## Electrocardiography

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# Electrocardiographic Predictors of Right Ventricular Volume Measured by Magnetic Resonance Imaging Late after Total Repair of Tetralogy of Fallot

WENDY M. BOOK, M.D., W. JAMES PARKS, M.D.,\* KATHERINE L. HOPKINS, M.D., † J. WILLIS HURST, M.D.

Department of Medicine, Division of Cardiology, Emory University School of Medicine; \*Departments of Pediatrics and Radiology, Division of Pediatric Cardiology, Emory University, The Children's Heart Center and Egleston Children's Hospital; †Department of Radiology, Emory University and Egleston Children's Hospital, Atlanta, Georgia, USA

#### Summary

*Background:* Right ventricular dysfunction occurs in many patients with significant pulmonary valve regurgitation late after initial total repair of tetralogy of Fallot. Methods to predict which of these patients are at increased risk of late morbidity and mortality are not yet known.

*Hypothesis:* This study evaluated electrocardiographic (ECG) predictors of severe right ventricular dilatation determined by magnetic resonance imaging (MRI) volumes in patients with tetralogy of Fallot late after initial corrective repair.

*Methods:* We retrospectively reviewed the ECGs and MRI right ventricular volume measurements of 20 patients (age 4.4 to 19.3 years, mean 10.0 years) with significant pulmonary valve regurgitation late after repair of tetralogy of Fallot. All patients had enlarged, hypokinetic right ventricles by echocardiography. The patients were grouped based on an indexed right ventricular end-diastolic volume (RVEDV/BSA) of < 102 ml/m<sup>2</sup> (Group 1) or ≥ 102 ml/m<sup>2</sup> (Group 2). We determined the sensitivity, specificity, positive and negative predictive values of QRS duration, and mean frontal plane QRS axis for predicting right ventricular volumes.

*Results:* A maximal QRS duration of  $\geq 150$  ms or a northwest quadrant frontal plane QRS axis had 85% sensitivity, 86% specificity, 92% positive predictive value, and 75% negative predictive value for predicting an RVEDV/BSA of

Address for reprints:

Wendy M. Book, M.D. Emory University Center for Heart Failure Therapy 1364 Clifton Road NE Suite F508 Atlanta, GA 30322, USA

Received: January 8, 1999 Accepted with revision: March 31, 1999  $\geq$  102 ml/m<sup>2</sup>. The mean QRS duration was significantly longer in Group 2 than in Group 1 patients (156 ms vs. 123 ms, p = 0.005).

*Conclusions:* In patients late after repair of tetralogy of Fallot with significant pulmonary valve regurgitation, a maximal manually measured QRS duration of  $\geq$  150 ms and/or a frontal plane QRS northwest quadrant axis can predict patients with marked right ventricular enlargement. The presence of either of these findings on the ECG signifies patients who require further evaluation and consideration for pulmonary valve replacement.

**Key words:** congenital heart disease, right bundle-branch block, right ventricle, ventricular dysfunction

#### Introduction

Although long-term survival in repaired tetralogy of Fallot has improved since Lillihei first described surgical repair in 1955, sudden death and ventricular arrhythmias are frequent contributors to late morbidity and mortality in these patients.<sup>1-7</sup> Electrocardiographic (ECG) predictors of sudden death and ventricular tachycardia late after repair have been described by several authors.<sup>8–12</sup> A QRS duration > 180 ms has been associated with right ventricular dysfunction, malignant ventricular arrhythmias, and sudden death.8, 10, 12 Increased JT dispersion has also been associated with sustained ventricular tachycardia and sudden death.9, 10 Low amplitude root mean square voltage  $\leq 100 \,\mu\text{V}$  has been shown to be a predictor of inducible ventricular tachycardia at electrophysiologic study.<sup>11</sup> However, nonsustained ventricular tachycardia has not been shown to be a predictor of late sudden death.<sup>13</sup> The initial repair of tetralogy of Fallot often requires a valvotomy and/or a transannular outflow tract patch to relieve the outflow tract obstruction adequately.<sup>14</sup> Surgical repair often leads to significant pulmonary valve regurgitation

and chronic right ventricular volume overload that was initially thought to be well tolerated.<sup>15</sup> However, chronic right ventricular volume overload has been associated with diminished exercise tolerance, decreased right and left ventricular ejection fraction, arrhythmias, and sudden death.<sup>16–24</sup>

Murphy *et al.* showed that patients with tetralogy of Fallot whose pulmonary valve annulus and structure was preserved during the initial repair had late survivals similar to population normals.<sup>3</sup> Those with a transannular patch had diminished survival compared with normals.<sup>3</sup> Patients with residual severe pulmonary valve regurgitation and chronic right ventricular volume overload may require closer follow-up than those with an intact pulmonary valve and annulus.

