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Original Research Article

A Hospital-Based Assessment of the Outcome of Pulmonary Thromboendarterectomy

Madhav Kumar[1], Tushar Kumar[2], Namita Mishra[3], Aandrei Jivendera Jha[4], Devi Shetty[5]

[1]Assistant Professor, Department of CTVS, IGIMS, Patna, Bihar, India

[2]Associate Professor, Department of CTVS, IGIMS, Patna, Bihar, India

[3]Assistant Professor, Department of Anaesthesiology, ESIC, Medical College and Hospital, Bihta, Patna, India

[4]Associate Professor, Department of Cardiothoracic and Vascular Surgery, IGIMS, Patna, Bihar, India

[5]Senior Consultant Cardiac Surgeon, Department of Cardiac Surgery, Narayana Institute of Cardiac Sciences, Bangalore, India

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Corresponding author: Dr. Aandrei Jivendera Jha
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Abstract

Aim: The aim of the present study was to assess the one-year outcome of Pulmonary Thromboendarterectomy surgery.

Methods: The present study was conducted in newly diagnosed consecutive patients with CTEPH from a period ranging from May 2011 to May 2014. 90 patients were selected in the study.

Results: Of the 90 subjects who qualified for inclusion in the study, there were 63 males (70%) and 27 females (30%). The majority of the patients were in the 21 – 50 years group, with almost equal numbers in the 21 – 35 year and 36-50-year age group. Two third of the patients were admitted with NYHA Class 3 (66.67%). Patients recorded with NYHA Class 2 were 27.78%, while patients recorded with NYHA Class 4 were only 5.56%. No patient was recorded with NYHA Class 1. Cough was also a common symptom, being present in 70 patients (77.77%). Haemoptysis was also a fairly common symptom, being present in 39 patients (43.33% of patients), at some point in their history. Only 4 (4.44%) of the patients were diabetic. Functional status according to the Karnofsky Performance Status score in 90 patients at late follow-up after pulmonary endarterectomy and in 70% of the patients, the Karnofsky Performance Status score was 80% or higher (i.e., "able to carry on normal activity").

Conclusion: Success of PTE has now been confirmed. It remains the primary treatment for CTEPH. Longer life expectancy is expected in these patients. PTE is safe and effective operative procedure. PTE is successful, curative alternative to lung transplant. Compared to lung transplant, PTE offers lower surgical mortality rate, better long term survival and fewer chronic complication.

Keywords: one year outcome, Pulmonary Thromboendarterectomy surgery

Introduction

Chronic thromboembolic pulmonary hypertension (CTEPH) is classified as group IV pulmonary hypertension (PH) and defined as precapillary PH with mean pulmonary artery pressure (MPAP) ≥ 25 mmHg and pulmonary artery wedge pressure (PAWP) ≤ 15 mmHg and at least one detected segmental pulmonary perfusion defect despite at least 3 months of effective anticoagulant therapy. [1] Although the exact prevalence and annual incidence rates of CTEPH are still unknown, several studies have reported that it may occur in at least 5 per million individuals annually. [2,3] A history of pulmonary embolism (PE) has been reported in almost three-quarters of patients diagnosed with CTEPH. [4] The pathophysiology of CTEPH begins with obstruction of large or middle-sized pulmonary arteries by unresolved thrombi in most cases. [5] In contrast, small vessel remodeling occurs in non-obstructed vessels in the presence of high flow-related shear stress, inflammation, or cytokine release. [2] Both major vessel lesions and microvascular disease can lead to the progression of CTEPH and impaired hemodynamics. [5] Patients generally develop

symptoms of increased pulmonary artery pressure (PAP) and pulmonary vascular resistance (PVR), as well as a consequent reduction in exercise capacity. [6-8] Although CTEPH is life-threatening, it is potentially curable. Pulmonary endarterectomy (PEA) is the standard therapeutic approach for CTEPH. [1,9,10]

Acute pulmonary embolism has been said to result in more than 600,000 symptomatic episodes in the United States each year, and to be the principal cause of death in 200,000 patients. However, this may be an underestimation as necropsy studies have shown that the diagnosis of acute pulmonary embolism was unsuspected in 70% - 80% of patients in whom it was the principal cause of death. The majority of surviving patients appear gradually to resolve their pulmonary emboli in due course of time. Complete resolution of embolic material does not always occur; the pulmonary clots then organize, and narrow the pulmonary arterial branches leading to pulmonary hypertension. Failure to resolve the embolus causes hypertensive lesions in the open vascular bed and further increases pulmonary vascular resistance. CTEPH causes right ventricular (RV) pressure overload, which leads to functional and morphological alterations of both right and left ventricles. These changes result in a decreased cardiac index (CI). [11]

