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SYSTEMATIC REVIEW

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Prognostic significance of echocardiographic deformation imaging in adult congenital heart disease

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Abstract

Background: Due to medical and surgical advancements, the population of adult patients with congenital heart disease (ACHD) is growing. Despite successful therapy, ACHD patients face structural sequalae, placing them at increased risk for heart failure and arrhythmias. Left and right ventricular function are important predictors for adverse clinical outcomes. In acquired heart disease it has been shown that echocardiographic deformation imaging is of superior prognostic value as compared to conventional parameters as ejection fraction. However, in adult congenital heart disease, the clinical significance of deformation imaging has not been systematically assessed and remains unclear.

Methods: According to the Preferred Reporting Items for Systematic Reviews checklist, this systematic review included studies that reported on the prognostic value of echocardiographic left and/or right ventricular strain by 2-dimensional speckle tracking for hard clinical end-points (death, heart failure hospitalization, arrhythmias) in the most frequent forms of adult congenital heart disease.

Results: In total, 19 contemporary studies were included. Current data shows that left ventricular and right ventricular global longitudinal strain (GLS) predict heart failure, transplantation, ventricular arrhythmias and mortality in patients with Ebstein's disease and tetralogy of Fallot, and that GLS of the systemic right ventricle predicts heart failure and mortality in patients post atrial switch operation or with a congenitally corrected transposition of the great arteries.

Conclusions: Deformation imaging can potentially impact the clinical decision making in ACHD patients. Further studies are needed to establish disease-specific reference strain values and ranges of impaired strain that would indicate the need for medical or structural intervention.

KEYWORD

deformation strain imaging adult congenital echocardiography

1 | INTRODUCTION

Due to medical and surgical advancements, over 90% of newborns with congenital heart disease nowadays reach adulthood,[1] resulting in an increasing prevalence of congenital heart disease in adults. Despite successful therapy, adults with congenital heart disease (ACHD) still face structural sequalae, putting them at a higher risk for heart failure, significant valvular heart disease and arrhythmic events.[1] Therefore, lifelong surveillance in specialized care centres is recommended for ACHD patients, leading to better outcomes compared to follow-up in centres without specific ACHD expertise.[2] During follow-up visits, the assessment of left and right ventricular function using echocardiography or cardiac magnetic resonance (CMR) is pivotal. Impaired ventricular function is associated with adverse events, and guides the indication for heart failure therapy and intervention in significant valvular heart disease.[1,3,4] Nonetheless, optimal timing of intervention remains challenging, partly because ventricular volumes and ejection fraction, which are currently the most frequently used parameters, are not sensitive enough to reveal early myocardial dysfunction. The use of parameters with more sensitivity would lead to earlier intervention, which will presumably lead to improved outcomes.

In acquired and in genetic heart disease, echocardiographic deformation imaging has shown incremental value in early disease detection and risk stratification compared to traditional parameters.[5,6] Among the available strain parameters, left ventricular (LV) global longitudinal strain (GLS) is most frequently used in daily clinical practice all over the world,[5] and is endorsed by the guidelines for acquired valvular heart disease.[3] Normal reference values for LV GLS range from −16.7% to −26.7% in men, and −17.8% to −28.2% in women.[7] However, in ACHD patients, the prognostic implications of strain assessment have not been fully elucidated. Yet, the utility of this technique in ACHD is promising, since echocardiography is frequently used as first-line imaging modality in ACHD. We conducted a systematic literature search on the prognostic value of echocardiographic deformation imaging in ACHD patients, with the goals of evaluating the current evidence, identifying knowledge gaps, and determining future directions.

Key points

- Ventricular function is a pivotal prognostic factor in AHCD patients, yet the utility of deformation imaging remains uncertain.
- Echocardiographic deformation imaging can provide mid-term prognostic information for various types of ACHD patients.
- Future research could concentrate on defining disease-specific normal reference values, and values that might indicate intervention.

2 | METHODS

2.1 | Search strategy and selection criteria

This systematic review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist.[8] Studies that reported on the prognostic value of echocardiographic left and/or right ventricular strain by 2-dimensional speckle tracking in ACHD patients were included. To conduct the literature search, the PubMed and Embase databases were queried with the assistance of a university librarian. The search terms included keywords and synonyms related to (1) deformation imaging and (2) the most common forms of ACHD, including atrial septal defect, ventricular septal defect, tetralogy of Fallot, transposition of the great arteries (TGA), univentricular circulation. The following specific query for the search was:

("speckle tracking echocardiograp*" [tiab] OR strain*[tiab] OR deformation imag*[tiab] OR speckle track*[tiab] OR GLS*[tiab] OR mechanical dispersion*[tiab]) AND ("Heart Defects, Congenital" [Mesh] OR "congenital heart disease*" [tiab] OR "atrial septal defect*" [tiab] OR "ventricular septal defect*" [tiab] OR "tetralogy of fallot" [tiab] OR "transposition of the great arter*" [tiab] OR "univentricular circul*" [tiab] OR "Fontan Procedure" [Mesh] OR "Fontan Procedur*" [tiab]).

The titles and abstracts of the articles obtained in the initial search were reviewed and studies that described the assessment of deformation imaging in congenital heart disease, which were published in English peer reviewed journals were selected for further analysis of eligibility. When considered eligible, the full article was studied in depth, and the reference list was screened for potential additional studies. Studies that used deformation imaging by other modalities than echocardiography were excluded, as well as studies that used atrial strain and studies in paediatric populations. Abstracts and unpublished congress data were not considered for inclusion. The final search was conducted on 18 August 2023. The quality of the studies and the consequent risk of selection bias was evaluated by two observers (P.R. and K.T.) using the Newcastle–Ottawa quality assessment scale for cohort studies (Data S1).

2.2 | Data extraction

From each included article, the following characteristics were extracted: year of publication, design of the study, type of (repaired) congenital heart disease, number of patients, age, gender, investigated parameters of ventricular strain, manufacturer of software package, clinical end-points, time of follow-up, and the hazard ratio of the strain parameter for the clinical end-point.

3 | RESULTS

After screening the titles and abstracts, 505 articles were examined in full text. In total, 19 original articles were identified, all published between 2012 and 2023, Figure 1. The included studies are summarized in Table 1, and are presented according to the specific type of congenital heart disease (TGA, Ebstein's anomaly, or tetralogy of Fallot), or as miscellaneous if a particular ACHD condition was investigated in only one report.

