# Optimal timing of pulmonary valve replacement in tetralogy of Fallot

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# Preoperative Thresholds for Pulmonary Valve Replacement in Patients with Corrected Tetralogy of Fallot Using Cardiovascular Magnetic Resonance

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## Abstract

**Background**

To facilitate the optimal timing of pulmonary valve replacement, we analyzed preoperative thresholds of right ventricular (RV) volumes above which no decrease or normalization of RV size takes place after surgery.

**Methods**

Between 1993 and 2006, 71 adult patients with corrected tetralogy of Fallot underwent pulmonary valve replacement in a nationwide, prospective follow-up study. Patients were evaluated with cardiovascular magnetic resonance both preoperatively and postoperatively. Changes in RV volumes were expressed as relative change from baseline.

**Results**

RV volumes decreased with a mean of 28%. RV ejection fraction did not change significantly after surgery (from 42±10% to 43±10%; P=0.34). Concomitant RV outflow tract reduction resulted in a 25% larger decrease of RV volumes. After correction for surgical RV outflow tract reduction, higher preoperative RV volumes ($mL/m^2$) were independently associated with a larger decrease of RV volumes (RV end-diastolic volume: ß=0.41; P<0.001). Receiver operating characteristic analysis revealed a cutoff value of 160 $mL/m^2$ for normalization of RV end-diastolic volume or 82 $mL/m^2$ for RV end-systolic volume.

**Conclusion**

Overall, we could not find a threshold above which RV volumes did not decrease after surgery. Preoperative RV volumes were independently associated with RV remodeling and also when corrected for a surgical reduction of the RV outflow tract. However, normalization could be achieved when preoperative RV end-diastolic volume was <160 $mL/m^2$ or RV end-systolic volume was <82 $mL/m^2$.

## Introduction

In patients with corrected tetralogy of Fallot and residual long-standing pulmonary regurgitation, timing of pulmonary valve replacement (PVR) remains controversial [1,2]. Beneficial effects of PVR have to be weighed against the risk for repeat PVR [3,4]. Beneficial effects of PVR include improvement in functional class and exercise capacity, reduction of right ventricular (RV) size [2], and decrease in QRS duration [5]. Because data on long-term morbidity and mortality are lacking on this subject, cardiovascular magnetic resonance (CMR) can be used to accurately assess the effect of PVR on RV volumes and function. Although PVR may result in a decrease in RV volumes [2,5], it remains unknown whether a threshold can be found above which no RV remodeling occurs after PVR. Furthermore, it remains a subject of debate whether RV remodeling is the result of the intrinsic capacity of the RV or is largely dependent on surgically reducing the RV outflow tract (RVOT). Some reports have assessed the effects of PVR by examining normalization of RV volumes after surgery but only with a limited number of patients [5,6] Therefore, in a prospective, multicenter study we analyzed whether a threshold exists above which the RV does not improve further after surgery and whether preoperative thresholds can be identified for normalization of RV volumes after surgery.

## Methods

### Patient population

In a nationwide, prospective study, 71 patients with a previous correction for tetralogy of Fallot were followed up after PVR. Patient characteristics are listed in Table 4.1. Data on the first 25 patients, who were operated on between 1993 and 2002, were reported previously [2]. The remaining patients were operated on between 2002 and 2006 in 5 tertiary referral centers. CMR was performed preoperatively and 6 to 12 months postoperatively following clinical protocol. After the first year, patients were routinely followed up at the outpatient clinics of the participating centers, according to their local protocols. The medical records for all patients were reviewed. Data collected included patient characteristics, operations and concomitant procedures, echocardiographies, and

ECGs. The international research boards approved the study, and informed consent was obtained in all patients (Table 4.1).

