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Management of high-risk chronic thromboembolic pulmonary hypertension patients

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ABSTRACT

Objectives: In this study, we present our surgical results and postoperative management in high-risk chronic thromboembolic pulmonary hypertension (CTEPH) patients undergoing pulmonary thromboendarterectomy (PTE).

Patients and methods: Between December 2015 and December 2020, a total of nine patients with CTEPH (6 males, 3 females; median age: 52 years; range, 34 to 67 years) who were at high risk for mortality and underwent PTE in our cardiovascular surgery clinic were retrospectively analyzed. The PTE procedure was performed under cardiopulmonary bypass through total circulatory arrest. Pre- and postoperative data were compared.

Results: Of the patients with CTEPH, two had a hydatid cyst, two had a malignant tumor, and five had advanced right heart failure with poor end organ functions. Two patients required an additional intervention including tricuspid ring annuloplasty and atrial septal defect closure in each. Preoperatively, the mean pulmonary artery pressure (mPAP) was 78±22 mmHg, mean pulmonary vascular resistance (PVR) was 13±2.5 Wood Units, mean cardiac index (CI) was 1.27±0.6 L/min/m^2, and mean cardiac output (CO) was 2.62±0.5 L/min. Preoperatively, the mean systemic vascular resistance (SVR) was 25±1.5 Wood units and mean left ventricular ejection fraction (LVEF) was 55.5±%.

Conclusion: The PTE procedure is the gold-standard treatment of CTEPH. Patients diagnosed with CTEPH should be immediately referred to a PTE center, before the onset of persistent arteriopathy.

Keywords: Chronic thromboembolic pulmonary hypertension, progressive right heart failure, pulmonary hypertension, pulmonary thromboendarterectomy.

Chronic thromboembolic pulmonary hypertension (CTEPH) is characterized by intraluminal thrombus organization and fibrous stenosis or by total obliteration of pulmonary arteries.[1] Consequently, pulmonary vascular resistance increases, leading to pulmonary hypertension (PH) and right heart failure.[2] Vascular disobliteration by pulmonary thrombo-endarterectomy (PTE) is the treatment of choice for patients with CTEPH,[3] but not all patients are eligible for surgery.[4] Treatment of CTEPH usually requires a multidisciplinary approach and is provided through surgery or medical treatment or both. Pulmonary thromboendarterectomy is the actual gold-standard treatment.[5]

Postoperative courses of the PTE patients can be difficult in terms of hemodynamics and ventilation management.[4,5] Reperfusion edema of lungs in pulmonary endarterectomized segments and right ventricle dysfunction due to extracorporeal circulation, ischemia, hypothermia, residual pulmonary hypertension, are the most important issues. Maintaining the sufficient right ventricle function,

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the organ perfusion, the renal function, the adequate oxygenation and avoiding early pulmonary reocclusion are the mainstay of postoperative care.[6,7] It has been demonstrated that measurement of cardiac flow, mixed venous oxygen saturation, arterial blood gas samples are beneficial in terms of monitoring adequate ventilation and circulation.

In the present study, we present our surgical results and postoperative management in high-risk CTEPH patients undergoing PTE in our newly established center.

PATIENTS AND METHODS

This single-center, retrospective study was conducted at Dr. Siyami Ersek Thoracic and Cardiovascular Surgery Training and Research Hospital, Department of Cardiovascular Surgery between November 2015 and December 2020. Twenty-nine patients who were diagnosed with CTEPH and who underwent PTE based on a multidisciplinary assessment were screened. Nine of these patients (6 males, 3 females; median age: 52 years; range, 34 to 67 years) who had a higher risk of mortality were included in this study. The PTE procedure was performed under total circulatory arrest (TCA) and cardiopulmonary bypass (CPB). Data of these patients were reviewed retrospectively. Patients were initially evaluated in our preoperative CTEPH outpatient clinic and the Multidisciplinary Council decided on PTE surgery based on a set of prespecified criteria.

