Technical advances of pulmonary thromboendarterectomy for chronic thromboembolic pulmonary hypertension

Christian Hagla, Nawid Khaladj, Tina Peters, Marius M. Hoeper, Frank Logemann, Axel Haverich, Paolo Macchiarini

Abstract

Objective: To minimize the side-effects of circulatory arrest times and profound hypothermia in patients undergoing pulmonary thromboendarterectomy (PTE) for chronic thromboembolic pulmonary hypertension (CTEPH). Methods: Between March 2000 and June 2002, 30 patients (in New York Heart Association (NYHA) class III or IV) were operated for CTEPH using our modified technique. It includes moderate hypothermic (28–32°C), total cardiopulmonary bypass (CPB) and simultaneous selective antegrade cerebral perfusion and occlusion of the bronchial arteries by introducing an occlusive balloon catheter into the descending aorta. The preoperative pulmonary vascular resistance in the cohort was 873 ± 248 dynes/s/cm². Results: Mean total CPB, cross-clamp times and duration of anterograde cerebral perfusion were 132 ± 40, 98 ± 21 and 21 ± 10 min, respectively. Mean core temperature 29.5 ± 1.9°C. The duration of postoperative mechanical ventilatory support was 34 ± 44 h and the mean stay in the ICU was 5 ± 9 days. Seven patients had mild to moderate lung reperfusion injury, one transient neurological dysfunction. Three patients (10%) died during their hospital stay, two for multiorgan failure and one for persistent pulmonary hypertension. All patients had a significant pulmonary hemodynamic improvement and all achieved NYHA class I (P < 0.01) status 4 weeks after discharge, remaining stable at a median follow-up time of 16 months (range, 1–29 months) postoperatively. Conclusions: These technical advances improve neurological outcome, control back-bleeding from bronchial arteries and avoid prolonged rewarming phases in patients undergoing PTE.

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1. Introduction

Chronic thromboembolic pulmonary hypertension (CTEPH) usually results from incomplete lysis of large organized thrombus in the main pulmonary artery and secondary branches, leading to obliterative pulmonary hypertension, disabling right ventricular failure and subsequent death due to heart failure. By removing the organized thromboembolic material, pulmonary thromboendarterectomy (PTE) can be lifesaving by reducing pulmonary hypertension, improving right ventricular function and well-being in properly selected patients. The surgical technique of PTE for CTEPH has evolved over the past 5–10 years but is currently performed only in selected medical centers [1–5]. Basically, the technique involves a median sternotomy, total cardiopulmonary bypass, deep hypothermia and intermittent periods of hypothermic circulatory arrest (HCA). To minimize the sequelae of circulatory arrest times and profound hypothermia, we developed some technical modifications of the originally described PTE and present our early results.

2. Materials and methods

Between March 2000 and June 2002, 30 consecutive
patients underwent PTE at the Hannover Medical School. Their mean age was 58 ± 13 years. Fourteen were females and 16 males. Overall, the diagnosis of CTEPH was made 41 ± 22 months before surgery, and hemodynamic or ventilatory deterioration of exercise capacity occurred 8 ± 3 months before surgery. Preoperatively, all patients were in New York Heart Association (NYHA) functional class III (n = 21) or IV (n = 9). Three patients had a patent foramen ovale and one, impaired kidney function. All but one had a history of deep venous thrombosis and 15 patients had some coagulation disorders.

