Ultrasound in Med. & Biol., Vol. 48, No. 5, pp. 721−729, 2022

0301-5629/$ - see front matter

https://doi.org/10.1016/j.ultrasmedbio.2022.01.014

● *Review Article*

ULTRASOUND SHEAR WAVE ELASTOGRAPHY OF THE INTERVERTEBRAL DISC AND IDIOPATHIC SCOLIOSIS: A SYSTEMATIC REVIEW

STEVEN DE REUVER,[*,1] AARON J.B.W.D. MOENS,[*,1] MOYO C. KRUYT,[*] RUTGER A.J. NIEVELSTEIN,[†] KEITA ITO,[*,‡] and RENÉ M. CASTELEIN[*]

[*] Department of Orthopedic Surgery, University Medical Center Utrecht, Utrecht, The Netherlands; [†] Department of Radiology, University Medical Center Utrecht, Utrecht, The Netherlands; and [‡] Department of Biomedical Engineering, Eindhoven University of Technology, Eindhoven, The Netherlands

(*Received* 22 *October* 2021; *revised* 11 *January* 2022; *in final form* 23 *January* 2022)

Abstract—Ultrasound shear wave elastography is a radiation-free and low-cost technique for evaluating the mechanical properties of different tissues. This study systematically reviewed all relevant literature on shear wave elastography of the intervertebral disc. The purpose was twofold: first, to determine the validity of the elastography method, that is, the correlation between elastographically measured shear wave speed and disc mechanical properties, and inter-/intra-operator reliability; and second, to explore if disc elastography is potentially useful in identifying children at risk for idiopathic scoliosis. This systematic review was performed according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) guidelines. A comprehensive search was performed in PubMed and Embase, and study quality was assessed using the AXIS (Appraisal Tool for Cross-sectional Studies) critical appraisal instrument. Seven articles were included. Three animal *ex vivo* studies reported moderate-to-good correlations between shear wave speed and disc mechanical properties (r = 0.45−0.81). Three studies reported high intra-operator repeatability (intra-class correlation coefficient [ICC] 0.94−0.99) and inter-operator reproducibility (ICC 0.97−0.98). Four clinical studies measured shear wave speed in asymptomatic children. Two studies reported significantly higher shear wave speeds in scoliosis patients compared with healthy controls, measured in discs both inside and outside the scoliotic curve. In conclusion, shear wave elastography appears reliable in assessing intervertebral disc mechanical characteristics. Despite its promising capabilities to distinguish patients with asymptomatic from those with pathological discs, the exact correlation between disc mechanical properties and shear wave speed remains unclear. (E-mail: r.m.castelein-3@umcutrecht.nl)

Key Words: **Systematic review, Ultrasound shear wave elastography, Intervertebral disc, Mechanical properties, Stiffness, Elastic modulus, Adolescent idiopathic scoliosis.**

INTRODUCTION

Adolescent idiopathic scoliosis (AIS) is the most prevalent form of scoliosis: a 3-D structural deformity of the spine, which includes lateral curvature, anteroposterior deviation and axial rotation, without any obvious underlying condition (Kuklo et al. 2005; Illés et al. 2011). The prevalence is 2%−4% in the general population, and it affects mostly girls in early puberty (Cheng et al. 2015). AIS can lead to severe trunk deformities causing poor self-image, pain and in severe cases cardiopulmonary compromise, which often requires spinal fusion surgery (Koumbourlis 2006; Johnston et al. 2011; Tsiligiannis and Grivas 2012; Lonner et al. 2013; Choudhry et al. 2016). Despite decades of quality research, the exact etiology of AIS remains largely unknown, in contrast to congenital, neuromuscular and other types of scoliosis (Cheng et al. 2015).

Recently, it has been proposed that AIS is a multifactorial condition most likely involving a mismatch between the mechanical properties of the maturing intervertebral disc (IVD) and the rapidly increased loading caused by the pubertal growth spurt (Castelein et al. 2020). In patients with AIS, the

Address correspondence to: René M. Castelein, Department of Orthopedic Surgery, G05.228, University Medical Center Utrecht, PO Box 85500, 3508 GA Utrecht, The Netherlands. E-mail: r.m.castelein-3@umcutrecht.nl

[1] Shared first authorship

deformity occurs primarily in the IVD while the bony vertebral bodies retain their shape, and differences in mechanical properties between scoliotic IVDs and normal controls have been described (Yu et al. 2005; Grivas et al. 2006; de Reuver et al. 2020). The main problem with elucidating the role of the IVD in the etiology of AIS is the invasive nature of harvesting IVD tissue to study its mechanical properties, especially because it concerns a population of young age. Additionally, most studies on AIS etiology include patients with already established scoliotic curves; therefore, distinguishing between cause and effect is practically impossible. We hypothesize that in AIS patients, pathological mechanical IVD properties may already be present before the onset and/or progression of the scoliotic curve. If this were to be true, and these IVD properties could easily and safely be measured in children, this could potentially be used as a proxy for the risk of AIS development and progression of the scoliotic curve. Unfortunately, there currently is no established diagnostic method for non-invasive characterization of the IVD to determine the tissue's mechanical properties.