Relief of structural abnormalities, such as pulmonary valve regurgitation, by pulmonary valve replacement late after initial repair has been shown to reduce right ventricular size and improve exercise capacity and right ventricular function.<sup>25–29</sup> Currently it is not known whether pulmonary valve replacement reduces mortality, nor which patients will benefit from this surgical procedure.

The development of cardiac magnetic resonance imaging (MRI) has allowed accurate assessment of ventricular volumes and anatomy in patients with and without congenital heart disease.<sup>30–33</sup> Cardiac MRI is particularly useful in quantifying right ventricular volumes and pulmonary valve regurgitant fractions in repaired tetralogy of Fallot.<sup>34–36</sup> Echocardiography is useful in noting the presence of right ventricular enlargement after tetralogy repair, but is not accurate in quantifying right ventricular size, particularly if the right ventricular outflow tract is distorted by aneurysmal dilatation.

Although a QRS duration > 180 ms has been proposed as a predictor of malignant arrhythmias late after initial repair, the majority of patients with tetralogy of Fallot have a QRS duration < 180 ms.<sup>8</sup> Some patients may have symptoms or progressive deterioration prior to the development of a markedly prolonged QRS duration and sudden death.

We evaluated the usefulness of the 12-lead ECG in predicting right ventricular volumes as measured by cardiac MRI in patients with surgically corrected (repaired) tetralogy of Fallot who have significant pulmonary valve regurgitation and right ventricular enlargement.

#### Methods

Patients with a diagnosis of repaired (surgically corrected) tetralogy of Fallot (95% with a transannular patch) and moderate to severe pulmonary valve regurgitation and right ventricular enlargement defined by echocardiography were included in the study. All patients had previously undergone cardiac MRI as part of a separate study. Twenty patients who had an ECG within 30 months of the MRI were included. Patients ranged in age from 4.4 to 19.3 years (mean 10.0 years).

All MRI examinations were performed on a 1.5 Tesla Signa scanner (General Electric Medical Systems, Milwaukee, Wisc.) using gradient coils as appropriate with respect to subject size. Axial cine gradient echo images were obtained from the top of the aortic arch through the heart. Volume measurements were made by two investigators (KLH and WJP). After visual inspection, the gradient echo images most closely corresponding to end-diastole (just prior to mitral valve closure) and end-systole (just before mitral valve opening) were selected. From these, three-dimensional (3-D) shaded surface renderings of both the right and left ventricular lumina were generated. Reconstructions were performed on an independent Allegro workstation (ISG Technologies, Toronto, Canada) using a seeded volume of interest technique. The technique involved selecting a range of signal intensities to be included in the reconstructed volume. For this study, we included those signal intensities corresponding to moving blood and excluded those of myocardium. A computer "seed" was placed on each axial image within the ventricle being rendered. All contiguous voxels that had signal intensities within the specified range were then automatically selected, forming a 3-D cast of the ventricular lumen. Manual editing prevented erroneous inclusion of adjacent structures with similar signal characteristics. Atrioventricular and ventricular-arterial valve planes were used to define ventricular limits. Papillary muscles were excluded from the seeded volume. The process was carried out separately for end-diastolic and end-systolic images.

To correct for differences in patient sizes and ages, the volumes were indexed to body surface area (volume in ml/ body surface in  $m^2$ ).

