REVIEW

Management of patients with pulmonary atresia, ventricular septal defect, hypoplastic pulmonary arteries and major aorto-pulmonary collaterals: Focus on the strategy of rehabilitation of the native pulmonary arteries

Prise en charge des atrésies pulmonaires avec communication inter-ventriculaire, hypoplasie des artères pulmonaires et collatérales : mise au point sur la stratégie de réhabilitation des artères pulmonaires

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Received 20 June 2012; received in revised form 4 August 2012; accepted 17 August 2012
Available online 13 November 2012

KEYWORDS
Pulmonary atresia; Major aorto-pulmonary collateral arteries; Rehabilitation

Summary  Pulmonary atresia with ventricular septal defect (VSD), hypoplastic native pulmonary arteries (PAs) and major aorto-pulmonary collateral arteries (MAPCAs) is a rare and complex congenital cardiac disease. In broad outline, two surgical approaches are available for patients with this condition. The first is characterized by one or several stages of complete unifocalization of the supplying MAPCAs, with or without incorporation of the native pulmonary arteries (PAs), connection of the right ventricle to the ‘neo-Pas’ and, if possible, concomitant or delayed closure of the VSD. The second strategy is based on rehabilitation of the native pulmonary arteries. The first step is a direct right ventricle to native PA connection, to promote the growth of native PAs. The establishment of antegrade flow also allows an easier approach for
Management of patients with pulmonary atresia

Background

Pulmonary atresia with ventricular septal defect (VSD), hypoplastic native pulmonary arteries (PAs) and major aorto-pulmonary collateral arteries (MAPCAs) is a rare and complex congenital cardiac disease. In broad outline, there are two different surgical approaches to these patients. One of these approaches is characterized by one or several stages of complete unifocalization of the supplying MAPCAs, with or without incorporation of the native PAs, connection of the right ventricle (RV) to those ‘neo-PAs’ and, if possible, concomitant or delayed closure of the VSD [1, 2].

The other approach is based upon rehabilitation of the native PAs [3]. The first step is to create a direct connection from the RV to the native PAs, in order to promote native PA growth. Establishment of antegrade flow allows also an easier approach for interventional catheterization, making dilatation/stenting of stenosis and then closure of communicant collaterals possible. When the development of the native PAs is satisfactory, the complete repair is performed. If it is necessary to suture a MAPCA to the PA (‘unifocalization’), this is accomplished by connecting the collateral artery to an already developed native branch.

Our team developed this multidisciplinary strategy with good results [4]. Based on this experience as well as on the literature, we review this strategy for the management of patients with pulmonary atresia, VSD, hypoplastic PAs and MAPCAs.

Which patients are we talking about?

Anatomical description

To enter this category, a patient should present with pulmonary atresia, no persistent arterial duct and ‘hypoplastic’ but present central PAs. This excludes patients with ‘normal’ PAs vascularized through a ductal structure, with the atresia being simply at the valvular level or more complex. It excludes, of course, patients without any central PAs. In real life, it is not always easy at first examination to differentiate clearly between a tortuous arterial duct and an MAPCA but it is clear that none of these patients should be prostaglandin E1-dependent. ‘Hypoplastic’ PAs have to be determined according to the Nakata index [3] (below 90 mm/m² or 100 mm/m², depending on the authors). None of these patients should be readily accessible to complete repair without unifocalization, which means that a normal output will not be able to flow through the central PA before rehabilitation.

The origin of the pulmonary flow is completely due to the MAPCAs. The distribution of the native PAs and the MAPCAs to the pulmonary segments has to be appreciated and evaluated.

The location of the VSD is the same as in Tetralogy of Fallot—a conoventricular position. The anatomical investigations have to confirm that it is a single VSD. Furthermore, the position of the coronary arteries has to be checked. The aortic arch may be left- or right-sided, which may have importance for the surgical plans.
Some of the patients might have a 22q11 deletion (Di George syndrome), which seems to be correlated with smaller native PAs [4].

All of this information is established via echocardiography, tomodensitometry or angiography. In our hands, angiography is preferred because it has always permitted a more precise anatomical diagnosis. This point has to be re-evaluated with each improvement in the computed tomography scan technique. Typically, angiography shows the 'sea-gull' aspect, with retrograde filling of the extremely diminutive central PAs (Fig. 1A). The Nakata index can then be calculated.

