



The effect of a multidisciplinary team on the implementation rates of major diagnostic and therapeutic procedures of chronic thromboembolic pulmonary hypertension

Dong Kyu Oh, MD^a, Jong-Min Song, MD, PhD^{b,f}, Duk-Woo Park, MD, PhD^{b,f}, Sang Young Oh, MD^{c,f}, Jin-Sook Ryu, MD, PhD^{d,f}, Jaewon Lee, MD, PhD^{e,f}, Sang Do Lee, MD, PhD^a, Jae Seung Lee, MD, PhD^{a,f,*}

^a Department of Pulmonology and Critical Care Medicine, University of Ulsan College of Medicine, Asan Medical Center, Seoul, Republic of Korea

^b Department of Cardiology, University of Ulsan College of Medicine, Asan Medical Center, Seoul, Republic of Korea

^c Department of Radiology, University of Ulsan College of Medicine, Asan Medical Center, Seoul, Republic of Korea

^d Department of Nuclear Medicine, University of Ulsan College of Medicine, Asan Medical Center, Seoul, Republic of Korea

^e Department of Thoracic and Cardiovascular Surgery, University of Ulsan College of Medicine, Asan Medical Center, Seoul, Republic of Korea

^f Pulmonary Hypertension and Venous Thrombosis Center, University of Ulsan College of Medicine, Asan Medical Center, Seoul, Republic of Korea

ARTICLE INFO

Article history:

Received 10 February 2018

Received in revised form 16 July 2018

Accepted 16 July 2018

Available online 14 August 2018

Keywords:

Chronic thromboembolic pulmonary hypertension

Disease management

Interdisciplinary communication

Pulmonary embolism

Pulmonary hypertension

ABSTRACT

Background: Although guidelines have recommended that patients with chronic thromboembolic pulmonary hypertension (CTEPH) should be managed by a multidisciplinary team (MDT), there is a lack of clinical data indicating that the MDT improves CTEPH management.

Objectives: The study aimed to identify the effect of an MDT on CTEPH management.

Methods: We divided the study period into pre-MDT and post-MDT eras and compared the implementation rates of major diagnostic and therapeutic procedures.

Results: Of 116 patients with CTEPH, 42 (36.2%) were diagnosed in the post-MDT era. The implementation rates of right heart catheterization (10.8% vs. 97.6%, $p < 0.001$) and pulmonary endarterectomy (32.4% vs. 59.5%, $p < 0.005$) were significantly increased in the post-MDT era. Balloon pulmonary angioplasty was not performed in the pre-MDT era but was performed in the post-MDT era.

Conclusions: The MDT appears to be associated with improved CTEPH management.

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Introduction

Pulmonary hypertension is a pathophysiological disorder defined as an increase in the mean pulmonary arterial pressure (PAP) at rest (≥ 25 mmHg) and can complicate the majority of cardiovascular and respiratory diseases.¹ The prevalence of the disease has been reported

in 97 cases per million with a female to male ratio of 1.8, and the age-adjusted mortality rate ranges from 4.5 to 12.3 per 100,000 population.¹ Chronic thromboembolic pulmonary hypertension (CTEPH) is a distinct subtype of pulmonary hypertension (group 4) characterized by obstructive pulmonary artery remodeling resulting from major vessel thromboembolism.^{1–3} The prevalence and incidence of CTEPH have been reported in 3.2 cases per million and 0.9 cases per million each year, respectively, and the burden of the disease is expected to increase over the next decade.^{4–6}

However, the timely and accurate diagnosis of CTEPH remains a challenge due to non-specific signs and symptoms in the early phase of the disease.^{1,7} In addition, because of the complex nature of its pathophysiology, diagnosis requires multi-stage procedures including echocardiography, pulmonary function tests (PFTs), ventilation/perfusion scanning (V/Q scanning), computed tomography (CT) or conventional pulmonary angiography, and right heart catheterization (RHC).¹ Therefore, recent guidelines and review articles have recommended that patients should be referred to a CTEPH expert center with a multidisciplinary team (MDT) as soon as the disease is suspected.^{1,8}

