Echocardiographic Assessment of Adults with Repaired Tetralogy of Fallot: A Cardiovascular Magnetic Resonance Comparison Study

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Abstract

Background-Surgical management of the tetralogy of Fallot (TOF) results in anatomic and functional abnormalities in the majority of patients. Right ventricular (RV) dilation from pulmonary regurgitation (PR), residual atrial and/or ventricular septal defect, tricuspid regurgitation, right ventricular outflow tract (RVOT) aneurysm, and pulmonary artery peripheral stenosis are some of the abnormalities frequently encountered in patients with repaired TOF. Cardiovascular magnetic resonance (CMR) can provide assessments of anatomical connections, biventricular function, flow measurement, and more, without ionizing radiation. Echocardiography is the most frequently used modality for the initial assessment and follow-up of most patients with CHD. We sought to evaluate adult patients with repaired TOF by transthoracic echocardiography and compare them with CMR.

Methods-156 patients (52 women, mean age= 23 ± 5.5 years) late after TOF repair with severe PR were evaluated. Ventricular size and function and TOF -associated anomalies such as patent ductus arteriosus (PDA), peripheral pulmonary stenosis (PPS), and persistent left superior vena cava (LSVC) were evaluated by transthoracic echocardiography and CMR separately.

Results- Mean of LV ejection fraction by CMR was 52 ± 9 % and by echocardiography was 47 ± 5.1 %. We found a significant correlation between LVEF assessed by CMR and 2D visual assessment in multiple views. Mean of RVEF by CMR was 37± 8 % and RV end diastolic volume index was 161± 57.3 mm^3. Linear correlation between CMR-RVEF and RVEF measured by echocardiography was weak. There was almost perfect agreement between CMR and echocardiography for the diagnosis of LSVC (99.2%). Agreement was 88.3% in the diagnosis of PDA, 66.4% in the diagnosis of PPS, and 93% in the diagnosis of the right aortic arch was.

Conclusion- Adults late after repaired TOF have significantly reduced biventricular systolic function. Despite abnormal LV geometry, visual assessment of LV systolic function by an expert echocardiologist has an acceptable agreement compared to the quantitative measurement of LV systolic function by CMR. However, the correlation between CMR-RVEF and RVEF measured by echocardiography is weak. We found incremental diagnostic value of CMR in PPS and PDA. Atrial septal defect and ventricular septal defect are found more frequently by echocardiography***(Iranian Heart Journal 2011; 12 (2):26-33).***

Tetralogy of Fallot (TOF) is the most common form of cyanotic congenital heart disease (CHD) with a favorable outcome in most patients[1].

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(PR),

Nowadays, we are facing with an increasing number of patients with significant residual PR, late after TOF repair. [2-4] The deleterious effects of longstanding PR on the RV size and function results in an increased risk for severe arrhythmias and sudden death.[5-8] Although right ventricular volume load due to severe PR can be tolerated for many years, there is now evidence that the compensatory mechanisms of the RV myocardium ultimately fail and that if the volume load is not eliminated or reduced by pulmonary valve replacement the dysfunction might be irreversible.

It is, therefore, crucial to assess RV volume and systolic function in these patients. Cardiovascular magnetic resonance (CMR) has evolved during the last 2 decades as the reference standard imaging modality to assess the anatomic and functional sequelae in patients with repaired TOF.[9] Echocardiography (the bedrock of non-invasive cardiac imaging) is the most frequently used modality for the initial assessment and follow-up of most patients with CHD. [10]

In patients with repaired TOF, echocardiography provides the assessment of residual RVOT obstruction, degree of pulmonary regurgitation, residual VSD, RV dilatation and function, left ventricular function, tricuspid regurgitation, peripheral PA stenosis, aortic root size and insufficiency, persistent left SVC, and other associated anomalies. However, CMR is not limited by acoustic window and nor is it associated with exposure to ionizing radiation; furthermore, it is non-invasive. It provides accurate quantitative information on biventricular size and function, blood flow measurements, myocardial viability, and cardiovascular anatomy.

In many centers CMR has become the preferred method of non-invasive imaging in patients with repaired TOF. [11-15] We aimed to evaluate patients with repaired TOF by transthoracic echocardiography and compare them with CMR .

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and pulmonary atresia, pulmonary valve conduit, and patients with any contraindications to MRI were excluded .The study was approved by the institutional ethics committee, and there were no financial or other potentially conflicting relationships to the report.

