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Clinical Outcomes of Endoscope-Assisted Pulmonary Endarterectomy for Chronic Thromboembolic Pulmonary Hypertension

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Purpose: Pulmonary thromboembolism is a potentially life-threatening condition in patients with heart disease; however, limited studies discussing long-term outcomes exist. This study aimed to investigate the long-term outcomes of pulmonary endarterectomy (PEA) in patients with chronic thromboembolic pulmonary hypertension (CTEPH), focusing on the improvement of functional class and right ventricular (RV) pressure.

Materials and Methods: Clinical data of patients with CTEPH were obtained from Yonsei Hospital between May 2012 and December 2021, and reviewed retrospectively. Twenty-six patients underwent endoscope-guided PEA during the study period, and the mean follow-up duration was 24.8±23.4 months.

Results: After PEA, most patients (88.5%) were weaned from inotropes without extracorporeal membrane oxygenation support during the first few days. Two patients (7.6%) had cerebrovascular accidents without neurological deficits. On echocardiography, the RV systolic pressure and tricuspid regurgitation grades significantly improved (p<0.001). Furthermore, the mean left ventricle end-diastolic diameter was significant increased (p=0.003), and the left ventricular end-systolic diameter increased (p<0.001). The median intensive care unit stay was 3.0±9.4 days, and median hospital stay 16.0±26.5 days. The 5-year survival rate was 95.5%, and the 5-year freedom rate of cardiac death was 100%. There was a marked improvement in New York Heart Association (NYHA) status (p<0.001). Cox regression suggested that the main pulmonary artery (MPA) involvement is a significant predictor of non-improvement in functional class post-PEA.

Conclusion: Mortality rates are low and patients experience a marked improvement in NYHA class and health status after PEA. Moreover, MPA involvement may affect functional outcomes.

Key Words: Pulmonary arterial hypertension, endarterectomy, functional status

INTRODUCTION

Chronic thromboembolic pulmonary hypertension (CTEPH) is a rare cause of pulmonary hypertension that presents as obstructive pulmonary artery remodeling with organized and fibrotic changes secondary to acute pulmonary thromboembolism (PTE). CTEPH develops in approximately five individuals per million annually, and in 0.56% to 6.1% of individuals after acute thromboembolism.[1-3]

CTEPH is the leading cause of severe pulmonary hypertension; it is characterized by intraluminal thrombus organization and fibrous stenosis or complete obliteration of the pulmonary arteries.[4] The consequence is in increased pulmonary vascular resistance (PVR), pulmonary hypertension, and progressive right heart failure. Common symptoms of CTEPH include shortness of breath, fatigue, edema, palpitations, and dizziness. However, some patients with asymptomatic or non-specific symp-

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toms may experience delays in accessing treatment for CTEPH.

There are three major treatment options for CTEPH: pulmonary endarterectomy (PEA); balloon pulmonary angioplasty (BPA); and medications, such as phosphodiesterase (PDE)-5 inhibitors, endothelin receptor antagonists, and prostanoids. Several studies outside of Korea have reported the outcomes of these three treatment methods. Vascular disobliteration by PEA is the preferred treatment for patients with CTEPH,[5] but is not suitable for all patients. Poor functional status and chronic CTEPH may prevent open PEA, and the method may not succeed in patients with distal vessel lesions.[1] Patients who are deemed unsuitable for PEA should be evaluated for other treatment options, such as medications or BPA.

The aim of the present study was to investigate the long-term outcomes of PEA in patients with CTEPH, with a particular focus on the improvement in functional class and right ventricular (RV) pressure.

MATERIALS AND METHODS

Patients

This study was approved by the Institutional Review Board of Severance Hospital, Yonsei University College of Medicine (IRB approval no. 2021-1035-001), and informed consent was obtained from all the patients. We retrospectively investigated the patients who underwent PEA between May 2012 and December 2021.

Transthoracic echocardiography is the standard method for detecting pulmonary hypertension. It shows right atrial and ventricular enlargement and dysfunction with varying degrees of tricuspid regurgitation (TR) and paradoxical motion of the interventricular septum, leading to an impairment of left ventricular diastolic function. Pulmonary ventilation perfusion scanning is an important screening method to differentiate between CTEPH and idiopathic pulmonary arterial hypertension. All of the patients in this study underwent high-resolution helical CT to detect the distribution of the obstructive pulmonary artery lesions.

