Domains and outcome measures for the assessment of cardiac involvement in juvenile and adult systemic sclerosis: a scoping literature review

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ABSTRACT

Objective. *Cardiac involvement in juvenile systemic sclerosis (jSSc) is a leading cause of morbidity and mortality, yet structured protocols for its assessment remain poorly defined. To improve clinical and research practice, standardisation of paediatric outcome measures is pivotal.*

Methods. *As part of the broader IJOG initiative, a scoping review was conducted following PRISMA-ScR guidelines. PubMed, Embase, Web of Science, and CENTRAL were searched (1994–2026) for studies assessing cardiac involvement in juvenile and adult SSc with at least one outcome measure evaluated longitudinally.*

Results. *Of 3,858 cardiac-domain studies identified, 57 met the inclusion criteria. The majority were prospective and single centre. Six cardiac features were identified, assessed through seven categories of outcome measures, the majority classified as clinician reported outcomes. The most commonly used outcome measure was standard echocardiography (46 studies), followed by cardiac biomarkers (27 studies) and right heart catheterisation (25 studies). Advanced outcome measures such as speckle-tracking echocardiography (STE) and cardiac magnetic resonance imaging were seldom reported. Only three paediatric studies were identified, evaluating standard echocardiographic parameters, cardiac biomarkers, and STE. Few studies included control groups, evaluated responsiveness to intervention, or used cardiac outcome measures as primary trial endpoints.*

Conclusion. *This scoping review revealed significant heterogeneity in outcome measures used to assess cardiac involvement in SSc, limiting comparability across studies. Importantly, only three paediatric studies were identified, involving 38 children, evaluating only standard echocardiography, cardiac biomarkers, and speckle-tracking echocardiography. Most findings are therefore derived from adult data, and their applicability to paediatric practice requires cautious interpretation. These findings highlight a critical gap in paediatric cardiac evidence and underscore the need for the IJOG consensus process to identify feasible, paediatric-appropriate outcome measures for future jSSc research.*

Introduction

Juvenile systemic sclerosis (jSSc) is a rare connective tissue disease with multisystem involvement, characterised by autoimmunity, vasculopathy, and fibrosis. Although rare in children, it is associated with significant cardiopulmonary morbidity and mortality (1). In adult-onset SSc, cardiovascular complications are similarly recognised as a leading cause of morbidity, with a significantly increased risk of major adverse cardiac events (2).

Cardiac complications in jSSc may be either primary or secondary to pulmonary arterial hypertension (PAH) (1). Clinically evident cardiac involvement is reported in approximately 5–24% of paediatric cases and represents the major determinant of prognosis (3, 4). The most common manifestations include

pericardial disease and arrhythmias, followed by heart failure and pulmonary hypertension (3). Notably, certain paediatric subsets carry a particularly elevated cardiac risk: in sine scleroderma jSSc (ssJSSc), a subset defined by the absence of skin fibrosis, cardiac involvement was the presenting feature in 85.7% of patients compared with 15.6% in classic jSSc (p=0.001), with significantly higher rates of mortality or end-stage organ failure (42.9% *vs*. 6.2%, p<0.001) (5). A subsequent study comparing paediatric and adult sine scleroderma confirmed that children with ssJSSc have significantly higher cardiac involvement than their adult counterparts (50.0% *vs*. 2.6%, p<0.0001), with a more aggressive disease course and worse prognosis (6). These findings underscore the need for paediatric-specific cardiac outcome measures across all jSSc subsets, including those without overt skin involvement.

Despite the clinical importance of cardiac involvement, structured protocols for assessment in jSSc remain poorly defined. Unlike adult-onset SSc (aSSc), where clinical management is supported by robust evidence-based recommendations, high-quality evidence for jSSc is limited. Consequently, standardised clinical approaches remain underdeveloped. Harmonisation of paediatric outcome measures is essential to ensure comparability and improve both clinical practice and research.

Recommendations for managing jSSc were initially established in 2021 by the Single Hub and Access point for Paediatric Rheumatology in Europe (SHARE) initiative (7). These guidelines were based on a literature review up to 2014 that included only paediatric cohorts, omitting studies on adults, for which more robust evidence is available. A subsequent effort toward standardisation has been undertaken by a multidisciplinary collaboration that more recently proposed a set of outcome measures for use in clinical trials for jSSc through consensus meetings (8). Current recommendations, however, require broader validation across diverse clinical settings.

