Pulmonary endarterectomy: the treatment of choice for chronic thromboembolic pulmonary hypertension

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A percentage ranging from 0.1 to 4.0 of patients recovering from acute pulmonary embolism develop chronic thromboembolic pulmonary hypertension (CTEPH). Without intervention, CTEPH is a progressive and lethal disease for which there is no effective medical therapy. Pulmonary endarterectomy (PEA) is the treatment of choice. Lung transplantation is indicated only in few cases when PEA is not feasible. Since 1994 at the IRCCS San Matteo Hospital - University of Pavia (Italy), 134 PEAs have been performed. Preoperatively, NYHA class distribution was respectively 3-II, 56-III, and 75-IV; mean pulmonary artery pressure and pulmonary vascular resistances were 47 ± 13 mmHg and 1149 ± 535 dynes*s*cm^{-5} respectively. The overall operative mortality has been 9.7% (4.5% in 2004). Survival at 3-month, 1-year, and 3-year follow-up was 89.5 ± 2.6, 87.8 ± 2.9, and 83.3 ± 3.5% respectively; this last rate was unchanged up to 10 years. After PEA, mean pulmonary artery pressure and pulmonary vascular resistances were 25 ± 9 mmHg and 322 ± 229 dynes*s*cm^{-5} respectively and these results were stable over time. At the 3-year follow-up, 94% of patients were in NYHA class I or II and the only therapy is anticoagulation.

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Pulmonary endarterectomy (PEA) is the treatment for pulmonary arterial hypertension (PAH) resulting from chronic thromboembolic obstruction of major pulmonary arteries. It is a highly effective procedure, with relatively low operative mortality and associated with long-term improvement in functional and hemodynamic status in the presence of adequate prophylaxis against embolic recurrences. Yet, it remains an uncommon operation because it is little known to much of the medical community and because pulmonary thromboembolic disease is a severely under-diagnosed condition in both its acute and chronic stages. Patients generally present with non-specific signs and symptoms, and conventional diagnostic tools lack high specificity.

Epidemiology

In Italy, the number of new symptomatic cases of acute pulmonary embolism is about 65 000/year[1]. How many patients experiencing an episode of acute pulmonary embolism do develop chronic thromboembolic pulmonary hypertension (CTEPH)? Historical estimates indicate that CTEPH occurs in approximately 0.1 to 0.5% of patients surviving an acute pulmonary embolism[2,3]. However, recent studies suggest a significantly higher prevalence of about 4.0%[4,5]. Considering only the symptomatic acute pulmonary embolism cases, we can extrapolate that in Italy there should be between 65 and 2600 of new CTEPH cases annually.

The number of patients that would benefit from PEA is extremely high. Presti et al.[6] found evidence of chronic thromboembolic obstruction of major pulmonary arteries in approximately 1.0% of 7753 necropsies performed on subjects with an average age of 67 years. Yet, in many PEA patients the disease is localized to the minor pulmonary arteries, where chronic thrombi are often unnoticed in autopsy studies[7].

Natural history

Recurrences of pulmonary embolism[5,8], *in situ* thrombosis[8], vascular remodeling, and arteriopathic changes within the small, non-elastic pulmonary arteries[9,10] are thought to be responsible for the progression of the disease. The prognosis for medically-treated patients is poor, especially in the absence of any intracardiac communi-

cation, and is proportional to the degree of PAH at the time of diagnosis. The 5-year mortality is 70% for patients with mean pulmonary artery pressure (mPAP) > 40 mmHg and approaches 90% when mPAP is > 50 mmHg[11].

Understanding both the epidemiology and the natural history of CTEPH, along with the poor prognosis associated with this disease, should encourage physicians to screen for incomplete embolic resolution in all recovered patients from a documented pulmonary embolism. Screening for PAH in every patient with a new-onset dyspnea and a history of previous venous thromboembolism (deep venous thrombosis and/or pulmonary embolism) is mandatory. The absence of symptoms during the primary acute event does not preclude evolution into the chronic stage of the disease. Thus, PAH should also be considered in the differential diagnosis of dyspnea whenever there is no clear correlation with an underlying disorder, regardless of whether or not the patient's history seems to suggest non-thoracic causes. Only a high level of suspicion and the awareness of the extremely wide and non-specific clinical spectrum of CTEPH can allow a timely diagnosis.

