Current strategies in tetralogy of Fallot repair: pulmonary valve sparing and evolution of right ventricle/left ventricle pressures ratio

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Abstract

Objective: Chronic volume overload in repair of tetralogy of Fallot (TOF) with transannular patch leads to significant late morbidity and mortality. Preserving pulmonary valve integrity offers a better long-term prognosis, despite a risk of residual stenosis. In our study we analyzed the evolution of pressure gradients in patients operated with conservative approaches, with particular regard to those babies with an immediate postoperative Prv/Plv ratio >0.70. Methods: Between January 2000 and June 2008, 24 patients with TOF underwent reparative surgery with a valve sparing procedure (median age 8.1 months, range 1.1—86.6). The intraoperative post-repair echocardiography showed a Prv/Plv ratio >0.70 in eight patients (33%, group A) and <0.70 in 16 patients (67%, group B). We realized a retrospective study of pre-, intra-, and postoperative data and of clinical and echocardiographic follow-up data. Results: There was no early or late mortality, nor functional or rhythmic disturbances. One patient required re-operation for residual stenosis at annular level at one year. After a median follow-up of 32.8 months (range 0.6—73.1), the Prv/Plv ratio decreased by 16% (p = 0.001) in all patients. In group A the reduction was 28% (p = 0.018) and in group B it was 12% (p = 0.14). Conclusions: After a valve sparing procedure there is a reduction of Prv/Plv ratio at medium-term follow-up; in our study this reduction was statistically significant in all patients and in the subgroup with higher postoperative ratios. A valve sparing strategy reduces pulmonary regurgitation, preserves RV function and decreases the incidence of late arrhythmias, which are the determinants of long-term outcome.

Keywords: Tetralogy of Fallot; Pulmonary valve sparing; Cardiac congenital

1. Introduction

Tetralogy of Fallot (TOF) was one of the first congenital heart defects that cardiac surgeons were able to treat successfully. The original repair was carried out through a large right ventriculotomy, often placing a pulmonary transannular patch to relieve the right ventricular outflow tract (RVOT) obstruction [1].

Since then, many other operative techniques have been developed, including transatrial repair of the ventricular septal defect and transatrial relief of RVOT obstruction (when the pulmonary structures do not need any manipulation) [2] and the combined transatrial/transpulmonary repair when pulmonary valve commissurotomy and/or pulmonary trunk enlargement are needed [3,4]. The objectives of these modifications are the avoidance of a ventriculotomy and the preservation of pulmonary valve/annulus integrity, with the aim of maintaining at long-term follow-up a normal RV function [5,6]. These kind of conservative operations are normally planned when the pulmonary annulus Z-score is higher than −4 [7,8].

Nevertheless, when a patch is not used to enlarge the pulmonary annulus, there is a risk of residual RVOT obstruction, which is more likely to occur when the Z-score value is −3 or lower. In borderline cases (as referred to pulmonary valve Z-scores), if a transannular patch has not been used and intraoperative RV/LV pressure (Prv/Plv) ratio is below 0.75, the repair may be considered satisfactory, while if this value is higher than 0.75 a transannular patch should be considered.

The immediate postoperative course of a TOF patient submitted to a pulmonary annulus conservative operation may be more troublesome with respect to the transannular patch group, since in the early phase a residual pulmonary stenosis is worse tolerated than regurgitation.

The aim of our work was to analyze the general outcome and the specific evolution of Prv/Plv ratio in TOF patients operated on with conservative approaches, with particular
regard to those babies with an immediate postoperative ratio ≥0.70.

The potential advantages and disadvantages of a pulmonary valve sparing procedure are resumed in Table 1.

## 2. Materials and methods

### 2.1. Patients

All patients undergoing TOF repair between January 2000 and June 2008 at our institution (110 patients) were identified from our computerized database. Patients with prior palliative surgery, TOF with absent pulmonary valve or pulmonary atresia or with concomitant atrioventricular canal defect were excluded (59 patients). Of the remaining 51 patients, 24 (47%) underwent TOF repair with a valve sparing procedure and they represent our group of study. All these patients had a pulmonary annulus Z-score greater than −4 and their demographic data are reported in Table 2.

### 2.2. Surgical technique (conservative approach)

Under aorto-bicaval cardiopulmonary bypass with moderate hypothermia (28°C) the aorta was cross-clamped and antegrade crystalloid cardioplegia was administrated and repeated at 20–25 min intervals.

