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Original Research

Programmed Follow-up and Quality Control of Treatment Techniques Enhance Chronic Thromboembolic Pulmonary Hypertension Management: Lessons From a Multidisciplinary Team

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AUTHOR'S SUMMARY

The role of multidisciplinary team in managing chronic thromboembolic pulmonary hypertension (CTEPH) is growing. Our center has established multidisciplinary team in 2015 and set strict indication for both pulmonary endarterectomy (PEA) and balloon pulmonary angioplasty along with patient follow-up evaluation plan. Since the adoption of multidisciplinary team, the number of CTEPH treatment has dramatically increased. Only 38 CTEPH patients have been treated for 18 years before the team, but 125 patients were treated after the team. In-hospital death after treatment was reported in only one PEA-based case. Multidisciplinary team has proven to show positive synergy in CTEPH management.

ABSTRACT

Background and Objectives: The recent developments in chronic thromboembolic pulmonary hypertension (CTEPH) are emphasizing the multidisciplinary team. We report on the changes in clinical practice following the development of a multidisciplinary team, based on our 7 years of experience.
Methods: Multidisciplinary team was established in 2015 offering both balloon pulmonary angioplasty (BPA) and pulmonary endarterectomy (PEA) with technical upgrades by internal and external expertise. For operable cases, PEA was recommended as the primary treatment modality, followed by pulmonary angiography and right heart catheterization after 6 months

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Conflict of Interest

The authors have no financial conflicts of interest.

Data Sharing Statement

The data generated in this study is available from the corresponding authors upon reasonable request.

Author Contributions

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to evaluate treatment effect and identify patients requiring further BPA. For patients with inoperable anatomy or high surgical risk, BPA was recommended as the initial treatment modality. Patient data and clinical outcomes were closely monitored.

Results: The number of CTEPH treatments rapidly increased and postoperative survival improved after team development. Before the team, 38 patients were treated by PEA for 18 years; however, 125 patients were treated by PEA or BPA after the team for 7 years. The number of PEA performed was 64 and that of BPA 342 sessions. World Health Organization functional class I or II was achieved in 93% of patients. The patients treated with PEA was younger, male dominant, higher pulmonary artery pressure, and smaller cardiac index, than BPA-only patients. In-hospital death after PEA was only 1 case and none after BPA.

Conclusions: The balanced development of BPA and PEA through a multidisciplinary team approach proved synergistic in increasing the number of actively treated CTEPH patients and improving clinical outcomes.

Keywords: Pulmonary thromboembolism; Pulmonary heart disease; Pulmonary hypertension; Quality control; Treatment outcome

INTRODUCTION

Chronic thromboembolic pulmonary hypertension (CTEPH) is a group of pulmonary vascular diseases characterized by chronic thrombi that persist in the pulmonary arteries, leading to pulmonary hypertension (PH) and subsequent right heart failure. Pathologically, CTEPH is characterized by chronic thrombi which are characterized as endothelization and unresponsive to anticoagulation.[1]

Traditionally, treatment for CTEPH has relied on pulmonary endarterectomy (PEA).[2] However, about one-third of the patients are not operable because of peripheral lesions or comorbidities of the patients. The introduction of balloon pulmonary angioplasty (BPA)[3][4] has made it possible to treat patients who are not candidates for surgical treatment.[5][6] Moreover, with the recognition of the effectiveness of pulmonary vasodilator therapy for CTEPH, there has been development in medical therapy as well.[7-9] Therefore, the treatment approach for CTEPH has become more complex, and the importance of a multidisciplinary approach[6][10][11] has risen from diagnosis to treatment planning. However, the availability of different treatment modalities may vary across centers and countries.[5] Considering the complex nature of CTEPH treatment, some centers focus on PEA,[12][13] while others without expert surgeons may choose to utilize BPA more frequently.[5][13] Therefore, achieving a balance in management based on the benefits of both treatment modalities is challenging.

In Asian countries, there is a limited number of large-volume centers with experienced surgeons[14-16] and multidisciplinary teams for the management of CTEPH. Furthermore, despite the recognition and emphasis given to the importance of multidisciplinary teams in guidelines and statements, there is a lack of readily available information regarding the specific methods and outcomes associated with the development of multidisciplinary teams in these regions. In this article, we aim to present our experience on how the practice has evolved following the implementation of a multidisciplinary team approach for CTEPH. Our approach involves a balanced starting point that encompasses both intervention and surgery, along with programmed follow-up and quality control of treatment techniques based on our 7-year experience.

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METHODS

Ethical statement

The study protocol was approved and the requirement for informed consent of individual patients was waived by the Institutional Review Board (IRB) of Samsung Medical Center (IRB No. 2023-06-123). This study was conducted according to the principles of the latest version (2013) of the Declaration of Helsinki.

