Featured Article

Pulmonary thromboendarterectomy in chronic thromboembolic pulmonary hypertension: the Spanish experience

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Background: Chronic thromboembolic pulmonary hypertension (CTEPH) can be cured by pulmonary endarterectomy (PEA). It is considered the best and only curable treatment option for patients with accessible lesions evaluated as optimal candidates. We describe the experience of the two reference centers in Spain, in order to reinforce the need for referring CTEPH patients to a specialized center to be assessed by a Multidisciplinary Expert Team.

Methods: We included a population of 338 patients who met the definition for CTEPH and underwent PEA between January 2007 and December 2019. The surgery was indicated in almost 60% of patients assessed. Demographic, anthropometric, hemodynamic and echocardiographic features are listed for PEA patients. Immediate and one-year postoperative outcomes as well as overall mortality were analyzed.

Results: Mean age was 53.5±15.0 years, 53.8% were men; a total of 68.5% were in WHO functional class III–IV; and most of them were in a preoperative hemodynamic condition: mean pulmonary arterial pressure (mPAP) was 46.5±13.1 mmHg and mean pulmonary vascular resistance (PVR) was 764.5± 392.8 dyn·s·cm^{-5}. PEA surgery was performed with cardiopulmonary bypass (CBP) and circulatory arrest, with very few complications [including neurological, postoperative reperfusion edema, extracorporeal membrane oxygenation (ECMO) implant and cardiac failure] and optimal postoperative results, where exercise capacity increased and mPAP and PVR values decreased significantly. Presence of persistent pulmonary hypertension (PH) at the six-month right heart catheterization was evaluated. A 3.3% perioperative mortality was achieved. Overall, one-, three- and five-year survival rates were analyzed by Kaplan-Meier's method (94.8%, 93.3% and 90.5% respectively), as well as for residual PH patients. Mortality risk factors were assessed.

Conclusions: Outstanding PEA results were seen in the immediate, one-year and long-term outcomes. The incidence of complications, including in-hospital mortality and long-term mortality were also below European rates.

Keywords: Pulmonary thromboendarterectomy; pulmonary hypertension (PH); pulmonary vascular resistance (PVR); residual pulmonary hypertension, operability

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Introduction

Chronic thromboembolic pulmonary hypertension (CTEPH) is an infrequent evolution of acute pulmonary embolism (PE). Its prevalence varies from 0.57% to 9.1% (1); and several mechanisms behind the development of CTEPH have been suggested (2). It is a rare disease, associated with high morbidity and mortality when not treated (3,4). It is still underdiagnosed but slowly starting to gain visibility. It should be diagnosed in its early phases so that CTEPH patients can be offered the best possible treatment (1,5,6). Nowadays it is a potentially curable disease (6,7), with pulmonary endarterectomy (PEA) being considered the treatment of choice in a high number of patients. This intervention pursues three main goals: (I) hemodynamic stability, reducing the effect of pulmonary hypertension (PH) on the right ventricle by preventing right ventricular failure and secondary valvular disease; (II) respiratory stability, by improving ventilatory efficiency; and (III) improved exercise capacity (1,5,8). PEA is a technically demanding operation, currently only performed in very few selected centers around the world; optimal results are associated with better patient selection, better perioperative care and greater surgical experience (1,5,8). When performed in specialized centers, better results are found in terms of patient survival, functional class and exercise capacity due to the improvement of hemodynamics after the surgery (4,7,9-11). Furthermore, the ability of PEA to allow access to the lesions does not only depend on their anatomical distribution, but also on the surgeon's previous experience (2). There is a group of patients considered inoperable (around 35–40% of CTEPH patients) (6,12), who have two other treatments options: balloon pulmonary angioplasty (BPA), and PH-targeted medical therapy (MT) with riociguat (a stimulator of soluble guanylate-cyclase enzyme) (13), which was approved in 2015 in Spain for patients with inoperable CTEPH or persistent PH after PEA.

