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Circulatory Assistance and Surgery for Residual Pulmonary Hypertension Following Thromboendarterectomy

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INTRODUCTION

Chronic thromboembolic pulmonary hypertension (CTEPH) complicated by pulmonary hypertension is resistant to medical therapy and has a poor prognosis. The only therapy effective for CTEPH is thromboendarterectomy (TEA). CTEPH is divided into four types, depending on the presence of thrombus in the pulmonary arteries. In Japan, CTEPH is generally divided into central and peripheral types. The results of surgery for the central type have recently become more favorable. However, the results of surgery for the peripheral type are not favorable due to inadequate surgical indications, surgical procedures, and perioperative care. To improve the results of surgery for peripheral CTEPH, the most important issue is treating residual pulmonary hypertension. For patients with residual pulmonary hypertension, it is impossible to perform removal from extracorporeal circulation during surgery. In addition, it is difficult to save lives unless percutaneous cardiopulmonary support (PCPS) is introduced in all cases. However, with circulatory assistance with PCPS alone, several deaths have occurred due to left ventricular failure during the procedure. Therefore, the authors began to use circulatory assistance with intraaortic balloon pumping (IABP). The authors compared circulatory assistance with PCPS alone

with concomitant use of PCPS and IABP for postoperative residual pulmonary hypertension in patients with CTEPH. Although there have been few surgeries for this disease in Japan, we discuss the results of 30 recent surgical cases.

SUBJECTS AND METHODS

In our Department between August 2001 and April 2008, we performed bilateral pulmonary thromboendarterectomy in 66 patients with CTEPH under extracorporeal circulation and intermittent deep hypothermic circulatory arrest through a median sternotomy. After surgery, we evaluated only perioperative laboratory data and the results of surgery for patients with residual pulmonary hypertension by comparing the P group (PCPS alone) with the PI group (PCPS and IABP) for 30 patients who recently underwent surgery. Our recent method of perioperative management for CTEPH is epoprostenol, a pulmonary vasodilator, which is continuously administered before surgery. Then sivelestat, a neutrophil elastase inhibitor, is administered continuously after induction of anesthesia. Epoprostenol is used to reduce the load on the right ventricle and sivelestat for pulmonary congestion (postoperative reperfusion disorder).

Values are the mean $\pm$ standard deviation. The chi-square test was applied to male to female ratio. We used Student's t-test for PaCO₂, PaO₂, mean pulmonary artery pressure (mPA), pulmonary vascular resistance (PVR), cardiac index (C.I.), ejection fraction (EF), and brain natriuretic peptide (BNP). A finding of $P < 0.05$ was considered significant.

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Table 1 Residual PH

	group P	group PI	p value
n	10	10	
Male / female	2 / 8	2 / 8	
Average age	50.4 ± 15.4	55.4 ± 12.6	0.438
Timing of PCPS introduction			
pre. / post.	0 / 10	1 / 9	0.305
Timing of IABP introduction			
pre-op.	–	1	
intra-op.	–	9	

Table 2 Group P pre operation data

	group P	group PI	p value
PaCO ₂ (torr)	36.9 ± 4.67	34.1 ± 4.97	0.229
PaO ₂ (torr)	58.8 ± 10.6	55.7 ± 7.04	0.456
mPA (mmHg)	51.8 ± 10.5	50.8 ± 10.4	0.841
C.I. (L / min / m ²)	2.27 ± 0.46	2.02 ± 0.28	0.205
PVR (dyne·sec·cm ⁻⁵)	1035 ± 353	1182 ± 384	0.411
EF (%)	67.4 ± 8.72	66.4 ± 11.8	0.856
BNP (pg / ml)	379 ± 328	712 ± 483	0.090

mPA: mean pulmonary artery pressure, C.I.: cardiac index, PVR: pulmonary vessel resistance, EF: ejection fraction, BNP: brain natriuretic peptide

RESULTS

There were 20 cases of circulatory assistance for CTEPH with postoperative residual pulmonary hypertension (group P = 10 patient, group PI = 10 patients). The male to female ratios were 2:8 (P group) and 2:8 (PI group) and without significant difference. Mean age was 50.4 ± 15.4 years (P group) and 55.4 ± 12.6 years (PI group; $p = 0.438$). PCPS was introduced during surgery in all patients in the P group but for only one patient before surgery in the PI group. In the PI group, IABP was introduced in one patient before surgery and nine patients during surgery (**Table 1**).

