Right Ventricular Dysfunction and Pulmonary Valve Replacement After Correction of Tetralogy of Fallot

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Background. Correction of tetralogy of Fallot often leads to pulmonary regurgitation, sometimes warranting pulmonary valve replacement, for which indications and timing to achieve optimal results are not yet clear. This retrospective study describes follow-up and reinterventions in our tetralogy of Fallot population.

Methods. Review of all consecutive patients operated on for tetralogy of Fallot between 1977 and 2000 was conducted. Included are date and type of repair, Doppler echocardiography (two-dimensional echocardiography), electrocardiographs, reoperations, and physical condition.

Results. Total repair was performed in 171 patients at a mean age 1.9 ± 2.5 years, follow-up time counted 9.6 ± 7.0 years. Right ventriculotomy was used in 92%, and transatrial ventricular septal defect closure was used in 8%; 74% received a transannular outflow patch. Twenty-year survival was 91%. Last follow-up electrocardiographs showed right bundle branch block in 67% and serious arrhythmias in 11%. Two-dimensional echocardiography demonstrated severe pulmonary insufficiency and dilated right ventricle in 31% and 38%, respectively, increasing with postrepair age (p < 0.001). Poor clinical condition (New York Heart Association class II+) and echocardiographic proof of right atrial dilatation (p = 0.012) and arrhythmias (p = 0.03) were significantly associated. Furthermore, the influence of residual hemodynamic lesions, such as a remaining ventricular septal defect or pulmonary stenosis, or right ventricular dilatation was important (p = 0.04). Reintervention was necessary in 32 patients (19%; 10-year freedom, 83%), including angioplasty for residual stenosis and pulmonary valve replacement. At a mean age of 9.2 years after correction, 14 patients received a homograft, and 2 patients received a heterograft. In 7 patients the right ventricle returned to normal dimensions and symptoms disappeared. The incidence of right ventricular dilatation was considerably higher (p = 0.020) in patients with a transannular patch; the transatrial approach showed the opposite (p = 0.03), and patients presented with lower QRS duration (p = 0.007), although no difference could be found between survival after both surgical techniques. Effects of early timing (correction < 6 months) on right ventricular dysfunction could not be established.

Conclusions. Severe right ventricular dilatation and pulmonary regurgitation secondary to outflow tract repair in tetralogy of Fallot are frequently occurring sequelae developing slowly over time. Indications for pulmonary valve replacement remain controversial because echocardiographic findings or arrhythmias are not always accompanied by deterioration of clinical condition. However, right atrial dilatation and additional hemodynamic lesions demand increased vigilance. Transatrial repair is associated with a favorable outcome.


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Nowadays, clinical management of tetralogy of Fallot (obstruction of right ventricular [RV] outflow, malalignment ventricular septum defect, and RV hypertrophy) involves a total surgical correction in early childhood. This decreases the necessity of prior palliative shunt procedures and has a low operative mortality and excellent long-term results [1–5]. However, in the follow-up, pulmonary valve insufficiency is frequently encountered even in asymptomatic patients [5–7]. Severe longstanding pulmonary regurgitation (PR) can lead to deleterious complications [1, 2, 8–15]. In a small number of patients with both deterioration of symptomatic status and objective evidence of progressive right heart failure, pulmonary valve replacement (PVR) is considered to relieve symptoms [1, 4, 16–20]; this number is expected to grow [16, 21], especially those in whom a transannular patch was used [22]. But specific indications and timing of PVR remain unclear. This study is an inventory of our tetralogy of Fallot population from initial repair to present status, focusing on the development of RV indicators and occurrence of reinterventions in follow-up with special attention to PVR.
Material and Methods

Population
The reports of all consecutive surviving patients, operated on in the Children’s Heart Center Utrecht between 1977 and 2000 and residing in the Netherlands, were examined retrospectively. The population (n = 171) consisted of 106 (62%) male and 65 female patients with a mean follow-up time of 9.6 ± 7.0 years (range, 0.2 to 32.6 years; median, 8.0) and mean age of 13.8 ± 8.0 years (range, 0.2 to 37.8 years). Excluded from this survey were 99 patients with follow-up abroad directly after operation (82), pulmonary atresia (13), complete atrioventricular septal defect, subaortic conus, or death before complete correction (2).

Uncomplicated tetralogy of Fallot was encountered in 150 patients, 12% (n = 21) had additional cardiac complications (abnormal coronary artery, systemic to pulmonary collaterals, pulmonary artery hypoplasia, branch stenosis). Pentalogy (with atrial septal defect) was reported in 23 (13%), 12 had a persistent ductus arteriosus, and 21 a bicuspid pulmonary valve. Comorbidity included Down syndrome, velo-cardio-facial syndrome, and VATER association (vertebral defects, imperforate anus, tracheoesophageal fistula, and radial and renal dysplasia) in 47 patients (27%). In 33 patients (19%) a palliative shunt was initially required to overcome symptoms (age, 0.9 ± 1.4 years; Blalock-Taussig, 8; central aortopulmonary, 25).