2.1. Preoperative evaluation

Preoperatively, all patients underwent transthoracic echocardiography and contrast echocardiography to determine a patent foramen ovale, radioisotopic ventilation–perfusion scanning and helical computed tomography (CT) scanning. CT scans were evaluated for the presence of occluded or stenosed pulmonary vessels, definition of atheromatous debris in the aortic arch and descending aorta and origin and number of major bronchial arteries. Biplane pulmonary angiography was made to establish whether thromboembolic obstruction was present, to determine its location and extension and to calculate the number of the involved segmental vessels. Right heart catheterizations with measure of the right atrial, pulmonary artery and pulmonary wedge pressures were made routinely. Cardiac output (CO) was determined by thermodilution and pulmonary vascular resistance was calculated. Other non-invasive examinations included duplex scanning of both, lower and upper extremities, blood gas analysis to detect partial or severe hypoxia and pulmonary functional testing. Absolute surgical contraindications were severe underlying obstructive or restrictive lung disease, renal failure requiring dialysis and malignancy or other end-stage non-cardiac diseases. Coronary angiography was performed in all patients with risks of coronary atherosclerotic disease. All patients with a clearly defined source of emboli arising from the deep leg veins received inferior cava filter before surgery. For screening purposes, completing studies for platelet count, prothrombin time, partial thromboplastin time, fibrinogen, protein C, protein S, antithrombin III, homocysteine, factor V (Leiden) mutation, prothrombin mutation and antiphospholipid antibody were routinely performed.

2.2. Anesthesiological management

It includes pressure lines in both radial arteries as well as in one femoral artery. A Swan–Ganz thermodilution catheter is introduced via the right jugular vein and bilateral cerebral oxygen saturation (INVOS®, Cerebral Oximeter, Somanetics, Troy, MI, USA) as well as an electroencephalograph (EEG) is measured online. During surgery, artificial ventilation is performed with low tidal volume without positive endexpiratory pressure using a standard tracheal tube. Before CPB, a central venous pressure adjusted (high) volume infusion therapy is started. After CPB, a volume restriction is obligatory. During surgery, the head is packed in ice to achieve topical cooling. Additionally potentially neuroprotective drugs such as thiopentane and cortisol are added into the heart lung machine.

2.3. Surgical technique

All patients were basically operated using the technical recommendations described by other authors [2,6,7] with a few modifications. After median sternotomy and pericardiectomy, the following structures were stepwise dissected on the right: (i) superior vena cava (SVC) up to the innominate vein, (ii) proximal azygos vein, (iii) right pulmonary artery retrocavally and in the Thiele sinus and (iv) proximal Boyden artery to allow its clamping. On the left, the ascending aorta is separated from the pulmonary artery trunk, the ligamentum arteriosus is divided and the left intrapericardial pulmonary artery is mobilized up to its upper lobe branches. Umbilical tapes are passed around the azygos vein, pulmonary artery trunk and retroaortic right pulmonary artery for occlusion during the endarterectomy procedures.

Following systemic heparinisation (300 U/kg), cardiopulmonary bypass (CPB) is established via the ascending aorta and both caval veins, care being taken to place the SVC cannula right at the convergence of the innominate vein. Cooling is performed to reach a core temperature of 28–32°C as manifested by bladder and nasopharyngeal temperature. In the interim, a 22 F aortic occlusion balloon catheter (Edwards®, Booldingbrook, IL, USA) is introduced into the ascending aorta close to the inflow cannula and directed into the descending aorta beyond the left subclavian artery to reach the level of the previously CT established takeoff of the bronchial artery(ies) (Fig. 1); inflation of the balloon under control of the radial and femoral arterial pressure curves bilaterally proves the correct location. After induction of ventricular fibrillation, a 18 mm sump tube is inserted through the right upper lobe vein and directed into the left ventricle to minimize its distension and to further decrease the excessive bronchial artery flow. The aorta is then cross-clamped and cold cardioplegia is administered in the aortic root with additional doses being given every 20 min to allow optimal protection of the heart.

