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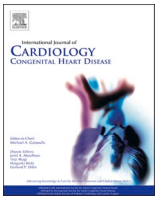

Correlation of ECG and cardiac MRI for assessment of ventricular hypertrophy and dilatation in adults with repaired tetralogy of Fallot

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A B S T R A C T

Background: Surgically repaired Tetralogy of Fallot (rTOF) is associated with progressive right ventricular hypertrophy (RVH) and dilation (RVD). Accurate estimation of RVH/RVD is vital for the ongoing management of this patient population. The utility of the ECG in evaluating patients with rTOF with pre-existing right bundle branch block (RBBB) has not been studied. We aimed to determine the sensitivity/specificity of currently established ECG criteria in detecting RVH/RVD in this patient population.

Methods: We included consecutive patients diagnosed with rTOF who underwent CMR performed at our regional referral centre between January 2012 and December 2019. Each CMR was assessed for LVH, LVD, RVH and or RVD. The ECG corresponding to the CMR was then used to determine RVH/LVH for specificity and sensitivity analysis.

Results: Our study included 163 consecutive rTOF patients. The specificity for ECG-based criteria for LVH was 100.00% (95% C.I. (87.75, 100.00)), and the sensitivity was 7.19% (95% C.I. (3.15, 12.83)). When RBBB was present, specificity for RVH was 100.00% (95% C.I. (84.56, 100.00)), and sensitivity was 7.69% (95% C.I. (3.75, 13.69)). When RBBB was absent, specificity for RVH was 100.00% (95% C.I. (15.81, 100.00)), and sensitivity was 0.00% (95% C.I. (0.00, 33.63)). A regression model with the entire group of 163 ToF patients, based on the Sokolow-Lyon criterion (sum of R in V1 + S in V5/V6), produced a new suggested criterion for the diagnosis of RVH in patients with rTOF, which was a sum of R in V1 + S in V5/V6 greater than 13.25 mm. This model's sensitivity for RVH detection was 69.1%, and specificity was 36.8%.

Conclusions: Standard ECG voltage criteria have poor sensitivity for detecting right and left ventricular chamber hypertrophy and dilatation in patients with rTOF, so current ECG criteria should not be used to monitor RVH/RVD in this patient population.

1. Introduction

Patients with surgically repaired tetralogy of Fallot (rTOF) often experience progressive right ventricular (RV) remodelling and dilation [1]. Longitudinal studies show that RV remodelling stabilizes in adolescence and early adulthood, but some patients may experience rapid progression of RV dilation in later adulthood, leading to adverse outcomes [2]. Monitoring RV size and function using cardiac MRI (CMR) is recommended from adolescence, but this is not always feasible due to resources and patient anxiety [3]. CMR is also not feasible in patients with non-MRI conditional devices such as pacemakers and defibrillators. Furthermore, assessing right ventricular hypertrophy/dilation (RVH/RVD) through conventional imaging with echocardiography is challenging due to the complex RV shape and difficulty in measuring RV-free wall motion [4].

Assessing cardiac chamber enlargement and hypertrophy using routine diagnostics like electrocardiogram (ECG) could benefit clinicians and patients. ECGs are widely available, inexpensive and provide valuable information on structural heart disease. In this study, we aim to determine the diagnostic accuracy of established ECG criteria in detecting both RVH/RVD or left ventricular hypertrophy/dilation (LVH/LVD) on CMR in the adult congenital heart disease (ACHD) population, specifically for patients with rTOF who often have right bundle branch block (RBBB).