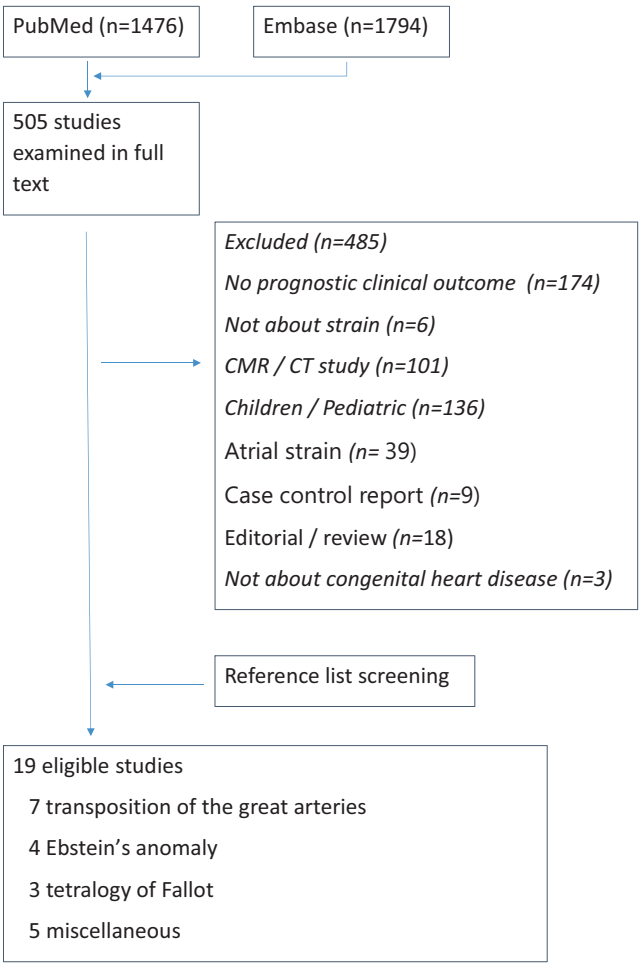

FIGURE 1 Flowchart of the study selection.

The mean or median age ranged from 20 to 41 years. The study of Rösner et al. included also adolescents (median 20, [12–70] years),[9] and we made this specific exception, since this was the only study assessing the prognostic value of strain in patients with a single-ventricle circulation after a Fontan palliation. It was deemed to provide important unique information relevant for the ACHD cardiologist. The number of patients included by the different studies varied from 24 to 821 (Table 1).

3.1 | Transposition of the great arteries

Six studies reported on the prognostic value of strain of the systemic ventricle in patients with a congenital corrected TGA (ccTGA) or in patients who had an atrial switch operation for TGA, reporting on a total of 758 patients. The most notable strain parameters in this population is GLS of the systemic right ventricle, Figure 2. Egbe et al showed in 186 patients with ccTGA that a reduction of GLS of the systemic right ventricle at baseline was associated with cardiovascular events (death, heart transplantation, heart failure hospitalization) during a median follow-up of 10 (interquartile range (IQR): 4–16) years: hazard ratio (HR) per 1% improve: .94 (95% confidence interval (CI): .90–.98).[10] This parameter was also studied in a retrospective analysis of the VALsartan in SystEmic Right VEntricle (VAL-SERVE) trial: Woudstra et al. showed in 60 patients with a systemic right ventricle in the context of ccTGA ($n=21$) or after an atrial switch operation for TGA ($n=39$) that, besides 3-dimensional CMR / computed tomographic derived ejection fraction, only echocardiographic assessed GLS of the systemic right ventricle was independently associated with heart failure during a median follow-up of 8 (IQR: 7–9) years (Table 1).[11]

One recent study ($n=151$) investigated the role of LV and RV strain in TGA patients who were operated with an arterial switch or Rastelli operation in whom the LV is connected to the systemic circulation. In these patients, the peak strain values of the RV septum and free wall were independently related to atrial arrythmia induced heart failure hospitalization ($n=9$) (Table 1).[12]

3.2 | Ebstein's anomaly

Four retrospective studies investigated the role of LV and RV strain assessment in the cohort of patients with Ebstein's anomaly from the Mayo Clinic (Table 1). An example of the echocardiographic analysis is provided in Figure 3. The total cohort comprised 673 individuals with Ebstein's anomaly (median age 37 [IQR 25–49] years) who underwent echocardiographic follow-up between the years 2000 and 2020. The studies investigated the prognostic performance of LV

TABLE 1 Included studies according to the subtype of adult congenital heart disease.

Author	Year	Design	Type of congenital heart disease	Number of patients	Age (years)	Male	Global deformation parameters
Systemic right ventricle in congenitally corrected transposition of the great arteries, or in patients operated with an atrial switch operation for transposition of the great arteries							
Egbe[10]	2022	Retrospective cohort	ccTGA	186	40 ± 12	50%	RV GLS
Egbe[26]	2022	Retrospective cohort	ccTGA	233	40 ± 15	50%	RV GLS LV GLS
Woudstra[11]	2020	Retrospective analysis of VAL-SERVE trial	ccTGA TGA after atrial switch	21 39	34 ± 11	65%	RV GLS
Geenen[27]	2019	Retrospective analysis of prospective cohort	ccTGA Atrial switch for TGA	21 65	37 ± 9	65%	RV GLS RV CS RV FWLS RV SWLS
Diller[28]	2012	Retrospective	Atrial switch ccTGA	87 42	35 ± 12	55%	RV GLS RV RS
Kalogeropoulos[29]	2012	Retrospective	TGA after atrial switch	64	29 ± 6	66%	RV GLS
Transpositon of the great arteries corrected with an arterial switch operation or Rastelli procedure							
Egbe[12]	2023	Retrospective	TGA after arterial switch TGA after Rastelli procedure	89 62	20 (18–22) 27 (19–33)	61% 63%	RV strain of the septum and free wall
Ebstein's anomaly							
Egbe[15]	2023	Retrospective	Ebstein's anomaly	620	37 (25–49) years	42%	RV GLS RV FWS LV GLS
Egbe[13]	2021	Retrospective	Ebstein's anomaly	673	37 (25–49) years	42%	LV GLS
Egbe[21]	2021	Retrospective	Ebstein's anomaly with severe TR undergoing surgery	76	36 (24–51) years	45%	RV GLS LV GLS
Egbe[14]	2021	Restrospective	Ebstein's undergoing surgery	371	39 (27–59)	42%	Occult LV systolic dysfunction (normal LVEF, but impaired LV GLS, less negative than −18%) RVGLS

