Pulmonary endarterectomy: an alternative to circulatory arrest and deep hypothermia: mid-term results

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Abstract

Background: The current surgical technique for pulmonary endarterectomy (PEA) involves the use of deep hypothermia and circulatory arrest at 18°C (DHCA). Our experience started in 2004 when we decided to use an original alternative strategy which consists of avoiding deep hypothermia and subsequent circulatory arrest by using moderate hypothermia at 26°C, and maintaining a bloodless field. This can be achieved by means of negative pressure in the left heart chambers and appropriate pump flow modulation in order to maintain the mixed venous oxygen saturation (SVO2) higher than 65%. Materials and methods: From June 2004 to June 2007, 40 consecutive patients were operated on in our department with this strategy. The aim of this article is to report the early results for all patients and the complete six-month follow-up for 30 subjects who have reached this end-point at the time of writing. The mean temperature during extracorporeal circulation was 25.9°C; core temperature was lowered to 21°C in only one patient and an 8 min DHCA was performed in order to complete the PEA. Results: Two patients died (6.6%): one on the third postoperative day due to myocardial infarct, requiring an ECMO implantation. The other patient died from septic shock. The six-month follow-up, performed in all other patients, included clinical and hemodynamic evaluation. Pulmonary vascular resistance (PVR) decreased from 793.5 ± 284 dyn/cm/s to 286 ± 143 (p = 0.000). A comparable reduction of mean pulmonary arterial pressure and an increase of cardiac output were also observed. Conclusions: The results confirm that adequate removal of pulmonary artery obstructive lesions can also be achieved with an operative procedure that avoids or reduces the use of DHCA while allowing a bloodless field during PEA interventions. This technique may limit the well known adverse effects of DHCA due to organ hypoperfusion, improving the postoperative recovery of the patients.

Keywords: Pulmonary endarterectomy; Pulmonary hypertension; Pulmonary thromboemboli; Deep hypothermic circulatory arrest

1. Introduction

Pulmonary endarterectomy (PEA) is the treatment of choice in patients with chronic thromboembolic pulmonary hypertension (CTPH). In-hospital mortality of PEA, reported in the literature, varies from 5% to 24% [1] and mostly depends on the preoperative clinical status and the individual center experience. Five-year survival is markedly improved with PEA (75–80%) [2] if compared with the natural history of the disease or with other surgical approaches such as lung (44%) or heart and lung transplantation (41%) [2].

When the mean pulmonary artery pressure in patients with CTPH exceeds 50 mmHg, the 5-year mortality approaches 90% [3].

The aims of PEA are related to the right ventricular afterload reduction because of the removal of elastic pulmonary artery obstructive lesions due to organized thromboemboli.

Initial surgical experience adopting cardiopulmonary bypass pumps (CBP) was severely hampered by poor results due to the massive blood back-flow coming from the enlarged bronchial arterial circulation typical of CTEPH. At the beginning of the 80s, the San Diego group led by Daily et al. [4] adopted periods of deep hypothermia and circulatory arrest at 18°C (DHCA) when performing PEA, thus limiting the blood back-flow into the operative field. In the literature, the mean hypothermic arrest time was about 36 ± 11 min [5,6]. This important innovation led to increased beneficial effects of the operation and a progressive reduction in mortality, which ranged in the San Diego center from 17% in the 90s to 4.4% in the last 500 cases. Other groups reported a variable overall mortality of 10.9% [7] or 4.5–9.7% [8]. The results are conditioned by the learning curve in each
center as well as the preoperative clinical and hemodynamic conditions of patients. For example, preoperative pulmonary vascular resistance (PVR) is an important risk factor; Dartevelle et al. as well as other authors reported a 4% mortality when PVR is less than 900 dyn/cm/s⁻², 10% when PVR varies from 900 to 1200 dyn/cm/s⁻² and 20% when PVR is higher than 1200 dyn/cm/s⁻² [7,9].

Although DHCA has been widely applied in cardiac surgery since the beginning of the 70s, particularly in the surgery of the thoracic aorta [10], it involves many complications due to histochemical changes and organ hypoperfusion [11]. The use of DHCA has therefore been progressively abandoned for thoracic aorta surgery and replaced by other equally effective techniques [12,13].

Despite the fact that DHCA is still the strategy of choice for performing PEA in many surgical groups, some authors have searched for other alternative techniques [14—17]. The aim of the present study is to present our surgical experience in performing PEA with an original and alternative strategy which limits or prevents DHCA, using moderate hypothermia at 26 °C, while maintaining a bloodless field.

