Original Article

Preoperative right ventricular longitudinal strain as a prognosticator of postoperative residual or recurrent tricuspid regurgitation in Ebstein anomaly: a cardiovascular magnetic resonance study

Xiahui Tian[1,2], Yuelong Yang[1], Xinyi Luo[1,3], Liqi Cao[1], Xiaobing Zhou[4], Huanwen Xu[1], Rui Chen[1], Ruohong Luo[1,5], Hui Liu[1,6]

[1]Department of Radiology, Guangdong Provincial People's Hospital (Guangdong Academy of Medical Sciences), Southern Medical University, Guangzhou, China; [2]Department of Radiology, Zhujiang Hospital, Southern Medical University, Guangzhou, China; [3]School of Medicine, South China University of Technology, Guangzhou, China; [4]Department of Radiology, The Fifth Affiliated Hospital of Sun Yat-sen University, Zhuhai, China; [5]Guangdong Cardiovascular Institute, Guangdong Provincial People's Hospital, Guangdong Academy of Medical Sciences, Guangzhou, China; [6]Guangdong Provincial Key Laboratory of Artificial Intelligence in Medical Image Analysis and Application, Guangdong Provincial People's Hospital (Guangdong Academy of Medical Sciences), Southern Medical University, Guangdong Academy of Medical Sciences, Guangzhou, China

Contributions: (I) Conception and design: X Tian, Y Yang, H Liu; (II) Administrative support: H Liu; Y Yang; (III) Provision of study materials or patients: X Tian; (IV) Collection and assembly of data: X Luo, L Cao; (V) Data analysis and interpretation: X Tian, H Xu, R Chen; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Hui Liu, MD. Department of Radiology, Guangdong Provincial People's Hospital (Guangdong Academy of Medical Sciences), Southern Medical University, No. 106, Zhongshan 2nd Road, Guangzhou 510080, China; Guangdong Provincial Key Laboratory of Artificial Intelligence in Medical Image Analysis and Application, Guangdong Provincial People's Hospital (Guangdong Academy of Medical Sciences), Southern Medical University, Guangdong Academy of Medical Sciences, Guangzhou, China. Email: liuhuijiujiu@gmail.com.

Background: The preoperative predictors of residual or recurrent tricuspid regurgitation (TR) after cone reconstruction (CR) remains unclear in patients with Ebstein anomaly (EA). We aimed to determine the predictive value of right ventricular longitudinal strain, assessed using cardiac magnetic resonance (CMR) imaging, for residual or recurrent TR after CR in patients with EA.

Methods: This single-centre, retrospective study analysed data from 48 patients with EA [mean ± standard deviation (SD), age, 35.0±13.6 years; 13 males] who underwent CMR before CR between January 2017 and February 2023. Two-dimensional colour Doppler echocardiography was performed before CR and mid-term (>6 months) after CR to evaluate the degree of TR in patients with EA. Thirty healthy volunteers served as controls. Univariate and multivariate logistic regression analyses were performed to identify CMR predictors of moderate or severe TR >6 months after CR.

Results: Mid-term postoperative results revealed severe, moderate, and mild TR in 8 (17%), 7 (15%), and 33 (69%) patients, respectively. For patients with EA and moderate or severe TR after CR, left ventricular global longitudinal strain (GLS), left ventricular ejection fraction, right ventricular global longitudinal strain (RVGLS), and right ventricular ejection fraction (RVEF) were significantly worse compared to patients with mild TR (all $P<0.05$). Multivariate logistic regression analyses revealed that RVGLS was independently associated with moderate or severe TR >6 months after CR [odds ratio (OR) 1.193, 95% confidence interval (CI): 1.025–1.388; P=0.02].

Conclusions: RVGLS was a significant predictor of moderate or severe TR >6 months after CR. This finding emphasizes that early and accurate measurement of RV function may help to identify patients at high risk for severe residual or recurrent TR.

Keywords: Ebstein anomaly (EA); cardiac magnetic resonance (CMR); global longitudinal strain (GLS); tricuspid regurgitation (TR)

Submitted Feb 06, 2024. Accepted for publication Jul 03, 2024. Published online Aug 05, 2024.
doi: 10.21037/cdt-24-63
View this article at: https://dx.doi.org/10.21037/cdt-24-63

Introduction

Ebstein anomaly (EA) is a rare congenital heart malformation (1), characterized by abnormally formed and apically displaced leaflets of the tricuspid valve (TV). Apical displacement of the TV means that the right heart consists of a morphological right atrium (RA), an atrialized portion of the right ventricle (RV), and the remaining functional RV, accompanied by varying degrees of tricuspid regurgitation (TR) (2). Patients with severe TR may experience cyanosis, paradoxical embolism, pulmonary embolism, tachyarrhythmia, and heart failure, requiring surgical intervention. Surgical intervention is inevitable for almost all patients with EA and is the treatment of choice for the lesion (3). Over the past several decades, cone reconstruction (CR) has become the procedure of choice at most centres. The CR procedure uses native valve tissue to reconstruct the tricuspid valve with a circumferential "cone" of tissue that is reattached at the anatomic annulus, thereby creating the most anatomic repair. The RV is then longitudinally folded at the posterior wall to exclude the atrialized portion of the RV, thus reducing the volume of the RV and the diameter of the annulus. However, postoperative residual or recurrent TR is a common complication, and reintervention may become necessary for recurrent TR (2).

Highlight box

Key findings

- Right ventricular global longitudinal strain (RVGLS) was a significant predictor of moderate or severe tricuspid regurgitation (TR) >6 months after cone reconstruction (CR) in patients with Ebstein anomaly (EA).

What is known and what is new?

- Right ventricular function and myocardial strain decreased in patients with EA.
- RVGLS provided independent prognostic value for predicting moderate or severe TR >6 months after CR in patients with EA.

