Preoperative thresholds for mid-to-late haemodynamic and clinical outcomes after pulmonary valve replacement in tetralogy of Fallot

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Aims
The right ventricle (RV) remodels early after pulmonary valve replacement (PVR) in tetralogy of Fallot (TOF) patients. Previously reported preoperative thresholds to achieve early postoperative RV normalization were consistently close to 80 mL/m² for end-systolic volume (ESV) and 160 mL/m² for end-diastolic volume (EDV). Our objective was to determine whether these thresholds were also associated with mid-to-late RV normalization and clinical events.

Methods and results
Out of a multicentre cohort of 157 TOF patients who had undergone PVR, in 65 patients (62% male, age 29 ± 8 years, homograft in 98%) cardiovascular magnetic resonance (CMR) imaging was performed preoperatively and 3 years (6.3 years, interquartile range: 4.9–9.5) postoperatively. Mid-to-late haemodynamic outcome was classified as: ‘RV normalization’ [RV ejection fraction (EF) > 48% and RV EDV < 108 mL/m²] in 14 of 65 (22%) patients, ‘intermediate’ in 34 of 65 (52%) patients, and ‘suboptimal’ (RV EF < 45% and RV EDV > 120 mL/m²) in 17 of 65 (26%) patients. Preoperative RV ESV < 80 mL/m² was strongly associated with favourable mid-to-late haemodynamic outcome in a proportional odds model [common odds ratio (OR): 0.04 for worse class, 95% confidence interval (CI): 0.01–0.17]. During 7.8 ± 4.0 years follow-up after PVR, adverse clinical events (death, sustained ventricular tachycardia, or heart failure) occurred in 18 of 106 (17%) patients with preoperative CMR available. Patients with preoperative RV ESV > 95 mL/m² were at increased risk for unfavourable mid-to-late haemodynamic outcome (common OR: 25.5, 95% CI: 5.35–122) and events (hazard ratio: 2.89, 95% CI: 1.03–8.11).

Conclusion
In TOF patients who had undergone PVR, the best preoperative threshold to achieve mid-to-late RV normalization was RV ESV < 80 mL/m². Patients with preoperative RV ESV > 95 mL/m² were at increased risk for suboptimal haemodynamic outcome and adverse clinical events. Our findings may assist in timing of PVR.

Keywords
Tetralogy of Fallot • Pulmonary valve replacement • Pulmonary regurgitation • Cardiovascular magnetic resonance imaging • Congenital heart disease

Introduction
Progress in surgical techniques and medical management have led to dramatic improvements in prognosis for patients born with tetralogy of Fallot (TOF).1,2 However, in adult patients right ventricular (RV) dilatation and dysfunction may persist even after correction of residual pulmonary regurgitation (PR) by pulmonary valve replacement (PVR).3,4 These patients are known to be at risk for heart failure.

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arrhythmias, and sudden cardiac death.\textsuperscript{5–9} Optimal timing of PVR may prevent such unfavourable late sequelae.\textsuperscript{4,10} Previous research has revealed preoperative RV volume thresholds above which early postoperative normalization of RV function and volume was unlikely.\textsuperscript{4,11–14} Reported thresholds were consistently close to 80 mL/m\textsuperscript{2} for end-systolic volume (ESV) and 160 mL/m\textsuperscript{2} for end-diastolic volume (EDV).\textsuperscript{4,11–14} Consequently, current European guidelines advise PVR in asymptomatic patients with progressive RV dilatation in order to prevent irreversible RV dysfunction.\textsuperscript{15} However, several factors such as pulmonary conduit degeneration, ventricular dysynchrony, and fibrosis may also have unfavourable effects on mid-to-late postoperative RV haemodynamics.\textsuperscript{16–19} Moreover, it remains unclear whether beneficial early effects of PVR persist during follow-up and whether operating before exceeding RV volume thresholds would also result into mid-to-late RV normalization and better clinical outcomes. Therefore, we aimed to determine preoperative thresholds associated with mid-to-late haemodynamic outcome and clinical events.