Abbreviations: Ao, aorta; BMI, body mass index; BPA, balloon pulmonary angioplasty; CO, cardiac output; CT, computed tomography; CTEPH, chronic thromboembolic pulmonary hypertension; IVC, inferior vena cava; LVEDD, left ventricle end-diastolic diameter; LVEF, left ventricle ejection fraction; MDT, Multidisciplinary team; Pa, pulmonary artery; PAP, pulmonary arterial pressure; PCWP, pulmonary capillary wedge pressure; PEA, pulmonary endarterectomy; PFTs, pulmonary function tests; PVR, pulmonary vascular resistance; RAP, right atrial pressure; RHC, right heart catheterization; SD, standard deviation; TRV, tricuspid regurgitation velocity; V/Q scanning, ventilation/perfusion scanning; WHO, World Health Organization

* Corresponding author. Department of Pulmonology and Critical Care Medicine, Pulmonary Hypertension and Venous Thrombosis Center, University of Ulsan College of Medicine, Asan Medical Center, 88, Olympic-ro 43-gil, Songpa-gu, Seoul 05505, Republic of Korea.

E-mail address: jsdoc1186@daum.net (J.S. Lee).

Although CTEPH may be treated by pulmonary endarterectomy (PEA), the lack of well-defined criteria for PEA can lead to wide variations in the assessment of operability between centers with low volumes and those with intermediate or high volumes, suggesting that both the center's and the medical professional's level of expertise may influence operability.⁹ As PEA is the only definitive treatment option for CTEPH, it has been strongly recommended that the patients should be managed by an MDT of experts including experienced PEA surgeons and CTEPH physicians.^{1,8–15}

Despite these theoretical advantages, there is a lack of clinical data indicating that the establishment of an MDT improves CTEPH management. Therefore, this study was conducted to identify the effect of an MDT on the management of CTEPH, especially on the implementation rates of major diagnostic and therapeutic procedures that are essential for the management of the disease. Additionally, we analyzed the effect of an MDT on post-PEA outcomes.

Methods

Study design and population

The study was performed in a tertiary referral teaching hospital with 2700 beds in Seoul, Korea. The data were retrospectively collected from patients who were ≥ 18 years old and diagnosed with CTEPH between December 1994 and October 2017. The hospital's CTEPH expert center with an MDT was established on 1 November 2013. Based on these dates, we divided the study period into two eras: pre-MDT (from December 1994 to October 2013) and post-MDT (from November 2013 to October 2017). Patients were followed up until death, loss to follow-up, or the end of the study period (31 December 2017).

The MDT met once or twice a week and consisted of CTEPH professionals including a pulmonologist, a cardiologist expert in pulmonary hypertension, an interventional cardiologist for RHC and balloon pulmonary angioplasty (BPA), a cardiothoracic surgeon for PEA, an experienced chest radiologist, and a clinical nurse specialist. In the clinic, the professionals reviewed patient medical records together and determined the best diagnostic and therapeutic strategies for the patients.

CTEPH was diagnosed based on the following criteria: (1) at least 3 months of effective anticoagulation prior to diagnosis, (2) ≥ 1 mismatched segmental perfusion defect on lung V/Q scanning with signs suggesting CTEPH on conventional and/or CT pulmonary angiography, and (3) a mean PAP of ≥ 25 mmHg with a pulmonary capillary wedge pressure (PCWP) of ≤ 15 mmHg on RHC.¹ For patients without RHC, pulmonary hypertension was assessed by echocardiography based on the following criteria: (1) a peak tricuspid regurgitation velocity (TRV) of > 3.4 m/s or (2) a peak TRV of 2.9–3.4 m/s and the presence of other signs of pulmonary hypertension on echocardiography.¹ These signs included (1) a right ventricle/left ventricle basal diameter ratio of > 1.0 , (2) a flattening of the interventricular septum, (3) a right ventricular outflow Doppler acceleration time of < 105 ms and/or mid-systolic notching, (4) an early diastolic pulmonary regurgitation velocity of > 2.2 m/s, (5) an inferior vena cava (IVC) diameter of > 21 mm with decreased inspiratory collapse, and (6) a right atrial area (end-systole) of > 18 cm.¹ Additionally, laboratory tests, PFTs, lung V/Q scanning, chest radiography, and CT pulmonary angiography were performed to discriminate CTEPH from other types of pulmonary hypertension.

