Long-term results after thromboendarterectomy for chronic pulmonary embolism

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Abstract

Objective: In patients with chronic thromboembolic pulmonary hypertension, pulmonary vascular resistance (PVR) can be reduced by pulmonary thromboendarterectomy (PTE). In this study, long-term symptomatic and hemodynamic effects were investigated. Methods: Twenty-two patients (12 female, 10 male, mean age 40 years, preoperative NYHA functional class II/III/IV: n = 1/12/9) were re-evaluated 48–72 months (mean 60 months) after surgery. In addition to clinical assessment, radiologic, hemodynamic and echocardiographic investigations were performed. Results: All patients reported a marked improvement of their clinical condition. At follow-up, 11 patients were identified as NYHA class I, 10 as NYHA class II and one patient was in class III. PVR and mean pulmonary artery pressure (mPAP) were significantly reduced (preoperative PVR 800–274 dynes/s per cm⁻⁵, follow-up PVR 180–28.3 dynes/s per cm⁻⁵; P < 0.001; preoperative mPAP 48.5–7.4 mmHg, follow-up mPAP 27.5–4.9 mmHg; P < 0.001). There was also a significant increase in arterial blood oxygen tension (preoperative PaO₂ 59–10 mmHg; follow-up PaO₂ 84–12 mmHg; P < 0.001). Chest roentgenograms and echocardiographic examinations revealed significantly decreased right heart dimensions and a recovery of right heart function. Conclusion: In patients with severe chronic thromboembolic pulmonary hypertension, persistent symptomatic and hemodynamic improvements can be achieved by PTE. © 1999 Elsevier Science B.V. All rights reserved.

Keywords: Pulmonary thromboendarterectomy; Chronic pulmonary embolism

I. Introduction

Chronic thromboembolic pulmonary hypertension induces right heart hypertrophy, right heart dilatation and right ventricular failure by the time. Pulmonary thromboendarterectomy (PTE) is an effective surgical procedure for an acute and significant reduction of pulmonary artery pressure and pulmonary vascular resistance. The reduction of right ventricular afterload results in a decrease of right heart dimensions and functional improvement immediately after surgery [1–5]. Long-term experience after PTE is scarce [1,4,6].

In this study, patients were re-evaluated 48–72 months after PTE to examine, if the significant reduction of mean pulmonary artery pressure (mPAP), pulmonary vascular resistance (PVR) and the improvement of right ventricular function are maintained on a long-term basis.

2. Materials and methods

Between June 1989 and June 1998, 160 PTE operations have been performed at our institution. From June 1989 to June 1992, 54 patients were treated by PTE. Twelve patients deceased perioperatively. Two patients died within 2 years after the operation, one due to right heart failure waiting for lung-transplantation and one due to sepsis. From the 40 long-term survivors, 10 patients were re-investigated at other institutions with good clinical results and five patients declined to have a reassessment, because they were completely asymptomatic. Three patients were lost to follow-up.
Twenty-two patients (12 women, 10 men, mean age 40 years, range 19–69 years) were reassessed at our institution 48–72 months (mean 60 months) after surgery.

2.1. Preoperative patient data

Preoperatively, nine patients were in NYHA functional class IV, 12 patients were in class III and one patient was in class II. Mean pulmonary artery pressure was elevated to 48.5 ± 7.4 mmHg. Cardiac index was reduced to 1.9 ± 0.7 l/min per m². Mean pulmonary vascular resistance was calculated as 800 ± 274 dyne/s per cm⁻². Coagulation abnormalities were found in nine patients: antithrombin III deficiency (n = 2), protein C deficiency (n = 2), Lupus anticoagulant (n = 1) and APC resistance (n = 4). Six patients presented a history of venous thrombosis, two in the upper and four in the lower extremities.

There were no differences in preoperative data between long-term survivors and the non-survivors (Table 1).

2.2. Operation

All patients were operated using a standardized technique [1,6,7] with extracorporeal circulation and periods of circulatory arrest in deep hypothermia. Additional cardiac procedures included: tricuspid annuloplasty in 12 patients, closure of atrial septal defect or persistent foramen ovale in three patients and coronary artery bypass operation in one patient.