***Table 4.1.*** *Patient and surgery characteristics.*

| Variable | |
|---|---|
| Male/female, n | 42/29 |
| Shunt procedure | 41 |
| Age at shunt procedure, y, median (IQR) | 2.1 (0.8 to 3.8) |
| Age at initial repair (n=66), y, median (IQR) | 5.0 (2.7 to 7.4) |
| Type of initial repair (n=66) | |
| Myectomy/valvulotomy | 14 |
| RV patch | 16 |
| Transannular patch | 69 |
| RV to pulmonary artery conduit | 1 |
| Indications for PVR (all patients had moderate to severe pulmonary regurgitation) | |
| Symptomatic | 71 |
| Asymptomatic with progressive RV dilatation | 24 |
| Ventricular arrhythmias or QRS >180 msec | 15 |
| Progressive tricuspid regurgitation | 4 |
| Age at PVR, y, median (IQR) | 29 (23 to 37) |
| Previous PVR | 6 |
| Diameter homograft, mm, mean±SD | 25±1.7 |
| Type of graft for RVOT reconstruction | |
| Pulmonary homograft | 96 |
| Contegra conduit | 3 |
| Aorta homograft | 1 |
| Concomitant procedures | |
| Tricuspid valve plasty or ring | 24 |
| RV reduction plasty | 18 |
| Pulmonary artery angioplasty | 15 |
| Ventricular septal defect closure | 4 |

Data are expressed as percentages unless otherwise noted. IQR indicates interquartile range.

*RV = right ventricle, PVR = pulmonary valve replacement, RVOT = right ventricular outflow tract.*

Guidelines for replacing the pulmonary valve in patients with severe pulmonary regurgitation included progressive RV enlargement, progressive tricuspid regurgitation, arrhythmias, or symptoms such as deteriorating exercise performance [7]. The exact interpretation of these guidelines was left to the participating centers.

**Pulmonary valve replacement**

All homografts were allocated by Bio Implant Services, Leiden, the Netherlands, from whom the data on homograft and donor characteristics were obtained. Additional procedures performed at the time of PVR are listed in Table 4.1. All patients were operated on with normothermic or moderately hypothermic cardiopulmonary bypass. Most pulmonary valve insertions were performed on beating hearts. Aortic cross-clamping was dependent on the surgeon's preference or on concomitant procedures. Arrhythmia surgery was not performed concomitantly. Cryopreserved pulmonary homografts were used for most RVOT reconstructions. Homografts were inserted in the orthotopic pulmonary position with one proximal and one distal end-to-end running suture after longitudinally opening the proximal pulmonary artery and slightly extending this incision if necessary across the former pulmonary annulus. The outflow tract patch material was resected as much as possible. Although the patch resection itself may decrease RVOT size, this procedure was performed in all patients, and information on the size of the resected material was not available to us. Therefore, we considered the RVOT surgically reduced when the RVOT proximal to the graft was reduced to overcome the size discrepancy with the pulmonary homograft. We expected that the reduction in RV size would be greatest in this situation. The indication for this procedure was left to the cardiac surgeon during the procedure.

**Cardiovascular magnetic resonance**

CMR data were acquired on local available magnetic resonance systems. Imaging sequences of the first 25 patients were previously reported [2]. For the remaining patients, CMR studies were performed with the use of local imaging protocols.8 CMR was performed at a median of 5 (3.4 to 7.6) months before and a median of 9 (6.2 to 15) months after PVR. Scout images were obtained in 3 orthogonal planes, and standard 2- and 4-chamber views were acquired. From these views, a stack of 12 to 14 slices was

acquired in the short-axis orientation (steady state free precession). Images were analyzed at the Leiden University Medical Center with standardized analysis techniques [8]. 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). Stroke volume (SV) was calculated by deducting the end-systolic volume (ESV) from the end-diastolic volume (EDV), and ejection fraction (EF) was defined as (SVx100)/EDV. All volumes were indexed for body surface area.

Velocity mapping was performed with the use of velocity-encoded phase contrast sequence [8]. For velocity mapping of the pulmonary artery, sagittal and coronal scout images were used to construct a double oblique plane perpendicular to the vessel. FLOW software (Medis) was used to calculate regurgitant flow and systolic forward flow. Pulmonary regurgitation was calculated as regurgitant flow x 100 / systolic forward flow.

**Statistical analysis**

Data are described as frequency, mean with SD, or median with interquartile range. Differences between parameters before and after surgery were analyzed with paired Student t test, Wilcoxon signed rank test, or McNemar test. Changes in CMR-derived ventricular volumes after surgery were expressed as percent change from baseline. One patient had 2 PVRs included in the analysis. Univariate predictors for change in hemodynamic parameters after surgery (patient characteristics (sex, age at repair, previous palliation, time from repair to PVR), surgical characteristics (age at PVR, homograft diameter, concomitant procedures), and CMR parameters at baseline) were analyzed with independent Student t test, ANOVA, or Pearson correlation coefficient, when appropriate. Independent predictors for change in hemodynamic parameters were analyzed with multivariable linear regression analysis. All significant predictors in univariate analysis entered the multivariable regression model with the use of forward stepwise analysis. The identification of a preoperative threshold in RV-EDV index (EDV-I) for normalization of RV-EDV-I (<108 mL/m$^2$) and RV-ESV index (ESV-I) (<47 mL/m$^2$) [9] was analyzed with the use of receiver operating characteristic curves. We considered situations in which surgery was performed "too early" (performing surgery