National Spanish outcomes in CTEPH management are scarce due to the current decentralized model (1,6). Currently, CTEPH can be treated in PH specialized centers or at general hospitals, where the decision of referring the patient for surgery is left to the treating doctor (1). However, all patients should be referred and carefully evaluated by a Multidisciplinary Expert Team, where every individual case is discussed, and the most suitable treatment is chosen. The Multidisciplinary Expert Team is made up of pulmonologists, cardiologists, radiologists and cardiac surgeons specialized in PEA (9). There are two PH specialized centers in Spain that bring together most CTEPH patients (>60%), designated as Centros, Servicios y Unidades de Referencia del Sistema Nacional de Salud (CSUR): Hospital Clínic, Barcelona, and Hospital Universitario 12 de Octubre, Madrid (5,14). These centers assess patients who belong to the corresponding health administrative area and those being referred from general hospitals (1). A recently published study shows that a low percentage of patients were referred to CSUR in Spain (61.4%), which led to a lower rate of total PEA (30.7%), and higher overall mortality (1). Furthermore, it is important to mention that, since 2007, a national observational registry of pulmonary hypertension (REHAP) has been running in order to evaluate national clinical management of CTEPH patients and its long-term outcomes in Spain (1,6). Both specialized centers participate in the REHAP Registry and in the International CTEPH Registry (14).

Our objective is two-fold: (I) to investigate demographics, echocardiographic and hemodynamic characteristics of the 338 CTEPH patients who underwent surgery in CSUR Centers in Spain; and (II) to analyze surgical outcomes, immediately and up to one-year after the surgery. In-hospital and long-term mortality were analyzed. With this data, we want to reinforce our idea of changing the current model of CTEPH management in Spain.

Methods

Inclusion criteria

In the aforementioned centers, 578 patients between January 1st 2007 and December 31st 2019 met the definition of CTEPH, fulfilling therefore, the specific hemodynamic criteria for right heart catheterization (RHC): mean pulmonary artery pressure (mPAP) ≥25 mmHg, pulmonary vascular resistance (PVR) ≥3 Wood units or ≥240 dyn.s.cm^{-5} and pulmonary capillary wedge pressure (PCWP) ≤15 mmHg, or below this level but with documented exercise PH. Of the evaluated patients, 338 were considered operable, the remaining were deemed inoperable and given other treatment options. Moreover, all patients (operable and inoperable) showed perfusion defects in ventilation/perfusion lung scintigraphy and CT angiography, consistent with CTEPH. They all received at least three months of anticoagulation treatment before the final diagnosis of CTEPH was given and continued receiving it long term. Data such as demographic and anthropometric parameters,

Table 1 Patient characteristics at diagnosis

Variables	Mean ± SD or n (%)
Demographic and anthropometric	
Age (years)	53.5±15.0
Male gender	182 (53.8)
BMI (kg/m^2)	28.0±5.2
Systemic hypertension	91 (35.0)
DM	25 (9.6)
Current/past smoking habit	105 (40.4)
Coronary artery disease	16 (6.2)
Cancer history	25 (9.7)
Hypercoagulability	115 (34.0)
PE history	290 (85.8)
DVT	153 (45.3)
Clinical	
WHO I–II	101 (31.5)
WHO III–IV	220 (68.5)
6MWD (m)	399.4±123.4
NT-proBNP (mg/dL)	1,403.3±2,034.9
Hemodynamic and echocardiographic	
mPAP (mmHg)	46.5±13.1
PVR (dyn·s·cm^{-5})	764.5±392.8
RAP (mmHg)	9.1±5.4
PCWP (mmHg)	10.3±4.0
Cardiac index (L/min/m^2)	2.30±0.59
TAPSE (mm)	17.4±4.3
Pericardial effusion	32 (12.8)

BMI, body mass index; DM, diabetes mellitus; PE, pulmonary embolism; DVT, deep vein thrombosis; WHO, World Health Organization; 6MWD, six-minute walk distance; NT-proBNP, N-terminal pro B-type natriuretic peptide; mPAP, mean pulmonary arterial pressure; PVR, pulmonary vascular resistance; RAP, right atrial pressure; PCWP, pulmonary capillary wedge pressure; SD, standard deviation; TAPSE, tricuspid annular plane systolic excursion.

PH clinical characteristics and supplementary diagnostic tests parameters (echocardiographic and RHC variables) (*Table 1*) were obtained from routine medical visits.