2.3. Long-term treatment

An inferior vena cava filter (LGM; FA Braun, Melsungen, Germany) was placed in three patients before and in 14 patients after surgery. All patients were anticoagulated with phenprocoumon (Marcumar®) to an international normalized ratio (INR) from 2.5 to 3.5.

Table 1
Preoperative, operative and early postoperative data of long-term survivors in comparison with non-survivors

<table>
<thead>
<tr>
<th></th>
<th>Long-term survivors</th>
<th>Non-survivors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age/ range (years)</td>
<td>40/19–69</td>
<td>44/21–63</td>
</tr>
<tr>
<td>History of symptoms (months)</td>
<td>27 ± 19</td>
<td>35 ± 21</td>
</tr>
<tr>
<td>Pre-OP NYHA functional class I / II / III / IV (n)</td>
<td>0/1/12/9</td>
<td>0/1/6/7</td>
</tr>
<tr>
<td>mPAP (mmHg)</td>
<td>48.5 ± 7.4</td>
<td>53.1 ± 14.3</td>
</tr>
<tr>
<td>Cardiac index (l/min/m²)</td>
<td>1.9 ± 0.7</td>
<td>2.0 ± 0.7</td>
</tr>
<tr>
<td>PVR (dyne/s per cm⁻²)</td>
<td>800 ± 274</td>
<td>1105 ± 478</td>
</tr>
<tr>
<td>Total operation time (min)</td>
<td>337 ± 82</td>
<td>400 ± 95</td>
</tr>
<tr>
<td>ECR bypass time (min)</td>
<td>236 ± 63</td>
<td>286 ± 76</td>
</tr>
<tr>
<td>Ischemia time (min)</td>
<td>113 ± 46</td>
<td>136 ± 57</td>
</tr>
<tr>
<td>Circulatory arrest time (min)</td>
<td>48 ± 20</td>
<td>61 ± 24</td>
</tr>
<tr>
<td>mPAP, 6 h post-op (mmHg)</td>
<td>32.5 ± 7.0</td>
<td>48.7 ± 15.7</td>
</tr>
<tr>
<td>Cardiac index, 6 h post-op (l/min per m²)</td>
<td>2.7 ± 1.1</td>
<td>2.6 ± 0.9</td>
</tr>
</tbody>
</table>

2.4. Reassessment

All 22 patients were clinically examined and their NYHA functional class was determined. Arterial blood gas analyses at rest under room-air conditions were obtained in all patients. Chest radiographs in the anteroposterior and lateral view were performed. Further investigations included high resolution computed tomography (n = 18), right heart catheterization (n = 20) and echocardiography (n = 22). The inferior vena cava filter was controlled by roentgenograms of the lumbar spine and angiography of inferior vena cava. These results were compared with preoperative data.

Using contrast high resolution computed tomography (FA Picker; Systems PQ5000 or PQ6000), pulmonary parenchymal and pulmonary artery morphology were depicted to avoid the invasive angiographic investigation [8,9].

Right atrial pressure, pulmonary artery pressure, wedge pressure and cardiac output were measured, using a Swan-Ganz thermodilution catheter. PVR and cardiac index were calculated.

Thoracostic echocardiographic examination (FA Hewlett-Packard; Andover, MA, Systems Sonos 2500 or Sonos 5500) was performed to quantify end-systolic and end-diastolic right ventricular areas from an apical four-chamber view by planimetry.

2.5. Statistics

Values are expressed as mean ± standard deviation. Paired t-test statistical analysis was applied to compare preoperative data with follow-up results. P-Values less than 0.05 were considered statistically significant.

3. Results

3.1. Clinical examination

At the time of re-investigation, all patients reported a functional improvement. Eleven patients were identified as NYHA class I, 10 as NYHA class II and one patient, preoperatively in NYHA class IV, was staged NYHA class III, but had been able to return to an appropriate level of activity (Fig. 1).

Mean arterial oxygen tension significantly increased from 59 ± 10 mmHg preoperatively to 84 ± 12 mmHg (P < 0.001).