**Methods**

For this retrospective, multicentre cohort study, we identified all patients with a previous surgical correction for TOF who had undergone PVR to correct PR in one of three participating academic centres (Academic Medical Center Amsterdam, Leiden University Medical Center, and Radboud University Medical Center Nijmegen) at an age of 12 years or older. The mid-to-late haemodynamic outcomes were studied in patients if both preoperative (<3 years before PVR) and mid-to-late (>3 years after PVR) cardiovascular magnetic resonance (CMR)-derived RV volume and function were available, and mid-to-late CMR was performed prior to redo-PVR or tricuspid valve (TV) plasty or replacement. Medical records were reviewed to obtain patient and surgical characteristics. In addition, peak systolic pressure gradient across the RV outflow tract was estimated by continuous wave Doppler echocardiography. Early effects of PVR and the course of RV function during follow-up were investigated in a subgroup of patients in whom early postoperative CMR was also available. Finally, the occurrence of a composite of clinical events [death, sustained ventricular tachycardia (VT) (>30 s or requiring cardioversion), or heart failure (increase in NYHA class requiring diuretics)] was determined in all patients in whom preoperative CMR was available. Surgical techniques used for PVR have been described previously.\textsuperscript{4,16} This study complies with the declaration of Helsinki and was approved by the institutional ethics committee. The need to obtain informed consent was waived by the ethics committee.

**Cardiovascular magnetic resonance**

Cardiovascular magnetic resonance imaging data were acquired on local available magnetic resonance systems. Cardiovascular magnetic resonance studies were performed with the use of previously described imaging protocols.\textsuperscript{3,10} The short-axis orientation was used to calculate both RV and left ventricular (LV) volumes from endocardial contours with the use of MASS software (Medis, Leiden, the Netherlands). Trabeculations and papillary muscles were considered part of the ventricular cavity.\textsuperscript{23} Ejection fraction (EF) was calculated as stroke volume (EDV minus the ESV) divided by EDV. Velocity mapping was used to determine PR fraction and was performed with the use of velocity-encoded phase contrast sequence.

**Definition of outcomes**

In line with previous studies, RV normalization was defined as normal RV volume (RV EDV < 108 mL/m\textsuperscript{2}) and function (RV EF > 48%) mid-to-late after PVR.\textsuperscript{4,12} Suboptimal mid-to-late haemodynamic outcome was defined as RV dilatation (RV EDV > 120 mL/m\textsuperscript{2}) and dysfunction (RV EF < 45%).\textsuperscript{13} Patients who did not fulfil criteria for either RV normalization or suboptimal outcome were considered to have ‘intermediate’ outcome.

**Statistical analysis**

Data were described as number with frequency, median with interquartile range, and mean with standard deviation. Mid-to-late haemodynamic outcome was classified as an ordinal variable (ranging from favourable to unfavourable class: (i) RV normalization, (ii) intermediate, and (iii) suboptimal). A proportional odds model was used to calculate the common odds ratio (odds for less favourable class) of different predictive variables. The assumption of proportional odds was checked with the test of parallel lines. Continuous variables were dichotomized on relevant cut-off values by plotting receiver operating characteristic curves and assessing the area under the curve (AUC) for RV normalization or suboptimal haemodynamic outcome. Univariate linear regression analysis was used to determine variables associated with changes in RV ejection fraction during serial follow-up. Variables with P-value < 0.10 were entered in a backward multivariable linear regression model. The predictive value of preoperative variables on a composite of clinical events was determined using univariate Cox hazards regression analysis. The differences in haemodynamic parameters between groups were assessed with independent samples t-test or Mann–Whitney U test, as appropriate. Changes in haemodynamic parameters within groups with paired t-test or Wilcoxon signed rank test, as appropriate. Analyses were performed with SPSS 21.0. A P-value < 0.05 was considered statistically significant.

**Results**

Out of a total of 157 TOF patients who had undergone PVR (Figure 1), haemodynamic mid-to-late outcomes were determined in a subgroup of 65 patients in whom preoperative, and mid-to-late CMR were available (Table 1). All patients had preoperative PR fraction of ≥25% on CMR and 10 of 65 (15%) patients also had significant preoperative pulmonic stenosis (>36 mmHg pressure gradient) on echocardiogram. Excluded patients without preoperative CMR

![Figure 1](https://example.com/flowchart.png)
Mid-to-late outcomes after PVR in TOF

3 years after PVR are listed in Table 1. In 11 of 53 (21%) patients, 27 of 106 (25%) patients with preoperative RV ESV < 80 mL/m² were at risk for the occurrence of adverse clinical events (HR: 2.89, 95% CI: 1.03–8.11, P = 0.044). There was no difference in the occurrence of adverse events between patients with preoperative RV ESV < 80 mL/m² and 95 mL/m² (2/20) (P = 0.009).