### 2. Materials and methods

From June 2004 to June 2007, 40 consecutive patients with CTEPH were operated on by PEA in our department. We considered only 30 consecutive patients treated up to December 2006, since we have a complete six-month follow-up for these 30 patients.

The annual distribution of the patients was as follows: 3 in 2004, 6 in 2005 and 21 in 2006.

The preoperative characteristics of the patients are described in Tables 1—4.

The purpose of our operating technique, already described [18], was to obtain a bloodless field with moderate hypothermia (26 °C) thanks to two principles:

- It is necessary to have negative pressure in the "left heart" in order to drain bronchial back bleeding. For this reason we place a 18 F Terumo 4334 cannula in the standard manner from the right upper pulmonary vein in the left ventricle. The cannula is connected to a reservoir (Dideco BT 844) inside which a negative pressure is created by the Baxter vacuum device [18]. At the beginning of our experience we also used another cannula placed in the left atrium through the left upper pulmonary vein, but this was abandoned as it was of no use. Another vacuum device has recently been added, placed on the venous return of the extracorporeal circulation and we pay attention to the cannulation of the superior vena cava to guarantee optimal azygos vein drainage.
- The cardiopulmonary bypass pump flow was adjusted to the lowest rate, able to maintain a mixed venous oxygen saturation, monitored on the CPB circuit and by a Swan-Ganz catheter in the superior vena cava. The mixed venous oxygen saturation (SVO₂) must be higher than 65%.

The extracorporeal circulation circuit is the traditional one used for this operation, with hypothermic circulatory arrest (HCA) (bicaval, aortic and pulmonary trunk cannulation).

#### 2.1. Intraoperative monitoring

Central venous pressure (CVP), peripheral oximetry and invasive systemic arterial pressure (ABP) are monitored as usual. A Swan-Ganz catheter is positioned in the pulmonary artery, and, in order to ensure continuous monitoring of cardiac output (CO) as well as volume, the PICCO system (Pulsion Medical Systems, Munich, Germany) is inserted through the left femoral artery.

Continuous CO₂ (capnometry) and transesophageal echocardiography (TEE) complete the monitoring.

#### 2.2. Surgical technique

After median sternotomy and systemic heparinization, the ascending aorta, bicaval veins and the pulmonary trunk are cannulated and the CPB is started. The left ventricle is drained through the right upper pulmonary vein. Cooling is started until 26 °C is reached, the aorta is cross-clamped and

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**Table 1**

<table>
<thead>
<tr>
<th>Preoperative profile</th>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Mean age (years)</td>
<td>61.6 (min 26—max 82)</td>
<td></td>
</tr>
<tr>
<td>M/F</td>
<td>12/18</td>
<td></td>
</tr>
<tr>
<td>NYHA III</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>NYHA IV</td>
<td>14</td>
<td></td>
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<tr>
<td>DVT</td>
<td>20</td>
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<tr>
<td>APA a</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>LAC b</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>Need for O₂ therapy</td>
<td>18</td>
<td></td>
</tr>
</tbody>
</table>

M/F: male/female; NYHA: New York Heart Association; DVT: prior history of pulmonary embolism and/or deep vein thrombosis.

a Antiphospholipid antibodies.

b Lupus anticoagulant.

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**Table 2**

<table>
<thead>
<tr>
<th>Preoperative hemodynamic data (mean values)</th>
<th>Mean ± SD (min—max)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PAP (mmHg)</td>
<td>48 ± 10 (min 28—max 70)</td>
</tr>
<tr>
<td>IC (l/min/m²)</td>
<td>2.3 ± 0.4 (min 1.2—max 3.6)</td>
</tr>
<tr>
<td>PVR (dyn/s⁻²)</td>
<td>791 ± 278 (min 360—max 1457)</td>
</tr>
<tr>
<td>RA (mmHg)</td>
<td>7.4 ± 3.6 (min 2—max 15)</td>
</tr>
<tr>
<td>TPG (mmHg)</td>
<td>39 ± 10.8 (min 8—max 60)</td>
</tr>
<tr>
<td>WEDGE (mmHg)</td>
<td>9.4 ± 3.4 (min 2—max 21)</td>
</tr>
<tr>
<td>RV EF</td>
<td>37 ± 7.5 (min 20—max 50)</td>
</tr>
</tbody>
</table>

PAP: pulmonary artery pressure (systolic (d); diastolic (m) mean; IC: cardiac index; PVR: pulmonary vascular resistance; RA: right atrium; TPG: transpulmonary gradient; RV EF: right ventricle ejection fraction; SD: standard deviation.