To address these gaps, the International Juvenile Systemic Sclerosis Outcome Group (IJOG) was created in partnership between the Childhood Arthritis and Rheumatology Research Alliance (CARRA) and the Paediatric Rheumatology European Society (PRES) (9). IJOG aims to develop feasible, meaningful consensus outcome measures to monitor treatment in diverse jSSc clinical setting and trials worldwide. According to the published protocol (9), the project begins with a scoping literature review regarding outcome tools in six key disease domains for both adult and juvenile SSc. International surveys and Delphi processes will then evaluate these measures to develop a standardised core outcome set for future multicentre jSSc trials.

This manuscript presents the results of the cardiac domain scoping review, focusing on outcome measures used to assess cardiac involvement in adult and juvenile SSc.

Methods

Scoping review search strategy

The IJOG study protocol, including the scoping review strategy, has been previously published (9). In summary, the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) guidelines were followed (10). The PubMed, Embase, Web of Science and Cochrane Central Register of Controlled Trials (CENTRAL) databases were searched with the assistance of a librarian from the Albert Einstein College of Medicine. All searches were initially conducted in June 2021 and covered the literature published in English, between 1994 and 2021. An updated search was completed from June 2021 to April 2026.

References were subsequently imported into Covidence. The screening process and identification of relevant studies were planned in four principal steps: 1) initial title and abstract screening, 2) title and abstract screening by disease domain, 3) full-text screening by disease domain, and 4) inclusion for data extraction by disease domain. Two reviewers independently completed each step, with a third reviewer resolving disagreements.

Eligibility criteria

Longitudinal paediatric and adult studies published in English from 1994 onward, with abstracts, were included if they reported at least two time points for the assessment of cardiac involvement in SSc, with or without a description of cardiac symptoms. Studies were required to include at least one outcome measure for cardiac involvement (electrocardiography [ECG], 24-hour Holter ECG monitoring, standard Doppler echocardiography, advanced echocardiography (speckle-tracking echocardiography [STE]), cardiac magnetic resonance imaging [cMRI], stress tests, right heart catheterisation [RHC], cardiac biomarkers). Outcome measures that were experimental, not commercially available, or highly specialised were excluded, as the aim of the IJOG study is to identify feasible and broadly applicable outcome measures for future international jSSc studies.

We also excluded case reports including less than three paediatric or ten adult SSc cases, narrative reviews, conference abstracts, editorials, lectures, animal studies, basic science research. Studies primarily focused on aSSc-related comorbidities, such as atherosclerosis, dyslipidaemia, and smoking, as well as those addressing malignancies or mortality outcomes other than sudden cardiac death, were also excluded.

Data extraction and analysis

Members of the advisory group, comprising paediatric rheumatologists (FZ, NVC, CP, SL, MT), and a paediatric cardiologist (BC), reached consensus on the characteristics of the studies to be extracted regarding cardiac features and outcome measures. A standardised Excel spreadsheet was pilot-tested by two members before being uploaded to Covidence as the structured data extraction form.

Extracted data were summarised using descriptive statistics to characterise the included studies. The following cardiac features were considered: myocardial function, PAH, arrhythmias, pericarditis/pericardial effusion, valvular disease, and exercise capacity. For each category of cardiac outcome measures,

the following parameters were extracted when available:

- ECG: standard ECG; 24-hour Holter ECG monitoring; P-QRS-T dispersion.
- Standard echocardiography: left ventricular ejection fraction (LVEF); LV diastolic function; right ventricular (RV) systolic function; valve function; estimated pulmonary artery pressure (PAP); pericardial effusion.
- Advanced echocardiography (STE): LV global longitudinal strain (LV-GLS); RV strain; 3D/4D parameters.
- Cardiac magnetic resonance imaging (cMRI): systolic function/volumes; speckle tracking MRI; tissue characterisation (late gadolinium enhancement [LGE] - T1/T2 mapping); pulmonary arterial pressure.
- Right heart catheterisation (RHC): performed either for PAH diagnosis or monitoring.
- Stress tests: Standard exercise testing; cardiopulmonary exercise testing (CPET); 6-minute walking test (6MWT); cMRI stress test.
- Biomarkers: N-terminal pro-B type natriuretic peptide (NT-proBNP); troponin.

Outcome measures were classified according to the U.S. Food and Drug Administration (FDA) Clinical Outcome Assessment framework into clinician-reported outcomes (ClinRO), performance outcomes (PerfOM), and biomarker assessments (11).