The natural history of acute pulmonary embolism is not entirely clear as most patients are not followed serially with lung scans or echocardiography, and acute pulmonary embolism is an under diagnosed condition. Presti found chronic massive thrombosis of major pulmonary arteries in nearly 1% of 7753 necropsies. Many patients who have had relief of their pulmonary hypertension following PTE have had disease confined to their minor pulmonary arteries, and chronic thrombus in these smaller pulmonary vessels is probably often overlooked in necropsy series. It is well known that pulmonary hypertension persists and may indeed be progressive long after evidence of the original thrombus has disappeared. For these reasons, the actual prevalence of the CTEPH is underestimated. Although the surgical operation for acute pulmonary embolism remains controversial, operation for chronic pulmonary embolism is well established. [12]

The aim of the present study was to assess the one year outcome of Pulmonary Thromboend - arterectomy surgery.

Materials and Methods

The present study was conducted in newly diagnosed consecutive patients with CTEPH from a period ranging from May 2011 to May 2014. 90 patients were selected in the study.

Inclusion Criteria

All patients undergoing PTE operation

A multidisciplinary team comprising Cardiologists, Cardiothoracic surgeons, Pulmonologists, Radiologists meticulously select patients for PTE at the weekly CTEPH meeting after thorough review.

Data Collection

Data has been obtained from assessments routinely performed for patients with CTEPH in clinical practice and includes medical history, clinical signs and symptoms, diagnosis, and treatment procedures.

Criteria for Non –operability

Type 4 -4a (Eisenmenger's syndrome); 4b (Primary pulmonary hypertension).

Modified New York Heart Association (NYHA)

Functional classification of heart disease

I. Asymptomatic except during severe exertion

II. Symptomatic with moderate activity

III. Symptomatic with minimal activity

IV. Symptomatic at rest

CTEPH Classification

Type I Main or Lobar pulmonary vessel wall disease with stasis and fresh propagation of clot into major pulmonary vessels .

Type II intimal thickening and fibrosis with or without organized thrombus proximal to segmental arteries

Type III Fibrosis, intimal webbing, and thickening with or without organized thrombus within distal segmental and subsegmental arteries only.

Type IV Microscopic distal arteriolar vasculopathy without visible thromboembolic disease

Clinico-Radiological Investigations

Preoperatively, all patients underwent:

1. 2D-Echocardiography
2. Chest Roentgenogram
3. CT angiography of the pulmonary arteries

After anaesthetic induction in the operating room, a 7.5 Fr, 110cms continuous cardiac output thermodilution pulmonary artery catheter (CCO 139F75 Edwards Life sciences) was placed through an 8.5 Fr sheath inserted in the right internal jugular vein. The catheter placement was confirmed by observing the pulmonary artery waveform trace and by transesophageal

echocardiography. The thermistor and thermal filament connectors were connected to the cardiac output monitor (Vigilance, Edwards Life sciences) and cardiac output monitoring started on the monitor. Pulmonary wedge pressure was determined by inflation of the balloon on the pulmonary artery catheter. Subsequently, measured and derived values of pulmonary and systemic circulation were obtained from the monitor.