3.2. Radiology

The marked reduction of heart dimensions is illustrated in the chest radiographs (Fig. 2). Computed tomography demonstrates reopening and improved perfusion of the pulmonary vessels and segmental branches (Fig. 3) and a reduction of right heart dimensions concomitant to the decreased right ventricular afterload. One patient in
NYHA stage III had partial reocclusion of major pulmonary vessels in both upper and in the right lower lobe and also a dilated right ventricle with leftward dislocation of the interventricular septum, similar to preoperative investigations. All implanted vena cava filters were in place and free of thrombotic material.

3.3. Hemodynamic indices

In correlation with the symptomatic improvements the mPAP was significantly decreased from preoperatively 48.5 ± 7.4 to 27.5 ± 4.9 mmHg (P < 0.001). In addition the cardiac index was significantly increased from 1.9 ± 0.7 to 3.9 ± 1.5 l/min per m² (P < 0.001), PVR was significantly reduced from 800 ± 274 to 180 ± 28.3 dynes/s per cm⁻⁵ (P < 0.001). The patient in NYHA class III had an elevated PVR of 600 dynes/s per cm⁻⁵ (1100 dynes/s per cm⁻⁵, preoperatively; 302 dynes/s per cm⁻⁵, early postoperatively).

3.4. Echocardiography

Mean end-systolic and end-diastolic right ventricular areas were significantly decreased. The end-systolic right ventricular area was reduced from 24.9 ± 5.6 to 15.9 ± 3.7 cm² (P < 0.001). Right ventricular end-diastolic area value was 31.5 ± 6.5 cm² preoperatively and 22.9 ± 4.5 cm² at follow-up (P < 0.001). The end-systolic right ventricular area decreased more than the end-diastolic area, demonstrating an improved right ventricular contractility (Fig. 4). Preoperatively, 19 of the 22 reassessed patients had tricuspid valve incompetence. Twelve of them received tricuspid valve annuloplasty. No patient had valvular insufficiency at the time of follow-up.
4. Discussion

PTE is an effective surgical treatment for acute reduction of PVR in patients with chronic thromboembolic pulmonary hypertension [1,6,10–12].

In the first reported series of patients, the perioperative mortality rate particularly in patients with severe pulmonary hypertension was rather high [1,10]. Reasons for early death were respiratory failure by pulmonary reperfusion edema, persistent pulmonary hypertension with right heart failure in case of insufficient thromboendarterectomy or both. After refinements in operative technique, early reports from the University of California in San Diego showed marked improvements in outcome and clinical symptoms in operated patients [7,12,13].

At our institution, the early mortality rate in 54 patients operated on between June 1989 and June 1992 was 22.2% (12/54). Multiple changes in operative and postoperative management have been implemented and with increasing surgical experience, significant improvements could be achieved. The perioperative mortality rate could be reduced to an acceptable level, currently below 7%, similar to the results in San Diego. These good results were persistent in mid-term follow-up studies, performed 2–4 years after surgery [14,15].

However, there is little information on long-term effects of this surgical procedure.

Late survival in patients with chronic pulmonary embolism is dependent on the mean pulmonary artery pressure representing the degree of pulmonary vessel obstruction [16]. Medical therapy using anticoagulants, thrombolytic agents or vasodilators is not effective in this entity [3,17]. Elevation of mPAP above 50 mmHg reduces the 5 year survival rate in these patients to less than 10%. All patients in our study-group had such severe pulmonary hypertension with a mean pulmonary artery pressure of 48.5 ± 7.5 mmHg, preoperatively.

In our study, all long-term survivors reported marked symptomatic improvements at the time of reassessment, after a mean follow-up time of 5 years after PTE.

Only one patient in NYHA functional class III, preoperatively class IV, had partial pulmonary reocclusion, demonstrated in high resolution (HR) computed tomography. In correlation, hemodynamic and echocardiographic indices in this patient were worse compared with early postoperative examinations of this patient. The reason could be inadequate anticoagulant therapy, although this patient had no coagulation disorder as risk-factor for thromboembolic events.