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Abbreviations

Non-standard Abbreviations and Acronyms

rTOF	repaired tetralogy of Fallot
RV	right ventricular
CMR	cardiac MRI
ECG	electrocardiogram
RVH	right ventricular hypertrophy
RVD	right ventricular dilation
RBBB	right bundle branch block
ACHD	adult congenital heart disease
LVH	left ventricular hypertrophy
LVD	left ventricular dilation
LBBB	left bundle branch block
PVR	pulmonary valve replacement

2. Methods

2.1. Study overview

We conducted a retrospective cohort study of patients with rTOF from our ACHD clinic (Pacific Adult Congenital Heart Centre, St. Paul's Hospital, Vancouver, British Columbia, Canada) who underwent a cMRI scan from January 2012 to December 2019. Our clinic is a provincial referral center for patients with confirmed or suspected adult congenital heart disease diagnoses, drawn from a population of 5.1 million residents. This study was approved by the University of British Columbia (UBC) research ethics board, REB H21-00615.

2.2. Cardiac MRI data

A secure, view-only electronic health record (CareConnect) was used to access patient CMR reports. All patients underwent multiplanar, multisequence, unenhanced and gadolinium-enhanced CMR on a 1.5-T platform (HDxT, GE Healthcare) according to a standard Tetralogy of Fallot protocol. LVH was determined using both left ventricular wall thickness and LV mass index. Similarly, RVH was determined using right ventricular wall thickness and RV mass index. Left/right ventricular dilation was determined using LV/RV end-diastolic diameter and LV/RV volume index. Published reference ranges for CMR in adults were utilized [5]. For patients with repeat CMRs, we included the first available CMR on record.

2.3. ECG data

The closest preceding ECG to each corresponding CMR was then used to determine RVH/LVH for sensitivity and specificity analysis. We used the Sokolow-Lyon and Cornell voltage criteria for the diagnosis of LVH and the Sokolow-Lyon and Myers' voltage criteria for diagnosis of RVH [6–8]. The Sokolow-Lyon criterion-based RVH was defined as a composite of amplitudes (R voltage of V1 + S voltage of V5 or V6) >10.5 mm,4 and the Myers et al. criterion-based RVH was defined as (1) R/S ratio of V1 >1 or (2) R/S ratio of V5 or V6 <1 or (3) R voltage of V1 >6 mm. An example ECG with a true positive RVH is provided in the supplemental material. If the ECG met either criteria, a diagnosis of LVH or RVH was made. A diagnosis of RBBB or left bundle branch block (LBBB) was made using the criteria provided in the supplemental material (S1). Automated records were used to determine the cardiac intervals and QRS width.

2.4. Definitions

CMRs meeting criteria for RVH/RVD diagnosis were used to establish underlying RVH/RVD for sensitivity and specificity analysis. Patients with RVH/RVD on CMR and ECG diagnosis of RVH/RVD were called true positives. Patients without RVH/RVD on CMR but no ECG diagnosis of RVH/RVD were called true negatives. Patients with RVH/RVD on CMR but no ECG diagnosis of RVH/RVD were called false negatives. Patients with no RVH/RVD on CMR but ECG diagnosis of RVH/RVD were called false positives. A similar process was repeated for patients with LVH/LVD on CMR to establish a diagnosis of underlying LVH/LVD for sensitivity and specificity analysis.

As there are no established criteria for the presence of RVH in patients with RBBB, we also performed a regression model with the entire group of 163 rTOF patients based on the Sokolow-Lyon criterion (R in V1 + S in V5/V6) and Meyer's criterion (R/S in V1, R/S in V5/V6, and R in V1).

2.5. Statistical analysis

The statistical analyses were completed using the IBM SPSS statistics software, version 27 (IBM Corp, Armonk, NY). Pearson chi-squared tests were used to compare categorical variables, and independent sample t-tests were used to compare continuous variables. Sensitivity and specificity analyses were completed on MedCalc statistical software [9]. Sensitivity, specificity, disease prevalence, positive and negative predictive value, and accuracy are expressed as percentages. Confidence intervals for sensitivity, specificity and accuracy are "exact" Clopper-Pearson confidence intervals. Confidence intervals for the predictive values are the standard logit confidence intervals given by Mercaldo et al.; except when the predictive value is 0 or 100%, a Clopper-Pearson confidence interval is reported [10].