Preoperative evaluation

Three are the goals for a physician dealing with a suspect case of CTEPH: 1) to identify the presence of PAH; 2) to define the etiology; and 3) to evaluate the most appropriate therapy for the patient.

The initial work-up consists of: ECG, chest X-ray, and echocardiography. These steps allow the physician to obtain an overview of the functional and anatomical picture and to estimate the pulmonary artery pressure. None of these studies are diagnostic for CTEPH. ECG and chest X-ray may be normal also in the presence of PAH. Echocardiography is the exam that justifies the need for more additional diagnostic testing.

Once the estimated pulmonary artery pressure is in the hypertensive range, scheduling for radionuclide ventilation-perfusion scan is indicated. The purpose of the ventilation-perfusion scan is to reveal ventilation-perfusion mismatch areas caused by the central pulmonary vascular obstruction. All patients with CTEPH have a scan characterized by the presence of one of more segmental, mismatched defects. Ruling out idiopathic PAH is the most important implication in patients with this disease process who have either normal perfusion scans or those characterized by mottling. The perfusion scan can never be used to evaluate the extension of the embolic disease because it underestimates the actual degree of vascular occlusion[4]. In patients with appropriate perfusion scan findings, the right heart catheterization assists in defining diagnosis, prognosis, and surgical indication. Pulmonary vascular resistance (PVR) at the time of clinical presentation is usually in excess of 8 Wood units (640 dynes*s*cm^{-5}). However, as far as organ damage secondary to right heart failure is deemed reversible, no patient should be refused surgery for hemodynamic reasons. Performing pulmonary function studies is mandatory to exclude restrictive or obstructive pulmonary disease as a cause of PAH. In planning the intervention, severe obstructive or restrictive components are seriously taken into account. If they are in an advanced stage, the risk for respiratory morbidity might be increased because of an expected prolonged ventilatory support and a higher susceptibility to respiratory infections.

Once the diagnosis of PAH is made and a thromboembolic etiology suggested by the ventilation-perfusion scan, pulmonary angiography must be carried out. It is actually the most significant exam in the evaluation process. To confirm the diagnosis of CTEPH the classical features have to be outlined[12]. In order to evaluate surgical accessibility, chronic emboli location has to be clarified. Computed tomography scan is also important to define anatomical details and plan surgical strategy. It localizes the lesions and also refines the vascular wall width, which is important in planning an endarterectomy. It also visualizes course, connections and size of the ectasic bronchial arteries. In addition, it helps in ruling out associated mediastinal or chest comorbidities (mediastinal carcinoma, fibrous mediastinitis, sarcoidosis, and pulmonary arteritis) or other diseases (pulmonary angiosarcoma).

In male patients older than 40 and in females over 45, coronarography and echo-Doppler of the supra-aortic trunks are routinely performed. Should these two exams and/or echocardiography show any further significant disease, additional cardiac surgery is carried out during PEA. Coronarography and bronchial artery angiography are always indicated whenever the history reveals previous hemoptysis. Coronarography will show possible anastomosis between coronary and bronchial circulations. Bronchial artery angiography will show all the collateral arterial vessels from the systemic to the pulmonary circulation.

Therapy

PEA must be pursued whenever the surgical indications are fulfilled. Medical therapy is not able to affect the natural history of the disease and is only supportive[13,14]. Preventing embolic recurrences and supporting the right ventricle are the frontlines for the medical management. An inferior vena caval filter in the subrenal position is usually also placed during preoperative work-up. Diuretics, digitalis and in advanced stages inotropic support are the mainstay for supporting the failing right ventricle. Few data are available regarding the use of prostanoids in CTEPH[15-17].

Indications to surgery

Selection criteria for PEA are multiple and aim to establish: 1) patient's need for intervention; 2) technical feasibility; and 3) potential for success of the procedure.