Different features of each MAPCA should be analyzed (Fig. 1B): its origin from the descending aorta or – rarely, if ever – from the main branches of the ascending aorta; its size, with or without stenosis; its course, mainly in relationship with the esophagus, carina and bronchus and native PAs; and its distribution to the lungs.

The most important point to determine about the MAPCAs is if each of them is ‘communicant’; in other words, if the pulmonary segments they vascularize are also filled by the native PA or not. Each segment has to be considered separately, hence great differences in flow origin and pressure are possible between them.

However, detailed angiographical (or radiological) analysis may be easier after the first stage procedure than at the first work up and should always be re-evaluated afterwards. In our experience, we have to admit that complete distribution of the native PAs was, in fact, found more often than expected.

Clinical status

Early outcome after birth is usually good, with blood saturation usually around 80% or less. The mean age of the first surgical procedure is ideally around three months [5], depending on the patient’s growth. If cyanosis is problematic, the surgery has to be done earlier. If, however, the pulmonary blood flow is too high, medical treatment is given and early surgery is considered, if necessary.

One also has to be wary of management that is 'too late' in such a patient. In the lung territories filled by large MAPCAs, hypertensive PA disease can develop early, with no reversibility, which might compromise the patient’s future. Alternatively some segments can receive a very small part of the total pulmonary flow, which will impair vasculogenesis. Complete closure of central native PA is also a risk to consider. It is likely that some patients when diagnosed late and then described as having absolutely no native central PA, had, in fact, a diminutive and low-flow central PA to begin with. It should be understood that the flow in the central PA is dependent on a subtle difference of pressure between the left and right segments, with communication between native branching and MAPCAs.

In conclusion, even if the clinical status is good — meaning that the total pulmonary blood flow is adequate — this balance is unlikely to be as satisfactory at the segmental level and postponing the therapeutic decision can be very deleterious in the long-term.

Multistage native pulmonary artery rehabilitation: How to do it?

Step 1: Surgical technique for right ventricle-to-pulmonary artery continuity establishment [5]

The procedure is performed via a median sternotomy with the use of cardiopulmonary bypass (CPB) on a beating and ejecting heart. Aortic cross-clamping is not indicated because of the MAPCAs: the blood flow would be preferentially towards the lungs (if the pulmonary resistances are low) and would end up in dilated unable-to-eject ventricles; the systemic perfusion would be poor, whereas the lung would be overfilled.

Typically, analysis of external anatomy shows a diminutive main PA, connected to an atretic infundibulum. After controlling the right and left PAs, and in the case of no major coronary artery crossing the infundibulum, the main PA and the infundibulum are incised longitudinally. When the latter is opened (in the last minutes of the procedure), blood is, of course, ejected and resuscutioned back in the CPB circuit. Despite this bleeding, the sucker is managed carefully to avoid air embolism through the VSD and to the aorta. A precisely tailored autologous pericardium patch treated with glutaraldehyde (and rinsed) is sutured to the edge of the arteriotomy and to the epicardium around the infundibulotomy (Fig. 2).

Step 2: Multistage catheterization [6,7]

After a delay of two months, we believe that catheterization can be safely performed. This procedure has several objectives (Fig. 3):

- the diagnostic objectives are:
  - visualization of the enlarged now-established right ventricle-to-pulmonary artery (RV-PA) continuity,
**Figure 2.** Peroperative view of step 1. A and B. The arrow shows the hypoplastic main pulmonary arteries. The right and left pulmonary arteries are controlled and occluded by blue rubber loops. C. The main pulmonary artery is opened longitudinally (arrow). This incision will ultimately be extended to the infundibulum, as far as to obtain a sufficient opening of the right ventricle. D. An autologous pericardium patch is sutured to the edge of the arteriotomy and infundibulotomy.

**Figure 3.** Example of incomplete pulmonary artery distribution. A. Angiography showing an incomplete distribution of the right pulmonary artery. Only the upper pulmonary lobes are perfused. B. Major aorto-pulmonary collateral artery perfusing the middle and lower right pulmonary lobes.
quantification of the growth of native PAs, with an increased Nakata index;
re-evaluation and identification of the distribution of the native PAs;
and re-evaluation of the pre-existing MAPCAs and research of new ones;
the haemodynamic objective is:
evaluation of PA pressures in the different pulmonary segments, downstream of the MAPCAs;
the interventional objectives are:
angioplasty/stenting of the native PAs,
and coil occlusion of communicant MAPCAs.

