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Usefulness of Right Ventricular Free Wall Strain Obtained with Two-Dimensional Speckle-Tracking Echocardiography in Patients with Repaired Tetralogy of Fallot and Pulmonary Regurgitation

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Right ventricular (RV) dysfunction caused by chronic pulmonary regurgitation (PR) is a major determinant of clinical outcome in adults with repaired tetralogy of Fallot (rTOF). However, the accurate assessment of RV function by conventional echocardiography remains challenging. This study tested the feasibility and usefulness of RV free-wall (RVFW) strain obtained by two-dimensional (2D) speckle-tracking echocardiography (STE) in evaluation of RV function in adults with rTOF by comparing cardiac magnetic resonance (CMR) imaging. We enrolled 22 consecutive patients (male/female, 8/14; mean age, 25.0 years) with rTOF who underwent transthoracic echocardiography at Tohoku University Hospital from July 2016 to June 2019. We measured RVFW strain by STE and compared them with 22 hemodynamically normal subjects (NOR) (male/female, 9/13; mean age, 32.0 years). The correlation between RV strain and CMR-derived RV ejection fraction (RVEF) or PR fraction (PRF) were also evaluated. All rTOF patients had more than moderate PR but were near asymptomatic. RVFW longitudinal strain (RVFW-LS) was significantly decreased in the rTOF group compared with that in the NOR group (−19.6 vs. −24.7, $P < 0.01$). In the rTOF group, RVFW-LS correlated with PRF ($r = 0.44$, $P < 0.05$), whereas RVFW circumferential strain at the mid-ventricular level correlated with RVEF ($r = 0.57$, $P < 0.01$). Intra-observer variability of RVFW strain was acceptable. These results indicate that RV systolic function and PR severity in rTOF could be assessed by RVFW strain measured by 2D STE. This method is feasible and can be used as a complement to CMR imaging.

Keywords: right ventricular free-wall strain; right ventricular function; tetralogy of Fallot; two-dimensional speckle-tracking echocardiography
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Introduction

Tetralogy of Fallot (TOF) is one of the most common causes of cyanotic congenital heart disease with the prevalence of 0.34 per 1,000 live births (van der Linde et al. 2011). Since the first total correction of TOF was reported in 1955, overall mortality has declined over the past several decades and the number of adults with repaired TOF (rTOF) has increased (Cuypers et al. 2014). However, accumulating evidence showed that late cardiovascular complications, such as ventricular arrythmia, heart failure, and sudden cardiac death (SCD), develop even after TOF repair (Gatzoulis et al. 2000; Cuypers et al. 2014). Pulmonary regurgitation (PR) is generally accepted as one of the most important risks for these complications (Khairy et al. 2004; Bouzas et al. 2005; Geva 2006).

PR is commonly observed following surgical repair of TOF, especially in case right ventricular (RV) outflow tract

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is reconstructed using transannular patch. Although young patients with rTOF usually well tolerate PR, RV volume overload from chronic PR causes RV dilation with time, leading to RV dysfunction (RVD). Several studies have shown that RVD in rTOF is associated with poor long-term outcome, including exercise intolerance, arrythmia, and SCD. Current guidelines recommend pulmonary valve replacement (PVR) in advance to avoid poor prognosis before the development of irreversible RVD (Stout et al. 2019; Baumgartner et al. 2021). However, optimal timing for PVR is still controversial due to inadequate knowledge about the exact mechanism for developing RVD in rTOF (Bhagra et al. 2017).

Several echocardiographic parameters have been studied for the assessment of RV function in patients with rTOF, such as RV fractional area change (RVFAC), tricuspid annular plane systolic excursion (TAPSE), isovolumic acceleration time, tissue Doppler-derived tricuspid systolic velocity (S'), and myocardial strain measured by tissue Doppler or two-dimensional (2D) speckle-tracking echocardiography (STE) (Valente et al. 2014). More recently, three-dimensional (3D) STE has been reported (Yu et al. 2014). However, the precise mechanisms by which RVD in rTOF is related to the echocardiographic parameters remain unclear. Many studies included patients with rTOF who had both PR and RVOT obstruction, which might have introduced a bias. Currently, cardiac magnetic resonance (CMR) imaging is the gold standard for the evaluation of RV function (Geva 2011). We hypothesize that we could demonstrate additional values of echocardiographic parameters for more accurate understanding of the mechanisms of RVD due to chronic PR if we analyze only patients with rTOF with PR but without significant RVOT obstruction.