Programming chronic thromboembolic pulmonary hypertension team development

Our center is a tertiary university hospital with over 2,000 in-hospital beds and previously relied solely on PEA with a small volume (less than 5 cases per year) before 2015. In 2015, we began developing a CTEPH team with the implementation of BPA. In the first stage, we selected dedicated team members and assigned roles, including PH specialist, interventionist, intensivist, thoracic surgeon, radiologist, pulmonologist, and nuclear medicine specialist. Interventionists and thoracic surgeon participated in short-term training at renowned overseas centers to assess the current state of the art and identify areas where new learning or improvement was needed.

The team conducted a review of the current state of technology and guidelines and identified areas of deficiency, utilizing a multidisciplinary team approach. The team standardized the diagnosis process, with an initial diagnostic work-up performed by PH specialists. This included laboratory testing, chest X-rays, electrocardiograms, transthoracic echocardiography (TTE), exercise tests, computed tomography (CT) angiography, lower extremity vein doppler, pulmonary function tests, lung ventilation/perfusion scans, right heart catheterization (RHC), and pulmonary angiography.

The diagnosis of CTEPH was confirmed through a multidisciplinary approach with input from radiologists, nuclear medicine specialists, and interventionists, based on the results from pulmonary angiography. Treatment planning was conducted with the discussion between thoracic surgeons, interventionists, and PH specialists.

For patients who required initial PEA, thoracic surgeons managed their care for 1 to 2 days postoperatively before transferring them to PH specialists and intensivists. Medical management was conducted by PH specialists, with follow-up imaging performed 6 months after PEA, including CT angiography, lung perfusion scans, TTE, exercise test, RHC, and pulmonary angiography. If significant residual lesions that produced symptoms remained, BPA was performed. Final mean pulmonary arterial pressure (mPAP) was acquired immediately after BPA in patients treated with BPA or during RHC without BPA procedures (in the case of PEA without additional BPA).

For BPA-treated patients, medical treatment and follow-up were also provided by PH specialists. The team shared the clinical course and final outcomes for both PEA and BPA strategies. Quality control and improvement were achieved through periodic meetings to provide feedback, and all patient data was stored in a database.

The decision for the final session of BPA (with no further plans for additional BPA procedures in the near future) was made by the multidisciplinary team based on several factors. These factors included achieving the desired level of hemodynamic improvement, as well as

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considering the patients' perspective on their exercise capacity and quality of life. Non-medical reasons, such as financial constraints, were also considered when determining the timing of the final BPA session.

Evaluation of clinical outcomes after development of the chronic thromboembolic pulmonary hypertension program

Since the development of the program in December 2015, CTEPH or chronic thromboembolic disease patients have been enrolled in the program's database. Patients who were lost to follow-up early, defined as those who had less than 3 outpatient clinic visits or declined treatment at our center after the initial diagnosis, were excluded from the registry database.

The patient information collected includes basic demographic data, examination results, hemodynamic information, treatment details (PEA vs. BPA, hybrid BPA), reasons for BPA treatment, treatment complications, mortality, and clinical outcomes after treatment. Major complication was defined as fatal event, non-fatal event with additional surgical procedures or interventions or cerebral vascular accident. Minor complications were transient complication with minimal support but prolonged the admissions or medical assistants.

Patients were further categorized into 2 groups: PEA-based group (patients who were treated with PEA with or without BPA) or BPA-only group (patients who were treated exclusively with BPA without surgery). Two patients who underwent surgery was considered as BPA-only group because review of the image suggested that surgery was under quality with thrombectomy only. Therefore, patients who underwent PEA in our center were only considered as PEA-based group. Those groups were analyzed separately to evaluate their respective outcomes and characteristics. The annual number of PEA procedures performed prior to the program was identified from the surgical records list covering the period from November 1994 to December 2015. To compare the clinical outcomes after PEA, a review of medical records was also conducted for those patients.

Statistical analysis

The baseline characteristics were summarized using continuous variables, expressed as mean ± standard deviation or median with interquartile range. Categorical data were presented as a percentage and the number of events. Paired t-tests or Wilcoxon rank sum tests were used for the analysis of continuous variables, depending on the data distribution. Chi-square test was employed for comparing the number of events. Correlation analysis was conducted using Spearman's rho for nonparametric parameters. All statistical analyses were performed using SPSS software version 23.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

Treatment patterns change after team development

Prior to the development of the multidisciplinary team, a total of 38 patients underwent PEA over a span of 18 years, averaging 2.1 patients per year. However, after the team's establishment, a total of 125 patients underwent either PEA or BPA over the course of the last 7 years, averaging 18 patients per year. Specifically, 64 patients underwent PEA, while 98 patients underwent BPA, totaling 342 BPA sessions. Among the 98 patients treated with BPA, 38 patients had also undergone PEA as part of a hybrid approach (**Figure 1**).