3. Results

3.1. Baseline characteristics

Seven hundred seventy-one consecutive patients were identified as having both a diagnosis of congenital heart disease and a CMR between Jan 2012–Dec 2019. Of these patients, a total of 163 patients had a diagnosis of rTOF and were included in our study. The mean age was 40.1 ± 11.5 years. Female patients accounted for 40.5% of the study cohort. The mean RV EF was 40.2% ± 8.7, and the mean RV volume index was 128.0 ml/m2 ± 43.9. The mean LV EF was 56.2% ± 8.3, and the mean LV volume index was 80.6 ml/m2 ± 23.8. The mean QRS duration was 131.1 ms ± 33.1 (Table 1).

Table 1
Tetralogy of Fallot cohort baseline statistics.

	Tetralogy of Fallot N = 163
Baseline characteristics [1]	
Age [2]	40.1 (11.5)
Male	97 (59.5)
RVEF (%) [2]	40.2 (8.7)
RV Volume Index (ml/m^2) [2]	128.0 (43.9)
LVEF (%) [2]	56.2 (8.3)
LV Volume Index (ml/m^2) [2]	80.6 (23.8)
QRS duration (ms) [2]	131.1 (33.1)
TOF repair subtype [1]	
Unknown	61 (37.4)
External conduit	5 (3.1)
Outflow tract patch	41(25.2)
Transannular patch	53 (32.5)
Without patch	3 (1.8)

[a]Data presented as: n (%) sunless otherwise specified.
[b]Data presented as: mean (SD) TOF; tetralogy of Fallot RVEF; right ventricular ejection fracture, RV; right ventricle, LVEF; left ventricular ejection fraction, LV; left ventricle.

3.2. MRI/ECG characteristics

One hundred thirty-nine patients had RVH/RVD confirmed on CMR, seven patients had CMR proven LVH/LVD. Fourteen patients had an ECG diagnosis of RVH, and five had LVH. One hundred fifty-two patients had a diagnosis of RBBB, and zero had a diagnosis of LBBB (Table 2).

3.3. Sensitivity/specificity analysis

For ECG-reported diagnosis, the specificity for LVH/LVD was 100.00% (95% CI (87.75, 100.00)), and the sensitivity was 7.19% (95% CI (3.50, 12.83)). When RBBB was absent, ECG sensitivity was 0.00% (95% CI (0.00, 33.63)). ECG specificity was 100.00% (95% CI (15.81, 100.00)). In subjects with RBBB, specificity for RVH was 100.00% (95% CI (84.56, 100.00)), and sensitivity was 7.69% (95% CI (3.75, 13.69)). (Table 3).

The regression model with the entire group of 163 ToF patients, based on the Sokolow-Lyon criterion (R in V1 + S in V5/V6), produced new suggested criteria for the diagnosis of RVH in patients with RBBB, which was a Sokolow-Lyon sum greater than 13.2 mm. This model's sensitivity for RVH detection was 69.1%, and the specificity was 36.8%. The regression model with the entire group of 163 ToF patients, based on the Meyers et al. criteria (R/S in V1, R/S in V5/V6, and R in V1) resulted in a negative correlation for the prediction of RVH and was therefore not applied.

4. Discussion

The majority of patients in our study had RBBB, as is expected for rTOF. Our findings indicate that currently established ECG criteria have high specificity for detecting right and left ventricular chamber enlargement or hypertrophy in rTOF patients. However, they have poor sensitivity for detecting LVH/LVD and even worse sensitivity for detecting RVH/RVD (Figs. 1–3). The presence of a right bundle branch block does not affect the sensitivity of the ECG in detecting RVH/RVD. We propose utilizing a sum of R wave amplitude in lead V1 and S wave amplitude in leads V5/V6 greater than 13.2 mm as a reliable indicator of RVH in this patient population, however this requires external validation.