Total correction was performed at a mean age of 1.9 ± 2.5 years (range, 0.2 to 21.7 years). Most patients were corrected using a transannular patch (n = 126, 74%) in the RV outflow tract. In the remaining 26% infundibulotomy or pulmonary valve commissurotomy was sufficient to overcome the obstruction. In the majority the ventricular septal defect (VSD) was repaired through right ventriculotomy (157 patients, 92%); only 14 patients underwent transatrial repair. Mean follow-up time postoperatively was 8.0 ± 6.5 years (range, 0 to 27.9 years; median, 6.3 years).

Doppler echocardiographic data (especially RV dimensions, pulmonary stenosis and regurgitation, right atrial dilatation, and tricuspid insufficiency), cardiac catheterizations, electrocardiographs, and 24-hour Holter recordings (QRS complex duration, dysrhythmias) were reviewed. Furthermore, physical condition (New York Heart Association functional class I to IV), cause and time of death, age, indications, and type of reintervention were recorded.

Right Ventricular Dilatation and Pulmonary Regurgitation
Echocardiographic data (two-dimensional views) describing the RV were categorized as follows: a normal RV, ie, left ventricle to RV ratio of 3:1, was attributed the number 0 or none, a severely dilated RV (RV size equal or even exceeding left ventricular dimensions) was assigned the value 2, and anything in between was classified as a (mildly) dilated RV, associated with the number 1. Pulmonary valve incompetence was classified by the cardiologist on a scale from 1 to 4, 1 meaning trivial, 2 mild, 3 and 4 are in this study regarded as severe.

Statistical Analysis
All data are presented as the mean value ± one standard deviation (range). Probability of survival, freedom of reintervention, and PVR after repair were calculated by Kaplan-Meier analysis with the use of the SPSS program (SPSS Inc, OH). Differences among groups were calculated with Fisher’s exact test, log rank test, and Student’s t test. For the time analysis of RV dilatation and PR, data were clustered and adjusted for dependence of the outcome within a patient. The Mixor program (version 2) [23] then provided a graph from the mean probability in every category and year after corrective operation.

Results

Follow-Up
A total of 16 patients died during follow-up after complete repair. However, of the 11 deaths almost immediately after the operation, 2 patients had tracheobroncho-malacia, 1 suffered from cystic fibrosis combined with septic shock, and 2 from trisomy 13 and VATER association. Late deaths included 3 unrelated deaths (eg, car accident) and 2 patients with sudden cardiac death. Actuarial survival was 91% at both 10 and 20 years (Fig 1). Total mortality attributed only to the heart disease itself counted 4.7%.

At latest follow-up date most patients are in New York Heart Association class I, yet a considerable number of them presented with some insufficiency of the pulmonary valve, RV dilatation, tricuspid valve regurgitation, and right atrial dilatation (Table 1).

A significant association between poor clinical condition (New York Heart Association functional class II+) and objective echocardiographic measurements was only found in the demonstration of right atrial dilatation (p = 0.012); tricuspid insufficiency came close (p = 0.08). The presence of arrhythmias was also related to poor condition (p = 0.03).
In 15% (26 patients), RV outflow tract aneurysms were detected (ranging from trivial to mild, only one requiring reoperation). In 26% (44 patients) echocardiography showed a residual VSD; 9 were closed and 35 were very small or closed spontaneously. Postrepair cardiac catheterization was performed in 38 patients, mostly associated with PVR or to quantify pulmonary stenosis before angioplasty.

**Arrhythmias**
Cardiac arrhythmias on routine electrocardiographic examinations were prevalent, especially complete right bundle branch block (67%). First-degree atrioventricular block was found in 16 patients; in 6 patients this preceded the onset of more complex rhythm disturbances. Postrepair cardiac catheterization was performed in 38 patients, mostly associated with PVR or to quantify pulmonary stenosis before angioplasty.

**Reinterventions**
A total of 32 patients (19%) underwent reoperation at a mean age of 8.7 ± 5.6 years (range, 1.3 to 22.3 years; at 6.3 ± 5.8 years after correction), of which 8 did it more than once (Fig 2). Follow-up time after first reintervention was 6.0 ± 5.8 years. The majority of reinterventions, PVR excluded (10-year freedom, 83%), consisted of angioplasty for residual pulmonary stenosis (n = 12) and residual VSD closure (n = 6).