What is the implication, and what should change now?

- Early and accurate measurement of right ventricular function may help to identify patients at high risk for severe residual or recurrent TR, and further large clinical trials need to address to confirm this conclusion.

It is well-known that severe TR imposes a volume overload on the RV that can lead to progressive RV dilation and dysfunction (4,5). Persistent postoperative TR in patients with EA can lead to right ventricular dysfunction and right heart failure, thus negatively affecting prognosis (6). Therefore, early identification of patients at high risk of postoperative TR is particularly important and may help guide clinical management. However, risk factors for residual or recurrent TR after CR have not been studied in patients with EA.

Abnormalities of myocardial strain may provide the earliest evidence of right ventricular dysfunction (7). Cardiac magnetic resonance (CMR) imaging is the currently accepted reference standard for assessing cardiac size and function in patients with congenital heart disease (8). CMR feature tracking (CMR-FT) techniques enable assessment of strain from routine cine-images without specialized pulse sequences. CMR has prognostic value and utility for the evaluation of patients with EA before and after surgery because it offers unrestricted views for assessment and quantification of the dilated right heart, and left ventricle (LV), RV, and TV function (2,9). Recent studies have correlated CMR-derived parameters with heart failure markers and/or exercise capacity in patients with EA (10,11), describing its prognostic value in those with unrepaired EA (12). However, the predictive value of CMR-derived strain parameters for postoperative residual or recurrent TR in patients with EA has not been determined.

As such, the purpose of this study was to identify the predictive value of right ventricular longitudinal strain for postoperative recurrent or residual TR using CMR imaging. We present this article in accordance with the STARD reporting checklist (available at https://cdt.amegroups.com/article/view/10.21037/cdt-24-63/rc).

Methods

Study population

The present investigation was a single-centre retrospective study performed at the Guangdong Provincial People's Hospital (Guangzhou, China). Data from adolescent and adult patients with EA (age ≥10 years), who underwent CR surgery with preoperative CMR examinations between

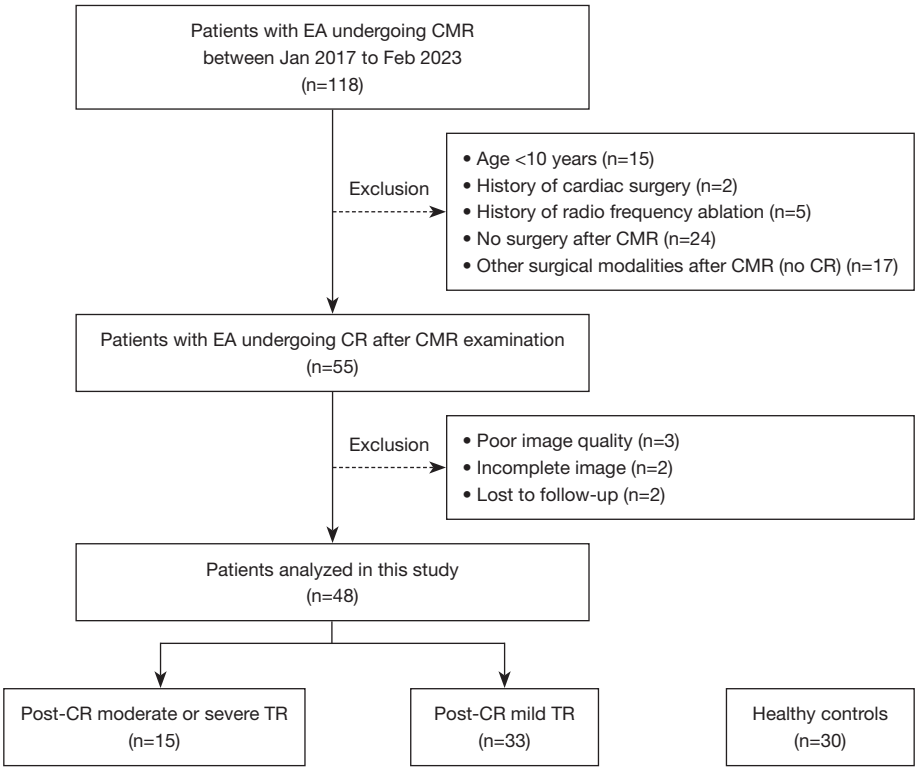

Figure 1 Flowchart depicting patient inclusion criteria. EA, Ebstein anomaly; CMR, cardiovascular magnetic resonance; CR, cone reconstruction; TR, tricuspid regurgitation.

January 2017 and February 2023, were retrospectively reviewed. Diagnostic criteria for EA were in accordance with current guidelines (2). The indications for operation included 1 or more of the following: symptoms or deteriorating exercise capacity, cyanosis, paradoxical embolism, progressive cardiomegaly on chest X-ray, and progressive RV dilation or reduction of RV systolic function. Two-dimensional colour Doppler echocardiography was performed in all patients before CMR examination to confirm the diagnosis of EA and evaluate the degree of TR. Patients with following conditions were excluded: (I) age <10 years; (II) history of cardiac surgery; (III) history of radiofrequency ablation; (IV) no surgery after CMR; (V) other surgical modalities after CMR; (VI) poor image quality; (VII) incomplete imaging data; (VIII) those lost to follow-up. Ultimately, 48 patients with EA were included (*Figure 1*). In addition, 30 age- and sex-matched (no significant differences) healthy volunteers without cardiovascular risk factors, clinical symptoms, cardiovascular disease or abnormal electrocardiograms, who underwent CMR scanning in the authors' hospital, were included as controls. The purpose of CMR scanning in healthy controls was to assess whether there were differences in CMR parameters between EA patients and healthy controls. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Institutional Review Board of Guangdong Provincial People's Hospital (No. 2019338H[R2]). Given the retrospective nature of the study, requirements for informed consent were waived.