Clinical outcomes

We determined the occurrence of the composite clinical outcome in a cohort including all 106 patients in whom preoperative CMR was available. There was no difference in preoperative CMR parameters between 65 patients who also had mid-to-late CMR and 41 patients without mid-to-late CMR (see Supplementary material online, Table S2). During a mean follow-up period of 7.8 ± 4.0 years, 18 of 106 (17%) patients experienced adverse clinical events (death in 4, sustained VT in 7, and heart failure in 7). Higher preoperative RV ESV was associated with adverse clinical outcomes [hazard ratio (HR): 1.16/10 mL/m², 95% CI: 1.03–1.28, P = 0.012] (Table 4). In particular, patients with preoperative RV ESV > 95 mL/m² were at risk for the occurrence of adverse clinical events (HR: 2.89, 95% CI: 1.03–8.11, P = 0.044). There was no difference in the occurrence of adverse events between patients with preoperative RV ESV < 80 mL/m² (3/34) or 80–95 mL/m² (2/20) (P = 0.73). Other variables predictive for adverse events were older age at PVR or surgical repair, lower RV EF, and lower LV EF (P < 0.05 for all).

Table 1 Patient and surgical characteristics

<table>
<thead>
<tr>
<th>Preoperative data</th>
<th>n = 65</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient characteristics</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>40 (62%)</td>
</tr>
<tr>
<td>Age at PVR (years)</td>
<td>29 ± 8.3</td>
</tr>
<tr>
<td>Initial correction</td>
<td></td>
</tr>
<tr>
<td>Myectomy/valvulotomy</td>
<td>8 (12%)</td>
</tr>
<tr>
<td>RV patch</td>
<td>10 (15%)</td>
</tr>
<tr>
<td>Transannular patch</td>
<td>46 (71%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Age at initial correction (years)</td>
<td>3.5 (2.1–5.8)</td>
</tr>
<tr>
<td>Previous shunt procedure</td>
<td>24 (37%)</td>
</tr>
<tr>
<td>Waterston</td>
<td>9 (38%)</td>
</tr>
<tr>
<td>Blalock–Taussig</td>
<td>13 (54%)</td>
</tr>
<tr>
<td>Other</td>
<td>2 (8%)</td>
</tr>
<tr>
<td>Age at shunt procedure (years)</td>
<td>1.7 (0.6–2.5)</td>
</tr>
<tr>
<td>Down syndrome</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>22q11 deletion</td>
<td>2 (3%)</td>
</tr>
<tr>
<td>QRS duration before PVR (ms)</td>
<td>150 ± 27</td>
</tr>
<tr>
<td>Preoperative NYHA class ≥II</td>
<td>33 (51%)</td>
</tr>
</tbody>
</table>

| Surgical characteristics                |        |
| Diameter graft (mm)                     | 25 ± 2.0 |
| Type of pulmonary valve                 |        |
| Pulmonary homograft                     | 62 (95%) |
| Contegra valved conduit                 | 1 (2%)  |
| Aortic homograft                        | 2 (3%)  |
| Concomitant procedures                  |        |
| Tricuspid valve plasty or ring          | 15 (23%) |
| RV aneurysm resection                   | 23 (35%) |
| Pulmonary artery angioplasty            | 12 (19%) |
| Ventricular septal defect closure        | 2 (3%)  |

Data were described as number with frequency, median with interquartile range, and mean with standard deviation.

NYHA, New York Heart Association; PVR, pulmonary valve replacement; RV, right ventricle.

assessment had undergone PVR before CMR became widely available, or had a pacemaker or internal cardioverter defibrillator implanted.

Course of haemodynamic parameters

In 53 patients (82% of total 65 patients), CMR was also performed early after PVR. Haemodynamic parameters before, early after, and >3 years after PVR are listed in Table 2. In 11 of 53 (21%) patients, early normalization of RV function and volume was achieved. During follow-up after PVR, 8 of 65 (12%) patients developed significant pulmonic stenosis (>36 mmHg on echocardiography), 6 of 65 (9%) patients developed significant PR (>20% on CMR), and 8 of 65 (12%) patients developed at least moderate tricuspid regurgitation. Overall, RV and LV volume and function generally remained stable during follow-up after PVR (Table 2 and Supplementary material online, Figure S1). However, in 13 of 53 (25%) patients, a decline of >5% in RV EF occurred. In multivariable linear regression analysis, only longer preoperative QRS duration was significantly associated with RV deterioration (see Supplementary material online, Table S1). Male sex was only associated with deterioration of RV EF in univariate analysis as QRS duration was longer in males when compared with females (157 ± 24 vs. 140 ± 27 ms, P = 0.009).
Table 2  Preoperative and early and mid-to-late postoperative imaging parameters