CTEPH was defined as symptomatic pulmonary hypertension (mean pulmonary artery pressure >25 mm Hg) with persistent lung perfusion defects.[6] A diagnosis of CTEPH was established before surgery was considered, and patients had undergone anticoagulation therapy for at least 3 months. Patients considered for surgery were evaluated by an interdisciplinary team of medical and surgical specialists experienced in PEA using high-quality imaging technologies.

The majority of patients selected for surgery were in the New York Heart Association (NYHA) functional class III or IV, with dyspnea at low levels of exertion or rest. Surgery may also be considered in patients with NYHA functional class II and with close to normal PVR at rest, if PVR increases significantly with exertion.[7]

The primary outcome of this study was overall survival and changes in functional status during follow-up. The secondary outcomes were post-operative outcomes, such as RV systolic pressure (RVSP) and changes in TR, measured by echocardiogram. Additionally, adverse events were defined as low cardiac output syndrome, bleeding requiring re-operation, respiratory complications requiring reintubation, infection, and cerebrovascular accident infarction.

Surgical technique

The aim of surgery is to remove the proximal fibrous pulmonary artery obstruction as completely as possible, while avoiding vascular injury within the lungs. The surgical technique has been well described by the San Diego group.[5] After a median sternotomy, PEA requires bilateral proximal pulmonary artery incisions, and endarterectomy is performed gently using double-action forceps and Jamieson dissecting aspirator. If the thrombus is localized to one side, as seen on the preoperative CT scan, unilateral pulmonary artery incision is performed. The procedure involves the establishment of bicaval cardiopulmonary bypass (CPB) under conditions of deep hypothermia to 25°C–28°C with brief periods of circulatory arrest, limited to 20 or 30 min, respectively.[5,8] Twenty-minutes of CPB support was performed after 20 min of total circulatory arrest, alternating until endarterectomy was complete. The surgeon established the correct endarterectomy plane, followed by the lobar, segmental, or subsegmental branches of each lobe. Since 2018, we have used a 5-mm videoscope to complete the resection of segmental and subsegmental lesions (Fig. 1).

Concomitant tricuspid valve repair (TAP) is usually performed due to severe tricuspid valve regurgitation and structural abnormalities of the tricuspid valve leaflets/chordae, or incomplete PEA. However, there was no incomplete PEA in this study.

Post-operative management

Cautious fluid and vasoactive drug administration, as well as pressure-controlled mechanical ventilation with a positive end-expiratory pressure of 8–10 cm H_2O, were used. This allowed prompt hemodynamic and respiratory stabilization, supporting early extubation 1–2 days post-operatively. Anticoagulation treatment to prevent re-occlusion was started with intravenous infusions within 12 hours of surgery. If there was no bleeding tendency for 12 hours after surgery, heparin infusion and oral aspirin therapy were started and switched to warfarin on the post-operative day (POD) 1. Lifelong anticoagulation was recommended for all patients after endarterectomy, and the target INR ranged from 2.0 to 3.0.

Veno-arterial extracorporeal membrane oxygenation (VA ECMO) was inserted in patients with severe RV failure with cardiogenic shock that did not respond to medical treatment, and veno-veno (VV) ECMO was inserted in patients with intractable hypoxia without RV failure.