This study tested the feasibility and usefulness of RV free-wall (RVFW) strain obtained by 2D STE in evaluation of RV function in adults with rTOF by comparing CMR imaging.

Methods

The study protocol was in accordance with the ethical guidelines of the 1975 Declaration of Helsinki and approved by the Ethics Committee of the Tohoku University Graduate School of Medicine (No. 2018-1-1003). Informed consent was obtained using the opt-out method.

Study population

We enrolled 22 consecutive patients with rTOF (including one patient with double outlet right ventricle) who underwent transthoracic echocardiography at Tohoku University Hospital from January 2016 to December 2019. Echocardiographic data were compared with 22 age-and sex-matched control subjects (NOR) to assess RV function. To eliminate the possible influence on RV function, we excluded patients with rTOF and significant residual hemodynamic abnormalities other than PR, including RV outflow tract and/or pulmonary stenosis, RV to pulmonary artery conduit (Rastelli type operation), pulmonary hypertension, and significant residual interventricular shunt. Patients who had undergone PVR after initial total correction were also excluded. The NOR group comprised subjects referred for echocardiography mainly for preoperative assessment before non-cardiac surgery.

Clinical data collections

The following baseline demographic information was collected from the medical records: age, sex, height, body weight, body mass index, New York Heart Association (NYHA) functional class, physical examination, laboratory data including brain natriuretic peptide level, 12-lead electrocardiogram (ECG), echocardiography, and CMR imaging. Surgical procedure and history of pacemaker implantation were also collected in rTOF.

Echocardiography

Transthoracic echocardiography was performed using EPIQ 7 ultrasound system (Philips Medical Systems, Andover, MA, USA) with X5-1 broadband phased-array transducer by experienced echocardiographers.

Conventional 2D echocardiographic measurements were obtained according to the American Society of Echocardiography guidelines, including left ventricular (LV) dimensions, left ventricular ejection fraction (LVEF), and RV dimensions. The degree of valve regurgitation was assessed by color-flow mapping and graded as none, mild, moderate, or severe (Zoghbi et al. 2017). RV systolic function was evaluated by four general echocardiographic indices: RVFAC, TAPSE, tricuspid annular systolic velocity (S'), and Tei index. Tei index is also known as myocardial performance index and consists of the sum of isovolumetric contraction time and isovolumetric relaxation time divided by RV ejection time. All indices for RV systolic function were measured according to the American Society of Echocardiography guidelines (Rudski et al. 2010).

Both RVFW longitudinal strain (RVFW-LS) and RVFW circumferential strain (RVFW-CS) by 2D STE were measured in apical four-chamber and three levels of short-axis views, respectively. The data were stored in Digital Imaging and Communications in Medicine files at a frame rate of 50 fps and transferred for offline analysis with TomTec Cardiac Performance Analysis software (TomTec Imaging System, Munich, Germany). After RV endocardial borders were traced manually on the end-systolic frame, the myocardium was divided into six segments in each of the short-axis and the four-chamber plane (Fig. 1A, B) (Khoo et al. 2011). Then, peak systolic strain for RVFW-LS and, basal, mid, and apical RVFW-CSs were calculated.

All echocardiographic analyses were performed by a single experienced operator who was blinded to other clinical data. Intra-observer variability was analyzed by Bland-Altman plots and coefficient of variation (CV) (Takigiku et al. 2012).