Software	Outcome	Follow-up	Prognostic implications univariate	Prognostic implications multivariate
GE Echopac	Composite of heart failure hospitalization, transplantation and death ($n=57$, 27%)	10 (4–16) years		RV GLS, for each % improving (more negative), HR: .94, 95% CI: .9–.98
TomTec	Composite of heart failure hospitalization, transplantation and cardiovascular death ($n=66$, 28%)	9 (4–13) years		RV GLS, for each % improving (more negative), HR: .9, 95% CI: .84–.92 LV GLS, for each % improving (more negative), HR: .92, 95% CI: .87–.97
GE Echopac	Heart failure free survival, including NYHA progression, hospitalization, increase diuretics, all-cause mortality $n=15$	8 (7–9) years		Impaired GLS sRV, less negative than −10.5%, HR, 95% CI: 37 (5–444), $p<.001$
TomTec	Composite of all-cause mortality and heart failure (hospitalization or increase in medication) $n=19$	5.9 (5.3–6.3) years		RV GLS not multivariate associated
TomTec	Composite of onset of heart failure (increase of NYHA class to ≥3), clinically relevant arrythmia, or death $N=41$	1.7 (.7–3.6) years		RV GLS, for % worsening (less negative), HR: 1.083, 95% CI: 1.021–1.150
GE Echopac	Composite of onset of heart failure or ventricular tachycardia $N=12$	2.4 (1.5–4.1) years		RV GLS, for % worsening (less negative), HR: 1.35, 95% CI: 1.14–1.58
TomTec	Heart failure hospitalization $N=9$	5.6 (3.1–8.9) years		RV strain, for each % improving (more negative), HR: .93, 95% CI: .88–.98
TomTec	All-cause mortality $n=47$, 8%	7.1 (3.4–10.2) years		RV GLS, for each % improving (more negative), HR: .94, 95% CI: .92–.96 LV GLS, for each % improving (more negative), HR: .96 (.94–.98)
TomTec	Death or heart transplantation $n=49$, 7%	51 (29–86) months		Impaired LV GLS, less negative than −18%, HR: 1.79, 95% CI: 1.25–4.98
TomTec	Post-operative improvement in VO_2 max $n=48$, 63%	15 (12–19) months		RA and LA reservoir strain, and not RV GLS and LV GLS predicted VO2 max improvement
TomTec	Death or heart transplantation $n=12$, 4%	68 (37–106) months		Occult LV systolic dysfunction, HR: 2.33, 95% CI: 1.85–2.90

(Continues)

TABLE 1 (Continued)

Author	Year	Design	Type of congenital heart disease	Number of patients	Age (years)	Male	Global deformation parameters
Tetralogy of Fallot							
Groote[17]	2019	Retrospective analysis of prospective cohort	Repaired ToF	151	33 (26–42) years	62%	LV GLS RV FWLS
Sabate Rotes (22)	2014	Retrospective cohort study	Patients with operated ToF prior undergoing first time PVR	146	36 ± 16	46%	LV strain in 4Ch view RV GLS
Diller[16]	2012	Retrospective	Repaired ToF	413	36 ± 13	51%	LV GLS RV GLS
Miscellaneous							
Rösner[9]	2022	Retrospective cohort	Single-ventricle, Fontan circulation Left morphology Right morphology	110	Median 20 (12–27)	57%	LS CS Strain pattern
Egbe[30]	2022	Retrospective	Patients with congenital heart disease and previous LV dysfunction (EF < 50%) and subsequent recovery LVEF > 50%	193	41 ± 17	57%	LV GLS
Egbe[19]	2021	Retrospective	Repaired and native coarctation	821 *645 repaired CoA* *176 native CoA*	Median 32 (21–46)	58%	RV GLS LV GLS
Moceri [31]	2017	Prospective cohort study	Eisenmenger syndrome (ASD, VSD, PDA, AP window) Other PAH aetiology	43 40	41 ± 15 years 60 ± 18 years	27% 45%	LV GLS LV CS RV FWLS RV FWTS
Chowdhury [32]	2015	Retrospective analysis of prospective trial	Patients with dysfunctional PA-RV conduits undergoing TPVR	24	32 ± 17 years	71%	RV LS RV FWS RV EDSR LV LS LV EDSR

Abbreviations: AP, aortopulmonary; ASD, atrial septal defect; ccTGA, congenital corrected transposition of the great arteries; CI, confidence interval; CS, circumferential strain; EDSR, early diastolic strain rate; EF, ejection fraction; FWLS, free wall longitudinal strain; FWS, free wall strain; FWTS, free wall transverse strain; GLS, global longitudinal strain; HR, hazard ratio; LS, longitudinal strain; LV, left ventricular; NYHA, New York Heart Association; PA, pulmonary artery; PAH, pulmonary arterial hypertension; PDA, patent ductus arteriosus; PVR, pulmonary valve replacement; RS, radial strain; RV, right ventricular; sRV, systemic right ventricle; SWLS, septal wall longitudinal strain; ToF, tetralogy of Fallot; TPVR, transcatheter pulmonary valve replacement; TR tricuspid valve regurgitation; VSD, ventricular septal defect; VT, ventricular tachycardia.