The selection process of candidates for BPA after PEA includ-

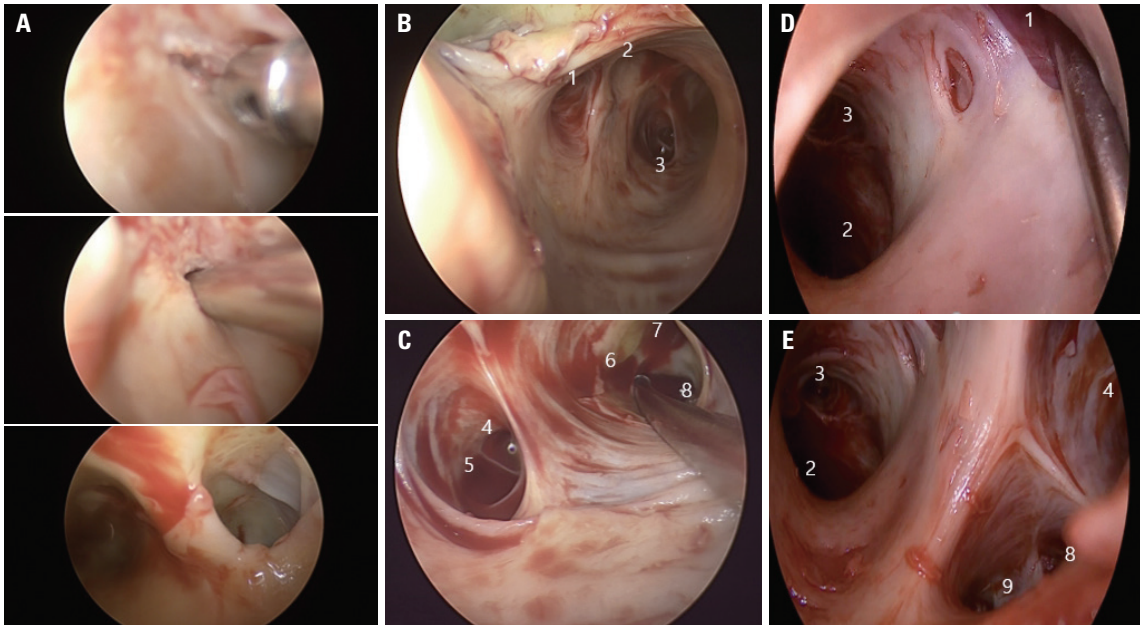

Fig. 1. Endoscope-assisted pulmonary endarterectomy for chronic thromboembolic pulmonary hypertension. (A) Endoscopic resection of segmental and subsegmental lesions during complete pulmonary endarterectomy surgery. (B) Post-surgical endoscopic image of the left upper lobe (1; apical, 2; posterior, 3; anterior segmental artery), (C) the left lower lobe (4; superior lingular, 5; inferior lingular segmental artery, 6; superior, 7+8; medical anterior), (D) the right upper lobe (1; apical, 2; posterior, 3; anterior segmental artery), (E) the right middle lobe (2; posterior, 3; anterior segmental artery, 4; lateral segmental artery), and the right lower lobe (8; anterior, 9; lateral segmental artery).

ed a complete reassessment of the patient with persistent symptomatic pulmonary hypertension at least 4 to 6 months after surgery using high-quality imaging techniques, such as CT angiograph, and right heart catheterization to assess the hemodynamic impairment.

Definitions

In this study, clinical improvement after PEA surgery was defined as a significant reduction in RVSP by 20% or more after surgery compared to before surgery. Improvement in NYHA functional class was defined as a change of grade 1 or higher to a lower class.

Routine post-operative & follow-up examination

Echocardiography was performed before discharge, and follow-up was performed at the outpatient clinic every 6 months after discharge. After 1 year, echocardiography was performed once every 2 years. Follow-up CT scans were performed in the first year and every 2 years thereafter.

Statistical analysis

Continuous data is presented as mean±standard deviation, or median and interquartile range. Categorical variables were analyzed using Fisher's exact test, and continuous variables were evaluated using Mann-Whitney U-test. The overall survival was estimated using Kaplan-Meier curve analysis, and differences between groups were compared using the log-rank test. *P*-values<0.05 were considered statistically significant. Data were analyzed using SPSS 25.0 (IBM Corp., Armonk, NY, USA).

RESULTS

Twenty-six patients underwent PEA between May 2012 and December 2021. The median follow-up duration was 36.5 months [interquartile range (IQR), 0.2–78.3]. The patient characteristics are shown in Table 1; median patient age was 59.5 years (IQR, 22–74), and 61.5% (n=16) of the participants were female. Half of the patients had systemic hypertension, 9 patients (34.6%) were diagnosed with deep vein thrombosis, and 5 patients (19.2%) had a history of cancer at the time of diagnosis. Five patients (19.2%) had a history of previous CTEPH intervention.

Deep hypothermic circulatory arrest (DHCA) was performed in all patients. Bilateral PEA was performed in 17 patients (65.3%); 5 patients (19.2%) underwent concomitant TAP, one an on-pump coronary artery bypass graft, and one a patent foramen ovale closure. The median aortic cross-clamping time was 96 minutes (IQR, 38–193), the median CPB time was 166 minutes (IQR, 92–225), and the mean total circulatory arrest time was 25 minutes (IQR, 7–54). Twenty-two patients (84.6%) were categorized as Jamieson classification type I, 2 patients (7.6%) as type II, and 2 further patients as type III (Table 2).