Several non-invasive elasticity imaging techniques exist that aim to quantify mechanical properties of the examined tissue. In general, elasticity imaging techniques are used to gather information on tissue elasticity and can be applied to organs located deeper in the body, which provides new opportunities for screening and diagnosis (Gennisson et al. 2013). Over the past few decades, numerous emerging elasticity imaging techniques have been developed and researched (Sarvazyan et al. 2011). Early elasticity imaging techniques in the 1970s and 1980s used static loading and an external vibrator to generate stress in tissues, after which modified color Doppler was used to track tissue displacement and measure tissue stiffness (Dickinson and Hill 1980, 1982). In the late 1990s an alternative quasi-static approach was developed to remotely measure tissue elasticity via manual compression or cardiovascular/respiratory pulsation, now known as strain elastography (Shiina et al. 2015). This was soon followed by the development of dynamic shear wave elastography to measure the shear wave speed (SWS), which directly relates to the elastic moduli of the tissue, as opposed to strain elastography (Garra 2015; Taljanovic et al. 2017). In contrast to strain elastography, shear wave elastography uses a focused acoustic radiation force to generate shear waves within the organ of interest, which allows for measurement of the propagation speed to locally quantify the tissue stiffness (Shiina et al. 2015). Since 2005, increasingly more manufacturers have added the shear wave elastography option to their standard ultrasound systems (Sarvazyan et al. 2011). Shear wave elastography is now regularly used in clinical practice to evaluate the breast, liver, prostate and musculoskeletal tissues (Moreau et al. 2016; Cong et al. 2017; Rouvière et al. 2017; Yoon et al. 2017). Therefore, in this systematic review, we explore the feasibility of using shear wave elastography to assess IVD mechanical properties through the measurement of SWS.

Non-invasive mechanical characterization of the IVD through shear wave elastography may provide new opportunities for early diagnosis and etiological research on AIS. However, to date, there is no systematic literature review on the current status of shear wave elastography of the IVD and its uses in AIS patients. Therefore, the purpose of this systematic review is twofold: The first goal is to determine the validity of shear wave elastography in quantifying IVD mechanical properties (*i.e.,* the correlation between SWS and apparent disc stiffness and/or elastic modulus, usually indirectly determined in *ex vivo* animal experiments) and the inter- and intra-operator reliability. The second goal is to analyze shear wave elastography measurements of the IVD in healthy populations and in children with AIS, and explore the usefulness of the method in identifying children at risk for idiopathic scoliosis.

METHODS

Search strategy and study selection

This systematic review was performed according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) guideline (Moher et al. 2009). A comprehensive search was performed in PubMed and Embase. The search string included all relevant terms and synonyms for "elastography," "ultrasonography" and "intervertebral disc," combined by "and." All terms were required to be mentioned in either the title or abstract of the study (Appendix A; see Supplementary Data, online only). Duplicates were removed. The reference lists of all included studies were reviewed for additional articles missed in the initial search. Two reviewers independently identified studies and reviewed title and abstract for relevance using predetermined inclusion and exclusion criteria. Any discrepancies were resolved through discussion. All articles irrelevant to the purpose of this study based on title or abstract were dismissed. Full text was reviewed if eligibility was uncertain after screening title and abstract. The search was conducted up until October 15, 2021. The search language was in English. There were no restrictions on publication date or status.

Inclusion and exclusion criteria

Both *ex vivo* animal studies and human *in vivo* studies on shear wave elastography of the IVD were included in this review if the full English text was available. Only studies that had their protocol approved by a local ethics committee, institutional review board and/or institutional animal care and use committee were included. *In vivo* studies had to be conducted in asymptomatic people or in patients with AIS. Studies in patients with pathology other than AIS were excluded. Further exclusion criteria were the use of elastography techniques other than ultrasound-based ones, such as MRI and optical coherence elastography, or when tissues different from the IVD were studied. When multiple articles were published on results within the same study population, only the most comprehensive or most recent article was included to prevent duplication bias.

Quality assessment

The AXIS critical appraisal tool for cross-sectional studies was used to assess the quality of the included studies (Downes et al. 2016). The criteria include 20 items scored "yes," "no," "don't know" or "not applicable (n/a)." The AXIS tool contains 7 criteria related to study design, 7 related to quality of reporting and 6 items on potential bias (Appendix B; see Supplementary Data, online only). The AXIS tool does not provide a fixed cut-off value for high or low study quality. Therefore, in line with earlier studies using AXIS, it was decided that in this systematic review, studies scoring 5 or more criteria negatively were considered low quality. Criteria scored "n/a" were not taken into account in this consideration.

Data extraction and analysis

A data form was created containing the following data from the included articles: title, first author, year of publication, country, study design, study population, study sample and the main results. The main outcomes of interest were the correlation between *ex vivo* SWS measurements of the annulus fibrosus and apparent IVD stiffness or elastic modulus, the repeatability (intra-operator) and reproducibility (inter-operator) of the elastography measurements and SWS measurements in healthy controls and AIS patients. Because of the heterogeneity of study designs and study populations, a quantitative meta-analysis was not performed. The intra-class correlation coefficient (ICC) was considered to be excellent (ICC >0.90), good (ICC 0.75−0.90), moderate (ICC 0.50−0.75) or poor (ICC <0.50) (Koo and Li 2016). The correlation coefficient (*r*) was regarded very good to excellent (*r* = 0.75−1.00), moderate to good (r = 0.50−0.75) or poor (r = 0.25−0.50) (Dawson and Trapp 2004).