Echocardiographic evaluation:

All the patients underwent a complete transthoracic echocardiography by an expert echocardiologist using Vivid 3 digital ultrasound system (GE Vingmed, Horten, Norway) with a 2.5 MHZ transducer. LV systolic function was evaluated by 2D visual assessment of the LV in the apical, parasternal long- and short-axis views in transthoracic echocardiography (TTE). The results were then averaged. The RV size and function were assessed based on the ASE guideline. Extra cardiac associated anomalies such as patent ductus arteriosus (PDA), peripheral pulmonary stenosis (PPS), and persistent left superior vena cava (LSVC) were evaluated by TTE right-sided saline injection and were compared with CMR.

CMR

The CMR protocols and technical acquisition parameters used at our institution were identical in all the patients. Clinical studies were analyzed and interpreted by two experienced CMR readers using a 1.5 T machine (Siemens Germany). Measurements of the ventricular systolic function were obtained on the axial views from the base to the apex (12 slices) covering the entire length of the ventricles with manual tracing of the endocardial contours at end systole and end diastole by including papillary muscles and trabeculae in the blood pool. Ventricular volumes and function were measured by ECG-triggered, breath-hold cine steady-state free (SSFP) precession imaging sequences.

Statistical Analysis

The data are described as mean ± standard deviation (SD) for the interval and count (%) for the categorical variables. Linear correlations between the interval variables were determined by the Pearson correlation coefficient (r). Associations between these variables were investigated by simple linear regression models. Associations between the RV function as an ordinal variable and the other echocardiographic parameters were investigated by several univariate or multivariate ordinal logistic regression models. P value<0.05 was considered a statistically significant result. SPSS 15 for Windows (SPSS Inc. Chicago, Illinois) was used for the statistical analyses. STATA 8 SE for Windows (STATA Corporation, Texas, USA) was also used for statistical modeling. Interobserver variability for the RV systolic function was tested by re contouring the right ventricles on 20 CMR studies. Also, there was a high correlation between the two measurements (Pearson's r = 0.90; p value < 0.001).

Results

Background Characteristics

156 patients (52 women) with a mean age of 23 ± 5.5 years (range= 12 to 42 years) participated. Descriptive results of the CMR and echocardiography are presented in Table I.

Assessment of ventricular function by CMR, compared to echocardiography:

LVEF was measured with both CMR and echocardiography (Table I). To investigate the agreement between the methods, the Bland-Altman plot was applied (Fig.1). The plot showed an acceptable agreement between CMR and echocardiography for the LV function assessment. The mean of the LVEF by CMR was 52 ± 9 % and by echocardiography was 47 ± 5.1 %. We found a significant correlation between the LVEF assessed by CMR and 2D visual assessment in multiple views (R = 0.218 and P value= 0.029).

Table I. Background and demographic descriptive data (n = 156)

Characteristic/ Variable	Mean ± SD/ count (%)	Min – Max
Age (year)	23 ± 5.5	12 – 42
Gender (F/M)	52/104	

CARDIAC MAGNETIC RESONANCE IMAGING		
Right Ventricle Ejection Fraction (%)	37 ± 8	12 – 61
Right Ventricle Diameter (cm)	4.5 ± 0.7	3 – 6.6
Right Ventricle End Diastolic Volume (mm^3)	263 ± 96.5	100 – 660
Right Ventricle End Diastolic Volume Index	161 ± 57.3	67 – 360
RVSP	40 ±12.4	25 – 95
PAP	27 ± 12.8	10 – 115
Left Ventricle Ejection Fraction (%)	52 ± 9	20 – 69
Associated Disease		
PDA	14 (9.0%)	
PPS	38 (24.3%)	
LSVC	3 (1.9%)	
VSD	20 (12.8%)	
ASD	3 (1.9%)	
ECHOCARDIOGRAPHY		
Left Ventricle Ejection Fraction (%)	47 ± 5.1	35 – 55
QRS Duration (ms)	147 ± 18.4	110 – 190
Visual Assessment of RV Function		
Mild Dysfunction	3 (1.9%)	
Moderate Dysfunction	11 (7.1%)	
Severe Dysfunction	119 (76.3%)	
Tricuspid Regurgitation		
Mild	40 (25.6%)	
Moderate	38 (24.4%)	
Severe	6 (3.8%)	
Associated Disease		
PDA	3 (1.9%)	
PPS	38 (24.3%)	
LSVC	4 (2.6%)	
VSD	24 (15.4%)	
ASD	9 (5.8%)	
Aortic Arch	9 (5.8%)	
Aortic Root Dilatation	4 (2.6%)	

The right ventricular ejection fraction (RVEF) as an index of the RV function was measured by CMR and its correlation with various echocardiographic parameters was determined. The mean of the RVEF by CMR was 37± 8 % and the RV end diastolic volume index was 161± 57.3 mm^3.