PEA selection

Most patients will benefit from PEA surgery, but the selection criteria remain subjective to each multidisciplinary team. It is based on several factors, such as lesion accessibility (anatomic distribution—assessed by CT angiography—and the cardiac surgeon's expertise), severity of the patient's disease including symptoms and hemodynamic status (severity of PH and right heart dysfunction) and presence of co-morbidities, including long-term expectations (1,12). Therefore, the selection of candidates for surgery depends on the combination of accessible surgical disease and the severity of PH and right ventricular dysfunction, but neither the severity of right ventricular dysfunction nor the value of PVR will exclude a patient from surgical consideration, however, the PEA and postoperative care are made more challenging. In terms of accessibility, if the disease is in the main, lobar or segmental pulmonary artery branches, endarterectomy is feasible; and it is only performed in the most expert centers even if subsegmental arteries are primarily affected (1,2,5,6,12). Nevertheless, distal segmental disease is much more difficult to remove and renders the patient inoperable (7,12,15). The decision to operate was always made in a meeting of members of the Multidisciplinary Pulmonary Hypertension Team.

Surgical technique and follow-up

PEA was performed in accordance with the University of California's protocol (San Diego, USA) (12). Surgical approach was through median sternotomy, and performed with full cardiopulmonary bypass, aortic cross-clamping and deep, hypothermia. Endarterectomy was performed during ten-minute periods of circulatory arrest, followed by five-minute reperfusion lapses. The extracted material during the PEA was grouped according to histopathological prognostic value established by the University of California group (16): type 1, fresh thrombus in the main-lobar pulmonary arteries; type 2, intimal thickening and fibrosis proximal to the segmental arteries, with no thrombus; type 3, disease within distal segmental arteries only; and type 4, distal arteriolar vascular disease. In-hospital mortality and all causes of death were collected. Postoperative complications were described as presence of reperfusion edema (postoperative respiratory failure causing hypoxia, accompanied by pulmonary infiltrates on chest X-ray in

some of the surgical areas, occurring in the first 72 hours after PEA, and needing mechanical ventilation for more than 96 hours), cardiac failure, need for extracorporeal membrane oxygenation (ECMO), neurological complications and residual PH. Both the definition of residual PH and the time for diagnosis are controversial; some authors establish it according to mPAP values and others to PVR values. In our study, residual PH was defined as having mPAP >25 mmHg at rest, and clinically relevant PH as having PVR >400 dyn·s·cm^{-5} (in the six-month RHC). All patients remained on long-term anticoagulant therapy. Follow-up time was at least one year.

Statistical analysis

Continuous variables were expressed as a mean ± standard deviation, or as a median with interquartile range (IQR) when not normally distributed. Quantitative variables were analyzed using the Student's *t*-test or Mann-Whitney U-test. Comparisons were made using the paired *t*-test or ANOVA. Categorical variables were expressed as frequencies, n (%) and compared using the Chi-square, Fisher's exact test or McNemar's for paired samples. All P values were two-sided, with a P value <0.05 being considered statistically significant. Preoperative, intraoperative, and postoperative variables were analyzed to evaluate if they statistically correlated with in-hospital mortality using logistic regression; those that were available in less than a 70% of patients were excluded [such as N-terminal pro B-type natriuretic peptide (NT-proBNP) which was firstly measured in 2009 in one of the two expert centers]. Multivariable logistic regression analysis was performed for variables considered risk factors, to calculate their relative risk and 95% confidence interval (CI). The univariate Cox regression model was used to evaluate proportional hazards for mortality, and those that revealed a P<0.05 significance were included in the multivariable analysis (again NT-proBNP was not included in this Cox analysis). The proportional hazards assumptions were checked using scaled Shoenfeld residual, using both hypothesis testing and graphical methods. The linearity assumptions were checked by plotting the Martingale residuals against continuous covariates. Survival curves were calculated using the Kaplan-Meier method and compared using the log rank test. The study date of entry was defined as the date of the first diagnostic RHC. The statistical analysis was performed using SPSS version 17 (SPSS Inc., Chicago, IL, USA) and R software version 4.1.1.