Inclusion criteria were as follows: age ≥18 years, documented PH diagnosis confirmed by right heart catheterization (RHC), a resting mean pulmonary artery pressure of ≥25 mmHg, or a post-exercise pulmonary capillary wedge pressure of ≥30 mmHg. Ventilation/perfusion scintigraphy studies were performed in all patients routinely. The patients with normal ventilation and large pulmonary perfusion defects or perfusion defects confined to minimum one segment were scheduled for surgery. The severity of pulmonary lesions and suitability for endarterectomy were routinely evaluated by pulmonary computed tomography (CT) angiography in all the patients. The patients should have been on anticoagulation for a minimum of three months before surgery. Coronary angiography was performed in all patients above 40 years of age. Echocardiographic studies were made in all the patients, and additional cardiac pathologies were investigated. The decision for surgery was made according to the severity of the symptoms and the deterioration in pulmonary hemodynamics. The selected patients had difficulty in their daily living activities and were usually intolerant to minimal effort or dyspneic at rest (New York Heart Association [NHYA] Functional Class III-IV). The RHC was performed to all patients. The 6-Minute Walk Test (6MWT) results were recorded preoperatively and postoperatively, including their fastest walking time and walking distances on a track of 60 meters per lap. All these data were considered by our Multidisciplinary CTEPH Council for eligibility for surgery. A written informed consent was obtained from each patient. The study protocol was approved by the Dr. Siyami Ersek Thoracic and Cardiovascular Surgery Training and Research Hospital Ethics Committee (Date: 21.12.2020, HNEAH-KAEK 2020/262-3121). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Surgical technique

The main goals of surgery are to restore pulmonary perfusion and ventilation-perfusion balance, to decrease the right ventricle (RV) afterload, and avoid secondary vasculopathies of pulmonary arteries. Necessary techniques and modifications allowing these goals within an acceptable operative risk are defined by San Diego group and carried out in CTEPH centers.[8]

Surgery was performed using intermittent circulatory arrest methods under CPB and deep hypothermia. Blood-free operative field was ensured for an accurate and effective endarterectomy. Surgery was not only the removal of the pulmonary thrombotic material, but a true endarterectomy implicating removal of a fibrotic material organized with neointimal and medial layers. In our clinic, operation was initiated by median sternotomy. The patient was heparinized and, then, connected to the CPB pump after aortic and bicaval cannulation. Through the aortic root cannula positioned into the ascending aorta, blood cardioplegia was administered to obtain cardiac arrest. Then, the body temperature was cooled down to 18°C. Two vent cannulas were introduced into the superior pulmonary vein and pulmonary artery during cool down. Antegrade blood cardioplegia was prepared and, through the aortic root cannula positioned into the ascending aorta, cardioplegia was administered to obtain cardiac arrest. Subsequently, during the intermittent TCA, the procedure was performed. Firstly, the right pulmonary artery was reached and incised longitudinally between the ascending aorta and superior vena cava. The correct plane was

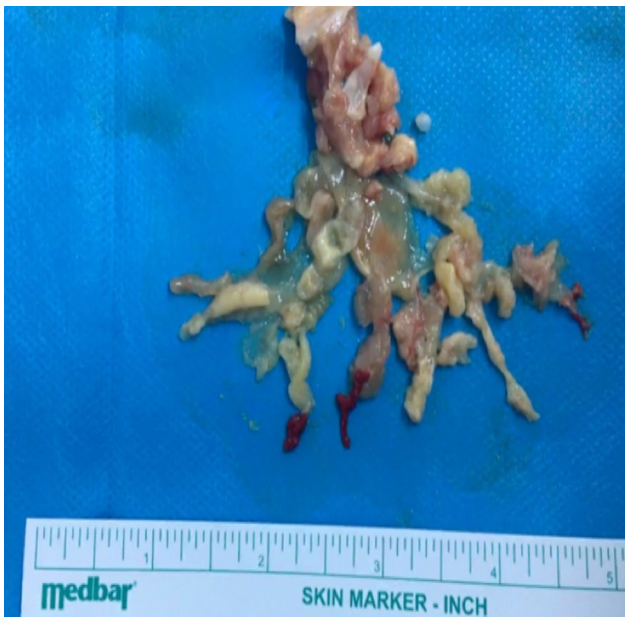

Figure 1. Pulmonary cyst and endarterectomy material.