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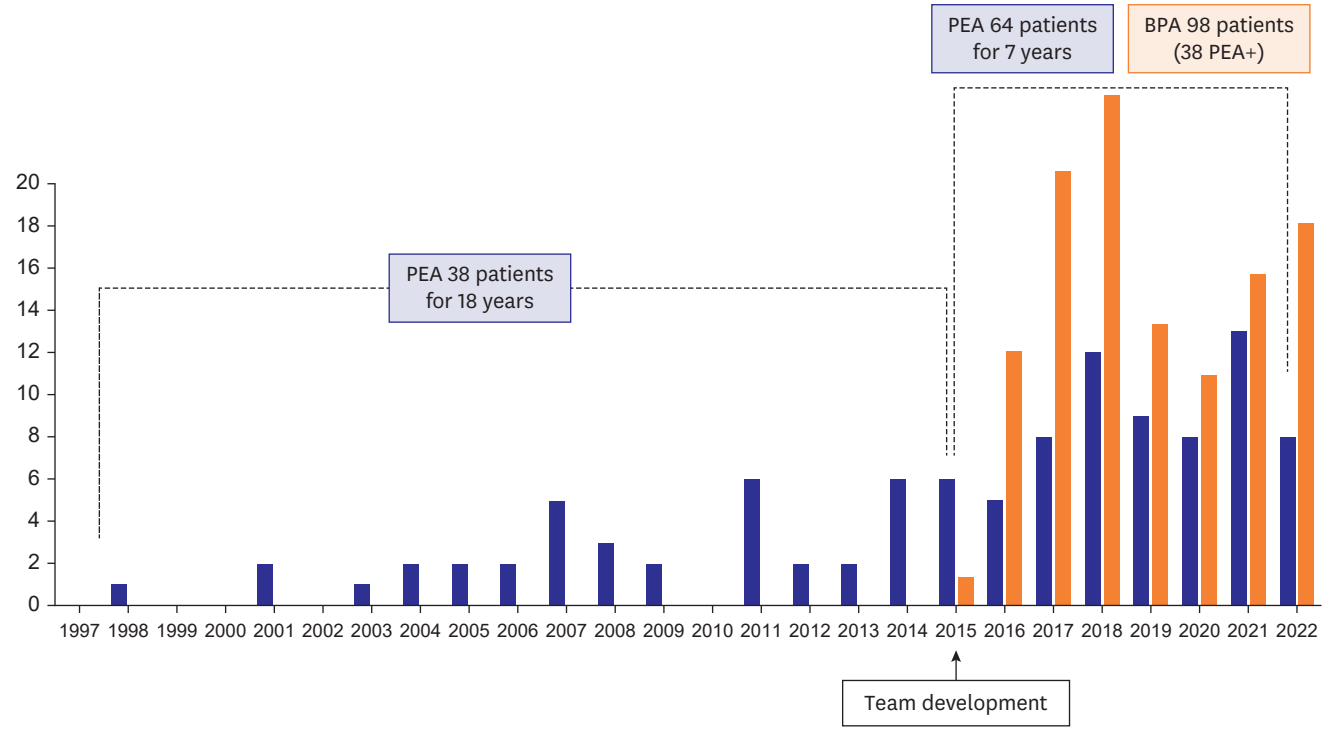

Figure 1. Number of CTEPH patients before and after CTEPH team development. The annual number of PEA cases is represented by the blue bar, while the orange bar represents the annual number of BPA cases.
BPA = balloon pulmonary angioplasty; CTEPH = chronic thromboembolic pulmonary hypertension; PEA = pulmonary endarterectomy.

Figure 2 provides a comprehensive summary of the treatment approaches for the patients in detail. Out of the total 125 actively treated patients, 64 underwent PEA in our center following the establishment of the multidisciplinary team. Among the PEA cases, 2 were redo procedures. Following PEA, 27 patients did not require additional treatment with BPA, while 35 patients underwent elective hybrid BPA performed 6 months after the surgery. In 2