Results

Study population and situation at diagnosis

The study population included a group of 338 patients with CTEPH who met the inclusion criteria and underwent surgery between January 1st 2007 and December 31st 2019; constituting 58.5% of the total assessed patients across the two specialized centers. Clinical and hemodynamic characteristics at diagnosis of all patients are listed in *Table 1*; mean age was 53.5±15.0 years, 53.8% were men and most of patients had severe clinical disease [68.5% were in World Health Organisation (WHO) functional class III–IV] and a severe hemodynamic condition (with a mPAP of 46.5± 13.1 mmHg and 80 patients (23.7%) had previous PVR >1,000 dyn·s·cm^{-5}).

Immediate and one-year outcomes

PEA immediate postoperative outcomes

In patients who underwent PEA, mean CBP time was 215.8±47.0 minutes, mean cross-clamp time was 113.1± 24.6 minutes, with a mean time of circulatory arrest of 42.8±14.5 minutes. Complete PEA was performed in 95.5% and concomitant surgery in 70 (20.6%) patients (*Table 2*). According to the San Diego classification system of the biological material extracted, 27.9% was classified as type 1, 49.8% as type 2 and 22.3% as type 3. Complications in postoperative care were registered; the global in-hospital mortality was 3.3%, postoperative reperfusion edema occurred in 14.2% of patients, cardiac failure in 6.5% and ECMO was required in 25 patients (7.4%), 18 of which were veno-venous and 7 were veno-arterial. Additionally, postoperative neurological complications occurred in 5.9% of patients, most of which were temporary (5.3%) but in two cases (0.6%) caused permanent damage. Median intensive care unit (ICU) stay was 6 (IQR 8) days; and in-hospital stay was 14 (IQR 12) days (*Table 2*). Patients' preoperative, intraoperative and postoperative characteristics potentially associated with greater in-hospital mortality were assessed by logistic regression univariate analysis; the items found to be risk factors for in-hospital mortality are specified in *Table 3*. Following multivariable analysis, only previous PVR >1,000 dyn·s·cm^{-5} remained an independent risk factor for in-hospital mortality (P=0.010) (*Table 3*).

PEA one-year clinical and hemodynamic outcomes

One-year outcomes in PEA patients were assessed: both exercise capacity [6-minute walk distance (6MWD)] and

Table 2 Intraoperative characteristics and immediate postoperative complications

Variables	Mean ± SD or n (%) or median [IQR]
CPB time (min)	215.8±47.0
Cross-clamp time (min)	113.1±24.6
Circulatory arrest (min)	42.8±14.5
Complete PEA	323 (95.5)
Concomitant surgery	70 (20.6)
San Diego anatomo-surgical classification	
Type 1	89 (27.9)
Type 2	159 (49.8)
Type 3	71 (22.3)
ICU stay (days)	6 [4–12.8]
In-hospital stay (days)	14 [9–21]
In-hospital mortality	11 (3.3)
Reperfusion edema	48 (14.2)
Cardiac failure	22 (6.5)
ECMO	25 (7.4)
Neurological complications	20 (5.9)

CBP, cardiopulmonary bypass; PEA, pulmonary endarterectomy: ICU, Intensive Care Unit; IQR, interquartile range; ECMO, extracorporeal membrane oxygenator; SD, standard deviation.

clinical functional class (WHO classification) improved, and NT-proBNP values decreased significantly. Moreover, hemodynamic and echocardiographic features improved significantly after surgery: mPAP, RAP and PVR values decreased, and statistical differences were found between preoperative and postoperative figures. Additionally, both cardiac index and tricuspid annular plane systolic excursion (TAPSE) values improved after PEA (*Table 4*).

Residual PH after PEA

For patients whose data was available (n=260), 130 (50%) had persistent residual PH (mPAP >25 mmHg); and clinically relevant residual PH (PVR >400 dyn·s·cm^{-5}) was seen in 59 (22.7%) patients. Mean preoperative PVR in the latter group of patients was 844.2±314.9 dyn·s·cm^{-5}, higher than the rest of the patients.

