEMATIC REVIEW OF THE LITERATURE TO IDENTIFY PATIENT-REPORTED AND CLINICAL MEASUREMENT TOOLS USED FOR ASSESSING PULMONARY FUNCTION IN PATIENTS WITH AIS.

In chapter 5, we focus on patients with AIS and the tools used to measure pulmonary function. As described in chapter 4, the availability of a measurement tool for pulmonary function in AIS is unexplored. For this reason, we performed a systematic review to identify patient-reported and clinical measurement tools used for assessing pulmonary function and -symptoms. A secondary objective was to assess the measurement properties of the identified instruments (i.e. the characteristics and quality of the measurement tools, such as reliability and validity). Following the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement, a comprehensive literature search and selection process was performed, resulting in the inclusion of 122 studies. In total, 50 different pulmonary parameters were identified, measured by seven distinct clinical measurement instruments. The most frequently used instruments were spirometry and plethysmography, with the most frequently reported parameters

being forced vital capacity (FVC, 99/122 papers, 81%), forced expiratory volume in one second (FEV_1, 97/122 papers, 80%), the FEV_1/FVC ratio (31/122 papers, 25%) and total lung capacity (TLC, 29/122 papers, 24%). Spirometry and plethysmography generally offer a reliable assessment of lung volume and flow functions, making them suitable for diagnosing restrictive or obstructive lung impairments.[24–26] However, we found no evidence regarding the adequacy of these instruments in an AIS population in terms of their measurement properties.

Concerning patient reported outcome measures (PROMs), five were identified that have been used for assessing pulmonary symptoms in patients with AIS. However, no studies were found addressing concurrent measurement properties to assess the adequacy of these measurement instruments. Consequently, factors such as floor-ceiling effects, validity, reliability, responsiveness, and interpretability[27] of the identified PROMs could not be evaluated within the AIS population. We concluded that an adequate and satisfactory patient-centered instrument for measuring pulmonary outcomes in patients with AIS is not available.

Since clinimetric measurement properties couldn't be established within an AIS population, we conducted a post-hoc literature search to determine if these measurement instruments were validated in populations other than AIS. Twenty studies of generally high methodological quality were discovered. None of these studies evaluated all measurement properties as described by Terwee et al.[27]

In assessing these twenty studies, the University of California, San Diego Shortness of Breath Questionnaire (UCSD SOBQ)[28] seems promising. It showed good clinimetric measurement properties in populations with lung diseases and includes the limitations of daily activities, which are important for an AIS population (as described in chapter 4). However, a direct comparison between patients with lung diseases and AIS patients is a challenge since AIS patients typically have restricted but generally healthy lungs.[16] Additionally, the UCSD SOBQ appears overly comprehensive for routine outcome assessment, especially when compared to the widely used Scoliosis Research Society-22 (SRS22) questionnaire. The SRS22 consists of 22 questions across five outcome domains, while the UCSD SOBQ comprises 24 questions focusing on one outcome domain.

Apart from the UCSD SOBQ, the Borg Rating of Perceived Exertion (RPE)[29] scale emerges as another promising PROM. It appeared to have a good criterion validity, which means that it strongly correlates with the gold standard.[27] However, it may be

inadequate for evaluating pulmonary issues in AIS patients due to its limited scope. That is, it primarily assesses breathlessness at a single point in time, typically during or immediately after exercise. It lacks information on other pulmonary symptoms such as increased fatigue, reduced exercise capacity and perceived limitations in daily functioning, which are commonly reported by AIS patients (as discussed in chapter 4).

The challenge in finding a suitable measurement instrument for pulmonary function in AIS is that the underlying cause and theoretical framework for the experienced pulmonary symptoms remain elusive. Are these limitations primarily attributed to lung dysfunction, such as restricted lung inflation, or does the fatigue originate from heightened energy expenditure by the musculoskeletal system? Could a cardiovascular etiology be ascribed to these symptoms? Recent research indicates that a subset of AIS patients may present with impaired right cardiac function and pulmonary hypertension, phenomena which normalize following scoliosis surgery.[30] This suggests potential benefits of spine surgery on cardiac function, possibly through spine realignment and its impact on cardiovascular structures and the rib cage.

Understanding the pulmonary symptoms experienced by AIS patients is crucial to develop an appropriate PROM for routine clinical assessment. This understanding will also facilitate the evaluation of aging, curve progression, or various treatment modalities on pulmonary function and symptoms in scoliosis patients. Therefore, we recommend to further explore this domain with patients to delineate the limitations they encounter and to identify pertinent questions or items for measurement. This collaborative approach will aid in establishing a theoretical framework for AIS-related pulmonary issues, ultimately leading to the identification and validation of existing PROMs (such as the UCSD SOBQ), or the development of new disease-specific PROM.

PART 3: PULMONARY FUNCTIONING

AIM 5: TO ASSESS THE FEASIBILITY OF UTILIZING A WEARABLE 'SMART SHIRT' FOR CONTINUOUS MONITORING OF LUNG VOLUMES AND HEART RATE, DURING ROUTINE ACTIVITIES IN PATIENTS WITH AIS.

As described in chapter 5, it is unclear how to adequately measure pulmonary function in AIS. It is commonly assessed using spirometry, involving a single-timed, forced measurement that does not accurately represent pulmonary functioning during typical daily activities or exercise. As such, we used a validated novel 'smart shirt'[31] in chapter 6, to continuously monitor and explore cardiopulmonary functioning during standardized daily activities, i.e. walking and climbing the stairs. The shirt continuously monitors chest circumference at two specific levels: at the upper chest and the abdomen. Depending on the sex, height and age of the patient, it calculates the lung volumes. Additionally, it has three electrocardiographic leads to continuously produce a 1-lead electrocardiogram (ECG, 256 Hz) and a 3-axis accelerometer. Alongside the shirt measurements, we performed a baseline spirometry and assessed the amount of breathlessness multiple times before, during and after walking with the modified Borg scale (ranging from 0 to 10). We included AIS patients with a thoracic curve of ≥30^0 and no respiratory comorbidities in this exploratory feasibility study. Due to the nature of the study, we used a small patient sample, analyzing data from a total of five patients.