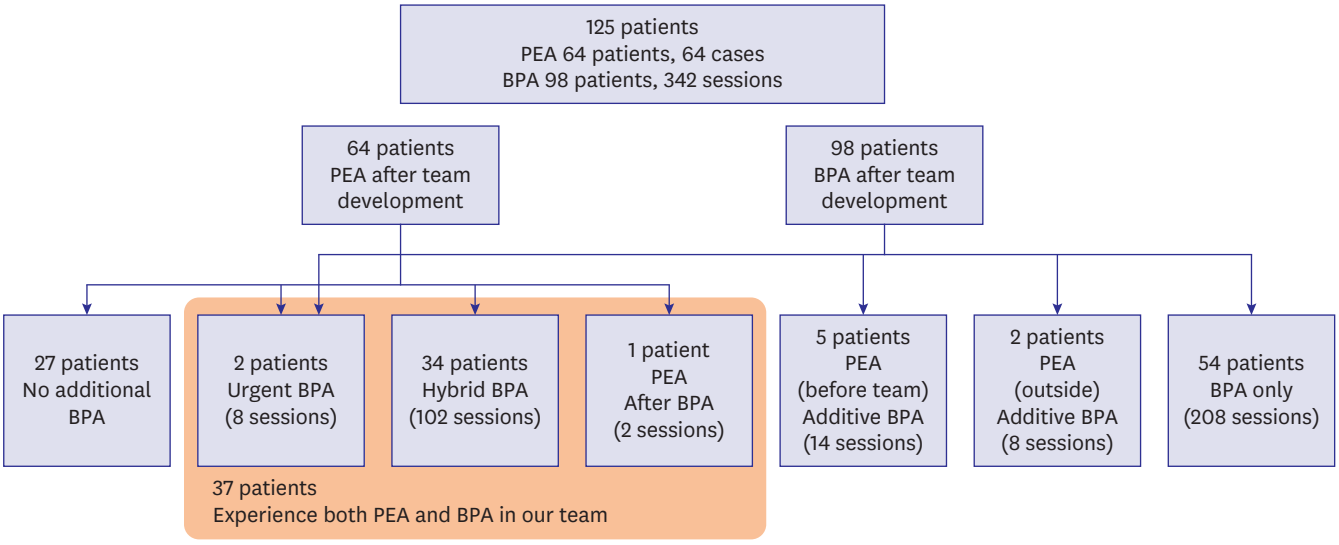

Figure 2. Details of treatment of chronic thromboembolic pulmonary hypertension patients after multidisciplinary team development.
BPA = balloon pulmonary angioplasty; PEA = pulmonary endarterectomy.

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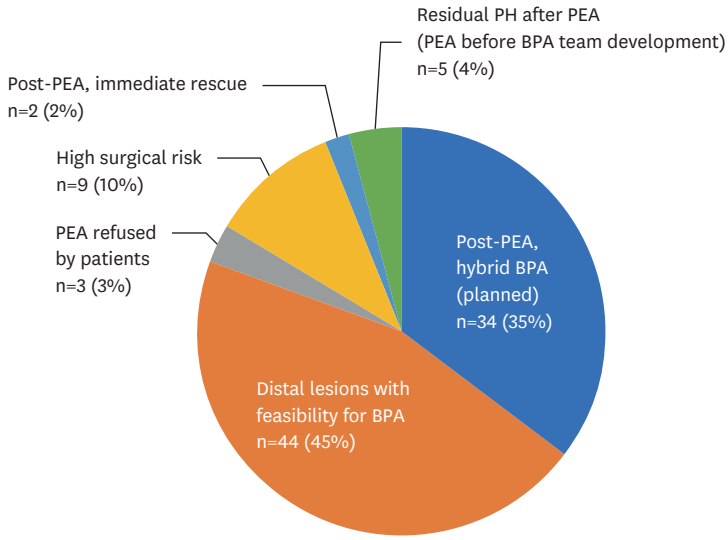

Figure 3. The reasons for performing BPA.
BPA = balloon pulmonary angioplasty; PEA = pulmonary endarterectomy; PH = pulmonary hypertension.

cases, urgent rescue BPA was performed due to the presence of recurrent or residual lesions accompanied by unstable vital signs. Remarkably, one of these patients was successfully rescued. One patient had a history of unsuccessful BPA (2 sessions) but achieved excellent outcomes following PEA. Additionally, 98 patients were treated with BPA, and 37 patients overlapped with those who had also undergone PEA (hybrid, rescue or preoperative BPA). Two patients had a history of PEA performed elsewhere and 5 underwent PEA in our center prior to the establishment of the team, and the indication for BPA in these cases was residual PH with symptoms or recurrence of CTEPH. Finally, 54 patients received BPA treatment exclusively, without any surgical intervention.

The reason for BPA was summarized in **Figure 3**. The most common reason is CTEPH with distal lesions which is feasible for BPA. The second was the post-PEA status with residual lesions (hybrid BPA). The third was a high surgical risk of the patients such as age, lung disease, and multiple comorbidities.

Baseline characteristics of patients by treatments

Table 1 provides an overview of the baseline clinical characteristics of the patients. All patients in the study presented with symptoms, and there was a slight predominance of female patients in the overall population. N terminal pro B-type natriuretic peptide (NT-proBNP) levels were elevated in all patients, and anticoagulant therapy was administered to all individuals. The use of vasodilators, specifically off-label sildenafil, was limited (11%).

