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Myocardial strain analysis by cardiac magnetic resonance associated with arrhythmias in repaired tetralogy of Fallot patients

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Abstract

Background Evaluating myocardial function using cardiac magnetic resonance (CMR) feature tracking provides a comprehensive cardiac assessment, particularly a detailed evaluation for patients with repaired tetralogy of Fallot (rTOF). This study aimed to identify factors associated with arrhythmias in rTOF patients utilizing conventional CMR techniques, including myocardial strain measurements.

Methods This single-center, retrospective study included 245 rTOF patients who underwent CMR between 2017 and 2023. Patients were stratified based on the presence or absence of arrhythmias during follow-up. The biventricular strain was assessed using CMR-derived feature tracking. Demographic, clinical, and imaging data were collected, and statistical analyses were performed to identify factors associated with arrhythmic events.

Results The median age at surgery was 5.6 years (range 1–44 years), with the median age at CMR was 27.5 years (range 15–69 years). Over the follow-up period, 25 patients (10.2%) experienced atrial or ventricular arrhythmias. Univariate analysis revealed significant associations between arrhythmic events and older age at surgery and CMR, lower functional class, larger heart size on chest radiograph, and prolonged QRS duration (QRSd). Additionally, arrhythmias were associated with increased right ventricular (RV) volume, reduced RV and left ventricular (LV) ejection fraction (EF), and impaired strain values. Multivariate binary logistic regression, adjusting for age at surgery, NYHA class, QRSd, and cardiothoracic ratio, identified that a lower RV EF (adjusted odds ratio [aOR] 6.97), RV global radial strain (GRS) (aOR 6.68), RV global circumferential strain (GCS) (aOR 6.36), RV global longitudinal strain (GLS) (aOR 3.14), and LV GRS (aOR 3.02) were all significantly associated with arrhythmias.

Conclusion This study highlights the significant contribution of CMR-derived myocardial strain measurements in predicting arrhythmic events in patients with rTOF. In addition to conventional RV EF, strain metrics—particularly those of the right ventricle- emerged as strong, independent predictors of arrhythmias, offering valuable prognostic information for clinical management in this patient population. These findings underscore the importance of

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myocardial strain analysis as a complementary tool to conventional imaging in evaluating arrhythmic risk in rTOF patients.

Clinical trial number Not applicable.

Keywords Tetralogy of Fallot, Myocardial deformation, Myocardial strain, Arrhythmia

Introduction

The tetralogy of Fallot (TOF) represents the most prevalent form of congenital cyanotic heart defect. Over the decades, surgical outcomes have improved significantly for TOF patients, leading to a longer life expectancy. As a result, individuals with repaired tetralogy of Fallot (rTOF) now represent the majority of patients seen in adult congenital heart disease clinics. Lifelong monitoring and early detection of long-term complications are crucial aspects of the management of care for patients with rTOF [1]. Two major issues in rTOF patients are postoperative pulmonary regurgitation (PR) and arrhythmias. Significant PR can lead to right ventricular enlargement (RVE) and decreased RV function. Both RVE and decreased RV function have been identified as predictors of arrhythmic events [2], which can increase the risk of mortality. Timely identification and intervention can potentially prevent ventricular dysfunction, thereby improving exercise capacity and reducing the incidence of arrhythmias [3].

Cardiac magnetic resonance imaging (CMR) plays a significant role in the comprehensive assessment and long-term management of these patients. It offers a non-invasive, high-resolution imaging modality that provides essential insights into both the structural and functional aspects. Through precise quantification of ventricular dimensions and function using CMR, it is possible to determine the optimal timing for pulmonary valve replacement (PVR) and assess the risk of sudden cardiac death [4]. One of the key advantages of CMR is its ability to evaluate myocardial strain. Using deep learning in feature tracking in CMR is increasingly recognized as a powerful tool for both clinical research and practice. The CMR feature tracking offers high spatial resolution and reproducibility, making it particularly useful in patients with complex conditions like rTOF, where other imaging modalities may be less accurate or limited. It also provides a more comprehensive, multidimensional assessment of ventricular function and tissue deformation, enabling the detection of subtle changes in myocardial performance that may not be apparent with conventional metrics like ejection fraction [5, 6]. Feature tracking using CMR is a standardized technique that allows for the non-invasive assessment of myocardial strain and deformation, providing a detailed evaluation of cardiac function [7]. Unlike strain measurements using echocardiography, strain assessment using CMR enables more precise quantification of myocardial mechanics, including longitudinal, circumferential, and radial strain, in both the RV and left ventricle (LV). With its high spatial resolution and reproducibility, CMR feature tracking is particularly useful in patients with complex conditions like rTOF, where other imaging modalities may be less accurate or limited, and more prone to operator dependence. Recent studies have underscored the prognostic value of myocardial strain, particularly LV strain, which is a strong predictor of adverse events, including heart failure and mortality, in various cardiac conditions. In the context of rTOF, LV strain has been associated with outcomes such as arrhythmias and worsening ventricular function [8, 9]. More recently, the role of the right ventricular (RV) strain has also been gaining attention. RV dysfunction is a hallmark of rTOF, and RV strain has been identified as an independent predictor of adverse cardiac events, including heart failure and sudden cardiac death [10, 11]. This is of relevance in rTOF patients, who are often at higher risk of long-term RV dysfunction and arrhythmias due to altered hemodynamics after surgical repair [12].

Traditionally, myocardial strain has been assessed using echocardiography, which remains the most widely accessible method. However, CMR is increasingly regarded as the gold standard for evaluating both RV and LV structure and function, including myocardial strain. Unlike echocardiography, which is subject to user variability and imaging limitations, CMR provides superior tissue characterization and is not limited by acoustic windows or other technical challenges. CMR also allows for more precise measurement of strain in the right ventricle, which is crucial for patients with rTOF who may experience progressive RV dysfunction over time.

However, there is limited information on the role of RV strain in patients with repaired tetralogy of Fallot (rTOF), who are at risk of arrhythmias. Therefore, this study aims to identify the value of strain changes concerning arrhythmic events in patients with repaired tetralogy of Fallot (rTOF) using clinical data and CMR parameters, including information on myocardial strain. Furthermore, the study aimed to examine the correlation between ventricular volumes and function assessed by conventional and strain evaluations.