The smart shirt proved to be feasible and well-tolerated by the patients (despite the asymmetry of their chest and trunk), showing promise for its use in monitoring pulmonary parameters among individuals with AIS. Data generated by the smart shirt showed an overall increase in tidal volumes, heart rate, breathing rate and minute ventilation during walking and stairclimbing. The amount of breathlessness varied greatly among patients.

The most notable result was the poor correlation between the degree of perceived breathlessness and the spirometry measurements or data obtained from the smart shirt. For example, two patients with similar thoracic Cobb angles (63^0) showed great differences in spirometric results and reported breathlessness levels. One of these participants demonstrated excellent spirometric measurements (e.g. FVC at 104% of predicted) but experienced severe breathlessness during stairclimbing (upper limit rated 8 out of 10).

Conversely, the other participant had poorer spirometric measurements (e.g. FVC at 66% of predicted) but reported much less breathlessness (upper limit rated 4 out of 10). This inconsistency suggests that spirometry in AIS patients may not offer the necessary insights which are important to understand the pulmonary symptoms as perceived by patients with AIS. Furthermore, the cardiopulmonary parameters continuously measured by the smart shirt also showed no correlation with the reported level of breathlessness.

To the best of our knowledge, this is the first study that continuously measures cardiopulmonary parameters in patients with AIS. Our findings question the conventional understanding of the underlying causes of pulmonary symptoms in patients with AIS. Generally, these symptoms were thought to stem from restricted lung volumes, which could be linked to various factors such as deformities in the thoracic cage, shortening of the thoracic spine, reduced chest wall compliance and increased chest wall stiffness.[32,33]

The results of our study and recent other research cited below question this conventional thinking. Recent investigations propose an obstructive (rather than restrictive) pattern originating from constriction of the right-sided bronchial passages.[34,35] This constriction of the right bronchial tree occurs due to the intrusion of the spine into the chest, caused by the endothoracic hump resulting from the deformity with a loss of thoracic kyphosis. Moreover, emerging evidence also points towards a potential cardiac origin for the perceived breathlessness and/or exercise intolerance, possibly due to compression of the right pulmonary artery, which could result in (mild) pulmonary hypertension.[30,36] Finally, dysfunction of the respiratory muscles has also been reported in patients with AIS.[37,38]

In summary, our findings provide valuable insights into cardiopulmonary changes during mild exercise in patients with AIS. Nevertheless, we were unable to establish any correlation between spirometry results, smart shirt measurements, or perceived breathlessness. To further explore the origins of the experienced pulmonary symptoms continued research is needed to gain deeper insights into this area.

AIM 6: TO BUILD A THEORETICAL FRAMEWORK AND IDENTIFY RELEVANT PATIENT EXPERIENCED OUTCOMES FOR SYMPTOMS RELATED TO BREATHING AND EXERCISE TOLERANCE IN PATIENTS WITH IDIOPATHIC AND ADULT SCOLIOSIS

As described in chapter 4 and 5, understanding the pulmonary symptoms as experienced by patients with AIS is crucial to develop an appropriate and adequate PROM for routine clinical assessment. To further explore relevant patient experienced outcomes with a focus on functioning and to establish a theoretical framework for scoliosis-related pulmonary issues, we performed an international multicenter qualitative study using structured patient interviews in chapter 7.

Six idiopathic and nine adult scoliosis patients who reported pulmonary symptoms from 5 centers in the Netherlands and the USA participated. In-depth structured interviews were conducted, transcribed and analyzed to identify the relevant patient experienced outcomes for symptoms related to breathing and exercise. These were identified based on the definitions in the International Classification of Functioning, Disability and Health (ICF) framework. Two main patient-experienced outcome categories were identified: 1) 'symptoms related to cardiovascular and respiratory functions', covering 'shortness of breath / breathlessness', 'wheezing', and 'chest pains', and 2) 'symptoms related to exercise tolerance' covering 'reduced exercise tolerance' and 'respiratory fatigue'.

1. SYMPTOMS RELATED TO SENSATIONS ASSOCIATED WITH CARDIOVASCULAR AND RESPIRATORY FUNCTIONS

All participants (15/15, 100%) reported 'shortness of breath' and/or 'breathlessness'. This indicates that this is the predominant pulmonary symptom in symptomatic patients with idiopathic and adult scoliosis. In chapter 4 'breathlessness' was also the primary reported symptom (10/26, 38%). 'Wheezing' and 'exercise-induced chest pains' were observed in specific cases (3/15 and 4/15, respectively).

2. SYMPTOMS RELATED TO EXERCISE TOLERANCE FUNCTIONS

Regarding the second category of complaints, patients frequently mentioned experiencing reduced exercise tolerance and limitations in physical activities. Among the participants, 10 out of 15 (67%) reported 'pulmonary fatigue,' and 13 out of 15 (87%) reported 'reduced exercise tolerance.' This often leads to frustration, isolation, and a decline in overall well-

being. These findings could explain the observation of avoidance of aerobic exercise in patients with AIS reported by Lenke et al.[18] Some patients reported to experience difficulties with performing daily tasks. Others did not experience this, but still reported a difference in ability compared to their healthy peers. Both adults and adolescents reported that these limitations worsen over time, impacting both their physical abilities and social interactions. The perceived disparity in physical abilities has also been associated with negative impacts on self-esteem and confidence.[39]

The identified patient experienced outcome categories as described above lays the groundwork for the development of a new PROM; a first step to standardize the measurement of pulmonary functioning of patients with spinal deformity.