when preoperative RV volumes were low and did normalize after surgery; low specificity) or "too late" (performing surgery when preoperative RV volumes were high and did not normalize after surgery; low sensitivity) equally adverse. Therefore, we selected the point at which sensitivity and specificity were equal. A probability value of <0.05 was considered statistically significant.

## Results

### Clinical events after surgery

Clinical characteristics of all patients are listed in Table 4.1. Median follow-up time after surgery was 1.6 (0.9 to 5.2) years. Of the 71 patients prospectively followed up, 1 patient died suddenly 18 months after PVR (age 33 years, no preoperative arrhythmias, latest QRS duration 156 msec). Ten months before his death, the patient underwent CMR with RV-EDV-I of 133 mL/$m^2$ and RV-EF 30%. In 1 patient, implantable cardioverter-defibrillator implantation was planned 1 week postoperatively because of ventricular arrhythmias before surgery and QRS duration of 192 msec (age 37 years, preoperative RV EDV-I 210 mL/$m^2$, and RV-EF 35%). One patient developed sustained ventricular tachycardias after PVR, which were hemodynamically tolerated, and underwent radiofrequency ablation (age 35 years, no preoperative arrhythmias, latest QRS duration 158 msec, preoperative RV-EDV-I 175 mL/$m^2$, and RV-EF 49%). This patient refused to undergo follow-up CMR. All of these patients were in New York Heart Association class I or II.

Three patients underwent a second PVR. Two of these patients underwent redo surgery <6 months after PVR because of kinking of the (long) pulmonary homograft in one and a false aneurysm with severe subvalvular stenosis in the other. These patients underwent their follow-up CMR after their second PVR. The remaining patient underwent redo PVR 2 years after the first PVR because of no improvement in RV volumes and functional class and significant residual pulmonary regurgitation after the first surgery. During the second PVR, the RVOT was reduced, and hemodynamics and functional class improved. Both PVRs of this patient were included in the analysis. In total, 70 PVRs were available

for analysis with CMR (Figure 4.1). The characteristics and indications of these PVRs are listed in Table 4.1.

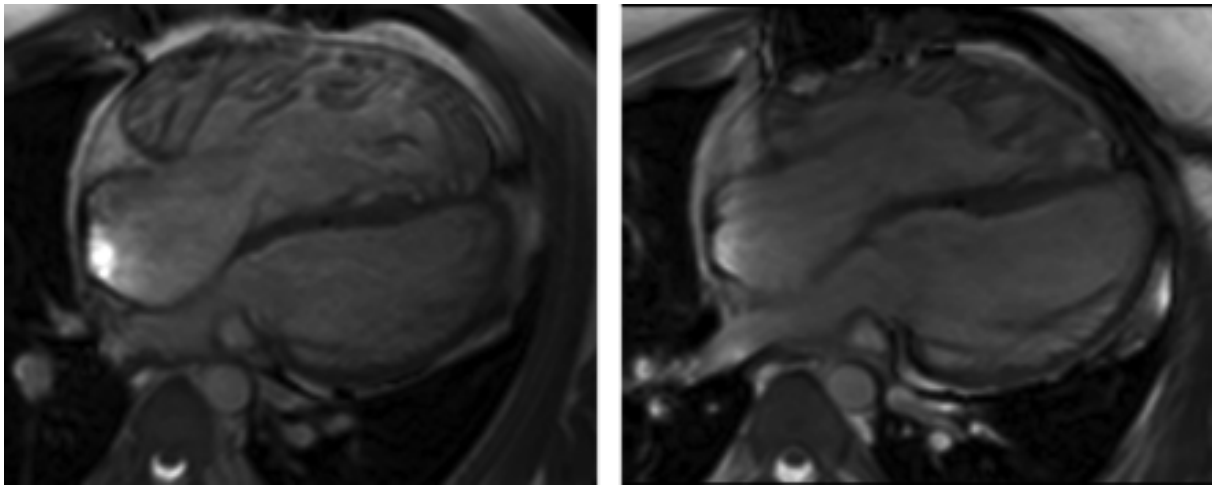

***Figure 4.1.*** *A still-frame image of 4-chamber cine imaging from CMR (steady state free precession) is shown; left, before PVR; right, after surgery. Note the severely enlarged RV before surgery and the reduction in RV volume after surgery, with a consequent small increase in LV size.*