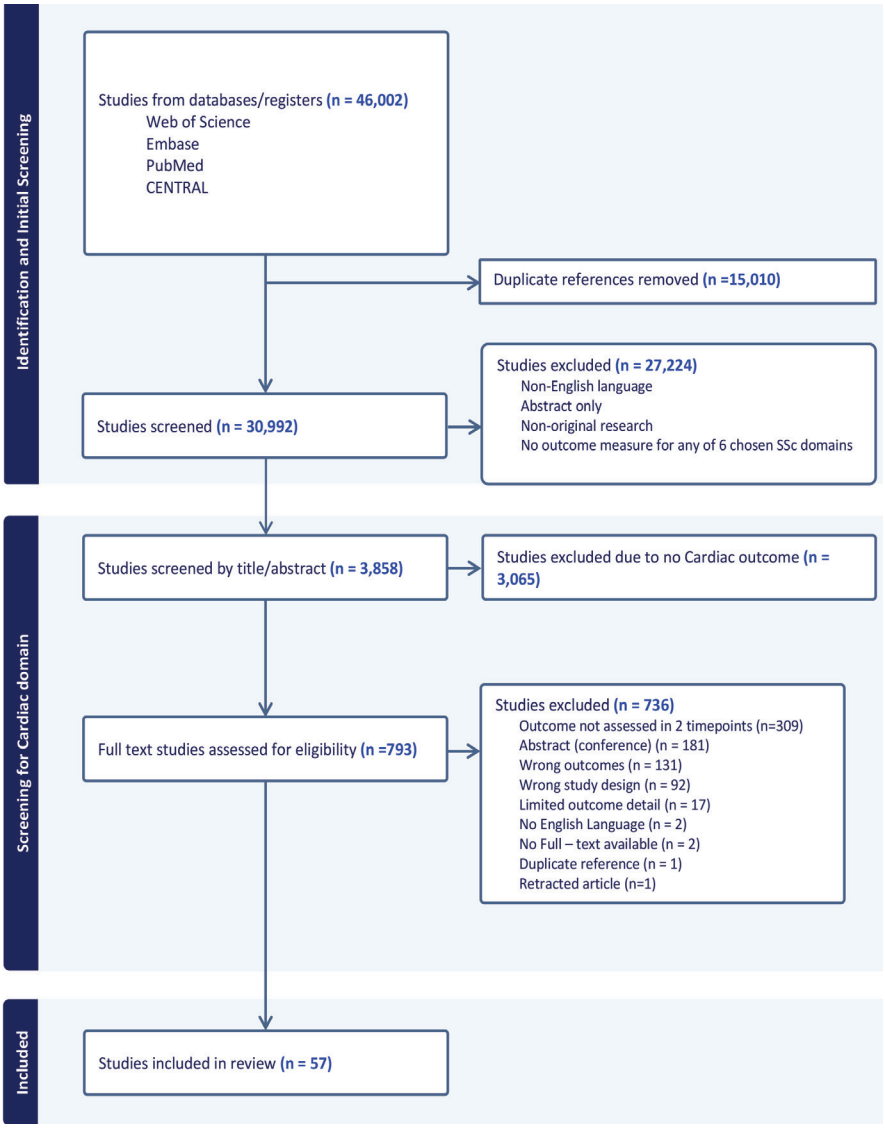

Fig. 1. PRISMA flow diagram of study selection.

Results

Search results

The initial search (1994-2021), previously published (9), and the updated search (2021-2026) combined identified a total of 46,002 records. After deduplication, 30.992 records were screened by title and abstract. A total of 3,858 records relevant to the cardiac domain were identified. Of these, 793 studies were selected for full-text review. Ultimately, 57 studies met the predefined inclusion criteria and were selected for data extraction (Supplementary references S1-S57). The complete study selection process is illustrated in the PRISMA flow diagram (Fig. 1).

Study characteristics

A total of 57 studies were included, comprising 10,214 patients. Of these, three studies (5.2%) included paediatric populations only (n=38 children) (Suppl. ref. S6, S8, S28), while the remaining included exclusively adults. The majority of studies were single-centre (78.9%). The most frequently reported study designs were prospective longitudinal cohort studies (57.8%) and retrospective cohort studies (35.1%). Most studies were conducted in Europe and North America. Characteristics of the included studies are reported in Table I.

Cardiac features

The frequency of the cardiac features assessed across the included studies is summarised in Table II. The most commonly evaluated features were myocardial dysfunction (54.4% of studies) and PAH (57.9%). Approximately half of the included studies assessed a single feature, whereas the remainder evaluated between two and four features. All three paediatric studies assessed both myocardial function and presence of arrhythmias.

Cardiac outcome measures

Of the 57 included studies, most used multiple categories of outcome measures. Only nine studies relied on a single category of outcome measures, while 17 (29.8%) and 18 (31.6%) studies used two or three categories, respectively. The most frequent com-

binations included an imaging-based outcome measure, most commonly echocardiography and less often cMRI, paired with either stress testing or biomarker assessment. The cardiac outcome measures identified across the included studies are summarised in Table III, classified by FDA outcome assessment category.