The study was approved by the institutional review board of our hospital (2015-0516). Because of the retrospective nature of the study, the requirement for informed consent was waived.

Data collection

Data on baseline characteristics were retrieved at the time of diagnosis, which included age, gender, body mass index (BMI), severity of

symptoms assessed by the World Health Organization (WHO) functional class, comorbidities assessed by the Charlson comorbidity index, and laboratory tests. For patients who underwent PEA, additional information was collected to evaluate post-PEA outcomes including the occurrence of reperfusion pulmonary edema, reoperation, in-hospital mortality, and residual pulmonary hypertension. Residual pulmonary hypertension was assessed by echocardiography after 3–6 months from PEA based on the outlined echocardiographic criteria for pulmonary hypertension.¹

Echocardiography was performed using the Philips echocardiography system (Philips MEDICAL Systems, Eindhoven, the Netherlands), and the left ventricle ejection fraction (LVEF), left ventricle end-diastolic diameter (LVEDD), and peak TRV were measured. The trans-tricuspid pressure gradient was calculated using a modified Bernoulli equation ($\Delta P = 4v^2$), and the systolic PAP was estimated by adding the trans-tricuspid pressure gradient to the right atrial pressure (RAP). The RAP was 3 mmHg when an IVC collapses $> 50\%$ (diameter of < 2.1 cm) with a sniff, and it was 15 mmHg when an IVC collapses $< 50\%$ (diameter of > 2.1 cm) with a sniff or $< 20\%$ with quiet inspiration.¹

For lung V/Q scanning, ^{99m}Tc-Technegas and ^{99m}Tc-macroaggregated human albumin were used, and ≥ 1 mismatched segmental perfusion defect indicated the possibility of pulmonary thromboembolism.¹

CT pulmonary angiography was performed from 1997, and all images were reviewed using the picture archiving and communication system (PetaVision, Asan Medical Center PACS, Seoul, Korea). Ring-like stenosis, webs/slots, and chronic total occlusions such as pouch or tapered lesions were considered as specific signs of CTEPH.¹ Additionally, the diameters of the pulmonary artery (Pa) and aorta (Ao) were measured at the level of the main pulmonary artery bifurcation, and the ratio of these diameters (Pa:Ao), a useful marker for predicting the presence of resting pulmonary hypertension, was assessed.^{1,16,17}

RHC was mainly performed in the intensive care unit (ICU) using a flow-directed balloon-tipped pulmonary artery catheter in the pre-MDT era. On the other hand, it was performed in the cardiac catheterization laboratory unit with fluoroscopic guidance in the post-MDT era. Hemodynamic variables including systolic PAP, diastolic PAP, mean PAP, RAP, PCWP, and arterial and venous oxygen saturation were measured. Cardiac output (CO) was calculated using thermodilution techniques. Pulmonary vascular resistance (PVR) was expressed in Wood units and calculated using the following equation: $PVR = (\text{mean PAP} - \text{mean PCWP}) / \text{CO}$.

For surgical treatment, we used the following general criteria to assess operability: (1) patients who complained of symptoms with WHO functional class $\geq \text{II}$, (2) patients who had surgically accessible lesions, and (3) patients who did not have significant comorbidities.¹ However, due to the lack of well-defined surgical criteria, operability was largely determined by a PEA surgeon and/or a CTEPH physician in the pre-MDT era and by an MDT of experts in the post-MDT era. BPA was performed in the cardiac catheterization laboratory unit and was performed only on patients who were inoperable or reluctant to undergo PEA.

Statistical analysis

For continuous variables, the data are presented as mean \pm standard deviation (SD) or median (interquartile range), and an independent *t*-test and Mann-Whitney *U* test were used for comparisons. For categorical variables, data are presented as number (%), and chi-square test, Fisher's exact test, and linear-by-linear association test were used for comparisons. A *p* value of < 0.05 was considered statistically significant. Statistical analyses were performed using SPSS 21.0 software (IBM Corporation, Armonk, NY, USA).