**Hemodynamic changes after PVR**

Changes in hemodynamics after PVR are listed in Table 4.2. In Table 4.2, a reduction in RV volumes and QRS duration can be observed as well as an increase in LV-EDV-I, net forward flow, and functional class. No improvement in RV volumes was observed in 4 patients. In 3 of these patients, residual pulmonary regurgitation (>20%) was observed, in 1 patient as a result of low-grade endocarditis. None of the 4 patients underwent a reduction of the RVOT. Individual lines for absolute change in RV-EDV-I are depicted for patients who did and did not undergo surgical RVOT reduction in Figure 4.2. Relative decrease in RV-EDV-I was higher in patients undergoing surgical RVOT reduction compared with those who did not (35±8% versus 27±20%; P=0.02). However, in patients not undergoing surgical RV reduction, RV-EDV-I could still decrease substantially when no residual pulmonary regurgitation was present (Figure 4.2).

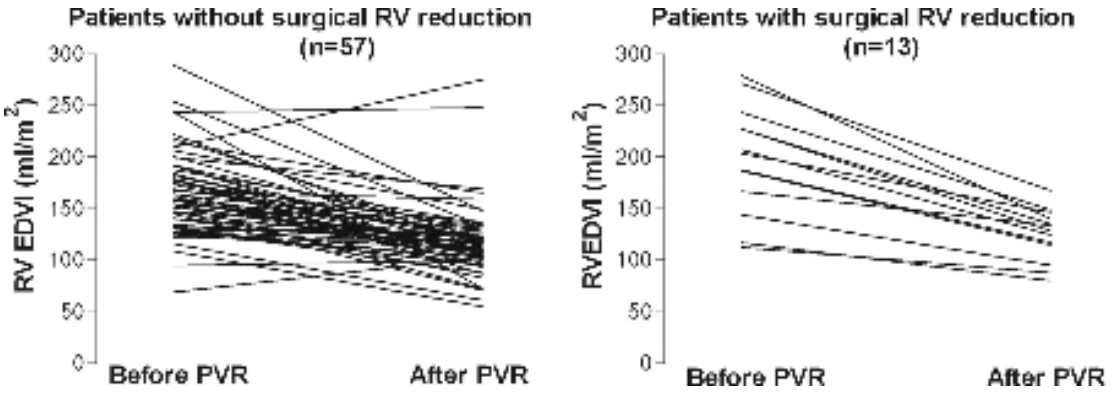


***Figure 4.2.*** *The actual decrease in RV-EDV is depicted for patients in the present study. Left, Patients who did not undergo a surgical RVOT reduction (n=58); right, patients with a surgical RVOT reduction (n=13). In 4 patients without surgical RVOT reduction, RV size did not decrease after surgery. Three of these patients developed postoperative pulmonary regurgitation >20%. Note that in patients without surgical RVOT reduction and high RV-EDV, RV size could decrease substantially. Furthermore, 2 patients were operated on with normal preoperative RV-EDV-I. Both patients became symptomatic with severe pulmonary regurgitation and a RV that was larger than the LV.*

**Predictors for hemodynamic improvement after PVR**

Decrease in RV volumes (RV-EDV-I and RV-ESV-I) was related to preoperative values, and a threshold above which RV did not decrease after PVR could not be observed (Figure 4.3). When the change in RV volumes was expressed as a relative change from baseline, average decrease in both RV-EDV-I and RV-ESV-I was 28% (Table 4.2). Although RV volumes changed substantially, RV-EF did not change significantly. However, net SV and LV-EDV improved after surgery. Table 4.3 depicts preoperative predictors that were multivariably associated with relative change in RV volumes after surgery. Patients with a surgical reduction of the RVOT had higher preoperative RV-EDV-I than patients without surgical reduction (198±53 versus 165±39 mL/m$^2$; P=0.01). After correction for a surgical reduction of the RVOT in a multivariable model, relative change in RV-EDV-I and RV-ESV-I remained independently associated with preoperative RV-EDV-I (ß=0.39, P=0.001; ß=0.43, P<0.001, respectively). Interestingly, we observed that lower preoperative RV-EF resulted in a greater increase in RV-EF after surgery (Table 4.3) and a smaller LV-EDV-I resulted in a greater increase in LV-EDV-I after surgery.