Clinician-reported outcomes

The majority of cardiac outcome measures identified in this review were classified as clinician-reported outcomes (ClinRO), encompassing all imaging-based and electrocardiographic assessments that require clinician interpretation. These included electrocardiography, standard and advanced echocardiography, cardiac MRI, and right heart catheterisation.

Electrocardiography

Electrocardiographic outcome measures were reported in 15 studies (Suppl. ref. S6, S8, S14, S17, S20, S23, S26, S28, S29, S31, S34, S36, S39, S52, S53), including all three paediatric studies. Three ECG-based outcome measures were identified (Table III). Seven studies used standard resting ECG alone, five employed Holter monitoring, one study combined both modalities, and one study assessed P-QRS-T dispersion using standard ECG. Across all ECG-based outcome measures, 4 studies included a control group, 4 assessed ECG changes in response to an intervention, and no RCTs used ECG parameters as a primary outcome. Standard ECG and 24-hour Holter monitoring are currently included in jSSc recommendations, whereas P-QRS-T dispersion is not (7, 8).

Standard echocardiography

Standard echocardiography was the most frequently reported category of outcome measures, assessed in 46 studies (80 %) (Suppl. ref. S3-13, S15-S19, S21-29, S31-S40, S44-S51, S53, S55, S56), including all three paediatric studies, and was primarily employed to assess myocardial function and pulmonary haemodynamics. Six distinct echocardiographic outcome measures were identified (Table III). LVEF was evaluated in 32 studies (56%) and was used to assess myocardial function. Of these, 14 included a control group, 14 assessed changes in response to an intervention, and no RCTs used LVEF as a primary outcome. LVEF is currently included in jSSc recommendations (7, 8).

LV diastolic function was assessed in 24 studies (42 %), and RV systolic function in 20 (35 %) for the assessment of myocardial function, including one RCT evaluating RV function as primary outcome (Suppl. ref. S46) Estimated PAP was assessed in 32 studies (56%). Notably, in 7 studies echocardiography was used exclusively for the estimation of PAP, without evaluation of other cardiac parameters. Estimated PAP is currently included in jSSc recommendations (7).

Advanced echocardiography

Advanced echocardiography (STE) outcome measures were reported in 10 studies (17.5%) (Suppl. ref. S4, S8, S13, S24-S26, S32, S40, S45, S46), including one paediatric study (Suppl. ref. S8). Three types of STE-based outcome measures were identified (Table III). Most of the studies report data on both LV-GLS and RV strain, one reports RV strain alone, while 3D/4D parameters were evaluated only in 1 study.

Across all STE-based outcome measures, 4 studies included a control group, 3 assessed STE changes in response to an intervention, and 1 RCTs used STE parameters as a primary outcome, specifically RV strain together with RV function evaluated with standard echocardiography (Suppl. ref. S46). None of the STE-based outcome measures are currently included in jSSc recommendations (7, 8).

Cardiac magnetic resonance

Cardiac MRI was reported as an outcome measure in nine studies (16 %), none of which included paediatric patients (Suppl. ref. S4, S31, S34, S39, S42, S43, S50, S52, S53). Four types of cMRI-based outcome measures were identified (Table III). Systolic function and cardiac chambers volumes were assessed in all nine studies, and all but one evaluated tissue characterisation via LGE and/or T1/T2 mapping. Two studies included additional features such as presence of pericardial effusion and myocardial perfusion.

Across all cMRI outcome measures, 2 studies included a control group, 3 assessed cMRI changes in response to an intervention, and no RCTs used cMRI parameters as a primary outcome. cMRI outcome measures are not currently included in jSSc recommendations (7, 8).

Right heart catheterisation

RHC was performed in almost half of the studies (43.9%) (Suppl. ref. S1, S3, S4-S6, S7, S9, S13S17, S21, S22, S24, S27, S30, S40, S47, S51, S52, S54-S57), used for PAH diagnosis or, in six studies, repeated more than once for PAH monitoring. None of the paediatric studies included RHC. Of the

Table I. Characteristics of the included studies (n=57).

Study design	n. of studies (%)
Randomised controlled trial	2 (3.5)
Non-randomised experimental study	0 (0)
Retrospective cohort study	20 (35.1)
Prospective cohort study	33 (57.8)
Case-control study	1 (1.8)
Case series	1 (1.8)
Number of participating centres	
Single centre	45 (78.9)
Multicentre	12 (21.1)
Population	
Adults only (<18)	54 (94.7)
Children only	3 (5.3)
Adults and children	0 (0)
Geographical region	
Europe	34 (59.6)
North America	12 (21.1)
South America	1 (1.8)
Asia	10 (17.5)
Australia	0 (0)

Table II. Cardiac features assessed in the included studies.