FUTURE PERSPECTIVES

In this thesis we studied various aspects of assessing patients with adolescent idiopathic scoliosis (AIS) and adult spinal deformity (ASD). Our research sheds light on the complex nature of these conditions and the diverse challenges they present. In the future trajectory of research in this field, several challenges lie ahead.

LONGITUDINAL STUDIES AND PREDICTIVE MODELING:

The evaluation of radiographic factors for predicting curve progression in adults with a spinal deformity (**chapter 2**) emphasizes the need for longitudinal studies in understanding disease progression patterns and prognostic factors. Future research could delve deeper into longitudinal studies with assessments over time, involving larger patient cohorts over extended follow-up periods. As recommended in **chapter 2**, it would be advantageous to include non-surgically treated ASD patients in spine registries. Doing so could enable the use of advanced statistical modeling techniques such as machine learning algorithms to develop predictive models to forecast individualized progression patterns. Additionally, this approach could offer valuable insights into the interplay between spinal alignment, aging, clinical outcomes and experienced symptoms. This could possibly enable tailored treatment strategies and optimized patient care.

DEVELOPMENT OF AN ADEQUATE PATIENT REPORTED OUTCOME MEASURE (PROM) FOR PULMONARY FUNCTIONING:

The recognition of pulmonary function as a vital yet underexposed domain in adolescent idiopathic scoliosis (AIS) and ASD patients (**chapter 4**) highlights the necessity of integrating the assessment of pulmonary function into clinical practice. The absence of an adequate measurement instrument for pulmonary function in AIS (**chapter 5**) highlights the necessity for developing such a measurement instrument. The discrepancy between spirometric measurements and reported breathlessness (**chapter 6**) further highlights the questionable utility of current clinical measurement instruments. To prioritize patient-centered care, we advise that future research efforts should concentrate on developing and validating a PROM for pulmonary functioning of patients with spinal deformity. This PROM could then be integrated into routine clinical assessments and potentially guide therapeutic decision-making.

The groundwork for this new PROM was laid in **chapter 7**. The next step involves defining the PROM items (questions), based on the theoretical framework and identified patient experienced outcomes. Future research should include a large-scale cross-sectional validation study based on the COnsensus-based Standards for the selection of health Measurement Instruments (COSMIN) checklist for PROMs.[27,40] This would ideally be conducted across multiple centers to assess the PROM's clinimetric properties. Ideally, this study can determine the PROM's internal consistency, measurement error and reliability, floor and ceiling effects, construct validity and responsiveness. This new PROM might be integrated into an existing PROM, such as the Scoliosis Research Society-22 (SRS-22) questionnaire, which is a validated and widely used tool for assessing health-related quality of life in patients with spine deformity.

The successful integration of the PROM to assess pulmonary functioning in patients with spinal deformity into clinical practice and research can offer valuable insights into disease progression, treatment efficacy, and patient-centered outcomes over time. By integrating the PROM into routine clinical assessments and research protocols, healthcare providers and researchers can monitor changes in pulmonary functioning and quality of life, aiding in the early detection of deterioration and optimization of treatment approaches. Additionally, the PROM can serve as a meaningful endpoint in clinical trials, allowing for the evaluation of interventions designed to enhance pulmonary functioning

and alleviate the effects of spinal deformities on patients' respiratory health and overall well-being.

TECHNOLOGICAL INNOVATIONS FOR CONTINUOUS MONITORING CARDIOPULMONARY PARAMETERS:

The feasibility assessment of using wearable technology for continuous monitoring of cardiopulmonary parameters (**chapter 6**) highlights the potential of technological innovations for the evaluation of pulmonary functioning in patients with spinal deformity. To further explore the possibilities of the smart shirt used in **chapter 6**, the shirt should be validated in a spine deformity population using spirometry to calibrate the measured pulmonary volumes. Moreover, a larger cohort with a healthy control group may possibly shed more light on the etiology of the experienced pulmonary symptoms.

In summary, the proposed future research directions in spinal deformity hold promise to drive the field toward more comprehensive, patient-centered management strategies that can significantly enhance the lives of those affected.

SUMMARY

In this thesis we studied multiple aspects of function and functioning in patients with spinal deformity, aiming to enhance our understanding of its progression, diagnostic techniques, impact on pulmonary function and the ability to routinely and adequately measure the pulmonary functioning. Furthermore, we encountered challenges in distinguishing the terms function and functioning, with function referring to the potential capacity of a body part or system and functioning to the actual realization of that potential in the context of an individual's life.

In **chapter 2** we performed a retrospective evaluation of curve progression in non-surgically treated adult spinal deformity (ASD) patients, shedding light on the challenges of predicting progression in both coronal and sagittal planes. Despite previous studies suggesting certain radiographic factors as predictors of progression, our findings revealed curve progression in the majority of patients and a lack of significant associations between

curve progression and variables such as curve direction, magnitude of the curve or level of the intercrest line. These inconsistencies highlight the complexity of ASD progression and emphasize the need for personalized follow-up strategies.

In **chapter 3** we compared the efficacy of prone bending radiographs versus supine traction radiographs in assessing curve flexibility which is essential for pre-operative planning in spinal fusion surgery. Our results favor the use of prone bending radiographs, offering greater curve correction and patient comfort compared to traction radiographs. This finding has had immediate implications for clinical practice, as we discontinued the use of traction radiographs in routine assessments of curve flexibility in AIS, AdIS and DNDLS patients.

In **chapter 4** we emphasized the underexposed impact of pulmonary symptoms in patients with spinal deformity, calling attention to the need for routine assessment and management strategies. By highlighting the prevalence of pulmonary symptoms and their impact on daily functioning, we underscored the importance of identifying and developing patient-centered outcome measures for pulmonary function. This to include a highly relevant factor into routine outcome assessment to comprehensively encompass all the relevant factors affecting the quality of life of patients with spinal deformity.