Methods

We retrospectively included adolescent and adult patients with post-repaired TOF who underwent CMR at our hospital between 2017 and 2023. Patients with inadequate follow-up data, incomplete CMR, associated myocardial diseases, or permanent pacemaker implantations were excluded. The patient selection process is illustrated in Fig. 1.

All data were collected through a review of hospital electronic medical records of arrhythmic events, including atrial and ventricular arrhythmias. An arrhythmia event was defined as atrial tachycardia, atrial flutter, atrial fibrillation, and ventricular tachycardia event as a documented occurrence recorded on previous electrocardiograms, holter monitoring, or medical records. Electrocardiograms and chest radiographs correlated within 6 months of the CMR were reviewed. The Institutional Review Board approved the protocol for this study under approval (COA no. Si 631/2023). Given the anonymous and retrospective nature of this study, written informed consent was not obtained from the study subjects.

CMR protocol and assessment of RV and LV strain

All CMR studies were performed on a 3-T whole-body scanner (Ingenia or Intera Achieva; Philips Healthcare, Best, the Netherlands) using a standardized protocol. Cine short-axis, 2-chamber, 3-chamber, and 4-chamber axis images were acquired during end-expiratory breath holds for ventricular and functional analyses. On short-axis cine images, biventricular end-diastolic volume (EDV), end-systolic volume (ESV), and ejection fraction were obtained using an IntelliSpace Portal (version 9) advanced visualization and analysis system (Philips Healthcare).

Accurate segmentation of the myocardium is crucial for reliable strain analysis. For deformation analysis, we semi-automatically delineated endocardial and epicardial borders and manually adjusted them, if necessary, throughout the cardiac cycles using CMR feature tracking software from a commercial provider (cvi42; Circle Cardiovascular Imaging Inc) (Fig. 2). This semi-automatic technique allows for more flexibility and accuracy. It allows for manual adjustments of endocardial and epicardial borders during the cardiac cycle, ensuring a more precise delineation of the myocardium. This capability is especially useful for cases where automatic segmentation

