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Is systemic right ventricular function by cardiac MRI related to the degree of tricuspid regurgitation in congenitally corrected transposition of the great arteries?☆

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ABSTRACT

Background and Methods: Systemic right ventricular dysfunction and tricuspid regurgitation (TR) are frequently encountered in patients with congenitally corrected transposition of the great arteries (CCTGA). Studies using echocardiography have suggested a relationship between the degree of TR and systemic right ventricular dysfunction; however, assessment of systemic right ventricular function by echocardiography is limited. Cardiac MRI (CMR) is the gold standard for volumetric assessment of the systemic right ventricle. We performed a retrospective cohort study at our center evaluating all adult patients with CCTGA who underwent a CMR between 1/1999 and 1/2013 to determine the relationship between the degree of TR and systemic right ventricular function.
Results: Of the 33 patients identified, 12 had ≤mild TR (37%), 13 had moderate TR (40%), and 8 had severe TR (24%). Mean age at CMR was 38 years (23–64). Mean right ventricular ejection fraction (45% vs. 41% vs. 42%, $p = 0.68$) and mean indexed right ventricular end diastolic volume (122 ml/m^2 vs. 136 ml/m^2 vs. 138 ml/m^2 $p = 0.36$) were not significantly different for patients with ≤mild TR, moderate TR or severe TR. The degree of TR was not associated with additional congenital lesions, prior procedures, presence of an intraventricular conduction delay, or decreased left ventricular function.
Conclusion: No association between the degree of TR and right ventricular volume or ejection fraction by CMR was identified. Failure to show worsening function or increased volume with greater degrees of TR suggests that the degree of regurgitation alone may not fully explain the heterogeneity in right ventricular size and function.

1. Introduction

In congenitally corrected transposition of the great arteries (CCTGA) there are both atrio–ventricular and ventriculo–arterial discordance resulting in a systemic right ventricle and a tricuspid systemic AV valve [1,2]. This lesion has been associated with late failure of the systemic right ventricle and varying degrees of tricuspid regurgitation (TR) resulting in significant morbidity and mortality [3,4]. TR has been reported in 20–50% of all patients with congenitally corrected transposition of the great arteries with autopsy studies demonstrating tricuspid valve abnormalities in 91% of all cases [5–7].

Although the etiology of systemic right ventricular failure in patients with CCTGA remains controversial, several studies have implicated tricuspid valve regurgitation as the cause of ventricular dysfunction [8–11]. However, these studies have relied largely on two-dimensional transthoracic echocardiography to delineate right ventricular size and function [5,7,8]. Assessment of the systemic right ventricle by two-dimensional transthoracic echocardiography is difficult because of the lack of reproducible methods for quantitative assessment and the complex ventricular geometry. In contrast, cardiac MRI (CMR) provides more accurate measurements and is now considered the gold standard for volumetric and functional assessment of the systemic right ventricle [12,13]. Using CMR, we sought to determine the quantitative relationships between the degree of TR in patients with CCTGA and right ventricular size and function.

2. Methods

2.1. Patient population

We conducted a retrospective observational study evaluating all patients age 18 years or older with CCTGA who underwent a CMR at the Columbia University Medical Center. Details regarding the patient's diagnosis and associated abnormalities were recorded. A predetermined set of clinical variables and imaging characteristics were defined prior to data acquisition. The Columbia University Medical Center Internal Review Board reviewed and approved this study prior to data acquisition and the study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki.

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2.2. Clinical variables

Information regarding the patient's clinical status was defined via review of electronic and written medical records. Patient specific data including symptoms, medications, and functional status were ascertained from the patient's clinical visit closest to the time of CMR. Functional status was categorized using the New York Heart Association (NYHA) classification. Patients were considered symptomatic if they reported any dyspnea, chest pain, or decreased exercise tolerance. Clinical arrhythmia was defined as sustained supraventricular tachycardia or sustained ventricular tachycardia documented on 12-lead ECG, Holter monitor, or electrophysiology study at any point in the patient's clinical course. The duration of the QRS complex was measured from available ECGs closest to the time of CMR.

2.3. Measurement of tricuspid regurgitation and echocardiographic parameters

Two-dimensional transthoracic echocardiograms (TTE) were reviewed for each patient. The time between each patient's TTE and CMR was recorded. A blinded reader with expertise in echocardiography assessed qualitative right ventricular function, the degree of TR, and the tricuspid apical displacement index for each patient using two-dimensional transthoracic echocardiography. The degree of TR was graded as mild, moderate, or severe using standard techniques. Patients with ≥mild right ventricular dysfunction were classified as having abnormal function by TTE. Tricuspid valves with an apical displacement index greater than 8 mm/m^2 were defined as Ebsteinoid based on prior literature [14]. When a patient had multiple transthoracic echocardiograms, the study closest to the patient's CMR was used.

2.4. CMR image acquisition

For patients with multiple CMRs, the latest CMR was utilized in this study. CMR studies were performed with breath holding and ECG gating at 1.5 Tesla (Signa, General Electric, Milwaukee, WI) using an 8-channel phased array coil for signal reception. Prior to June 2003 short axis cine gradient echo images were obtained with the following parameters: TR/TE/flip angle 8.8/15.2/15°, 8 views per segment, FOV = 30 cm, acquisition matrix 256 × 128, slice thickness 8 mm with no gap, and receiver bandwidth 31.25 kHz. From June 2003 onwards, short axis cine images were acquired using a steady-state free precession pulse sequence (FIESTA) with the following parameters: TR/TE/flip 3.6/1.5/45°, 24 views per segment, FOV = 35 cm, acquisition matrix 192 × 160, slice thickness 8 mm with no gap, and receiver bandwidth 125 kHz. Images were reviewed and analyzed using ReportCARD software (GE Healthcare).