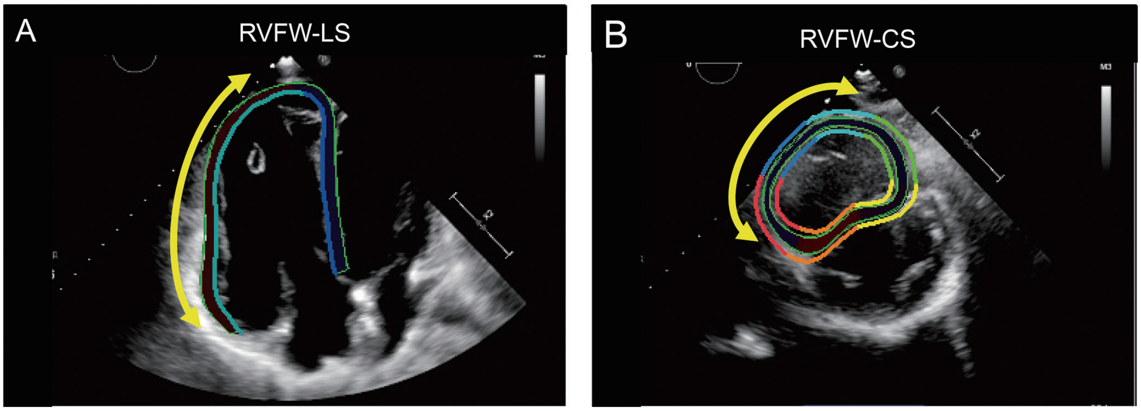

Fig. 1. Representative images of two kinds of right ventricular systolic strain measured by two-dimensional speckle-tracking echocardiography (2D STE).
A. Right ventricular free wall longitudinal strain (RVFW-LS) is obtained from apical four-chamber plane (yellow arrow). B. Right ventricular free wall circumferential strain (RVFW-CS) is measured from the mid-ventricular short-axis plane (yellow arrow).

CMR imaging

CMR was performed only in the group of rTOF using a whole-body 1.5 T MR scanner (Intera Achieva 1.5 T Nova Dual, Philips Medical Systems, Best, the Netherlands) with a five-channel cardiac coil. Cine imaging was obtained using a steady-state free precession sequence (echo time, 3.1 ms; repetition time, 1.5 ms; flip angle, 60°C; slice thickness, 10 mm; number of slices, 20; number of phases per 1 cardiac cycle, 20; field of view, 360 mm; matrix size, 192 × 192). Two-dimensional phase contrast imaging was performed to quantify through-plane blood flow velocity and volume in the main pulmonary artery approximately 1-2 cm above the pulmonary valve.

Quantitative measurement of CMR data was performed using commercially available workstation (ZIO Station 2; Ziosoft, Tokyo, Japan). We measured RV end-diastolic volume, RV end-systolic volume, and RV ejection fraction (RVEF) by tracing RV endocardial in the end-diastolic and end-systolic frames of short axial slices. We also measured pulmonary regurgitant fraction (PRF) from flow time curve in the main pulmonary artery.

Statistical analysis

Results were expressed as mean ± standard deviation (SD), median (interquartile range), or number (%). The difference between two groups was assessed by using an unpaired Student's t-test, Mann-Whitney test, or chi-square test, as appropriate. Linear regression analysis was used to evaluate correlation between variables. To determine the agreement between the two methods, a Bland-Altman plot was constructed. Data were considered to be statistically significant at a P-value < 0.05. All analyses were performed with JMP Pro 15.0. (SAS Institute Inc., Cary, NC, USA).

Results

Clinical characteristics of patients with rTOF

The clinical characteristics of 22 patients with rTOF are shown in Table 1. The median age was 25.0 years and two-thirds were women. The most common procedure for relieving RVOT obstruction was transannular patch used in 17 (77%) patients. One patient (5%) had muscle resection with preservation of the pulmonary valve. The median age at total correction was 3 years, and the median time between total correction and study enrollment was 22.5 years (Table 1). No patients had NYHA III or IV classification. ECG abnormalities were common in patients with rTOF. The mean QRS width was 153 ms, and more than 70% of patients had complete right bundle branch block (Table 1).

Conventional echocardiographic parameters

Table 2 shows the comparison of conventional echocardiographic parameters between the rTOF and NOR groups. In LV parameters, patients with rTOF had significantly decreased end-diastolic dimension and ejection fraction compared with the controls. There were no differences in LV mass index and left atrial volume index. Regarding diastolic function, significant differences were noted in deceleration time of mitral early diastolic velocity and ratio of early trans-mitral velocity to early diastolic septal velocity of the mitral annulus (septal E/e') between the two groups (Table 2).