A computed tomography scan is often very useful at this point to prepare for the catheterization procedure. Occlusion of communicant collaterals is important, even if the PA has not yet reached the expected diameter, to promote the flow, which will itself promote growth and presumably angiogenesis. The expected antegrade flow is always in competition with collateral flow and this has to be well understood and studied branch by branch. When a native pulmonary branch and MAPCA both fill one or several pulmonary segments, the occlusion of this MAPCA is performed as soon as the antegrade circulation (with or even without dilatation/stenting) is considered sufficient. When one or several pulmonary segments are only filled by a MAPCA (Fig. 3B), it will be ‘unifocalized’ (disconnected from origin and anastomosed to the now enlarged native PA) at the time of step 3 or during an additional step, before the total correction.

At this point of the pathway the dilatation/stenting process focuses on the central PAs, to promote growth of hilar and segmental branches and to allow safe occlusion of the communicant MAPCAs.

Sometimes an ‘ideal’ catheterization procedure cannot be done in one step; several procedures may be necessary, according to the development of the native PAs. Of course, the pulmonary blood flow and the subsequent oxygen saturation have to be evaluated throughout the whole process.

If the pulmonary blood flow has already increased before the first surgical step, occlusion of the communicant collaterals may be done earlier than two months, if necessary. As a matter of fact, in these specific cases, the first surgical step is necessary but does not improve and even impairs clinical status, increasing the failure to thrive and signs of congestive heart failure.

**Step 3: ‘Complete’ correction**

When all the communicant MAPCAs have been occluded and the Nakata index is considered sufficient (usually > 150 mm²/m²), a complete repair can be performed under CPB, this time with aortic cross-clamping and cardioplegic cardiac arrest. In patients with a Nakata index between 90 and 150 mm²/m², other criteria, such as transcutaneous oxygen saturation (SaO₂) greater or equal to 85% (without open MAPCA), might be considered as good evidence of feasibility of VSD closure.

The repair includes: reconstruction of the pulmonary bifurcation and branches as far as possible in both directions (the stents, if any, are longitudinally open and most of the time almost totally removed; some well included and perfectly endothelialized parts can be left in place; both the right and left PAs, from origin to hilum, are enlarged with PA homograft wall patches; patch closure of the VSD; and establishment of another RV-PA continuity with a cryopreserved pulmonary homograft. At the end of the procedure, even if the haemodynamics are perfect, the RV/left ventricle (LV) pressure ratio has to be calculated. Upon a 1/1 ratio, VSD reopening (perforating the patch with a hole punch) should be considered.

**Additional steps**

The management of MAPCAs that provide the only supply to one or several pulmonary segments may necessitate other surgical steps. Those MAPCAs have to be unifocalized to the homolateral native PA, when it is considered sufficiently well developed. This may be performed as an additional step, through a lateral thoracotomy, between two stages of catheterization; it can also be performed at the time of step 3. The choice between these two different approaches depends heavily on the feasibility of midline unifocalization. The course of each MAPCA with respect to the other structure is of importance. Easy access to the aortic origin of the MAPCAs depends also on the right or left position of the descending aorta.

Moreover, additional catheterizations should be performed after the last surgical step, in order to continue the PA rehabilitation programme. Those subsequent percutaneous procedures aim to: evaluate haemodynamic status (PA and RV pressures); continue to promote the development of native PAs with angioplasty and stenting, if necessary (this will now mainly address hilar and lobar branches); diagnose and occlude new aorto-pulmonary collaterals; if necessary and as soon as possible, occlude a fenestrated VSD patch; and, eventually, redilate the central homograft and/or reevaluate the RV outflow tract.

The schedule and frequency of those additional catheterization procedures are determined according to each patient’s characteristics. Clinical status (even if the patient is doing well) and RV pressures (even if pleasantly low) have to be taken in account. The distribution can also be still very heterogeneous between the right and left side (perfusion scans are very helpful) and in each side between lobes and segments.

**Outcomes**

Long-term results were published in 2011 [8]; 20 patients (Table 1) were included in the study. The mean follow-up was 8.2 ± 4.5 years and the mortality rate was 15%. Three patients did not survive (respectively 0.3, 0.4 and 11.8 years after surgery) in the clinical setting of RV failure. The first patient died from a cardiac arrest and could not be resuscitated, in the context of severe respiratory distress and fever. The second died during an interventional catheterization, in the setting of acute RV failure with arrhythmia. The third patient had an interrupted follow-up for ten years; at this time, RV dysfunction could not be improved despite emergent RV-PA conduit replacement of a very stenotic homograft. This last case shows how the follow-up of these patients matters. The PA rehabilitation process has to be considered and managed as a continuum. The team has to
Management of patients with pulmonary atresia

Example of management: Case study

Pulmonary atresia with VSD, hypoplastic PAs and MAPCAs was diagnosed a few days after birth. The baby boy was referred to our institution after anatomical evaluation in another centre. The characteristics of the patient are shown in Table 3.

