Mid-term results of surgery for chronic thromboembolic pulmonary hypertension

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Abstract

Pulmonary thromboendarterectomy is an effective surgical treatment for chronic thromboembolic pulmonary hypertension (CTEPH). In this study, we review our short- and mid-term results in the recent series of patients undergoing pulmonary thromboendarterectomy. Twenty-three patients (54±12 years) were re-evaluated 7–59 months (mean, 34 months) after surgery. Nine patients were in New York Heart Association functional class II, 11 patients in class III and three patients in class IV. All patients used supplemental oxygen therapy. After surgery, pulmonary hemodynamics were significantly improved: pulmonary vascular resistance (PVR) decreased from 925±342 to 337±260 dynes-s-cm⁻¹ (P<0.01); mean pulmonary artery pressure (MPAP) decreased from 47±12 to 25±10 mmHg (P<0.01). Three patients developed severe residual pulmonary hypertension and one of them died soon after surgery. During the follow-up period there were no deaths, but one recurrence of pulmonary embolism. Nineteen patients (86%) were in New York Heart Association functional class I or II and thirteen patients (59%) were weaned from oxygen therapy. In conclusion, pulmonary thromboendarterectomy provided remarkable early and late results with acceptable hospital mortality rate, normalization of pulmonary hemodynamics, and improvement in clinical functional status with relief of hypoxemia.

Keywords: Chronic thromboembolic pulmonary hypertension; Pulmonary hypertension; Pulmonary thromboendarterectomy; Surgical outcomes

1. Introduction

Chronic thromboembolic pulmonary hypertension (CTEPH), caused by intraluminal thrombus organization and fibrous stenosis or complete obliteration of pulmonary arteries, is a rare but life-threatening complication of acute pulmonary embolism. The prognosis of medically treated patients with CTEPH is poor and worsens as pulmonary hypertension exacerbates. Patients with mean pulmonary artery pressure of >30 mmHg have a 30% 5-year survival rate, and those with mean pulmonary artery pressure (MPAP) exceeding 50 mmHg have only a 10% 5-year survival rate [1]. On the contrary, pulmonary thromboendarterectomy can substantially improve pulmonary hemodynamics immediately after surgery [2–4], and improve prognosis and clinical functional status on a long-term basis [5–7]. In this study, we review our short- and mid-term outcomes in our recent series of patients undergoing pulmonary thromboendarterectomy, to evaluate restoration of pulmonary hemodynamics soon after surgery, and improvement in the prognosis, clinical functional status, and hypoxemia at follow-up.

2. Material and methods

2.1. Patients

Twenty-three patients with CTEPH underwent pulmonary thromboendarterectomy at the National Hospital Organization Chiba Medical Center between April 2002 and March 2007. Institutional approval for this study was obtained, and written informed consent to use of clinical data was obtained from each patient. The mean age of the patients was 54±12 years (range 20–70 years). There were 13 male and 10 female patients. All patients were clinically examined and medically treated at Chiba University Hospital. Nine patients were in New York Heart Association (NYHA) class II, 11 patients in class III and three patients in class IV. All patients used supplemental oxygen therapy.

2.2. Surgical technique

An inferior vena cava filter was inserted in all patients preoperatively. All patients underwent surgery in accordance with the standardized technique described by the University of California, San Diego group [2]. A median sternotomy was made for bilateral pulmonary thromboendarterectomy and intermittent hypothermic circulatory...
arrest was applied for achieving bloodless operative field [8]. The mean cardiopulmonary bypass time was 289 ±
42 min and aortic cross-clamp time was 161 ± 33 min. The mean circulatory arrest time was 77 ± 17 min.

2.3. Hemodynamic measurement

Pulmonary hemodynamics were assessed at Chiba University Hospital by right-sided heart catheterization, preoperatively in all patients and at one month after surgery in surviving patients.

2.4. Follow-up

All surviving patients were followed up for 7–59 months (mean, 34 ± 17 months) after surgery and 10 patients were followed up for 36 months or longer. Follow-up information on functional status and use of supplemental oxygen was obtained by questionnaire, mailed to the patient or the referring physician. Mean arterial oxygen pressure under room-air conditions (PaO₂) was obtained for all patients.