In RV parameters, the rTOF group had significantly larger diameters of right ventricle and right atria than the NOR group (Table 2). Significant increases in systolic peak flow velocity of RVOT and tricuspid valve regurgitant pressure gradient were noted in the rTOF. Conventional measures for RV systolic function were significantly impaired in the rTOF group compared with those in the NOR group, including RVFAC, TAPSE, and S' (Table 2).

Table 1. Characteristics of the study patients.

	rTOF (N = 22)	NOR (N = 22)
Age (years)	25.0 (22.0-33.0)	32.0 (24.8-40.3)
Female (N, %)	14 (64)	13 (59)
BMI (kg/m2)	23.1 ± 2.9	22.4 ± 5.9
Diagnosis (N, %)		
TOF	21 (95)	
DORV	1 (5)	
Operative procedure (N, %)		
Trans-annular patch	17 (77)	
Muscle resection	1 (5)	
Unknown	4 (18)	
Age at total correction (years)	3.0 (2.0-5.0)	
Time between total correction and study enrollment (years)	22.5 (20.0-27.8)	
NYHA (N, %)		
I/II	22 (100)	
III/IV	0 (0)	
BNP (pg/ml)	6.8 (5.8-27.5)	
Electrocardiography		
HR (beats/minute)	71 ± 10	71 ± 8
QRS width (ms)	153 (104-170)	96 (91-103)
CRBBB (N, %)	16 (73)	0 (0)

Results are expressed as median (interquartile range), number (%) or mean ± SD.
AF, atrial fibrillation; BMI, body mass index; BNP, brain natriuretic peptide; CRBBB, complete right bundle branch block; DORV, double outlet right ventricle; HR, heart rate; NYHA, New York Heart Association functional class; NOR, hemodynamically normal subjects; rTOF, repaired tetralogy of Fallot; TOF, tetralogy of Fallot.

RV speckle-tracking strain analysis in rTOF

Differences of RVFW systolic strains between the rTOF and NOR groups are shown in Table 3. The rTOF group had significantly lower RVFW-LS compared with the NOR group (−19.6 ± 4.1 vs. −24.7 ± 3.0, $P < 0.01$). No difference was noted in RVFW-CS at the basal, mid, and apical levels between the two groups (Table 3).

Correlation between echocardiographic and CMR imaging measurements

Table 4 shows the correlation between 2D echocardiographic parameters and CMR measurements in the rTOF group. CMR-derived RVEF was significantly associated with four 2D echocardiographic parameters, including LVEF ($r = 0.48$, $P = 0.02$), RVFAC ($r = 0.71$, $P < 0.01$), Tei index ($r = -0.59$, $P < 0.01$), and RVFW-CS at the mid-ventricular level ($r = 0.57$, $P < 0.01$) (Table 4 and Fig. 2A). A significant correlation was also noted between CMR-derived PRF and Tei index ($r = 0.51$, $P = 0.02$), and RVFW-LS ($r = -0.44$, $P = 0.04$) (Table 4 and Fig. 2B).

Intra-observer variability of RVFW strain measurement by 2D speckle-tracking echocardiography

The mean bias (95% limits of agreement) and CV were as follows: −0.58 (−1.30 to 0.14) and 6.2% for RVFW-LS, −1.2 (−2.71 to 0.24) and 7.5% for basal RVFW-CS, −0.41 (−1.68 to 0.85) and 9.6% for mid-RVFW-CS, and −1.8 (−3.56 to −0.05) and 13.4% for apical RVFW-CS.

Discussion

In the present study, the relation between RVD in patients with rTOF and significant PR was evaluated using 2D STE. We were able to demonstrate the following: (1) patients with rTOF showed impaired biventricular systolic function compared with the NOR group; (2) among strain parameters, only RVFW-LS was significantly decreased in the rTOF compared with the NOR group; (3) in the patients with rTOF, a significant negative correlation was found between mid-RVFW-CS and CMR-derived RVEF, whereas RVFW-LS correlated negatively with CMR-derived PRF; (4) intra-observer variability of RVFW strain by 2D STE was acceptable. These results indicate that RVD due to chronic PR in rTOF could be evaluated more comprehensively by using both RVFW-LS and RVFW-CS.