Table 2 shows a comparison of preoperative data in the P and PI groups: PaCO₂ before surgery, 36.9 ± 4.67 torr (P) and 34.1 ± 4.97 torr (PI: $p = 0.229$); PaO₂, 58.8 ± 10.6 torr (P) and 55.7 ± 7.04 torr (PI) ($p = 0.456$); mPA, 51.8 ± 10.5 mmHg (P) and 50.8 ± 10.4 mmHg (PI: $p = 0.841$); CI, 2.27 ± 0.46 l / min / m² (P) and 2.02 ± 0.28 l / min / m² (PI: $p = 0.205$); PVR, 1035 ± 353 dyne·sec·cm⁻⁵ (P) and 1182 ± 384 dyne·sec·cm⁻⁵ (PI: $p = 0.411$); EF, 67.4

Table 3 Outcome

	group P	group PI
alive	6	6
death	4	4

± 8.72% (P) and 66.4 ± 11.8% (PI: $p = 0.856$); BNP, 379 ± 328 pg / ml (P) and 712 ± 483 pg/ml (PI: $p = 0.090$). There were no significant differences between the two groups in any of these parameters. Surgery results were as follows: survival 6 and death 4 for both P and PI groups (**Table 3**).

Table 4 shows a comparison of perioperative laboratory data for patients resistant to surgery. Other than PaO₂ and EF, all laboratory data for the P group were improved after surgery. Other than PaCO₂, PaO₂, and EF, all laboratory data for the PI group were improved. We compared postoperative data for surgery-resistant patients in the two groups. Only PVR differed significantly,

Table 4 Postoperation data

	pre-op.	group P post-op.	p value	pre-op.	group PI post-op.	p value
PaCO ₂ (torr)	34.3 ± 2.87	43.7 ± 5.64	0.022	33.7 ± 4.53	39.1 ± 3.05	0.858
PaO ₂ (torr)	56.5 ± 7.43	67.6 ± 16.4	0.133	55.9 ± 7.10	56.1 ± 9.34	0.496
mPA (mmHg)	50.3 ± 10.5	21.5 ± 5.09	0.001	55.2 ± 6.59	34.2 ± 14.0	0.040
C.I. (L / min / m ²)	2.20 ± 0.41	3.21 ± 0.81	0.015	2.01 ± 0.34	2.94 ± 0.47	0.004
PVR (dyne·sec·cm ⁻⁵)	992 ± 298	205 ± 140	0.002	1217 ± 370	541 ± 259	0.010
EF (%)	67.8 ± 10.6	56.4 ± 11.2	0.032	70.0 ± 8.51	69.1 ± 2.94	0.588
BNP (pg / ml)	332 ± 218	60.3 ± 50.0	0.015	540 ± 360	71.4 ± 63.5	0.028

Table 5 Postoperation data

	Group P	Group PI	p value
PaCO ₂ (torr)	43.7 ± 5.64	39.1 ± 3.05	0.121
PaO ₂ (torr)	67.6 ± 16.4	56.1 ± 9.34	0.131
mPA (mmHg)	21.5 ± 5.09	34.2 ± 14.0	0.064
C.I. (L / min / m ²)	3.21 ± 0.81	2.94 ± 0.47	0.505
PVR (dyne·sec·cm ⁻⁵)	205 ± 140	541 ± 259	0.025
EF (%)	56.4 ± 11.2	69.1 ± 2.94	0.068
BNP (pg/ml)	60.3 ± 50.0	71.4 ± 63.5	0.759

with the P group exhibiting a lower value.

PCPS assist periods were 3.33 ± 2.42 days (P group) and 9.17 ± 5.19 days (PI group) ($p = 0.041$). The PI group received assistance significantly longer. The IABP assist period was 12.0 ± 6.39 days. Patients were removed from IABP after removal from PCPS.