Cardiac feature	n. of studies (%)
Myocardial function	31 (54.3)
Pulmonary arterial hypertension	33 (57.9)
Arrythmias	11 (19.3)
Pericarditis/pericardial effusion	3 (5.3)
Valvular disease	0 (0)
Exercise capacity	13 (22.8)
Other	
- myocarditis	1 (1.8)
Studies assessing more than one feature	26 (45.6)

Table III. Cardiac outcomes measures identified in 57 selected studies.

Outcome Measure	n. of studies (%)	FDA Classification	n. of studies with control group (comparison with control group)	n. of studies with intervention (response to intervention)	n. of studies using as primary outcome (n. of RCT)	Included in current jSSc recommendations
ECG		**ClinRo**				**Yes**
Total number of studies	14 (24)		4 (4)	4 (4)	0 (0)	
Number of studies with children	3 (5.2)		1 (1)	1 (1)	0 (0)	
Parameters assessed						
Standard ECG	9 (15.8)		4 (3)	1 (0)	0 (0)	Yes
24H Holter monitoring	6 (10.5)		1 (0)	3 (1)	0 (0)	Yes
P-QRS-T Dispersion	1 (1.8)		1 (1)	0 (0)	0 (0)	No
Other	1 (1.8)		0 (0)	0 (0)	0 (0)	N/A
STANDARD ECHO		**ClinRo**				**Yes**
Total number of studies	46 (80)		14 (14)	14 (11)	25 (1)	
Number of studies with children	3 (5.2)		1 (1)	1 (1)	1 (0)	
Parameters assessed						
LVEF	32 (56.1)		12 (12)	10 (2)	15 (0)	Yes
LV diastolic function	24 (42.1)		11 (11)	7 (1)	8 (0)	No
RV systolic function	20 (35.1)		10 (10)	6 (0)	6 (1)	No
Valve function	12 (21.1)		5 (5)	1 (0)	0 (0)	No
PAP	31 (54.4)		11 (11)	7 (3)	1 (0)	Yes
Pericardial effusion	5 (8.8)		1 (1)	0 (0)	8 (0)	No
Other	3 (5.2)		0 (0)	2 (0)	0 (0)	N/A
SPECKLE-TRACKING ECHO		**ClinRo**				**No**
Total number of studies	10 (17.5)		4 (4)	3 (2)	3 (1)	
Number of studies with children	0 (0)		0 (0)	0 (0)	0 (0)	
Parameters assessed						
LV-GLS	9 (15.8)		4 (4)	3 (2)	3 (0)	
RV strain	8 (14.0)		3 (3)	3 (2)	3 (1)	
3D/4D parameters	1 (1.8)		1 (1)	1 (0)	1 (0)	
CARDIAC MRI		**ClinRo**				**No**
Total number of studies	9 (15.8)		2 (2)	3 (3)	6 (0)	
Number of studies with children	0 (0)		0 (0)	0 (0)	0 (0)	
Parameters assessed						
Systolic function	9 (15.8)		2 (2)	3 (3)	6 (0)	
Speckle tracking MRI	0 (0)		0 (0)	0 (0)	6 (0)	
Tissue characterisation (LGE - T1/T2 mapping)	8 (14.0)		2 (2)	3 (3)	6 (0)	
PAP	0 (0)		0 (0)	0 (0)	0 (0)	
Other	2 (3.5)		0 (0)	0 (0)	0 (0)	
STRESS TESTS		**PerfOM**				**Yes**
Total number of studies	19 (33.3)		5 (5)	7 (4)	5 (1)	
Number of studies with children	0 (0)		0 (0)	0 (0)	0 (0)	
Parameters assessed						
Standard exercise testing	1 (1.8)		0 (0)	0 (0)	0 (0)	No
Cardiopulmonary exercise testing	4 (7.0)		1 (1)	3 (1)	2 (0)	No
6-minute walking test	16 (28.1)		3 (3)	6 (1)	3 (1)	Yes
cMRI stress test	0 (0)		0 (0)	0 (0)	0 (0)	No
Other	1 (1.8)		1 (1)	0 (0)	0 (0)	N/A
CARDIAC BIOMARKERS		**Biomarker**				**Research agenda**
Total number of studies	26 (45.6)		7 (7)	11 (10)	4 (0)	
Number of studies with children	1 (1.8)		1 (1)	0 (0)	0 (0)	
Parameters assessed						
NT-proBNP	25 (43.9)		7 (7)	11 (3)	4 (0)	**Research agenda**
Troponin	7 (12.3)		1 (1)	2 (1)	2 (0)	No
Other	3 (5.2)		1 (0)	0 (0)	0 (0)	N/A
RHC		**ClinRo**				**Research agenda**
Total number of studies with procedure performed at least once	25 (43.9)		5 (5)	9 (2)	6 (0)	
Number of studies performing RHC longitudinally for PAH monitoring	6 (10.5)		1 (1)	4 (2)	2 (2)	
Number of studies with children	0 (0)		0 (0)	0 (0)	0 (0)	