Importance of RV function in adult patients with repaired TOF

Along with progress in surgical and medical management, the number of adults with rTOF is increasing

Table 2. Comparison of conventional echocardiographic parameters between the rTOF and NOR groups.

	rTOF (N = 22)	NOR (N = 22)	P value
Left ventricular parameters			
LVDd (mm)	42.7 ± 4.7	46.2 ± 3.8	< 0.01
LVDs (mm)	30.6 ± 4.6	29.5 ± 3.4	0.40
LVEF (%)	56.9 ± 5.5	66.9 ± 4.7	< 0.01
LVMI (g/m²)	63.3 ± 15.1	69.0 ± 13.8	0.20
LAVI (ml/m²)	26.1 ± 8.0	23.7 ± 4.5	0.24
DcT (ms)	187.1 ± 37.4	219 ± 43.7	0.01
E/A	1.9 (1.5-2.4)	1.5 (1.3-1.7)	0.09
Septal E/e’	8.6 (6.7-12.1)	7.3 (6.2-8.6)	0.01
Lateral E/e’	5.8 (4.6-6.6)	5.4 (4.3-6.2)	0.29
Right ventricular parameters			
RVDd (mm)	43.6 ± 6.9	28.6 ± 3.7	< 0.01
RAd (mm)	44.4 ± 8.1	31.6 ± 3.4	< 0.01
Systolic peak flow velocity of RVOT (m/s)	1.6 ± 0.4	0.9 ± 0.1	< 0.01
TRPG (mmHg)	28 .0 ± 8.1	19.1 ± 4.2	< 0.01
RVFAC (%)	39.5 ± 7.7	45.7 ± 3.2	< 0.01
TAPSE (mm)	15.4 ± 3.0	23.1 ± 3.5	< 0.01
S’ (cm/s)	9.0 ± 1.4	12.4 ± 1.8	< 0.01
Tei Index	0.26 (0.17-0.38)	0.24 (0.14-0.30)	0.50

Results are expressed as mean ± SD or median (interquartile range).
DcT, deceleration time of mitral early diastolic velocity; E/A, the ratio of early (E) to late (A) mitral inflow velocity; E/e’, the ratio of early transmitral velocity to early diastolic velocity of the mitral annulus; LAVI, left atrial volume index; LVDd, left ventricular end-diastolic dimension; LVDs, left ventricular end-systolic dimension; LVEF, left ventricular ejection fraction; LVMI, left ventricular mass index; NOR, normal control subjects, RAd, right atrial dimension; RVDd, right ventricular-end diastolic dimension; RVFAC, right ventricular fractional area change; RVOT, right ventricular outflow tract; S’, velocity of the tricuspid annular systolic motion; TAPSE, tricuspid annular plane systolic excursion; Tei Index, the sum of isovolumetric contraction time and isovolumetric relaxation time divided by ejection time; TRPG, tricuspid valve regurgitant pressure gradient. See Table 1 for other abbreviations.

Table 3. Comparison of right ventricular free wall systolic strains between the rTOF and NOR groups.

	rTOF (N = 22)	NOR (N = 22)	P value
LS (%)	−19.6 ± 4.1	−24.7 ± 3.0	< 0.01
Basal CS (%)	−28.8 ± 6.0	−26.6 ± 8.2	0.30
Mid-CS (%)	−26.8 ± 5.9	−24.2 ± 7.6	0.22
Apical CS (%)	−26.6 ± 5.8	−28.2 ± 7.0	0.41

Results are expressed as mean ± SD.
CS, circumferential strain; LS, longitudinal strain.
See Tables 1 and 2 for other abbreviations.

(Cuypers et al. 2014). Accumulating evidence showed that RV dilation due to chronic PR after TOF repair causes RVD with time, leading to late cardiovascular complications, such as ventricular arrythmia, heart failure, exercise intolerance and SCD (Gatzoulis et al. 2000; Khairy et al. 2004; Geva 2006; Cuypers et al. 2014). Thus, to prevent these late complications, accurate evaluation of RV function in rTOF is essential. Although the current guidelines recommend PVR in advance before irreversible RVD develops (Stout et al. 2019; Baumgartner et al. 2021), optimal timing for PVR is still controversial due to inadequate knowledge about the exact mechanism for the development of RV remodeling (Bhagra et al. 2017).