All operations were performed by the same surgeon. The chest was opened through a median sternotomy. The patient was placed on extracorpereal cireutation by bicaval and aortic cannulation and was cooled to a nasopharyngeal temperature of 18±20°C. The central pulmonary arteries were opened and a dissection plane developed which was then followed to segmental level. Deep hypothermic circulatory arrest was used in all procedures to achieve accurate visualization during peripheral dissection. Using head light and surgical loupes, the pulmonary arterial tree could be visualized directly approximately 2±3 cm beyond the origin of the segmental arteries. Repeated periods of circulatory arrest limited to 20 min were used; usually endarterectomy of one pulmonary arterial bed could be accomplished within one 20 min period. After complete endarterectomy extracorporeal circulation was resumed and the patient rewarmed. Concomitant cardiac procedures (closure of patent foramen ovale, aortic valve replacement or coronary bypass grafting) usually were performed during the rewarming period. Dobutamine and Adrenaline were used to support the weaning from cardiopulmonary bypass. Postoperatively, hemodynamic monitoring was continued for the first 48±72 h after the operation. Decreased systemic vascular resistance was treated by norepinephrine if necessary. Residual pulmonary hypertension was treated by nitrates. After hemodynamic stabilization the patients were weaned from ventilator support and extubated once normal gas exchange was present. Anticoagulation was started with intravenous heparin 6 hours postoperatively. Oral warfarin therapy was restarted on postoperative day 1 with a target INR of 3±3.5. For identification of risk factors we analyzed the influence of preoperative parameters (age, sex, NYHA class, right atrial pressure, pulmonary artery pressure, pulmonary vascular resistance, cardiac output, number of angiographically involved segments, diameter of bronchial artery and presence of coronary artery disease,) on hospital mortality and hemodynamic improvement.

Postoperatively, all patients underwent:

1. 2D-Echocardiography at the time of shifting to ward from intensive care

2. Chest Roentgenogram on the first postoperative day and at the time of shifting to ward from intensive care.

On one year follow up -2 D Echocardiography was used to assess the changes in heart function. The data was collected according to protocol and tabulated for analysis. The data thus collected was subject to statistical analysis using appropriate tests.

Statistical Analysis

Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean±SD (Min-Max) and results on categorical measurements are presented in Number (Count) as well as percentage (%) of the total subjects under study. Significance is assessed at 5% level of significance. Student "t" test (two tailed, dependent) has been used to find the significance of study parameters on continuous scale within each group. 95% Confidence Interval has been computed to find the significant features. Confidence Interval with lower limit more than 50% is associated with statistical significance. Regression analysis has been used to understand the dependency of dependent variables due to independent variables. Chi square test and paired “t” test has been done to understand the variations in PASP and mPAP values. The statistical software namely IBM SPSS Statistics 21.0 was used for the analysis of the data. Microsoft Office Excel was used for collection and pictorial representation of the patient data.

Results

Table 1: Demographic data

Gender	Count	Percentage
Male	63	70.00%
Female	27	30.00%
Age		
Less than 20 years	2	2.22%
21 - 35 years	38	42.22%
36 - 50 years	36	40.00%
51 - 65 years	12	13.33%
66 and above years	2	2.22%
NYHA Class		

Class 1	0	0.00%
Class 2	25	27.78%
Class 3	60	66.67%
Class 4	5	5.56%
Pre Operative Symptoms		
Cough	70	77.78%
Past History of Deep Vein Thrombosis	46	51.11%
Haemoptysis	39	43.33%
Pulmonary Embolism	36	40.00%
Syncope	32	35.56%
Chest Pain	29	32.22%
Palpitations	22	24.44%

Of the 90 subjects who qualified for inclusion in the study, there were 63 males (70%) and 27 females (30%). Patients were divided in age bands of 15 years between 21 – 65 years, and those less than 20 years and greater than 65 years. The majority of the patients were in the 21 – 50 years group, with almost equal numbers in the 21 – 35 year and 36 – 50 year age group. There were only 2 patients in the age group of less than 20 years and greater than 65 years. Two third of the patients were admitted with NYHA Class 3 (66.67%). Patients recorded with NYHA Class 2 were 27.78%, while patients recorded with NYHA Class 4 were only 5.56%. No patient was recorded with NYHA Class 1. Breathlessness was the commonest symptom, with the majority of the patients having Class 3 NYHA symptoms (60 patients). Cough was also a common symptom, being present in 70 patients (77.77%). Haemoptysis was also a fairly common symptom, being present in 39 patients (43.33% of patients), at some point in their history.

Table 2: High Risk Factors

High Risk Factors	Count	Percentage
Prothrombotic state	57	63.33%
Previous surgery/ Procedures	22	24.44%
Smoking	19	21.11%
Hypertension	11	12.22%
Long term immobilization	9	10.00%
Diabetes	4	4.44%
Hyperlipidemia	2	2.22%

Only 4 (4.44%) of the patients were diabetic. Hypertension again was not a common co morbidity being found in only 11 (12.22%) patients. 21.11% of the patients admitted were smokers. Hyperlipidemia was recorded in only 2 (2.22%) patients. 24.44% of the patients had a history of previous surgery. Only 10% of the patients were immobilised since a long time. 63.33% of the patients were in a Prothrombotic state.