The patients were placed into two groups based on their right ventricular volume indexed to body surface area (RVEDV/BSA) by MRI measurement. Patients in Group 1 had an indexed right ventricular volume of  $< 102 \text{ ml/m}^2$ . Group 2 patients had a right ventricular volume  $> 102 \text{ ml/m}^2$ . A volume of  $102 \text{ ml/m}^2$  was chosen because it represents the median indexed volume and the cutoff for the lower and upper fiftieth percentiles for patients with repaired tetralogy of Fallot and with pulmonary valve regurgitation late after initial repair based on an MRI study of 42 such patients at our institution (personal communication, Parks WJ, May 1998).

The ECGs were performed using the standard 12 leads on patients aged > 8 years. A V<sub>4</sub>R lead was included in patients  $\leq$  8 years of age. The ECGs were performed with a Marquette VU (Milwaukee, Wisc.) at a paper speed of 25 mm/s.

The ECGs were interpreted by two investigators; one was blinded to the patients' history and MRI results (JWH), the other had access to the patients' history and MRI results (WMB). Both investigators independently reviewed all ECGs. The patient's age was indicated on the ECG. All patients but one were in normal sinus rhythm (one had junctional tachycardia) and all had either a right bundle-branch block pattern or right ventricular conduction delay on the 12-lead ECG. One patient also had a left anterior fascicular block pattern in addition to the right bundle-branch block pattern.

The 12-lead ECG was examined in all patients, except in one in whom only a rhythm strip from a Holter monitor was available. The ECGs were examined for rhythm, PR interval, P-wave abnormalities, frontal plane QRS axis, QRS duration, and T-wave axis. The mean frontal plane QRS axis was determined by measuring the total net area of the QRS complex by



FIG. 1 Illustration of "northwest" quadrant mean frontal plane QRS axis.  $\blacksquare$  = Range of mean frontal plane QRS axis considered "northwest."

estimating the area above and below the baseline and relating the result to the extremity lead axis. This method is described in detail by Grant and Estes.<sup>37</sup> For the purposes of analysis, the frontal plane QRS axis was classified as "northwest quadrant" (+ 180 to  $-90^{\circ}$ ) or "not northwest quadrant" (Fig. 1). The computer-derived QRS axis was not utilized.

Maximal QRS duration was recorded as the longest manually measured duration from the beginning of the Q or R wave to the end of the S wave. Computer-calculated QRS durations were not used.

The P wave was analyzed for direction and morphology. For purposes of analysis, the P wave was classified as "normal" or "abnormal." P-wave abnormality was defined as the presence of abnormalities of duration, axis, amplitude, or morphology for age.<sup>38</sup> The PR interval was measured manually and recorded. First-degree atrioventricular block was also noted if present as defined by a PR interval exceeding the normal limits for rate and age.<sup>38</sup>

All ECGs were examined by two observers (JWH and WMB). These observers agreed on the direction of the frontal plane QRS axis within 10° and on QRS duration within 0.01 s on all ECGs. In no situation did the observers place the patients in different QRS axis categories.

The MRI scans were interpreted and volumes quantified by two observers experienced in cardiac MRI (KLH and WJP).

#### **Statistical Analysis**

Sensitivity, specificity, and positive and negative predictive value were then determined for QRS duration and frontal plane axis in predicting right ventricular volume indexed to body surface area. For comparison of proportions, the exact mid-p p value was calculated.<sup>39</sup> To compare means, the independent *t*-test was used. A p value of <0.05 was considered to be statistically significant.

### Results

The ECGs and cardiac MRI scans of 20 patients late after repair of tetralogy of Fallot were reviewed. A 12-lead ECG was reviewed in 19 patients. One patient had review of a Holter monitor rhythm strip as the ECG recorded nearest to her MRI.

	Group 1 (n = 7)	Group 2 (n = 13)	p Value
No transannular patch	0	1	0.68
Operative note missing	2	2	NS
Transannular patch	5	10	0.66
Mean age at repair (months)	13.8	22.0	0.35
Mean age at MRI years	10.7	9.3	0.35
Mean time from repair to			
MRI (years)	13.4	7.6	0.16
Male (%)	3 (43)	11 (85)	0.09
Palliative shunt prior to			
repair (%)	1 (14.2)	4 (30.7)	0.45
Pulmonary valve replacement			
late after repair (%)	2 (28.5)	8(61.5)	0.20
Mean RVEDV/BSA (ml/m <sup>2</sup> )	82.3	128.7	< 0.001 a

<sup>a</sup>p<0.05 considered significant.