In this study, 5 patients (19.2%) underwent concomitant procedure of TAP. The mean RVSP of the patients who underwent TAP during the immediate postoperative period decreased to 42 mm Hg from 85 mm Hg. However, among the patients who received TAP, patient number 10 (Fig. 2) showed an increase in RVSP immediately after surgery. In non-TAP patients, RVSP decreased from 79 mm Hg to 40 mm Hg. There was no difference in the amount of change in RVSP (p=0.264) or the value of imme-

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Table 1. Baseline Characteristics of Patients (n=26)

Variables	Value
Age, yr	59.5 (22–74)
Female sex	16 (61.5)
Body mass index, kg/m^2	23.7 (19.7–30.8)
Hypertension	13 (50.0)
Diabetes mellitus	2 (7.6)
Chronic renal failure	5 (19.2)
PAOD	1 (3.8)
COPD	2 (7.6)
Cerebrovascular accident	2 (7.6)
Comorbidities	
Deep vein thrombosis	9 (34.6)
Antiphospholipid syndrome	1 (3.8)
Antithrombin III deficiency	1 (3.8)
Protein C and protein S deficiency	1 (3.8)
Smoking history	5 (19.2)
Current smoker	4 (15.3)
Former smoker	1 (3.8)
NYHA functional class (III/IV)	15 (57.6)
Clinical characteristics	
Dyspnea	26 (100.0)
Chest pain	4 (15.3)
Syncope	5 (19.2)
Hemoptysis	2 (7.6)
Fatigue	2 (7.6)
Edema	3 (11.5)
Palpitations	1 (3.8)
Prior intervention history	5 (19.2)
Cancer history	5 (19.2)
Lung function test	
DLCO (% pred.)	79 (53–93)
FEV1 (% pred.)	85 (63–112)
FVC (% pred.)	92 (62–116)
FEV1/ FVC (% pred.)	74 (64–87)

PAOD, peripheral arterial occlusive disease; COPD, chronic obstructive pulmonary disease; NYHA, New York Heart Association; DLCO, diffusing capacity of the lung for CO; FEV1, forced expiratory volume in one second; FVC, forced vital capacity.
Data are presented as interquartile range or n (%).

Table 2. Pulmonary Endarterectomy Intraoperative Data (n=26)

Variables	Value
Deep hypothermic circulatory arrest	26 (100)
Bilateral pulmonary thromboendarterectomy	17 (65.3)
Concomitant tricuspid valve repair	5 (19.2)
CPB time, min	166 (92–225)
ACC time, min	96 (38–193)
TCA time, min	25 (7–54)
Jamieson classification	
I	22 (84.6)
II	2 (7.6)
III	2 (7.6)
IV	0 (0)

CPB, cardiopulmonary bypass; ACC, aortic cross clamp; TCA, total circulatory arrest.
Data are presented as interquartile range or n (%).

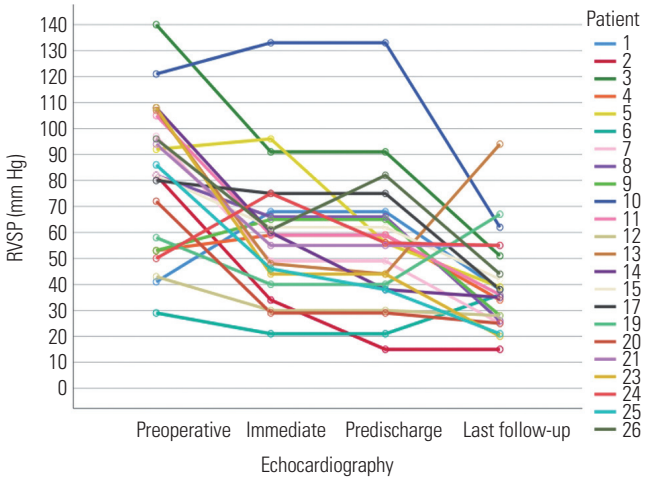

Fig. 2. The change in right ventricular systolic pressure (RVSP) post-pulmonary endarterectomy surgery.

diate postoperative RVSP between these two groups (p=0.772).

After surgery, sustained pulmonary hypertension may lead to persistent right ventricle pressure overload, tricuspid annular dilatation, and regurgitation. In this study, 4 patients (15.3%) had a rather elevated RVSP in the immediate postoperative period compared to before surgery. These patients were treated with oral PDE-5 (Sildenafil; Viagra, Pahtension), inhaled nitric oxide (iNO), and/or inhaled iloprost (Ventavis). During the last follow-up, these patients showed a significant decrease in RVSP compared to the immediately elevated RVSP.

After PEA, most patients (88.5%) were weaned from inotropes without ECMO support during the first few days. There were three ECMO support patients (11.5%, 1 VA ECMO, 2 VV ECMO). After surgery, one patient was tachypneic and hypoxic, and the patient was started on Epinephrine, milrinone, and inhaled Epoprostenol but was persistently hypoxic with a rising lactic acid and worsening metabolic acidosis. With evidence of worsening RV failure on bedside echocardiography, the patient was cannulated for VA ECMO to facilitate optimization for advanced management. ECMO was withdrawn 9 days after insertion.