In **chapter 5** we performed a comprehensive systematic review of the literature of measurement instruments used to assess pulmonary function in adolescent idiopathic scoliosis (AIS) patients. Despite numerous parameters and instruments being reported, the clinimetric measurement properties specific to the AIS population have not been established. Spirometry and plethysmography are very frequently used measurement instruments, but the relevance to or the correlation with the experienced pulmonary symptoms is not known. Although two patient-reported outcome measures (PROMs) have had their clinimetric properties studied in populations other than AIS, their applicability in AIS patients remains uncertain. In conclusion, our findings revealed the lack of an adequate measurement instrument for routine outcome monitoring of pulmonary function. Additionally, we highlight the elusive nature of the underlying cause and theoretical framework for the pulmonary symptoms. This emphasizes the necessity for further research and development of patient-centric measurement instruments.

In **chapter 6** we explored the feasibility of using a smart shirt for continuous monitoring of cardiopulmonary functioning during routine activities in AIS patients. The smart shirt was found to be feasible and well-tolerated by patients despite the asymmetry of their

trunk, indicating its potential for further exploration in understanding the experienced pulmonary symptoms. By enabling the continuous measurement of cardiopulmonary parameters during various activities, the smart shirt can offer valuable insights. However, our findings also underscored the complexities in understanding pulmonary symptoms in AIS. Discrepancies were observed between spirometry measurements, data collected from the smart and the reported amount of experienced breathlessness. These inconsistencies raise questions about the usability of objectively measured pulmonary function in the assessment of the pulmonary symptoms or pulmonary functioning. In conclusion, our findings suggest that the pulmonary symptoms experienced by AIS patients may have other underlying causes, such as a cardiovascular origin.

In **chapter 7** we conducted a qualitative study to build a theoretical framework and identified relevant patient experienced outcomes related to breathing and exercise tolerance in idiopathic and adult scoliosis patients. Based on the interviews with idiopathic and adult scoliosis patients, two main categories were identified with multiple sub-categories. The main categories were 1) *'symptoms related to cardiovascular and respiratory functions'* and 2) *'symptoms related to exercise tolerance functions'*. Subcategories being 1) *'shortness of breath'/'breathlessness', 'wheezing', 'exercise-induced chest pains'* and 2) *'pulmonary fatigue'* and *'reduced exercise tolerance'*. By identifying these patient experienced outcomes, we laid the groundwork for developing a new patient reported outcome measure (PROM) to standardize the measurement of pulmonary functioning of patients with spinal deformity. Further research is necessary to develop the items (questions) of the PROM and validate this in a large-scale cross-sectional validation study. By integrating this new PROM into routine clinical assessments and research protocols, healthcare providers and researchers can monitor changes in pulmonary functioning and quality of life, aiding in the early detection of deterioration and optimization of treatment approaches. Additionally, the PROM can serve as a meaningful endpoint in clinical trials, allowing for the evaluation of interventions designed to enhance pulmonary functioning and alleviate the effects of spinal deformities on patients' respiratory health and overall well-being.

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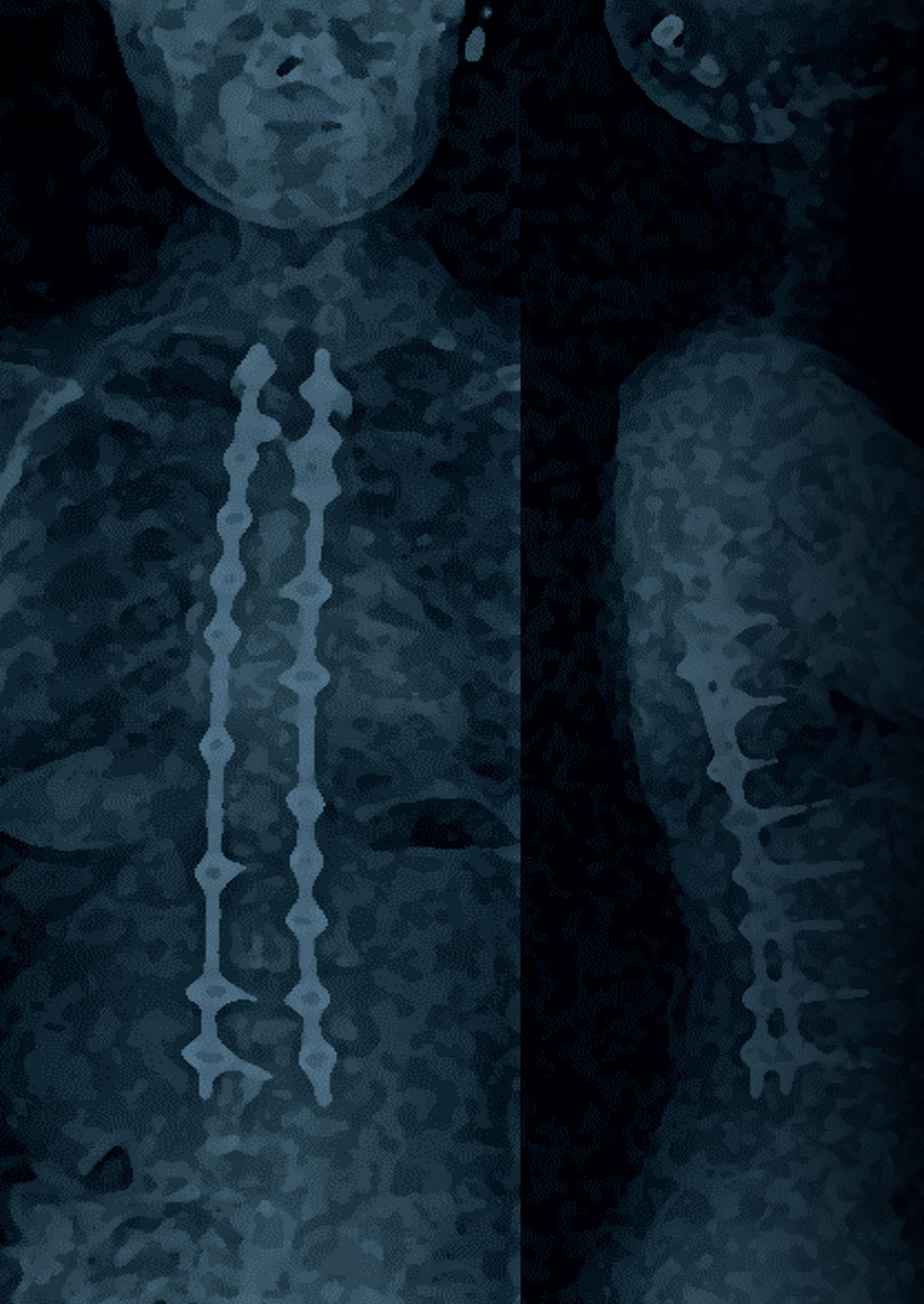