Abbreviations: RVEDV/BSA = right ventricular end-diastolic volume in milliliters divided by body surface area in meters squared, MRI = magnetic resonance imaging, NS = not significant.

All ECGs except four were performed within 7 months of the MRI date. Two ECGs in each group which were performed within 7–30 months from the MRI date were included.

The baseline characteristics of the two groups are shown in Table I. There were no significant differences between the two groups in baseline characteristics although there was a trend toward more males in Group 2 (p=0.09). The groups were defined based on their right ventricular volumes, and this difference did reach statistical significance. The mean RVEDV indexed to body surface area as determined by MRI volume measurements of 14 children without structural heart disease is 41 (± 9) ml/m<sup>2</sup> (personal communication, K. Hopkins 1999).

The ECG features of the two groups are shown in Table II. The mean QRS duration was significantly longer in Group 2.

TABLE II Electrocardiographic features of Group 1 and 2 patients

	Group 1	Group 2	p Value
Mean QRS duration (ms)	123	156	0.005 "
Range of QRS duration	80-150	130-200	
Northwest QRS axis (%)	1(14)	6(50)	0.25
Mean PR interval (ms)	134	192	0.06
First-degree AV block (%)	0(0)	6(46)	0.034
P wave abnormal (LAA, RAA,			
or bilatrial enlargement) (%)	2 (28.5)	4 (30.1)	0.80

<sup>*a*</sup> p Value of <0.05 considered statistically significant. The mean maximally measured QRS duration was significantly longer in Group 2 patients (RVEDV/BSA  $\geq$  102 ml/m<sup>2</sup>) than in Group 1 patients. Firstdegree AV block was present significantly more in Group 2 patients. *Abbreviations:* AV = atrioventricular, LAA = left atrial abnormality, RAA = right atrial abnormality, RVEDV/BSA = right ventricular end-diastolic volume divided by body surface area.



FIG. 2 Sample electrocardiogram from a Group 1 patient. Mean frontal plane QRS axis is + 115. Maximally measured QRS duration (lead II) is 100 ms.

First-degree atrioventricular (AV) block was seen in a significantly higher proportion of Group 2 patients and in none of the Group 1 patients. A representative ECG from Groups 1 and 2 are shown in Figures 2 and 3, respectively.

Using a QRS duration  $\ge 150$  ms alone, the sensitivity and specificity for predicting a right ventricular volume indexed to body surface area of  $\ge 102$  ml/m<sup>2</sup> was 69 and 86%, respectively. A northwest quadrant frontal plane QRS axis and/or a QRS duration  $\ge 150$  ms increases the sensitivity without affecting the specificity (Table III). The range of QRS duration in the Group 2 patients was 130 to 200 ms. Four patients in Group 2 had both a QRS duration  $\ge 150$  ms and a northwest quadrant axis, six patients had a QRS duration  $\ge 150$  ms without a northwest quadrant axis, two had a northwest quadrant axis alone with a QRS duration of 140 ms in one and 130 ms in the other, and two patients had neither. Five patients in Group 2 had serial ECGs available for comparison. In the first patient, the initial QRS duration prior to repair was 60 ms with a frontal plane QRS axis of  $+ 125^{\circ}$ . One year after repair, the QRS duration was 110 ms with an axis of  $-130^{\circ}$ . The patient then underwent closure of a residual ventricular septal defect. Two years after initial repair and 1 year after the VSD closure (at the time of MRI), the QRS duration was 140 ms with a left-axis deviation (left anterior fascicular block pattern). This same patient then underwent a pulmonary valve replacement, and the ECG done 2 years after the MRI showed a QRS duration of 160 ms and persistent left anterior fascicular block pattern.

A second patient had an ECG available 6 years after initial repair, which was essentially the same as the one obtained at the time of MRI 9 years after repair showing a QRS duration of 150 ms with a normal axis in both tracings. First-

![](_page_3_Figure_7.jpeg)

FIG. 3 Sample electrocardiogram from a Group 2 patient. Mean frontal plane QRS axis is -100. The maximally measured QRS duration (lead V<sub>1</sub>) is 190 ms.