After being on total CPB, any preoperative known patent foramen ovale is traditionally closed. The SVC is then fully transected (after retraction of the Swan–Ganz catheter) [7] and using head light and angiography [2], the endarterectomy is then made in the usual fashion starting generally on the right side. The standard procedure is modified as follows: (1) the Boyden artery on the right side is cross-clamped with a bull-dog and its endarterectomy is made at the end to avoid significant back-bleeding and blood spillage into the distal
part of the right pulmonary artery branches during their endarterectomy (Fig. 2); (2) as soon as the intravascular dissection is disturbed with back-bleeding from the bronchial arteries, the aortic occlusive balloon is inflated and the flow in the aortic cannula reduced to maintain a perfusion pressure of 50–60 mmHg in the right radial artery. If oxygen saturation decreases, arterial pressure is adjusted or vasoactive drugs (e.g. dehydrobenzperidole or papverine) to avoid cerebral vessel spasm are administered; (3) on the left side, the proximal left pulmonary artery is completely transected from the pulmonary trunk (Fig. 3) and an endarterectomy is started in the usual fashion; holding the left lung hyperinflated during the endarterectomy facilitates deobstruction especially of the lower lobe branches. An end-to-end anastomosis reestablishes the continuity thereafter (Fig. 4). The procedure is finished by conventional deairing, clamping the ascending aorta and rewarming and weaning the patients from CPB.

2.4. Postoperative management

All patients are placed on volume-controlled mechanical ventilation during the early postoperative period with a PEEP level of 6–8 and a tidal volume of 10 ml/kg body weight. Inhaled nitric oxide at doses of 15–20 ppm are routinely given for the first 4 h postoperatively and gradually withdrawn. The postoperative cardiac index is held as preoperative and a positive endexpiratory pressure of 8–10 is set. Low-dose inotropic support (e.g. dobutamine or epinephrine) is usually necessary in the majority of patients. Continuous intravenous heparin is given as soon as the patient has stabilized and bleeding from the chest tubes is minimal. Oral coumadin therapy usually starts after 48–72 h with a target international normalized ratio (INR) of 2.5–3.5.

2.5. Statistics

Results were computed with the StatView® software and data are presented as mean ± standard deviation. Comparisons of pre- and postoperative results were made via the Wilcoxon sign rank test. Mortality was defined as early
(before hospital discharge or within 30 days after operation) or late (occurring thereafter).

3. Results

Preoperatively, the number of involved segmental pulmonary arteries was 9.4 ± 1.4, and a tricuspid insufficiency was present as grade I in two patients, grade II in 13 and grade III in 15 patients. Mean total cardiopulmonary bypass time was 132 ± 41 min, mean cross-clamp time 98 ± 21 min, mean duration of anterograde cerebral perfusion 21 ± 10 min and mean core temperature 29.5 ± 1.9°C. There were neither intraoperative deaths nor any major intraoperative complications. The duration of postoperative mechanical ventilatory support was 34 ± 44 h, and the mean median stay in ICU was 5 ± 9 days. Seven had mild to moderate lung reperfusion injury and one suffered from transient neurological dysfunction (agitation, delirium). Three patients (10%) died during hospital stay, two for multiorgan failure and one for persistent pulmonary hypertension. No late deaths occurred.

As expected, there was a significant postoperative improvement of patients’ hemodynamics (Table 1). None of the surviving patients had a tricuspid insufficiency and all patients achieved NYHA class I (P < 0.01) status 4 weeks after discharge and remained in this functional class during the median follow-up time of 16 months (range, 4–29 months) postoperatively.

4. Discussion

Circulatory arrest during PTE is necessary because of the continuous severe retrograde blood flow obscuring the operative field during the process of endarterectomy, primarily due to the bronchial arteries hyperplasia induced

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Preoperative</th>
<th>Immediate postoperative</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PAP (mmHg)</td>
<td>56 ± 17</td>
<td>26 ± 10</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CI (l/min/m²)</td>
<td>1.8 ± 0.3</td>
<td>2.8 ± 0.4</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CO (l/min)</td>
<td>4.2 ± 0.8</td>
<td>5.9 ± 1.4</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>PVR (dynes/s/cm⁻⁵)</td>
<td>873 ± 248</td>
<td>290 ± 117</td>
<td>&lt;0.0001</td>
</tr>
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PAP, mean pulmonary arterial pressure; CI, cardiac index; CO, cardiac output; PVR, pulmonary vascular resistance.
by the underlying chronic hypoxia. Because of the intrinsic co-morbidity of HCA and to minimize the retrograde bronchial arteries flow during the endarterectomy, we hypothesized that by transaxial placement of an aortic occlusion catheter beyond the left subclavian artery to occlude the ostia of the bronchial arteries, it would enable us to (i) perform a selective antegrade cerebral perfusion at 28–32°C while (ii) minimizing the retrograde bronchial arteries retrograde flow.