Currently, CMR is the gold standard for evaluation of RV size and function (Geva 2011). Several guidelines recommend RV assessment using CMR as a key factor for determining the timing for PVR in asymptomatic patients with rTOF (Stout et al. 2019; Baumgartner et al. 2021). However, CMR has limitations in terms of cost, availability, routine use in follow-up, and contraindication in patients with pacemakers, implantable defibrillators, and other CMR-incompatible devices. In daily practice, 2D transthoracic echocardiography remains the modality of choice for noninvasive cardiac assessment in rTOF (Valente et al. 2014).

Table 4. Correlation between echocardiographic parameters and CMR-derived RVEF or PRF in the rTOF group.

	CMR-RVEF		CMR-PRF	
	r	P value	r	P value
Left ventricular parameters				
LVDd	−0.07	0.74	0.14	0.52
LVEF	0.48	0.02	−0.16	0.48
DcT	0.16	0.48	−0.14	0.52
Septal E/e’	0.11	0.63	0.28	0.20
Conventional right ventricular parameters				
RVFAC	0.71	< 0.01	−0.12	0.61
TAPSE	−0.12	0.61	−0.06	0.78
S’	0.19	0.40	−0.07	0.74
Tei index	−0.59	< 0.01	0.51	0.02
Right ventricular free wall strains				
LS	0.29	0.19	−0.44	0.04
Basal CS	0.11	0.63	0.05	0.84
Mid-CS	0.57	< 0.01	0.16	0.48
Apical CS	0.06	0.80	0.26	0.24

RVEF, right ventricular ejection fraction; PRF, pulmonary regurgitant fraction; r, correlation coefficient.
See Tables 1, 2 and 3 for other abbreviations.

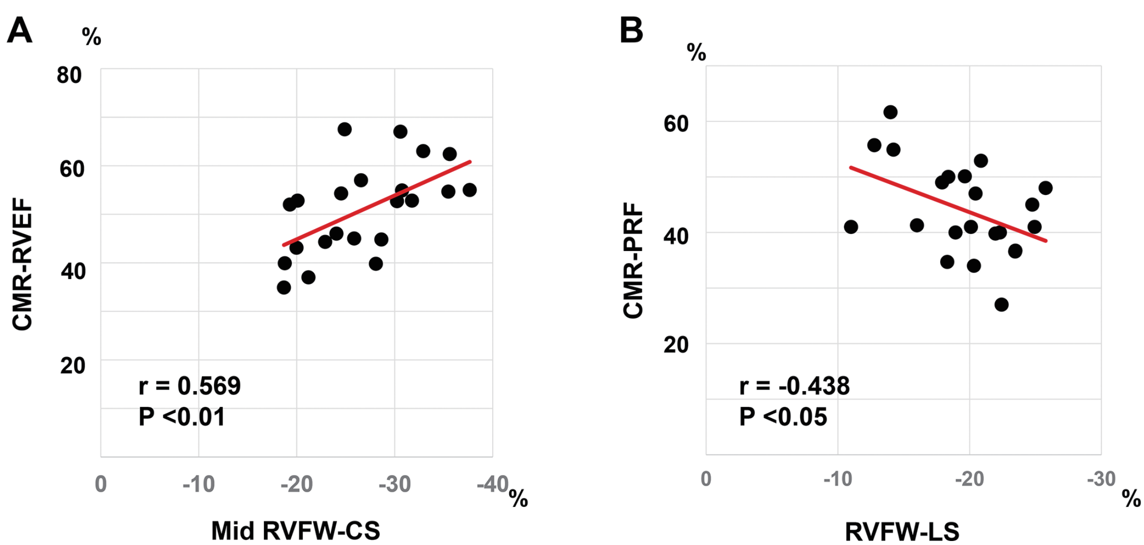

Fig. 2. Correlations between right ventricular free wall circumferential strain at mid-ventricular level (Mid RVFW-CS) and cardiac magnetic resonance imaging-derived right ventricular ejection fraction (CMR-RVEF) (A), and between right ventricular free wall longitudinal strain (RVFW-LS) and CMR-derived pulmonary regurgitant fraction (CMR-PRF) (B).

