



Clinical research

# Reduction of QRS duration after pulmonary valve replacement in adult Fallot patients is related to reduction of right ventricular volume

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## KEYWORDS

Electrocardiography;  
Magnetic resonance  
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Pulmonary valve  
replacement

**Aims** Late after total correction, Fallot patients with a long QRS duration are prone to serious arrhythmias and sudden cardiac death. Pulmonary regurgitation is a common cause of right ventricular (RV) failure and QRS lengthening. We studied the effects of pulmonary valve replacement (PVR) on QRS duration and RV volume.

**Methods and results** Twenty-six consecutive Fallot patients were evaluated both pre-operatively and 6–12 months post-operatively by cardiac magnetic resonance (CMR). In this study, we present the computer-assisted analysis of the standard 12-lead electrocardiograms closest in time to the CMR studies. For the whole group, QRS duration shortened by  $6 \pm 8$  ms, from  $151 \pm 30$  to  $144 \pm 29$  ms ( $P = 0.002$ ). QRS duration decreased in 18 of 26 patients by  $10 \pm 6$  ms, from  $152 \pm 32$  to  $142 \pm 31$  ms. QRS duration remained constant or increased slightly in eight of 26 patients by  $3 \pm 3$  ms, from  $148 \pm 27$  to  $151 \pm 25$  ms. CMR showed a decrease in RV end-diastolic volume from  $305 \pm 87$  to  $210 \pm 62$  mL ( $P = 0.000004$ ). QRS duration changes correlated with RV end-diastolic volume changes ( $r = 0.54$ ,  $P = 0.01$ ).

**Conclusion** Our study shows that PVR reduces QRS duration. The amount of QRS reduction is related to the success of the operation, as expressed by the reduction in RV end-diastolic volume.

## Introduction

Tetralogy of Fallot (TOF) is the most common cyanotic congenital abnormality.<sup>1</sup> Surgical total correction has resulted in an increasing number of patients reaching adulthood. However, late after total correction, TOF

patients with a QRS duration  $>180$  ms are prone to ventricular tachycardia and sudden cardiac death.<sup>2</sup> An important causative factor of increased QRS duration is residual pulmonary valve regurgitation, which may lead to severe right ventricular (RV) dilatation and heart failure.<sup>3,4</sup> Pulmonary valve replacement (PVR) has been reported to stabilize the gradual progression of the QRS duration in the long run.<sup>5</sup> Additionally, risk stratification by QRS duration may be further refined by analysis of

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QRS dispersion and QT dispersion.<sup>6</sup> The aim of our study was to evaluate the short-term effects of PVR on the QRS duration, QRS- and QT-dispersion. We also examined whether changes in QRS duration were related to changes in RV volume as obtained with cardiac magnetic resonance (CMR).

## Methods

From 1997 to 2002, twenty-six (15 male/11 female) consecutive TOF patients were evaluated with CMR pre-operatively and 6–12 months post-operatively.<sup>7</sup> In the present study, we present the retrospective serial analysis of the standard 12-lead electrocardiograms (ECGs) closest in time to the pre- and post-operative CMR studies. All patients were treated according to our routine clinical protocol.

## Patients

Baseline patient characteristics and surgical procedures are summarized in *Table 1*. The median age at which initial total repair had been performed was 5.0 years [interquartile range (IQR) 2.8–6.8 years]. A transannular patch was applied in 10 patients. Prior to total repair, a palliative procedure had been performed in 11 patients.

Major indications for PVR were pulmonary regurgitation in combination with RV dilatation and a reduced validity. Only two patients were in NYHA class I, but these patients had severely dilated RVs, defined as an increase in RV end-diastolic volume (EDV) more than twice the left ventricular EDV. Overall, 15 patients had severe pulmonary regurgitation and 11 patients had moderate pulmonary regurgitation. Severe RV dilatation was seen in 13 patients. Residual pulmonary valve regurgitation was corrected by PVR at a median age of 29.2 years (IQR 24.3–39.4 years).