RESULTS

Study selection and quality assessment

The procedure for inclusion of articles in this systematic review is illustrated in the PRISMA flow diagram (Fig. 1) (Moher et al. 2009). A total of seven studies were included. Three animal *ex vivo* studies reported on the correlation between SWS measurements of the annulus

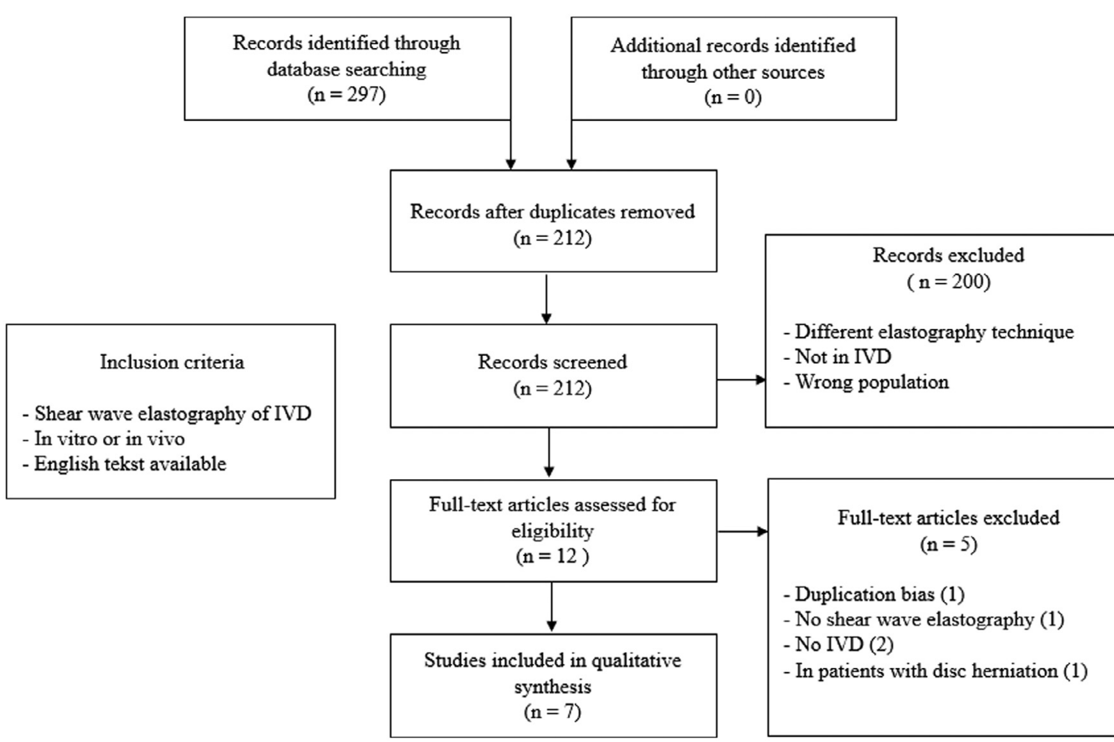

Fig. 1. Preferred Reporting Items for Systematic Reviews and Meta-analyses flow diagram. IVD = intervertebral disc.

fibrosus and apparent IVD stiffness and/or elastic modulus. Repeatability and/or reproducibility was reported by one *ex vivo* and two clinical studies. Two studies reported the SWS in healthy controls, and two other studies compared SWS in healthy controls with that in patients with AIS. All seven included studies were of high quality according to the AXIS critical appraisal tool (Appendix B). Recurrent negative criteria were either a lack of sample size justification, a lack of discussion of study limitations, unclear funding sources and/or conflicts of interest possibly affecting study outcomes.

Study characteristics

All included studies were published between 2013 and 2020. The majority of included studies were conducted at the same institute (Table 1). Three *ex vivo* studies reported on correlations between SWS and mechanical properties of either bovine or porcine IVDs (Vergari et al. 2013; Vergari et al. 2014a; Chotar-Vasseur et al. 2015). A total of four clinical studies included a population of asymptomatic adults, asymptomatic children and a combination of asymptomatic children and children with AIS (Langlais et al. 2018; Vergari et al. 2014b, 2016, 2020).

Correlation between SWS and mechanical properties

Three *ex vivo* studies reported on the correlation between SWS measurements in the annulus fibrosus and apparent stiffness and/or elastic modulus. In these studies, multiple cycles of axial compression, at loads ranging between 0 and 400 N, were applied to the bovine or porcine intervertebral segments to produce a repeatable mechanical response. The slope in the produced force-displacement curve represents the material stiffness. As IVD height and surface area are known, stress−strain curves can be calculated from force-displacement curves, from which the elastic modulus can be calculated. After the final cycle, the segment is unloaded and then loaded again, after which the position is held to induce stress relaxation, during which the elastography measurements were taken. The reported correlation coefficient (r) in these three studies varied from 0.45 to 0.81 (Table 2). The first study by Vergari et al. (2013) reported a significant correlation (r = 0.45) between SWS and IVD stiffness for pooled data (n = 40). A later study reported significant correlations (r = 0.63−0.70) between three measured variables under axial loading: SWS, IVD stiffness and the apparent elastic modulus (Vergari et al. 2014a) Chotar-Vasseur et al. (2015). performed a linear regression analysis between the IVDs' apparent elastic modulus and elastographically measured SWS of the annulus fibrosus at different preloads of 10, 200 and 400 N. A coefficient of determination R^2 of 0.66 was reported, corresponding to a correlation coefficient of r = 0.81.

Repeatability and reproducibility

One *ex vivo* study and two clinical studies reported on the repeatability (intra-operator) of shear wave elastography to measure the SWS in the annulus fibrosus (Table 2). The variation within repeated measurements was 0.20−0.39 m/s (7.0%−7.5% coefficient of variation), while the ICCs for intra-operator reliability ranged between 0.94 and 0.99 (Vergari et al. 2014a, 2014b, 2016). Two clinical studies reported reproducibility (inter-operator), in which the SWS variation was 0.25−0.30 m/s (8.7%−10.0% coefficient of variation). The ICCs for inter-operator reliability ranged between 0.97 and 0.98 (Vergari et al. 2014b, 2016).