Software	Outcome	Follow-up	Prognostic implications univariate	Prognostic implications multivariate
TomTec	Composite of death or heart failure (change in diuretics, or hospitalization) $N=14$	72 (64–75) months		in a ridge regression model including LVEF, LVGLS, RV FWS, only RV FWS is associated with outcome, per improving tertile, HR: .6, 95% CI: .38–.95
Velocity Vector Imaging	NYHA class improvement	3 ± 2.7 years	RV FWS associated with NYHA ≥ 2, odds ratio, per % worsening (less negative): 1.3, $p=.02$	
TomTec	Composite of sudden cardiac death or life threatening arrhythmia $n=19$	2.9 (1.4–4.4) years	for each % improving (more negative) LV GLS, %, HR: .87, 95% CI: (.77–.99) RV GLS, %, HR: .96, 95% CI: .86–1.07	In combination with right atrial area, RV fractional area change, LV GLS was associated with outcome, $p<.001$, c statistic: .70
TomTec Velocity Vector Imaging	Composite of death or transplantation ($n=35$, 32%)	85 ± 35 months		Classic dyssynchrony pattern, HR: 9.4, 95% CI: 3–35
TomTec	Composite of heart failure hospitalization, sustained VT, heart transplant, or death; $N=37$	5.3 (2.6–8.4) years		Impaired LVGLS, less negative than −18%, HR: 2.61, 95% CI: 1.97–3.05, $p<.001$
TomTec	Composite of heart failure hospitalization, heart transplant and cardiovascular death ($n=111$, 14%)	8 (4–11) years	Right heart hemodynamic score, including RVGLS LVGLS	Validation cohort: Right heart hemodynamic score, per unit, HR: 1.51, 95% CI: 1.32–2.04 LVGLS, per unit increment in cox model, HR: 1.1, 95% CI: 1.02–1.23
Qlab 9.0 Philips TomTec	Cardiopulmonary death $n=22$ (27%)	23 (3–32) months		RVFWTS, for % worsening (less negative), HR: .94, 95% CI: .89–.98, $p=.03$
TomTec	Ventilatory efficiency (VE/VCO_2 slope) after TPVR	6 months after TPVR		RVLS, % ($r=-.60$, $p<.001$)

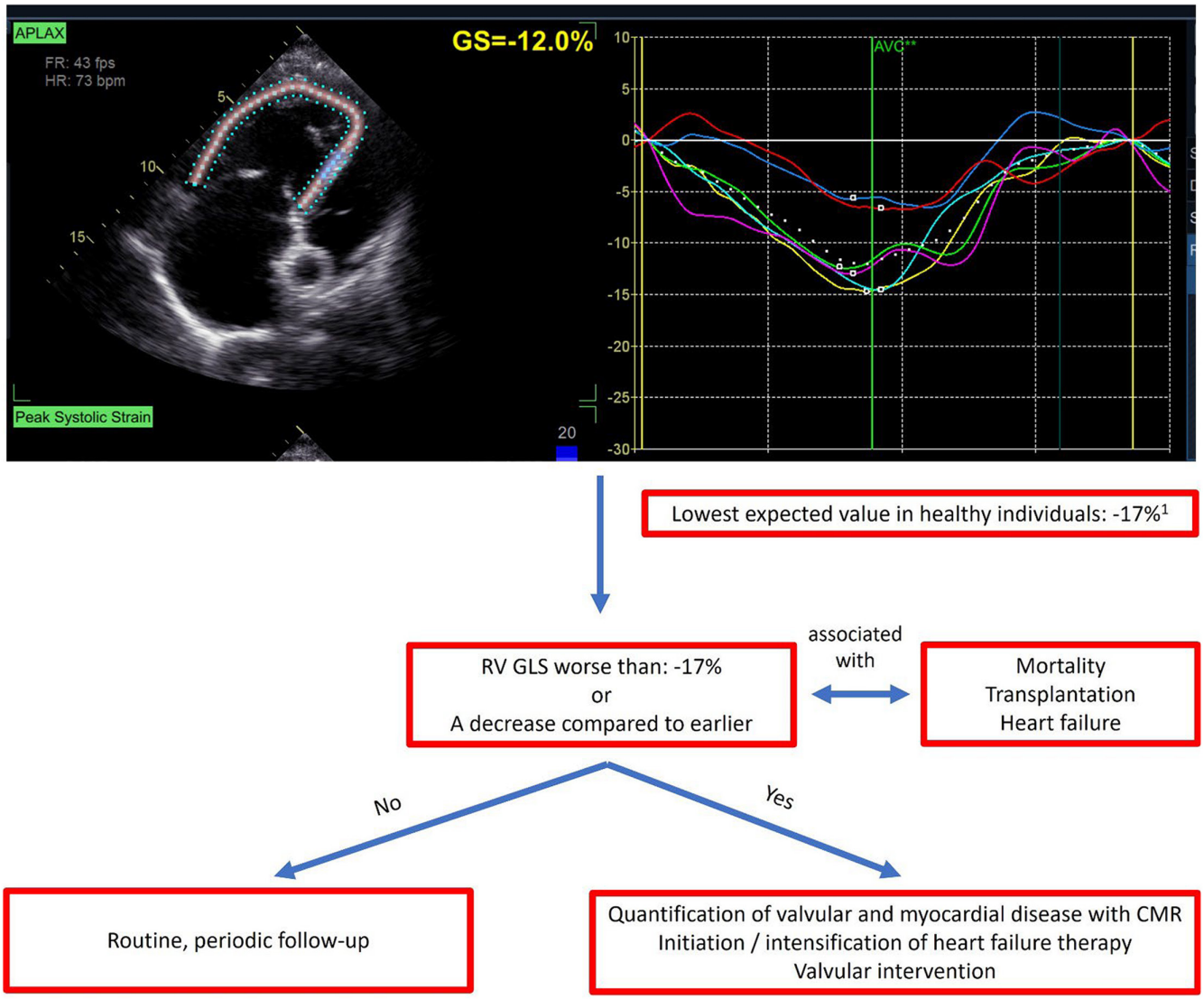

FIGURE 2 Strain assessment of the systemic right ventricle in patients with a congenital corrected transposition of the great arteries or after an atrial switch operation, and potential implications. CMR, cardiac magnetic resonance; RV GLS, right ventricular global longitudinal strain. [1]As observed by Morris et al[25] in apparently healthy individuals with a systemic right ventricle; more studies are needed to define more robust normal reference values for GLS of the systemic RV.

GLS[13,14] and of RV GLS,[15] in either the total population,[13,15] or with a specific focus on the 371 patients who underwent tricuspid valve surgery.[14] The presence of impaired LV GLS (less negative than −18%) was independently associated with cardiac transplantation or death during a median follow-up of 51 (IQR: 29–86) months, HR: 1.79 (95% CI: 1.25–4.98) in the entire cohort.,[13] It also independently predicted long term post-operative mortality in the patients who underwent tricuspid valve surgery, despite a preserved LV ejection fraction, Table 1.[14]

3.3 | Tetralogy of Fallot

Three unique studies investigated the prognostic value of left and right ventricular strain in patients with repaired tetralogy of Fallot ($n = 710$), Table 1. The assessment of both LV GLS and RV free wall strain (RV FWS) appeared to have clinical value, see for an example Figure 4.