reached and endarterectomy was performed starting from proximal side proceeding toward the distal vessel. Correct endarterectomy plane was obtained after extracting the larger thrombotic material. The most distal-end endarterectomy was executed during 20-min TCA period. Endarterectomy specimens were circumferentially tracked in each lobe until reaching segmental and subsegmental branches (Figure 1). After reperfusion and closure of the right pulmonary artery incision, the left pulmonary artery was incised. Left pulmonary artery endarterectomy required another TCA period. Cardiopulmonary bypass was reinitiated and the left pulmonary artery incision was repaired. Tricuspid valve repair was not necessary, as tricuspid insufficiency usually recovers during the following days of the successful PTE. Weaning from CPB was performed carefully after reheating. Hemostasis was assured and the operation was completed.

Table 1. Baseline demographic and clinical data of patients

Patient characteristics	n	%	Median	Range
Age (year)			52	34-67
Sex				
Male	6	66.6		
Female	3	33.3		
Hypertension	1	0.52		
Diabetes Mellitus	1	0.26		
Coronary artery disease	1	0.26		

Postoperative management

In our institution, careful fluid management and vasoactive medication administration, and pressure-controlled mechanical ventilation were maintained to provide prompt stabilization of hemodynamics and gas exchange, leading early extubation on the first or second postoperative day. Long-term ventilatory support was needed in 15% of the patients, due to RV failure caused by reperfusion edema and/or residual PH. In order to avoid reocclusion, we administered prophylactic intravenous unfractionated heparin at postoperative 2 and 4 h and, then, warfarin was initiated between the postoperative Days 3 to 5 to provide continuous anticoagulation. We strongly recommended life-long anticoagulation following endarterectomy for all patients.

Table 2. Overview of the individual characteristics and clinical processes of patients

Patient	Age/Sex	CTEPH type	CTEPH-etiology	PVR pre-op	PVR post-op	Initial NYHA	Outcome NYHA	Outcome	Causes of death	ECMO days
1	53/F	4	RVF	922	340	3	1	Following		7
2	67/F	1	PAS	1066	248	4	x	Dead 1st month after PEA	Angiosarcoma	x
3	34/M	1	Hydatid cyst	800	310	3	2	Following		x
4	58 /M	1	Adeno-CA	1120	298	4	x	Dead 3rd month after PEA	Adeno-CA	x
5	56/M	2	RVF	1257	248	3	1	Following		6
6	61/F	4	RVF	1040	428.5	4	x	Dead 38th days after PEA	MOF	7
7	50/M	1	Hydatid cyst	653	345	3	x	Dead 3rd days after PEA	Anaphylactic shock	x
8	48/M	4	RVF	800	350	4	2	Following		5
9	44/M	3	RVF	798	250	3	2	Following		7

PVR: Pulmonary vascular resistance; NYHA: New York Heart Association; RVF: Right heart failure; PAS: Pulmonary angiosarcoma; PEA: Pulmonary endarterectomy; CA: Cancer; MOF: Multiorgan failure.

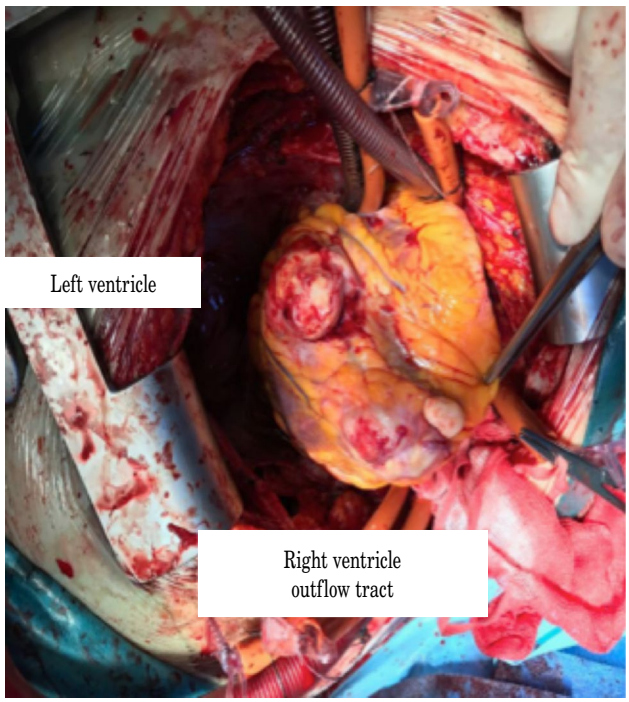

Figure 2. Right ventricular outlet and right ventriculotomy.