***Table 4.2.*** *Hemodynamic changes after surgery.*

| Variable | Before Surgery | After Surgery | Mean Difference | Percent Change |
|---|---|---|---|---|
| RV-EDV-I, mL/m$^2$ | 171±44 | 119±34* | –52±37 | –28±19 |
| RV-ESV-I, mL/m$^2$ | 102±38 | 70±29* | –32±28 | –27±31 |
| RV-SV index, mL/m$^2$ | 70±16 | 49±10* | –21±15 | –28±17 |
| RV-EF, % | 42±10 | 43±10 | 1.0±8.7 | 4.7±22 |
| RV-EF$_{cor}$, % | 24±8.1 | 41±11* | 17±12 | 87±64 |
| LV-EDV-I, mL/m$^2$ | 85±22 | 94±20* | 8.3±20 | 17±43 |
| LV-EF, % | 52±9 | 53±8 | 1.1±7.4 | 4.0±15 |
| Pulmonary regurgitant fraction, % | 44±13 | 5±9* | 39±17 | 90±17 |
| Net forward flow, mL/m$^2$ | 38±16 | 46±12* | 7.3±19 | 34±47 |
| Tricuspid regurgitation grade ≥2, % | 26 | 19 | ... | ... |
| QRS duration, msec | 155±29 | 144±29* | –11±11 | –7.0±6.1 |
| NYHA class ≥II, % | 53 | 11* | ... | ... |

Values are expressed as mean±SD unless otherwise noted. NYHA indicates New York Heart Association.
*Statistically significant difference compared with baseline ($P$<0.05).

When postoperative predictors for change in RV-EDV-I (%) are taken into account, postoperative pulmonary regurgitation (%) entered the model as well (ß=–0.50 (SE 0.09), P<0.001). Decrease in RV-EDV-I (%) was related to both increase in RV-EF (R=0.42, P<0.001) and increase in LV-EDV-I (R=0.30, P=0.012) and LV-EF (R=0.35, P<0.001).
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***Table 4.3.*** *Univariable predictors for hemodynamic change after surgery in multivariable analysis.*

| Parameter | Predictor | ß (SE) | *P* |
|---|---|---|---|
| RV-EDV-I decrease (%) | Presurgery RV-EDV-I (mL/m$^2$) | 0.41 (0.11) | <0.001 |
| | Surgical RV reduction (yes, no) | 0.06 (0.12) | 0.58 |
| RV-ESV-I decrease (%) | Presurgery RV-EDV-I (mL/m$^2$) | 0.39 (0.12) | 0.001 |
| RV-EF increase (%) | Presurgery RV-EF (%) | –0.64 (0.19) | 0.001 |
| | Presurgery RV-ESV-I (mL/m$^2$) | –0.23 (0.19) | 0.23 |
| LV-EDV-I increase (%) | Presurgery LV-EDV-I (mL/m$^2$) | –0.44 (0.11) | <0.001 |
| LV-EF increase (%) | Presurgery LV-EF (%) | –0.47 (0.12) | <0.001 |
| | Presurgery RV-EDV-I (mL/m$^2$) | 0.10 (0.12) | 0.39 |
| | Age at PVR (y) | –0.14 (0.11) | 0.21 |
| | Graft diameter (mm) | –0.09 (0.11) | 0.41 |
| NYHA class improvement (%) | Presurgery NYHA class (I–IV) | 0.71 (0.09) | <0.001 |

NYHA indicates New York Heart Association.