ECG: electrocardiogram; LV: left ventriculum; RV: right ventriculum; PAP: pulmonary arterial pressure; LVEF: left ventricular ejection fraction; LV-GLS: left ventriculum global longitudinal strain; MRI: magnetic resonance imaging; LGE: late gadolinium enhancement; ECHO: echocardiogram; RHC: right heart catheterisation; PAH: pulmonary arterial hypertension; ClinRo: clinician reported outcome; PerfOM: performance outcome measure.

studies employing RHC, 5 included a control group and 9 assessed haemodynamic changes in response to an intervention. No RCTs used RHC-derived parameters as a primary outcome. RHC is currently included in the jSSc research agenda but not in routine recommendations (8).

Performance outcomes

Nineteen studies reported performance-based outcome measures (Suppl. ref. S1, S2, S5, S7, S9, S14–S16, S22, S26, S35, S36, S41, S44, S46, S49, S54, S56, S57). Four types of Performance outcomes (PerfOM) were identified (Table III).

The 6MWT was the most frequently assessed PerfOM (16 studies, 28.1%), used for the evaluation of exercise capacity and functional impairment in the context of PAH. No paediatric studies included the 6MWT despite current recommendations in jSSc (7, 8). CPET was adopted in four studies, while standard exercise testing and stress echocardiography were used only once, respectively. Across all PerfOM measures, 5 studies included a control group, 7 assessed response to an intervention, and 1 RCTs used a PerfOM as a primary outcome, specifically the 6MWT (Suppl. ref. S57).

Cardiac biomarkers

Twenty-seven studies assessed the use of biomarkers (Suppl. ref. S4, S6, S7, S16, S22-24, S26, S27, S29, S36-43, S45, S47, S48, S50, S52-S54, S56, S57). Two types of biomarker outcome measures were identified (Table III). NT-proBNP was the most frequently assessed biomarker, evaluated in all 27 studies, including one paediatric study (Suppl. ref. S6). Of these, 7 included a control group and 11 assessed biomarker changes in response to an intervention. One RCT used NT-proBNP as a primary outcome. NT-proBNP is currently included in the jSSc research agenda (7, 8). Troponin was assessed in six studies, while other biomarkers were included in a minority of studies. No paediatric studies evaluated troponin.

Based on the findings of this review, Supplementary Table S1 provides a qualitative summary of the strengths, limitations, feasibility, and paediatric applicability of each category of cardiac outcome measures identified.

Discussion

This study explored the available evidence regarding cardiac outcome measures currently used to evaluate adult and paediatric patients with SSc, as part of the broader IJOG initiative to identify feasible outcome measures for future jSSc treatment studies. The findings reveal significant heterogeneity in the outcome measures used across studies, a predominance of ClinRO-classified measures, and a critical gap in paediatric evidence.

The first finding is the limited representation of paediatric patients. Only three of the 57 included studies enrolled children, comprising just 38 patients. Most studies included only adults, were single-centre and were observational, with prospective cohorts predominating, likely reflecting the requirement for longitudinal assessment at ≥2 timepoints.

The 57 identified studies evaluated several cardiac features, with myocardial function and PAH being the most commonly assessed. Overall, 21 outcome measures were classified into three FDA categories: ClinRo, PerfOM, and biomarker. Most studies employed a multimodal assessment approach, combining multiple outcome measures categories.

ClinRO measures predominated and included electrocardiography, standard and advanced echocardiography, cMRI, and RHC. This predominance reflects the central role of clinician-interpreted imaging and electrophysiological assessments in the evaluation of cardiac involvement in SSc.