Although several conventional echocardiographic parameters have been proposed to evaluate RV function in rTOF, such as RVFAC, TAPSE, isovolumic acceleration time and S’ (Rudski et al. 2010; Valente et al. 2014), there is no single echocardiographic parameter that can be consistently used to evaluate RV function in rTOF. One possible explanation for this is that many studies investigating RVD in rTOF examined all subsets of patients, including patients with and without RV outflow tract obstruction. Coexisting RV outflow tract obstruction is reported as a confounding factor in assessing RV function in patients with rTOF with PR (Spiewak et al. 2011).

There is a clear need for better echocardiographic measures for assessing RV function in rTOF. Recently, myocardial deformity by 2D STE has emerged as a more reliable parameter that can measure RV global and regional function. RV global longitudinal strain (RVGLS) has been significantly associated with CMR-derived RVEF and is an independent predictor for prognosis in several cardiovascular diseases, such as pulmonary hypertension, heart failure, ischemic heart disease, and cardiomyopathy (Lee and Park 2018). The present study aimed to evaluate RV function using conventional and 2D STE in adult patients with PR after TOF repair and no significant RV outflow tract obstruction.

RV strain for systolic dysfunction in repaired TOF

A significant impairment of RV function by conventional echocardiography was noted in the rTOF group compared with the NOR group, as in the previous study (Kavurt et al. 2019). Among these conventional echocardiographic methods, there was a significant but moderate correlation between RVFAC and CMR-derived RVEF. Our findings are similar to those of previous studies (Bernard et al. 2014; Kavurt et al. 2019) and may support the notion that RVFAC can be a better parameter over other conventional methods in the evaluation of RV systolic function in rTOF (Savla et al. 2017).

RV strain by 2D STE can measure RV intrinsic myocardial contractility, defined as percentage change in myocardial deformation, and provide both regional and global RV systolic function (Rudski et al. 2010). It has advantages in terms of relative independence of angle insonation and is less affected by volume loading conditions compared to other echocardiographic parameters (Savla et al. 2017). Although most studies have focused on RVGLS (Scherptong et al. 2009; Bernard et al. 2014; Li et al. 2015; Toro et al. 2016; Kavurt et al. 2019), we also evaluated RV circumferential strain to obtain better understanding of the mechanism of RVD in rTOF. Furthermore, we chose not RV global strains but RVFW strains to exclude the effect of septal motion, which may reflect non-RV intrinsic myocardial factors, such as RV conduction delay (Lu et al. 2013).

In the present study, the rTOF group showed significant decrease in RVFW-LS than the NOR group, while there was no significant difference in RVFW-CS at all three levels between the two groups. This may reflect an abnormal RV contraction pattern where longitudinal contraction is more vulnerable than circumferential contraction in patients with rTOF with RVD. Regarding preserved RVFW-CS, there may be a possibility of an adaptive response to the chronic RV volume overload due to PR after TOF repair. Kempny et al. (2012) reported that RV global circumferential strain, measured by CMR feature tracking, is significantly increased in adult patients with rTOF compared with controls, although the exact mechanism remains unknown. Interestingly, they demonstrated significant association between RV global circumferential strain and VE/VCO2 slope, an index of ventilatory inefficiency. Recent studies have showed moderate to good correlation between RVGLS and RVEF derived from CMR imaging in patients with rTOF (Scherptong et al. 2009; Bernard et al. 2014; Toro et al. 2016; Kavurt et al. 2019). However, we were unable to demonstrate significant correlation between RVFW-LS and CMR-derived RVEF. In contrast, we observed moderate correlation between RVFW-CS at the mid-ventricular level and CMR-derived RVEF. The reason for these differences is unclear, but taken together with significant reduction in RVFW-LS in the rTOF group than in the NOR group, RVFW-LS could detect early subtle change in RV systolic function before RVEF declines. Conversely, RVFW circumferential function seems to be a more important determinant of RVEF. Orwat et al. (2016) demonstrated that the correlation between RV global circumferential strain and RVEF is better than that between RVGLS and RVEF in rTOF using CMR feature tracking method. Our findings may suggest that compensatory mechanism to preserve RV circumferential function, especially at mid-ventricular level, where TOF surgery may have less impact, unlike RV outflow tract, contributes to the good correlation between RVFW-CS and RVEF.