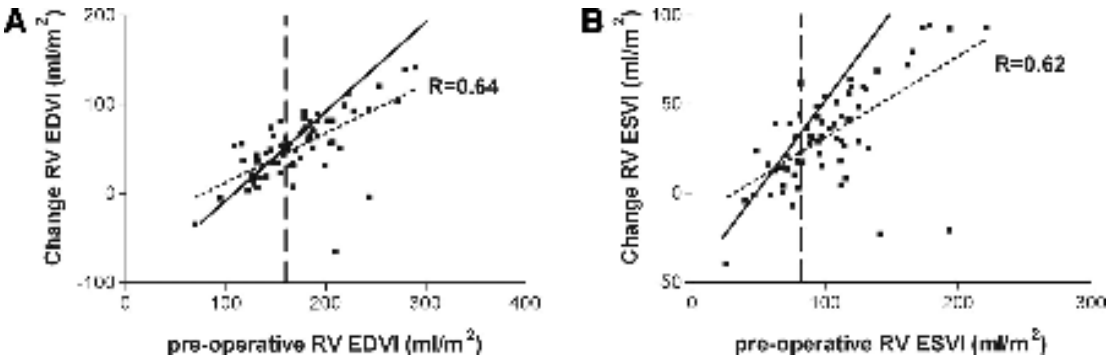


***Figure 4.3.*** *The association with preoperative RV-EDV-I (A) or RV-ESV-I (B) and the absolute decrease in RV volumes after surgery is depicted (dashed line is the regression line). Note that a threshold for reduction in RV volumes after surgery could not be identified. Individuals on the left side of the solid line are patients in whom ventricular volume returned to normal after surgery. The vertical dashed line represents the preoperative cutoff value for normalization after surgery.*

### Cutoff values for normalization of RV-EDV-I and RV-ESV-I

In 37% of the patients RV-EDV-I returned to normal values (<108 mL/m$^2$), and in 17% RV-ESV-I returned to normal values (<47 mL/m$^2$). Sensitivity and specificity for normalization of RV-EDV-I were 55% and 92%, with a preoperative RV-EDV-I cutoff value of 160 mL/m$^2$ (Figure 4.4A). At <120 mL/m$^2$, all patients normalized, and at >190

mL/m$^2$, none of the patients normalized after surgery. For normalization of RV-ESV-I, a preoperative cutoff value of 82 mL/m$^2$ was observed, with a sensitivity of 74% and a specificity of 82% (Figure 4.4B).

Patients with normalization of RV-EDV-I and RV-ESV-I after surgery had a lower postoperative QRS duration (133±30 versus 152±26 msec; P=0.02) and a higher postoperative RV-EF (48±9.9% versus 40±8.8%; P=0.001) than patients with no normalization, respectively. No significant difference in New York Heart Association class after surgery was observed between patients with or without normalization (1.3±0.36 versus 1.2±0.33, respectively; P=0.31)

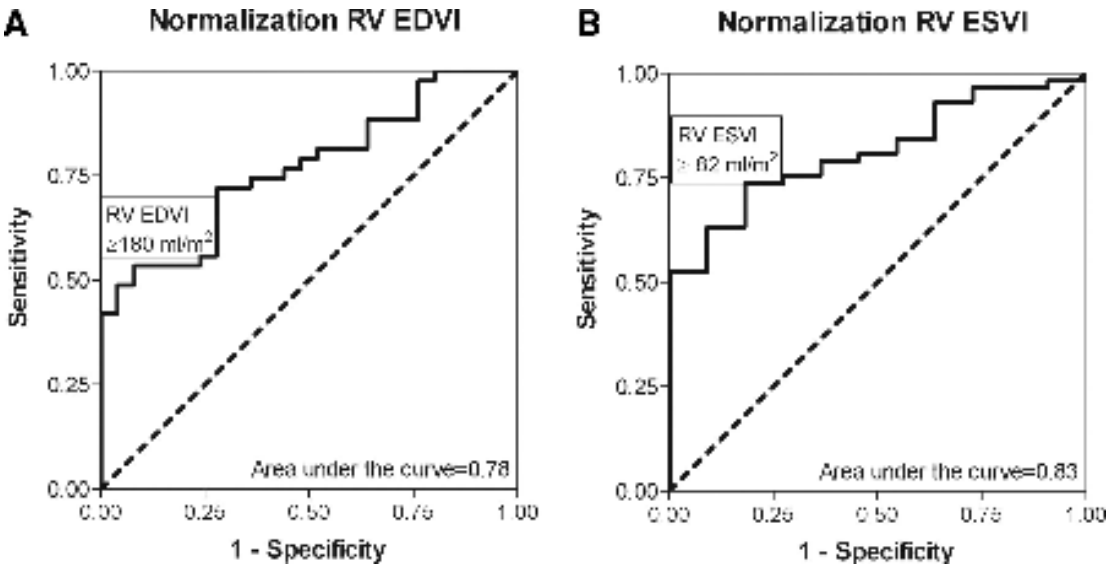


***Figure 4.4.*** *Receiver operating characteristic curves are depicted for normalization of RV-EDV-I (A) and RV-ESV-I (B) after PVR.*