Table 1. Overview of included studies

Article	Year	Study population	n	IVD level	Main outcome
Ex vivo					
Vergari et al.	2013	Oxtails	8	n/a	SWS and IVD stiffness correlation
Vergari et al.	2014	Oxtails	11	n/a	SWS and IVD stiffness correlation, intra-operator ICC, repeatability
Chotar-Vasseur et al.	2015	Porcine IVDs	8	Pig 1: T15−L5 Pig 2: L1−L4	SWS and IVD stiffness correlation
In vivo					
Vergari et al.	2014	Asymptomatic adults	47	C6−C7 or C7−T1	SWS, intra-/inter-operator ICC, repeatability, reproducibility
Vergari et al.	2016	Asymptomatic children	31	L5−S1 or L4−L5	SWS, intra-/inter-operator ICC, repeatability, reproducibility
Langlais et al.	2018	Asymptomatic children AIS patients	30 30	L3−L4, L4−L5 and L5−S1	SWS
Vergari et al.	2020	Asymptomatic children AIS patients	59 25	L3−L4, L4−L5 and L5−S1	SWS

AIS = adolescent idiopathic scoliosis; ICC = intra-class correlation coefficient; IVD = intervertebral disc; n/a = not available; SWS = shear wave speed.

Table 2. Main results

Article	Year	Repeatability (intra-operator)		Reproducibility (inter-operator)		SWS and IVD stiffness correlation	Average SWS (m/s)	
		SWS variation (m/s)	ICC	SWS variation (m/s)	ICC	Correlation coefficient, *r*	Asymptomatic	AIS
Ex vivo								
Vergari et al.	2013					0.45		
Vergari et al.	2014	±0.39 (7%)	0.96−0.99			0.63−0.70		
Chotar-Vasseur et al.	2015					0.81		
In vivo								
Vergari et al.	2014	±0.20 (7%)	0.94−0.98	0.30 (10%)	0.97		3.0 ± 0.4	
Vergari et al.	2016	±0.22 (7.5%)	0.96−0.98	0.25 (8.7%)	0.98		2.9 ± 0.5	
Langlais et al.	2018						3.0 ± 0.3	3.5 ± 0.3
Vergari et al.	2020						3.1 ± 0.5	4.0 ± 0.5

AIS = adolescent idiopathic scoliosis; ICC = intra-class correlation coefficient; IVD = intervertebral disc; SWS = shear wave speed.

Shear wave speed in asymptomatic patients

Two studies reported solely on SWS measurements in healthy controls (Table 2). In 47 asymptomatic adults (mean age: 36.5 ± 12.6), a mean SWS of 3.0 ± 0.4 m/s was reported, measured at level C6−C7 and C7−T1 (Vergari et al. 2014b). Similar values for SWS were reported in 31 asymptomatic children aged 6 to 17, with a mean SWS in the annulus fibrosus of the IVD at levels L4−L5 and L5−S1 of 2.9 ± 0.5 m/s (Vergari et al. 2016).

Shear wave speed in AIS and healthy controls

Two other studies measured SWS values in asymptomatic children, but also compared with measurements in children with AIS. In the study by Langlais et al. (2018), SWS measurements in IVDs of 30 asymptomatic children (mean age 13 ± 1.9) were compared with those of 30 patients with thoracic or lumbar AIS (mean age 13 ± 2.0, mean Cobb angle 28.8 ± 10.4°). In this study, the SWS was measured with ultrasound elastography at the lower lumbar level (L3−S1), which in AIS patients is mostly outside of the spinal area affected by scoliosis. In asymptomatic children, the SWS measured 3.0 ± 0.3 m/s, and in AIS patients, 3.5 ± 0.3 m/s (2.7−4.8 m/s), while it is known from earlier *ex vivo* studies that a higher SWS is correlated with increased disc stiffness (Vergari et al. 2013, 2014a; Chotar-Vasseur et al. 2015). No significant difference between IVD levels (L3−L4, L4−L5, L5−S1) was observed within both groups, and SWS was significantly higher at all disc levels in AIS patients compared with healthy controls ($p < 0.02$). Furthermore, in this study, a high SWS measured in multiple consecutive discs was associated with increased risk of curve progression. Subgroup analysis revealed mean SWSs in stable scoliosis of 3.3 ± 0.3 m/s, in progressive scoliosis of 3.7 ±0.3 m/s, in pre-treatment progressive scoliosis of 4.0 ± 0.3 m/s and in scoliosis during treatment of 3.3 ± 0.3 m/s (Fig. 2). These data might suggest a possible form of regenerative capacity of the disc during treatment; however, the SWS is usually measured in IVDs outside of the affected part of the spine.

The latest study by Vergari et al. (2020) reported SWS data in lower lumbar discs of 59 asymptomatic children (mean age 13 ± 2) and 25 severe AIS patients with mostly thoracic curves (mean age 15 ± 1.5, mean Cobb angle 57 ± 14°), before and after surgical intervention. SWS was significantly higher in pre-operative AIS patients at 4.0 ± 0.5 m/s compared with asymptomatic children at 3.1 ± 0.5 m/s. Three months post-operatively, the mean SWS in AIS patients exhibited a non-statistically significant decrease to 3.5 ± 0.3 m/s, and after a further year a significant decrease to 3.3 ± 0.4 m/s, a value similar to that of asymptomatic controls. Furthermore, a weak correlation between Cobb angle and a lower SWS was observed ($r = 0.40$, $p = 0.05$). Similar SWS values were found for AIS patients with thoracic (3.8 ± 0.4 m/s) and thoracolumbar (3.9 ± 0.4 m/s) curves. Only one of the included patients had a lumbar curve, with a mean SWS of 5.1 m/s.