CHAPTER 9

NEDERLANDSE SAMENVATTING

9

NEDERLANDSE SAMENVATTING

In dit proefschrift hebben we verschillende aspecten van de functie en het functioneren van patiënten met scoliose bestudeerd, met als doel om de bochtprogressie, de diagnostische technieken en de impact op de longfunctie beter te begrijpen. Tevens hebben we de basis gelegd voor de ontwikkeling van een vragenlijst (patiënt-gerapporteerde uitkomstmaat, *PROM*) die het mogelijk zal maken om het functioneren van de longen van patiënten met scoliose routinematig en adequaat te meten. Daarnaast stuitten we op uitdagingen bij het onderscheid maken tussen de termen functie en functioneren, waarbij functie verwijst naar de potentiële capaciteit van een lichaamsdeel of systeem en functioneren naar de daadwerkelijke realisatie van die capaciteit in de context van iemands leven.

In **hoofdstuk 2** hebben we een retrospectief onderzoek uitgevoerd naar de progressie van de bocht (functie) bij niet-chirurgisch behandelde volwassen patiënten met scoliose (*adult spinal deformity, ASD*). We benadrukten de uitdagingen die komen kijken bij het voorspellen van progressie in zowel coronale als sagittale vlakken. Hoewel eerdere onderzoeken bepaalde radiologische factoren hebben gesuggereerd als voorspellers van progressie, konden wij dit niet bevestigen. Onze resultaten toonden allereerst een progressie van de bocht bij de meerderheid van de patiënten. Daarnaast lieten onze bevindingen een gebrek aan significante verbanden zien tussen de progressie van de bocht en variabelen zoals de richting van de kromming, de grootte van de kromming of de hoogte van de lijn tussen de bekkenvleugelranden. Deze inconsistenties onderstrepen zowel de complexiteit van de bochtprogressie bij volwassen patiënten met scoliose als de noodzaak voor gepersonaliseerde follow-upstrategieën.

In **hoofdstuk 3** hebben we twee radiologische technieken met elkaar vergeleken voor de beoordeling van de flexibiliteit van de bocht (functie) bij scoliose: buigopnamen in buikligging en tractieopnamen in rugligging. Deze flexibiliteitsbeoordeling is cruciaal in het maken van een preoperatief plan voor een fusie van de wervelkolom. Onze resultaten geven de voorkeur aan het gebruik van buigopnamen in buikligging. Deze laten meer correctie zien van de bocht en het maken hiervan is vergeleken met tractieopnames

veel comfortabeler voor de patiënt. Deze bevinding leidde tot een directe aanpassing in onze klinische praktijk, waarbij we zijn gestopt met het routinematige gebruik van tractieopnamen bij (jong)volwassen patiënten met idiopathische of degeneratieve scoliose.