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**Table 3**

<table>
<thead>
<tr>
<th>Risk factors for PEA</th>
<th>Pt no.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Permanent central venous catheters</td>
<td>3</td>
</tr>
<tr>
<td>Tricupid valve prosthesis</td>
<td>1</td>
</tr>
<tr>
<td>PVR &gt; 1000 dyn/s⁻²</td>
<td>10</td>
</tr>
<tr>
<td>PAPs &gt; 100 mmHg</td>
<td>10</td>
</tr>
<tr>
<td>Unilateral lesion</td>
<td>2</td>
</tr>
<tr>
<td>No history of thromboembolic events</td>
<td>10</td>
</tr>
<tr>
<td>Heart failure</td>
<td>2</td>
</tr>
</tbody>
</table>
Cardiocirculatory arrest 1(8
Mean lowest temperature 25.9
Mean aortic cross-clamp time (min) 180.9
Mean CPB time (min) 280.7

CPB: cardiopulmonary bypass.

Table 4
Main perioperative parameters

<table>
<thead>
<tr>
<th>Main perioperative parameters</th>
<th>Mean ± SD (min–max)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean CPB time (min)</td>
<td>280.7 ± 67.1 (171–513)</td>
</tr>
<tr>
<td>Mean aortic cross-clamp time (min)</td>
<td>180.9 ± 40.3 (91–287)</td>
</tr>
<tr>
<td>Mean lowest temperature</td>
<td>25.9 ± 1.2 (21–28)</td>
</tr>
<tr>
<td>Cardiocirculatory arrest</td>
<td>1(8 a 21 °C)</td>
</tr>
</tbody>
</table>

The cannulas are removed and protamine is administered.

cold crystalloid cardioplegia (Custodial — Dr Koehler GMBH Chemie-Alabsbach-Haehlein) is administered. The cardioplegia administration is repeated after the endarterectomy of the right pulmonary branch (usually requiring about 90–100 min). A right pulmonary artery longitudinal arteriotomy is performed and the operation starts. It is very important to identify the cleavage plane with a part of the medial layer (Fig. 1). In the event of a severely compromised Boyden branch or, if the preoperative CT scan showed a significant bronchial artery hyperplasia, we believe that it is better to clean the Boyden branch last. This is because the right superior pulmonary lobe is higher than the left atrium, so when the Boyden artery is reopened, an extensive retrograde blood flow would impair the operative field and visualization of the distal vessels would then become more difficult.

The core temperature usually reaches 26 °C but in some cases [12] 27 °C or 28 °C may be sufficient (median 26 °C). When the back bleeding is severe, the pump flow can be reduced, maintaining a central venous saturation of about 65% to facilitate the visualization of the more distal vessels.

PEA was considered successfully and radically performed in all patients, by using the above technique, except in one case (1/30) in which the core temperature was lowered to 21 °C and an 8 min circulatory arrest was performed in order to complete the PEA.

Before CPB is stopped, 60 min of myocardial and lung reperfusion is performed with low pulmonary pressure (8–10 mmHg) to limit reperfusion injury. Protective ventilation is also adopted (VC = 8–10 ml/kg, Fi O₂ 50%, PEEP + 4 cmH₂O).

The cannulas are removed and protamine is administered.

2.3. Statistical analysis

The software SPSS for Windows was used for statistical analysis (SPSS 8.0 for Windows, SPSS Inc., Chicago, IL). Continuous data are expressed as mean and standard deviation while categorical data are expressed as total plus frequency. Preoperative and follow-up hemodynamic data were analyzed using Student’s t-test.

3. Results

Two patients died: one on the third postoperative day due to myocardial infarction and despite an ECMO implantation. The other patient died from septic shock on the sixth day.

3.1. Morbidity

Rethoracotomy was performed in two patients because of bleeding. In one case, massive bleeding came from a pulmonary artery lesion complicated by a significant hypotensive episode and cardiac arrest. In this case, we temporarily used an ECMO procedure.

There were two pulmonary infections. In one case we temporarily used an ECMO for respiratory failure.