In 413 patients (mean age 36 ± 13 years) Diller et al showed that LV GLS was predictive for the composite endpoint of sudden cardiac death, and life-threatening ventricular arrhythmias during a follow-up of 3 (IQR: 1–4) years: HR for each % improving LV GLS: .87 (95% CI: .77–.99), independently from QRS duration.[16] In the study by Grootel et al including 151 patients with repaired tetralogy of Fallot (median age 33 [IQR: 25–42] years), the composite end-point of death or heart failure (defined as change in heart failure therapy or hospitalization) occurred in 14 (9%) patients during a follow-up of 72 (IQR: 64–75) months.[17] Heart-failure free survival

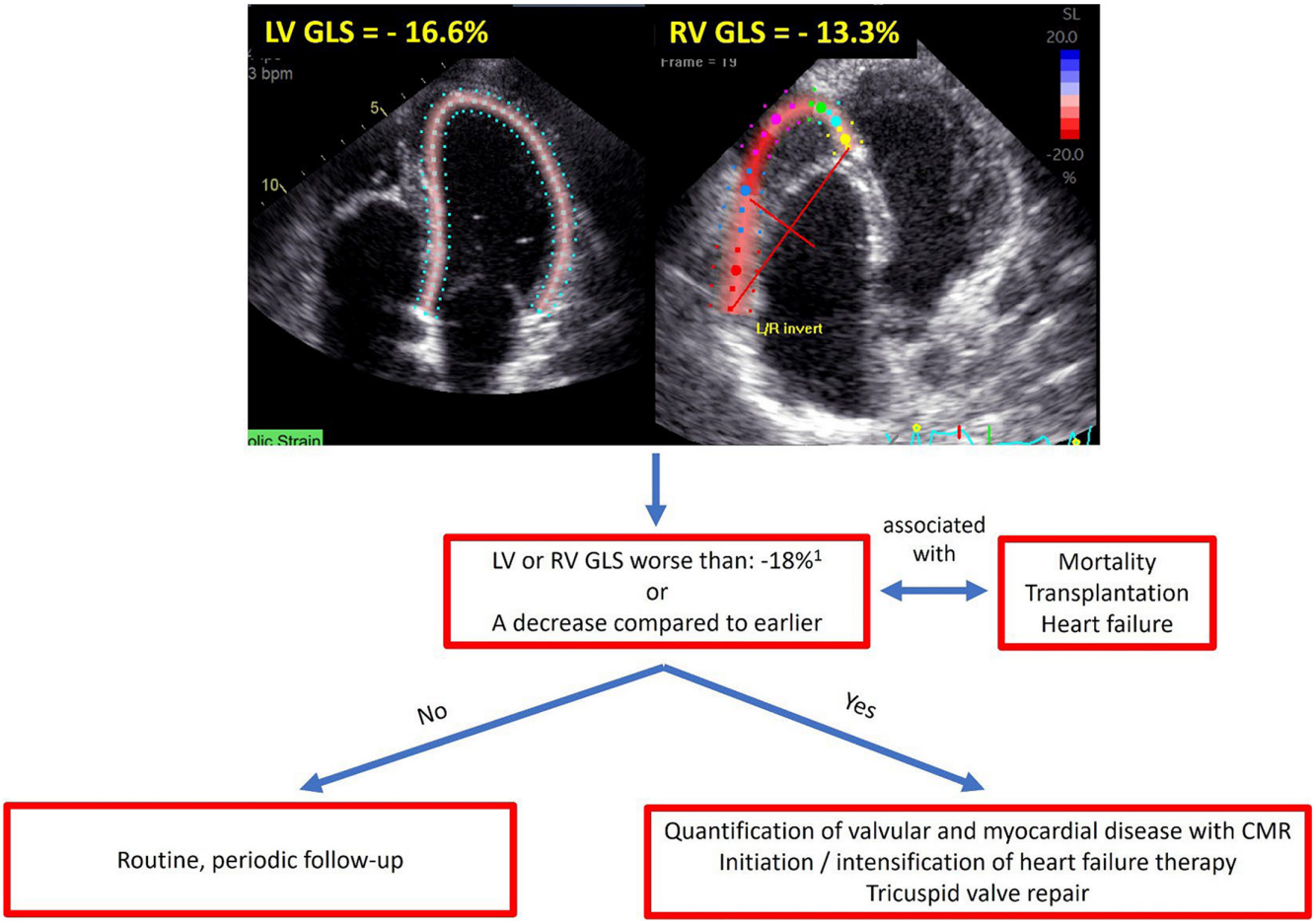

FIGURE 3 Assessment of the left and right ventricular global longitudinal strain in a patient with Ebstein's anomaly, and potential implications. CMR: cardiac magnetic resonance, LV, left ventricular; GLS, global longitudinal strain; RV, right ventricular. [1]As proposed by Egbe et al,[13,15] more studies are needed to define robust normal reference values for LV and RV GLS in patients with Ebstein's anomaly.

was significantly higher in the patients with a preserved LV GLS (more negative than −17.8%) as compared to their counterparts (97% vs. 84%, $p = .004$), and in the patients with better RV FWS values (most preserved tertile vs. most impaired tertile: 100% vs. 81%, $p = .001$), Table 1.[17]

3.4 | Miscellaneous

Rösner et al performed an echocardiographic strain analysis in 110 patients (median 20 [IQR:12–27] years, 11% pacemaker), who had undergone a Fontan procedure, see Figure 5. Of these patients, 39% had a univentricular morphological LV, 33% a univentricular, morphological right ventricle, 6% a univentricular but morphological undefinable ventricle, and 22% had a biventricular system. The dominant ventricles were analysed for longitudinal (apical long-axis) and circumferential strain (parasternal short axis).[9] Furthermore, the strain curve plots were also visually inspected for the extent and synchronicity of contraction. The classic dyssynchrony (CPD) pattern, where earlier systolic contraction of one of the walls results in an opposite-directed outward stretch and subsequent rebound of the opposing wall, and thereby limiting the total extent of contraction of the first contracting wall, was identified in 15% of the patients.[18] The multivariate analyses revealed that the presence of the CPD pattern remained independently associated with the primary endpoint of death or heart transplantation during a follow-up of 85 ± 35 months: HR: 9.4 (95% CI: 3–35). Interestingly, longitudinal and circumferential strain as individual markers of disease were not significantly predictive for transplantation free survival.[9] In a cohort of 821 patients with native ($n = 176$) or repaired ($n = 645$) coarctation of aorta, described by Egbe et al.,[19] LV GLS was independently associated with the composite endpoint of heart failure hospitalization, hear transplantation and cardiovascular mortality, Table 1.