## Discussion

In our study on optimal timing of PVR in patients with corrected tetralogy of Fallot, we could not find a threshold above which RV volumes did not decrease after surgery. Preoperative RV volumes were independently associated with RV remodeling and also when corrected for a surgical reduction of the RVOT. Despite the substantial decrease in

patients with very high preoperative RV volumes, normalization could be achieved when preoperative RV-EDV was <160 mL/m$^2$ or RV-ESV was <82 mL/m$^2$.

**Improvement of RV size and function after PVR**

After the disappointing results of PVR reported by Therrien et al in 2001 [1], several reports have shown beneficial effects of PVR [2,6] including a report by Therrien et al as well [5], all using CMR to quantify RV dimensions. In this report, we confirm the decrease in RV volumes of (approximately) 30% and an increase in effective SV of both ventricles [2,5,6]. Besides these beneficial effects of PVR on RV size and effective SV, we confirm an overall improvement in functional New York Heart Association class [10]. RV function did not change after surgery, but it remains unknown whether RV function stabilizes after surgery or declines steadily over time, as is the case before PVR.

After the report by Vliegen et al [2], an important issue was the question of whether the reported decrease in RV dilatation after surgery was only the result of the surgical reduction of the RV. In this report, we have shown that in patients with no surgical reduction of the RV during PVR, reduction of RV volumes may take place as well. Although most patients underwent resection of the transannular patch, it seems unlikely that placing a homograft over the defect without additionally tailoring the RVOT results in a large additional reduction in RV size. Furthermore, in the multivariable model for decrease in RV volumes, only preoperative dilatation remained significant in the model. We think that it is important to perform a surgical reduction of the RVOT in severely dilated RVOTs to prevent postoperative pulmonary regurgitation.

In patients with tetralogy of Fallot, RV dysfunction may negatively affect LV function [11]. Geva et al. [12] emphasized that LV function plays an important role in the patient's functional class. Interestingly, our study confirms a right-to-left ventricular interaction after surgery. We observed that change in RV volumes after surgery related directly to changes in LV volumes and function. In our opinion, changes in RV volumes are the most important benefit of PVR, and changes in patient's functional class, LV function,

and QRS duration are secondary to changes in RV volumes. Therefore, the main focus of our report is the change in RV volumes after surgery.

**Can we operate too late?**

Our study population consisted of patients from both centers that are considered "conservative" in timing of PVR and centers that advocate "early" PVR [2]. Of interest is that in our study, factors associated with delaying surgery (age at PVR, time from initial repair to PVR, high RV-EDV-I) were not associated with less decrease in RV volumes. Moreover, patients with higher RV-EDV-I before surgery showed a higher relative decrease in RV-EDV-I and RV-ESV-I. We could not find a threshold above which RV volumes do not decrease after surgery. Only patients with postoperative pulmonary regurgitation showed no decrease in RV volumes after surgery [13]. Possibly, the difference between our study and the study from Therrien et al.[1], in which no change in RV volumes was observed, is the use of CMR in our study versus the use of radionuclide angiography, which is considered less accurate in quantifying RV dimensions. Our results suggest that PVR substantially reduced RV dilatation, even in patients with very high RV volumes and RV dysfunction.

**Delaying PVR**

The risk of "late" PVR includes irreversible RV dysfunction after PVR. The risk of timing of early PVR in asymptomatic patients primarily comprises the need for repeat PVR. In our study, homografts were primarily used for RVOT reconstruction, and we have shown in a previous study that on average a homograft is replaced 10 to 20 years after PVR [3]. As long as an ideal graft is yet to be found, delaying surgery has substantial benefits.

However, despite the ability of the RV to reduce dilatation substantially when preoperative RV volumes are high, not many patients showed normalized RV volumes after surgery (normalized RV-EDV-I in 37% and normalized RV-ESV-I in 17%). One might speculate that the RV improves further after the 9 months in the present study.

However, in a report by van Straten et al,13 RV-EDV-I decreased only 1.8 mL/m$^2$ from 7 to 18 months after PVR.