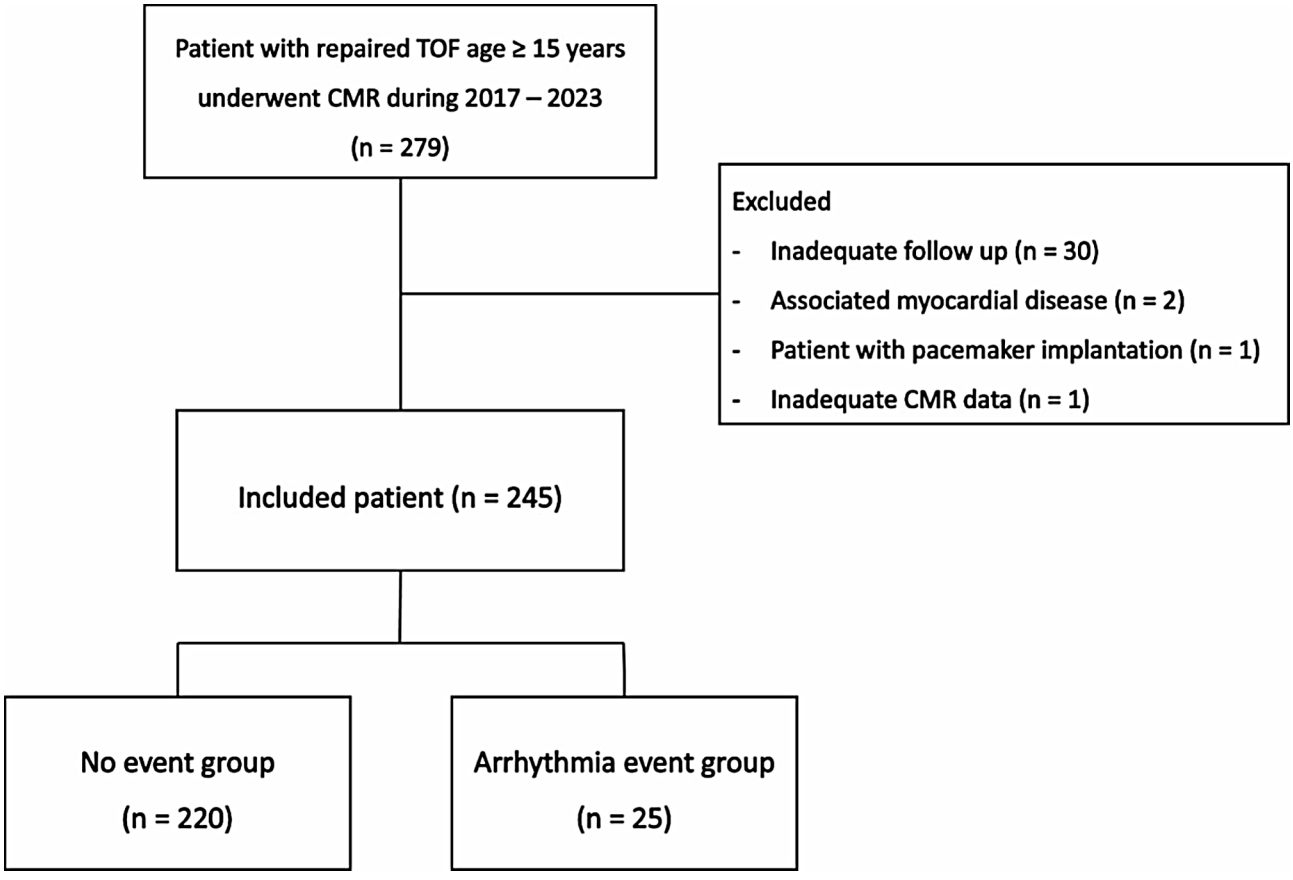


Fig. 1 Summary of patients with repaired TOF who underwent CMR during 2017–2023

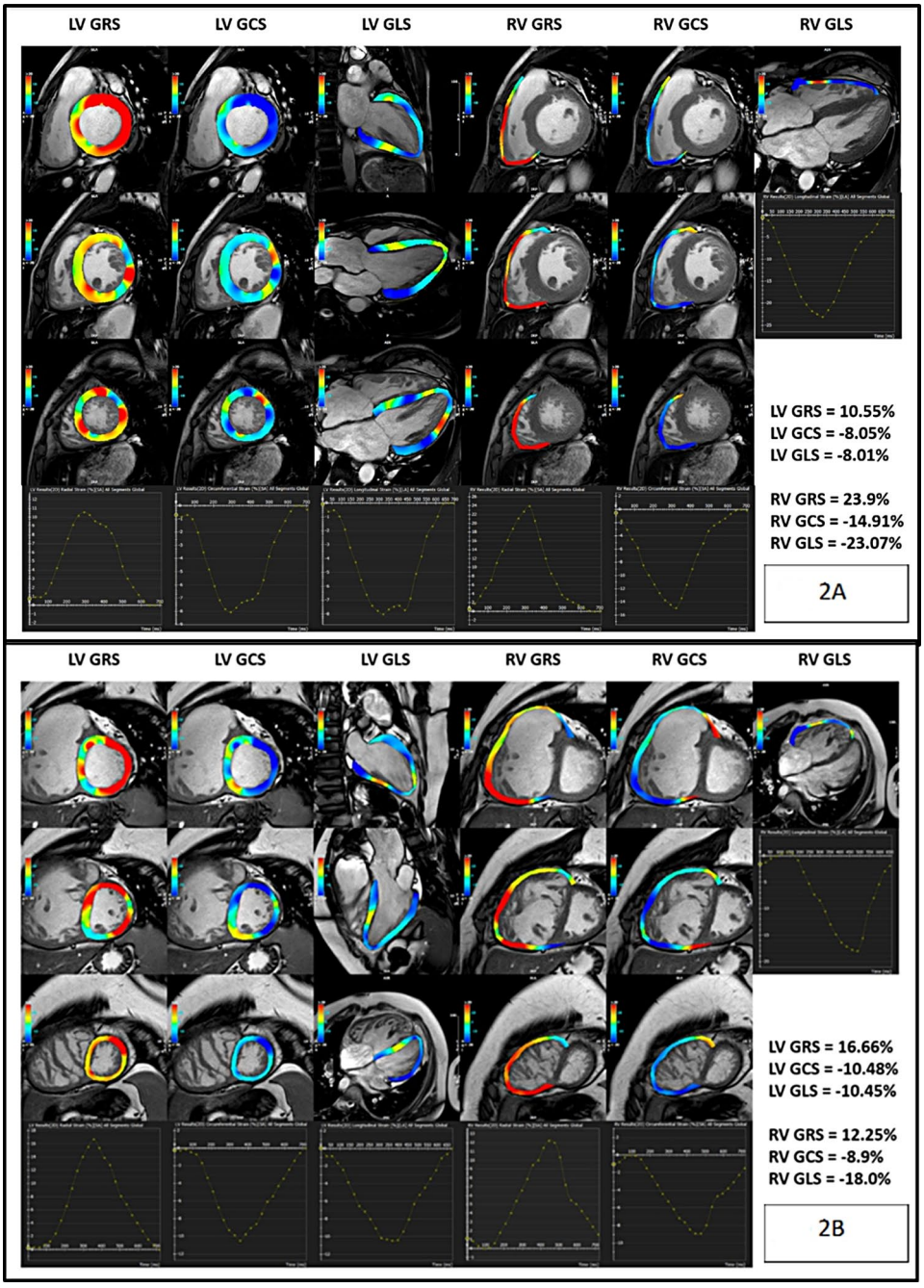


Fig. 2 Feature-tracking strain analysis in patients with significant abnormal LV strain (**A**) and abnormal biventricular strain (**B**)

might fail due to low image quality or motion artifacts. Furthermore, the inclusion of multiple strain measures—longitudinal strain (LS), circumferential strain (CS), and radial strain (RS)—provides a more comprehensive assessment of myocardial deformation compared to traditional methods, which may focus on just one strain measurement.

This approach is novel primarily in how it addresses the segmentation and delineation of myocardial borders during the cardiac cycle, while also integrating multiple strain measurements (longitudinal, circumferential, and radial strain) derived from different imaging. Longitudinal strain (LS) is the measurement of longitudinal shortening from the base to the apex. LS was obtained from 4-chamber images for the RV and two-, three-, and four-chamber long-axis cine images for the LV [13]. The circumferential strain (CS) demonstrates circumferential shortening of the short-axis, and the radial strain (RS) represents myocardial deformation from the endocardium to the epicardium, indicating a thickening motion

throughout the cardiac cycle. Both CS and RS are analyzed from short-axis images. Greater shortening, or better systolic function, is indicated by more negative GLS and GCS, while greater thickening, or better systolic function, is indicated by more positive GRS. Although the technique is semi-automatic, it still requires manual adjustments for boundary delineation, which introduces potential variability and user bias. To evaluate intraobserver and interobserver variability, 30 patients were randomly selected. Intraobserver reliability was assessed by repeated measurements by an interpreter (YS) after at least 2 weeks of blinding to previous results. Interobserver variability was evaluated by two observers (SN and YS) independently performing post-processing with blinded results, and then comparing those results.

Statistical analysis

Categorical data are presented as frequencies with percentages and were compared using the chi-square test or Fisher's exact test. Continuous data with a normal distribution are presented as mean ± standard deviation, while those with a nonnormal distribution are presented as median and interquartile range. Group comparisons for normally distributed data were conducted using Student's t-test and for comparisons involving more than two groups, the one-way ANOVA test was employed. Pearson's correlation tests were utilized to quantify correlations. Binary logistic regression analysis and multivariate regression analysis were employed to determine the impact of baseline characteristics, CMR parameters, and myocardial strain on the likelihood of arrhythmia events. The multivariate analysis involved separate models incorporating clinical variables and one CMR parameter to assess the likelihood of arrhythmia events. Receiver operating characteristic (ROC) analysis was conducted to determine the highest sensitivity and specificity of the parameters to predict arrhythmia events and to determine the optimal cutoff value. Variables with a *p-value* of <0.1 from the univariate binary logistic regression analysis were entered into the multivariate logistic regression analysis. The results of the univariate and multivariate binary logistic regression analysis are shown as the odds ratio (OR) and the 95% confidence interval (95%CI) and as the adjusted OR (aOR), the 95%CI, respectively. Interobserver and intraobserver reliability of strain measurement was assessed by intraclass correlation coefficient (ICC). All statistical analyses were performed using the statistical package for Social Science version 22 (SPSS Inc.). The $P<0.05$ was considered statistically significant.