2.5. CMR image analysis

A single reader with expertise in CMR and blinded to clinical status and the results of echocardiography performed CMR image analysis. Cine loops were used to select images at end-diastole (ED) and end-systole (ES). ED was defined as the phase with the largest volume and ES as the phase with the smallest volume for the right and left ventricles independently. Manual tracing was performed on each ED and ES short axis view and summed to calculate right ventricular and left ventricular volumes. By convention, right ventricular trabeculations were considered part of the right ventricular cavity in both systole and diastole. Ejection fraction was calculated using the EDV and ESV values ((EDV − ESV / EDV) × 100%).

2.6. Statistics

Statistical analysis was performed using STATA statistical software (Version 12.1, Stata Corp, 4905 Lakeway Drive, College Station, TX, USA). Univariate analyses comparing discrete clinical variables between degrees of TR were performed using a χ^2 test. A one-way ANOVA was performed to compare the means of continuous variables in groups with different degrees of TR. *P* values <0.05 were considered statistically significant.

3. Results

3.1. Patients

We identified 55 patients with CCTGA seen at the Schneeweiss Adult Congenital Heart Center. Thirty-three of the 55 patients (60%) underwent CMR and 63% were female. Mean age at the time of CMR was 38 (range 23–64) years. Twelve patients (36%) had an Ebsteinoid tricuspid valve. Twelve patients (36%) had associated congenital lesions including pulmonary stenosis in 8 patients (24%), ventricular septal defect (VSD) in 6 patients (18%), atrial septal defect (ASD) in 3 patients (9%), and 1 patient each with pulmonary atresia and coarctation of the aorta (Table 1). Prior procedures are listed in Table 1 and included resection of sub-pulmonary stenosis in 2 patients (6%), VSD closure in 2 patients (6%), ASD closure in 3 patients (9%), LV-PA conduit and VSD closure in 2 patients (6%), and pulmonary valvotomy and VSD closure in 2 patients (6%). Of the patients who underwent CMR, 8 (24%) had severe TR, 13 had moderate TR (40%) and 12 (36%) had mild or less TR. The median time between CMR and TTE was 36 days (interquartile range: 114 days). Of the patients with CCTGA who underwent CMR, 8 patients (24%) went on to tricuspid valve replacement after CMR.

Table 1
Patient characteristics.

	All patients (n = 33)
Gender (female)	21 (63%)
Mean age at CMR	38 years (23–64)
Associated lesions	
Pulmonary stenosis	8 (24%)
Ventricular septal defect	6 (18%)
Atrial septal defect	3 (9%)
Pulmonary atresia	1 (3%)
Coarctation of the aorta	1 (3%)
Prior procedures	
VSD closure	2 (6%)
Sub PS repair	2 (6%)
LV-PA conduit/VSD closure	2 (6%)
Pulmonary valvotomy/VSD closure	2 (6%)
ASD closure	3 (9%)
RF ablation	2 (6%)
Degree of tricuspid regurgitation	
≤Mild	12 (36%)
Moderate	13 (40%)
Severe	8 (24%)
Ebsteinoid tricuspid valve	12 (36%)

VSD = ventricular septal defect, PS = pulmonary stenosis, ASD = atrial septal defect, LV-PA conduit = Left ventricular to pulmonary artery conduit, RF = radio frequency ablation.

Twenty-two of the 55 patients (40%) with CCTGA did not have a CMR. Twelve (54%) patients did not have a CMR secondary to an implanted pacemaker and ten (46%) opted to not have the test. There was no significant difference between the patients who did and did not have a CMR with respect to severity of TR, qualitative systemic right ventricular function by TTE, NYHA classification, cardiovascular symptoms, clinical arrhythmia, eventual tricuspid valve surgery or beta-blocker or diuretic use (Table 2).

3.2. Clinical variables

Clinical data was available on all 33 patients with CCTGA who underwent CMR. Table 3 describes the effect of different degrees of TR on selected clinical variables. Patients with a greater degree of TR were more likely to go on to tricuspid valve surgery, be NYHA class II or higher, report symptomatic dyspnea, and have decreased stamina. We found no association between the degree of TR and medications, arrhythmia burden, QRS duration or prior procedures (Table 3).

3.3. CMR findings

The mean right ventricular ejection fraction (RVEF) by CMR for patients with severe TR was 42% compared to 41% patients with moderate

Table 2
Comparison of characteristics of patients who did and did not undergo CMR.

	CMR (n = 33)	No CMR (n = 22)	*P*-value
≥Moderate TR	21 (64%)	10 (45%)	0.84
Severe TR	8 (24%)	2 (9%)	0.14
RV dysfunction by TTE	12 (36%)	7 (32%)	0.57
NYHA Class ≥II	9 (27%)	3 (14%)	0.48
Any cardiac symptom	22 (66%)	8 (36%)	0.23
Any arrhythmia	10 (30%)	5 (23%)	1.00
Beta blocker use	11 (33%)	6 (27%)	0.83
Diuretic use	3 (9%)	3 (14%)	0.36
Tricuspid valve surgery	8 (24%)	4 (18%)	0.70

CMR = cardiac MRI, TR = tricuspid regurgitation, TTE = transthoracic echo.