DISCUSSION

The purpose of this systematic review was twofold. The first aim was to determine the validity of shear wave elastography (*i.e.,* the correlation with mechanical disc properties) and inter-/intra-operator reliability. The second aim was to examine if disc elastography is potentially useful in identifying children at risk for idiopathic scoliosis. Studies were reviewed that reported on the correlation between elastographically measured SWS in the annulus fibrosus and apparent IVD stiffness and/or elastic modulus. Furthermore, studies that reported on the repeatability and reproducibility of SWS measurements were reviewed, as were studies that measured the SWS in IVDs of patients with AIS and asymptomatic controls.

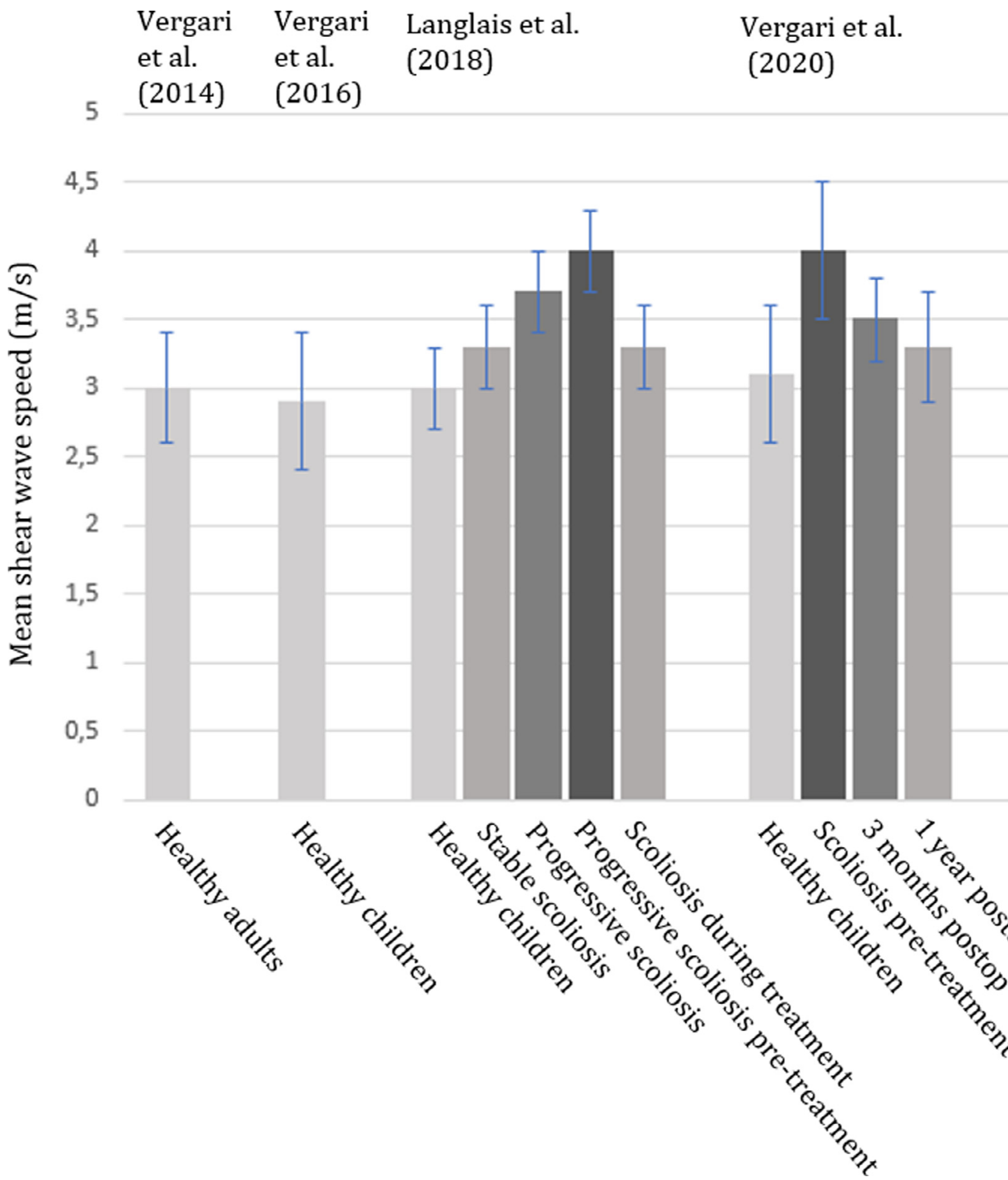

Fig. 2. Subgroup analysis of shear wave speed. Error bars indicate standard deviations.

The initial search resulted in 262 records, of which seven articles were included. Three *ex vivo* studies of animal tissue reported a moderate to good correlation between SWS measured in the annulus fibrosus and apparent IVD stiffness or elastic modulus (r = 0.45−0.81). Excellent intra-operator repeatability (ICC 0.94−0.99) and inter-operator reproducibility (ICC 0.97−0.98) were reported. Four *in vivo* studies were included in this review, of which two were solely in asymptomatic controls and two in both asymptomatic children and patients with (mostly) thoracic AIS. In these two studies, a significantly higher SWS was observed in AIS patients compared with asymptomatic controls. This may suggest that the IVDs in AIS patients both inside and outside the scoliotic curve are stiffer than in asymptomatic children, as a higher SWS correlates with an increased IVD stiffness. This could indicate that AIS involves pathological IVDs in the entirety of the spinal column, although it is most likely that IVDs adjacent to or within the curve will be affected more. But because only two studies included patients with AIS, no definitive conclusions can be drawn and more studies are necessary to investigate the uses of shear wave elastography in identifying children at risk for scoliosis.