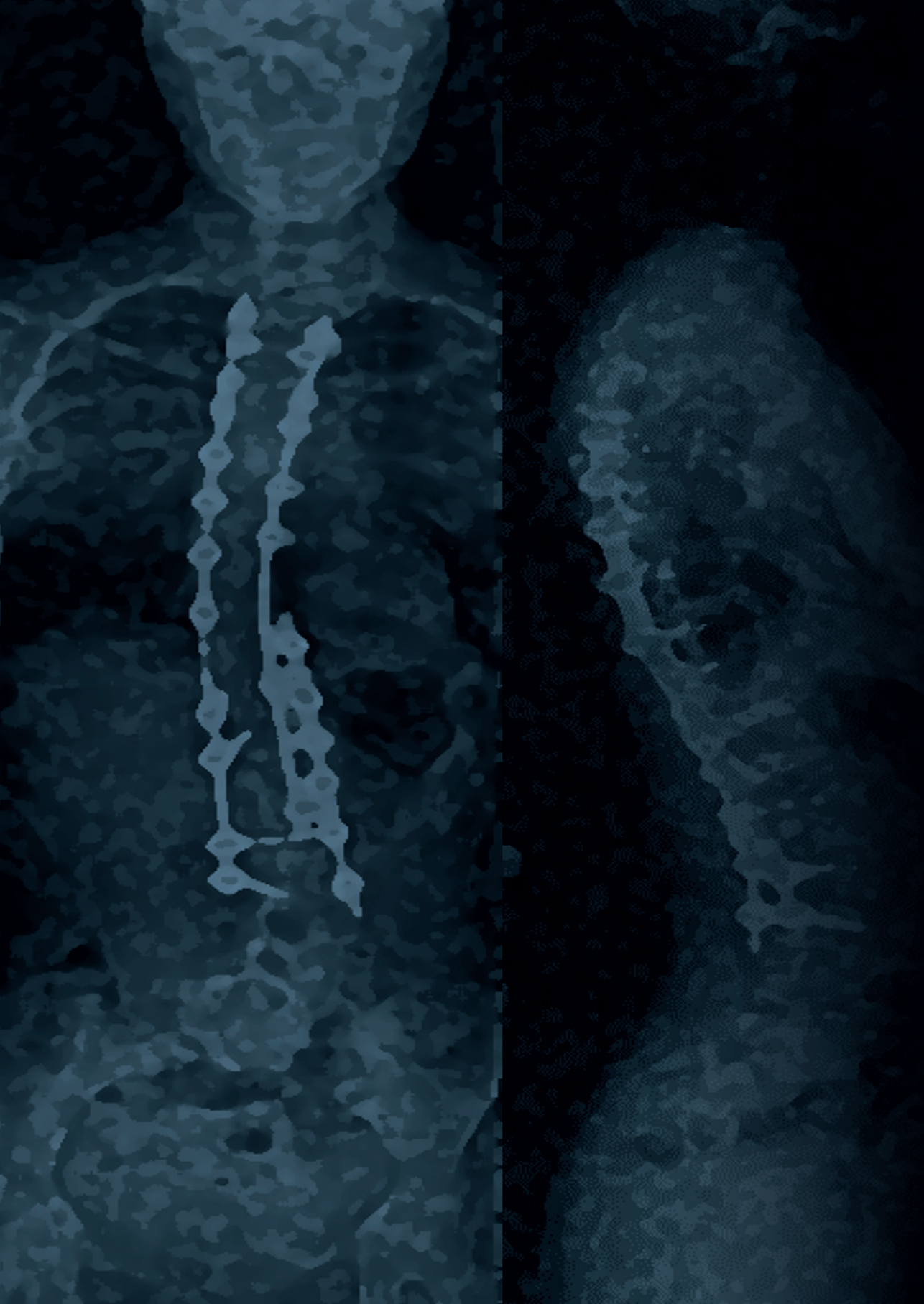
In **hoofdstuk 4** hebben we de vaak onderbelichte impact van longgerelateerde symptomen bij scoliosepatiënten benadrukt en gewezen op de noodzaak van routinematige evaluatie hiervan. Door de prevalentie en impact van longgerelateerde symptomen op het dagelijks functioneren te belichten, onderstrepen we het belang van het ontwikkelen en implementeren van patiëntgerichte uitkomstmaten voor longfunctie als onderdeel van de routinematige zorg voor scoliosepatiënten.

In **hoofdstuk 5** voerden we een systematische review uit van de literatuur betreffende meetinstrumenten die worden gebruikt om de longfunctie bij patiënten met adolescent idiopathische scoliose (AIS) te beoordelen. Ondanks de vele gerapporteerde parameters en instrumenten zijn de clinimetrische meeteigenschappen specifiek voor de AIS-populatie nog niet vastgesteld. Spirometrie en plethysmografie worden vaak gebruikt, maar de relevantie en correlatie met de ervaren longgerelateerde symptomen zijn niet duidelijk. Hoewel twee patiënt gerapporteerde uitkomstmaten (PROM's) veelbelovende clinimetrische eigenschappen vertoonden, zijn deze geëvalueerd in andere populaties dan AIS. Hierdoor is hun toepasbaarheid bij AIS-patiënten niet vastgesteld. Onze bevindingen tonen een gebrek aan een adequaat meetinstrument voor routinematige monitoring van longfunctie aan en benadrukken de noodzaak van verder onderzoek naar de nog onbekende onderliggende oorzaken van de longgerelateerde symptomen.

In **hoofdstuk 6** onderzochten we de haalbaarheid van het gebruik van een 'slim shirt' voor de continue monitoring van het functioneren van het cardiopulmonale systeem tijdens alledaagse activiteiten bij patiënten met AIS. Het slimme shirt werd goed verdragen door de patiënten ondanks de asymmetrie van de borstkas, wat de potentie aantoont voor verder onderzoek naar het functioneren van de longen. Hoewel het shirt waardevolle inzichten biedt, benadrukken onze bevindingen ook de complexiteit van deze symptomen. We observeerden discrepanties tussen spirometriegegevens, de gegevens van het slimme shirt en de gerapporteerde mate van kortademigheid, wat vragen oproept over de

bruikbaarheid van objectief gemeten longfunctie bij de beoordeling van longgerelateerde symptomen. Onze resultaten suggereren dat de longgerelateerde symptomen bij AIS-patiënten mogelijk een andere oorzaken hebben, zoals een cardiovasculaire oorzaak.

In **hoofdstuk 7** voerden we een kwalitatieve studie uit om een theoretisch kader te ontwikkelen en relevante patiënt-gerapporteerde uitkomsten te identificeren met betrekking tot ademhaling en inspanningstolerantie bij patiënten met idiopathische en volwassen scoliose (ASD). Op basis van interviews identificeerden we twee hoofdcategorieën: *1) 'symptomen gerelateerd aan cardiovasculaire en respiratoire functies'* en *2) 'symptomen gerelateerd aan inspanningstolerantie'*. Subcategorieën waren: *1) 'kortademigheid'/'benauwdheid'*, *'piepende ademhaling'*, *'pijn aan de bortkas'* en *2) 'ademhalingsvermoeidheid'* en *'verminderde inspanningstolerantie'*. Door deze patiënt-gerapporteerde uitkomsten te identificeren, hebben we de basis gelegd voor de ontwikkeling van een nieuwe patiënt-gerapporteerde uitkomstmaat (PROM) voor het functioneren van de longen bij patiënten met scoliose. Verder onderzoek is nodig om de vragen voor de PROM te ontwikkelen en te valideren in een grootschalige cross-sectionele studie. Door deze PROM te integreren in klinische- en onderzoeksprotocollen, kunnen zorgverleners veranderingen in het functioneren van de longen en kwaliteit van leven monitoren, wat bijdraagt aan vroegtijdige detectie van verslechtering en optimalisatie van behandelstrategieën. Bovendien kan de PROM dienen als een waardevol eindpunt in klinische onderzoeken, waarmee het effect van scoliosebehandelingen op longgerelateerde symptomen kan worden geëvalueerd en de impact van scoliose op het functioneren van de longen beter in kaart kan worden gebracht.