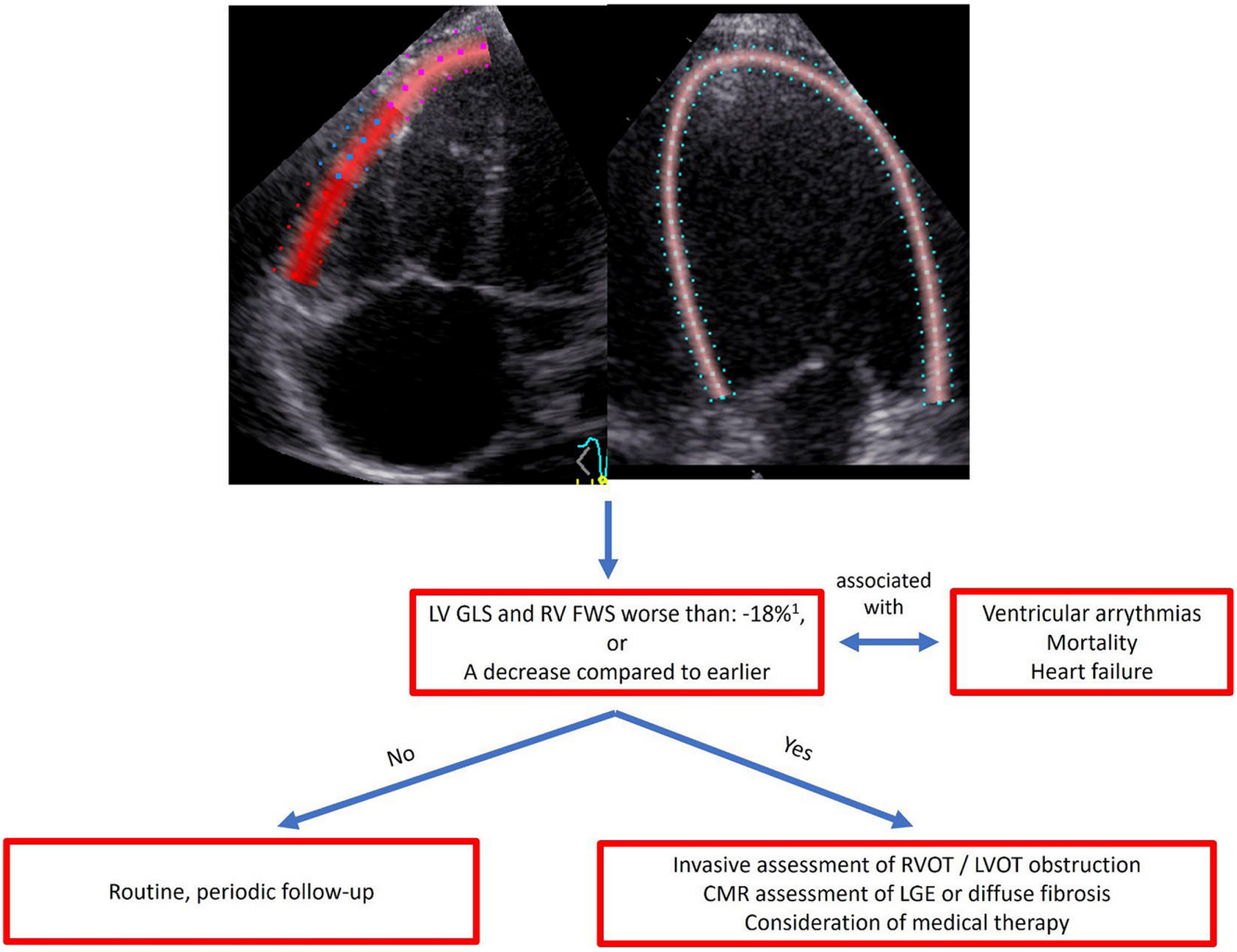

FIGURE 4 Assessment of the left ventricular global longitudinal, and the right ventricular free wall strain in a patient with a repaired tetralogy of Fallot, and potential implications. CMR, cardiac magnetic resonance; FWS, free wall strain; GLS, global longitudinal strain; LGE, late gadolinium enhancement; LV, left ventricular; LVOT, left ventricular outflow tract; RV, right ventricular; RVOT, right ventricular outflow tract. [1]As proposed by Grootel et al,[17] more studies are needed to define robust normal reference values for LV GLS and RV RWS in patients with a repaired tetralogy of Fallot.

4 | DISCUSSION

This systematic review highlights two main findings. First, the clinical value of deformation imaging in ACHD patients is a subject of active research, indicating its growing importance in clinical practice. Second, prognostic mid-term follow-up data on left and right ventricular strain for hard clinical end-points is available for specific subtypes of ACHD. These findings underscore the potential of deformation imaging as a promising tool for risk stratification and clinical decision making in ACHD patients. The current findings also supports the need for multi-centre collaboration to expand the patient cohort and identify disease-specific ranges of strain values that can indicate a clinical benefit for therapeutic intervention.

4.1 | Current implications of strain in ACHD

4.1.1 | Transposition of the great arteries

Patients with a TGA are born with two separate circulations: the right ventricle is connected to the systemic circulation, and the LV to the pulmonic circulation. To survive, shunting at atrial, ventricular or arterial level is required, resulting in a mixed oxygen saturated circulation. Initially, TGA patients underwent surgical repair with an atrial switch procedure, connecting the pulmonic venous atrium to the systemic right ventricle, and connecting the caval veins to the subpulmonic LV. Due to the high systemic afterload posed on the right ventricle, these patients are at high risk for failure of the systemic right ventricle, significant tricuspid regurgitation,