Among ClinRO measures, standard echocardiography was the most frequently used. This was expected, given the widespread availability and non-invasive nature of this test. In the adult SSc population, the utility of echocardiography in the assessment of myocardial dysfunction is well established, and annual assessment is recommended as part of the cardiovascular screening used to identify primary SSc heart involvement (12). Recent evidence confirms that LV dysfunction remains one of the most prevalent complications of SSc cardiac involvement, further supporting the central role of LVEF in longitudinal assessment (13). Most studies included conventional echocardiographic parameters, with LVEF being the most commonly reported, including in all three paediatric studies. LVEF is included in current jSSc recommendations (8) and in the J4S score as a measure of cardiac disease severity (14). Its consistent use likely reflects its reproducibility and established role in clinical practice. LV diastolic function and RV systolic function were also frequently assessed but are not currently included in jSSc recommendations, despite their potential relevance to the detection of early myocardial involvement. Pericardial disease and valve function were seldom assessed as outcome measures.

In a substantial proportion of the studies, echocardiography was used for PAP estimation, either alongside myocardial function assessment or as the sole echocardiographic outcome measure. Consistently, more than half of the included studies evaluated PAH as a cardiac feature, and 43% included RHC as an outcome measure for PAH diagnostic confirmation or longitudinal monitoring. This finding likely reflects the high prevalence of PAH in adult patients, where it represents one of the leading causes of mortality (15) and is therefore included in diagnostic algorithms to screen potential patients for RHC (16). In contrast, none of the paediatric studies evaluated PAH, and none reported RHC as an outcome measure. In jSSc, PAH has a much lower prevalence (3) than in adults, and given its invasiveness, the routine use of RHC has not yet been standardised in paediatric recommendations, although it remains the diagnostic standard when PAH is suspected.

Unlike standard echocardiography, STE use was assessed in only a minority of studies. Interest in STE has increased because it detects subclinical myocardial dysfunction before reductions in LVEF become apparent (17, 18). Despite the limited paediatric lit-

erature, one study evaluated LV-GLS as an outcome measure in jSSc (Suppl. ref. S8). Nonetheless, STE-based outcome measures are not yet considered part of the routine cardiac evaluation, even in adult guidelines, and require further validation before inclusion in jSSc recommendations, bearing in mind that these techniques remain less accessible than standard echocardiography and that feasibility and interpretation may vary across different settings.

Cardiac MRI was reported in only nine longitudinal studies, none including children. cMRI allows for accurate characterisation of cardiac morphology and function, along with identification of tissue alterations indicative of inflammation and/or fibrosis (19). All studies evaluated systolic function through this outcome measure, and all but one evaluated tissue characterisation with LGE and/or T1/T2 mapping. Its limited use likely reflects lower availability, higher costs and need for specialised expertise compared with other outcome measures. Current adult recommendations support individualised rather than routine use while recognising its value for detecting subclinical disease (12). cMRI is not currently included in jSSc recommendations (7, 8).

Electrocardiographic measures, both standard ECG and 24-hour Holter monitoring, were reported in about one quarter of the studies, including all three paediatric studies. ECG is a simple, readily available, and non-invasive measure that allows for diagnosis and monitoring of cardiac rhythm disturbances, a serious complication of cardiac involvement in SSc. The routine use of ECG is already well established in both adult and paediatric recommendations (7, 8, 12). Its relatively infrequent reporting likely reflects its routine use in clinical practice rather than omission from patient assessment.

Overall, the ClinRO category demonstrated the greatest heterogeneity in outcome measures, with 14 distinct parameters identified across five subcategories. While several ClinRO measures are already included in current jSSc recommendations (standard ECG, Holter, LVEF, estimated PAP), the majority, including LV diastolic function, RV systolic function, all STE parameters, and all cMRI parameters, are not. This discrepancy highlights the need for the IJOG consensus process to determine which measures should be incorporated into future paediatric protocols.

Stress tests, classified as PerfOM, were reported in 19 studies. The 6MWT was the most commonly assessed (16 studies, 28%) while CPET was reported in only four. None of the paediatric studies included any PerfOM measure.

In the context of the studies included in this review, which focused only on cardiac involvement, 6MWT was generally used as an outcome measure for the assessment of functional impairment in patients with suspected or confirmed PAH. This test, which is simple to administer, safe, and non-invasive, is indicated for functional assessment with diagnostic and prognostic purposes in several conditions, including all types of PAH, pulmonary fibrosis, and heart failure (20-22). Current guidelines include the 6MWT among the outcome measures to assess pulmonary involvement in jSSc (5), which underscores the nonspecific nature of this test and warrants further clarification on whether it should also be used as an outcome measure in the cardiac evaluation. The absence of PerfOM in paediatric studies represents an important gap. While the 6MWT is already recommended for pulmonary assessment in jSSc, its role as a cardiac-specific outcome measure (and the potential role of CPET) should be addressed in the IJOG consensus process.