When comparing the PEA-based and BPA-only patient groups, the PEA-based group was found to be younger ($p=0.004$) and had a higher proportion of male patients ($p<0.001$). Diabetes was more prevalent in the BPA-only group ($p=0.02$), while hemoglobin levels were higher in the PEA-based group ($p<0.001$). Thrombophilia, both hereditary and antiphospholipid syndrome, was more common in the PEA-based group ($p<0.001$). The PEA-based group also had a higher number of patients with unstable vital signs, including cases of acute-on-chronic or unstable chronic severe CTEPH (11.6%), which required urgent

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Table 1. Clinical data at baseline

Characteristics	Total (n=125)	PEA-based (n=69)	BPA-only (n=56)
Age* (year)	54.2±16.0	50.6±14.9	58.7±16.2
Sex† (male %)	54 (43)	36 (52)	18 (32)
Body surface area (m^2)	1.74±0.26	1.77±0.26	1.71±0.27
Previous DVT	32 (26)	19 (28)	13 (23)
Previous acute PE	111 (89)	61 (88)	50 (89)
Thrombophilia‡	35 (28)	25 (36)	10 (18)
Hereditary	23 (18)	16 (23)	7 (13)
APLS	12 (10)	9 (13)	3 (5)
Hypertension	24 (19)	10 (15)	14 (25)
Diabetes†	6 (7.2)	1 (11)	8 (14)
Cancer	6 (4.8)	3 (4.3)	3 (5.4)
WHO FC (II/III/IV)	50/58/17 (40/46/14)	25/32/12 (36/46/17)	25/26/5 (40/46/14)
Previous PEA	5 (4)	3 (4.3)	2 (3.6)
Mode of presentation			
Acute on chronic	6 (4.8)	6 (8.7)	0
Unstable chronic severe	2 (1.6)	2 (2.9)	0
Stable chronic	117 (93.6)	61 (88.4)	56 (100)
Hemoglobin†	13.8±1.9	14.3±2.0	13.2±1.8
D-dimer	1.29±2.90	1.51±3.14	1.0±2.6
Cholesterol	170.8±37.5	171.7±37.0	170.0±38.5
GFR (mL/min/1.73 m^2)	84.6±21.3	86.9±20.6	81.8±21.9
NT-proBNP (pg/dL)	1,321.7±1,982.9	1,479.5±2,156.1	1,123.0±1,740.1
Anticoagulation			
Warfarin	68 (54)	37 (54)	26 (46)
NOAC	67 (46)	32 (46)	29 (52)
Sildenafil use	14 (11)	5 (7.2)	9 (16.1)

Values are presented as number (%) or mean ± standard deviation.
APLS = antiphospholipid syndrome; BPA-only = patients who were treated exclusively with balloon pulmonary angioplasty without surgery; DVT = deep vein thrombosis; GFR = glomerular filtration rate; NOAC = novel oral anticoagulant; NT-proBNP = N terminal pro B-type natriuretic peptide; PE = pulmonary embolism; PEA = pulmonary endarterectomy; PEA-based = patients who were treated with pulmonary endarterectomy with or without balloon pulmonary angioplasty; WHO FC = World Health Organization functional class.
*p=0.004, †p<0.001, ‡p = 0.02.

or emergent surgery. Although NT-proBNP levels were higher in the PEA-based group, the difference was not statistically significant.

Hemodynamic data were obtained for a total of 118 patients, excluding 7 patients from the PEA-based group who could not undergo evaluation before PEA due to unstable vital signs. Therefore, hemodynamic data were available for 62 patients in the PEA group. **Table 2** presents the baseline hemodynamic parameters for both groups. The PEA-based group demonstrated higher mPAP and mean pulmonary arterial pulse pressure. Additionally, the PEA-based group exhibited a lower cardiac index (CI). However, there were no significant differences observed in pulmonary vascular resistance (PVR) and the distance covered in the 6-minute walk test distance (6MWD) between the 2 groups.

Clinical outcomes

Functional improvement was assessed in the patient population. At baseline, all patients exhibited significant symptoms, with 60% experiencing World Health Organization functional class (WHO FC) III or IV dyspnea. Following treatment, 63 patients (50.4%) achieved asymptomatic status, and 90% of patients (n=113) achieved a mild symptomatic status (WHO FC I or II).

Figure 4 illustrates the functional improvement observed after treatment in the overall population and within each treatment strategy. The baseline distribution of WHO FC did not

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Table 2. Hemodynamics at baseline

Parameters	Total (n=118)	PEA-based (n=62)	BPA-only (n=56)
PCWP	9.3±4.0	9.5±4.2	9.0±3.6
mPAP*	40.6±12.2	44.4±11.7	36.2±11.4
mSAP	93.3±15.0	91.7±12.9	95.0±16.8
mRAP	8.12±5.6	8.4±5.0	7.8±6.2
mPAPP*	42.7±15.4	47.7±15.0	37.0±13.9
Heart rate	75.3±14.1	75.9±13.4	74.6±14.9
SvO_2	66.6±10.8	65.4±11.2	68.0±10.0
Cardiac output	4.59±1.61	4.44±1.50	4.75±1.72
Cardiac index†	2.63±0.80	2.48±0.71	2.79±0.87
PVR	667.2±425.7	749.3±429.1	573.1±405.5
6MWD	390.0±114.5	388.6±119.8	391.3±110.7