Table 3: Description of Chest X –Ray, coronary angiogram, ECG

Description Of Chest X-Ray	Count	Percentage
Enlarged RA/ RV	46	90.20%
Enlarged LPA/ RPA/ MPA	44	86.27%
Peripheral Pruning	15	29.41%
Coronary Angiogram	**Percentage**	
Normal	93.33%	
Abnormal	6.67%	
ECG	**Count**	**Percentage**
T - Wave Inversion	75	83.33%
Right Axis Deviation	63	70.00%

Out of the 51 patients (56.67%) with Abnormal Chest X-Ray, 44 (86.27%) had an Enlarged LPA/ RPA/ MPA, 46 (90.19%) patients had Enlarged RA/RV, while only 15 (29.41%) patients had Peripheral pruning. 6.67% patients had an abnormal coronary angiogram, while majority 93.33% patients had normal coronary angiogram. For the Evaluation of ECG, RV overload was considered which includes Right Axis Deviation and T – Wave inversion in V1 – V5. Right Axis Deviation was present in 63 patients (70%), while T – Wave inversion was present in 75 patients (83.33%).

Table 4: Description of Abnormal CBC of patients

Description of Abnormal CBC	Count
Microcytic Hypochromic Anemia	5
Polycythemia	4
Macrocytic Anemia	2
Megaloblastic Anemia	2
Leukocytosis	1
Thrombocytopenia	1
Normocytic Hypochromic Anemia	1

Out of 15 (16.67%) patients with Abnormal CBC, 4 had Polycythemia while 5 patients had Microcytic Hypochromic Anaemia. 2 patients had Macrocytic Anaemia and Megaloblastic Anaemia and 1 patient had Leukocytosis, Normocytic Hypochromic Anaemia and Thrombocytopenia.

Table 5: ANCA assay, APLA assay, Factor V Leiden mutation, Homocysteine assay and Other thrombotic work up

ANCA ASSAY	Percentage
Yes	3.33%
No	96.67%
APLA ASSAY	
Yes	20.00%
No	80.00%
FACTOR V LEIDEN MUTATION	
Yes	5.56%
No	94.44%
Other Thrombotic Work Up	
Protein C negative	17
Protein S negative	16
Factor VIII Assay positive	12
Antithrombin III Deficiency	10
Fibrinogen	2
Factor IX Assay positive	1
Heparin PF 4 Antibody positive	1
Resistance APC - R positive	1

The ANCA Assay was positive in only 3 of the 90 patients (3.33%). The APLA Assay was positive in 18 out of 90 patients (20%). The Factor V Leiden mutation was normal in 94.44% patients while it was present in only 5.55% patients. Homocysteinemia was present in 41.11% patients. The thrombotic work up also includes factors such as – Factor VIII Assay, Resistance APC – R, Heparin PF 4 Antibody, Factor IX Assay, Protein S, Fibrinogen, Protein C, Antithrombin III deficiency. 16 patients had Protein S deficiency, while 17 patients had protein C deficiency. Factor VIII Assay was positive in 12 patients while there was Antithrombin III deficiency in 10 patients.

Table 5: Karnofsky Performance Status

Karnofsky Performance Status	N (%)
60	7
70	20
80	17
90	23
100	23

Functional status according to the Karnofsky Performance Status score in 90 patients at late follow-up after pulmonary endarterectomy and in 70% of the patients, the Karnofsky Performance Status score was 80% or higher (i.e., “able to carry on normal activity”).

Discussion

Recent developments in the medical treatment of pulmonary arterial hypertension have overshadowed the role of interventions in the treatment of pulmonary arterial hypertension

(PAH). Pulmonary thromboendarterectomy (PTE) offers a potential surgical cure for a subset of patients with chronic thromboembolic pulmonary arterial hypertension (CTEPH). [13] Chronic thromboembolic pulmonary hypertension (CTEPH) is the result of chronic obstruction of the pulmonary arteries by thrombi and it is estimated to follow after, 1%-2% of all cases of acute pulmonary embolism. [14] Obstructed pulmonary arteries contribute to the development of pulmonary hypertension, which leads to right heart failure and death. The description of this clinical entity evolved from an autopsy finding to a recognized cause of chronic pulmonary hypertension. Several mechanisms are postulated to be responsible for the development of embolic event. Recurrence of embolism has been reported subsequent to 2.5% to 7% of adequately treated pulmonary embolic events.