The RVOT was inspected both through the right atrium/tricuspid valve and through the pulmonary valve (except in those cases in which the anatomy could be fully understood through the atrial inspection and, from preoperative study, it was judged unnecessary to repair any pulmonary structure, either valve or trunk). After VSD inspection, the muscular resection was always started from the atrium, addressing RVOT parietal and septal trabeculations, and usually it was possible to reach the very subpulmonary region (and to visualize the pulmonary valve) from this access. Then, from a vertical incision in the pulmonary trunk, we inspected the pulmonary valve and, when necessary, any commissural fusion of the valve leaflets was sharply incised, taking care to avoid any deep incision in the annulus. The infundibulum was inspected through the pulmonary valve and additional resection was performed if necessary. Very rarely, when infundibular resection was more complex than usual or in very small babies, we created a small ventriculotomy in the anterior aspect of RVOT to better relieve through it any subpulmonary residual obstruction (this incision respected the pulmonary annulus integrity). Then the RVOT and the pulmonary valve annulus were measured with Hegar dilators and their sizes were recorded as the larger dilator that fitted them without forcing. The Z-score values were calculated from a nomogram [9].

The ventricular septal defect was then repaired via the right atrium, aortic clamp was removed and, with beating heart, right atrium was closed and the pulmonary artery was repaired, using an appropriate enlargement patch, extended toward a PA branch when necessary.

At the end of the procedure, after the modified ultrafiltration, pressures in the right and left ventricles were measured and recorded, and two-dimensional transesophageal echocardiography was performed. We considered the repair satisfactory when no significant residual defects were found at the echo exam and either the Prv/Plv ratio was below 0.75 or, if slightly higher, we were quite sure of the appropriateness of muscular resection and we believed the residual gradient to be due only to the small annulus (and always in presence of hemodynamic stability). Otherwise, we went back on bypass and we realized a more aggressive muscular resection (or we placed a transannular patch, but these patients are not included in this study).

### 2.3. Postoperative management

#### 2.3.1. Inotropic support

Weaning from bypass was generally realized with dopamine 5–6 mcg/kg/min, milrinone 0.5–0.6 mcg/kg/min, and urapidil 0.5–0.6 mg/kg/h. Exceptionally, in patients with very high RV pressures in which the correction was considered satisfactory, low dose adrenaline was started (0.02–0.04 mcg/kg/min). In the first few postoperative hours urapidil was generally stopped, raising milrinone up to 0.7 mcg/kg/min. In cases of severe RV failure with reduction of cardiac output and constant need of fluid administration to maintain an adequate preload, we utilized low dose noradrenalin until the low cardiac output status was reverted. In the last two years we have been using levosimendan in cases of diastolic ventricular failure or myocardial injury secondary to the extracorporeal circulation and aortic cross-clamping, with good results. We used to

### Table 1

Advantages and disadvantages of a pulmonary valve sparing procedure.

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary valve sparing</td>
<td>• PR</td>
<td>• Immediate risk</td>
</tr>
<tr>
<td></td>
<td>• RV dysfunction</td>
<td>• Residual stenosis risk (reintervention)</td>
</tr>
<tr>
<td>Transannular patch</td>
<td>• PV reintervention</td>
<td>• Free PR</td>
</tr>
<tr>
<td></td>
<td>• Immediate risk</td>
<td>• RV dysfunction</td>
</tr>
<tr>
<td></td>
<td>• Residual stenosis risk</td>
<td>• PV reintervention</td>
</tr>
</tbody>
</table>

### Table 2

Demographic data of the study cohort.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>24</td>
</tr>
<tr>
<td>Age (months)</td>
<td>8.1 (1.1–86.6)</td>
</tr>
<tr>
<td>Gender (male/female)</td>
<td>13/11</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>8.05 (5.0–16.5)</td>
</tr>
<tr>
<td>Body surface area (m²)</td>
<td>0.39 (0.29–0.72)</td>
</tr>
<tr>
<td>Preoperative pulmonary annulus Z-score</td>
<td>−1.5 (−3 to 0)</td>
</tr>
</tbody>
</table>

* Values are expressed as median (range) or number of patients.
administrate a 6 mcg/kg bolus followed by a 0.1 mcg/kg/min infusion during 24 h.

2.3.2. Fluid management
An adequate preload was maintained by intravascular fluid administration (in the first hours blood, plasma, or albumin), looking for a generally high target CVP (being patients with a restrictive RV physiology). Furosemide (± hydrochlorothiazide) was started as continuous infusion soon after patient arrival in ICU. Any effusion (pleural and/or abdominal) was evacuated as soon as diagnosed.

2.3.3. Ventilation strategy
Mechanical ventilator was settled in the modality of ‘pressure regulated volume control’, with a low tidal volume, PEEP low/physiologic, ventilation rate as to get normocapnia, and the FiO2 necessary to have an adequate arterial blood oxygenation. In cases of moderate RV failure, not preventing the patient from being extubated, we optimized the weaning from mechanical ventilator with the use of non-invasive ventilation (BiPAP or CPAP) by nasal or facemask.