Number of 6MWD was available in 52 and 50 in each group (total n=112).
6MWD = 6-minute walk test distance; BPA-only = patients who were treated exclusively with balloon pulmonary angioplasty without surgery; mPAP = mean pulmonary arterial pressure; mPAPP = mean pulmonary arterial pulse pressure; mRAP = mean right atrial pressure; mSAP = mean systolic arterial pressure; PCWP = pulmonary capillary wedge pressure; PEA-based = patients who were treated with pulmonary endarterectomy with or without balloon pulmonary angioplasty; PVR = pulmonary vascular resistance; SvO_2 = mixed venous oxygen saturation.
*p<0.001, †p=0.026.

differ significantly between the PEA-based and BPA-only treatment groups. However, a higher proportion of patients in the PEA-based group (n=47, 70%) achieved WHO FC I compared to the BPA-only group (n=24, 42%) (p<0.001). After treatment, more than 90% of patients in both the PEA-based and BPA-only groups achieved a mild symptomatic status (WHO FC I or II).

Significant changes were observed in 6MWD, NT-proBNP levels, and mPAP after treatment in both the PEA-based and BPA-only groups (**Table 3**). Although the baseline mPAP was higher in the PEA-based group compared to the BPA-only group (p<0.001), the final mPAP was significantly lower in the PEA group than the BPA-only group (p=0.006).

In the group of patients who underwent PEA with hybrid BPA, 60 out of 64 patients had follow-up RHC 6 months after surgery. Among these patients, mPAP measurements after 6 months were available for 57 patients. It was found that 17 patients (26.6% of the overall PEA patients) had mPAP levels ≥30 mmHg at this follow-up. After undergoing hybrid BPA, 11 patients still had mPAP levels ≥30 mmHg. Notably, there was a statistically significant decrease in mPAP from 28.5 mmHg before BPA to 24.8 mmHg after hybrid BPA (p=0.002). In the BPA-only group, 18 patients (32.1% of the group) still had mPAP levels ≥30 mmHg

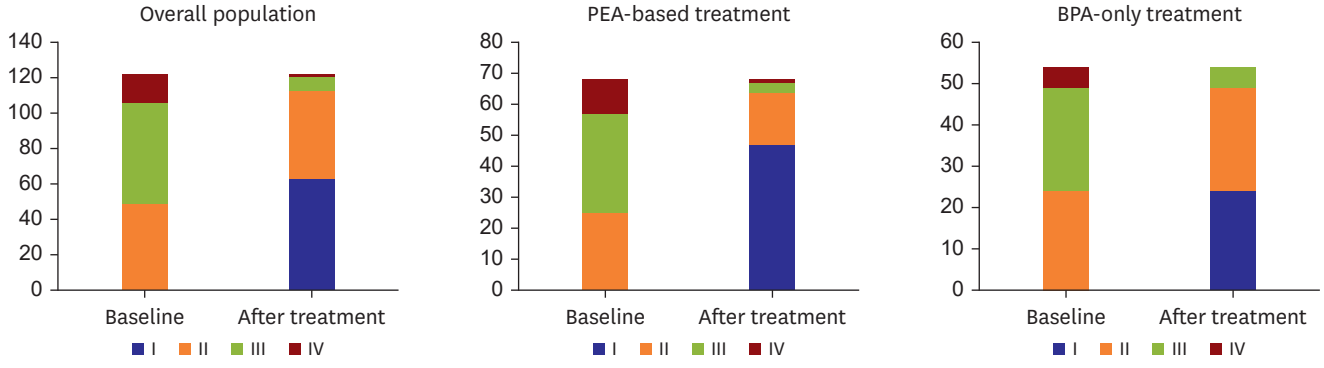

Figure 4. Functional improvement after treatment in overall population and by treatment strategy.
BPA-only = patients who were treated exclusively with balloon pulmonary angioplasty without surgery; PEA-based = patients who were treated with pulmonary endarterectomy with or without balloon pulmonary angioplasty.