PEA survival

During a mean follow-up of 38.5±27.3 months, there were a total of 27 deaths. One-, three- and five-year survival rates from diagnosis were 94.8%, 93.3% and 90.5%, respectively (*Figure 1*). Residual PH mortality was also evaluated; one-, three-, and five-year survival rates were 94.8%, 87.8% and 87.8%, respectively, and were slightly lower in those patients with normalized PVR after surgery, although, survival rates equalized six years after surgery (log-rank 0.004) (*Figure 2*). Univariate Cox regression was performed to evaluate mortality risk factors during follow-up (*Table 5*). For multivariable Cox analysis, only a higher 6MWD (P=0.009), therefore better physical capacity and higher cardiac output (by every 0.5 L/min increase) (P=0.033), remained an independent protective factor for mortality during follow-up (*Table 5*).

Discussion

CTEPH is a rare disease, with 8.9 cases per million inhabitants in Spain, despite it being thought to be underdiagnosed (1,2). Our study provides characteristics at diagnosis from 338 operable patients assessed in the CSUR expert centers for the management of complex PH, and outcomes after PEA including survival rates. Clinical guidelines (7) and consensus documents (1,2,17) establish the need to refer these patients to Multidisciplinary Expert Teams with expert surgeons to treat CTEPH. In fact, surgery should not be ruled out in any patient before being evaluated by an expert team. In the International CTPEH Registry (11), up to 43% of the patients evaluated were not considered candidates for surgery. A proportion of 75.7% of patients in the Spanish Registry (REHAP) did not undergo surgery (1). However, as previously shown, in CSUR specialized centers, almost 60% (58.5% of 578 patients) underwent surgery, after being evaluated by a Multidisciplinary Expert Team.

Analysis of the data revealed that the results of our series are excellent, despite severe previous hemodynamic condition. In our study population, 68.5% were classified as WHO III–IV functional class at the time of surgery (5.3% as WHO IV), and mPAP was 46.5±13.1 mmHg and mean PVR was 764.5±392.8 dyn·s·cm^{-5}. Furthermore, PEA surgical times were similar to international specialized centers, including a mean total arrest time of 42.8±14.5 minutes

Table 3 Univariate and multivariate logistic regression analysis for in-hospital mortality

Risk factor	Univariate analysis		Multivariate analysis	
	RR [95% CI]	P	RR [95% CI]	P
WHO functional class IV	10 [23–47]	0.001		
RAP	1.1 [1.0–1.2]	0.034		
Cardiac output	0.5 [0.2–0.9]	0.042		
PVR >1,000 dyn·s·cm^{-5}	8 [2–27]	0.009	10.5 [1.8–85.0]	0.010
Reperfusion edema	11 [4–99]	<0.001		
Cardiac failure	12 [2–57]	0.001		
ECMO	22 [5–150]	<0.001		

WHO, World Health Organization; RAP, right atrial pressure; PVR, pulmonary vascular resistance; ECMO, extracorporeal membrane oxygenator; RR, relative risk; CI, confidence interval.

Table 4 Comparison between preoperative and postoperative patient characteristics after PEA

Variables	Preoperative	One-year outcomes	P (bilateral)
Clinical			
WHO classification, n (%)			<0.001
I–II	76 (27.8)	261 (95.6)	
III–IV	197 (72.2)	12 (4.4)	
6MWD (m), mean ± SD	403.9±113.0	466.5±96.3	<0.001
NT-proBNP (mg/dL), mean ± SD	1315.3±1,589.5	288.6±322.7	<0.001
Hemodynamic and echocardiographic, mean ± SD			
mPAP (mmHg)	46.4±13.0	27.3±10.3	<0.001
PVR (dyn·s·cm^{-5})	757.8±375.2	329.0±477.5	<0.001
RAP (mmHg)	9.2±5.3	6.3±3.7	<0.001
PCWP (mmHg)	10.6±4.0	10.5±6.7	0.932
Cardiac index	2.30±0.59	2.70±0.57	<0.001
TAPSE (mm)	17.8±4.3	16.7±3.5	0.034

PEA, pulmonary endarterectomy; WHO, World Health Organization; 6MWD, six-minute walking distance; NT-proBNP, N-terminal pro B-type natriuretic peptide; mPAP, mean pulmonary arterial pressure; PVR, pulmonary vascular resistance; RAP, right atrial pressure; PCWP, pulmonary capillary wedge pressure; SD, standard deviation; TAPSE, tricuspid annular plane systolic excursion.