The second patient required continuous ventilatory assistance with a high oxygen concentration fraction of inspired oxygen (FiO2) of 0.8 to 0.9 without RV failure evidence. Seven days post-surgery, VV ECMO was initiated due to desaturation and decreased oxygen partial pressure (pO2); and this was continued for 10 days. The last patient was extubated 1 day after surgery; however, on post-operative day 2, the patient's dyspnea worsened and sputum increased despite high-flow nasal cannula support. On chest radiography, the patient's pulmonary edema had worsened, so venovenous ECMO was initiated. ECMO was withdrawn 8 days after insertion. All three patients

who underwent ECMO were discharged without any further major incident.

Furthermore, postoperatively, a few patients recovered slowly after moderate to severe systemic inflammatory response syndrome. Among them, 3 patients (11.5%) had persistent or recurrent symptomatic pulmonary hypertension. Therefore, we followed them carefully with regular visits at our clinic with CT scan and echocardiogram evaluation, and no recurrence of thrombus was observed on these exams. Therefore, we treated these patients by adding medications, such as Riociguat (Adempas). One patient had a stent inserted into the right main pulmonary artery (MPA) due to external compression following BPA after 6 months after PEA surgery.

In our institution, anticoagulation strategy for PTE patients with complete resolution was controlled with vitamin K antagonist. Recently, Humbert, et al.[9] reported that exposure-adjusted hemorrhagic event rates were similar in the vitamin K antagonist group and new oral anticoagulant (NOAC) group, while exposure-adjusted embolic and/or thrombotic event rates were higher in the NOAC group. In this study, no re-operation was performed for bleeding, but 2 patients (7.6%) experienced cerebrovascular accidents. One patient with underlying protein C and S deficiency had a seizure on POD 1, but brain magnetic resonance imaging and electroencephalography revealed no lesions. One patient suffered hypoxic brain damage and underwent rehabilitation. Five patients (19.2%) experienced delirium, two of whom had long-lasting delirium that delayed general ward transfer and discharge. After surgery, 96.2% of the patients remained free of continuous renal replacement therapy (Table 3).

The mean follow-up duration with echocardiography was 2.04±1.93 years. The RVSP and TR grades significantly improved (p<0.001, respectively) (Fig. 2). The mean left ventricular end-diastolic diameter increased from 43±5.53 mm to 46±5.28 mm (p=0.003), and the mean left ventricular end-systolic diameter increased from 28±4.11 mm to 31±5.54 mm (p<0.001). There were no significant differences in left ventricular ejection fraction (Table 4). One patient died 28 months after surgery due to cancer dissemination. The median intensive care unit stay was 3 days, and the median hospital stay was 14 days. The 5-year survival rate was 95.5%, and the 5-year freedom rate of cardiac death was 100% (Fig. 3). Overall, the mortality rate was low, and there were significant improvements in NYHA class and health status (p<0.001) (Fig. 4).

Cox univariate regression analysis demonstrated that the male sex, chronic kidney disease grade III–IV, and MPA involvement were independent predictors of non-improvement

Table 3. Short-Term Outcomes of Pulmonary Endarterectomy Surgery

Variables	Value
In-hospital death	0 (0)
Low cardiac output syndrome	0 (0)
ECMO insertion	3 (11.5)
Re-operation for bleeding	0 (0)
Newly required dialysis	1 (3.8)
Early cerebrovascular accident	2 (7.6)
Delirium	5 (19.2)
Sternal wound infection	0 (0)
Reintubation	1 (3.8)
Tracheostomy	1 (3.8)
ICU stay, days	3 (2–9)
Hospital stay, days	14 (9–22)

ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit.
Data are presented as interquartile range or n (%).

Table 4. Changes in Hemodynamic Parameters after Pulmonary Endarterectomy Surgery

Variables	Pre-operative	Post-operative	*p* value
LVEDD, mm	43±5.53	46±5.28	0.003
LVESD, mm	28±4.11	31±5.54	<0.001
LAVI, mL/m^2	20.95±7.04	23.7±12.56	0.052
LVEF, %	67±6.96	65±7.04	0.029
RVSP, mm Hg	82±28.47	36±19.64	<0.001
RAP, mm Hg	10±5.28	5±3.68	0.007
mPAP, mm Hg	61.4±13.8	48.6±14.8	0.046
TR grade			<0.001
I	7 (26.9)	9 (34.6)	
II	5 (19.2)	3 (11.5)	
III	6 (23.0)	0 (0)	
IV	3 (11.5)	0 (0)	
E	0.47±0.22	0.67±0.19	0.053
E/E'	9.26±3.49	9.67±3.02	0.896
Mean follow-up period: 2.04±1.93 years			

LVEDD, left ventricular end-diastolic diameter; LVESD, left ventricular end-systolic diameter; LAVI, left atrial volume index; LVEF, left ventricle ejection fraction; RVSP, right ventricular systolic pressure; RAP, right atrial pressure; mPAP, mean pulmonary arterial pressure; TR, tricuspid regurgitation; E, early mitral filling velocity; E', early diastolic mitral annular velocity.
Data are presented as mean±standard deviation or n (%).