2.3.4. Echocardiographic assessment
All patients received a transesophageal echocardiographic examination intraoperatively to assess the appropriateness of surgical repair. In ICU, trans-thoracic echocardiograms were realized on the first PO day and then according to the clinical status of each patient. All patients received an echocardiographic examination prior to discharge from hospital (generally the day before).

2.4. Data analysis
We divided the patients into two groups according to the intraoperative post repair Prv/Plv ratio: ≥ 0.70 (group A, 33% patients) and < 0.70 (group B, 67% patients). We realized then a retrospective study of pre-, intra-, and postoperative data and a clinical and echocardiographic data review at last follow-up. Student’s t-test (one sample paired test) was employed to assess the statistical significance of Prv/Plv evolution in the whole cohort of patients and in each subgroup; a p value < 0.05 was regarded as significant. Variables are expressed as mean (± SD) or median (range).

3. Results
There was no early or late mortality, nor functional or permanent rhythm disturbances. Functional tachycardia occurred in six patients (25%), and it was generally controlled in a few hours by lowering the patient’s core temperature to 34 °C and/or by atrial pacemaker overriding. Pleural effusion affected four patients (17%) and one of them suffered a cardiac pre-tamponade due to sub acute pericardial effusion, which was evacuated by echo-guided catheter placement.

A total of three patients (12.5%) underwent redo procedures: only one of them (4%) was re-operated (at 11.7 months) due to significant stenosis at annular level, and a transannular patch was placed; another patient underwent redo surgery at 12.9 months for additional muscular bands resection, but pulmonary annulus was respected; the third patient underwent an interventional cath lab procedure at 15.3 months to solve a pulmonary artery stenosis (cutting balloon angioplasty). Characteristics of these patients are given in Table 3.

In all patients, the median Prv/Plv ratio as measured in operating room was 0.59 (range 0.30–0.90), with a median pressure gradient in RVOT of 31.5 mmHg (range 14–120). Eight patients (33%) had a Prv/Plv ratio ≥ 0.70 (group A), ranging from 0.70 to 0.90. Interestingly, from this group only one patient underwent a re-operation, and she was the one who had residual muscular obstruction; she had an annulus Z-score of 0 at first operation and of −2 at re-operation. The patient who required a transannular patch was in group B: at first operation he had a pulmonary annulus Z-score of −2 and a Prv/Plv ratio of 0.63; he developed a severe subvalvular and valvular obstruction, which could not be treated with an annulus sparing procedure (he had, at re-operation, a borderline annulus Z-score of −3).

Mean intraoperative pulmonary annulus Z-score was −1.62 (± 0.98), with three patients having −3 and two having −2.5 (that is 21% of patients with pulmonary annulus smaller than Z −2). There was an adequate concordance with the preoperative value (measured with echocardiography) in 75% of patients, while in the rest the preoperative Z-score value was slightly underestimated.

After a median follow-up of 32.8 months (range 0.6–73.1), Prv/Plv ratio decreased by 16% in all patients (from 0.61 ± 0.16 to 0.49 ± 0.20, p = 0.001); in group A the reduction was 28% (from 0.79 ± 0.06 to 0.57 ± 0.21, p = 0.018) and in group B it was 12% (from 0.52 ± 0.10 to 0.45 ± 0.19, p = 0.14) (Fig. 1). Excluding the 3 patients that had to be re-intervened, only 2 (out of 21, 9.5%) had a Prv/Plv ratio > 0.65, and they are among the patients with the shorter follow-up period (1 month and 0.57 month, respectively), so that we expect these pressure ratios to lower with time.

Mean value of pulmonary regurgitation was mild at follow-up control; it was severe in only two patients (8.3%), and in none at early postoperative control. The mechanism of PV

<table>
<thead>
<tr>
<th>Initial surgical approach</th>
<th>Age (months)</th>
<th>Weight (kg)</th>
<th>Pulmonary annulus Z-score</th>
<th>Prv/Plv ratio</th>
<th>Interval to re-operation (months)</th>
<th>Corrective procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>TA</td>
<td>1.1</td>
<td>5.2</td>
<td>−2</td>
<td>−3</td>
<td>0.63</td>
<td>8.0</td>
</tr>
<tr>
<td>TA/TP</td>
<td>7.0</td>
<td>7.1</td>
<td>0</td>
<td>−2</td>
<td>0.77</td>
<td>1.00</td>
</tr>
<tr>
<td>TA</td>
<td>7.5</td>
<td>8.2</td>
<td>−2.5</td>
<td>−3</td>
<td>0.57</td>
<td>0.80</td>
</tr>
</tbody>
</table>
regurgitation in these two severe cases was leaflet retraction (at operation the valve was bicuspid in both cases and commissurotomy was performed).