Statistical analysis

Statistical analysis was performed using the STATA for Macintosh version 12.0 software (STATA Corp., College Station, TX, USA). Descriptive data were expressed in mean ± standard deviation (SD), median (min-max), or number and frequency, where applicable. The Fisher's exact test was used to compare categorical data, while the Students t-test was used to compare continuous variables. A p value of <0.05 was considered statistically significant.

RESULTS

Baseline demographic and clinical characteristics of the patients are shown in Table 1. Of the patients, 99% had dyspnea, 33% had edema, 22.2% had fatigue, 11.1% had chest pain, and 11.1% had hemoptysis.

Of the patients with CTEPH, two had a hydatid cyst, two had a malignant tumor, and five had advanced right heart failure with poor end organ functions. Two patients required an additional intervention including tricuspid ring annuloplasty and atrial septal defect closure in each. Preoperative severe PH was observed in all of the patients. Left ventricular dimensions and functions were normal in all patients. All the patients had significant RV dilatation and dysfunction, and one of these patients had very severe RV dysfunction and could not survive. An overview of the individual characteristics and clinical processes of the patients is shown in Table 2.

Table 3. Pre- and postoperative data for hemodynamic variables

	Preoperative		Postoperative		
	n	Mean±SD	n	Mean±SD	*p*
LVEF (%)		55.5±7		57.5±5	NS
Right ventricular basal diameter (mm)		5.5±1.2		5.2±0.8	NS
TAPSE (mm)		13.9±3		16.5±3	NS
RVS velocity (cm/sn)		8±1.5		9.5±1.2	NS
PAP (systolic) mmHg		78±22		41±20	≤0.05
PVR Woods (Unite)		13±2.5		7±3	≤0.05
SVR Woods (Unite)		25±1.5		21±1.8	≤0.05
CI (L/ min/m^2)		1.27±0.6		2.2±0.6	≤0.05
CO (L/min)		2.62±0.5		4.1±0.5	≤0.05
Oxygen saturation (%)		85±3.5		95±4	≤0.05
6 Minute Walk Test (m)		345±10		460±10	≤0.05
NYHA Class					
1	-		2		
2	-		3		
3	5		-		
4	4		-		

SD: Standard deviation; LVEF: Left ventricular ejection fraction; TAPSE: Tricuspid annular plane systolic excursion; RVS: Right ventricular systolic; PAP: Pulmonary artery pressure; PVR: Pulmonary vascular resistance; SVR: Systemic vascular resistance; CI: Cardiac index; CO: Cardiac output; NYHA: New York Heart Association; NS: Not significant.

Table 4. CTEPH etiology

	n	%	*p*
Angiosarcoma	1	11	NS
Adenocarcinoma	1	11	NS
Hydatid cyst	2	22	NS
End-stage right heart failure	5	55	NS

CTEPH: Chronic thromboembolic pulmonary hypertension; NS: Not significant.

Table 5. Operative data

Operative data	Minutes	*p*
Cardiopulmonary bypass time	297	NS
Cross-clamp time	132	NS
Total circulatory arrest time	37	NS

NS: Not significant.

Of two patients with a pulmonary hydatid cyst, one had RV outlet involvement. Beside the common surgical procedure, we fastened both vena cava superior and inferior and incised the right atrium in our patients. Contents of the RV hydatid cyst was aspirated, and its capsule was excised from the inferior vena cava. The RV was further examined for cysts, and the other cysts were in the RV outlet and were excised successfully via right ventriculotomy (Figures 1 and 2).

Blood-free area with TCA under CPB was necessary for removing cysts without causing rupture, anaphylactic shock or systemic embolism. The other two patients with a pulmonary angiosarcoma (PAS) and pulmonary adenocarcinoma presented with severe CTEPH manifestations.