ADDENDUM

DATA MANAGEMENT AND MEDICAL RESEARCH ETHICS

PHD PORTFOLIO

LIST OF PUBLICATIONS

DANKWOORD

CURRICULUM VITAE

10

DATA MANAGEMENT AND MEDICAL RESEARCH ETHICS

ETHICS AND PRIVACY

MEDICAL AND ETHICAL APPROVAL OF THE STUDIES

This thesis is based on the results of research involving human participants (or existing data from published papers), which were conducted in accordance with relevant national and international legislation and regulations, guidelines, codes of conduct and Radboudumc policy.

For **chapters 6** and **7** of this thesis, the Radboud university medical center medical ethical review board gave the approval to conduct both studies. The study protocols from both studies were reviewed and approved by the recognized Medical Ethics Review Committee 'METC-Oost Nederland'. File numbers; **Chapter 6**: 2022-13282; **Chapter 7**: 2021-7428).

The study described in **chapter 5** was a systematic literature review performed in the Radboud university medical center according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. The protocol of this review was registered in PROSPERO (ID 129174), an international prospective registry of systematic reviews.

PRIVACY STATEMENT

According to Dutch legislation, data collection from electronic patient files was performed by personnel with a treatment relationship with the patient or by the researcher upon consent by the study participant. The privacy of the participants of studies described in **chapters 2, 3, 4, 6,** and **7** was warranted by the use of pseudonymization. The pseudonymization key was stored on a secured network drive of the Sint Maartenskliniek or the Radboudumc that was only accessible to members of the project who needed access to it because of their role within the project. The pseudonymization key was stored separately from the research data.

INFORMED CONSENT

Written informed consent was obtained from all research participants of **chapters 6** and **7** to collect and process their data for this research project. The sensitivity and confidentiality of the raw qualitative data (i.e. interviews) makes sharing of the data without compromising confidentiality and privacy impossible, therefore consent for sharing of the raw data was not asked from the participants. Where possible, the raw qualitative data will be anonymized by data aggregation to enable sharing for reuse.

DATA COLLECTION AND STORAGE

Pseudonymized data from **chapters 2** and **3** was obtained from the Electronic Health Records (HiX) and stored on local, secured servers of the Sint Maartenskliniek in .csv documents.

Anonymized data from **chapter 4** was obtained from the questionnaires and pseudonymized data from **chapters 6** and **7** was obtained from the Electronic Health Records (EPIC). This data and the raw data from recording devices (archived in their original form) was stored on local, secured servers from the Radboud university medical center.

DATA SHARING ACCORDING TO THE FAIR PRINCIPLES

All studies are published open access. Interoperable file formats have been used for **all chapters** (e.g. .csv or ATLAS.ti formats).

The datasets from **chapters 2, 3** and **6** are suitable for reuse and are published in the Radboud Data Repository (**Chapter 2**: ru.rumc.nhasd_t0000043a_dsc_405, **Chapter 3**: ru.rumc.tvsbsd_t0000042a_dsc_147, chapter 6: ru.rumc.svpfais_t0000032a_dsc_538). Data were made reusable by adding sufficient documentation, by using preferred and sustainable data formats and by publishing under the CC BY-NC license. Requests for access will be checked by a data access committee (DAC) formed by the department, if necessary. The data not suitable for reuse will be archived for 15 years after termination of the study.

Due to the sensitivity and confidentiality of the raw qualitative data from **chapter 7**, which makes sharing of the data without compromising confidentiality and privacy impossible, no online data repository was made.

PHD PORTFOLIO

PhD period: 01-11-2019 to 01-05-2025
Department: Orthopedic Surgery
Promotor: Prof. dr. M. de Kleuver
Copromotors: Dr. M.L. van Hooff, Dr. M.H. Pouw
Mentor: Dr. J.H. Peters

TRAINING ACTIVITIES	HOURS
COURSES AND WORKSHOPS	
Radboudumc introduction day Radboudumc (2019)	6.00
Introduction days for PhD Candidates (2023)	15.00
E-learning for research involving human subjects (2023)	4.00
Scientific integrity course (2023)	20.00
Ziekenhuisfinanciën en Medisch Management	8.00
Cursus opleiden van coassistenten in de klinische praktijk	9.00
Courses orthopaedic resident training 2020-2024	368.00
Fundamental Critical Care Support (FCCS) cursus (20.00)	
Advanced Trauma Life Support (ATLS) cursus (36.00)	
AO Basic Principles of Fracture Management cursus (30.00)	
AO Advanced Principles of Fracture Management cursus (50.00)	
Laparoscopie cursus BCIG (20.00)	
Cursorisch onderwijs AioS Heelkunde (CASH) 1.1-1.4 (32.00)	
Post Academisch Chirurgisch Onderwijs Nijmegen-Utrecht (PACONU) 1-4 (32.00)	
Heupprothesiologie cursus (8.00)	
Knieartroscopie cursus basis (8.00)	
Knieprothesiologie cursus (8.00)	
Dutch Foot and Ankle Society (DFAS) basiscursus (8.00)	