Results

Baseline characteristics

From December 1994 to October 2017, a total of 116 patients were diagnosed with CTEPH. The mean age was 53.3 ± 13.8 years, and 61 (52.6%) were male. Table 1 shows the baseline characteristics of the study population. All patients complained of symptoms with WHO functional class \geq II. The elevated peak TRV on echocardiography (4.3 ± 0.7 m/s), Pa:Ao ratio on CT pulmonary angiography (1.2 ± 0.2), and mean PAP on RHC (46 [37–54] mmHg) indicated the presence of pulmonary arterial hypertension. All patients who underwent lung V/Q scanning showed ≥ 1 mismatched segmental perfusion defect, which indicated the possibility of pulmonary thromboembolism. Overall, 74 (63.8%) were diagnosed in the pre-MDT era, whereas 42 (36.2%) were diagnosed in the post-MDT era. Baseline characteristics including age, gender, BMI, symptoms, comorbidities, and physiologic findings were not significantly different between the eras.

Major diagnostic procedures

Table 2 shows the implementation rates of major diagnostic procedures at the time of diagnosis. The implementation rates of echocardiography (98.6% vs. 100.0%, $p > 0.999$) and lung V/Q scanning (93.2% vs. 92.9%, $p > 0.999$) were not significantly different between the pre-MDT and post-MDT eras. Considering its delayed introduction, the implementation rate of CT pulmonary angiography was also not significantly different between the eras (94.0% vs. 100.0%, $p = 0.158$). However, those of conventional pulmonary angiography (18.9% vs. 97.6%, $p < 0.001$) and RHC (10.8% vs. 97.6%, $p < 0.001$) were significantly increased in the post-MDT era. Furthermore, there were 12 additional cases of delayed performed conventional pulmonary angiography and RHC in the post-MDT era, indicating that the patients were diagnosed in the pre-MDT era, but the procedures were performed in the post-MDT era.

Fig. 1 shows the number of annual cases of major procedures including conventional pulmonary angiography and RHC. The number of annual cases of conventional pulmonary angiography and RHC

was ≤ 3 until 2013, and it was sharply increased from 2014. The number for both conventional pulmonary angiography and RHC peaked at 20 in 2016.

Major therapeutic procedures

Table 3 shows the implementation rates of major therapeutic procedures and the changes in the treatment of CTEPH between the eras. The implantation rate of PEA was significantly increased in the post-MDT era (32.4% vs. 59.5%, $p = 0.005$). The time to PEA after diagnosis was significantly decreased in the post-MDT era (42 [37–62] vs. 14 [11–17], $p < 0.001$). BPA was not performed in the pre-MDT era; it was only performed after the establishment of the MDT (not available vs. 35.7%). Furthermore, there were 6 and 13 additional cases of delayed performed PEA and BPA, respectively.

Fig. 1 shows the number of annual cases of major procedures for CTEPH, which demonstrated a marked increase in PEA and BPA after the establishment of the MDT. The number of annual cases of PEA and BPA peaked at 12 and 27, respectively, in 2017.

Post-PEA outcomes

Table 4 shows the *post-hoc* analysis of post-PEA outcomes. A total of 55 PEAs were performed, and 31 (56.4%) were performed in the post-MDT era. The percentages of patients who suffered from reperfusion pulmonary edema (29.2% vs. 12.9%, $p = 0.180$), reoperation (4.2% vs. 0.0%, $p = 0.436$), in-hospital mortality (12.5% vs. 3.2%, $p = 0.307$), and residual pulmonary hypertension (41.7% vs. 29.0%, $p = 0.328$) were decreased in the post-MDT era; however, these reductions were not statistically significant.