We anticipate a significant increase in our ACHD follow-up programs, particularly for patients with rTOF, as their outcomes continue to improve [11]. While their survival rate in early childhood is excellent, morbidity remains high as they reach middle age [12]. Risk assessment in rTOF continues to be a topic of investigation, and imaging markers of

Table 2
cMRI and ECG diagnosis of Tetralogy of Fallot cohort.

	Tetralogy of Fallot N = 163
cMRI data [1]	
LVH	0 (0)
LVD	7 (4.3)
RVH	69 (42.3)
RVD	128 (78.5)
ECG data [1]	
LVH	5 (3.1)
RVH	10 (6.1)
RBBB	152 (93.3)
LBBB	0 (0)

cMRI; cardiac magnetic resonance imaging, ECG; electrocardiogram, LVH; left ventricular hypertrophy, LVD; left ventricular dilation, RVH; right ventricular hypertrophy, RVD; right ventricular dilation, RBBB; right bundle branch block.
[a]Data presented as: n (%) unless otherwise specified; 2data presented as: mean (SD).

Table 3
Sensitivity, specificity, PPV and NPV of the ECG in detecting right and left ventricular chamber hypertrophy and dilatation on cardiac MRI in adults with repaired tetralogy of Fallot.

	Specificity (%)	Sensitivity (%)
LVH/LVD	100.00 [87.75–100.00]	7.19 [3.50–12.83]
RVH/RVD, without RBBB	100.00 [15.81–100.00]	0.00 [0.00–33.63]
RVH/RVD, with RBBB	100.00 [84.56–100.00]	7.69[3.75–13.69]

PPV; positive predictive value, NPV; negative predictive value, ECG; electrocardiogram, LVH; left ventricular hypertrophy, LVD; left ventricular dilation, RVH; right ventricular hypertrophy, RVD; right ventricular dilation, RBBB; right bundle branch block.

		(PREDICTED) By MRI: Positive	(PREDICTED) By MRI: Negative
(ACTUAL) By ECG	Positive	10 (True Positive)	129 (False Negative)
(ACTUAL) By ECG	Negative	0 (False Positive)	24 (True Negative)

Fig. 1. Contingency table of diagnosis of LVH/LVD.

		(PREDICTED) By MRI: Positive	(PREDICTED) By MRI: Negative
(ACTUAL) By ECG	Positive	10 (True Positive)	120 (False Negative)
(ACTUAL) By ECG	Negative	0 (False Positive)	22 (True Negative)

Fig. 2. Contingency table of diagnosis of RVH/RVD with RBBB.

		(PREDICTED) By MRI: Positive	(PREDICTED) By MRI: Negative
(ACTUAL) By ECG	Positive	0 (True Positive)	9 (False Negative)
(ACTUAL) By ECG	Negative	0 (False Positive)	2 (True Negative)

Fig. 3. Contingency table of diagnosis of RVH/RVD without RBBB.

adverse right ventricular remodelling include RV dilation and increasing RV mass [3]. These imaging markers, however are currently only available using CMR [4]. Although there are published guidelines for routine imaging follow up of patients with rTOF, some patients do require expediated imaging referral and assessment by local experts [4]. Monitoring disease progression is imperative in patients with rTOF as a referral for pulmonary valve replacement (PVR) is recommended before the deterioration in RVEF occurs, as RV dysfunction has shown to correlate poorly with postoperative outcomes [13]. However, due to the growing number of follow-ups in the current environment, many patients now receive shared care with primary care physicians, internists, and community cardiologists. To aid community cardiologists in monitoring rTOF patients, establishing ECG criteria to detect chamber hypertrophy/enlargement would be helpful and could allow for more urgent referrals for CMR if necessary.