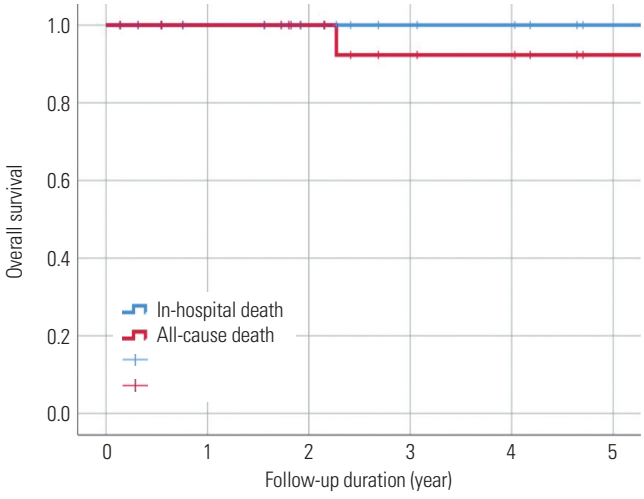

Fig. 3. Kaplan-Meier survival analysis post-pulmonary endarterectomy surgery.

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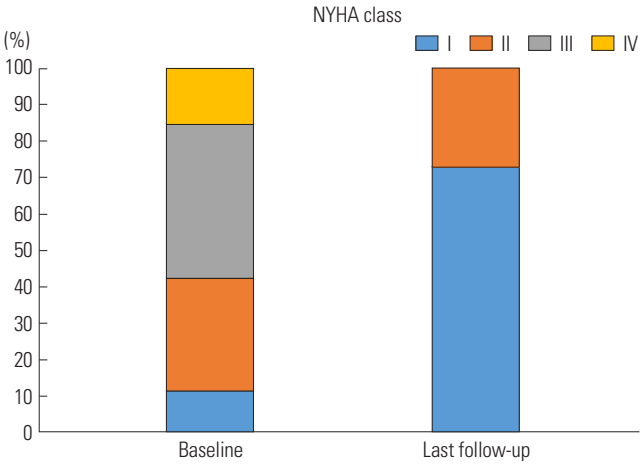

Fig. 4. Functional outcomes post-pulmonary endarterectomy surgery. NYHA, New York Heart Association.

Table 5. Multivariate Cox Proportional Hazards Regression Analysis of Ventricular Systolic Pressure Reduction Post-Pulmonary Endarterectomy

Variables	Univariate	Multivariate		
	p value	*p* value	HR	95% CI
Age >70 years	0.841			
Male sex	0.031	0.860		
BMI	0.826			
Diabetes mellitus	0.999			
CKD (grade III–IV)	0.041	0.079		
Smoking history	0.999			
Prior PTE intervention	0.705			
MPA involvement	0.006	0.014	1.6	1.15–2.14
Bilateral involvement	0.197			
Neoplasia cause	0.029			
RVSP	0.203			
Low LVEF (≤35%)	0.185			

BMI, body mass index; CKD, chronic kidney disease; PTE, pulmonary thromboembolism; MPA, main pulmonary artery; RVSP, right ventricular systolic pressure; LVEF, left ventricle ejection fraction; HR, hazard ratio; CI, confidence interval.

after PEA, based on RVSP reduction. The multivariate Cox regression analysis confirmed MPA involvement to be a significant predictor of non-improvement in functional class (Table 5).

DISCUSSION

PTE is a major cause of morbidity and mortality worldwide. The pathophysiology of CTEPH gradually increases PVR and afterload of the right ventricle, resulting in morphological and functional changes in the right and left ventricles. As a result, cardiac output decreases, leading to death.