Three animal *ex vivo* studies reported a correlation coefficient varying from 0.45 to 0.81 between SWS of the annulus fibrosus and apparent IVD stiffness or elastic modulus under different loads, suggesting that the variability in SWS might also be confounded by something other than just the IVD stiffness. For example, in the study by Chotar-Vasseur et al. (2015), almost a doubling of the SWS was demonstrated under 400-N axial compression compared with 10 N. In addition, there was no significant correlation between the stiffness of unloaded IVDs and SWS (Vergari et al. 2014a). Therefore, elastographically measured SWS is most likely also influenced by other tissue properties of the IVD such as hydration status, age and size, or even technical variability in the elastography method itself. It has been determined by denucleation that the nucleus pulposus plays a more pronounced role in IVD stiffness in the low force range, whereas at a higher reference force of 400 N, the mechanical behavior of the IVD is dominated by the annulus fibrosus and stiffness is minimally affected by denucleation (Shea et al. 1994; Cannella et al. 2008). The three *ex vivo* studies included in this review reported the correlation between SWS and apparent IVD mechanical properties in different circumstances, making it challenging to draw robust conclusions on the true relationship between shear wave elastography and IVD mechanical properties. Ideally, SWS measured with ultrasound elastography should reflect solely changes in disc stiffness. However, it remains unclear exactly what and to what extent external factors are involved and how these should be accounted for. A further investigation into the role of the IVD anisotropy caused by its lamellar buildup should be performed to better understand how loading affects the elastic modulus in different planes.

Three studies reported excellent values (ICC >0.90) with moderate to strong evidence for both repeatability and reproducibility. Elastography of the IVD seems to be less operator dependent compared with that of superficial organs, breasts or muscles. Because the IVD is located deeper inside the body, it might be less susceptible to operator-dependent force of application of the ultrasound probe, which could explain the high repeatability and reproducibility compared with other tissues (Kot et al. 2012).

Four clinical studies provided values for healthy controls, and two studies observed in AIS an increase in SWS with progression of the scoliotic curve, while a decrease was observed after surgical correction and stabilization (Fig. 2). Overall, the SWS in lower lumbar discs measured by elastography was significantly higher in patients with (mostly) thoracic AIS than in healthy controls (Langlais et al. 2018; Vergari et al. 2020). This may suggest that throughout the spine, in both the scoliotic and unaffected areas, the IVDs are stiffer in patients with AIS than in asymptomatic controls. In an earlier study, it was suggested that the spinal curvature severity in scoliosis patients was associated with a stiffer spine (Deviren et al. 2002). Therefore, it was expected that a positive correlation between SWS and Cobb angle would exist. However, no significant positive correlation was found in Langlais et al. (2018) nor even a trend toward a negative correlation in Vergari et al. (2020). This can be due to a lack of statistical power or, as mentioned in Vergari et al. (2020), the aggressive bracing of more severely affected patients, which may influence disc hydration and its mechanical properties.

In the clinical elastography studies in this review, the IVDs at the lower lumbar levels were measured, whereas the scoliosis was present (mostly) in the thoracic spine. One MRI study in AIS patients determined that the deterioration of the IVD is greater within the spinal curvature than in asymptomatic regions of the spine (Huber et al. 2016). Therefore, the measured SWS differences between AIS patients and asymptomatic controls could be an underrepresentation of the IVD stiffness differences within the curve. Support for this hypothesis could be found in the study by Vergari et al. (2020), in which there was one patient included with a lumbar scoliosis. In this patients the SWS was measured in or close to the scoliotic curve with a mean SWS of 5.1 m/s, which was the highest value reported among all patients. The studies by Langlais et al (2018) and Vergari et al. (2020) measured SWS in lower lumbar IVDs in patients with AIS. A similar increase in SWS was observed in both patients with thoracic and those with (thoraco)lumbar scoliosis, compared with asymptomatic controls. This suggests that in patients with AIS, the characteristics of the IVD may be different throughout the entire spine and not just in the affected area. Therefore, the different IVD mechanical properties may not be solely a result of the scoliotic deformity, but might already be present before the onset of scoliosis.

The main limitations of this systematic review were not methodological but related to the outcome, as six of seven included studies were carried out at the same institute. Furthermore, only two included studies tested shear wave elastography in a clinical setting on patients with AIS. There were a limited number of studies on the subject, with large variability in both study design and study population characteristics. Of the seven included studies, data were only analyzed descriptively, as no meta-analysis could be performed. Finally, relatively small sample sizes and heterogeneity in reported data made thorough comparison and interpretation of the results difficult, and therefore, this systematic review provides only an overview of current literature on ultrasound-based shear wave elastography of the IVD in relation to scoliosis, with a few tentative conclusions.

Current diagnostic techniques for early-stage AIS have a high accuracy when used together; for instance, a sensitivity of 93.8% and a specificity of 99.2% can be reached with the Adam's forward bend test, scoliometer measurement and Moiré topography combined (Dunn et al. 2018). Despite this, these techniques are applicable only in patients with an already established curve. This systematic review illustrates that ultrasound shear wave elastography is able to make a distinction between scoliotic and non-scoliotic patients by measuring shear wave speed through the annulus fibrosus of IVDs outside the scoliotic curve, as a proxy for mechanical properties of the IVD, specifically stiffness. This could imply that disc properties of patients that develop scoliosis are different even before the onset of scoliosis. If that is true, this technique can be used as a predictor, especially in high-risk populations, before the onset of a scoliosis. Such a high-risk population could be patients with 22q11.2 deletion syndrome, a group that was described as a human model for idiopathic scoliosis in the general population, as they develop an idiopathic-like scoliosis with an incidence of ~50% (Homans et al. 2019a, 2019b). Another possible use of ultrasound elastography could be in the follow-up of AIS patients to detect those at risk for progression at an early state, allowing for more aggressive non-surgical treatment and possibly preventing surgery in the long run.