We believe that in patients undergoing PEA, a femoro-femoral cannulation (Biomedicus percutaneous kit venous and arterial femoral — Medtronic Inc. MN) with centrifugal device (Jostra Rotaflow Pump Maquet Cardiopulmonary AG Hirrlingen Germany) and oxygenator (Quadrox Jostra D — Maquet Cardiopulmonary AG) is preferable [19,20]. With this configuration, the right heart preload is very well controlled. Despite the increase of systemic vascular resistance, left ventricle diastolic dysfunction, usually present in this type of disease, tends to improve with this ECMO configuration, training the left ventricle to a progressive and slow increase of diastolic filling. Extubation of the patient may also be achieved as well as normal oral feeding.

It was possible to wean the two patients from the ECMO on the 12th and 20th postoperative days, respectively.

Mean postoperative ventilation time was 38 h (SD 38.2) with a median of 25 h.

Platelet transfusion was not necessary during the postoperative period, except in the two patients who were reoperated for bleeding.

We usually keep the patients in the intensive care unit (ICU) for around 5–6 days after the operation, even in the absence of complications. The mean time of ICU stay was therefore not evaluated.

3.2. Follow-up

All 28 surviving patients were reassessed after an average of 7 ± 2 months by clinical evaluation, 6-min walk test and right heart catheterization.

All patients were in NYHA functional classes I (16) or II (12). The 6-min walk distance improved from 371.1 ± 108.9 before PEA to 483.0 ± 114.1 at follow-up (p = 0.01) (Fig. 2). Fig. 3a and b shows the reduction of mean pulmonary arterial pressure and pulmonary vascular resistance from baseline (before surgery) to the immediate postoperative period and

Fig. 1. Histological images of surgical samples: a different degree of medial layer thickness is present. (By courtesy of Ornella Leone, Institute of Pathology, S. Orsola Hospital, Bologna).
to the follow-up assessment: both parameters are clearly reduced in all patients.

4. Discussion

The results of the present study confirm that an adequate removal of pulmonary artery obstructive lesions (Fig. 4) and excellent mid-term clinical, functional and hemodynamic results can be achieved in CTEPH patients adopting a new strategy for PEA interventions. This technique made it possible to avoid DHCA use in all but one case.

The limitations related to DHCA have recently led some authors to look for alternatives, such as those proposed by Masuda and Macchiarini [15—17]. None of these solutions ensure the perfusion of the bronchial vascular tree, causing lung ischemia, particularly with Macchiarini’s technique in which the core temperature is maintained at 28—32 °C without any hypothermic protection [17].

Great improvements have recently been achieved in the field of CPB technology, such as the development of devices, which improve the venous drainage with negative pressures. These devices, designed to allow cardiopulmonary bypass even with small cannulas (usually applied in minimally invasive surgery such as Heart-Port), ensure optimal venous drainage. We have taken advantage of these techniques [18], which were adopted in our PEA procedures for systemic venous as well as for pulmonary venous drainage, thus achieving a completely bloodless field. In addition, pump flow was modulated and modified according to temperature and, most of all, according to mixed venous O₂ saturations.

It is also important to note that the following aspects are relevant in order to obtain the best result by applying our technique: proper positioning of the left ventricular suction, through the mitral valve, correct superior vena cava drainage by using large size cannulas (30—32 Fr) and careful CPB management, maintaining negative central venous pressure.

Another advantage of our approach is related to the possibility of reverting to DHCA, when needed, in cases with considerable blood back-flow. In fact, it is possible to lower core temperature and perform systemic arrest as we did in one case (8 min of circulatory arrest at 21 °C).

Regarding in-hospital mortality (6.6%), two patients died: the first one was a 77-year-old man, who underwent emergency surgery due to respiratory distress and cardiac insufficiency, and thus without previous coronary angiography. Weaning from CPB was not possible and ECMO was started. The patient died on the third postoperative day because of heart rupture. The second patient was a 55-year-old female, who presented respiratory insufficiency and septic status on the third postoperative day, in spite of the large spectrum antibiotic treatment we always use in these patients, which consists of Vancomicine, Ceftazidine and Levofloxacine. The patient worsened, she developed septic shock and then died on the sixth postoperative day.
5. Conclusions

DHCA is the technique that has made PEA feasible and widely used in many centers. However, recent technological advances (the use of vacuum by new cannulas and continuous monitoring of mixed venous oxygen saturation) have opened new possibilities for the application of CPB, allowing novel surgical approaches. We have adopted these new technologies in order to limit the use of DHCA and maintain a bloodless field for PEA interventions. The excellent clinical, functional and hemodynamic short- and mid-term results reported in this study confirm that the proposed strategy is feasible and effective.

References