Because it is not yet known whether reducing the size of the RV is enough to improve long-term outcomes after PVR, it is not clear whether delaying PVR is a good approach. Possibly, achieving normalization in RV volumes is important in improving long-term outcomes. When the latter is assumed, patients should be operated on before the RV-EDV-I reaches 160 mL/m$^2$ or RV-ESV-I reaches 82 mL/m$^2$. Our cutoff value of 160 mL/m$^2$ for RV-EDV-I lies slightly below the reported values by Therrien et al. [5] in adults (170 mL/m$^2$) and Buechel et al. [6] in children (200 mL/m$^2$).

**Other factors influencing optimal timing of PVR**

Associated factors may alter the timing of PVR. Patients with long-standing pulmonary regurgitation with subsequent RV dilatation and severe ventricular arrhythmias should be evaluated for PVR. Risk for these ventricular arrhythmias is higher when QRS duration is >180 msec [14]. It has been observed that QRS duration decreases after PVR, related to the reduction in RV volumes [15]. Ventricular arrhythmias or sudden cardiac death occurred in 3 of 71 (4%) of the patients. In a recent study, we observed that when patients were operated on when QRS was >180 msec, the risk for ventricular arrhythmias remained high (25%) [16]. In our opinion, PVR should be performed before the QRS duration reaches 180 msec.

In some of the participating centers, PVR is delayed until the patient becomes symptomatic. We have observed that patients with high preoperative New York Heart Association class showed an improvement in functional class after surgery. However, some patients with severely dilated RVs were not symptomatic in our study, and these patients were at increased risk for increased RV volumes and reduced RV-EF after surgery. However, from our report, we cannot conclude that delaying surgery until symptoms occur is unfavorable because the long-term outcomes of increased RV volumes and decreased RV-EF after surgery are not known to us.

Other factors influencing timing of PVR include the occurrence of significant hemodynamic abnormalities requiring surgery: tricuspid regurgitation, residual ventricular septal defect, and pulmonary stenosis. When 1 of these lesions is present, PVR can be considered before the RV reaches the preoperative cutoff values.

**Limitations**

Although, in our opinion, the patient population in the present study reflects the wide clinical spectrum normally seen in clinical practice, the present study lacks sufficient statistical power to determine with confidence that there is no ceiling effect, particularly in the range of very large RV-EDV-I (e.g. >220 $mL/m^2$). Future studies should incorporate data on hard outcome variables, acquired during a longer follow-up period, and use objective assessment of functional outcome to make definitive conclusions on the effectiveness and indications for PVR.

We used a standard gradient echo imaging technique for the first 25 previously described patients, whereas the subsequent patients were imaged with a steady state free precession technique. These 2 techniques have been shown not to yield equivalent results [17]. However, baseline measurements and measurements after PVR were performed with the same imaging technique in all individual patients. Therefore, differences before and after surgery could be assessed reliably.

**Conclusion**

Even in patients with very high preoperative RV volumes and RV dysfunction, our results suggest that PVR substantially reduced RV dilatation. A threshold could not be observed, and RV size before surgery was independently associated with reduction in RV volumes after surgery. A reduction of RV volumes to normal values could be achieved when PVR was performed before RV-EDV-I reached 160 $mL/m^2$ or RV-ESV-I reached 82 $mL/m^2$.

## Clinical Perspective

Patients with corrected tetralogy of Fallot and residual long-standing pulmonary regurgitation are at risk for heart failure and sudden cardiac death. With pulmonary valve replacement, pulmonary regurgitation is targeted, and right ventricular volume decreases after surgery. However, once a graft is placed in the pulmonary position, the patient will need to undergo future redo surgery for graft failure. Controversy remains regarding the optimal timing of pulmonary valve replacement. How long can pulmonary valve replacement be delayed, and above which right ventricular dimensions does remodeling not occur after surgery? We analyzed preoperative and postoperative right ventricular volumes and function in 71 adult patients with corrected tetralogy of Fallot using cardiovascular magnetic resonance. We observed that even in patients with very severe preoperative right ventricular dilatation and dysfunction, pulmonary valve replacement substantially reduced right ventricular dilatation. A threshold for remodeling after surgery could not be observed. Although greater right ventricular dilation was associated with a greater reduction in right ventricular size, "normalization" of the right ventricle occurred in only 37% of the patients. A substantial decrease in right ventricular size can still be obtained when surgery is delayed until the right ventricle becomes severely dilated. However, when normalization in right ventricular size is achieved, surgery should be performed at an earlier stage.

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