Three are the historical indications for this intervention[8,18,19]. Functional and hemodynamic data indicate the need for the operation. The anatomic aspect defines the suitability for surgery (Table I). Thus, the ideal candidate has to present with a moderate to severe functional impairment, PVR > 300 dynes*s*cm^{-5}, and chronic emboli located within and proximal to the segmental arteries. Generally, patients referred for PEA are experiencing severe functional limitation and are often oxygen-dependent. CTEPH is a progressive disease. Small vessel arteriopathy is a major and irreversible component in the hemodynamic decline that steadily occurs over time[3,9]. As surgical mortality is now acceptably low, patients within NYHA class II are often deemed suitable candidates. PVR is the main hemodynamic reference in the evaluation process and is often very high. Thus, hemodynamic impairment is typically severe. However, in few occasions it may be worthwhile to favor the global clinical context over the global single indications. Then, operating on patients within NYHA class II, with evidence of PAH only during exercise, but with a complete vascular obstruction of one lung will be appropriate. Here, the reason to operate is intended to prevent the evolution of the disease and to diminish the dead space ventilation which is contributing to the patient's dyspnea. In patients who are either mildly symptomatic with an adequate (low range) cardiac output or have broad bronchial artery anastomosis with an overestimated measured wedge pressure the calculated PVR may result < 300 dynes*s*cm^{-5}. In these cases mPAP at rest > 25 mmHg is the hemodynamic cut-off. In general, whenever the surgical risk is individually reasonable it is advisable to operate with the purpose of avoiding the evolution of the disease and the onset of the Eisenmenger-like arteriopathy. This should be taken into account especially in young people. Therefore, the range of CTEPH patients needing PEA is wide. It spans from young and mildly symptomatic patients, with hemodynamic impairment only during exercise but with an extensive vascular obstruction to very sick, frankly symptomatic subjects with a severe right ventricular dysfunction due to an aggressive or long-lasting hypertension but only a modest vascular impediment.

Table I. Formal indications to pulmonary endarterectomy.

Clinic: moderate to severe functional impairment (typical patients referred to surgery are in NYHA class III or IV)
Hemodynamic: PVR > 300 dynes*s*cm^{-5}
Anatomic: organized thromboembolic lesions located along the pulmonary vascular bed within and proximal to the segmental arteries

NYHA = New York Heart Association; PVR = pulmonary vascular resistance.

The presence of a surgically accessible thromboembolic disease is always required. Surgical accessibility is a purely operative concept and relates to the feasibility of the intervention. It is assessed mainly by pulmonary angiography and high-resolution computed tomography scan. Ability and experience of the surgical team play an important role in this evaluation. Lesions located along the main, lobar or segmental arteries are considered as surgically accessible. If the chronic emboli are only within subsegmental or even more distal branches, the disease is considered surgically inaccessible. In this case lung transplantation is advisable.

Once the need for PEA and the technical feasibility are established, the next step is to estimate the operative outcome. The principal risk factor for early mortality is the persistence of high PVR after intervention. Postoperative PAH leads to acute right ventricular failure, which carries high mortality. The risk/benefit ratio of PEA is drawn from a comparative evaluation between pulmonary angiography/high resolution computed tomography scan and right heart catheterization. If the preoperative PVR is too elevated compared to the extension of vascular embolic obstruction, secondary arteriopathy or idiopathic PAH are likely to be involved. Such an integrative interpretation of the radiologic images and right heart catheterization is not trivial, and requires good quality films, appropriate projections for each lung, experience, and teamwork among physicians. Any mistake at this point very often carries a high mortality and absence of hemodynamic improvement by the intervention.

In conclusion, each patient with radiologic signs of chronic thromboembolic lesions should be evaluated for PEA. In the presence of symptoms, either at rest or during exercise and surgically accessible lesions, eligibility for PEA will be a consequence. Age, status and rate of progression of the underlying disease, and operative risk are then considered to make the final decision. Thus, selection criteria for PEA are several. Only experience and a large number of patients to evaluate and treat can guarantee excellent results. This is the reason why patients suffering from CTEPH should be referred to institutions with a solid background in both PEA and lung transplantation.

Intra- and postoperative management

PEA is a true endarterectomy of the obstructed major pulmonary arteries. It aims to remove the organized thromboembolic lesions and restore a normal segmen-

tary perfusion. It is accomplished through a median sternotomy incision, using cardiopulmonary bypass with deep hypothermia and periods of circulatory arrest.