## CMR

CMR was performed using a 1.5 T system (NT15 Gyroscan, Philips Medical Systems, Best, The Netherlands). The CMR protocol has

been described previously.<sup>7</sup> Briefly, a multiphase, ECG-triggered, multishot echoplanar gradient echo technique was used to acquire short axis images. Images were acquired during breath holds. Slice thickness was 10 mm with a 0.8–1.0 mm section gap. The flip angle was 30° and echo time was 5–10 ms. Eighteen to twenty-five frames per cycle resulted in a temporal resolution of 22–35 ms.

## ECG

For this study, we used all ECGs of these patients that had been stored digitally. Such ECGs were recorded at a median of 7.8 months (IQR 12.4–2.5 months) before PVR and at a median of 14.3 months (IQR 3.8–20.1 months) after PVR. The pre-operative ECGs closest in time to the pre-operative CMR studies were recorded at a median of 2.0 months (IQR 3.8 to –1.1 months) before CMR. The post-operative ECGs closest in time to the post-operative CMR studies were recorded at a median of 2.7 months (IQR –2.3 to 13.8 months) after CMR. All ECGs were standard 12-lead recordings with a sample frequency of 500 Hz.

The ECGs were analysed by our MATLAB computer program LEADS (Leiden ECG Analysis and Decomposition Software). LEADS first computed an averaged beat, to minimize noise. In this averaged beat, the beginning and end of the QRS complex were automatically detected. Finally, the observer, blinded to the patient data, corrected this interval if necessary. To facilitate easy identification of the first deflection in any lead (onset QRS) and the last sharp deflection in any lead (offset QRS), the 12 standard ECG leads were superimposed on the screen. By using the zoom function, the ECG could be magnified at will, which allowed for the most accurate crosshair-cursor measurement of the QRS duration. QRS- and QT-dispersion were calculated as the longest minus the shortest interval in any of the 12 leads. The end of the T-wave was defined as the moment of return to the baseline. If U-waves were present, the end of the T-wave was set at the T-U nadir.

## Statistical analysis

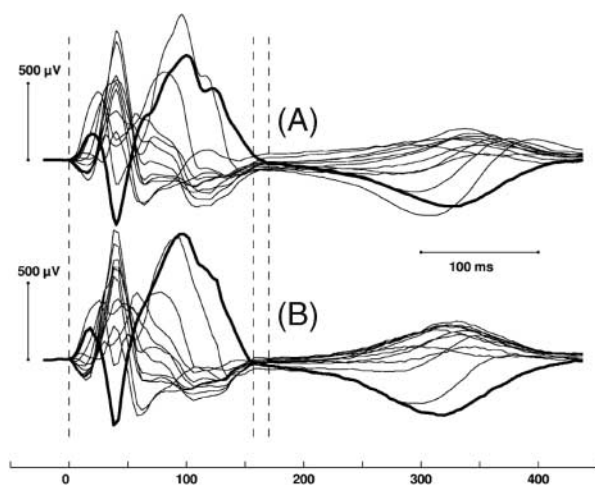
Two-sided paired Student's *t*-tests were used to compare pre- and post-operative data. *P*-values were Bonferroni corrected for multiple testing. Linear regression analysis was performed to assess the relation between the changes in QRS duration and the changes in RV EDV. A probability value of *P* < 0.05 was considered significant.

## Results

A typical example of a pre- and post-operative ECG is shown in *Figure 1*. Twenty-four of 26 patients had a right bundle branch block pattern before and after PVR. For the whole group, QRS duration shortened by  $6 \pm 8$  ms, from  $151 \pm 30$  to  $144 \pm 29$  ms (*P* = 0.002, *Table 2*). QRS duration decreased in 18 of 26 patients by  $10 \pm 6$  ms, from  $152 \pm 32$  to  $142 \pm 31$  ms and remained constant or increased slightly in eight of 26 patients by  $3 \pm 3$  ms, from  $148 \pm 27$  to  $151 \pm 25$  ms. QRS- and QT-dispersion did not change significantly, from  $22 \pm 14$  to  $23 \pm 9$  ms (*P* = 0.97) and from  $47 \pm 21$  to  $47 \pm 20$  ms (*P* = 0.99), respectively. RV EDV could be obtained in 20 patients both before and after PVR. (In six patients, CMR could not be obtained owing to technical difficulties, the quality of four pre-operative and two post-operative CMRs appeared unsatisfactory