Discussion

Owing to the lack of clinical data, the recommendation to manage CTEPH patients with an MDT of experts has been based solely on experts' opinions.^{1,8} Therefore, in this study, we aimed to investigate the effect of an MDT on the management of CTEPH and found that the MDT was associated with improved management by increasing

Table 1
Comparison of the baseline characteristics of patients with CTEPH between the pre-MDT and post-MDT eras

	Whole era n = 116	Pre-MDT era n = 74	Post-MDT era n = 42	p value
Age, years	53.3 (13.8)	53.9 (13.4)	52.3 (14.6)	0.543
Male	61 (52.6)	40 (54.1)	21 (50.0)	0.674
BMI, kg/m ²	24.0 (3.7)	23.6 (3.0)	24.8 (4.5)	0.123
WHO functional class				>0.999
Class I	0 (0.0)	0 (0.0)	0 (0.0)	
Class II	62 (53.4)	40 (54.1)	22 (52.4)	
Class III	46 (39.7)	29 (39.2)	17 (40.5)	
Class IV	8 (6.9)	5 (6.8)	3 (7.1)	
Charlson comorbidity index	2 (1–3)	2 (1–3)	2 (1–3)	0.206
Echocardiography	n = 115	n = 73	n = 42	
LVEF, %	63.2 (7.8)	63.1 (9.0)	63.3 (5.4)	0.887
LVEDD, mm	42.3 (5.7)	42.7 (5.9)	41.6 (5.2)	0.314
Peak TRV, m/s	4.3 (0.7)	4.2 (0.7)	4.4 (0.7)	0.154
CT angiography	n = 105	n = 63	n = 42	
Pa diameter, mm	38.3 (6.4)	38.6 (5.8)	38.0 (7.2)	0.653
Ao diameter, mm	32.8 (5.1)	33.2 (4.9)	32.2 (5.5)	0.350
Pa:Ao ratio	1.2 (0.2)	1.2 (0.2)	1.2 (0.3)	0.739
Hemodynamics by RHC	n = 61	n = 20	n = 41	
Mean PAP, mmHg	46 (37–54)	45 (34–54)	46 (37–56)	0.639
Cardiac index, L/min/m ²	2.4 (1.9–2.9)	2.5 (2.1–3.2)	2.3 (1.8–2.7)	0.110
PVR, wood units	9.9 (7.2–13.4)	7.3 (4.5–14.4)	10.7 (8.5–13.4)	0.137

Values are presented as mean (SD), median (IQR), or number (%).

Abbreviations: Ao, aorta; BMI, body mass index; CT, computed tomography; CTEPH, chronic thromboembolic pulmonary hypertension; LVEDD, left ventricle end-diastolic diameter; LVEF, left ventricle ejection fraction; MDT, multidisciplinary team; PAP, pulmonary arterial pressure; Pa, pulmonary artery; PVR, pulmonary vascular resistance; RHC, right heart catheterization; TRV, tricuspid regurgitation velocity; WHO, World Health Organization.

Table 2

Comparison of the implementation rates of major diagnostic procedures for CTEPH between the pre-MDT and post-MDT eras

	Whole era n = 116	Pre-MDT era n = 74	Post-MDT era n = 42	p value
Echocardiography	115 (99.1)	73 (98.6)	42 (100.0)	>0.999
V/Q scanning	108 (93.1)	69 (93.2)	39 (92.9)	>0.999
CT angiography	105 (96.3) ^a	63 (94.0) ^a	42 (100.0)	0.158
Pulmonary angiography	55 (47.4)	14 (18.9)	41 (97.6)	<0.001
RHC	49 (42.2)	8 (10.8)	41 (97.6)	<0.001

Values are presented as number (%).

Abbreviations: CT, computed tomography; CTEPH, chronic thromboembolic pulmonary hypertension; MDT, multidisciplinary team; RHC, right heart catheterization; V/Q scanning, ventilation/perfusion scan.

^a Because of the delayed introduction of CT pulmonary angiography, the total number of patients in the whole era and pre-MDT era is 109 and 67, respectively.

the implementation rates of major diagnostic and therapeutic procedures recommended by guidelines.^{1,2} To the best of our knowledge, this is the first study to demonstrate the clinical effect of an MDT on the management of CTEPH. Our findings suggest that patients with CTEPH should be managed by an MDT of experts.¹

In our hospital, CTEPH experts such as pulmonologists, cardiologists, and thoracic surgeons treated patients independently in the pre-MDT era. On the other hand, after the establishment of the MDT, the professionals regularly met once or twice a week and actively communicated with each other. This led to an improvement in patient management in the post-MDT era, which may be attributed to increased collaboration and inter-departmental communication. For example, although it is well known that fluoroscopy-guided RHC is more convenient and safer than conventional flow-directed balloon-tipped pulmonary artery catheterization,¹⁸ it was rarely performed in the pre-MDT era because it was difficult for the pulmonologists and thoracic surgeons to form a team that can provide fluoroscopic guidance in the cardiac catheterization laboratory unit. On the other hand, in the post-MDT era, it could be performed under fluoroscopic guidance in the cardiac catheterization laboratory unit following increased inter-departmental cooperation, which improved patient safety and procedure quality.