Pulmonary embolism should always be considered a bilateral disease[3]. In a series of more than 1500 PEAs, < 1.5% of cases were purely unilateral[3]. Even though imaging studies suggest a unilateral involvement, intraoperative inspection is always needed. The highest number of chronic thromboembolic lesions possible will be detected, maximizing the efficacy of the intervention and preventing the consequences of an incomplete operation (higher perioperative morbidity and mortality, poor long-term outcome, and reintervention). A bloodless operative field is crucial to define an appropriate endarterectomy plane and to develop it deep into the vessels as they become progressively smaller. A scarce visibility increases the risk of breaking distally the endarterectomy specimen leaving residual obstruction. This material will never be reachable a second time and the intervention will loose part of its efficacy. Circulatory arrest is the only way to arrest bronchial blood flow and exsanguinate the patient. Deep hypothermia is then required. A true endarterectomy in the medial tunica is the key of the operation. It does not have to be confused with an embolectomy, which is a completely different intervention for a different disease. After general anesthesia has been induced, cardiopulmonary bypass is instituted and the patient is cooled to 18°C. The first arteriotomy is carried out on the right main pulmonary artery. Visual inspection is started and a clivage plane developed in the tunica media. Once an appropriate plane has been defined, it will be developed deep into the most distal vessels possible of each lobe. Circulatory arrest will be necessary to gain an optimal visibility. Periods of reperfusion through cardiopulmonary bypass may be necessary to avoid long periods of ischemia. The same procedure is followed on the left pulmonary artery. At the end of the endarterectomy, cardiopulmonary bypass is re-instituted and the patient slowly re-warmed. Right ventricular remodeling will quickly restore the competence of the tricuspid valve.

During the immediate postoperative period, the leading principles are: 1) adequate mechanical ventilation; 2) proper inotropic drug management; 3) aggressive diuresis; and 4) early beginning of anticoagulation.

Results

The "Pulmonary Endarterectomy Program" at the IRCCS San Matteo Hospital - University of Pavia (Italy) started in 1994. Ever since, our series has steadily grown and patients are now referred nationally and internationally. In 2004, we evaluated 54 patients for suspected CTEPH. The diagnosis was confirmed in 34 of those. Twenty-five patients had indication for PEA (operability rate 74%). Seven of the remaining 9 patients were added to our lung transplantation waiting list because the embolic lesions were determined to be too distal (n = 5) or associated with severe emphysema (n = 2); 2 patients were given medical therapy because of their ineligibility for lung transplantation due to their advanced age.

Between April 1994 and June 2005, 134 PEAs were performed in 131 patients. In 3 cases redo PEA was required respectively at 39, 40, and 56 months of follow-up. Recurrence of CTEPH occurred because of non-adequate anticoagulation during the follow-up. Candidates for surgery ranged in age from 11 to 81 years (median 53 years), with predominance of males (77/134, 57.5%). Only 69% of them had a diagnosed positive history for deep venous thrombosis. Functional impairment ranged from NYHA class II to IV (3, 56 and 75 respectively). The duration of severe functional impairment (NYHA class III/IV) was 21 ± 26 months (range 2-264 months). The clinical picture had a broad spectrum. We operated on young patients with dyspnea and PAH only during exercise as well as old and high-risk patients with florid right ventricular failure. Nearly 50% (68/134) of our patients were oxygen-dependent. In 33.8% the operation has been carried out on an urgent/emergency regimen. No patient was refused because of hemodynamic impairment; exclusion from surgery happened only because of the presence of distal lesions or severe lung parenchymal disease. In 11.3% of the cases, the presence of other concomitant cardiac diseases required associated procedures (8 patent foramen ovale repairs and 7 coronary artery bypass).

The overall operative mortality rate was 9.7%, reflecting the learning curve for this operation. In 2004, the mortality rate was 4.5% (1/22). Major causes of death were airways bleeding, right ventricular failure, and sepsis. Compared to other institutions, we experienced a lower mortality due to reperfusion pulmonary edema (1/134). However, it represented one of the major postoperative complications. It occurred in 23 patients (17.2%) and has been responsible for an increase in the time of recovery. Duration of mechanical ventilation, intensive care unit and hospital stay progressively decreased over the years. In 2004, the mean intubation length was 1.8 ± 1.3 days (range 1-6 days); the mean intensive care unit and hospital stay were 3.7 ± 2.2 days (range 1-10 days) and 10.6 ± 3.3 days (range 6-19 days), respectively.