More early postoperative and follow-up data are given in Table 4.

### 4. Discussion

In literature there are several reports showing the problems of long-term pulmonary incompetence, although this remains a controversial issue. Some studies [10,11] report good long-term outcomes after TOF repair with transannular patch, with low incidence of redo procedures, despite a significant, high degree of pulmonary regurgitation, and this is ascribed to the adaptive properties of the right ventricle. These findings are contraindicated by other studies showing the deleterious effect of pulmonary insufficiency on the right ventricle when more sensitive measurements are made, such as MR examinations [5,12–14]. Arrhythmias may complicate the long-term evolution, especially in those cases in which a ventriculotomy is associated to the transannular patch [15,16]. Stewart and colleagues [6] showed that the pulmonary valve (annulus) preservation is possible in most patients presenting for a complete repair of tetralogy of Fallot. They demonstrated that favorable prognostic factors for a conservative strategy are a pulmonary annulus $Z$-score greater than $-4$, a tricuspid pulmonary valve, and a postoperative Prv/Plv ratio less than 0.7. The ability to preserve the valve function should prevent the deleterious effect of free pulmonary regurgitation, preserving RV function and decreasing the incidence of late arrhythmias.

At our institution we have made a strong effort to avoid both a ventriculotomy and/or a transannular patch in patients with pulmonary annulus $Z$-score greater than $-4$, in order to preserve both RV and pulmonary valve function. So, whenever possible, we used the transatrial/transpulmonary approach, accepting postoperative Prv/Plv ratio even higher than 0.75 when we were quite sure that residual obstruction was due to the small pulmonary annulus (and not to residual infundibular stenosis) and, always, in presence of stable hemodynamics.

The present study does not address the issue of which patients can be treated with a conservative approach, which is a very interesting argument deserving a different analysis. Our objective was to analyze, in the selected group of patients operated on with a pulmonary annulus sparing procedure, the general outcome and the more specific evolution of Prv/Plv ratio and pulmonary annular dimensions with time. Our results show a significant mean reduction in Prv/Plv ratio at medium-term follow-up (from $0.61 \pm 0.16$ to $0.49 \pm 0.20$, $p < 0.01$), and a consequent growth of pulmonary annulus from a mean $Z$-score of $-1.62 \pm 1.01$ to $-0.37 \pm 1.62$ even if this last reduction did not reach statistical significance. On the contrary, in those cases in which, at follow-up, a significant residual stenosis was found (at subvalvular, valvular or supravalvular level) the annulus got smaller with time: it is the case of our three patients who needed the redo procedures. This suggests that when infundibular and supravalvular stenosis are fully removed.
The incidence of arrhythmias, which are the determinants of residual RVOT obstruction, it reduces pulmonary artery pressure on medium-term follow-up, which in our series was statistically significant in the whole cohort and in the group of babies with medium-term follow-up, which in our series was statistically significant.}

### References

Dr Di Donato: I agree only partially with your statement that you make in the paper that any residual RV-to-PA gradient is due only to the small annulus, even with an aggressive valve sparing approach like yours. In our experience, as well as in that of others, a progressive decrease in right ventricular pressure is seen in the first few hours after surgery and, in fact, on postoperative day 1 the right ventricular pressure is most often significantly lower than the value recorded intraoperatively. This observation would suggest an important dynamic component of the initial RV-to-PA gradient destined to fade away with the ensuing infundibular relaxation. The role of this dynamic infundibular component is also confirmed by the lack of correspondence between severity of intraoperative right ventricle to left ventricle pressure ratio to left ventricle pressure ratio greater than 0.75 and the need for late RVOT revision. Concerning the measurement of right ventricular pressure and of the right ventricle to systemic pressure ratio, based on which you decide whether to accept the repair, my questions are:
What is the maximum level of intraoperative right ventricular pressure that you tolerate?
Do you routinely leave a pressure line in the right ventricle to monitor the pressure over the following 24–48 h?

Dr Boni: As for the first comment, I do agree with you, and that’s why we accept high gradients or high pressures in the right ventricle: because it is well known that pressures decrease in a few hours, and when you measure pressures in the operating room, the patient may be in a hyperdynamic state.

What I meant was that when the only residual obstruction is at annular level, this does not prevent the other structures from having a normal development.

Regarding the question about which maximum RV/LV pressure ratio we accept, we have accepted up to 0.9, because in that case we believed that the annulus was in the limit and the muscular resection was deep enough. So we thought that it was for the hyperdynamic state and in fact that patient did not require any reoperation. Finally, it depends on the single individual, maybe we can accept ratio up to 80% or 90%.

Dr C. Schreiber (Munich, Germany): I think we can probably fill a breakfast session next year on this or some postgraduate day. I think we should move on.