<table>
<thead>
<tr>
<th>CMR</th>
<th>Before PVR</th>
<th>Early after PVR</th>
<th>Late after PVR</th>
<th>Δ PVR</th>
<th>Δ FU</th>
</tr>
</thead>
<tbody>
<tr>
<td>n = 65</td>
<td>n = 53</td>
<td>n = 65</td>
<td>n = 53</td>
<td>n = 53</td>
<td>n = 53</td>
</tr>
<tr>
<td>Time CMR from PVR (years)</td>
<td>−0.4 (−0.8 to −0.3)</td>
<td>0.7 (0.5–1.5)</td>
<td>6.3 (4.9–9.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RV EDV (mL/m²)</td>
<td>172 ± 39</td>
<td>114 ± 26</td>
<td>115 ± 26</td>
<td>59 ± 28</td>
<td>0 ± 18</td>
</tr>
<tr>
<td>RV ESV (mL/m²)</td>
<td>98 ± 30</td>
<td>64 ± 23</td>
<td>65 ± 21</td>
<td>35 ± 21</td>
<td>0 ± 17</td>
</tr>
<tr>
<td>LV EDV (mL/m²)</td>
<td>89 ± 22</td>
<td>98 ± 22</td>
<td>99 ± 23</td>
<td>8 ± 19</td>
<td>0 ± 15</td>
</tr>
<tr>
<td>LV ESV (mL/m²)</td>
<td>44 ± 14</td>
<td>47 ± 17</td>
<td>48 ± 17</td>
<td>3 ± 13</td>
<td>1 ± 12</td>
</tr>
<tr>
<td>RV EF (%)</td>
<td>44 ± 8</td>
<td>45 ± 9</td>
<td>45 ± 7</td>
<td>1.5 ± 9</td>
<td>0 ± 10</td>
</tr>
<tr>
<td>LV EF (%)</td>
<td>51 ± 11</td>
<td>53 ± 9</td>
<td>52 ± 9</td>
<td>1.9 ± 8</td>
<td>−1 ± 8</td>
</tr>
<tr>
<td>PR fraction (%)</td>
<td>47 ± 13</td>
<td>0 (0–4)</td>
<td>0 (0–7)</td>
<td>−42 ± 14</td>
<td>0 (0–3)</td>
</tr>
<tr>
<td>Echocardiography n = 57</td>
<td>n = 62</td>
<td>n = 62</td>
<td>n = 55</td>
<td>n = 60</td>
<td></td>
</tr>
<tr>
<td>Time echo from PVR (years)</td>
<td>−0.4 (−0.7 to −0.2)</td>
<td>0.02 (0.01–0.06)</td>
<td>8.4 (6.3–12.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PV gradient (mmHg)</td>
<td>22 ± 16</td>
<td>17 ± 9</td>
<td>20 ± 13</td>
<td>−5 ± 17</td>
<td>3 ± 10</td>
</tr>
<tr>
<td>PV gradient &gt;36 mmHg</td>
<td>10 (15%)</td>
<td>4 (6%)</td>
<td>8 (11%)</td>
<td>−9%</td>
<td>+5%</td>
</tr>
<tr>
<td>Tricuspid regurgitation</td>
<td>n = 55</td>
<td>n = 61</td>
<td>n = 49</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None/mild (%)</td>
<td>35 (64%)</td>
<td>58 (95%)</td>
<td>41 (84%)</td>
<td>+31%</td>
<td>−11%</td>
</tr>
<tr>
<td>Moderate/severe (%)</td>
<td>20 (36%)</td>
<td>3 (5%)</td>
<td>8 (16%)</td>
<td>−31%</td>
<td>+11%</td>
</tr>
</tbody>
</table>

Data were described as number with frequency, median with interquartile range, and mean with standard deviation. Δ PVR, change between preoperatively and early postoperatively; Δ FU, change between early postoperatively and mid-to-late postoperatively; CMR, cardiovascular magnetic resonance; EDV, end-diastolic volume; ESV, end-systolic volume; FU, follow-up; LV, left ventricle; PR, pulmonary regurgitation; PV, pulmonary valve; PVR, pulmonary valve replacement; RV, right ventricle.