Although the series is small, the obtained results suggest that the presented technical advances are feasible in the vast majority of patients. The only failure we had in one patient probably resulted from other mediastinal and pleura parietalis to pulmonary vessels collaterals that may have contributed to the significant retrograde blood flow. However, we were still able to complete successfully the operation in the classic way by cooling the patient down to reach a core temperature of 19°C. The idea of an antegrade cerebral perfusion during PTE is not new since Zeebregts and coworkers [8] already used, in 1998, a selective antegrade cerebral perfusion technique similar to that used by Kazui [9] for total aortic arch repairs, and concluded that their technique offers substantial benefits with regard to cerebral protection. However, the technique by Zeebregts et al. requires manipulation and cannulation of the innominate artery and left common carotid artery, jeopardizing the risks of embolization due to calcifications of the arch branches. Furthermore, additional canulas reduce the visibility of the already small operative field and may increase the risk of air embolism.

Compared to the Zeebregts’s technique, we feel that ours is easier to perform, does not require additional canulas or modification of the bypass circuit, minimizes the risks of air embolism and, most importantly, provides blood flow for the head vessels while remarkably reducing retrograde bronchial arterial flow. The antegrade flow during isolated perfusion can be adjusted to maintain a blood pressure of 50–60 mmHg in the radial arteries, and continuous cerebral oxygen saturation measurements serve as an additional tool to improve safety of the technique. Preoperative radiological imaging of the bronchial arteries arising from the aorta is extremely helpful to assess the location and number of the major bronchial arteries, and especially designed balloons may further improve the efficiency of this technique. To avoid longer periods of relative warm ischemia (28°C) in the lower body parts distal the inflated balloon, intermittent periods of reperfusion are required to protect the other organs. Since the balloon inflation times usually add up to a maximum of 30 min, interrupted by short reperfusion intervals, this procedure was well tolerated without any end organ failure.

All our operations were made with a 28–32°C core temperature, avoiding thus deep hypothermia with its potentially negative side-effects and reducing CPB times and its associated complication as well. The type of lung reperfusion injury observed in this study was always a lung reperfusion edema and rated as mild to moderate; there were no signs of ischemia or hemorrhage. Since the postoperative management did not change as compared to our previous experience with PTE under HCA (P. Macchiarini, personal communication), we might speculate that the introduced technical changes might be responsible for the reduced incidence and severity of reperfusion injury. Additionally, by performing an antegrade selective cerebral perfusion at 28–32°C, the risks of imperfect cerebral protection during the critical period of interruption of the cerebral circulation under HCA were minimized, as was the cerebral global ischemia resulting in the temporary neurological dysfunction or embolic stroke complications. From our experience, we do not feel the necessity for cold cerebral perfusion as advocated by others [10,11], but are using topical cooling of the head, starting with the beginning of surgery. Furthermore, potentially neuroprotective drugs are administered before antegrade cerebral perfusion is planned.

Two other major technical advances were introduced. On the right, once the endarterectomy plane is raised posteriorly, the dissection continues gradually to include the middle and lower segmental branches without endarterecomizing the first mediastinal pulmonary artery branch. This is endarterectomized at the end to avoid retrograde blood flow spillage into the middle and lower lobe branches during their endarterectomy; we found it helpful to leave a rim of thromboembolic material around its takeoff during the initial dissection to be used thereafter. One of the major difficulties on the left side are the need of a relatively long arteriotomy, risks of extensive tearing during its closure because of its residual thin and fragile wall and the difficulties to visualize directly the anteromedial segments. Based on the lessons learned from the eversion technique in patients with carotid artery stenosis, we postulated that by completely transecting the left pulmonary artery 0.5–1 cm from its takeoff, we would be able to (i) gain an excellent 360° endoluminal visualization with consequent optimal circumferential deobstruction, especially if the left lung is kept inflated during the endarterectomy of the lower lobe branches and (ii) reduce the anastomotic risks by starting the endarterectomy 1.0 cm beyond the section of the left pulmonary artery so that the anastomosis will be made on a thicker wall. Compared to our previous experience with longitudinal arteriotomies, we never experienced tearing or postoperative bleedings deriving from the left closure insufficiency, even in patients with transient pulmonary hypertension.