Echocardiographic measurements

Patient history, treatment, and echocardiographic results were retrieved from medical and hospital records. Two-dimensional colour Doppler echocardiography (EPIQ Diagnostic Ultrasound System CVX, Philips Healthcare, Erlangen, The Netherlands; Vivid E95 Echocardiography System, GE Healthcare, Chicago, IL, USA) were performed before CR and >6 months after CR to evaluate the degree of TR. The distal jet area of TR on two-dimensional colour Doppler images was used to semi-quantitative estimate of TR severity (13). Recurrent or recurrent TR identified by post-operative echocardiography. Residual or recurrent

severe, moderate, and mild TR were defined by TR distal jet areas of >10, 5–10, and <5 cm^2, respectively.

CMR image acquisition

All CMR examinations were performed on a 3.0 Tesla scanner (Ingenia, Philips Healthcare, Erlangen, The Netherlands) equipped with a 32-coil element. The study consisted of cine imaging, T1 mapping and late gadolinium enhancement (LGE) imaging. A single-shot balanced steady-state free-precession sequence was used for cine acquisitions. A stack of short-axis planes from the apex to the base, along with long-axis planes (2-, 3-, and 4-chamber views) was collected. LGE imaging was acquired 10 minutes after injection of gadopentetate dimeglumine. LGE imaging was performed in the long-axis views and short-axis slices covering the entire LV region. Detailed parameters of the cine and LGE sequences are provided in the Supplementary file (Appendix 1).

CMR image analysis

All CMR cine images, T1 mapping, and strain were analysed using a post-processing workstation (cvi42, version 5.13, Circle Cardiovascular Imaging, Calgary, AB, Canada) by experienced cardiologist (X.T., >8 years' experience). The detailed process for conventional CMR parameters and T1 mapping parameters are shown in the Supplementary file (Appendix 1). All long-axis slices (2-, 3-, and 4-chamber views) and short-axis slices were selected for the CMR feature tracking strain analysis. Details of the process for the strain parameters are described in the Supplementary file (Appendix 1). In line with Mayo Clinic's standard method, we include the atrialized RV (aRV) since this could give more insight into volume and function changes and make it a more reproducible method (14).

Reproducibility analysis

Twenty patients with EA were randomly selected for reproducibility assessment of strain and T1 mapping measures. For intra-observer variability, the same investigator analysed the samples at least one month later, and was blinded to the initial results. For inter-observer variability, another investigator (Y.Y., >8 years' experience), who was blinded to the clinical data and results, analysed the same samples.

Statistical analysis

Normality of the continuous variables was tested using the Shapiro-Wilk test. Continuous variables are expressed as mean ± standard deviation (SD) and were compared using the unpaired Student's *t*-test. The Wilcoxon signed-rank test was used for continuous data that were non-normally distributed. Comparisons of mean values among the three groups were performed using one-way analysis of variance (ANOVA) or Kruskal Wallis. Categorical variables are expressed as percentage and were compared using the chi-squared test or Fisher's exact test.

Univariate and multivariate logistic regression analyses were performed to identify CMR predictors of moderate or severe TR after CR. Receiver operating characteristic (ROC) curves were used to determine the best cut-off values for predicting moderate or severe TR after CR. The area under the ROC curve (AUC) was calculated to assess the predictive power of the variables of interest at mid-term (>6 months) postoperative moderate or severe TR. Intraclass correlation coefficient with corresponding 95% confidence interval (CI) and Bland-Altman plots were used to assess inter- and intra-observer variabilities. Differences with a two-sided $P<0.05$ were considered to be statistically significant. Statistical analyses were performed using SPSS version 25.0 (IBM Corporation, Armonk, NY, USA) and Prism version 9.0 (Graph-Pad Inc., San Diego, CA, USA).

Results

Study population characteristics

Patients with age <10 years (n=15), history of cardiac surgery (n=2), history of radiofrequency ablation (n=5), no surgery after CMR (n=24), other surgical modalities after CMR (n=17), poor image quality (n=3), incomplete imaging data (n=2), and those lost to follow-up (n=2) were excluded. Ultimately, forty-eight patients with EA were included (*Figure 1*), with baseline clinical characteristics summarized in *Table 1*. The mean ± SD age of the patients was 35.0± 13.6 years, with a predominance of females [35 of 48 (73%)]. New York Heart Association (NYHA) class I and NYHA II predominated in all patients with EA [43/48 (90%)]. Preoperatively, the mean distal jet area of TR was 17.7± 8.8 cm^2 in patients with EA, and severe, moderate, and mild TR was observed in 39 (81%), 8 (17%), and 1 (2%) patients, respectively. Patients with moderate or severe TR after CR exhibited a higher preoperative TR distal jet area, although

Table 1 Baseline characteristics of the study population

Variables	All patients (n=48)	Post-CR moderate or severe TR (n=15)	Post-CR mild TR (n=33)	P
Age (years)	35.0±13.6	34±14.6	35.4±13.2	0.73
Sex				0.05
Female	35 [73]	8 [53]	27 [82]	
Male	13 [27]	7 [47]	6 [18]	
Body mass index (kg/m^2)	1.56±0.16	1.59±0.20	1.55±0.14	0.39
Heart rate (beats/min)	83.2±15.0	80.4±9.7	84.8±16.8	0.31
Symptoms				0.24
Chest distress	12 [25]	3 [20]	9 [27]	
Shortness of breath	8 [17]	5 [33]	3 [9]	
Palpitation	13 [27]	4 [27]	9 [27]	
NYHA class				0.28
NYHA I	24 [50]	4 [27]	20 [61]	
NYHA II	19 [40]	8 [53]	11 [33]	
NYHA III	5 [10]	3 [20]	2 [6]	
NYHA IV	0 [0]	0 [0]	0 [0]	
Electrocardiogram				0.06
Normal	19 [40]	3 [20]	16 [48]	
CRBBB	14 [29]	7 [47]	7 [21]	
IRBBB	9 [19]	3 [20]	6 [18]	
Atrial flutter	2 [4]	2 [13]	0 [0]	
Pre-excitation syndrome	2 [4]	0 [0]	2 [6]	
Carpentier's classification				0.57
Type A	21 [44]	6 [40]	15 [45]	
Type B	21 [44]	6 [40]	15 [45]	
Type C	6 [13]	3 [20]	3 [10]	
Type D	0 [0]	0 [0]	0 [0]	
Distal jet area of TR (cm^2)	17.7±8.8	19.4±9.3	17.0±8.6	0.39
Preoperative comorbidities				0.42
ASD	19 [40]	7 [47]	12 [36]	
PFO	9 [19]	3 [20]	6 [18]	
Cardiothoracic ratio (%)	0.58±0.07	0.60±0.07	0.58±0.07	0.40