Table 3

Comparison of the implementation rates of major therapeutic procedures for CTEPH between the pre-MDT and post-MDT eras

	Whole era n = 116	Pre-MDT era n = 74	Post-MDT era n = 42	p value
PEA	49 (42.2)	24 (32.4)	25 (59.5)	0.005
BPA ^a	15 (35.7)	NA	15 (35.7)	NA
Both PEA and BPA ^a	3 (7.1)	NA	3 (7.1)	NA
Medical treatment only	55 (47.4)	50 (67.6)	5 (11.9)	< 0.001

Values are presented as number (%).

Abbreviations: BPA, balloon pulmonary angioplasty; CTEPH, chronic thromboembolic pulmonary hypertension; MDT, multidisciplinary team; NA, not available; PEA, pulmonary endarterectomy

^a BPA was not performed in the pre-MDT era.

Moreover, the implementation of RHC in the cardiac catheterization laboratory unit led to the introduction of BPA for CTEPH treatment in the post-MDT era.

In this study, the baseline characteristics (age, gender, BMI, severity of symptoms, and comorbidities) were not significantly different between the eras. The equal gender distribution is in agreement with the results of previous studies.^{6,9,19–22} However, the mean age was 5–10 years younger than that in previous studies, particularly studies performed in Western countries.^{6,9,19–22} Considering the relatively younger age distribution in the studies performed in Asia and Australia,^{23–26} regional, cultural, and/or racial factors may cause the differences in age distribution. Therefore, further studies are required to investigate the association between these factors and the findings.

A comparison of the diagnostic procedures indicated that the implementation rates of conventional pulmonary angiography and RHC were significantly different between the eras. These procedures are essential especially for discriminating CTEPH from other types of pulmonary hypertension; however, they were less frequently performed in the pre-MDT era. This suggests that these vital procedures might be overlooked or improperly performed in the pre-MDT era. Considering that the disease can be treated, some patients might lose the chance of proper treatment because of the absence of an MDT.

A comparison of the therapeutic procedures revealed that the implementation rate of PEA was significantly increased in the

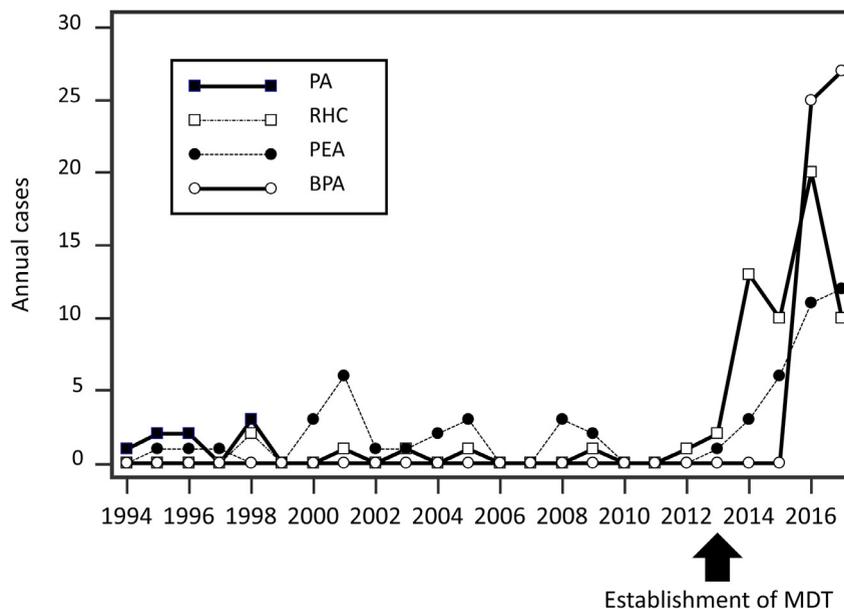


Fig. 1. Annual cases of major diagnostic and therapeutic procedures for CTEPH. Abbreviations: BPA, balloon pulmonary angioplasty; CTEPH, chronic thromboembolic pulmonary hypertension; MDT, multidisciplinary team; PA, pulmonary angiography; PEA, pulmonary endarterectomy; RHC, right heart catheterization.