Results

The final analysis included 245 adolescent and adult patients with rTOF. The median age at surgery was 5.6 years (range 1–44 years) and the median age at CMR was 27.5 years (range 15–69 years). During the follow-up period, 25 patients experienced documented arrhythmias: 10 had ventricular tachycardia, 13 had atrial flutter, 6 had atrial tachycardia, and 2 had atrial fibrillation. Among these cases, 10 patients required electrophysiological studies and underwent radiofrequency ablation. There was no new onset of complete AV block after the CMR study. Patients with arrhythmia events had a wider QRS duration and a larger cardiothoracic ratio (CT ratio) on chest radiographs. On conventional CMR measurements, higher LV and RV volumes as well as lower RVEF were significantly more common in the arrhythmia event group. However, LVEF only showed a tendency towards lower values in this group. In addition, the detailed functional study using feature tracking strain demonstrated significantly worse strain of LV and RV in the arrhythmia event group. A summary of information from all patients on baseline characteristics and CMR findings, including strain measurements, is provided in Table 1. Intraobserver and interobserver variability in the measurement of RVGRS, RVGCS, RVGLS, LVGRS, LVGCS, and LVGLS is presented with good reproducibility, as reflected by high ICC (ICC=0.88–0.98 and 0.80–0.97, respectively).

There were strong correlations between RVEF and RVGRS (r=0.665, P value<0.001) and RV GCS (r = -0.673, P value<0.001). It was a moderate correlation with RV GLS (r = -0.443, P value<0.001) (shown in Fig. 3). The RVESVi had a moderate correlation with RVGRS (r = -0.520, P value<0.001), RVGCS (r=0.545, P value<0.001), and RVGLS (r=0.427, P value<0.001). The RVEDVi also showed a moderate correlation with RVGRS (r = -0.375, P value<0.001), RVGCS (r=0.395, P value<0.001), and RVGLS (r=0.354, P value<0.001). The LVEF had a moderate correlation with RV strain, RVGRS (r=0.340, P value<0.001), RVGCS (r = -0.339, P value<0.001) (shown in Fig. 3), and weak correlation with RVGLS (r = -0.290, P value<0.001). Similarly, the LVEF also had a strong correlation with all myocardial LV strains, LVGRS (r=0.605, P value<0.001), LVGCS (r = -0.569, P value<0.001), and moderate correlation with LVGLS (r = -0.476, P value<0.001). The LVESVi had a moderate correlation with LV strain, LVGRS (r = -0.531, P value<0.001), LVGCS (r=0.488, P value<0.001) and LVGLS (r=0.464, P value<0.001). The LVEDVi also had weak correlations with LV strain, LVGRS (r = -0.275, P value<0.001), LVGCS (r=0.218, P value=0.001), and LVGLS (r=0.283, P value<0.001).

Of the 225 patients, 65 had mild right ventricular enlargement (RVE), defined by RVEDVi of less than 120 ml/m^2; 87 had moderate RVE, with RVEDVi ranging from 120 to 160 ml/m^2; and 93 had severe RVE, with RVEDVi equal to or greater than 160 ml/m^2. When comparing RV volume, patients with severe RVE exhibited

Table 1 Demographic and CMR parameters for all patients with comparison between the group without events and the arrhythmia event group

Clinical characteristics	All patients ($n=245$)	Arrhythmia event ($n=25$)	No event ($n=220$)	P value
Age at surgery (years)	8.26 ± 7.4	10.01 ± 6.09	8.06 ± 7.45	0.085
Age at CMR (years)	31.07 ± 12.6	41.02 ± 11.18	29.93 ± 12.24	**< 0.001**
Female	126 (51.4%)	12 (48.2%)	114 (51.8%)	0.717
BMI (kg/m^2)	22.21 (± 4.84)	23.04 ± 4.48	22.12 ± 4.88	0.369
TAP	151 (61.6%)	16 (64%)	135 (61%)	0.797
Previous palliative shunt	54 (22.0%)	6 (25%)	48 (22%)	0.714
NYHA class > 1	33 (13.5%)	12 (48%)	21 (9%)	**< 0.001**
QRS duration (msec)	152 ± 26.7	173.84 ± 32.05	149.93 ± 25.04	**< 0.001**
Cardiothoracic ratio	0.53 ± 0.06	0.59 ± 0.07	0.52 ± 0.05	**< 0.001**
LVEDVi (ml/m^2)	77.48 ± 16.2	83.52 ± 17.6	76.79 ± 16.01	**0.050**
LVESVi (ml/m^2)	30.11 ± 11.2	35.00 ± 12.35	29.55 ± 10.95	**0.021**
LVEF (%)	61.80 ± 8.4	58.76 ± 8.9	62.15 ± 8.3	0.056
RVEDVi (ml/m^2)	155.01 ± 52.8	195.16 ± 71.09	150.45 ± 48.46	**< 0.001**
RVESVi (ml/m^2)	83.24 ± 39.5	122.50 ± 58.21	78.78 ± 34.26	**< 0.001**
RVEF (%)	47.95 ± 8.7	39.40 ± 9.60	48.92 ± 8.15	**< 0.001**
PRRF (%)	37.45 ± 19.68	35.67 ± 24.20	37.65 ± 19.18	0.702
LV GRS (%)	36.59 ± 9.96	31.78 ± 9.65	37.14 ± 9.87	**0.010**
LV GCS (%)	-18.05 ± 3.13	-15.77 ± 3.2	-18.31 ± 3.02	**< 0.001**
LV GLS (%)	- 16.95 ± 2.4	-15.60 ± 2.30	-17.10 ± 2.37	**0.003**
RV GRS (%)	27.86 ± 7.01	22.05 ± 7.82	28.52 ± 6.62	**< 0.001**
RV GCS (%)	-16.15 ± 2.77	-13.47 ± 3.36	-16.45 ± 2.53	**< 0.001**
RV GLS (%)	-20.45 ± 3.32	-18.31 ± 4.50	-20.70 ± 3.08	**0.001**

BMI, body mass index; NYHA, New York Heart Association; TAP, transannular patch; LVEDVi, left ventricular end-diastolic volume index; LVESVi, left ventricular end-systolic volume index; LVEF, left ventricular ejection fraction; RVEDVi, right ventricular end-diastolic volume index; RVEF, right ventricular ejection fraction; RVESVi, right ventricular end-systolic volume index; PRRF, pulmonary regurgitation regurgitant fraction; LV, left ventricle; RV, right ventricle; GRS, global radial strain; GCS, global circumferential strain; GLS, global longitudinal strain

significantly lower RV myocardial strain compared to those with mild and moderate RVE (Table 2). Considering the LV function, the LVEF and LV GCS were significantly lower in severe RVE.