TABLE III Sensitivity, specificity, positive and negative predictive value of maximal QRS duration  $\geq$  150 ms and /or a northwest (NW) quadrant axis (mean frontal plane QRS axis ± 180 to -90 degrees) for predicting right ventricular end-diastolic volume indexed to body surface area (RVEDV/BSA)  $\geq$  102 ml/m<sup>2</sup> as measured by MRI

	Group 2 (RVEDV/BSA ≥ 102 ml/m <sup>2</sup> )	Group 1 (RVEDV/BSA <102 ml/m <sup>2</sup> )
QRS duration $\ge 150 \text{ ms}$ and/or NW axis <sup><i>a</i></sup>	11	1
QRS duration < 150 ms and axis other than NW	2	6

a p = 0.002.

Positive predictive value of ECG 92%, negative predictive value of ECG 75%, sensitivity 85%, specificity 86%.

See Figure 1 for diagram of a northwest quadrant frontal plane QRS axis.

Abbreviations: NW = northwest, RVEDV/BSA = right ventricular end-diastolic volume divided by body surface area, MRI = magnetic resonance imaging, ECG = electrocardiogram.

degree AV block with a PR interval of 210 ms was present on both tracings.

A third patient had ECGs from 9 and 11 years after initial repair. The QRS duration was unchanged in these two tracings but the frontal plane QRS axis had shifted from right-axis deviation to the northwest quadrant in the later tracing. This patient also had first-degree AV block present on both tracings.

The fourth patient had an ECG available 5 years after initial repair, 7 years after repair (at the time of MRI), and 1 year after MRI (following pulmonary valve replacement). The QRS durations on these tracings were 140, 150, and 130 ms, respectively, with the frontal plane QRS axis of + 180, -170 and + 130, respectively. This patient also had first-degree AV block with a PR interval of 250 ms present on all three tracings.

The fifth patient also had an ECG available before and after pulmonary valve replacement (3 and 4 years after initial repair, respectively). The QRS duration and frontal plane QRS axis were unchanged in this patient.

The range of QRS durations for the Group 1 patients was 80 to 150 ms. Only one patient had a QRS duration  $\geq$  150 ms (150 ms) and also was the only patient in the group with a northwest quadrant axis. This patient had a right ventricular volume indexed to body surface area of 64 ml/m<sup>2</sup>.

#### Discussion

Approximately 5% of patients with tetralogy of Fallot die suddenly late after total repair.<sup>1–8</sup> Another 9 to 10% undergo pulmonary valve replacement for chronic right ventricular volume overload from chronic pulmonary valve regurgitation.<sup>17, 19, 20, 27–29</sup> Cardiac MRI is a relatively new method for following ventricular volumes and right ventricular func-

tion.<sup>31–36</sup> Pulmonary valve replacement in repaired tetralogy of Fallot with right ventricular dysfunction has been shown to improve right ventricular ejection fraction and exercise tolerance.<sup>27</sup> The impact of pulmonary valve replacement on arrhythmias and mortality is not known. The timing of pulmonary valve replacement and the identification of which patients with right ventricular enlargement are most likely to benefit from the procedure remains unknown.

Electrocardiographic markers have been associated with arrhythmic complications later after repair. An association between ECG findings such as the QRS duration, the QTc interval, the JTc interval, QTc dispersion, and JTc dispersion with malignant ventricular arrhythmias late after repair has been described in several studies.<sup>8–12</sup> Gatzoulis *et al.* describe a QRS duration > 180 ms as being associated with life threatening arrhythmias and right ventricular dysfunction.<sup>8</sup> Recognition of earlier ECG abnormalities may assist in determining which patients are at higher risk and require further evaluation.

Routine MRI measurements in all patients with tetralogy of Fallot is not feasible due the cost of the procedure and limited availability of centers trained in cardiac MRI studies. The 12-lead ECG is a simple and noninvasive method that can be followed serially to predict which patients might benefit from closer follow-up of their clinical status and right ventricular volumes in the setting of significant pulmonary valve regurgitation and right ventricular enlargement late after repair of tetralogy of Fallot.