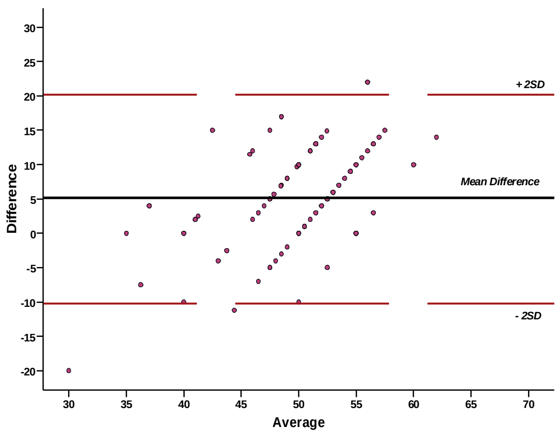

Fig. 1. Bland-Altman plot for agreement between CMR and echocardiography to determine LVEF

Linear correlation between CMR-RVEF and RVEF measured by echocardiography was weak, but statistically significant (Pearson's r = 0.218, p value = 0.029). On the other hand, the function of the RV was assessed visually by echocardiography and the dysfunction was determined and ranked as mild, moderate, and severe. A reverse association existed between the severity of RV dysfunction and CMR-RVEF (p value= 0.001) (Table II).

Table II. Association between right ventricular ejection fraction assessed by CMR and visual assessment of right ventricle function from echocardiography

	RVEF % (Mean ± SD)	P value
Visual Assessment of RV Function		0.003
Mild Dysfunction (n = 3)	41 ± 4	
Moderate Dysfunction (n = 11)	45 ± 6.4 *	
Severe Dysfunction (n = 142)	37 ± 7.9 *	
		0.001
Mild & Moderate Dysfunction	44 ± 6.1	
Severe Dysfunction	37 ± 7.9	

* significant difference in pairwise comparison (Bonferroni post-hoc test, p = 0.003)

The linear regression models for the association between the right ventricle diameter in echocardiography and CMR parameters are demonstrated in Table III.

Table III. Linear regression models for the association between right ventricle diameter in echocardiography and CMR parameters †

Model No		r *	Model r^2	Model β ± SE	P value for β	constant
1	RVEDV	0.631	0.398	0.005 ± 0.001	<0.001	3.22
2	RVEDVI	0.579	0.335	0.007 ± 0.001	<0.001	3.33

* Pearson's Correlation Coefficient
† RV diameter measured by echocardiography as dependent variable

Association between RV parameters in CMR and the diameter of right ventricle, visually assessed by echocardiography, is summarized in Table IV.

Table IV. Association between RV parameters in CMR and the diameter of right ventricle, visually assessed by echocardiography

	RV enlargement (Mean ± SD)			P value
	Mild (n = 3)	Moderate (n = 11)	Severe (n = 117)	
RVEDV	149 ± 57.4 *	174 ± 37.5 †	281 ± 94.8 *, †	<0.001
RVEDVI	84 ± 28.6 *	110 ± 28.9 †	171 ± 57 *, †	<0.001

*, † Significant difference in Bonferroni post-hoc test (p <0.005)

Practically, we categorized the measure of CMR-RVEF to 4 sub-groups: normal RV (CMR-RVEF>50%), mild RV dysfunction (CMR-RVEF from 40% to 50%), moderate RV dysfunction (CMR-RVEF from 30% to 40%), and severe RV dysfunction (CMR-RVEF <30%). [16,17] The associations between the categorized RVEF and echocardiographic parameters were investigated by several ordinal logistic regression models.

Agreement between CMR and Echocardiography to Diagnose Patients' Associated Anomalies

Kappa statistics was computed to investigate the agreement of the two diagnostic modalities. It was found that the agreement between CMR and echocardiography for the diagnosis of LSVC was almost perfect (kappa = 0.854, p value <0.001). Agreement in the diagnosis of PDA was 88.3%, in PPS was 66.4%, in LSVC was 99.2%, and in the right aortic arch was 93%. No agreement existed between the two modalities for the diagnosis of PDA and PPS. The findings are summarized in Table V.