Several treatment options are available, but PEA is widely accepted as the gold standard due to improvements in symptoms, survival rates, and its curative outcomes. For patients who are considered unsuitable for surgery, targeted medical therapy and BPA are good alternatives. Lung or cardiopulmonary transplantation is the last available option.[10]

After initial positive outcomes at the University of California, PEA has become widely accepted as an appropriate treatment, with ongoing modifications to the technique. The recent worldwide in-hospital mortality rate is approximately 4.4% to 16%. Several studies have suggested that patients' NYHA class, 6-minute walk outcomes, and general condition are improved post-PEA. With the reduction of immediate post-operative complications and mortality rates, outcomes can be further improved.

In 2018, our team modified our surgical technique using a videoscope to remove lobar, segmental, and subsegmental lesions based on the techniques used at the University of California, San Diego. Since then, we have reported no in-hospital mortality and one case of overall mortality, with a 5-year survival rate of 95.5%. The effect of changes in surgical technique on the clinical outcomes and NYHA class needs to be studied in a larger patient group.

Most patients with CTEPH belong to NYHA class III or IV, with oxygen demands and severe dyspnea secondary to a ventilation-perfusion mismatch. Post-PEA, the mismatch was corrected by improved perfusion, resulting in better gas exchange. This led to improved symptoms, reduced oxygen requirements, and improved NYHA classification. Similarly, in our study, NYHA class III or IV, which accounted for 60% of the total patient group, improved to NYHA class I or II.

RV afterload generally decreases immediately post-PEA due to reduced pulmonary arterial pressures, leading to RV remodeling and improved TR. However, some patients with preoperative TR grade III and IV showed no post-operative improvement. Although controversial, tricuspid annuloplasty is a common concomitant surgery; RV hypertrophy exacerbates TR due to tricuspid annulus enlargement. Our center performed concomitant TAP in patients with severe tricuspid valve regurgitation or structural abnormalities of the tricuspid valve leaflets/chordae.[11-13] Among the uncorrected TR grade I or II patients, most gradings were improved, but none worsened. In addition, we confirmed that RVSP decreased gradually over time after PEA.

Our study also showed that MPA involvement was an independent predictor of non-improvement after PEA surgery. However, MPA involvement does not imply that surgical resection was difficult compared to lesions located in the subsegmental area. It means the patients with MPA involvement had higher disease severity. The patients had higher preoperative RVSP than those without MPA involvement (74.2 mm Hg vs. 67.1 mm Hg, p=0.012), suggesting more severe RV dysfunction preoperatively.

CTEPH is characterized by intraluminal thrombus organization, fibrosis, and subsequent unobstructed small vessel remodeling. These characterizations result in pulmonary hypertension and progressive right heart failure. Sustained pulmonary hypertension may lead to persistent right ventricle pressure

overload, tricuspid annular dilatation, and regurgitation. Therefore, TAP procedure is associated with better long-term right-side remodeling in CTEPH patients.[14] In this study, 19.2% of the patients underwent concomitant procedure of TAP. In both TAP and non-TAP groups, TR significantly improved after PEA with the exception of patients with severe RV dysfunction preoperatively. Furthermore, TAP was not a risk factor of poor prognosis after PEA (p=0.788).

Reperfusion lung injury accounted for the largest proportion of post-operative complications and usually occurred within 48 hours. Pulmonary edema, caused by increased blood flow and permeability in the lungs, leads to hypoxia and a new increase in opacity on chest radiography. Treatment methods for reperfusion injury include diuretics, hematocrit maintenance, ventilator management, and VV ECMO initiation. Post-operative corticosteroids can also be used to reduce complement activity and cytokine release after CPB. In recent studies, the obstructive ratio was found to be a predictor of reperfusion injury. One theory is that neurological injury is caused by DHCA; however, there is no clear evidence that DHCA causes cognitive decline post-PEA. Regular follow-up at 3, 6, and 12 months after surgery is important to determine any cognitive impairment. Pulmonary hypertension of 500 dynes/cm^{-5} or more persists post-PEA in a third of cases. According to the international CTEPH registry, persistent pulmonary hypertension occurs in 16.7% of patients, causing high early mortality. Although the cause remains unclear, further research is difficult since right-sided catheterization is not routine at most centers.[15]

The present study was limited in that it was a retrospective study conducted by a single surgeon in a single institution with a small number of patients. In addition, there were cases where CTEPH and acute PTE were mixed, leading to an ambiguous diagnosis. Some cases were also lost to follow-up. In future studies, we would perform CT and echocardiography within the first year, and then once every 2 years thereafter, according to the follow-up protocol of our hospital.

This study aimed to determine the clinical outcomes of CTEPH patients after PEA. We successfully performed PEA in 26 patients with CTEPH, with no in-hospital 30-day mortality. Few patients had post-operative complications, and RVSP and TR significantly decreased on post-operative echocardiography. The NYHA classifications of our patients improved post-operatively.