Analysis of the receiver operator characteristics was used to assess the predictive value of RV and LV strain for arrhythmia events. The results showed that the area under the curves (AUC) of RVGRS (0.758, $p<0.001$) and RVGCS (0.765, $p<0.001$) were greater than that of other parameters (see Fig. 4). The best cutoff values for all strain values to detect arrhythmia events are shown in Table 3.

Univariate binary logistic regression analysis was performed to determine independent factors associated with arrhythmia events, and their p-values, and odds ratios with 95% confidence intervals are shown in Table 3. Significant factors, including age group > 6 years, age at CMR, QRS duration > 180 msec, CT ratio > 0.55, NYHA class > 1, LVEDVi, LVESVi, RVEDVi, RVESVi, RVEF, LVEF, and all strain values, were significant in the univariate analysis. To avoid collinearity issues, separate models were used in the multivariate regression analysis. Due to its strong correlation with the age group at surgery, we omit the age at CMR from the multivariable regression analysis model. Instead, we include the age group at surgery, NYHA, QRS duration, CT ratio, and one MRI parameter (LVEDVi, LVESVi, RVEDVi, RVESVi, RVEF, LVEF, and all strain values) to determine independent factors associated with arrhythmia events. Apart from RVEF < 40% (aOR 6.97), RVGRS (aOR 6.68), RVGCS (aOR 6.36), RVGLS (aOR 3.14) and LVGRS (aOR 3.02) were found to be the factors associated with arrhythmia events.

Discussion

Our retrospective study examines arrhythmic events in patients with repaired Tetralogy of Fallot (TOF) across a wide age range at the time of cardiac magnetic resonance (CMR) imaging, as well as in patients of varying ages at primary repair. Because our center is situated in a resource-limited setting, the median age at repair was older and the age range was wider compared to TOF cases reported in Western countries [14]. However, this median age and range are comparable to those seen in low- to middle-income countries [15]. Although older age at repair has not been identified as a mortality risk factor [15, 16], it is associated with a longer duration of cyanosis and may increase the risk of arrhythmias. Therefore, our population might differ from those evaluated in other studies. We aim to identify factors associated with

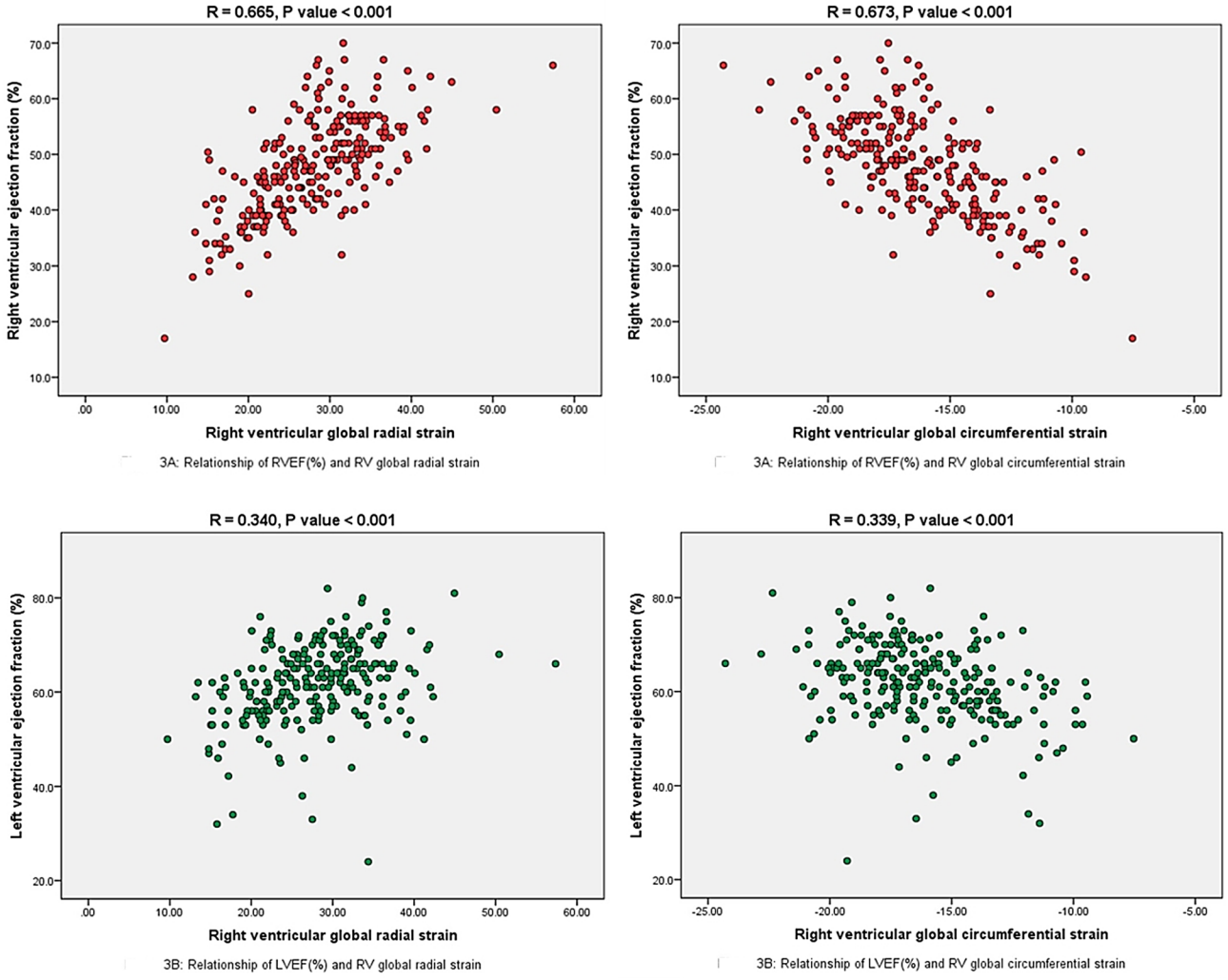


Fig. 3 The correlation of RV strain and RV ejection fraction and left ventricular ejection fraction

arrhythmic events using clinical data, basic investigations such as ECG and CXR, and conventional CMR, including myocardial strain.