CONCLUSIONS

This study systematically reviewed all relevant literature on shear wave elastography of the intervertebral disc, with the purpose of determining its validity, reliability and potential usefulness in identifying children at risk for idiopathic scoliosis. Excellent repeatability and reproducibility were reported with moderate to strong levels of evidence. Multiple studies determined a correlation between elastographically measured SWS and the apparent stiffness/elasticity of IVDs under axial loading, however with a large variation and in different circumstances. Although it is promising that in clinical studies ultrasound elastography could make a distinction between IVDs in patients with and without AIS, the correlation between SWS measurements and disc stiffness and possible confounding factors is not yet fully understood.

Acknowledgments—The authors thank the Scoliosis Research Society and Fondation Yves Cotrel for sponsoring their research on exploring ultrasound elastography of the intervertebral disc.

Conflict of interest disclosure—S.D.R reports a Scoliosis Research Society and Fondation Yves Cotrel research grant. All other authors have no disclosures to declare.

SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ultrasmedbio.2022.01.014.

REFERENCES

Cannella M, Arthur A, Allen S, Keane M, Joshi A, Vresilovic E, Marcolongo M. The role of the nucleus pulposus in neutral zone human lumbar intervertebral disc mechanics. J Biomech 2008;41:2104–2111.
Castelein RM, Pasha S, Cheng JCYC, Dubousset J. Idiopathic scoliosis as a rotatory decompensation of the spine. J Bone Miner Res 2020;35:1850–1857.
Cheng JC, Castelein RM, Chu WC, Danielsson AJ, Dobbs MB, Grivas TB, Gurnett CA, Luk KD, Moreau A, Newton PO, Stokes IA, Weinstein SL, Burwell RG. Adolescent idiopathic scoliosis. Nat Rev Dis Prim 2015;1:15–30.
Chotar-Vasseur Y, Cachon T, Ponsard B, Carozzo C, Viguier E. In vitro comparison between mechanical properties and elastographic characterization of porcine intervertebral disc. Comput Methods Biomech Biomed Eng 2015;18:1906–1907.
Choudhry MN, Ahmad Z, Verma R. Adolescent idiopathic scoliosis. Open Orthop J 2016;10:143–154.
Cong R, Li J, Guo S. A new qualitative pattern classification of shear wave elastograghy for solid breast mass evaluation. Eur J Radiol 2017;87:111–119.
Dawson B, Trapp RG. Basic & clinical biostatistics. 4th edition New York: Lange Medical Books/McGraw-Hill Medical; 2004.
de Reuver S, Brink RC, Homans JF, Vavruch L, Tropp H, Kruyt MC, van Stralen M, Castelein RM. Anterior lengthening in scoliosis occurs only in the disc and is similar in different types of scoliosis. Spine J 2020;20:1653–1658.
Deviren V, Berven S, Kleinstueck F, Antinnes J, Smith JA, Hu SS. Predictors of flexibility and pain patterns in thoracolumbar and lumbar idiopathic scoliosis. Spine (Phila Pa 1976) 2002;27:2346–2349.
Dickinson R, Hill CR. An ultrasonic method of analyzing tissue motion. Br J Radiol 1980;53:626–627.
Dickinson RJ, Hill CR. Measurement of soft tissue motion using correlation between A-scans. Ultrasound Med Biol 1982;8:263–271.
Downes MJ, Brennan ML, Williams HC, Dean RS. Development of a critical appraisal tool to assess the quality of cross-sectional studies (AXIS). BMJ Open 2016;6 e011458.
Dunn J, Henrikson NB, Morrison CC, Blasi PR, Nguyen M, Lin JS. Screening for adolescent idiopathic scoliosis. JAMA 2018;319:173.
Garra BS. Elastography: History, principles, and technique comparison. Abdom Imaging 2015;40:680–697.
Gennisson JLL, Deffieux T, Fink M, Tanter M. Ultrasound elastography: Principles and techniques. Diagn Interv Imaging 2013;94:487–495.
Grivas TB, Vasiliadis E, Malakasis M, Mouzakis V, Segos D. Intervertebral disc biomechanics in the pathogenesis of idiopathic scoliosis. Stud Health Technol Inform 2006;123:80–83.
Homans JF, Baldew VGM, Brink RC, Kruyt MC, Schlösser TPC, Houben ML, Deeney VFX, Crowley TB, Castelein RM, McDonald-McGinn DM. Scoliosis in association with the 22q11.2 deletion syndrome: An observational study. Arch Dis Child 2019a;104:19–24.
Homans JF, de Reuver S, Breetvelt EJ, Vorstman JAS, Deeney VFX, Flynn JM, McDonald-McGinn DM, Kruyt MC, Castelein RM. The 22q11.2 deletion syndrome as a model for idiopathic scoliosis - A hypothesis. Med Hypotheses 2019b;127:57–62.
Huber M, Gilbert G, Roy J, Parent S, Labelle H, Périé D. Sensitivity of MRI parameters within intervertebral discs to the severity of adolescent idiopathic scoliosis. J Magn Reson Imaging 2016;44:1123–1131.
Illés T, Tunyogi-Csapó M, Somoskeöy S. Breakthrough in three-dimensional scoliosis diagnosis: Significance of horizontal plane view and vertebra vectors. Eur Spine J 2011;20:135–143.

Johnston CE, Stephens Richards B, Sucato DJ, Bridwell KH, Lenke LG, Erickson M. Correlation of preoperative deformity magnitude and pulmonary function tests in adolescent idiopathic scoliosis. Spine 2011;36:1096–1102.

Koo TK, Li MY. A guideline of selecting and reporting intraclass correlation coefficients for reliability research. J Chiropr Med 2016;15:155–163.