**Pulmonary Valve Replacement**
In 16 patients (9%) both physical and heart condition deteriorated to such an extent that PVR was considered (mean age after repair, 9.2 ± 6.7 years). Predominant clinical symptoms include diminished exercise tolerance and fatigue; indications for and outcome of repeated operative solution are depicted in Table 2. Most valves used were homografts, although two were Hancock heterografts. Good results were reported in 7 patients: an RV that returned to normal dimensions and disappearance of symptoms. A QRS complex exceeding 180 ms predicted serious problems in at least 2 of 3 patients. All important arrhythmias present before reoperation persisted after the procedure.

Four patients had a reintervention for residual pulmonary stenosis first. Tricuspid insufficiency as indication for PVR was documented in patients with both good and less favorable outcome.

**Time and Type of Repair and Outcome**
Figure 3 demonstrates that RV dimensions in patients without or before PVR slowly increase over time. A...
Table 2. Details of Pulmonary Valve Replacements

<table>
<thead>
<tr>
<th>Patient</th>
<th>Postrepair Age (y)</th>
<th>Clinical Condition</th>
<th>PR</th>
<th>RV Dilatation</th>
<th>Tricuspid Insufficiency</th>
<th>Pulmonary Stenosis</th>
<th>Arrhythmias</th>
<th>QRS &gt; 180 ms</th>
<th>Homograft</th>
<th>Other Problems</th>
<th>Follow-up After PVR (y)</th>
<th>Outcome</th>
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<td>x</td>
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<td>x</td>
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<td>Death shortly postoperatively</td>
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<tr>
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<td>x</td>
<td>x</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Abnormal lung vein, extra TAP, pacemaker</td>
<td>2nd PVR 7 yr later, sudden cardiac death 12 y later</td>
<td></td>
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<tr>
<td>3</td>
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<td>x</td>
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<td>x</td>
<td>0.6</td>
<td>Good</td>
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</table>

DCRV = double chamber right ventricle; PR = pulmonary regurgitation; PS = pulmonary stenosis; PVR = pulmonary valve replacement; RV = right ventricular; TAP = transannular patch; VSD = ventricular septal defect.

100% 100% 94% 75% 38% 38% 19% 88%
pulmonary atresia needs to be distinguished, as they congenital heart defects. The group of patients with very reasonable outcome compared with other serious pointed out by Murphy and colleagues [1], but it is still a

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Comment

In conjunction with recent large studies, the prognosis of a newborn with tetralogy of Fallot is excellent [1–4, 21]. Most patients were in New York Heart Association functional class I, and we found a 20-year actuarial survival of 91%. This is lower than the general population, as pointed out by Murphy and colleagues [1], but it is still a very reasonable outcome compared with other serious congenital heart defects. The group of patients with pulmonary atresia needs to be distinguished, as they present with more problems in follow-up, confirming the results of Knott-Craig and associates [3].

We doubt whether changes toward earlier timing of the initial repair greatly affect the late outcome. Our data show that patients operated on after the age of 6 months have a comparable probability of needing reintervention or PVR, and there is no difference in RV dimensions. The fact that their follow-up time was significantly longer and most operations were performed in the early days of our center certainly militate for a time-dependent or surgically dependent effect. Evaluating transannular patching, this time factor was ruled out, and our results met those of previous observations [22], indicating that both severe PR and RV dilatation were more prevalent in those patients who received this outflow patch. The positive impact of the transatrial approach was confirmed, although this technique was not used extensively in our population; we have more recently changed to a more frequent implementation of this technique.

The shorter duration of the QRS complex, did not result in fewer dysrhythmias in follow-up, in accordance with Oechslin and coworkers [19], pointing out that the site of ventricular arrhythmia is predominantly around the margins of the VSD patch and not the ventriculotomy per se, therefore putting every patient at equal risk. In regard to the severity of late RV outflow tract complications, our results did confirm those of Dietl and colleagues [24], who are in favor of the right atrial technique. Recommending preservation of the pulmonary valve or, if a transannular patch is necessary, restricting its width (minimizing regurgitant flow) and having a preference for the transatrial approach seems logical.

Right ventricular dysfunction and pulmonary valve insufficiency slowly develop after repair of tetralogy of Fallot and become present in almost all patients to some degree. Similar to Meijboom and coworkers [21], Zakha and associates [9], Jonsson and colleagues [7], and Hornfeffer and associates [2], who also used echocardiography in follow-up, we found evidence of more than trivial PR in a considerable number of patients. Meijboom and colleagues [21], however, did not confirm the increase we found with time of both PR and RV dilatation. Exercise capacity is found to be decreased in patients with dilated RV [13, 21], but most patients remain asymptomatic. Although some argue that long-standing PR has no adverse effect on survival [1, 2, 21, 22, 25, 26], PVR will become a more frequent consideration as the population ages. Shimazaki and coworkers [27] reported that in patients without operation and with anatomically normal hearts, except for a congenitally incompetent pulmonary valve, symptoms of right heart failure will develop 30 to 40 years later in life.