Table V. Comparison and agreement between CMR and echocardiography to detect associated anomalies (n = 156)

	Diagnostic Modality		P value*	Kappa ± SE
	Cardiac MR	echocardiography		
PDA	14 (9%)	3 (1.9%)	0.007	0.089 ± 0.105
PPS	38 (24.4%)	38 (24.4%)	0.999	0.130 ± 0.104
LSVC	3 (1.9%)	4 (2.6%)	0.999	0.854 ± 0.144 †
VSD	20 (12.8%)	24 (15.4%)	0.557	0.313 ± 0.103 †
ASD	3 (1.9%)	9 (5.8%)	0.070	0.314 ± 0.175 †

PDA: , PPS: ,LSVC: , VSD: , ASD: * McNemar test † p value <0.001

Discussion

This study provides data on the spectrum of ventricular volumes, function, and associated anomalies in adults with repaired TOF. Furthermore, our study demonstrates the agreement between CMR and transthoracic echocardiography in the evaluation of associated anomalies. We found that most of our adult patients with repaired TOF had severe RV enlargement (117 out of 156, mean of RV end diastolic volume index= 161± 57.3 mm^3). The mean of the RVEF was 37% ±

8, which was significantly reduced. Severe chronic PR was considered an important, treatable cause of RV dilatation and failure. [9] Severe pulmonary regurgitation was associated with substantial right ventricular dilation or dysfunction (i.e., right ventricular diastolic volume index >150 to 170 mL/m2 or a right ventricular ejection fraction <45% has been suggested as indications for pulmonary valve replacement). [18,19]

It shows that most of our adult patients with repaired TOF need pulmonary valve replacement. The mean of the LVEF was significantly lower than normal in the adult patients with repaired TOF, suggesting an unfavorable ventricular-ventricular interaction. The adverse impact of the RV dilatation and dysfunction on the LV geometry and function (both diastolic and systolic) has been demonstrated in patients with congenital heart disease. Ventricular dyssynchrony, both intra- and inter-ventricular, is likely to contribute to adverse RV-LV interaction. [20, 21]

We found an acceptable agreement between CMR and echocardiography for LV function assessment. The mean of the LVEF by CMR was 52 ± 9 % and by echocardiography was 47 ± 5.1 %: It shows a significant correlation between the LVEF assessed by CMR and 2D visual assessment in multiple views. LV systolic dysfunction has been observed in patients with repaired TOF. In the Broberg et al. study, LV systolic dysfunction was found in 21% of adult patients with TOF: 14.4% had mildly decreased and 6.3% had moderately to severely decreased systolic function. LV systolic dysfunction was associated with shunt duration, RV dysfunction, and arrhythmia. [22]

Linear correlation between CMR-RVEF and RVEF measured by echocardiography was weak, but statistically significant (Pearson's $r = 0.218$, p value $= 0.029$). Greutmann et al. found a poor agreement between the echocardiographic visual estimation of the degree of RV dilatation and the degree of RV dilatation on CMR. Visual estimates of the RV size systematically underestimated the RV volumes in patients with moderate or severe RV dilation. [23] Recent publications have shown that the measurement of the tricuspid annulus plane systolic excursion (TAPSE) has better reproducibility than other echocardiographic indices of RV function and a high specificity for detecting abnormal RV systolic function in adults.

Associated anomalies and complications in repaired TOF *may* warrant intervention after repair. Residual atrial and/or ventricular septal defect (VSD), right aortic arch, persistent left SVC, aorto-pulmonary collaterals, patent ductus arteriosus (PDA), tricuspid regurgitation, right ventricular outflow tract (RVOT) aneurysm, peripheral pulmonary artery stenosis (PPS), and tachyarrhythmias are some of the abnormalities frequently encountered in patients with repaired TOF. [9] Our study showed the incremental diagnostic value of CMR in detecting PDA and right aortic arch but TTE with contrast study found more atrial and/or ventricular septal defect. The best agreement was found in the diagnosis of persistent left SVC. Our data confirm the usefulness of performing preoperatively routine CMR in patients with repaired TOF. 24% of our patients had some degrees of peripheral pulmonary artery stenosis; the severity should be estimated by cardiac catheterization. Davlouros et al. reported 14.1% moderate to severe peripheral pulmonary artery stenosis in repaired TOF patients. [24]

Since CMR provides accurate quantitative information on biventricular size and function, blood flow measurements, myocardial viability, and cardiovascular anatomy, in many centers CMR has become the preferred method of non-invasive imaging in patients with repaired TOF. [9,25]

Conclusions

Adults late after repaired TOF have significantly reduced biventricular systolic function. Despite abnormal LV geometry, visual assessment of LV systolic function by an expert echocardiologist has an acceptable agreement compared to the quantitative measurement of LV systolic function by CMR. However, the correlation between CMR-RVEF and RVEF measured by echocardiography was weak. Because CMR is not limited by acoustic window, we found an incremental diagnostic value of CMR in PPS, PDA, and right aortic arch. Atrial and ventricular septal defect were found more by echocardiography. Our data confirm the usefulness of performing both transthoracic echocardiography and preoperatively routine CMR in patients with complex congenital heart disease as in repaired TOF.

Conflict of interest

No conflicts of interest have been claimed by the authors.

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