Prolongation of the QRS duration beyond 150 ms was predictive of a larger right ventricular volume in our patient population. A northwest quadrant frontal plane QRS axis, when present, was observed in combination with a QRS duration  $\geq$  150 ms in all but two patients. Using a northwest quadrant frontal plane QRS axis and/or a QRS duration of  $\geq$  150 ms increased the sensitivity of the ECG for detecting a larger right ventricular volume to 85% without affecting the specificity.

With an isolated right bundle-branch block one would not expect a QRS duration  $\geq 150$  ms or a northwest quadrant frontal plane QRS axis; thus either of these findings suggests that an intramyocardial conduction abnormality is present beyond the bundle branches themselves. Such abnormalities could be the result of marked dilatation of the right ventricle. The cause of the dilatation in the group we studied is probably longstanding pulmonary valve regurgitation. However, additional surgical factors might predispose to marked dilatation in the setting of long-term pulmonary valve regurgitation. Although 95% of our group had a transannular patch as part of their initial repair and all had moderate to severe pulmonary valve regurgitation, there was a vast difference in their QRS durations that could not be accounted for by age or time from surgery. Why the dilatation occurs in some patients with tetralogy and not in others with the same degree of pulmonary valve regurgitation is not clear. This could be due to differences in surgical technique involved in infundibular resection or patching the ventricular septal defect, although we found no such differences in review of available operative notes. Gatzoulis et al. noted that their patients with a restrictive right ventricular pattern by echocardiography had a better outcome.8

To answer this question, a prospective study with serial ECGs starting in the immediate postoperative period should be performed. If the QRS duration is markedly prolonged immediately postoperative, this implies a surgical etiology. If, however, serial ECGs show gradual increases in the QRS duration, long-standing pulmonary valve regurgitation is the more likely culprit. This is an important question to answer as we send more patients with repaired tetralogy of Fallot for late pulmonary valve replacements in the hope of improving their right ventricular function.

We examined serial ECGs in the five patients in whom they were available. Unfortunately, we did not have a sufficient number of tracings available from the time of initial repair to answer the question of cause and effect satisfactorily. Clearly, without a large number of sequential tracings the question of cause and effect cannot be answered.

The presence of first-degree AV block on the ECG could be surgical in origin. We found this only in the larger right ventricular volume group which again may represent a group who required more extensive resection of the infundibular area. Its presence on the ECG also indicates a group of patients with repaired tetralogy of Fallot who require further evaluation of their right ventricular size and function.

Prolongation of the QRS duration beyond 150 ms did indicate a larger right ventricle in the majority of patients studied. Right ventricular dilatation has been associated with decreased exercise tolerance, right ventricular dysfunction, and arrhythmias.<sup>16–19, 22</sup> Routine ECGs with manual measurement of the maximal QRS duration may be helpful in determining which patients with repaired tetralogy of Fallot and significant pulmonary valve regurgitation require closer follow-up or more extensive evaluation. The northwest quadrant frontal plane QRS axis signifies a patient who requires further evaluation and follow-up. This finding was present in only one patient with a smaller right ventricular volume.

### Limitations

Our study is limited by its small number of patients and the lack of serial ECGs on most patients. We also chose to include four patients (two in each group) whose ECGs were performed 13 to 30 months prior to the MRI date. We assumed significant changes did not occur on the ECG during that time period in the absence of interim surgery.

## Conclusion

We describe a method of utilizing the electrocardiogram of patients with repaired tetralogy of Fallot as a tool for predicting marked right ventricular enlargement and dysfunction late after repair. A QRS duration of  $\geq 150$  ms and/or a northwest quadrant frontal plane QRS axis has a 85% sensitivity and a 86% specificity for detecting marked enlargement of the right ventricle as measured by MRI. By examining both the maximal manually measured QRS duration, frontal plane QRS axis, and the PR interval, one can noninvasively predict patients with marked enlargement of the right ventricle in the setting of pulmonary valve regurgitation late after tetralogy of Fallot repair. Prospective follow-up of these patients with serial ECGs is necessary to determine the long-term predictive value of ECG abnormalities for predicting events such as arrhythmias and sudden death.

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