In conclusion, the presented technical modifications represent, in our opinion, a further contributive step towards a better postoperative outcome in terms of lung reperfusion injuries and rate of neurological complications in patients undergoing PTE for CTEPH.
References


Appendix A. Conference discussion

Dr J. Bachet (Paris, France): Why do you put a balloon catheter in the descending aorta instead of just having circulatory arrest of the lower body while maintaining the cerebral perfusion as we do in my group when we replace the arch?

Dr Hagl: With the balloon catheter in the descending aorta, first of all, it’s very easy to perform. You don’t have to introduce a new cannula, like other people do, like you and Dr. Kazui do, in aortic arch surgery where you put the catheter in the heart vessels. You don’t have to do that. So you minimize, I think, the risk for air embolism and the manipulation of potentially calcified vessels. So therefore, to put the catheter into the descending aorta is very easy. You guide them with your hand, and you have more or less the same effect. And because we have not too long circulatory arrest times for the lower body, it is not really a problem. People tolerate that very easily. And between the right side and the left side of the PTE, you always have a time of reperfusion. So I think that is not a real problem.

Dr Bachet: You said that you use antegrade cerebral perfusion, but you didn’t tell us what kind of and at what temperature. How do you put the cannulas in the carotid arteries?

Dr Hagl: We measure the pressure in the right radial artery actually, and we try to achieve a pressure of 50 to 60 mmHg. So we are not going by flow, but we are going by pressure in the radial artery. If we got the impression, as I said, we do continuous neuromonitoring in these patients. And if you realize that saturation goes down, this is sometimes due to cerebral spasm. And what we do then is we give some vasoactive drugs, like papaverine, and then you can see that the flow increases against and you avoid these spasms and you see the increase in your saturation again.

Dr Bachet: And how do you cannulate the cerebral vessels?

Dr Hagl: You don’t have to cannulate it. The inflow is via your …. Dr Bachet: Through the arterial cannula?

Dr Hagl: No, just via the originally introduced aortic cannula in the ascending aorta.

Dr T. Carrel (Bern, Switzerland): When I read your abstract, I was amazed that the time of cerebral perfusion came up to 55 minutes. And I’m always surprised that there is no concern about the lower body part ischemia. There is never any report about paraplegia in those patients having had antegrade perfusion of the cerebrum, but deep or modest hyperthermic circulatory arrest in the lower body part. So you stop the circulation at 28, 30 degrees, and you have no concern for the spinal cord up to 50 minutes?

Dr Hagl: Actually we don’t, because we allow reperfusion in between the right and the left side, as one point.

The second one is if you realize that it takes longer to do the endarterectomy, you just allow a short period of reperfusion. And that’s from experience of the descending aortic surgery, we know that if you go down to, let’s say, 29 degrees, you have pretty long time before you get paraplegia in these patients. I agree, it could happen in patients, especially if the blood supply to the spinal cord is poor for whatever reasons; but so far we haven’t seen it and, hopefully, we’ll not see it in the future.

Dr J. Bachet (Paris, France): I can support Dr. Hagl’s answer, because in our experience of more than 200 patients with cerebral perfusion and circulatory arrest of the lower part of the body, we have seen only 3 paraplegias. We stop the circulation at about 28 degrees Celsius. Those 3 paraplegias occurred in people with acute dissection already having neurologic disorders, and we never saw a new one. So I think it’s rather safe.