Discussion

To our knowledge, this study is the first to report preoperative thresholds for mid-to-late RV normalization after PVR in TOF patients. Preoperative RV ESV < 80 mL/m², which has previously been associated with early RV normalization, was highly associated with mid-to-late RV normalization and superior to thresholds in other preoperative variables. Mid-to-late RV normalization was achieved in only 22% of the total study population as opposed to 69% of patients with preoperative RV ESV < 80 mL/m². Patients with preoperative RV ESV > 95 mL/m² were at increased risk for both suboptimal (RV dilation and dysfunction) mid-to-late haemodynamic outcome and adverse clinical events during follow-up.

Mid-to-late right ventricular normalization

Optimal timing of PVR is a matter of interest and continuing debate because adverse RV modulation can be irreversible when PVR is performed too late.4,10,12 Persistent RV dysfunction and dilation after PVR may impact mid-to-late clinical outcomes.5–7 On the other hand, performing PVR too early may lead to numerous reoperations or interventions for conduit dysfunction.11,12,16,23,24

In our study, preoperative RV ESV was superior to RV EDV and RV EF in predicting mid-to-late RV normalization, possibly because RV ESV reflects both volume and systolic function and is a valid estimate of intrinsic RV function.25 Our reported thresholds for mid-to-late RV normalization are in line with those previously published for early haemodynamic outcome. For instance, Geva et al.13 reported RV ESV (<90 mL/m²) and QRS duration (<140 ms) as predictors for early RV volume and function normalization while the study by Oosterhof et al.4 reported RV ESV (<82 mL/m²) and RV EDV (<160 mL/m²) as thresholds for early RV volume normalization. Patients with mid-to-late RV normalization also had favourable LV haemodynamic outcome, which is also associated with clinical events in TOF.6,7,18,26 These differences may be explained by continuous adverse RV-LV interaction in patients with persistent RV dysfunction.

Postoperative course of right ventricular function

We furthermore explored the course of CMR-derived RV function during serial follow-up after PVR. Although RV ejection fraction and volumes generally remained stable, a significant decline (>5%) in RV EF occurred in 25% of patients. Prolonged preoperative QRS duration was associated with RV deterioration during follow-up. Previously, QRS prolongation has been related to RV dilation and mortality in TOF patients.5,27 We hypothesize that QRS prolongation may reflect the presence of deleterious factors such as ventricular fibrosis and regional RV outflow tract dysfunction and dysynchrony.18,19,28

Recently, Hallbergson et al.29 reported an unfavourable course of RV function parameters in adults and children after PVR. Their less favourable postoperative results in a study with a partly cross-sectional design may be related to a later timing of PVR (mean preoperative RV EDV 200 mL/m² vs. 172 mL/m²) and a higher prevalence of postoperative conduit dysfunction in their population. Indeed, in our study, there was a trend towards postoperative RV function deterioration in patients with higher postoperative PVR gradient. We hypothesize that conduit dysfunction will negatively impact RV function parameters if left untreated. However, as...
most patients with severe conduit dysfunction rapidly underwent re-intervention before mid-to-late CMR, we were unable to demonstrate these effects.

Conservative approach

As it is still not entirely clear which extent of RV dysfunction and/or dilation leads to an adverse prognosis in TOF patients,\textsuperscript{6,7} we investigated predictors for mid-to-late suboptimal haemodynamic outcome (RV dysfunction and dilation). About half of the patients operated with preoperative RV ESV > 95 mL/m\(^2\) had suboptimal mid-to-late outcome, while in patients operated when preoperative RV ESV was 80–95 mL/m\(^2\) suboptimal mid-to-late outcome was unlikely. In the setting of gradually progressive RV dilation, such a conservative approach can postpone PVR for several years and has the potential to limit the number of re-interventions.\textsuperscript{30}

We found a high rate of adverse clinical events (17% after a mean of 7.8 years of follow-up) in our population. Patients operated with preoperative RV ESV > 95 mL/m\(^2\) were at increased risk for the occurrence of adverse clinical events. These findings are in line with a previous report by our group, which found more adverse events (including supraventricular tachycardias) in patients with larger