Table 1 (*continued*)

Table 1 (*continued*)

Variables	All patients (n=48)	Post-CR moderate or severe TR (n=15)	Post-CR mild TR (n=33)	P
Laboratory exam				
HCT (L/L)	0.41±0.03	0.42±0.03	0.40±0.02	0.20
NT-proBNP (pg/mL)	188.9±435.5	405.7±744.5	90.4±64.2	0.02*
Hemoglobin (g/L)	137.1±13.2	142.2±17.6	134.8±10.2	0.07
Creatinine (μmol/L)	62.2±13.9	71.2±15.0	58.2±11.4	0.001*
Albumin (g/L)	40.0±2.7	40.9±2.2	39.6±2.9	0.14
Total bilirubin (μmol/L)	14.9±5.2	15.6±5.3	14.6±5.2	0.55

Values are mean ± standard deviation or n [%]. *, P values <0.05. NYHA, New York Heart Association; CRBBB, complete right bundle branch block; IRBBB, incomplete right bundle branch block; TR, tricuspid regurgitation; ASD, atrial septal defect; PFO, patent foramen ovale; HCT, hematocrit; NT-proBNP, N-terminal pro-brain natriuretic peptide; CR, cone reconstruction.

the difference was not statistically significant (P=0.39). Regarding Carpentier's classification, preoperative Type A and B predominated, though with no significant difference between the two groups (P=0.57). Patients with moderate or severe TR exhibited significantly higher N-terminal pro-B-type natriuretic peptide (P=0.02) and creatinine (P=0.001) levels. The healthy control group (n=30) consisted of 18 (60%) females and 12 (40%) males, with a mean age of 39.4±8.6 years.

Echocardiographic mid-term TR outcomes after CR

More than 6 months after CR [median follow-up duration, 30.3 months (range, 6–78 months)], severe TR was observed in 8 (17%) patients, moderate TR in 7 (15%), and mild TR in 33 (69%).

Comparison of preoperative CMR parameters

Preoperative CMR features in patients with controls, all EA patients, moderate or severe TR and mild TR are summarized in *Table 2*. For LV parameters in patients with EA, the end-diastolic volume index (EDVi), stroke volume index (SVi), left ventricular mass index (LVMi), and cardiac output (CO) were significantly lower (all P≤0.001), and left ventricular global longitudinal strain (LVGLS) (P=0.006) and left ventricular global radial strain (LVGRS) (P=0.002) were significantly higher compared with those of controls. Although left ventricular ejection fraction (LVEF) in patients with EA was lower, the difference was not statistically significant compared with that of controls (P=0.17). Native T1 values and extracellular volume (ECV) were significantly increased in patients with EA, compared with those of controls (all P<0.001). Regarding RV features in patients with EA, the EDVi, end-systolic volume index (ESVi), SVi, and CO were significantly higher compared with those of controls (all P<0.001). Meanwhile, right ventricular ejection fraction (RVEF) was significantly lower and right ventricular global longitudinal strain (RVGLS) was significantly higher in patients with EA (all P<0.001) compared with those of controls.

As shown in *Table 2*, LVEF (P=0.01) and RVEF (P<0.001) were significantly lower and LVGLS (P=0.004) and RVGLS (P=0.001) were significantly worse in those with moderate or severe TR, compared with those of patients with mild TR. The right ventricular end-systolic volume index (RVESVi) was significantly higher in patients with moderate or severe TR (P=0.008). LVEF (P=0.01) and LVGLS (P=0.004) were significantly impaired in patients with moderate or severe TR, compared with those of mild TR and controls; however, not significantly impaired in patients with mild TR compared with those of controls (P=0.51 and P=0.07, respectively). Native T1 values and ECV were significantly increased in patients with mild TR and moderate or severe TR compared with those of controls (all P<0.001), whereas not significantly different between patients with mild TR and moderate or severe TR (P=0.98 and P=0.06, respectively). RVEF and RVGLS were significantly impaired in patients with mild TR and moderate or severe TR compared with those of controls (all P<0.001).