One patient with adenocarcinoma had also pneumonectomy simultaneously. This patient had chronic thrombi occluding the left upper and left middle lobar arteries. Another patient with a PAS had bilateral main pulmonary artery stenosis with severe CTEPH manifestations. Preoperative and postoperative data, etiologies, and variables of operations are presented in Table 3, 4, and 5, respectively.

DISCUSSION

In some studies, residual PH with PVR ≥425 dyn·s·cm–5 correlated with worse survival.[9] Objective definitions of the operation are still unclear, but some features are more likely to predict a good outcome (Table 6). While selected patients may technically be operative, they may not benefit from endarterectomy due to significant comorbidities. The best treatment for these strains remains unclear.

The international registry of incident cases of CTEPH reported a three-year survival of 90% in the operated patients and 70% in non-operated patients.[8-10] The mortality rates have significantly decreased after the definition of PTE for CTEPH in 1970s.[11] The surgical procedure is considered therapeutic and safe. Patients should be evaluated in multidisciplinary clinics and PTE should be proposed to all of them, even if they have distal vessel disease as the cause of CTEPH.[12] However, diffuse pulmonary edema due to reperfusion, persistent PH, or hypoxia-related life-threatening complications can be still seen in a few number of patients, despite advances in surgical techniques and increasing experience level.

In general, favorable results are obtained by the removal of large amounts of thromboembolic material and, on the other side, residual PH is one of the main reasons of mortality in the postoperative period.[13] Classical methods for treatment are insufficient for hemodynamic stabilization after residual PH. These

Table 6. Favorable risk-benefit assessment for pulmonary endarterectomy

Characteristics	Lower risk with predictable good long-term outcome	Higher risk with less predictable long-term outcome (not contraindications)
History	History of DVT/PE	No history of DVT/PE
Examination	No signs of right heart failure	Signs of right heart failure
Comorbidity	None	Significant concomitant lung or left heart disease
Functional limitation	Functional Class II or III	Functional Class IV
Imaging	Clear disease concordant on all images	Inconsistency on imaging modalities
Type of disease	Bilateral lower lobe disease	No disease appreciable in lower lobes
Hemodynamics	PVR <1,000 dyn·s·cm^{-5} , in proportion to site and number of obstructions on imaging; higher PA pulse pressure	PVR >1,200 dyn·s·cm^{-5} , out of proportion to site and number of obstructions on imaging; higher PA diastolic pressure

DVT: Deep vein thrombosis; PE: Pulmonary embolism; PVR: Pulmonary vascular resistance; PA: Pulmonary artery.

patients need full cardiopulmonary support using venous-arterial extracorporeal membrane oxygenation (VA-ECMO) to avoid multiorgan failure and death as an inevitable result of increasing pulmonary resistance, hypoxia, and RV failure.

Pre- or postoperative VA-ECMO in patients undergoing PTE can be successfully used for bridging to recovery in patients worsening cardiopulmonary functions. We suggest that support devices, that we use in our clinic since 2008, are helpful for stabilizing patients in a safe and effective way. The ECMO is used for the management of acute decompensation. Conventionally, ECMO is considered for the patients with severe cardiopulmonary failure, despite maximal pharmacological and ventilatory support. In our study, we used central ECMO and none of the patients had any complication. In addition, two patients were supported with VA-ECMO due to oxygenation insufficiency related to reperfusion injury, while the other three patients were supported with VA-ECMO due to RV failure. In these patients, cardiac function and certain RV functions could be a critical factor for survival. Of note, all patients in need of ECMO had poor preoperative RV function. All four patients with ECMO were weaned from ECMO and their postoperative course was uneventful. One of the patients supported with ECMO who had nephrotic syndrome died from multiorgan failure.

Pulmonary vascular hemodynamics can return to normal after successful PTE.[9] Some studies have shown that RV has an extraordinary ability to undergo reverse remodeling after PTE, despite severely suppressed function prior to surgery.[14-16] The hemodynamic changes are paralleled by inverse remodeling of the RV volumes and an improvement in ejection fraction.