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Table 3. Clinical outcomes

Outcome measures	PEA-based		BPA-only	
	Baseline	Final	Baseline	Final
WHO FC	2.79±0.70	1.38±0.65	2.65±0.65	1.80±0.60
6MWD (m)	344.7±159.7	475.5±107.5	366.3±130.5	432.2±118.3
NT-proBNP (pg/dL)	1,434.9±2,181.5	233.0±535.0	1,130.4±1,741.3	311.9±793.8
mPAP (mmHg)	44.5±11.3*	23.9±7.2†	37.5±11.3*	27.3±6.8†

Available number of data was as follows: WHO FC 68/46, 6MWD 41/49, NT-proBNP 64/54, mPAP 47/40 for PEA-based (total n=69)/BPA-only (total n=56), respectively.
6MWD = 6-minute walk test distance; BPA-only = patients who were treated exclusively with balloon pulmonary angioplasty without surgery; mPAP = mean pulmonary artery pressure; NT-proBNP = N terminal pro B-type natriuretic peptide; PEA-based = patients who were treated with pulmonary endarterectomy with or without balloon pulmonary angioplasty; WHO FC = World Health Organization functional class.
*p<0.001, †p=0.006.

at the final measurement of mPAP obtained during RHC. It is important to note that these measurements were taken either at the beginning of the last session of BPA or immediately after the completion of the last BPA procedure.

For overall BPA procedures, the number of BPA sessions per patient was 3.40±2.49 sessions (range 1–12), and the number of segmental arteries per session was 4.64±1.37 vessels (range 1–8) in overall patients. In the hybrid group, the number of BPA sessions per patient was 2.90±0.35, while in the BPA-only group, it was 3.77±2.60. The number of vessels per session was 4.40±1.60 for the hybrid group and 4.81±1.14 for the BPA-only group, respectively. Although the number of BPA sessions per patient was higher in the BPA-only group, there was no significant statistical difference (p=0.09).

The number of BPA sessions per patient was significantly correlated with mPAP and PVR measured before BPA (r=0.57, p<0.001 and r=0.50, p<0.001 by Spearman's rho). However, the number of branches per session did not show a significant correlation with mPAP or PVR, as the number of BPAs per session was mainly dependent on the procedural time limit (within 2 hours) and technical difficulties encountered during clinical practice. CI was not correlated with the number of BPA sessions per patient.

Complications

Table 4 summarized the complications of each procedure. PEA related in-hospital death was only one patient one month after surgery because of multiple complications including reperfusion injury, persistent PH, subdural hemorrhage, and failure to weaning

Table 4. Complications of each procedure

Major	Minor
· Persistent more than a month · Need mechanical support or redo surgery or rescue BPA	· Resolved within a week with medical support
· PEA related (6/65 cases) - In-hospital death after one month d/t multiple complications (n=1)* - Persistent thrombus with CPB weaning failure (n=1) - Postoperative bleeding (n=1) - Cerebral vascular accident (n=3)	· PEA related (14/65 cases) - Reperfusion injury (n=7)† - New onset atrial fibrillation (n=1) - Postoperative pericarditis (n=5) - Wound dehiscence (n=1)
· BPA related (0/342 sessions) - None	· BPA related (18/342 sessions) - Vessel dissection (n=7) - Vessel perforation (n=8) - Hemoptysis (delayed) (n=2) - Reperfusion injury (n=1)

BPA = balloon angioplasty; CPB = cardiopulmonary bypass; PEA = pulmonary endarterectomy.
*Reperfusion injury, persistent pulmonary hypertension, subdural hemorrhage, failure to weaning.
†Mild reperfusion injury resolved within a week.

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cardiopulmonary bypass. Major complications were less than 10% and minor complication including mild reperfusion injury was noted in 21% of the cases. Reperfusion injury was noted in 8 patients (12.5%) however most of them (n=7) were fully recovered with medical therapy. There was no major complication in BPA and minor complications were reported in 5% of the BPA sessions.

When compared to the clinical outcomes before team development, there were 38 patients who underwent PEA before 2015. In-hospital mortality (including lung transplantation) after PEA was 13.2% (n=5). Four of them (10.5%) died within a month after PEA, and one was treated by heart-lung transplantation. The 1-year survival rate was 86.8% (n=33).

Sixty-four patients underwent PEA after 2015 (including 2 cases of redo-PEA), and in-hospital mortality was 1.6% (n=1). There were no deaths within 1 month after PEA. The 1-year survival rate was 96.9% (n=62). In-hospital mortality and 1-year survival between PEA before the team and after the team were significantly different (p=0.016). The complication rate was also different. RV failure and reperfusion injury were common in patients undergoing PEA before the team, with a rate of 39.5% (n=15), while it was only 12.5% (n=8) after the team (p=0.003).

DISCUSSION

This study aimed to investigate the implementation and clinical impact of a multidisciplinary team approach in the management of CTEPH. The utilization of a predetermined and collaborative clinical decision-making process, along with a standardized treatment pathway and regular feedback, led to notable improvements both in terms of quality and quantity. Moreover, the inclusion of routine pulmonary angiography follow-up after PEA and the administration of adjuvant BPA played a crucial role in resolving residual PH in the majority of patients. This feedback mechanism also contributed to the refinement and enhancement of surgical techniques.