Stralingshygiëne voor medisch specialisten (20.00) Masterclass pathologische fracturen (8.00) Regionale Opleidingsgroep Orthopedie Oost (ROGOO) onderwijsdagen (32.00) Centrale Cursus Orthopedische Chirurgie (CCOC) 1 en 2 (56.00)	
CONFERENCES / PRESENTATIONS:	
Research presentations Scoliosis Research Society Travelling Spine Fellowship	5.00
Deutsche Wirbelsaulen Kongress (DWG, 2020): "Supine traction versus prone bending radiographs for assessing the curve flexibility in spinal deformity", presentation	14.00
Scoliosis Research Society (SRS, 2023) grant outcome symposium, presentation	8.00
Nederlandse Orthopedische Vereniging (NOV, 2022, 2023)	32.00
Dutch Foot and Ankle Society (DFAS) congress (2023)	8.00
Research presentations orthopaedic research department (2019), Radboudumc and Sint Maartenskliniek	3.00
GRANTS	
SRS Micro Research Grant (Chapter 6; Pulmonary Function in patients with Adolescent Idiopathic Scoliosis: a Feasibility Study of a wearable smart Shirt as a Measurement Instrument	30.00
TEACHING ACTIVITIES	
Praktische en psychomotore vaardigheden (PPV) bachelor geneeskunde (2023, 2024)	52.00
Minor Snijdende specialismen 2023	24.00
Supervising VLJM Steegh (medical student) Chapter 6; Pulmonary Function in patients with Adolescent Idiopathic Scoliosis: a Feasibility Study of a wearable smart Shirt as a Measurement Instrument	44.00
Supervising I.L. Kik (medical student) Chapter 7; "Building a theoretical framework for patient-experienced symptoms related to breathing and exercise tolerance in adolescent and adult scoliosis – An explorative study based on structured interviews"	20.00
TOTAL	**670.00**

LIST OF PUBLICATIONS

1. *The Natural History of Progression in Adult Spinal Deformity: A Radiographic Analysis*
   Faraj SSA, **Te Hennepe N**, Van Hooff ML, Pouw M, De Kleuver M, Spruit M.
   Global Spine J. 2020;10(3):272-279. DOI: 10.1177/2192568219845659
   https://pubmed.ncbi.nlm.nih.gov/32313792/

2. *Supine Traction Versus Prone Bending Radiographs for Assessing the Curve Flexibility in Spinal Deformity*
   Te Hennepe N, Spruit M, Pouw MH, Hinderks M, Heesterbeek P.
   Global Spine J. 2022 Sep;12(7):1345-1351. DOI: 10.1177/2192568220979136.
   https://pubmed.ncbi.nlm.nih.gov/33504207/

3. *Dysfagie door osteofyten van de cervicale wervelkolom [Dysphagia caused by osteophytes of the cervical spine].*
   Te Hennepe N, Hosman AJF, Pouw MH.
   Ned Tijdschr Geneeskd. 2020 Apr 30:164:D4278.
   https://pubmed.ncbi.nlm.nih.gov/32395960/

4. *Pulmonary function in patients with spinal deformity: have we been ignorant?*
   Van Hooff ML, **Te Hennepe N**, De Kleuver M.
   Acta Orthop. 2020 Oct;91(5):503-505. DOI: 10.1080/17453674.2020.1786267
   https://pubmed.ncbi.nlm.nih.gov/32619109/

5. *Pulmonary symptoms in adolescent idiopathic scoliosis: a systematic review to identify patient-reported and clinical measurement instruments*
   Te Hennepe N, Faraj SSA, Pouw MH, de Kleuver M, van Hooff ML.
   Eur Spine J. 2022 Jul;31(7):1916-1923; DOI: 10.1007/s00586-022-07204-z
   https://pubmed.ncbi.nlm.nih.gov/35438343/

6. *Pulmonary Function in patients with adolescent idiopathic scoliosis: an explorative study of a wearable smart shirt as a measurement instrument*
   Te Hennepe N, Steegh VLJM, Pouw MH, De Kleuver M, Van Hooff ML
   Spine Deform. 2024 Jul 31. doi: 10.1007/s43390-024-00938-4
   https://pubmed.ncbi.nlm.nih.gov/39085742/

7. *Building a theoretical framework for patient-experienced symptoms related to breathing and exercise tolerance in adolescent and adult scoliosis – An explorative study based on structured interviews*
   Kik IL, **Te Hennepe N**, Abma I, Bisseling P, Van de Fliert D, Hassan DF, Kempen D, Lenke LG, Roukema J, Schlösser T, De Kleuver M, Van Hooff ML
   Status: submitted to Spine Deformity

DANKWOORD

Promoveren doe je gelukkig niet alleen. Er zijn vele mensen bij betrokken die een onschatbare bijdrage hebben geleverd dat direct of indirect heeft bijgedragen aan het boekwerk dat nu voor je neus ligt. Promoveren naast je opleiding tot medisch specialist is een drukke en uitdagende periode, maar ook ontzettend leerzaam en soms zelfs leuk. Voor iedereen die ik niet persoonlijk noem en die op welke manier dan ook hebben bijgedragen aan dit proefschrift: ontzettend bedankt! Of het nu ging om administratieve ondersteuning, technische assistentie of inspirerende gesprekken, jullie bijdrage wordt zeer gewaardeerd.

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ABOUT THE AUTHOR

Niek te Hennepe was born on the 9th of April 1994, in Winterswijk, the Netherlands. He spent most of his youth in Lichtenvoorde. After graduating from secondary school in 2012, he pursued a medical degree at Radboud University in Nijmegen, which he obtained in 2019.

Niek's interest in orthopedic surgery developed early in his medical education. After finishing his bachelor's degree, while awaiting his clinical rotations, he undertook a traveling internship at the department of Orthopedic Trauma Surgery at the Tamale Teaching Hospital in Ghana where he first encountered the world of surgery firsthand.

Nieks medical research career started during his clinical rotations of his Master's program, where he wrote the first chapters of this thesis. This PhD journey officially commenced in 2019, after he graduated from medical school and started his career as a doctor-not-in-training (ANIOS). He entered the orthopedic surgery residency program in 2021. After completing general surgery training at Rijnstate Hospital in Arnhem, he continued his orthopedic surgery training at Sint Maartenskliniek and Radboud University Medical Centre, both in Nijmegen. He is currently in the fifth year of his residency and will complete his training to become an orthopedic surgeon at Rijnstate Hospital, Arnhem. Niek currently lives in Malden with his wife, Lea, and their son, Aron.