In this study, five patients had RV failure. One of these patients died of multiple organ failure. The remaining four patients were still under follow-up in our PH outpatient clinic with the RV ejection fraction values being almost doubled. It is noteworthy that RV maintained the ability to reverse remodeling, despite severely decreased function prior to PTE. A study has shown that these parameters play a critical role in remodeling and reverse remodeling, as RV afterload and ventriculoarterial connection are substantially altered.[17] Chronic pulmonary thromboembolism accompanied by intracardiac and pulmonary hydatid disease is a rare medical occurrence. Heart involvement is seen in 0.5 to 2% of the patients.[18] Left ventricular involvement is more common than RV (60% *vs.* 15%, respectively),[19] but the involvement of pulmonary arteries is rare. Its relation with chronic pulmonary thromboembolism is uncommonly reported.[20,21] In our study, pulmonary cystic hydatid disease was the cause of CTEPH in two of our patients, involving RV and pulmonary artery. One patient had right lower pulmonary lobe wedge resection for pulmonary hydatid disease and removal of RV hydatid cyst (under CPB) and PTE under TCA. The other patient had PTE under TCA, after right PTE and right ventriculotomy to remove intracardiac cysts in the RV outlet. The first patient died from anaphylactic shock, while the second patient was discharged with cure without any postoperative complications and was still under follow-up. The hydatid cyst disease is a parasitic infection caused by *Echinococcus granulosus*. Even cystic disease involvement in pulmonary circulation can be manifested as early thromboembolic PH, pulmonary embolization due to cysts or sudden death following anaphylactic shock due to rupture of cysts have been defined in the literature.[22]

In our study, two patients had PTE using Jameson aspirators and Madani forceps, and the cysts and their branches were removed without rupture via right pulmonary arteriotomy. Thrombotic material was organized around the cystic wall. Excision of this cyst-thrombus complex was not different than other PTE procedures. Cardiac hydatid cyst rupture is a serious complication and risk of intracavitary rupture in right heart cysts is higher.[19,20] Thromboendarterectomy should be performed under circulatory arrest to remove cysts carefully in a blood-free environment without rupturing them. Therefore, these patients should be referred to multidisciplinary centers without delay.

Pulmonary angiosarcoma is a rare, but aggressive disease with poor prognosis. Primary PAS is usually mistaken for chronic pulmonary thromboembolism. Surgical intervention is the mainstay of the treatment of PAS; however, postoperative prognosis is still poor despite prolonged survival. In several studies, additional PTE patients showed better survival rates than those with isolated tumor excision.[22-26] In our study, two of our patients had a malignant tumor. One had pulmonary adenocarcinoma and the other had a PAS. Both patients with CTEPH manifestations underwent routine PTE procedure. There was no complication in the postoperative course. The patient with a PAS died one month after discharge, while the patient with adenocarcinoma died three months after discharge.

Patients with operable CTEPH should receive PTE as a treatment option. For inoperable cases, the highest level of evidence supports initiation of medical therapy and evaluation of balloon pulmonary angioplasty (BPA). Patients with persistent/recurrent symptomatic PH following PTE should seek medical treatment and consider for BPA or undergo re-endarterectomy in case of reocclusion.[27] Finally, given the subjectivity of the workability assessment, it is possible for a patient initially considered to be inoperable to receive PTE with or without any treatment for inoperable CTEPH. Therefore, the new algorithm allows for fluidity between these treatment modalities, as it gains knowledge and expertise.

Riociguat is the approved medical therapy for inoperable CTEPH patients, based on the Chronic Thromboembolic Pulmonary Hypertension Soluble Guanylate Cyclase-Stimulator Trials (CHEST).[28,29] Recently, the Macitentan in Subjects With Inoperable Chronic Thromboembolic Pulmonary Hypertension-1 (MERIT-1) trial provided the first evidence on combination drug therapy in inoperable CTEPH cases.[30] In the study of CHEST-1, riociguat was beneficial for patients with residual PH after endarterectomy.[31] Nonetheless, further studies are needed to clarify whether PH-targeted medical therapy is harmful or beneficial in operable patients prior to PTE.