Table 2 Comparison of preoperative CMR features in patients with controls, all EA patients, moderate or severe tricuspid regurgitation and mild tricuspid regurgitation >6 months after cone reconstruction

Parameters	Controls (n=30)	All EA patients (n=48)	Post-CR moderate or severe TR (n=15)	Post-CR mild TR (n=33)	P value	P_1 value	P_2 value	P_3 value	P_4 value
LV									
EDVi (mL/m^2)	71.7±7.3	62.7±13.1	66.2±18.6	61.1±9.7	0.002*	0.001*	0.13	<0.001*	0.15
ESVi (mL/m^2)	28.8±4.2	25.6±8.8	28.3±12.7	24.4±6.1	0.04*	0.06	0.82	0.02*	0.08
SVi (mL/m^2)	42.8±4.6	36.8±7.4	36.5±8.8	37.0±6.8	0.001*	<0.001*	0.003*	0.001*	0.80
LVMi (g/m^2)	44.1±8.0	33.2±6.0	34.8±5.1	32.4±6.3	<0.001*	<0.001*	<0.001*	<0.001*	0.26
CO (mL)	5.4±1.0	4.2±1.0	4.3±1.4	4.2±0.8	<0.001*	<0.001*	0.001*	<0.001*	0.83
EF (%)	60.2±3.5	58.1±6.1	55.0±6.0	58.9±5.5	0.01*	0.17	0.004*	0.51	0.01*
GLS (%)	−16.6±1.9	−15.1±2.1	−13.6±2.0	−15.5±2.1	<0.001*	0.006*	<0.001*	0.07	0.004*
GCS (%)	−17.6±1.8	−19.0±3.3	−17.6±3.5	−19.6±3.0	0.01*	0.02*	0.98	0.005*	0.02*
GRS (%)	29.8±4.8	34.5±8.0	31.0±8.7	36.1±7.3	0.001*	0.002*	0.59	0.001*	0.02*
Native T1 value (ms)	1,260.9±38.7	1,320.0±51.8	1,320.2±53.7	1,319.8±51.8	<0.001*	<0.001*	<0.001*	<0.001*	0.98
Post contrast T1 value (ms)	613.9±43.3	561.9±54.1	582.2±64.8	552.6±46.6	<0.001*	<0.001*	0.046*	<0.001*	0.06
Extracellular volume (%)	26.8±2.6	34.2±4.2	33.4±4.4	34.5±4.1	<0.001*	<0.001*	<0.001*	<0.001*	0.32
RV									
EDVi (mL/m^2)	77.2±12.0	197.1±94.5	225.6±126.9	184.1±74.2	<0.001*	<0.001*	<0.001*	<0.001*	0.07
ESVi (mL/m^2)	38.8±7.5	130.3±68.8	160.6±86.6	116.6±55.1	<0.001*	<0.001*	<0.001*	<0.001*	0.008*
SVi (mL/m^2)	39.1±6.3	79.4±35.2	81.6±42.2	78.5±32.2	<0.001*	<0.001*	0.002*	<0.001*	0.72
CO (mL)	5.0±1.0	9.5±4.7	10.3±6.0	9.1±4.1	<0.001*	<0.001*	0.004*	<0.001*	0.34
EF (%)	50.3±4,6	40.7±8.1	36.3±5.4	43.4±5.9	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*
GLS (%)	−22.1±5.2	−15.6±4.7	−13.2±3.0	−17.7±3.9	<0.001*	<0.001*	<0.001*	<0.001*	0.001*
LGE presence	0	5	2	3	0.60	0.07	0.36	0.45	0.66

Values are mean ± standard deviation or n. *, P values <0.05. P: difference among controls, post-CR moderate or severe TR and post-CR mild TR groups; P_1, controls *vs.* all patients; P_2, controls *vs.* post-CR moderate or severe TR; P_3, controls *vs.* post-CR mild TR; P_4, post-CR moderate or severe TR *vs.* post-CR mild TR. CMR, cardiovascular magnetic resonance; EA, Ebstein anomaly; LV, left ventricular; EDVi, end-diastolic volume index; ESVi, end-systolic volume index; SVi, stroke volume index; LVMi, left ventricular mass index; CO, cardiac output; EF, ejection fraction; RV, right ventricular; GLS, global longitudinal strain; LGE, late gadolinium enhancement; GCS, global circumferential strain; GRS, global radial strain; CR, cone reconstruction; TR, tricuspid regurgitation.

CMR predictors of mid-term outcome of CR

Univariate and multivariate logistic regression analyses were performed to identify CMR predictors of moderate or severe TR >6 months after CR, with results summarized in *Table 3*. Univariable logistic regression analyses revealed that LVEF (P=0.04), LVGLS (P=0.04), RVEF (P=0.04), and RVGLS (P=0.02) were significantly associated with moderate or severe TR at mid-term postoperative CR. In multivariate logistic regression analyses, RVGLS remained a significant predictor for moderate or severe TR at mid-term postoperative CR [odds ratio (OR) 1.193, 95% CI: 1.025–1.388; P=0.02].

ROC analysis was used to determine the cut-off values for abnormal parameters. Only the cut-off values of the parameters that were significant in the univariate analysis (P<0.05) were evaluated. More than 6 months after surgery, severe TR was detected in 8 (17%) patients, moderate TR in 7 (15%), and mild TR in 33 (69%). The sensitivity

Table 3 Univariate and multivariate logistic regression analyses for moderate or severe tricuspid regurgitation >6 months after cone reconstruction

Parameters	Univariate		Multivariate	
	OR (95% CI)	P value	OR (95% CI)	P value
LV				
EDVi	1.030 (0.982–1.080)	0.23		
ESVi	1.053 (0.975–1.137)	0.19		
SVi	0.990 (0.911–1.077)	0.82		
LVMi	0.929 (0.840–1.027)	0.15		
CO	1.075 (0.581–1.989)	0.82		
EF	0.894 (0.801–0.998)	0.04*	0.922 (0.810–1.049)	0.24
GLS	1.427 (1.011–2.104)	0.04*	1.048 (0.661–1.663)	0.84
GCS	1.212 (0.990–1.484)	0.06		
GRS	0.919 (0.843–1.001)	0.052		
Native T1 value	1.000 (0.988–1.012)	0.98		
Post contrast T1 value	1.011 (0.999–1.023)	0.09		
Extracellular volume	0.934 (0.803–1.087)	0.38		
RV				
EDVi	1.005 (0.998–1.011)	0.17		
ESVi	1.010 (1.000–1.020)	0.06		
SVi	1.003 (0.985–1.020)	0.77		
CO	1.051 (0.926–1.193)	0.44		
EF	0.907 (0.828–0.993)	0.04*	0.946 (0.852–1.050)	0.30
GLS	1.193 (1.025–1.388)	0.02*	1.193 (1.025–1.388)	0.02*

*, P values <0.05. LV, left ventricular; EDVi, end-diastolic volume index; ESVi, end-systolic volume index; SVi, stroke volume index; LVMi, left ventricular mass index; CO, cardiac output; EF, ejection fraction; GLS, global longitudinal strain; GCS, global circumferential strain; GRS, global radial strain; RV, right ventricular; OR, odds ratio; 95% CI, 95% confidence interval.

and specificity in predicting moderate to severe TR were 93% and 68% for RVEF <42.66%, and 93% and 71% for RVGLS >–17.16%, respectively (*Table 4*).