AUTHOR CONTRIBUTIONS

Conceptualization: Hyun-Soo Lee and Hyo-Hyun Kim. Data curation: Hyun Sik Kim. Formal analysis: Hyo-Hyun Kim. Investigation: Hyo-Hyun Kim. Methodology: Hyo-Hyun Kim. Project administration: Young-Nam Youn. Resources: Hyo-Hyun Kim. Software: Hyo-Hyun Kim. Supervision: Young-Nam Youn. Validation: Young-Nam Youn. Visualization: Hyo-Hyun Kim and Hyun Sik Kim. Writing—original draft: Hyun-Soo Lee and Hyo-Hyun Kim. Writing—review & editing: Young-Nam Youn. Approval of final manuscript: all authors.

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REFERENCES

1. Mahmud E, Madani MM, Kim NH, Poch D, Ang L, Behnamfar O, et al. Chronic thromboembolic pulmonary hypertension: evolving therapeutic approaches for operable and inoperable disease. J Am Coll Cardiol 2018;71:2468-86.
2. Lang IM, Pesavento R, Bonderman D, Yuan JX. Risk factors and basic mechanisms of chronic thromboembolic pulmonary hypertension: a current understanding. Eur Respir J 2013;41:462-8.
3. Ende-Verhaar YM, Cannegieter SC, Vonk Noordegraaf A, Delcroix M, Pruszczyk P, Mairuhu AT, et al. Incidence of chronic thromboembolic pulmonary hypertension after acute pulmonary embolism: a contemporary view of the published literature. Eur Respir J 2017;49:1601792.
4. Klepetko W, Mayer E, Sandoval J, Trulock EP, Vachiery JL, Dartevelle P, et al. Interventional and surgical modalities of treatment for pulmonary arterial hypertension. J Am Coll Cardiol 2004;43(12 Suppl):73S-80.
5. Jamieson SW, Kapelanski DP, Sakakibara N, Manecke GR, Thistlethwaite PA, Kerr KM, et al. Pulmonary endarterectomy: experience and lessons learned in 1,500 cases. Ann Thorac Surg 2003;76:1457-62; discussion 1462-4.
6. Keogh AM, Mayer E, Benza RL, Corris P, Dartevelle PG, Frost AE, et al. Interventional and surgical modalities of treatment in pulmonary hypertension. J Am Coll Cardiol 2009;54(1 Suppl):S67-77.
7. Mayer E. Surgical and post-operative treatment of chronic thromboembolic pulmonary hypertension. Eur Respir Rev 2010;19:64-7.
8. Mayer E, Klepetko W. Techniques and outcomes of pulmonary endarterectomy for chronic thromboembolic pulmonary hypertension. Proc Am Thorac Soc 2006;3:589-93.
9. Humbert M, Simonneau G, Pittrow D, Delcroix M, Pepke-Zaba J, Langleben D, et al. Oral anticoagulants (NOAC and VKA) in chronic thromboembolic pulmonary hypertension. J Heart Lung Transplant 2022;41:716-21.
10. Kim NH, Delcroix M, Jais X, Madani MM, Matsubara H, Mayer E, et al. Chronic thromboembolic pulmonary hypertension. Eur Respir J 2019;53:1801915.
11. D'Armini AM, Zanotti G, Ghio S, Magrini G, Pozzi M, Scelsi L, et al. Reverse right ventricular remodeling after pulmonary endarterectomy. J Thorac Cardiovasc Surg 2007;133:162-8.
12. Menzel T, Kramm T, Wagner S, Mohr-Kahaly S, Mayer E, Meyer J. Improvement of tricuspid regurgitation after pulmonary thromboendarterectomy. Ann Thorac Surg 2002;73:756-61.
13. Thistlethwaite PA, Auger WR, Madani MM, Pradhan S, Kapelanski DP, Jamieson SW. Pulmonary thromboendarterectomy combined with other cardiac operations: indications, surgical approach, and outcome. Ann Thorac Surg 2001;72:13-8.
14. Chikwe J, Itagaki S, Anyanwu A, Adams DH. Impact of concomitant tricuspid annuloplasty on tricuspid regurgitation, right ventricular function, and pulmonary artery hypertension after repair of mitral valve prolapse. J Am Coll Cardiol 2015;65:1931-8.
15. Jenkins D. Pulmonary endarterectomy: the potentially curative treatment for patients with chronic thromboembolic pulmonary hypertension. Eur Respir Rev 2015;24:263-71.

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