2.5. Statistical analysis

Results are described as mean ± S.D. Pre- and postoperative variables were compared with Wilcoxon sign rank test. Discrete variables were analyzed using the Fisher’s exact test. Mean arterial oxygen pressure before surgery, soon after surgery, and at the time of follow-up were compared using one-way analysis of variance for repeated measures, followed by Scheffe’s multiple comparison test. A value of P < 0.05 was considered to be statistically significant.

3. Results

Early results: Pulmonary hemodynamics were substantially improved after pulmonary thromboendarterectomy (Fig. 1): pulmonary vascular resistance (PVR) decreased from 925 ± 342 to 337 ± 260 dynes·s·cm⁻¹ (P < 0.01); mean pulmonary artery pressure decreased from 47 ± 12 to 25 ± 10 mmHg (P < 0.01); and cardiac index increased from 2.2 ± 0.5 to 2.7 ± 0.6 l/min·m² (P < 0.01). Mean percentage decrease in PVR was 61 ± 25%, and pulmonary hypertension was relieved in 17 patients (74%) with mean pulmonary artery pressure of < 30 mmHg.

There was one hospital death (4.3%). The patient, who had preoperative PVR of 1089 dynes·s·cm⁻¹ and MPAP of 48 mmHg, developed postoperative residual pulmonary hypertension hemodynamic collapse and disruption of pulmonary artery suture line, but died of multiple organ failure on postoperative day 12. Six patients (26%) developed residual pulmonary hypertension with mean pulmonary artery pressure > 30 mmHg after surgery (Table 1). Two patients who experienced severe pulmonary hypertension with unchanged pulmonary artery pressure after surgery suffered respiratory insufficiency requiring prolonged (> 14 days) ventilator support with tracheostomy. Three patients (13%) developed pulmonary hemorrhage. One patient who developed severe hypoxemia due to pulmonary hemorrhage was successfully treated with veno-arterial extracorporeal membrane oxygenation support. Severe reperfusion lung edema that exacerbated gas exchange did not occur in any patient.

Late results: During the follow-up period there were no deaths, and no major adverse events related to CTEPH, but there was one recurrence of pulmonary embolism. The patient who had a recurrence experienced postoperative residual pulmonary hypertension with mean pulmonary artery pressure of 35 mmHg, and suffered dyspnea on exertion 39 months after surgery. CT-scan showed progression of the disease with re-occlusion of the right lower lobar arteries, and echocardiography revealed an increase in tricuspid pressure gradient from 34 mmHg soon after surgery to 50 mmHg at the time of follow-up. Nineteen

Fig. 1. Changes in hemodynamic variables, (a) pulmonary vascular resistance, (b) mean pulmonary artery pressure, (c) cardiac index. *P < 0.01, Preop, preoperative; Postop, postoperative.
patients (86%) were asymptomatic, in NYHA class I or II (8 patients were in NYHA class I and 11 patients were in class II) (Fig. 2). Fourteen patients (64%) had improved functional status compared with their preoperative status, while five patients preoperatively in NYHA class II owing to effective medical therapy had unchanged functional status at the time of follow-up. Three patients were in NYHA class III: two patients with severe residual pulmonary hypertension remained in NYHA class III, and one patient with a recurrence worsened NYHA class from II to III. Mean arterial oxygen pressure under room-air conditions had significantly increased at the time of follow-up compared with the preoperative and early postoperative value (Fig. 3) (57.7 ± 7.7 mmHg, preoperative; 64.2 ± 11.6 mmHg, soon after surgery; 78.8 ± 16.0 mmHg, at follow-up; P < 0.01 vs. preoperative and soon after surgery). There were five patients (23%) who had mean arterial oxygen pressure of < 60 mmHg at follow-up, whereas there were 15 patients (65%) preoperatively (P = 0.12). Thirteen patients (59%) weaned from supplemental oxygen therapy at follow-up, although all patients used it preoperatively. Of 9 patients on oxygen therapy, two patients used it only during exertion or sleeping.