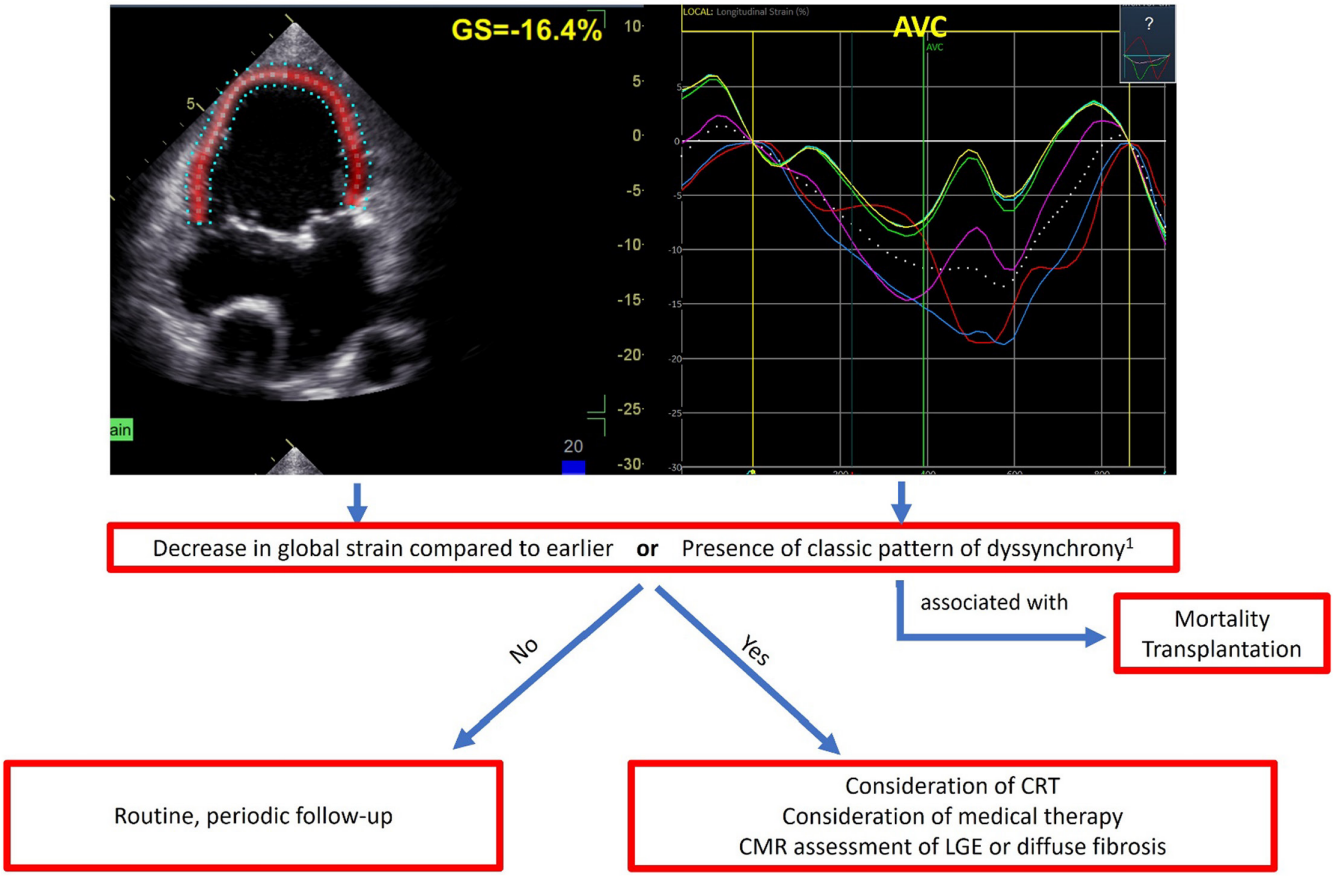

FIGURE 5 Strain assessment of the systemic ventricle in patients with a single ventricle physiology that is palliated with a Fontan procedure, in this example a double inlet left ventricle. AVC, aortic valve closure; CMR, cardiac magnetic resonance; CRT, cardiac resynchronization therapy; GS, global strain; LGE, late gadolinium enhancement. [1]As observed in the study by Rösner et al,[9] more studies are needed to define robust normal reference values for global strain of the systemic ventricle in patients with a single ventricle physiology that is palliated with a Fontan procedure.

pulmonary hypertension, and arrhythmia's. In larger series with follow-up of 40 years, survival ranges from 60% to75%, with only 20% having event-free survival.[1] The therapeutic arsenal for these patients include the treatment with heart failure medications, including sodium-glucose cotransporter 2 inhibitors for which initial promising results on outcome have been observed,[20] the consideration of earlier valvular surgery in the presence of significant tricuspid regurgitation, or eventually, a ventricular assist device or heart transplantation.

Functional assessment of the systemic right ventricle is currently performed with echocardiography using a multiparametric approach (eyeballing, tricuspid annular plane systolic excursion, fractional area change), or with CMR to determine the RV ejection fraction. This review shows that assessment of the GLS of the systemic RV is feasible, and that it provides incremental, functional insights associated with clinical outcomes (heart failure, transplantation, mortality). When observing a temporal decrease in the GLS of the systemic RV, this might argue for earlier consideration of the available therapeutic options. The available studies revealed that a decrease in function as assessed by strain was independently associated with adverse events, but the datasets and number of events were not large enough to identify specific reference values, or cut-off values that could clearly indicate the need for intervention.

Nowadays, patients born with a TGA are operated with the arterial switch operation so that the left and right ventricle pump to the concordant systemic and pulmonic circulation, respectively. While these patients are at risk for supravalvular right ventricular outflow tract (RVOT) obstruction, neo-aortic root dilatation (due to high systemic pressure in the intrinsic pulmonary valve annulus), and potential ischemic problems of the re-implanted coronary arteries, 30-year event-free and overall survival rates are fairly good (80% and >90%, respectively).[1]

This systematic review shows that the evidence for strain assessment in TGA patients after the arterial switch procedure is currently limited to one study, which shows that a decrease in RV GLS is associated with atrial arrhythmia induced heart failure.[12] The scarcity of available studies may, in part, be attributed to the relative low

occurrence of clinical events that patients with TGA experience once there are no major anatomical sequelae after a successful arterial switch operation, as far as is known from the available clinical follow-up. Nonetheless, the use of echocardiographic strain assessment might specifically be helpful in the individuals with significant neoaortic or pulmonic valve disease in order to identify early stages of LV or RV damage. Subsequently, CMR could be used to further quantify the degree of valvular disease and the extent of diffuse myocardial fibrosis, in order to further enhance the clinical decision making regarding a timely valvular (re-) intervention.[1,3]