The first angiography was performed (Fig. 1; Table 4). The angiograms showed a very hypoplastic 'sea-gull' with hypoplastic native PAs (right PA, 1.7 mm; left PA, 2 mm) and three MAPCAs. The distribution of the pulmonary vasculization was hypoplastic but apparently complete. The Nakata index was 25 mm/m². MAPCA 1 was emerging from the descending aorta and was connected to the inferior right pulmonary lobe. MAPCAs 2 and 3 were emerging from the descending aorta and were connected to the inferior left and right pulmonary lobe. The saturation decreased very slowly to 65% during the first weeks, due to the obstructive evolution of the MAPCAs.

Step 1

At the age of 3.4 months (4.5 kg), the patient underwent a surgical procedure under CPB, with establishment of RV-PA continuity, with an autologous pericardium patch. The postoperative course was simple and SaO₂ increased to 90%. The length of stay in the intensive care unit was three days and the patient was discharged home on the 13th day.

Step 2

The second catheterization was performed 3.5 months later (Table 5) and the third catheterization was performed two months later (Table 6).

Step 3

The second surgical procedure was performed at the age of 11 months (8.5 kg). Under CPB, the pulmonary bifurcation and branches were reconstructed, the RV-PA connection was done with a pulmonary homograft (diameter 20 mm) and the VSD was closed. At the end of the procedure, the RV/LV pressure ratio was 0.7. Haemodynamics were satisfactory. The length of stay in the intensive care unit was five days and the patient was discharged on the 10th day. SaO₂ was 98%. Early outcomes were good.

Table 1 Characteristics of patients, from [8].

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men/women</td>
<td>12/8</td>
</tr>
<tr>
<td>Microdeletion 22q11</td>
<td>7</td>
</tr>
<tr>
<td>Nakata index (mm/m²)</td>
<td>26 ± 14</td>
</tr>
<tr>
<td>SaO₂ (%)</td>
<td>76 ± 5</td>
</tr>
<tr>
<td>Number of MAPCAs</td>
<td>4 (2–6)</td>
</tr>
<tr>
<td>Right aortic arch</td>
<td>7</td>
</tr>
<tr>
<td>Right subclavian artery in lusoria position</td>
<td>1</td>
</tr>
<tr>
<td>Left superior vena cava</td>
<td>3</td>
</tr>
<tr>
<td>Additional ventricular septal defect</td>
<td>1</td>
</tr>
</tbody>
</table>

Data are number, mean ± standard deviation or median range. MAPCA: major aorto-pulmonary collateral artery; SaO₂: transcutaneous oxygen saturation.

Table 2 Example of continuation of pulmonary artery rehabilitation process after surgical complete repair, from [8].

<table>
<thead>
<tr>
<th>Follow-up after complete surgical repair (years)</th>
<th>8.2 ± 4.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>17</td>
</tr>
<tr>
<td>Percutaneous interventions</td>
<td>51</td>
</tr>
<tr>
<td>Balloon angioplasty</td>
<td>52</td>
</tr>
<tr>
<td>Stent placement</td>
<td>17</td>
</tr>
<tr>
<td>Residual collateral occlusion</td>
<td>12</td>
</tr>
<tr>
<td>Surgical RV-PA conduit replacement</td>
<td>3</td>
</tr>
</tbody>
</table>

Data are number or mean ± standard deviation. RV-PA: right ventricle-to-pulmonary artery.

Table 3 Characteristics of the patient.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td></td>
</tr>
<tr>
<td>Weight at birth (kg)</td>
<td>3.3</td>
</tr>
<tr>
<td>22q11 deletion</td>
<td>No</td>
</tr>
<tr>
<td>Nakata index (mm/m²)</td>
<td>25</td>
</tr>
<tr>
<td>SaO₂ (%)</td>
<td>80</td>
</tr>
<tr>
<td>Number of MAPCAs</td>
<td>3</td>
</tr>
<tr>
<td>Angiographic 'sea-gull'</td>
<td>Yes</td>
</tr>
<tr>
<td>Complete pulmonary artery distribution</td>
<td>Yes</td>
</tr>
<tr>
<td>Associated cardiac anomaly</td>
<td>Atrial septal defect</td>
</tr>
</tbody>
</table>

MAPCA: major aorto-pulmonary collateral artery; SaO₂: transcutaneous oxygen saturation.