This study included patients from the Indian subcontinent, mainly from south and west India and 70% were male. In our study, mean patient age was 38.34± 11.37 years with 82% patient in their 2nd, 3rd, 4th and 5th decade of their life. The median age in our study was 37.5 years with range from 19 to 70 years. In Thistlethwaite et al [15] study, the number of patients, Male percentage and mean patient age and standard deviation in years were – 743, 45.76 and 50.2 ± 14.9 respectively. In Eckhard Mayer et al [16] study, the number of patients, Male percentage and median age in years were – 386, 54.1 and 60 (18 - 84) respectively.

The NYHA functional class in our study is comparable to other studies from other centres. In B. Yildizeli et al [17] study of 49 patients following observations were made. 42.8% patients presented with history of pulmonary embolism, 28.5% had a history of DVT and 16.32 % patients had coagulation disorders.18.36% patients had diabetes mellitus, while 34.69% were smokers. Most patients were symptomatic for a long time before diagnosis of the disease. The mean duration of illness (in months) was 38.91 ± 35.27. In our study, the following risk factors were observed - Prothrombotic state (63.33%), Previous Surgery/ Procedures (24.44%), Smoking (21.11%), Hypertension (12.22%), Long Term Immobilization (10%), Hypothyroidism (8.88%), Diabetes (4.44%), Prolonged Travel (2.22%) and Hyperlipidemia (2.22%). Takashi Kunihara et al[20] noted Diabetes Mellitus (3.9%), Hyperlipidemia (17.2%) and History of Smoking (20.8%) a In our study, Coronary angiogram was abnormal in 6.67 % patients (6 Patients). CAD was present in 2 while myocardial bridling was present in 4 patients. Functional status according to the Karnofsky Performance Status score in 90 patients at late follow-up after pulmonary endarterectomy and in 70% of the patients, the Karnofsky Performance Status score was 80% or higher (i.e., “able to carry on normal activity”). The San Diego group conducted the first study on QOL in patients after PEA for CTEPH in 1999.[17] The group investigated a cohort of 514 survivors that were discharged after PEA between 1970 and 1994. Of 514 patients, 123 were lost to follow-up, 51 had died, and 14 and 3 were excluded because of language difficulties and lung transplantation, respectively. A study in Japan investigated QOL before and after PEA or BPA for CTEPH.18 The SF-36 was completed by 39 patients (n = 15 for PEA, n = 24 for BPA) before and after treatment. Significant differences in baseline characteristics were observed between the groups. Patients who underwent PEA had higher mPAP and pulmonary vascular resistance and lower exercise tolerance than patients treated with BPA. [18]

B. Yildizeli et al [19] univariate analyses of factors to predict mortality and morbidity following PTE with respect to history of CAD found no significant correlation between the variables risk factors in their study of population (n=279). In Madani et.al. study, the Preoperative mean PASP, Postoperative mean PASP, Preoperative mean mPAP and the Postoperative mean mPAP in Group I were - 75.7 ± 18.8, 46.8 ± 17.3, 46.1 ± 11.4 and 28.7 ± 10.1 respectively whereas, in Group II, the above values were - 75.5 ± 19.1, 41.7 ± 14.1, 45.5 ± 11.6 and 26.0 ± 8.4 respectively. According to Madani et al [21], patients in Group II with residual pulmonary hypertension did better postoperatively possibly because of the availability of newer medical agents for the treatment of Pulmonary hypertension. The Preoperative workup, ensuring that patients were haemodynamically stable before surgery was the main reason for increased pre-operative stay. Complexity of surgery, postoperative complications and postoperative recovery in ward in difficult cases can be accounted for longer hospital stay than routine cardiac surgery operations. At present, neither the prognosis nor the risk of progression to more a severe form of pulmonary hypertension in these patients is clear. [22] The optimal therapeutic option has also not been defined for patients with CTED; however, an increasing number of patients have undergone PEA in expert centers over the last few years for symptomatic improvement. Recently, the Cambridge group reported their results of PEA in patients with symptomatic CTED. [21] The authors reported significant improvement in symptoms and quality of life after PEA, with 95% survival rate at 1 year following surgery. [23]

Held et al [24] analyzed the exercise capacity and limiting factors in 10 patients with CTED and compared RHC and cardiopulmonary exercise test results of patients with CTEPH and control patients. They found that patients with CTED show

reduced oxygen uptake and work rate. They concluded that patients with CTED show objective functional impairment and similar limitations to patients with CTEPH. Functional limitation is characterized by gas exchange disturbance and ineffective ventilation.