4.2 | Ebstein's anomaly

In patients with Ebstein's anomaly, the tricuspid valve is characterized by an apical displacement of the septal and posterior leaflets, so that the right ventricle consists of atrial tissue, and the remaining (smaller than normal) functional right ventricle. The clinical presentation and hemodynamic disturbances depend on the extent of atrialization, the severity of tricuspid valve regurgitation, and the contractility of the remaining functional right ventricle, in addition to frequently associated arrhythmias. Indications for surgical correction include progressive right heart dilatation or dysfunction and symptomatic severe tricuspid valve regurgitation.[1] For a comprehensive, volumetric evaluation of RV function and tricuspid valve regurgitation, CMR is the golden standard. Nonetheless, the studies by Egbe et al[13–15,21] from the Mayo clinic demonstrate that also echocardiographic assessment of RV and LV strain can provide prognostic information. A decrease in RV GLS and, due to the distorted septal motion, also in LV GLS is associated with mortality and heart transplantation. These data suggest a role for echocardiographic strain assessment as a first line imaging technique to detect subtle forms of LV and RV dysfunction, which can be further analysed by CMR. Importantly, all strain analyses at the Mayo clinic were performed using TomTec software (TomTec Imaging Systems). Therefore, additional data are required to assess the feasibility of RV FWS and RV GLS assessment in Ebstein patients using different software vendors, as the unconventional RV anatomy might challenge the automated contour recognition algorithms. As the data are derived from a single cohort, multicentre validation is required.

4.3 | Tetralogy of Fallot

The surgical correction of tetralogy of Fallot includes augmentation of the obstructed RVOT and closure of the ventricular septal defect, posing patients at risk for significant pulmonic valve regurgitation, residual RVOT obstruction, LV or RV failure (due to the septal patch) and scar related ventricular arrhythmias. Moreover, a substantial number of patients are treated with a pulmonic valve prosthesis, prone to degeneration. The three studies included in current review provide clues that assessment of RV FWS and LV GLS could enhance the systematic follow-up of patients with repaired tetralogy of Fallot by enabling the early detection of RV or LV damage, associated with heart-failure, mortality and life-threatening arrhythmias.[16,17,22] It is important to realize that although strain imaging is less dependent on loading conditions as compared to ejection fraction, the increased after- or preload by valvular disease still directly influences the ventricular contractility and as a consequence, strain.[23] Therefore, a decrease in strain in the presence of valvular disease can reflect chronic myocardial damage in the form of fibrosis, or a direct effect due to an increased afterload. More data from myocardial work analysis and CMR-derived fibrosis imaging are needed for a more comprehensive understanding of ventricular mechanics in the presence of valvular disease. From a clinical perspective, once a decrease in strain is detected in a patient with tetralogy of Fallot, further invasive hemodynamic assessment of valvular disease or CMR quantification of diffuse fibrosis could help to determine the best treatment strategy regarding valvular intervention, or medical heart failure treatment.

Regarding the risk for ventricular arrhythmias in patients with tetralogy of Fallot, further research studying strain curve patterns might reveal deeper insights into the relationship between mechanical dispersion and the risk of ventricular arrhythmia's, These data could help to identify those patients who could benefit from electrophysiological investigation, prophylactic ventricular ablation or defibrillator therapy.[4]

4.4 | Future directions

A decrease in ventricular strain indicates (subclinical) myocardial dysfunction, which might prompt consideration for heart failure medication, resynchronization therapy in the presence of conduction abnormalities, or transcatheter/surgical intervention when impending volume or pressure overload due to structural heart disease. Before deformation imaging could be adapted in the clinical decision-making process regarding ACHD patients, there are some steps that need to be taken. First, it is crucial to establish normal values of LV and RV strain specific to the subtypes of ACHD, as these might differ for example between patients with a repaired tetralogy of Fallot and patients after an atrial switch for TGA. For this purpose, feature tracking CMR is a promising development,

enabling strain measurements from the routinely acquired cine images.[24] Correlating CMR feature tracking analysis with the degree and severity of diffuse and irreversible fibrosis will help to define normal ranges strain values. More data are needed to clarify the correlation between CMR and echocardiography derived strain values.

Second, comparing strain analyses before and after medical and surgical intervention can help to identify the most optimal strain ranges associated with a preservation or improvement in ventricular function. Subsequently, prospective studies comparing follow-up and intervention guided by strain values versus standard care can provide valuable insights into the true clinical impact of standard strain assessment during follow-up.

To ensure a sufficient number of patients for these analyses, and to enable validation, multicentre collaboration is pivotal.

4.5 | Limitations

All studies were retrospective cohort studies, and this study design inherently leads to inclusion bias. To increase the total population, several studies comprised heterogenous populations, including for example both patients with a congenitally corrected TGA and patients after an atrial switch operation to study the prognostic implications of GLS of the systemic right ventricle. This strategy might constrain the interpretability for the specific subgroups.

Before initiating multicentre corroboration studies, harmonization of study protocols and overcoming several limitations are essential. From the included studies in this review, it becomes clear that various software vendors were used for the strain measurements. Although that it has been demonstrated that the intervendor differences are small for global measurements in acquired heart diseases, the differences between software packages might remain an important concern in patients with abnormal anatomy as in congenital heart disease. The reproducibility of the strain measurements was not systematically provided. Furthermore, the included studies focused mainly on LV GLS, and RV GLS and FWS; additional insights might be provided by concomitant assessment of radial and circumferential strain.

5 | CONCLUSIONS

Deformation imaging of the left and right ventricle is associated with mid-term prognosis in various types of ACHD, making it a potential additional parameter in clinical decision making, alongside clinical variables and conventional imaging. Current research primarily involves patients with a systemic right ventricle and TGA, Ebstein's anomaly, and tetralogy of Fallot. Future research, combined with CMR, could concentrate on establishing normal strain values specific to each type of congenital heart disease and determining optimal strain ranges that indicate the most opportune timing for intervention.

AUTHOR CONTRIBUTIONS

PJR, KT, MJC and HBZ conceptualized and planned for the systematic review. PJR and KT did the systematic literature search and article inclusion. PJR, KT, MG, AJT, PH, GS, MJC and HBZ supported the analysis write-up and review of the manuscript. All authors approved the final manuscript for submission.

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CONFLICT OF INTEREST STATEMENT

The authors declare no relationship with industry and financial associations relevant to the content of this paper to disclose.

DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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