While an abnormal EF usually implies late systolic dysfunction, myocardial strain offers greater sensitivity to detect ventricular dysfunction. Myocardial strain evaluates myocardial deformation in terms of shortening, lengthening, thickening, and rotation throughout the cardiac cycle. This allows for early detection of systolic dysfunction, even when EF is preserved, and provides insight into diastolic function [17]. The assessment, including strain measurement by CMR, is widely recognized as a standardized and accurate technique, demonstrating high interobserver reliability in our study. Therefore, myocardial strain is useful for early diagnosis, prognosis, risk stratification, and treatment decision-making [13]. Most studies have utilized echocardiography for strain analysis, but only a few studies focus on arrhythmic events in patients with repaired tetralogy of Fallot (rTOF) using strain analysis by CMR. Several studies have recently compared the prognostic value of myocardial strain measured by echocardiography and found that it is a strong predictor of adverse events and mortality in various diseases, including in patients with rTOF [18, 19]. Like our results, Li Jiang et al. observed a reduction in RV strain and increased RVEDVi and RVESVi in TOF patients compared to controls [20]. However, the previous study did not demonstrate the ability to predict ventricular dysfunction based on ventricular dysynchrony and global strain in rTOF patients [6]. Our results demonstrated strong correlations of RVEF and moderate correlations of volumes with all RV strains in rTOF patients. The 2018 American Heart Association/American College of Cardiology (AHA/ACC) adult congenital heart disease guidelines and the 2020 European Society of Cardiology (ESC) Guidelines for the management of adult congenital heart disease recommend performing pulmonic valve replacement (PVR) at the appropriate time to improve

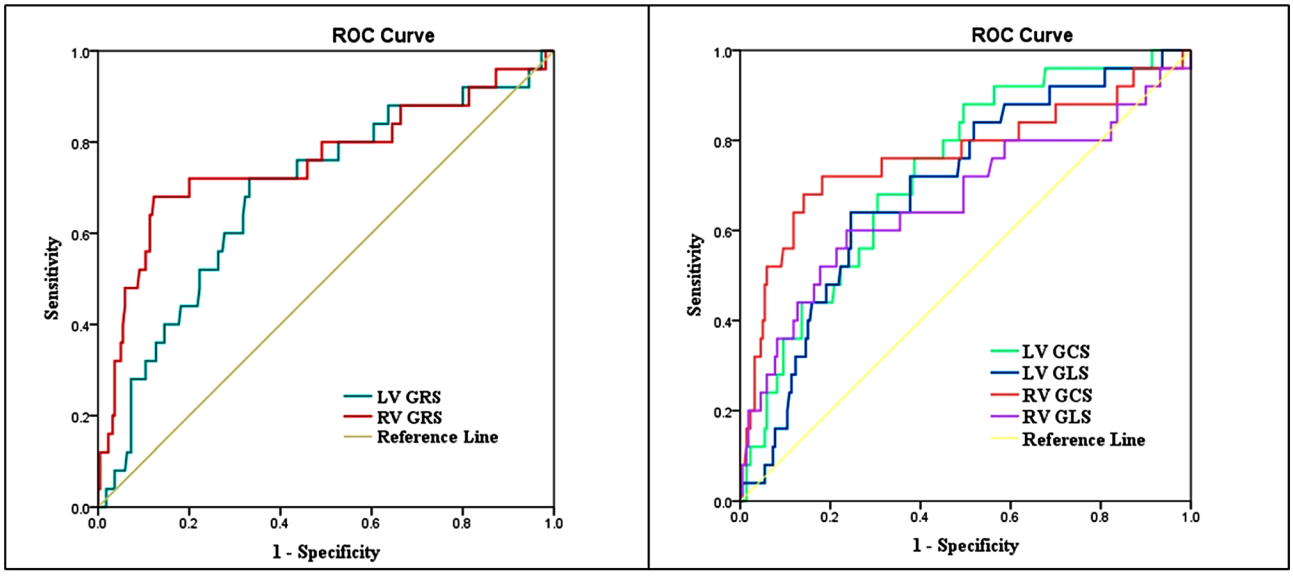
Table 2 Relationship between RV diastolic volume index and ventricular function including myocardial strains

	RV enlargement	Mean ± SD	95% CI	*P* value
LVEF (%)	Mild RVE	63.60 ± 9.43	Ref.	
	Moderate RVE	62.84 ± 7.40	0.75 (-2.51, 4.02)	1.000
	Severe RVE	59.59 ± 8.15	4.01 (0.79, 7.23)	**0.009**
LV GRS (%)	Mild RVE	38.33 ± 9.99	Ref.	
	Moderate RVE	36.21 ± 8.51	2.12 (-1.81, 6.06)	0.583
	Severe RVE	35.74 ± 11.10	2.59 (-1.28, 6.47)	0.324
LV GCS (%)	Mild RVE	-19.11 ± 3.19	Ref.	
	Moderate RVE	-18.23 ± 2.71	-0.88 (-2.09, 0.32)	0.236
	Severe RVE	-17.16 ± 3.24	-1.96 (-3.15, -0.77)	**< 0.001**
LV GLS (%)	Mild RVE	-17.35 ± 2.37	Ref.	
	Moderate RVE	-17.14 ± 2.13	-0.21 (-1.16, 0.73)	1.000
	Severe RVE	-16.51 ± 2.61	-0.84 (-1.77, 0.94)	0.094
RVEF (%)	Mild RVE	52.80 ± 8.59	Ref.	
	Moderate RVE	49.00 ± 7.24	3.80 (0.65, 6.96)	**0.012**
	Severe RVE	43.58 ± 8.20	9.23 (6.12, 12.34)	**< 0.001**
RV GRS (%)	Mild RVE	30.14 ± 7.34	Ref.	
	Moderate RVE	28.70 ± 6.44	1.44 (-1.24, 4.11)	0.591
	Severe RVE	25.48 ± 6.64	4.66 (2.02, 7.29)	**< 0.001**
RV GCS (%)	Mild RVE	-17.05 ± 2.62	Ref.	
	Moderate RVE	-16.51 ± 2.58	-0.54 (-1.6, -0.52)	0.655
	Severe RVE	-15.17 ± 2.77	-1.88 (-2.9, -0.38)	**< 0.001**
RV GLS (%)	Mild RVE	-21.55 ± 2.98	Ref.	
	Moderate RVE	-20.96 ± 3.07	-0.59 (-1.85, -0.67)	0.779
	Severe RVE	-19.21 ± 3.41	-2.33 (-3.57, -1.09)	**< 0.001**