In our country, the performance of PEA was limited to a few large university hospitals, including our own, and there was a shortage of qualified surgeons who met international standards. BPA had not yet been introduced before team development, requiring technical upgrading and training for both techniques. To initiate the team approach, it was crucial to establish mutual trust, leading both parties to visit expert centers abroad as an initial step. Additionally, the appointment of PH specialists to oversee patient diagnosis, perioperative and periprocedural treatments, and subsequent medical therapy was implemented to ensure a balanced approach between surgery and intervention, as well as to facilitate mutual feedback on clinical outcomes. Despite the emphasis placed on multidisciplinary teams in CTEPH management by European Society of Cardiology/European Respiratory Society guidelines, the formation of such teams presents various challenges in reality. Moreover, there is a scarcity of comprehensive data from large centers that specifically present the methods and outcomes of multidisciplinary teams. Therefore, this study provides valuable insights by demonstrating the specific methods employed to establish a multidisciplinary team and the process through which an expert center was developed.

The number of patient recruitments has rapidly increased for both BPA and PEA candidates, driven by the growing interest in diagnosing and treating patients both within and outside the hospital. This increase can be attributed to factors such as increased referrals, patients

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seeking treatment based on the team's reputation, and a heightened focus on recruiting eligible patients. The number of patients treated with the PEA-based strategy is comparable to the number treated with the BPA-only approach.

When comparing the clinical characteristics of the 2 strategies, the PEA-based group tends to have more severe disease, including a higher prevalence of thrombophilia, higher mPAP, and lower CI. Additionally, this group has a lower medical risk profile, characterized by younger age, less percentage of diabetes and anemia. Considering that a significant percentage of patients in the BPA-only group had high surgical risk or refused surgery as the reason for their treatment choice, the characteristics of the BPA-only group are not surprising. The BPA-only group in our study had a higher proportion of women, which aligns with previous reports[17] indicating a trend toward avoiding cardiac surgery procedures.

The significant symptomatic improvement observed in the PEA-based group compared to the BPA-only group can be attributed to the fact that the PEA-based group primarily consisted of patients with central lesions and a heavy disease burden. Successful removal of these central lesions through PEA has a greater impact on functional improvement in patients. However, it should be noted that not all patients in either group achieved normal pulmonary arterial pressure. The presence of residual lesions that cannot be resolved by additional BPA or possible endothelial dysfunction requiring additional medical therapy may contribute to the incomplete normalization of pulmonary arterial pressure in some cases. Furthermore, some patients may have been satisfied with their symptomatic status and opted not to undergo further BPA procedures. Additionally, it's important to mention that our study did not include additional RHC after the completion of BPA. Therefore, the final achievement of hemodynamic profiles may be lower than initially described, as pulmonary vascular remodeling can take several months to stabilize following BPA.[3]

It is true that preferred treatment methods for CTEPH can differ depending on medical circumstances and regional practices. The worldwide prospective CTEPH registry[5] reported data from 34 centers in 10 countries, with the majority from European countries (78%), 11% from America and other regions, and 11% from Japan. The data revealed significant variations in treatment practices across regions. In Europe, PEA was the primary treatment choice for 72% of CTEPH cases, while in Japan, that number was only 23.5%. Conversely, BPA was more commonly utilized in Japan, accounting for 68.7% of cases compared to 13.7% in Europe. The distribution in America and other regions resembled that of Europe. Recently published data from China[18] and Poland[19] also showed a similar distribution of PEA and BPA treatment strategies. On the other hand, it is worth noting that until recently, BPA was not available in some developing countries.

Our multidisciplinary team, employing a hybrid approach, has developed in a setting where previous systems were limited. Despite this, we have achieved a similar distribution in treatment strategies between PEA-based and BPA-only approaches. It is important to recognize that both PEA and BPA play vital roles in the treatment of CTEPH, and there is no definitive guidance applicable to all cases. The choice of treatment strategy should be tailored to each patient's unique medical conditions. Our experiences can provide guidance for the development of multidisciplinary CTEPH teams in settings with limited prior infrastructure.

The development of such teams should consider the local context, available resources, and expertise. Regional practices and preferences may influence the selection of treatment

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methods. By sharing our experiences and lessons learned, we can contribute to the advancement of CTEPH management globally.

Medical treatment plays a significant role in the management of CTEPH.[7-9] However, it is unfortunate that insurance reimbursement and the availability of certain drugs for CTEPH treatment are still limited in some countries, including ours. As a result, our data regarding the use and effectiveness of medical therapy in CTEPH is limited.

The development of a multidisciplinary team approach for CTEPH, incorporating both technical improvements in BPA and PEA, has demonstrated significant enhancements in the quality and quantity of patient care. By fostering synergy among team members, this approach has facilitated a balanced upgrade of both treatment modalities. The systematic integration of various disciplines has contributed to improved clinical outcomes and expanded treatment options for patients with CTEPH.

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