and mean CBP of 215.8±47.0 minutes; despite concomitant surgery being performed in a group of 70 (20.6%) patients. Overall perioperative mortality was 3.3%, similar to the largest series reported in the literature by international specialized centers (8,17-19), and below mean European rates (7); placing Spanish CSUR CTEPH Centers in an outstanding international position. Our success is due to the expertise of our surgeons and the procedural protocol developed by the Multidisciplinary Expert Team. Surgical outcomes and survival in both centers in Madrid and Barcelona have improved as there has been a gradual increase in the number of surgical candidates and the team acquired more experience (2,20,21). The accessibility of lesions varies according to the level of experience of the

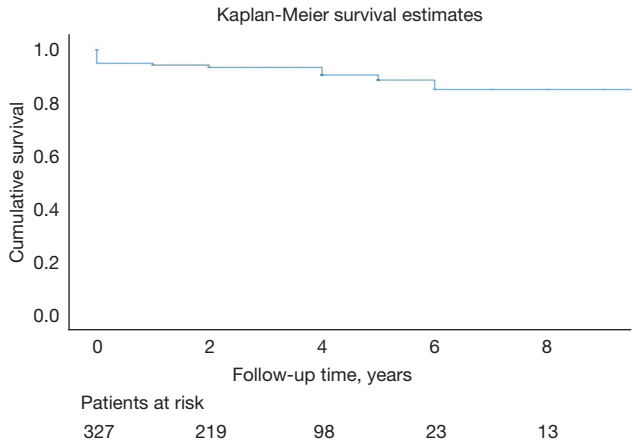

Figure 1 Kaplan-Meier survival estimates, including in-hospital mortality.

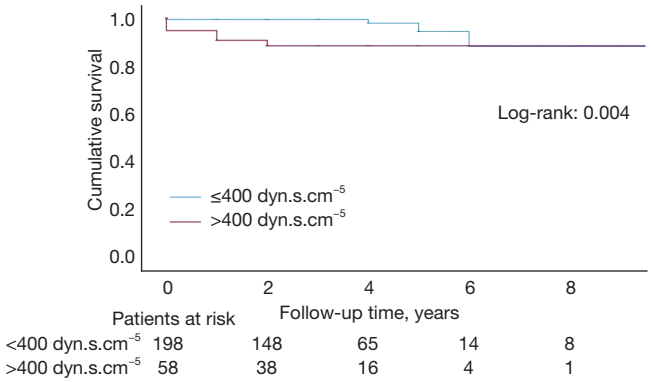

Figure 2 Kaplan-Meier survival estimates in residual PH patients and those with no residual PH. PH, pulmonary hypertension.

surgical team. In most experienced teams, the percentage of patients with segmental branch involvement (San Diego type 3) increases over time, constituting 22.3% of total operated patients in CSUR centers (12,19). It is remarkable that our series registers very few cases of neurological complications (5.9%), most of them being transitory after PEA intervention, despite not performing PEA with continuous cerebral perfusion as suggested by other groups (22). Other postoperative complications were also rare, such as cardiac failure (6.5%), or ECMO implant, where only 2.1% of PEA patients required veno-arterial ECMO and 5.3% veno-venous ECMO. Reperfusion injury is inherent to PEA and its incidence ranges from 5% to 20%, as published by different series (10,12,14). According to our outcomes, reperfusion injury was recorded in 14.2% of patients. It is noteworthy that after PEA, hemodynamic and echocardiographic outcomes improved significantly; patients' exercise capacity (6MWD), cardiac index and TAPSE index also improved; and NT-proBNP values decreased, as did mPAP and RAP values. Two important features must be highlighted; on one hand, PVR values decreased significantly (preoperative 757.8±375.2 *vs.* postoperative 329.0±477.5 dyn·s·cm^{-5}, P<0.001), although 50% of patients had residual PH (mPAP >25 mmHg), while only 22.7% of patients had clinically relevant residual PH in RHC (PVR >400 dyn·s·cm^{-5}) performed at six months after PEA, according to international registries (12,14,23). All such patients were individually assessed in order to choose further treatment options; 16.7% were candidates for BPA after surgery, and the rest were evaluated to receive targeted-MT such as riociguat, after its approval in Spain in 2015. Moreover, in our series we performed a six-month follow-up visit for two reasons: hemodynamic changes immediately following surgery will affect estimates of PVR, and also because the prevalence of residual PH increases over time when the cause is distal vascular disease (24).