Table 4

Comparison of the clinical outcomes of pulmonary endarterectomy between the pre-MDT and post-MDT eras

	Whole era n = 55	Pre-MDT era n = 24	Post-MDT era n = 31	p value
Reperfusion pulmonary edema	11 (20.0)	7 (29.2)	4 (12.9)	0.180
Reoperation	1 (1.8)	1 (4.2)	0 (0.0)	0.436
In-hospital mortality	4 (7.3)	3 (12.5)	1 (3.2)	0.307
Residual pulmonary hypertension	19 (34.5)	10 (41.7)	9 (29.0)	0.328

Values are presented as number (%).

Abbreviations: MDT, multidisciplinary team.

post-MDT era. The number of annual cases of PEA was rapidly increased after the establishment of the MDT and peaked at 12 in 2017. Furthermore, the time to PEA was significantly decreased in the post-MDT era, suggesting improved patient management. In addition, the in-hospital mortality rate after PEA was decreased from 12.5% to 3.2% in the post-MDT era (not statistically significant). These findings are consistent with the results of an international CTEPH registry, which showed that the in-hospital mortality rates for centers that performed >50, 11–50, and 1–10 PEAs per year were 3.4%, 4.5%, and 8.8%, respectively.¹¹ Considering that the recently proposed criteria in CTEPH management that emphasizes an in-hospital mortality rate of <5.0% following PEA,¹⁵ both the increased implementation rate of PEA and the decreased in-hospital mortality rate in the post-MDT era indicated that our hospital's level of expertise was improved after the establishment of the MDT.

Balloon pulmonary angioplasty (BPA) is an emerging treatment modality for CTEPH, which may be considered for patients with technically inoperable.¹ In this study, BPA was not performed in the pre-MDT era and was only performed after the establishment of the MDT. BPA was first performed in 2016 when the center's volume reached an intermediate level (11–50 PEAs per year). These findings are in agreement with recent recommendations indicating that BPA should be performed in an experienced center.²⁷

This study has several limitations. First, it is a retrospective before/after study performed at a single center, which has inherent limitations in terms of selection and assignment biases. Moreover, as we were unable to control possible confounding factors that have changed over time, the changes in the management of CTEPH in this study might be affected not only by the establishment of an MDT but also by other factors, such as temporal changes in available treatments and recommended management by guidelines. Although the similar baseline and demographic characteristics between the eras, which are also similar to those of previous studies,^{6,9,19–26} suggest that the possible selection and assignment biases may be minimal in this study, our findings need to be confirmed by larger, prospective, randomized studies. Second, although RHC is mandatory for the diagnosis of CTEPH, only a small number of patients underwent RHC in the pre-MDT era, indicating that the diagnosis might be inaccurate. Nevertheless, we believe that the low implementation rate of RHC in the pre-MDT era itself is meaningful since it demonstrates a possible scenario without the MDT. Furthermore, potential errors in the diagnosis of CTEPH would be minimal since we referred to well-established echocardiographic criteria, which indicate a high probability of pulmonary hypertension.¹ Third, we were unable to compare the mortality rates between the eras due to the small number of patients. However, both the well-established long-term clinical outcomes of PEA and the increased implementation rate of the procedure in the post-MDT era suggest that the establishment of an MDT could contribute to improved long-term clinical outcomes.

In conclusion, the establishment of an MDT appears to be associated with improved CTEPH management by increasing the implementation rates of major diagnostic and therapeutic procedures.

Therefore, the establishment of an MDT should be encouraged for the proper management of CTEPH.

Acknowledgments

This study was supported by the University of Ulsan College of Medicine, Seoul, Korea.

Declarations of interest

None.

Supplementary data

Supplementary data related to this article can be found at <http://dx.doi.org/10.1016/j.hrtlng.2018.07.008>.

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