As we were a newly established center, our patient number was small and we did not have a wide range of options. We made patients who had the chance to have an operation at the border. This was the limitation of our study.

In conclusion, PTE remains the treatment of choice for patients with operative CTEPH. Thromboendarterectomy under circulatory arrest is the effective and the unique treatment in patients with severe pulmonary artery involvement accompanying distinctive dyspnea and heart failure manifestations. Myocardial protection, management of right heart failure and management of TCA are the cornerstone of a successful surgical result.

Declaration of conflicting interests

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REFERENCES

1. Klepetko W, Mayer E, Sandoval J, Trulock EP, Vachiery JL, Dartevelle P, et al. Interventional and surgical modalities of treatment for pulmonary arterial hypertension. J Am Coll Cardiol 2004;43(12 Suppl S):73S-80S.
2. Gerges M, Yacoub M. Chronic thromboembolic pulmonary hypertension - still evolving. Glob Cardiol Sci Pract 2020;2020:e202011.
3. Jamieson SW, Kapelanski DP, Sakakibara N, Manecke GR, Thistlethwaite PA, Kerr KM, et al. Pulmonary endarterectomy: Experience and lessons learned in 1,500 cases. Ann Thorac Surg 2003;76:1457-62.
4. Madani MM. Surgical Treatment of Chronic Thromboembolic Pulmonary Hypertension: Pulmonary Thromboendarterectomy. Methodist Debakey Cardiovasc J 2016;12:213-8.
5. Hoeper MM, Mayer E, Simonneau G, Rubin LJ. Chronic thromboembolic pulmonary hypertension. Circulation 2006;113:2011-20.
6. Fedullo PF, Auger WR, Dembitsky WP. Postoperative management of the patient undergoing pulmonary thromboendarterectomy. Semin Thorac Cardiovasc Surg 1999;11:172-8.
7. Kramm T, Eberle B, Krummenauer F, Guth S, Oelert H, Mayer E. Inhaled iloprost in patients with chronic thromboembolic pulmonary hypertension: Effects before and after pulmonary thromboendarterectomy. Ann Thorac Surg 2003;76:711-8.
8. Delcroix M, Lang I, Pepke-Zaba J, Jansa P, D'Armini AM, Snijder R, et al. Long-term outcome of patients with chronic thromboembolic pulmonary hypertension: Results from an international prospective registry. Circulation 2016;133:859-71.
9. Mayer E, Dahm M, Hake U, Schmid FX, Pitton M, Kupferwasser I, et al. Mid-term results of pulmonary thromboendarterectomy for chronic thromboembolic pulmonary hypertension. Ann Thorac Surg 1996;61:1788-92.
10. Kim NH, Delcroix M, Jais X, Madani MM, Matsubara H, Mayer E, et al. Chronic thromboembolic pulmonary hypertension. Eur Respir J 2019;53:1801915.
11. Moser KM, Braunwald NS. Successful surgical intervention in severe chronic thromboembolic pulmonary hypertension. Chest 1973;64:29-35.
12. Simonneau G, Gatzoulis MA, Adatia I, Celermajer D, Denton C, Ghofrani A, et al. Updated clinical classification of pulmonary hypertension. J Am Coll Cardiol 2013;62(25 Suppl):D34-41.
13. Thistlethwaite PA, Kemp A, Du L, Madani MM, Jamieson SW. Outcomes of pulmonary endarterectomy for treatment of extreme thromboembolic pulmonary hypertension. J Thorac Cardiovasc Surg 2006;131:307-13.
14. Reesink HJ, Marcus JT, Tulevski II, Jamieson S, Kloek JJ, Vonk Noordegraaf A, et al. Reverse right ventricular remodeling after pulmonary endarterectomy in patients with chronic thromboembolic pulmonary hypertension: Utility of magnetic resonance imaging to demonstrate restoration of the right ventricle. J Thorac Cardiovasc Surg 2007;133:58-64.