### Table 3

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mid-to-late RV haemodynamic outcome</th>
<th>ORa</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative CMR</td>
<td></td>
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<tr>
<td>RV EF (per %)</td>
<td></td>
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<tr>
<td>41 ± 8</td>
<td>42 ± 8</td>
<td>51 ± 7</td>
<td>0.90</td>
<td>0.85–0.96</td>
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<tr>
<td>RV EF &gt; 48%</td>
<td></td>
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<tr>
<td>2 (12%)</td>
<td>9 (27%)</td>
<td>11 (79%)</td>
<td>0.10</td>
<td>0.03–0.34</td>
</tr>
<tr>
<td>LV EF (per %)</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>49 ± 9</td>
<td>51 ± 11</td>
<td>56 ± 10</td>
<td>0.96</td>
<td>0.92–1.01</td>
</tr>
<tr>
<td>RV EDV (per mL/m(^2))</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>194 ± 48</td>
<td>173 ± 35</td>
<td>142 ± 24</td>
<td>1.03</td>
<td>1.01–1.04</td>
</tr>
<tr>
<td>RV EDV &lt; 160 mL/m(^2))</td>
<td></td>
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<td></td>
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<tr>
<td>4 (24%)</td>
<td>12 (35%)</td>
<td>11 (79%)</td>
<td>0.20</td>
<td>0.07–0.58</td>
</tr>
<tr>
<td>RV EDV &gt; 180 mL/m(^2)</td>
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<tr>
<td>11 (65%)</td>
<td>14 (41%)</td>
<td>0 (0%)</td>
<td>7.10</td>
<td>2.33–21.7</td>
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<tr>
<td>RV ESV (per mL/m(^2))</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>115 ± 30</td>
<td>101 ± 26</td>
<td>70 ± 14</td>
<td>1.04</td>
<td>1.02–1.07</td>
</tr>
<tr>
<td>RV ESV &lt; 80 mL/m(^2)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (6%)</td>
<td>4 (12%)</td>
<td>11 (79%)</td>
<td>0.04</td>
<td>0.01–0.17</td>
</tr>
<tr>
<td>RV ESV &gt; 95 mL/m(^2)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15 (88%)</td>
<td>17 (50%)</td>
<td>0 (0%)</td>
<td>25.5</td>
<td>5.35–122</td>
</tr>
<tr>
<td>LV EDV (per mL/m(^2))</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>105 ± 28</td>
<td>86 ± 18</td>
<td>80 ± 16</td>
<td>1.04</td>
<td>1.02–1.07</td>
</tr>
<tr>
<td>LV ESV (per mL/m(^2))</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>54 ± 15</td>
<td>42 ± 13</td>
<td>36 ± 12</td>
<td>1.07</td>
<td>1.03–1.11</td>
</tr>
<tr>
<td>PR fraction (per %)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>48 ± 12</td>
<td>48 ± 12</td>
<td>47 ± 10</td>
<td>1.01</td>
<td>0.97–1.05</td>
</tr>
</tbody>
</table>

Data were described as number with frequency, median with interquartile range, and mean with standard deviation.

AUC, area under the curve; CI, confidence interval; CMR, cardiovascular magnetic resonance; EDV, end-diastolic volume; EF, ejection fraction; ESV, end-systolic volume; LV, left ventricle; NYHA, New York Heart Association; OR, odds ratio; PR, pulmonary regurgitation; PVR, pulmonary valve replacement; RV, right ventricle.

\textsuperscript{a}Common OR refers to the odds of a worse outcome class.

\textsuperscript{b}Univariate AUC reported for continuous variables and refers to the area under the receiver operator curve with mid-to-late RV normalization as binary outcome variable.

**Figure 2**

Probability of mid-to-late RV normalization, intermediate, or suboptimal haemodynamic outcome. Number of patients with mid-to-late RV normalization, intermediate, or suboptimal mid-to-late haemodynamic outcome depending on preoperative RV ESV. RV, right ventricle; ESV, end-systolic volume.
CMR was performed. The number of patients with significant postoperative conduit dysfunction was small. Secondly, CMR imaging was performed according to local protocols and there was variation in the timing of CMR. Cardiac volumes may vary depending on imaging technique and contouring.21,32 Thirdly, due to a limited number of adverse clinical events in our cohort, multivariable analysis of predictive variables was not feasible. Finally, this is a retrospective cohort of PVR patients, a comparison of PVR with a conservative non-surgical approach to RV volume overload was therefore not feasible.

Conclusions

In TOF patients who had undergone PVR, preoperative RV ESV < 80 mL/m² was the best threshold to achieve mid-to-late RV normalization. Patients operated when RV ESV was > 95 mL/m² were at increased risk for both suboptimal haemodynamic outcome and adverse clinical events. These thresholds are in line with those previously reported on early outcome and may assist in timing of PVR.

Supplementary material

Supplementary material is available at European Heart Journal online.

Author’s contributions


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References

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