4. Discussion

Pulmonary thromboendarterectomy has proven to be effective for patients with CTEPH [2–4, 6, 7, 9]. However, this operation is a technically and surgical experience demanding procedure associated with an increased operative mortality rate of around 10% [3, 4, 6, 7, 10], although the rate is below 5% at the center with the most experience, the University of California, San Diego [2]. Residual pulmonary hypertension is the major complication associated with perioperative mortality [4, 6, 10]. Jamieson et al. reported that 17 of 22 hospital death (77%) were related to residual pulmonary hypertension, and that the mortality rate was 31% when the postoperative pulmonary vascular resistance was > 500 dynes-s-cm⁻², but only 0.9% when it was < 500 dynes-s-cm⁻² [2]. Management of residual pulmonary hypertension is difficult, and depends on the severity of pulmonary hypertension, because pulmonary vascular resistance is commonly fixed, and usually does not respond to vasodilators [11]. In extreme cases, extracorporeal circulation may be required for severe hemodynamic collapse and disruption of pulmonary artery suture line.

Follow-up studies show significant improvement in prognosis and clinical functional status with relief of symptoms in patients undergoing pulmonary thromboendarterectomy [3, 5, 6, 9]. Archibald et al. demonstrated that 75% of the patients survived beyond six years after pulmonary thromboendarterectomy [5], and Ogino et al. reported 5-year survival rate of 86% [6]. In addition, 90% of patients were shown to be in NYHA class I or II at follow-up [5–7, 9]. While patients with CTEPH preoperatively use supplemental oxygen therapy for hypoxemia due to the ventilation/perfusion mismatch and decreased cardiac output [12], it
has shown that >68% of patients do not use oxygen therapy with an increase in arterial oxygen pressure at follow-up [6, 7, 9]. In the present study, there was no mortality during a mean follow-up period of 34 months. Nineteen patients (86%) were in NYHA class I or II, and fourteen patients (64%) had improved functional status compared with their preoperative status. These results are comparable to the previous results, and confirm the favorable and sustained effect of pulmonary thromboendarterectomy on late outcomes. Our result that there were 13 patients (59%) who were weaned from oxygen therapy at follow-up seems to be inferior to previous results. However, it should be noted that all our patients used oxygen therapy preoperatively, and there were only five patients who had mean arterial oxygen pressure of <60 mmHg at follow-up, whereas there were 15 such patients preoperatively. In contrast to marked improvement in functional status in patients with restoration of pulmonary hemodynamics, patients with residual or recurrent pulmonary hypertension had a poor functional status, NYHA class III. Residual pulmonary hypertension has been shown to prevent improvement of functional status. One year after surgery patients achieve a significant increase in 6-min walk distance, which correlates with the clinical and hemodynamic severity of disease. However, patients with residual pulmonary hypertension have a lower 6-min walk distance than hemodynamically normalized patients [11]. In addition, residual pulmonary hypertension and recurrence of pulmonary embolism have been shown to be major causes of late death after pulmonary thromboendarterectomy [5].

In order to reduce PVR and relieve pulmonary hypertension sufficiently, complete removal of thromboembolic obstructions in the segmental and sub-segmental pulmonary arteries is essential, and can be accomplished by establishment of the correct endarterectomy plane at the level of proximal, surgically accessible pulmonary arteries. We therefore believe that the presence of proximal thromboembolic material extending to distal branches is the most determinant factor of operability [8]. In the University of California, San Diego experience, patients with predominantly distal disease have higher perioperative mortality rate and higher incidence of postoperative complications than those with central disease [13]. In addition to pulmonary angiography CT-scan can help to evaluate the presence of proximal thromboembolic disease [14]. Although a reliable modality for evaluating the presence and degree of distal artery involvement remains to be established, PVR disproportionately high to the degree of pulmonary vascular obstruction seen on angiography and low upstream resistance on pulmonary artery occlusion waveform analysis suggest the presence of surgically inaccessible distal disease [2, 10, 15].

In conclusion, pulmonary thromboendarterectomy provided remarkable early and late results with acceptable hospital mortality rate, normalization of pulmonary hemodynamics, and improvement in clinical functional status with relief of hypoxemia. However, severe residual pulmonary hypertension was associated with perioperative mortality and poor functional status at follow-up. We believe that the most important determinant of whether a patient may benefit from pulmonary thromboendarterectomy is careful patient selection, based on preoperative evaluation of the presence of surgically accessible central disease and absence of distal small vessel disease.

References