RVE, right ventricular enlargement; LVEF, left ventricular ejection fraction; RVEF, right ventricular ejection fraction; LV, left ventricle; RV, right ventricle; GRS, global radial strain; GCS, global circumferential strain; GLS, global longitudinal strain

RV volume and myocardial function [21, 22]. In asymptomatic patients with severe pulmonic regurgitation, the criteria are based on severe RVE (RVEDVi ≥ 160 ml/m2) and progressive or mild/moderate RV systolic dysfunction. However, Monti et al. found that RV strain did not improve after pulmonic valve replacement and continued to deteriorate over time, regardless of whether PVR was performed [6]. Similarly, previous studies have reported improvements in RV volume after PVR, but RV myocardial motion remained irreversible [23, 24]. Our study highlights that all RV strains decreased significantly in patients with severe RVE, with reductions beginning even in moderate RVE. Therefore, early detection of RV dysfunction through RV strain may provide a better opportunity for early intervention and improved outcomes.

Independent predictors of major adverse clinical events, including death, sustained VT, and poor NYHA class, were identified as increased RVEDV (z-score > 7) along with LVEF < 55% or RVEF < 45% [25]. A recent systematic review and meta-analysis demonstrated that risk factors for VT included older age, older age at repair, a history of palliative shunt and ventriculotomy, number of thoracotomies, longer QRS duration, as well as more than moderate RVEF, lower LVEF, and larger RV size [26]. Additionally, either LV systolic or diastolic dysfunction, non-sustained VT, QRS duration ≥ 180 msec, extensive RV scarring, and inducible sustained VT at electrophysiological study have been identified as robust prognosticators for sudden cardiac death [21, 27]. Not only conventional CMR parameters but also myocardial strain in patients with rTOF are associated with outcomes. In patients with rTOF, biventricular dysfunction which affects long-term outcomes has been recognized [8, 28]. Berganza et al. and Jiang et al. demonstrated a significant decrease in LV GRS and LVGCS in rTOF patients compared to the control group [28, 29]. Thomas et al. and Orwat et al. demonstrated a strong association between LV longitudinal strain and both death and sustained ventricular tachycardia [30, 31]. Hagdorn et al. reported that the LV strain rate predicts ventricular arrhythmias [12]. Similarly, our results indicated that the left ventricular global radial strain (LVGRS) is also associated with arrhythmic events. In addition to LV strain, Ying Gao et al. identified lower right ventricular (RV) free wall strain as a predictive factor for poor outcomes using two-dimensional speckle tracking echocardiography [32]. In contrast, RV dyssynchrony and RV strain in the CMR study were not correlated with adverse events, including arrhythmias, hospitalization for heart failure, and death in patients with rTOF [33]. However, our results identified that all RV strains, particularly RVGRS and RVGCS,



Variables	AUC (95%CI)	Cut-off value	Sensitivity	Specificity
LV GRS	0.686 (0.572,0.801)	32.9%	72.00%	66.81%
LV GCS	0.732 (0.635,0.828)	-17.9%	76.00%	61.40%
LV GLS	0.699 (0.595,0.802)	-16.7%	72.00%	62.30%
RV GRS	0.758 (0.635,0.880)	22.8%	72.00%	80.00%
RV GCS	0.765 (0.642,0.888)	-14.0%	72.00%	81.80%
RV GLS	0.667 (0.534,0.800)	-18.7%	60.00%	76.40%

Fig. 4 Receiver operator characteristic (ROC) analysis for the association of arrhythmias in patients with rTOF

were strongly associated with arrhythmia events. Importantly, these strains remained independently associated factors even after adjusting for age group, NYHA class, QRS duration, and cardiothoracic ratio. With good inter- and intraobserver reliability, strain assessment using CMR provides consistent measurements and has been associated with arrhythmic events. It is especially sensitive in detecting abnormal ventricular function, making it crucial for early intervention. Our results suggest that rTOF patients with abnormal RV or LV strain should be closely monitored for potential arrhythmic events. Additionally, we established cut-off values for the myocardial strain parameters from both the LV and RV that are useful for anticipating arrhythmic events.

Limitations

This study has certain limitations that should be acknowledged. First, its retrospective design implies susceptibility to missing or incomplete data and potential biases. Second, our study may not represent the entire population of rTOF patients, as it only includes those who underwent CMR. Data on patients who did not undergo CMR, such as those with severe PS, are lacking. Third, the relatively small size of our population experiencing arrhythmic events raises the possibility that our statistical analyses may have lacked the necessary power to identify all significant differences and associations. Fourth, motion artifacts, particularly from breathing and heartbeats, can compromise image quality and reduce tracking accuracy. Additionally, restricted spatial and temporal resolution can impede the precise delineation of myocardial borders. Feature tracking and strain analysis can be computationally demanding, often requiring substantial processing time and resources [34]. The method may also be sensitive to noise in the input images. To enhance the robustness of the model, preprocessing steps or additional regularization techniques may be needed to address these issues [35]. Finally, the occurrence of arrhythmic events before or after CMR studies presents a challenge. While we could identify associated factors over time, we may not be able to determine predictors that precede the events. Further prospective longitudinal studies that focus on detailed myocardial function over time may yield better predictors of arrhythmic events.