Recent surgery results were favorable, with only one death in 30 cases. **Table 4** shows perioperative laboratory data. PaCO₂ was 37.0 ± 3.73 torr before surgery and 39.0 ± 3.68 torr after surgery ($p = 0.445$). PaO₂ was 60.6 ± 9.87 torr before surgery and 71.2 ± 14.3 torr after surgery ($p = 0.456$). mPA was 51.4 ± 13.2 mmHg before surgery and 23.8 ± 12.2 mmHg after surgery ($p < 0.001$). CI was 2.41 ± 0.62 l / min / m² before surgery and 2.96 ± 0.60 l / min / m² ($p = 0.214$) after surgery. PVR was 1035 ± 426 dyne·sec·cm⁻⁵ before surgery and 285 ± 173 dyne·sec·cm⁻⁵ ($p < 0.001$) after surgery. EF was $65.4 \pm 7.30\%$ before surgery and $63.1 \pm 6.41\%$ ($p = 0.012$) after surgery. BNP was 308 ± 325 pg / ml before surgery and 79.8 ± 73.0 pg / ml ($p = 0.001$) after surgery. mPA, PVR, and BNP were significantly improved.

DISCUSSION

PCPS is a biventricular assist device with a centrifugal pump and artificial lung to assist circulation by oxygenation and reduce right-sided preload. The device is effective in patients with severe heart failure and cardiac failure after heart surgery.²⁻⁴⁾ PCPS is used for CTEPH when pulmonary arterial blood pressure exceeds body blood pressure due to perioperative residual pulmonary hypertension. It is used for reduced gas exchange accompanying reperfusion abnormality of the lungs in the acute stage and to reduce right heart load against residual pulmonary hypertension rather than for ordinary cardiac failure. The indications for use of PCPS in patients with severe heart failure are different from those for patients with CTEPH, as shown above. Therefore, if PCPS is not introduced in patients with this disease, death will be unavoidable. Circulatory assistance by PCPS and PCPS+IABP has a mortality rate of 40%. However, considering that all patients without circulatory assistance would have died, it is clear that PCPS and IABP are useful. For duration to removal of PCPS, Oshima et al.⁵⁾ noted that the PCPS assistance period for 32 patients with severe heart failure was 134 ± 117 hours (5.58 ± 4.88

days) on average. Murashita et al.⁶⁾ noted that patients who could be removed from PCPS were included in a group with an assistance period of 24 hours or less. In our case, it was 3.33 ± 2.42 days for group P, the same as the assistance period for common cardiac failure therapy. However, for the PI group, the assistance period was 9.17 ± 5.19 days, four days longer than that reported by Oshima et al. We thus performed assistance over a longer period of time. For CTEPH, the indications for use differ from those patients with severe heart failure. Removal tends to be performed on the third day or later, since residual pulmonary hypertension continues 72 hours after surgery (3 days).⁷⁾ It appears that this accounts for the difference in time of removal in ordinary patients with severe heart failure. According to the perioperative laboratory data in the P and PI groups, pulmonary vascular resistance and BNP were significantly improved in both groups. It thus appears that favorable results were obtained even in patients saved by circulatory assistance. Comparison of postoperative laboratory data in surgery-resistant patients in the two groups, as shown in **Table 5**, indicates that the P group exhibited favorable pulmonary vascular resistance. This means that patients in the PI group have higher residual pulmonary hypertension and that patients who might have died with circulatory assistance performed with PCPS alone were saved with combined use of PCPS and IABP. Assistance by IABP yields myocardial protection due to reduced preload during left ventricular systole and increased coronary blood flow in diastole.⁸⁾ In CTEPH, preoperative left ventricular failure is not observed. However, postoperative left ventricular failure may be caused by intermittent deep hypothermic circulatory arrest. Therefore, circulatory assistance in CTEPH should be in the form of PCPS+IABP rather than PCPS alone.

However, pulmonary vascular resistance was $541 \text{ dyne} \cdot \text{sec} \cdot \text{cm}^{-5}$ and not satisfactory. It appeared that right heart failure was not sufficiently improved. These patients should be carefully followed in the future.

For the last three years, we have tried to improve surgical results. As perioperative care for CPTE, we have continuously administered epoprostenol from before surgery and sivelestat after administration of anesthetics. With these surgical improvements, the mortality rate in the group of our 30 recent patients improved to 3.3%. Additionally, postoperative pulmonary vascular resis-

tance has been significantly reduced. These results are acceptable. However, since the cause of CTEPH is unknown, it is important to investigate its pathogenesis in attempts to improve surgical outcomes.

CONCLUSION

Circulatory assistance by PCPS and IABP was useful for CPTE postoperative pulmonary hypertension. As a result of improved management in the perioperative period, mortality was 3.3% in 30 recent cases.

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