Conclusion

Success of PTE has now been confirmed. It remains the primary treatment for CTEPH. Longer life expectancy is expected in these patients. PTE is safe and effective operative procedure. PTE is successful, curative alternative to lung transplant. Compared to lung transplant, PTE offers lower surgical mortality rate, better long term survival and fewer chronic complication.

PTE remains the primary treatment for CTEPH. Physicians must have a broader knowledge of CTEPH as part of pulmonary arterial hypertension disease and more referrals to units having expertise in CTEPH management should be achieved. Routine clinical follow up after acute pulmonary embolism should be performed during the first two years and patients with acute PE showing signs of Pulmonary hypertension should receive a follow up echocardiography after discharge(usually 3-6 months). Prevention of Pulmonary Thromboembolism with early mobilization in postoperative period, elastic stockings, intermittent pneumatic compression and appropriate anticoagulation should be more aggressive. PTE program can be started in other cardiothoracic units of the country. Undergraduate and Postgraduate teaching programs should emphasize on the detection and treatment of pulmonary embolism in general and CTEPH in particular.

References

1. Galiè N, Humbert M, Vachiery JL, Gibbs S, Lang I, Torbicki A, Simonneau G, Peacock A, Vonk Noordegraaf A, Beghetti M, Ghofrani A, Gomez Sanchez MA, Hansmann G, Klepetko W, Lancellotti P, Matucci M, McDonagh T, Pierard LA, Trindade PT, Zompatori M, Hoeper M; ESC Scientific Document Group. 2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension: The Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS): Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC), International Society for Heart and Lung Transplantation (ISHLT). Eur Heart J. 2016 Jan 1;37(1):67-119.
2. Lang IM, Madani M. Update on chronic thromboembolic pulmonary hypertension. Circulation. 2014 Aug 5;130(6):508-18.
3. Pepke-Zaba J, Jansa P, Kim NH, Naeije R, Simonneau G. Chronic thromboembolic pulmonary hypertension: role of medical therapy. Eur Respir J. 2013 Apr;41(4):985-90.
4. Pepke-Zaba J, Delcroix M, Lang I, Mayer E, Jansa P, Ambroz D, Treacy C, D'Armini AM, Morsolini M, Snijder R, Bresser P, Torbicki A, Kristensen B, Lewczuk J, Simkova I, Barberà JA, de Perrot M, Hoeper MM, Gaine S, Speich R, Gomez-Sanchez MA, Kovacs G, Hamid AM, Jaïs X, Simonneau G. Chronic thromboembolic pulmonary hypertension (CTEPH): results from an international prospective registry. Circulation. 2011 Nov 1;1 24(18):1973-81.
5. Simonneau G, Torbicki A, Dorfmüller P, Kim N. The pathophysiology of chronic thromboembolic pulmonary hypertension. Eur Respir Rev. 2017 Mar 29;26(143):160112.
6. Mayer E, Jenkins D, Lindner J, D'Armini A, Kloek J, Meyns B, Ilkjaer LB, Klepetko W, Delcroix M, Lang I, Pepke-Zaba J, Simonneau G, Dartevelle P. Surgical management and outcome of patients with chronic thromboembolic pulmonary hypertension: results from an international prospective registry. J Thorac Cardiovasc Surg. 2011 Mar; 141(3):702-10.
7. Lang I. Chronic thromboembolic pulmonary hypertension: a distinct disease entity. Eur Respir Rev. 2015 Jun;24(136):246-52.
8. 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 Feb;41(2):462-8.
9. Madani M, Mayer E, Fadel E, Jenkins DP. Pulmonary Endarterectomy. Patient Selection, Technical Challenges, and Outcomes. Ann Am Thorac Soc. 2016 Jul;13 Suppl 3:S240-7.
10. Guth S, Wiedenroth CB, Kramm T, Mayer E. Pulmonary endarterectomy for the treatment of chronic thromboembolic pulmonary hypertension. Expert Rev Respir Med. 2016 Jun;10 (6):673-84.
11. Jamieson SW. Pulmonary throm boendarterectomy. Heart 1998; 79: 118-20 Pulmonary endarterectomy: experience and lessons learned in 1500 Casses. ats. Ctsnet joumals.org/cgi/content/ful1/78/2/746.
12. Nagaya N, Ando M, Oya H, Ohkita Y, Kyotani S, Sakamaki F, Nakanishi N. Plasma brain natriuretic peptide as a noninvasive marker for efficacy of pulmonary thromboendarterectomy. The Annals of thoracic surgery. 2002 Jul 1;74 (1):180-4.
13. Doyle RL, McCrory D, Channick RN, Simonneau G, Conte J. Surgical treatments/interventions for pulmonary arterial hypertension: ACCP evidence-based clinical