The predictive efficacy of different CMR parameters for moderate to severe TR after CR was evaluated using ROC curve analysis (*Figure 2*). The highest predictive efficacy of moderate to severe TR in mid-term postoperative CR was observed in RVGLS, with an AUC of 0.826.

Measurement reproducibility

Inter- and intra-observer variabilities for measurements of LV parameters [i.e., global longitudinal strain (GLS), global circumferential strain (GCS), global radial strain (GRS), native T1 value, and ECV] and RVGLS were determined in 20 randomly selected patients with EA (Table S1). Intra-observer intraclass correlation coefficient (ICC) (95% CI) for the analysis of LVGLS, LVGCS, LVGRS, RVGLS, native T1 value, and ECV were 0.85 (0.66–0.93), 0.94 (0.86–0.97), 0.94 (0.85–0.98), 0.97 (0.93–0.98), 0.97 (0.92–0.99), and 0.90 (0.78–0.99), respectively. Additionally, the ICC (95% CI) for inter-observer analysis in LVGLS, LVGCS, LVGRS, RVGLS, native T1 value, and ECV were 0.77 (0.52–0.90), 0.93 (0.85–0.97), 0.92 (0.78–0.97), 0.94 (0.87–0.98), 0.92 (0.82–0.97), and 0.81 (0.58–0.92), respectively. The inter-observer reproducibility (ICC ranging from 0.81 to 0.94) of all parameters was slightly lower than the intra-observer reproducibility (ICC

Table 4 Receiver operating characteristic curve analysis for predicting moderate and severe tricuspid regurgitation mid-term after cone reconstruction

Parameters	AUC (95% CI)	Cut-off value	Sensitivity (%)	Specificity (%)
LVEF (%)	0.727 (0.585–0.870)	58.94	87	58
LVGLS (%)	0.741 (0.592–0.891)	–15.00	80	64
RVEF (%)	0.804 (0.679–0.929)	42.66	93	68
RVGLS (%)	0.826 (0.709–0.943)	–17.16	93	71

LVEF, left ventricular ejection fraction; LVGLS, left ventricular global longitudinal strain; RVEF, right ventricular ejection fraction; RVGLS, right ventricular global longitudinal strain; AUC, area under curve; CI, confidence interval.

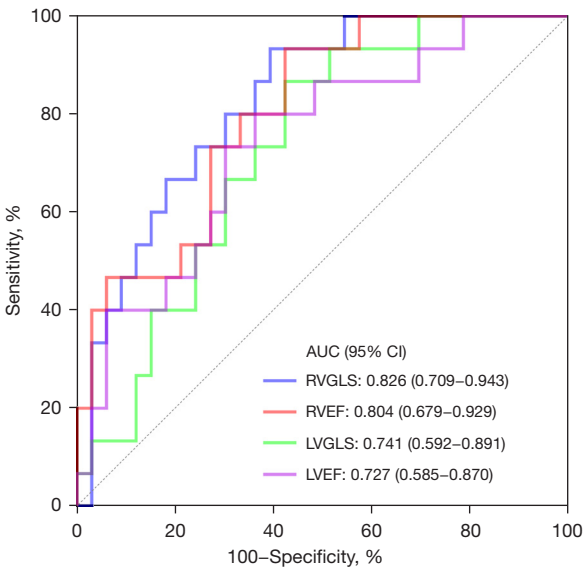

Figure 2 Receiver-operating characteristics curves for predicting moderate or severe tricuspid regurgitation >6 months after cone reconstruction. The highest predictive efficacy of moderate to severe tricuspid regurgitation >6 months after cone reconstruction was observed in RVGLS. AUC, area under curve; CI, confidence interval; RVGLS, right ventricular global longitudinal strain; RVEF, right ventricular ejection fraction; LVGLS, left ventricular global longitudinal strain; LVEF, left ventricular ejection fraction.

ranging from 0.85 to 0.97). These results for ICC indicate strong inter- and intra-observer agreement for the above parameters. Results of Bland-Altman analysis of LVGLS, LVGCS, LVGRS, RVGLS, native T1 value, and ECV are presented in *Figure 3*.

Discussion

To the best of our knowledge, the current study was the first to identify preoperative predictors of residual or recurrent TR in patients with EA using CMR imaging. The major findings of this study are summarized as follows. Firstly, for patients with EA, biventricular GLS and RVEF were significantly impaired, and diffuse myocardial fibrosis was present in the LV. Secondly, patients with EA and moderate or severe TR after CR exhibited significantly worse preoperative biventricular ejection fraction and biventricular longitudinal strain compared to those with mild TR. Thirdly, imaging determined that RVGLS was a significant predictor of moderate or severe TR at mid-term (i.e., >6 months) postoperative CR.