A considerable variation exists among patients in ability to tolerate PR and, as a result, development of RV dilatation. Especially additional lesions make the detrimental effects more difficult to endure: 5 of our patients already had one reoperation before undergoing PVR [8, 13, 22, 26]. Furthermore, Norgard and colleagues [28] and Gatzoulis and associates [29] demonstrated the protective effect (limited PR, less ventricular dilatation, and superior exercise performance) of a poorly compliant RV.
A high percentage of our population (9%) underwent PVR. In a few patients symptoms clearly diminished and the severity of regurgitation and dilatation improved, but unlike other reports [16, 18–20], objective outcome was not as good as expected. Some can be explained by normal deterioration of the implanted valve (in this case, mostly homografts), as also seen in groups with pulmonary atresia. Discovering a high-risk individual in an earlier stage, and offering PVR before the onset of myocardial degeneration, is now becoming the ultimate quest. Answers to this search are to be found in more specific indications for the replacement.

Some authors have emphasized the importance of coexisting tricuspid valve insufficiency [17, 26], resulting from progressive RV dilatation, and advocate earlier replacement because the onset of tricuspid regurgitation may represent a very late and possibly irreversible stage of RV failure [20].

Scar tissue is an important factor in the development of malignant ventricular arrhythmias. When this is combined with poor hemodynamics, a high-risk situation can evolve [30]. In contrast to Nienz and associates [11], Meijboom and colleagues [21] could not show a correlation between RV dilatation and arrhythmias (and sudden death). Neither could be confirmed in our study, but we agree with the findings of Gatzoulis and colleagues [31, that QRS prolongation (> 180 ms) is their most sensitive predictor. The presence of significant arrhythmias by itself alone cannot be an indication for PVR.

Perhaps a great factor in this problem is not the indication itself, but the evidence of its presence. Different patients have different ways of responding to hemodynamics after complete repair, and this should be accounted for in diagnostic methods. Doubts about a deteriorated RV function by echocardiographic data should best be confirmed by magnetic resonance imaging mapping studies to allow optimal timing in the decision-making process tailored to the individual patient [11, 32].

Limitations

In the 23 years of cardiac surgery for tetralogy of Fallot in our center, techniques and timing of the operation have changed and the experience of the surgeons has increased, suggesting a more favorable outcome in the youngest patients. During follow-up, electrocardiograph and echocardiography devices were modernized, presenting clearer pictures and allowing detection of problems earlier. Moreover, observations were performed by different cardiologists. Comparison of results may also be hazardous, because no standardized method is used in literature to quantify either PR or RV dilatation.

Conclusions

Severe RV dilatation and PR secondary to outflow tract repair in tetralogy of Fallot are frequently occurring sequelae in respectively 38% and 32% of our population, developing slowly with time. Indications for PVR remain controversial because warning echocardiographic findings or arrhythmias are not always accompanied by deterioration of clinical condition. However, right atrial dilatation and additional hemodynamic lesions demand increased vigilance. Transatrial repair is associated with a favorable outcome.

References

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DISCUSSION

DR DARRYL S. WEIMAN (Memphis, TN): Doctor Kanter seems to think that the porcine valve replacement is superior to the homograft. Did you have a chance to look at your data in that regard?

DR BENNINK: It is very interesting. In Holland, research was done by the Leiden group in which they put in the growing pig a biologic valve, mainly the Freestyle Medtronic valve, and because of the disastrous results, we did not dare to use that valve in humans. Now that I have seen this result of Dr Kanter, I can see that the pig is a little bit different from the human being. I knew that before, but it is not always wise to extrapolate all the results you get from animal experiments. But mainly it is homograft insertion that we do, and the Groningen group in Holland even implants mechanical valves in the pulmonary position.

DR CONSTANTINE MAVROUDIS (Chicago, IL): Some of the very important work on postoperative arrhythmias in these patients has been done by Michael Gatzoulis in Great Britain. He showed that atrial reentry tachycardia is more common than ventricular tachycardia in these patients. You did note in one of your slides that you used arrhythmias as part of your indications for operation. But did you do anything about these arrhythmias at the time of operation? In other words, did you perform a maze procedure in any of these patients? It would be interesting to hear what your thoughts are on this subject.

DR BENNINK: Thank you for your comments, Dr Mavroudis. We have not done anything with it yet, but, as you probably know, one of your former fellows is now working in our institute and we are planning to come and visit you in Chicago in January to see exactly how to do those procedures, so we are really considering it. One of our cardiologists is interested in electrophysiology. I think it is a wise thing to do, especially if the procedure is not too much prolonged. Then I think it will contribute to the outcome of the patients. Up until now we did not perform any arrhythmia surgical procedures.