Kot BCW, Zhang ZJ, Lee AWC, Leung VYF, Fu SN. Elastic modulus of muscle and tendon with shear wave ultrasound elastography: Variations with different technical settings. PLoS One 2012;7: e44348.

Koumbourlis AC. Scoliosis and the respiratory system. Paediatr Respir Rev 2006;7:152–160.

Kuklo TR, Potter BK, O'Brien MF, Schroeder TM, Lenke LG, Polly DW. Reliability analysis for digital adolescent idiopathic scoliosis measurements. J Spinal Disord Tech 2005;18:152–159.

Langlais T, Vergari C, Pietton R, Dubousset J, Skalli W, Vialle R. Shear-wave elastography can evaluate annulus fibrosus alteration in adolescent scoliosis. Eur Radiol 2018;28:2830–2837.

Lonner B, Yoo A, Terran JS, Sponseller P, Samdani A, Betz R, Shuffelbarger H, Shah SA, Newton P. Effect of spinal deformity on adolescent quality of life: Comparison of operative scheuermann kyphosis, adolescent idiopathic scoliosis, and normal controls. Spine 2013;38:1049–1055.

Moher D, Liberati A, Tetzlaff J, Altman DG, Altman D, Antes G, Atkins D, Barbour V, Barrowman N, Berlin JA, Clark J, Clarke M, Cook D, D'Amico R, Deeks JJ, Devereaux PJ, Dickersin K, Egger M, Ernst E, Gøtzsche PC, Grimshaw J, Guyatt G, Higgins J, Ioannidis JPA, Kleijnen J, Lang T, Magrini N, McNamee D, Moja L, Mulrow C, Napoli M, Oxman A, Pham B, Rennie D, Sampson M, Schulz KF, Shekelle PG, Tovey D, Tugwell P. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. PLoS Med 2009;6 e1000097.

Moreau B, Vergari C, Gad H, Sandoz B, Skalli W, Laporte S. Non-invasive assessment of human multifidus muscle stiffness using ultrasound shear wave elastography: A feasibility study. Proc Inst Mech Eng H 2016;230:809–814.

Rouvière O, Melodelima C, Hoang Dinh A, Bratan F, Pagnoux G, Sanzalone T, Crouzet S, Colombel M, Mège-Lechevallier F, Souchon R. Stiffness of benign and malignant prostate tissue measured by shear-wave elastography: A preliminary study. Eur Radiol 2017;27:1858–1866.

Sarvazyan A, Hall TJ, Urban MW, Fatemi M, Aglyamov SR, Garra BS. An overview of elastography - An emerging branch of medical imaging. Curr Med Imaging Rev 2011;7:255–282.

Shea M, Takeuchi TY, Wittenberg RH, White AA, Hayes WC. A comparison of the effects of automated percutaneous diskectomy and conventional diskectomy on intradiscal pressure, disk geometry, and stiffness. J Strength Cond Res 1994;8:317–325.

Shiina T, Nightingale KR, Palmeri ML, Hall TJ, Bamber JC, Barr RG, Castera L, Choi BI, Chou YH, Cosgrove D, Dietrich CF, Ding H, Amy D, Farrokh A, Ferraioli G, Filice C, Friedrich-Rust M, Nakashima K, Schafer F, Sporea I, Suzuki S, Wilson S, Kudo M. WFUMB guidelines and recommendations for clinical use of ultrasound elastography: Part 1: Basic principles and terminology. Ultrasound Med Biol 2015;41:1126–1147.

Taljanovic MS, Gimber LH, Becker GW, Latt LD, Klauser AS, Melville DM, Gao L, Witte RS. Shear-wave elastography: Basic physics and musculoskeletal applications. Radiographics 2017;37:855–870.

Tsiligiannis T, Grivas T. Pulmonary function in children with idiopathic scoliosis. Scoliosis 2012;7:7.

Vergari C, Rouch P, Dubois G, Tanter M, Gennisson J, Skalli W. Intervertebral disc characterisation by elastography: A preliminary study. Comput Methods Biomech Biomed Eng 2013;16:275–277.

Vergari C, Rouch P, Dubois G, Bonneau D, Dubousset J, Tanter M, Gennisson JL, Skalli W. Intervertebral disc characterization by shear wave elastography: An in vitro preliminary study. Proc Inst Mech Eng H 2014a;228:607–615.

Vergari C, Rouch P, Dubois G, Bonneau D, Dubousset J, Tanter M, Gennisson JL, Skalli W. Non-invasive biomechanical characterization of intervertebral discs by shear wave ultrasound elastography: A feasibility study. Eur Radiol 2014b;24:3210–3216.

Vergari C, Dubois G, Vialle R, Gennisson J-L, Tanter M, Dubousset J, Rouch P, Skalli W. Lumbar annulus fibrosus biomechanical characterization in healthy children by ultrasound shear wave elastography. Eur Radiol 2016;26:1213–1217.

Vergari C, Chanteux L, Pietton R, Langlais T, Vialle R, Skalli W. Shear wave elastography of lumbar annulus fibrosus in adolescent idiopathic scoliosis before and after surgical intervention. Eur Radiol 2020;30:1980–1985.

Yoon HM, Kim SY, Kim KM, Oh SH, Ko G-Y, Park Y, Lee JS, Jung AY, Cho YA. Liver stiffness measured by shear-wave elastography for evaluating intrahepatic portal hypertension in children. J Pediatr Gastroenterol Nutr 2017;64:892–897.

Yu J, Fairbank JCT, Roberts S, Urban JPG. The elastic fiber network of the anulus fibrosus of the normal and scoliotic human intervertebral disc. Spine 2005;30:1815–1820.