Coagulation abnormalities were found in almost 30% of our patients. None of these patients had recurrent pulmonary embolism within the follow-up period. So, life-long strict anticoagulant therapy seems to be effective. The implantation of an inferior vena cava filter in patients with history of deep veinous thrombosis might have provided additional safety.

At follow-up, all patients had an improved arterial oxygen tension. None of them required oxygen therapy after the operation. An improved lung parenchymal perfusion after restoration of pulmonary artery blood flow, visualized by Fig. 3. High resolution CT: preoperative typical thromboembolic lesions, beginning in the major pulmonary vessels (A) and restoration of pulmonary artery blood flow at follow-up (B).

![Fig. 3.](image)

Fig. 3. High resolution CT: preoperative typical thromboembolic lesions, beginning in the major pulmonary vessels (A) and restoration of pulmonary artery blood flow at follow-up (B).

![Fig. 4.](image)

Fig. 4. Significant reduction of right heart dimensions demonstrated by transthoracic echocardiography.
HR computed tomography [8,9], is considered as the reason for better oxygenation. The concomitant relief of right ventricular pressure overload leads to a reduction of right heart dimensions, recovery of right ventricular function and increased left ventricular pre-load. Subsequently, normalization of left ventricular geometry and diastolic function is induced and an improved cardiac index can be documented [2,18,19].

Correlating hemodynamic indices, mPAP and PVR were also significantly and persistently reduced. At the time of follow-up, mPAP was reduced to 27.5 ± 4.9 mmHg, anticipating an improved long-term survival [16].

The only therapeutic alternative to PTE, isolated lung or heart-lung transplantation, reveals limited mid-term results with a 3 year survival rate of 60%, due to the development of obliterative bronchiolitis (International Lung Transplant Registry, Suite 3107 Queeny Tower, One Barnes Hospital Plaza, St. Louis, MO). The long-term outcome is unknown [20,21]. Patients treated by PTE revealed a marked symptomatic improvement immediately after surgery, after a mid-term follow-up period and reported sustained improved condition in long-term follow-up 4–6 years after surgery. Therefore, transplantation is only indicated in patients with chronic thromboembolic pulmonary hypertension, when exclusively distant pulmonary artery obstructions are not considered to be surgically accessible.

We conclude that pulmonary thromboendarterectomy is the best therapeutic procedure in selected patients with thromboembolic pulmonary hypertension to achieve an improvement of clinical symptoms. This benefit is persistent on a long-term basis. The results suggest that a longer life expectancy can be anticipated in these patients.

References


Appendix A. Conference discussion

Dr H. Borst (Munich, Germany): I find this a rather amazing series in terms of numbers and also results. Of course your group has been doing this kind of surgery for quite a few years now and I would be very curious whether you have made any principal innovative changes in your technique. Are you still doing it the way you did it originally or are you doing the operations now quite differently?

Dr Kramm: No. Many changes in operative and postoperative management have been implemented since January 1995. In the first years we had a rather high preoperative mortality rate, more than 22%. And after these changes, we implemented and we perform now the endarterectomy in complete circulatory arrest and deep hypothermia of 18 degrees and we prefer the central access to the pulmonary vessels, and also with changes in...
the intensive care management, we could reduce our mortality rate to less than 7%. The operative changes are the main changes in the procedure.

_**Dr Borst:** How about the radicality? Are you going further out now with thromboendarterectomy or are you more conservative now?

_**Dr Kramm:** I think sometimes we are perhaps not radical enough, because we learned that a successful reduction of mean pulmonary artery pressure is the most important result of this operation. Even when you don’t get each scar removed from the vessel, when you reach a significant reduction of pulmonary artery pressure, the outcome or the late survival rate in these patients will be improved and the clinical symptoms will be improved.

_**Dr U. von Oppell (Cape Town, South Africa):** One of the factors that influence long-term outcome is recurrent pulmonary embolism. You only had 17 patients in the study group who had an IVC filter. Do you advise routine insertion of a Greenfield or other IVC filter in these patients prior to or after a thromboendarterectomy?