Our results could be interpreted in term of anatomy and physiology of the heart. The RV wall is mainly composed of two muscle layers. The superficial fibers of the right ventricle are arranged circumferentially parallel to the atrioventricular groove, whereas the deep muscle fibers are longitudinally aligned from base to apex (Ho and Nihoyannopoulos 2006). Physiologically, the RV stroke volume predominantly depends on longitudinal shortening. In contrast, the LV wall contains obliquely arranged myofibers in the superficial layer, longitudinal myofibers in the subendocardium, and circumferential myofibers in between (Ho and Nihoyannopoulos 2006). Smedsrud et al. (2011) reported reduced longitudinal strain with preserved LVEF and preserved circumferential strain in patients with chronic aortic regurgitation. They discussed that preserved circumferential function might be explained by the compensatory increase in stroke volume due to aortic regurgitation. In addition, the enlarged LV cavity with elevated ventricular wall stress might imply that the subclinical LV dysfunction starts in the subendocardium (Smedsrud et al. 2011). In the course of RVD progression in rTOF, RV volume overload due to chronic PR results in increased ventricular wall stress. Consequently, subclinical RVD in TOF also seems to start in the subendocardial myocardium, which can be reflected by reduced RVFW-LS with preserved RVFW-CS.

We demonstrated significant reduction in both LV end-diastolic dimension and LVEF in the rTOF. It is reported that ventricular interdependence is associated with LV dysfunction in rTOF. Geva et al. (2004) demonstrated the close relationship between LVEF and RVEF in long-term survivors of rTOF. Zervan et al. (2009) in their longitudinal follow-up study, reported that LV diameters of TOF patients after repair were significantly lower than those of normal population at any time. Leftward shifting of ventricular septum in RV volume overload has been suggested as mechanism for LV dysfunction (Louie et al. 1995). Given that myocardial fibers are shared between the two ventricles, LV dysfunction in rTOF could be mainly explained by ventricular interdependence mediated through ventricular septum.

RV strain for PR in repaired TOF

Chronic PR is an important factor associated with RV dysfunction and long-term outcomes in patients with rTOF. Multiple echocardiographic measures have been attempted to better evaluate PR severity, such as PR pressure half time, pulmonary jet to annulus width ratio, and diastolic flow reversal from the branch pulmonary arteries (Valente et al. 2014). However, to date there is no single echocardiographic measure of PR that is used uniformly due to limitations in each method. In the present study, we demonstrated that CMR-derived PRF was significantly associated with RVFW-LS. Previous studies investigating the effect of PR on RV regional function by using tissue Doppler derived RV strain showed conflicting results (Frigiola et al. 2004; Eyskens et al. 2010; Kowalik et al. 2011). Recently, Li et al. (2015) have reported that RVGLS assessed by 2D STE correlates significantly with CMR-derived PRF in pediatric patients with rTOF. STE has its advantages in terms of angle dependency. Our study and those of past studies suggest that RV longitudinal strain by using STE seems to be a better echocardiographic marker for evaluating PR severity than that by using tissue Doppler imaging. Strain has been used for assessing myocardial function. Thus, its application for PR needs to be elucidated by further investigation.

Regarding Tei index, Ibrahim (2014) found that there was no correlation between RV myocardial performance index and PR index, which is inconsistent with our finding. Importantly, we measured PRF quantitatively by using CMR imaging.

Limitations

Several limitations should be mentioned for the present study. First, since this is a cross-sectional study with a small sample size, the possibility of selection bias cannot be ruled out. Second, we enrolled only patients with rTOF with PR but without significant RVOT obstruction, which may not be generalizable to all rTOF population. Third, we did not evaluate 3D STE that have been reported as a more accurate method for assessing RV function in rTOF (Yu et al. 2014). Fourth, CMR RVFW strain analysis is unavailable in our hospital. We were unable to compare RVFW strain between echocardiography and CMR. Finally, we did not collect outcome measures such as morbidity and mortality. Future study needs to be considered.

Conclusion

These results indicate that RVFW-LS and RVFW-CS measured by 2D STE could be useful in evaluating RVD due to chronic PR in adult patients with rTOF. RVFW-LS may be sensitive to detect early subclinical RV myocardial impairment and PR severity, whereas RVFW-CS seems to be a good variable for evaluating RVEF. This method is feasible and can be used as a complement to CMR imaging.

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Conflict of Interest

The authors declare no conflict of interest.

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