In 2009, the AHA/ACCF/HRS published standardized criteria for interpreting ECGs, including RVH. There is however, no published criteria for the detection of RVH in the presence of RBBB [14]. This criterion was derived from studies that used cadaveric dissection of patients. These studies were small, mainly in patients with previously diagnosed RV pathology and not in the presence of RBBB. Validation of this criteria using CMR as the gold standard in the general population has shown that most ECG criteria for RVH have low sensitives (<10%) and, therefore should not be used as a screening tool [7,15–18]. As these validation studies were done in patients without cardiovascular disease, the findings do not apply to a population at increased risk for RVH, and the AHA/ACCF/HRS concludes that the greatest accuracy of ECG RVH criteria is in patients with congenital heart disease [14].

In this study, we analyzed the sensitivity and specificity of established ECG criteria in detecting chamber enlargement or hypertrophy, with correlation from CMR, in adults with rTOF. While we initially included all patients with congenital heart disease, we focused our analysis on a subgroup of patients with rTOF due to their anatomical homogeneity. The majority of patients in our study had RBBB, as is expected for rTOF. Our findings indicate that currently established ECG criteria have high specificity for detecting right and left ventricular chamber enlargement or hypertrophy in rTOF patients. However, they have poor sensitivity for detecting LVH/LVD and even worse sensitivity for detecting RVH/RVD. The presence of a right bundle branch block does not affect the sensitivity of the ECG in detecting RVH/RVD.

These findings suggest that similar to screening in a healthy population, the surface ECG alone is insufficient for excluding progressive RVH/RVD in rTOF patients CMR should be used for routine follow-up and symptomatic patients. However, since CMR is resource-intensive, new ECG criteria for diagnosing RVD/RVH in rTOF patients are needed. We propose utilizing a sum of R wave amplitude in lead V1 and S wave amplitude in leads V5/V6 greater than 13.2 mm as a reliable indicator of RVH in this patient population, however this requires external validation.

5. Limitations

This study has a few key limitations. It is important to note that different phenotypes for patients with rTOF exist depending on their surgical history. Transannular patch repair typically results in RV dilatation with eccentric hypertrophy and RV-PA conduit repair typically results in lower volumes and concentric hypertrophy [3]. Our study did not differentiate between types of repair, and it is feasible that this would result in a more accurate analysis. Study size is another limitation of our study and may prevent the findings from being extrapolated. This is particularly true for patients with LVH/LVD, as majority of the study population had RVH/RVD.

6. Conclusion

The current ECG voltage criteria are insufficient in detecting right ventricular hypertrophy and dilatation in rTOF patients. Despite the limitations of our study due to phenotypic variation in congenital heart disease, our findings strongly indicate the necessity for new ECG criteria to be implemented for follow-up of rTOF patients. We propose a new ECG standard: R in V1 + S in V5/V6 sum >13.2 mm to detect RVH in the rToF, however this requires external validation.

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CRediT authorship contribution statement

Shanjot Brar: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Validation, Visualization, Writing – original draft, Writing – review & editing. **Mehima Kang:** Data curation, Formal analysis, Validation, Writing – review & editing. **Amit Sodhi:** Conceptualization, Data curation, Formal analysis, Methodology. **Marc W. Deyell:** Formal analysis, Supervision, Validation, Writing – review & editing. **Zachary Laksman:** Formal analysis, Supervision, Validation, Writing – review & editing. **Jason G. Andrade:** Supervision, Validation, Writing – review & editing. **Matthew T. Bennett:** Supervision, Validation, Writing – review & editing. **Andrew D. Krahn:** Supervision, Validation, Writing – review & editing. **John Yeung-Lai-Wah:** Supervision, Validation, Writing – review & editing. **Richard G. Bennett:** Supervision, Validation, Visualization, Writing – review & editing. **Amanda Barlow:** Supervision, Visualization, Writing – review & editing. **Jasmine Grewal:** Supervision, Validation, Visualization, Writing – review & editing. **Gnalini Sathananthan:** Supervision, Visualization, Writing – review & editing. **Santabhanu Chakrabarti:** Conceptualization, Formal analysis, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing, John Shadarevian, Data curation, Formal analysis, Methodology, Resources, Software, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcchd.2024.100508.

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