_**Dr Kramm:** We implant LGM filters and we prefer to implant them when you have diagnosed deep venous thrombosis in the lower extremity. And when in older patients there is an additional risk factor for thromboembolic events like APC resistance, for example, then we implant an inferior vena cava filter. In younger patients who can perform the INR self-control and who have no history of deep venous thrombosis but history of thrombosis from other sources, we don’t implant an inferior vena cava filter.

_**Dr von Oppell:** So those patients are kept on life-long anticoagulation?

_**Dr Kramm:** Yes, this is the most important point to prevent reoccurrence of pulmonary embolism.

_**Dr R. Przybylski (Zabrze, Poland):** I would like to ask you about your experience with nitric oxide, because we started using nitric oxide in this group of patients, but results are bad, they are not so good as we expected.

_**Dr Kramm:** We used nitric oxide a few years ago, but we have seen that successful surgery is the means to reduce the pulmonary artery pressures. Everything else is only an additional help perhaps, but in a long-term view it is not the point. The point is a successful surgery. And with our increasing surgical experience, we don’t need nitric oxide at the time and we don’t need any other substance like intravenous or inhalative prostacycline.

_**Dr W Harringer (Hannover, Germany):** You have mentioned that you have implemented a few changes. What will you be interested in are the specific changes in your postoperative intensive care unit protocol, because we do see quite an amount of reperfusion injury in these patients.

_**Dr Kramm:** All patients are hyperventilated with high-flow and low-pressure ventilation. We hold a PEEP of 6 mmHg, and the aim is to get a blood pH of 7.50. Also, in addition, we prefer a catecholamine regimen where we give arterenol to keep the mean systemic arterial pressure at a level of about 80 mmHg, and we reduce our adrenaline doses to keep the cardiac index low, below 3 l/min per m². With this lowered cardiac output, we don’t see any, or very seldom, reperfusion edema. The alkalosis in the blood reduces the pulmonary vascular resistance and the low cardiac output is the second point to avoid reperfusion edema, and with a high mean systemic arterial pressure, you have always the chance for high dose application of diuretic drugs. And we give all patients fresh frozen plasma to keep the protein concentration in the serum high.

_**Dr F. Casselman (Cleveland, OH, USA):** I have a question regarding the technique. Do you routinely expose both sides and do an endarterectomy on both sides, because we found that on the pulmonary angiography you don’t always see particularly a peripheral emboli, and therefore we found it very useful to do intravascular ultrasound. I wonder whether you use any intravascular ultrasound.

_**Dr Kramm:** We always perform the endarterectomy on both sides, because in our diagnostics it is important that the thromboembolic lesions begin in the central pulmonary vessels and you always have thromboembolic lesions on both sides normally. When you have only peripheral lesions, these patients won’t undergo surgery, because in our experience with peripheral lesions, the operation is not as successful as you would wish, and mostly 2–3 years after this operation the patients have to be listed for transplantation.

_**Dr U. Althaus (Bern, Switzerland):** Dr. Kramm, in addition to the question of Dr. Casselman, I would like to ask you if you sometimes use pulmonary angioscopy for more accurately identifying the surgical accessibility of the lesions? As you certainly know, in San Diego, California, this preoperative investigation is frequently performed in order to visualize the most proximal location of the disease.

_**Dr Kramm:** No, we don’t perform angioscopy because we use for the last 2 years magnetic resonance tomography. It is possible to visualize the lesions and the membranes very sufficiently by using MRT. So we don’t need any angioscopy.

_**Dr Althaus:** What is your attitude towards the concomitant tricuspid annuloplasty? As you know, some authors do not recommend this procedure in view of the excellent recovery in right ventricular geometry following pulmonary thromboendarterectomy.

_**Dr Kramm:** In the first years, nearly every patient received tricuspid valve reconstruction, and we have learned that it is not necessary. The reduction of right heart volumes is enough to reach competent valvular closure. In our actual series, none of our patients received tricuspid valve reconstruction even if there was high-grade insufficiency preoperatively. I unfortunately have no slide, but recovery of valvular competence is significant and we don’t need valve reconstruction.