practice guidelines. Chest. 2004 Jul 1;126(1):63S-71S.
14. Nagaya N, Sasaki N, Ando M, Ogino H, Sakamaki F, Kyotani S, Nakanishi N. Prostacyclin therapy before pulmonary thromboendarterectomy in patients with chronic thromboembolic pulmonary hypertension. Chest. 2003 Feb 1;123(2):338-43.
15. Reddy S, Rajanbabu BB, Kumar NK, Rajani I. Temporary clamping of branch pulmonary artery for pulmonary hemorrhage after endarterectomy. The Annals of Thoracic Surgery. 2013 Oct 1;96(4):1459-61.
16. Shetty DP, Nair HC, Shetty V, Punnen J. A novel treatment for pulmonary hemorrhage during thromboendarterectomy surgery. The Annals of Thoracic Surgery. 2015 Mar 1;99(3):e77-8.
17. Archibald CJ, Auger WR, Fedullo PF, Channick RN, Kerr KM, Jamieson SW, Kapelanski DP, Watt CN, Moser KM. Long-term outcome after pulmonary thromboendarterectomy. American journal of respiratory and critical care medicine. 1999 Aug 1;160(2):523-8.
18. Tamada N, Nakayama K, Yanaka K, Onishi H, Shinkura Y, Taniguchi Y, Kinutani H, Tsuboi Y, Izawa KP, Satomi-Kobayashi S, Otake H. Pulmonary Endarterectomy and Balloon Pulmonary Angioplasty for Chronic Thromboembolic Pulmonary Hypertension―Similar Effects on Health-Related Quality of Life―. Circulation Reports. 2019 May 10;1(5):228-34.
19. Yıldızeli B, Taş S, Yanartaş M, Kaymaz C, Mutlu B, Karakurt S, Altınay E, Eldem B, Ermerak NO, Batırel HF, Koçak T. Pulmonary endarterectomy for chronic thrombo-embolic pulmonary hypertension: an institutional experience. European Journal of Cardio-Thoracic Surgery. 2013 Sep 1;44(3):e219-27.
20. Kunihara T, Gerdts J, Groesdonk H, Sata F, Langer F, Tscholl D, Aicher D, Schäfers HJ. Predictors of postoperative outcome after pulmonary endarterectomy from a 14-year experience with 279 patients. European journal of cardio-thoracic surgery. 2011 Jul 1;40(1):154-61.
21. Madani MM, Auger WR, Pretorius V, Sakakibara N, Kerr KM, Kim NH, Fedullo PF, Jamieson SW. Pulmonary endarterectomy: recent changes in a single institution's experience of more than 2,700 patients. The Annals of thoracic surgery. 2012 Jul 1;94(1):97-103.
22. de Perrot M, Mayer E. Chronic thromboembolic pulmonary hypertension: do we need a new definition? Eur Respir J. 2014 Dec;44(6):1401-3.
23. Taboada D, Pepke-Zaba J, Jenkins DP, Berman M, Treacy CM, Cannon JE, Toshner M, Dunning JJ, Ng C, Tsui SS, Sheares KK. Outcome of pulmonary endarterectomy in symptomatic chronic thromboembolic disease. Eur Respir J. 2014 Dec;44(6):1635-45.
24. Held M, Kolb P, Grün M, Jany B, Hübner G, Grgic A, Holl R, Schaefers HJ, Wilkens H. Functional Characterization of Patients with Chronic Thromboembolic Disease. Respiration . 2016;91(6):503-9.