Table 3 Factors associated with arrhythmia events in rTOF patients by univariate and multivariate binary logistic regression analysis

Variables	Arrhythmia event	No event	*P*-value	OR (95% CI)	Adjusted OR (95% CI)	*P*-value
Age at surgery (years)						
Age ≥ 6	20 (16.7%)	100 (83.3)	**0.003**	4.76 (1.72,13.14)		
Age < 6	5 (4%)	119 (96%)				
Age at CMR (years)						
Age ≥ 28	22 (18.5%)	97 (81.5%)	**< 0.001**	9.29 (2.70,31.98)		
Age < 28	3 (2.4%)	123 (97.6%)				
NYHA						
Class > 1	12 (36.4%)	21 (63.6%)	**< 0.001**	8.74 (3.54,21.60)		
Class 1	13 (5.6%)	199 (94.4%)				
QRS duration (msec)						
QRSd ≥ 180	10 (37.0%)	17 (63.0%)	**< 0.001**	7.96 (3.10,20.39)		
QRSd < 180	15 (6.9%)	203 (93.1%)				
Cardiothoracic ratio						
CTR ≥ 0.55	16 (20.3%)	63 (79.7)	**0.001**	4.43 (1.86,10.54)		
CTR < 0.55	9 (5.4%)	157 (94.6%)				
LVEDVi (ml/m2)						
LVEDVi ≥ 80	16 (15.7%)	86 (84.3)	**0.02**	2.77 (1.17,6.55)	2.15 (0.80,5.80)	0.129
LVEDVi < 80	9 (6.3%)	134 (93.7%)				
LVESVi (ml/m2)						
LVESVi ≥ 30	14 (13.2%)	92 (86.8%)	**0.179**	1.77 (0.77,4.08)		
LVESVi < 30	11 (7.9%)	128 (92.1%)				
RVEDVi (ml/m2)						
RVEDVi ≥ 160	15 (16.1%)	78 (83.9%)	**0.02**	2.73 (1.17,6.36)	1.85 (0.68,5.04)	0.228
RVEDVi < 160	10 (6.6%)	142 (93.4%)				
RVESVi (ml/m2)						
RVESVi ≥ 80	17 (16%)	89 (84%)	**0.011**	3.12 (1.29,7.55)	2.66 (0.97,7.28)	0.058
RVESVi < 80	8 (5.8%)	131 (94.2%)				
RVEF (%)						
RVEF ≤ 40	16 (30.2%)	37 (69.8%)	**< 0.001**	8.793 (3.61,21.40)	6.97 (2.44,19.97)	**< 0.001**
RVEF > 40	9 (4.7%)	183 (95.3%)				
LVEF (%)						
LVEF ≤ 55	10 (22.2%)	35 (77.8%)	**0.005**	3.52 (1.46,8.47)	2.16 (0.74,6.29)	0.158
LVEF > 55	15 (7.5%)	185 (92.5%)				
LV GRS (%)						
LV GRS ≤ 32.9	18 (19.8%)	73 (80.2%)	**< 0.001**	5.18 (2.07,12.95)	3.02 (1.04,8.79)	**0.043**
LV GRS > 32.9	7 (4.5%)	147 (95.5%)				
LV GCS (%)						
LV GCS ≤ -17.9	18 (17.5%)	85 (82.5%)	**0.003**	4.08 (1.63,10.19)	2.08 (0.73,5.87)	0.169
LV GCS > -17.9	7 (4.9%)	135 (95.1%)				
LV GLS (%)						
LV GLS ≤ -16.7	18 (17.8%)	83 (82.2%)	**0.002**	4.24 (1.70,10.59)	2.44 (0.87,6.89)	0.091
LV GLS > -16.7	7 (4.9%)	137 (95.1%)				
RV GRS (%)						
RV GRS ≤ 22.8	18 (29%)	44 (71%)	**< 0.001**	10.28 (4.04,26.16)	6.68 (2.35,18.97)	**< 0.001**
RV GRS > 22.8	7 (3.8%)	176 (96.2%)				
RV GCS (%)						
RV GCS ≤ -14	17 (30.4%)	39 (69.6%)	**< 0.001**	9.86 (3.98,24.47)	6.36 (2.28,17.76)	**< 0.001**
RV GCS > -14	8 (4.2%)	181 (95.8%)				
RV GLS (%)						
RV GLS ≤ -18.7	14 (21.2%)	52 (78.8%)	**0.001**	4.11 (1.76,9.60)	3.14 (1.11,8.90)	**0.031**
RV GLS > -18.7	11 (6.1%)	168 (93.9%)				

NYHA, New York Heart Association; CTR, cardiothoracic ratio; RVEDVi, right ventricular end-diastolic volume index; RVEF, right ventricular ejection fraction; RVESVi, right ventricular end-systolic volume index; LVEF, left ventricular ejection fraction; regurgitant fraction; LV, left ventricle; RV, right ventricle; GRS, global radial strain; GCS, global circumferential strain; GLS, global longitudinal strain

Conclusions

Our study provides valuable insights into the relationship between myocardial strain and arrhythmic events in patients with rTOF, underscoring the importance of comprehensive cardiac evaluation for risk stratification and management. In patients with severe RVE, all RV strain measures were significantly reduced, with noticeable declines even observed in cases of moderate RVE. We highlight the role of all RV strain measures, particularly RVGRS and RVGCS, as well as LVGRS from CMR imaging, as independent factors associated with arrhythmic events. Myocardial strain proves to be a valuable tool for prognostic assessment in patients with rTOF.

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Author contributions
Study conception and design: PChung and WK. Data collection: WK, YS and SN. Analysis and interpretation of the data/results: PChung and WK. Manuscript preparation: PChung and WK. Evaluation and revision of the manuscript for important intellectual content: PChung, WK, KD, CV, PChant, SK, TP, PT, YS, SN and JS. All authors have read and approved the final version of the manuscript to be submitted for journal publication.

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Data availability
The dataset used and analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Ethical approval and consent to participate, consent for publication
Electrocardiograms and chest radiographs correlated within 6 months of CMR were reviewed. The Siriraj Institutional Review Board, Faculty of Medicine Siriraj Hospital, Mahidol University approved the protocol for this study (COA no. Si 631/2023). Given the anonymous and retrospective nature of this study, written informed consent was not obtained from study subjects.

Competing interests
The authors declare no competing interests.

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