**Table 1** Baseline patient characteristics and surgical characteristics

Male sex ( <i>n</i> )	15
NYHA class	2.0 ± 0.6
Median age at initial repair (years)	5.0 (IQR 2.8–6.8)
Previous palliative shunt ( <i>n</i> )	
Blalock–Taussig	7
Watterston	3
Potts	1
Type of repair ( <i>n</i> )	
No patch	10
RV patch	6
Transannular patch	10
Median age at PVR (years)	29.2 (IQR 24.3–39.4)
Additional procedure ( <i>n</i> )	
Resection of infundibulum	2
Tricuspid valve repair	4
Closure of VSD	3
Closure of atrial septal defect (type II)	1



**Figure 1.** Example of the averaged beat of a patient before (A) and after (B) PVR. To make the difference in QRS duration clearly visible, the ECGs were plotted on a stretched time scale, with all 12 ECG leads superimposed. Lead V1, relevant for the end of the QRS complex, is plotted as a thick line. Start and end of the QRS complexes are indicated by vertical dashed lines. QRS duration shortened by 14 ms (from the right dashed line that marks the end of the QRS complex in the pre-operative ECG to the left dashed line that marks the end of the QRS complex in the post-operative ECG).

at the moment of analysis.) CMR showed an RV EDV decrease from  $305 \pm 87$  to  $210 \pm 62$  mL ( $P = 0.000004$ ). In patients with reduced QRS durations, RV EDV reduced from  $325 \pm 86$  to  $220 \pm 69$  mL ( $P = 0.00004$ ) and in patients with constant or slightly increased QRS duration, RV EDV decreased from  $253 \pm 72$  to  $190 \pm 42$  mL ( $P = 0.03$ ). These volume reductions, of 105 and 63 mL, respectively, tended to be larger in the group with reduced QRS duration, but this did not reach statistical significance ( $P = 0.08$ ). QRS duration changes correlated with RV EDV changes ( $r = 0.54$ ,  $P = 0.01$ , see Figure 2).

## Discussion

Our study demonstrated a decrease in QRS duration after PVR in patients with TOF. This reduction in QRS duration appeared to be related to the reduction of RV EDV. Until now, only a stabilization of QRS duration after PVR has been reported.<sup>5</sup> The use of a computer-assisted ECG measurement technique allowed us to show that PVR actually reduced QRS duration in most patients. In addition, our results demonstrate a relationship between the structural improvement and the improvement of electrical function. To our knowledge, our study is the first that showed a decrease in QRS duration following PVR in TOF patients.

Gatzoulis *et al.*<sup>6</sup> showed that QRS- and QT-dispersion could be used to refine risk stratification on top of QRS duration. Although according to present insights QT dispersion only indirectly estimates repolarization disturbances,<sup>8</sup> gross changes in de- and repolarization may still be detected by QRS- and QT-dispersion. However, in our

patient group no changes in QRS- and QT-dispersion were induced by PVR.

## Relation between QRS duration, RV dilatation, and arrhythmias

Gatzoulis *et al.*<sup>2</sup> reported a QRS duration  $>180$  ms as a risk marker for ventricular arrhythmias and sudden cardiac death.<sup>2</sup> Other studies confirmed a relation between QRS duration and late arrhythmias.<sup>9,10</sup> This relation may be explained by common factors that contribute to both the increased QRS duration and the vulnerability to arrhythmias. A central role is probably played by ventricular dilatation. Dilatation of the right ventricle increases wall stress, which leads to fibrosis of the right ventricle.<sup>11</sup> Fibrotic areas form blockades and areas of slow conduction that facilitate re-entry tachycardias.<sup>12-15</sup> Furthermore, stretch is known to induce premature ventricular excitations, which may serve as an arrhythmogenic trigger.<sup>16</sup> Additionally, ventricular dilatation may increase QRS duration by increasing the distance that the electrical activation front has to travel in the right ventricle, as most of our patients had a right bundle branch block pattern.

In previous studies,<sup>17-19</sup> a relation between RV EDV and QRS duration was found in a group of Fallot patients. The present study shows that this relation also holds for changes in RV EDV and QRS duration.