Our data demonstrated that LVEF was not significantly reduced in patients with EA compared with controls, whereas LVGLS was significantly impaired in patients with EA. Over the years, numerous studies have confirmed the feasibility of CMR-FT in the field of deformation imaging and validated its application in strain assessment in the biventricular region (15,16). CMR-derived strain parameters can provide additional information over LVEF for the evaluation of myocardial function. LVEF is a simple global analysis parameter that reflects the integrated assessment of longitudinal, circumferential, and radial functions (17,18); however, it fails to distinguish functional reduction in one of these components (19). Thus, LVEF could often appear normal even in the presence of an abnormal deformation. It is possible that, to some extent, the circumferential function compensates for the reduction in the longitudinal function, ensuring a stable LVEF. Furthermore, patients with EA exhibited increased LVGRS and decreased LVGCS, which may be due to paradoxical motion of the ventricular septum. Our findings demonstrated the presence of more subtle abnormalities in LV systolic function in patients with EA. Meanwhile, preoperative LVEF and the LVGLS were significantly worse in patients with moderate or severe TR after CR compared to those with mild TR. Derangements

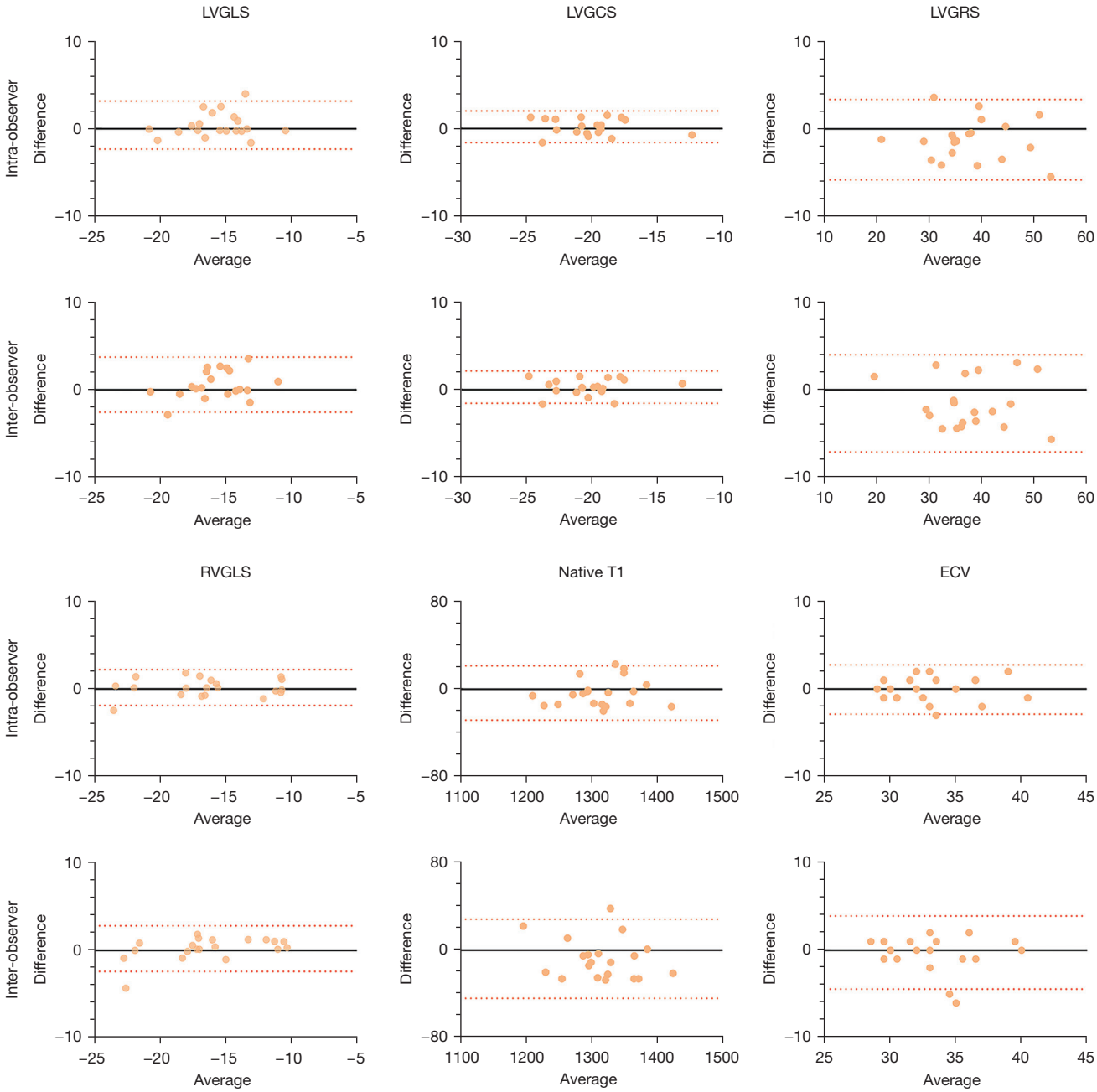

Figure 3 Bland-Altman plots for intra- and inter-observer reproducibility of left ventricular strain and T1 mapping parameters. The above parameters are strongly inter- and intra-observer agreement. LVGLS, left ventricular global longitudinal strain; LVGCS, left ventricular global circumferential strain; LVGRS, left ventricular global radial strain; RVGLS, right ventricular global longitudinal strain; ECV, extracellular volume.

in right heart morphology and function contribute to significant alterations in LV geometry, thus confirming the presence of biventricular interaction. A chronic volume overload of the RV in patients with EA leads to progressive RV dilation and dysfunction (20), and that RV dilatation and abnormal septal motion compress the LV, resulting in LV dysfunction (21).

At the same time, we demonstrated that RVGLS was

significantly impaired in patients with EA compared with controls. EA is understood as not just valve disease but also a myopathic process, and the abnormality with the leaflets are secondary to the myopathy. Shortening of the longitudinal fibers located subendocardially in RV draws the TV toward the apex. Thus, injured RVGLS may affect the function of the TV and thus cause TR. All of the maneuvers that we do in the operating room do not take away the fact that a myopathy is still present. Since this is a disease of the myocardium and results in a myopathy, RV function improvement may be limited (22). TR of varying degrees is present in most postoperative patients.