Regarding cardiac biomarkers, NT-proBNP was the most frequently assessed, evaluated in all 27 studies. This is likely related to the high prevalence of PAH in the adult population, as NT-proBNP is a well-established biomarker for PAH detection in SSc (16). Only one paediatric study has evaluated this biomarker, which is currently included in the research agenda for jSSc (8). Cardiac troponin was assessed in only six adult studies, possibly suggesting a less established role as an outcome measure for the assessment of myocardial injury related to SSc. The biomarker category had the fewest distinct outcome measures (two), yet NT-proBNP was among the most frequently reported outcome measures overall. The discrepancy between its widespread use in adult studies and its near-absence in paediatric studies highlights an important area for the IJOG consensus process to address, particularly given the practical advantages of biomarkers, including their objectivity, low cost, and ease of serial measurement.

Notably, no patient-reported outcomes were identified among the cardiac outcome measures in any of the 57 included studies. The absence of cardiac-specific PROs represents an important gap, particularly given the emphasis placed on patient-centred measurement by the OMERACT framework. While cardiac symptoms such as dyspnoea, palpitations, and exercise intolerance are clinically relevant, no validated PRO instruments specific to cardiac involvement in SSc were identified. This gap should be considered in the subsequent IJOG consensus process.

Several overarching observations emerge. Few studies included control groups, evaluated responsiveness to intervention, or used cardiac outcome measures as primary trial endpoints, limiting assessment of responsiveness and discriminative validity. Paediatric evidence was particularly sparse, with studies limited to standard echocardiography, ECG, one STE study, and one NT-proBNP study, necessitating substantial extrapolation from adult data when considering paediatric outcome measures. Finally, several outcome measures commonly used in aSSc, including LV diastolic function, RV systolic function, STE, and cMRI, are absent from current jSSc recommendations, whereas recommended measures such as the 6MWT have not been evaluated in paediatric longitudinal cardiac studies. In keeping with the scoping review methodology, this study was designed to identify and map the outcome measures used to assess cardiac involvement in SSc, rather than to formally evaluate their measurement properties. Accordingly, the findings reflect patterns of use

across the literature and should not be interpreted as endorsements of specific measures. The assessment of measurement performance, including reliability, validity, and responsiveness, will be addressed in subsequent phases of the IJOG initiative through structured consensus-building methodologies. To support the subsequent IJOG consensus process, the qualitative summary presented in Supplementary Table S1 is intended as a practical resource to inform expert deliberation rather than as a formal assessment of measurement performance.

This study has different limitations to be considered. First, the literature search was limited to English-language studies, which may have restricted the identification of relevant publications in other languages. Second, in accordance with the scoping review methodology, no formal assessment of methodological quality or risk of bias was conducted, nor was the diagnostic performance of the outcome measures evaluated. Third, the search covered a very broad time span, which may have introduced additional variability given the many advances in cardiac outcome measures over the past three decades. Finally, a critical limitation of the current evidence base is the near-complete reliance on adult-derived data. Only three of the 57 included studies enrolled paediatric patients, comprising just 38 children, and these studies evaluated a narrow range of outcome measures: standard echocardiography, ECG, one STE study, and one NT-proBNP study. Key outcome measures widely used in aSSc, including cMRI, RHC, 6MWT, CPET, and troponin, have not been evaluated longitudinally in jSSc. Direct extrapolation from adult data to paediatric practice must be approached with caution, given the well-recognised differences in disease phenotype, cardiac physiology, developmental considerations, and the distinct cardiac risk profile of certain jSSc subsets such as ssJSSc. These differences may affect both the performance and the clinical relevance of outcome measures validated in adults. The findings of this review should therefore be interpreted as a mapping of the available evidence landscape rather than as direct recommendations for paediatric use.

This scoping review provides the first comprehensive overview of cardiac outcome measures reported in aSSc and jSSc. The wide range of outcome measures identified reflects the complexity of primary cardiac involvement in SSc, which can manifest as both left and right myocardial dysfunction, arrythmias, pericarditis and PAH (3, 23). At the same time, this heterogeneity limits comparability and underscores the need for greater standardisation of outcome assessment. Importantly, this study highlights that available evidence from paediatric literature is limited, representing a significant knowledge gap that hinders the development of paediatric-specific guidelines. Given that most evidence identified in this review derives from adult populations, the applicability of these findings to paediatric practice cannot be assumed. While extrapolation from adult data remains a reasonable and necessary approach given the current paucity of paediatric evidence, future efforts should focus on the progressive generation of paediatric-specific data to validate and refine cardiac outcome measures for the jSSc population. Within this context, this first phase of the IJOG project has built a solid evidence base to guide future steps. The next stages will aim to reach agreement on the outcome measures for future jSSc research through structured consensus-building methodologies.

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