## Surgery in TOF patients

Total repair itself may contribute to the arrhythmogenicity. Scars made during the transventricular approach and applied patches may form anatomical blockades facilitating re-entry.<sup>15</sup> On the other hand, surgical resection of aneurysms and correction of ventricular septal defects could reduce the amount of potential contributors to arrhythmias.

Pulmonary regurgitation is the predominant haemodynamic lesion in Fallot patients with ventricular tachycardias and sudden cardiac death.<sup>3,20</sup> However, the timing of PVR remains a subject of debate: too late may cause irreversible damage to the RV, whereas too early may lead to multiple re-operations. Our study shows that in TOF patients with dilated RVs, PVR leads not only to mechanical but also to electrical beneficial effects. Hopefully, re-operations might be prevented in the future by the use of percutaneous implantation of pulmonary valves.<sup>21</sup>

## Limitations

As we had to restrict ourselves to digitally stored ECGs, there was a time lag between the ECGs and CMR studies [pre-operative ECGs 2.0 months (IQR  $-1.1$  to 3.8 months) before CMR and post-operative ECGs 2.7 months (IQR  $-2.3$  to 13.8 months) after CMR]. This imposes a limitation upon the conclusions that can be drawn from our study. However, we think that the observed effect of a reduction in QRS duration after

**Table 2** QRS durations and RV EDVs before and after PVR

	Pre-PVR		Post-PVR	
	QRS (ms)	RV EDV (mL)	QRS (ms)	RV EDV (mL)
QRS shortened ( <i>n</i> = 18)	152 ± 32	325 ± 86 ( <i>n</i> = 16)	142 ± 31	220 ± 69* ( <i>n</i> = 16)
QRS constant or lengthened ( <i>n</i> = 8)	148 ± 27	253 ± 72 ( <i>n</i> = 6)	151 ± 25	190 ± 42† ( <i>n</i> = 8)
QRS overall ( <i>n</i> = 26)	151 ± 30	305 ± 87 ( <i>n</i> = 22)	144 ± 29‡	210 ± 62¶ ( <i>n</i> = 24)

Values are mean ± standard deviations.

*n*, number of patients.

\**P* = 0.00004 vs. pre-operative value.

†*P* = 0.03 vs. pre-operative value.

‡*P* = 0.002 vs. pre-operative value.

¶*P* = 0.000004 vs. pre-operative value.

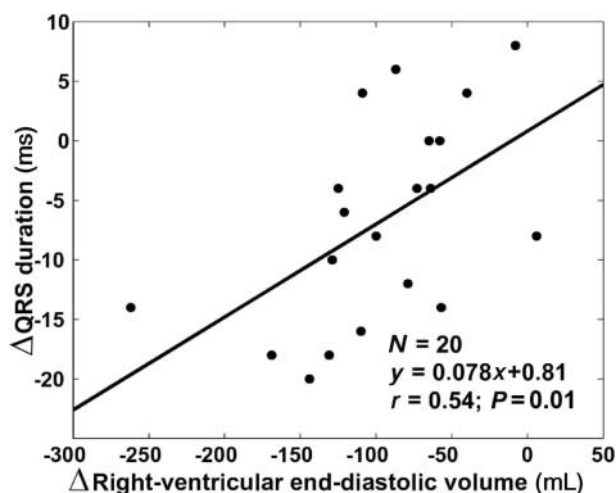


Figure 2. Correlation between changes in RV EDV and QRS duration.

PVR was weakened rather than strengthened by these time differences: relatively early pre-operative ECGs may have rendered smaller QRS durations before PVR, whereas relatively late post-operative ECGs may have rendered larger QRS duration after PVR. Both effects may have reduced the observed changes in QRS duration after PVR.

This study did not directly assess the effects of PVR on arrhythmias. However, as previous studies with longer follow-up of non-operated TOF patients have found a strong relation between QRS duration and arrhythmias, PVR resulting in reduced QRS duration is likely to protect against arrhythmias.

## Conclusion

PVR reduces QRS duration, a risk marker for ventricular tachycardias and sudden death in TOF patients. The structural success of the operation, measured as the reduction of the RV EDV, is related to the reduction of QRS duration.

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