In this study, potential factors associated with greater in-hospital mortality were also investigated. Previous PVR >1,000 dyn·s·cm^{-5} was a risk factor for in-hospital mortality in both the univariate and multivariable logistic regression analysis, similarly to other published series (12,19). Regarding follow-up, multiple mortality risk factors were found in the univariate Cox analysis. In the multivariable analysis, only longer preoperative distances in the six-minute walking test and high cardiac output were found to be independent protective factors for mortality, most likely due to better previous physical and hemodynamic conditions. Kaplan-Meier survival analysis showed outstanding survival rates of 94.8%, 93.3% and 90.5% in the one-, three- and five-year follow-up, respectively, similar to results reported in other major studies (12,15,19,23). For residual PH patients, survival rates were only slightly lower (94.8%, 87.8% and 87.8% at one-, three- and five-year follow-up, respectively) when compared with those patients whose PVR normalized after surgery (log-rank 0.004).

Excellent follow-up was achieved in 98.8% of patients; only 4 patients did not attend any check-up. A significant limitation when interpreting the results is that the data were collected by two different centers, where some data may be missing or inconclusive.

This study highlights the favorable results obtained in CSUR centers for CTEPH in Spain, with Multidisciplinary Expert Teams that evaluate patients according to their

Table 5 Univariate and multivariate Cox analysis for follow-up mortality

Variables	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P	HR (95% CI)	P
Demographic				
Age	1.01 (0.99–1.07)	0.156		
Female gender	2.22 (1.20–11.02)	0.01		
BMI	0.95 (0.83–1.08)	0.414		
DM	0.04 (0.00–2.91)	0.488		
Cancer history	3.60 (1.57–10.58)	0.009		
Current/past smoking habit	1.26 (0.45–3.51)	0.657		
Hypercoagulability	1.01 (0.36–2.82)	0.984		
PE history	0.15 (0.06–0.55)	0.002		
Clinical				
WHO functional class III-IV	2.00 (0.45–9.00)	0.214		
6MWD (increase by 30 m)	0.70 (0.65–0.85)	<0.001	0.80 (0.75–0.94)	0.009
Hemodynamic				
RAP (increase by 10 mmHg)	0.99 (0.40–2.35)	0.973		
mPAP (increase by 10 mmHg)	1.15 (0.77–1.76)	0.475		
PVR (increase by 200 dyn·s·cm^{-5})	1.34 (1.10–1.60)	0.001		
CO (increase by 0.5 L/min)	0.62 (0.48–0.82)	0.001	0.61 (0.39–0.96)	0.033
Time from diagnosis to surgery	0.95 (0.93–1.04)	0.644		
Residual PH	1.25 (0.34–4.60)	0.714		

HR, hazard ratio; CI, confidence interval; BMI, body mass index; DM, diabetes mellitus; PE, pulmonary embolism; WHO, World Health Organization; 6MWD, six-minute walk distance; RAP, right atrial pressure; mPAP, mean pulmonary arterial pressure; PVR, pulmonary vascular resistance; CO, cardiac output; PH, pulmonary hypertension.

specific case and recommend the most appropriate treatment.

Conclusions

A cohort of 338 patients out of 578 patients diagnosed with CTEPH from 2007 to 2019, underwent PEA at two Spanish CTEPH specialized centers. Surgical patients had outstanding survival rates at one-, three- and five-year follow-up, and a high in-hospital survival rate for PEA patients was confirmed. Pulmonary endarterectomies were performed within short CBP and circulatory arrest times, with very few complications (including neurological, postoperative reperfusion edema, ECMO implant and cardiac failure) and good one-year results, where exercise capacity increased, and mPAP and PVR values significantly decreased. Mortality risk factors were also evaluated. Due to the optimal results obtained in CSUR centers, we reinforce our statement that all patients should be referred for operability assessment at specialized centers established by international guidelines.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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