Table 4 First catheterization and angiographic assessment.

<table>
<thead>
<tr>
<th>Diagnostic evaluation</th>
<th>Main PA: 'sea-gull’</th>
<th>RPA: 1.7 mm, probably complete distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>LPA: 2 mm, probably complete distribution</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Nakata index: 25 mm/m²</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>

MAPCAs

| Haemodynamic evaluation | —                     |

Interventional procedure

| —                  |

LPA: left pulmonary artery; MAPCA: major aorto-pulmonary collateral artery; PA: pulmonary artery; RPA: right pulmonary artery.
RV pressure then increased progressively to a systemic level, as the native PAs were still moderately hypoplastic; their growth was not as good as expected and echocardiography showed a left PA stenosis.

**Additional steps**

The fourth catheterization was performed 2.5 years after the second surgery (Table 7) (Fig. 4). The fifth catheterization was performed when the patient was eight years old, five years after the most recent catheterization (Table 8). The immediate results were reserved. Despite the angioplasties, a reduction in RV and distal PA pressure was not observed, most likely due to the consequences of this new aorto-pulmonary collateral.

Shortly afterwards, the sixth catheterization re-evaluated haemodynamics: the distal PA and RV/LV ratio pressures were decreased to 18 and 0.6, respectively. The Nakata index was 260 mm/m² (10 times the original!).

Follow-up was satisfactory, with a standard quality of life (normal schooling, normal physical activities). Exercise test and 24-hour Holter-electrocardiogram were normal. A cardiological follow-up was organized for each year; this should be combined with magnetic resonance imaging and another haemodynamic evaluation in the following years.

Fig. 5 summarizes the evolution of this patient, throughout his first decade.
Figure 4. Example of additional step in the rehabilitation of pulmonary artery procedure. A. Angioplasty and stenting of the right pulmonary artery. B. Angioplasty and stenting of the left pulmonary artery.

Figure 5. Retrospective view of the rehabilitation procedure in patients with extremely hypoplastic pulmonary artery, ventricular septal defect and major aorto-pulmonary collateral arteries: one reported case. KT: catheterization.
However, small patients imply a small RV-PA conduit, which means an early replacement. It is likely that the infundibulotomy requires to be extended towards the RV. Lofland [9], who reported a median weight of 3 kg at the time of surgery, forget to mention the size of the cryopreserved pulmonary allografts he used. We can guess that they were less than 16 mm, which raises the problem of long-term outcome and the issue of the accessibility of such allografts. Moreover, even if he argues that the late results are good, the length of follow-up was not specified in his study.

In a 14-year survival study, Carotti et al. [10] demonstrated that long-term outcomes were affected negatively by low body weight and positively by staged VSD.

In low-weight patients, some authors perform a central or a modified Blalock-Taussig shunt as a first approach, to promote antegrade pulmonary flow [11]. We think that establishment of the RV-PA continuity avoids the potential distortion of native PAs because of the shunt anastomosis, especially in severely hypoplastic native PAs.

### Discussion

The strategy of rehabilitation of the native PA in the management of patients with pulmonary atresia, VSD, hypoplastic PAs and MAPCAs is a demanding challenge. It requires constant and collaborative efforts of surgeons, interventionists, anesthesiologists, intensivists and referring cardiologists. A team strategy must be defined, thoroughly re-evaluated and followed for each of these difficult-to-treat patients. Fig. 6 summarizes this PA rehabilitation programme, exactly as it is managed in our team.

Moreover, support from the family is an important point in the management of such long-lasting care. That implies supplying good, clear and exhaustive information from the very beginning of the story. In these circumstances, it is possible to achieve good quality biventricular repair. This approach frequently avoids using collateral tissue to create the long-term pulmonary bed, thus avoiding questions about long-lasting value of this tissue [12]. We believe that, although only one of the multiple therapeutic protocols is possible for these patients, this strategy may offer good long-term results for patients who may otherwise never even reach the step of biventricular repair.

### Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

### References


Management of patients with pulmonary atresia