In our study, diffuse myocardial fibrosis of the LV was observed in adolescent and adult patients with EA. T1 mapping images from CMR is a powerful non-invasive imaging modality to evaluate myocardial fibrosis. The ECV calculated from pre- and post-contrast T1 mapping images exhibited a strong correlation with collagen volume fraction histologically obtained from endomyocardial biopsies (23,24). Previous studies have shown that patients with EA exhibit focal and diffuse myocardial fibrosis in the LV, and autopsy studies have reported that patients with EA of all ages exhibit varying degrees of LV fibrosis (25-27). Diffuse myocardial fibrosis has been implicated as a culprit in ventricular dysfunction in patients with acquired and congenital heart disease (28,29). In the present study, we confirmed that patients with EA exhibited significantly higher T1 and ECV values for the LV than the healthy controls, suggesting the presence of diffuse myocardial fibrosis in the LV. However, there were no statistical differences between patients with moderate or severe TR and mild TR after CR.

Results of this study demonstrated that CMR-FT-derived RVGLS is a significant predictor of moderate or severe TR at mid-term after CR. CR is widely recommended for the treatment of EA; however, the mechanisms of residual or recurrent TR after CR are unclear. Significant TR that reappears after surgical management jeopardizes long-term outcomes after cardiac surgery (30). The RV volume overload caused by TR leads to eventual RV dilation and dysfunction. In addition, RV dilation and dysfunction leads to worsening TR, resulting in a vicious cycle (4,5). Therefore, early identification of patients at high risk for severe residual or recurrent TR is particularly important. This study demonstrated that the feature tracking derived RVGLS is a significant predictor for moderate or severe TR in mid-term postoperative CR and had greater predictive efficacy than RVEF. It highlights the value of evaluating longitudinal strain of RV to provide a more complete assessment of RV function than that provided by RVEF. These are assessed by the gold standard technique of CMR volumetric measurements. The RV wall consists of circumferential fibers and longitudinal fibers, with the longitudinal fibers passing through the apex toward the papillary muscles, tricuspid annulus, and RV outflow tract and are continuous with those of the septum. Shortening of the longitudinal fibers draws the tricuspid valve toward the apex (7). RV longitudinal strain is a parameter, which measures only the shortening of the RV along the base-to-apex direction, which is a consequence of the contraction of the longitudinal myocardial fibers in the subendocardial layer. Due to their subendocardial location, longitudinal fibers maybe more sensitive to disturbance by various pathologies. We have shown that worse RV longitudinal strain is an independent predictor of moderate or severe TR in patients with EA, possibly because it is an early marker of subclinical pathological processes affecting the subendocardial longitudinal fibers. It is worth noting that the aRV is included in the RV volume measurements for analysis of the RV parameters. Therefore, the worse RV longitudinal strain is may partly due to the impaired GLS in the atrialized RV. Prospective studies with a larger sample size are needed to confirm the relationship between aRV and RV longitudinal strain in the future study.

There were some limitations to our study, the first of which were its single-centre retrospective design and relatively small sample size. However, we are prospectively collecting data from patients with EA, and the results of this study are undergoing validation in an ongoing prospective study with a larger sample size. Secondly, selection bias should be addressed because this study included EA patients undergoing CMR imaging and cone reconstructive surgery. Thirdly, we used elevated ECV assessed by CMR to indicate the presence of myocardial fibrosis in the LV, and no histological examinations were performed. However, ECV is accepted as an early and sensitive marker of myocardial fibrosis. Finally, there are limitations in evaluating the severity of TR using jet area. Evaluation of TR severity has been hampered by the lack of a quantitative standard for severity. The echocardiographic examination provides only a semi-quantitative estimate of severity. However, color Doppler flow mapping of TR severity using jet area correlates well with angiographic evaluation and clinical measures of regurgitant severity (13). The CMR-derived indices we found to be associated with residual or recurrent TR after CR in our study should be examined in

future larger studies with a longer period of observation to identify patients at high risk for severe residual or recurrent TR.

Conclusions

In conclusion, this study demonstrated that preoperative assessment of RVGLS using CMR imaging provided independent prognostic value for predicting moderate or severe TR mid-term after CR in patients with EA. This finding emphasizes that early and accurate measurement of RV function may help to identify patients at high risk for severe residual or recurrent TR.

Acknowledgments

Funding: This work was supported by the National Natural Science Foundation of China (Grant No. 82371903) and the Guangzhou Clinical High-tech, Major, and Distinctive Technology Projects (No. 2023P-TS43).

Footnote

Reporting Checklist: The authors have completed the STARD reporting checklist. Available at https://cdt.amegroups.com/article/view/10.21037/cdt-24-63/rc

Data Sharing Statement: Available at https://cdt.amegroups.com/article/view/10.21037/cdt-24-63/dss

Peer Review File: Available at https://cdt.amegroups.com/article/view/10.21037/cdt-24-63/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://cdt.amegroups.com/article/view/10.21037/cdt-24-63/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by institutional review board of Guangdong Provincial People's Hospital (No. 2019338H[R2]). Given the retrospective nature of the study, requirements for informed consent were waived.

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Cite this article as: Tian X, Yang Y, Luo X, Cao L, Zhou X, Xu H, Chen R, Luo R, Liu H. Preoperative right ventricular longitudinal strain as a prognosticator of postoperative residual or recurrent tricuspid regurgitation in Ebstein anomaly: a cardiovascular magnetic resonance study. Cardiovasc Diagn Ther 2024;14(4):563-575. doi: 10.21037/cdt-24-63