15. Kreitner KF, Ley S, Kauczor HU, Mayer E, Kramm T, Pitton MB, et al. Chronic thromboembolic pulmonary hypertension: Pre- and postoperative assessment with breath-hold MR imaging techniques. Radiology 2004;232:535-43.
16. D'Armini AM, Zanotti G, Ghio S, Magrini G, Pozzi M, Scelsi L, et al. Reverse right ventricular remodeling after pulmonary endarterectomy. J Thorac Cardiovasc Surg 2007;133:162-8.
17. Rolf A, Rixe J, Kim WK, Börgel J, Möllmann H, Nef HM, et al. Right ventricular adaptation to pulmonary pressure load in patients with chronic thromboembolic pulmonary hypertension before and after successful pulmonary endarterectomy--a cardiovascular magnetic resonance study. J Cardiovasc Magn Reson 2014;16:96.
18. Besir Y, Gucu A, Surer S, Rodoplu O, Melek M, Tetik O. Giant cardiac hydatid cyst in the interventricular septum protruding to right ventricular epicardium. Indian Heart J 2013;65:81-3.
19. Shojaei E, Yassin Z, Rezahosseini O. Cardiac hydatid cyst: A case report. Iran J Public Health 2016;45:1507-10.
20. Orhan G, Bastopcu M, Aydemir B, Ersoz MS. Intracardiac and pulmonary artery hydatidosis causing thromboembolic pulmonary hypertension. Eur J Cardiothorac Surg 2018;53:689-90.
21. Kohlmaier B, Trobisch A, Pfurtscheller K, Knez I, Klepetko W, Pilhatsch A, et al. Cardiac and pulmonary cystic echinococcosis with massive obstruction of the pulmonary vessel system in a 16-year-old girl. Pediatr Infect Dis J 2018;37:e273-e275.
22. Şahpaz A, İrez A, Gülbeyaz H, Şener MT, Kök AN. Non-thrombotic pulmonary embolism due to liver hydatic cyst: A case report. Balkan Med J 2017;34:275-7.
23. Bandyopadhyay D, Panchabhai TS, Bajaj NS, Patil PD, Bunte MC. Primary pulmonary artery sarcoma: A close associate of pulmonary embolism-20-year observational analysis. J Thorac Dis 2016;8:2592-601.
24. Mussot S, Ghigna MR, Mercier O, Fabre D, Fadel E, Le Cesne A, et al. Retrospective institutional study of 31 patients treated for pulmonary artery sarcoma. Eur J Cardiothorac Surg 2013;43:787-93.
25. Lee Y, Kim HJ, Yoon H, Choi CM, Oh YM, Lee SD, et al. Clinical characteristics and treatment outcomes of primary pulmonary artery sarcoma in Korea. J Korean Med Sci 2016;31:1755-60.
26. Srivali N, Yi ES, Ryu JH. Pulmonary artery sarcoma mimicking pulmonary embolism: A case series. QJM 2017;110:283-6.
27. Mo M, Kapelanski DP, Mitruka SN, Auger WR, Fedullo PF, Channick RN, et al. Reoperative pulmonary thromboendarterectomy. Ann Thorac Surg 1999;68:1770-6.
28. Ghofrani HA, D'Armini AM, Grimminger F, Hoeper MM, Jansa P, Kim NH, et al. Riociguat for the treatment of chronic thromboembolic pulmonary hypertension. N Engl J Med 2013;369:319-29.
29. Simonneau G, D'Armini AM, Ghofrani HA, Grimminger F, Jansa P, Kim NH, et al. Predictors of long-term outcomes in patients treated with riociguat for chronic thromboembolic pulmonary hypertension: Data from the CHEST-2 open-label, randomised, long-term extension trial. Lancet Respir Med 2016;4:372-80.
30. Ghofrani HA, Simonneau G, D'Armini AM, Fedullo P, Howard LS, Jaïs X, et al. Macitentan for the treatment of inoperable chronic thromboembolic pulmonary hypertension (MERIT-1): Results from the multicentre, phase 2, randomised, double-blind, placebo-controlled study. Lancet Respir Med 2017;5:785-94.
31. Wiedenroth CB, Liebetrau C, Breithecker A, Guth S, Lautze HJ, Ortmann E, et al. Combined pulmonary endarterectomy and balloon pulmonary angioplasty in patients with chronic thromboembolic pulmonary hypertension. J Heart Lung Transplant 2016;35:591-6.