We established a postoperative follow-up protocol in order to monitor survival, functional, hemodynamic, and coagulative status, heart remodeling, and lung function. While the program was growing, we decided to progressively introduce further tests to better study our surgical candidates and investigate the course of the disease after PEA. Accordingly, for different studies we had different sized study populations. When patients were too compromised, func-

tional tests were not performed preoperatively. At present, 92% of the PEA patients are actively participating in the follow-up study. We collect survival and clinical data for the remaining 8% via a phone-call basis. Follow-up visits are at 3 months after PEA, yearly for the following 5 years, and then at 7 and 10 years postoperatively.

Both early and late survivals were excellent. Survival rate at 3 months, 1 year, and 3 years were 89.5 ± 2.6, 87.8 ± 2.9, and 83.3 ± 3.5%, respectively. Survival rates had not changed at 5, 7, and 10 years postoperatively.

On the whole, post-PEA improvement was dramatic and immediate. PVR and pulmonary artery pressure fell to nearly normal levels and cardiac output steeply increased[20] (Table II). This was typically evident while the patient was still in the operating room. Right ventricular remodeling also occurred early in the post-PEA course (Table III). Functional recovery steadily continued during the following year after the intervention[21] (Tables IV and V). Considering pre- and post-PEA data at 1, 2, and 3 years, a statistically significant correlation between mPAP and peak oxygen consumption was present ($p < 0.05$, $r > 0.8$); data at 3 months were not considered because discrepancy in the recovery pattern of hemodynamic and functional data. Fifty patients completed follow-up at 3 years. Preoperatively, 29 of the 50 patients (58%) were in NYHA class III, 21 (42%) in NYHA class IV, and 0 in NYHA class II due to chronological reasons (first NYHA class II case operated on in December 2002). Three months after PEA, 29 (58%) subjects were in NYHA class I, 18 (36%) in NYHA class II, and 3 (6%) in NYHA class III. At 1-year follow-up, 40 (80%) patients were in NYHA class I, 10 (20%) in NYHA class II. After 3 years, 1 patient moved from NYHA class II to NYHA class III, and 2 patients moved from NYHA class II to NYHA class IV, due to recurrence of the disease. These 2 patients had a redo PEA. A statistically significant difference exists not only between the preoperative and the postoperative data ($p < 0.0001$), but also between the functional status at 3 months and the other two postoperative controls ($p < 0.001$).

Conclusions

CTEPH is very often misdiagnosed. It is a lethal disease whose natural history cannot be modified by medical therapy. Yet, it is the only form of PAH that can be radically cured by a conservative intervention called PEA. PEA is a very demanding procedure that is routinely performed in about 10 centers worldwide. Proper patient selection, meticulous surgical technique, and adequate postoperative management are mandatory in order to get excellent and permanent results. Thus, experience and multidisciplinary approach are required as well as a high turn over of patients. Poor survival rate

Table II. Hemodynamic data (35 patients with complete 3-year follow-up).

	CVP (mmHg)	mPAP (mmHg)	CO (l/min)	CI (l/min/m^2)	PVR (dynes*s*cm^{-5})	PVRI (dynes*s*cm^{-5}/m^2)	RV-EF (%)
A: Before PEA	7 ± 6	48 ± 12	3.3 ± 0.9	1.8 ± 0.5	1125 ± 412	2027 ± 731	15 ± 8
B: Before discharge	5 ± 4	25 ± 10	5.2 ± 1.1	2.9 ± 0.5	289 ± 142	505 ± 234	32 ± 8
C: 3 months	2 ± 2	24 ± 11	5.1 ± 1.4	2.8 ± 0.6	231 ± 198	542 ± 271	32 ± 7
D: 1 year	1 ± 2	23 ± 12	5.0 ± 1.1	2.7 ± 0.6	290 ± 191	531 ± 343	35 ± 8
E: 3 years	2 ± 2	24 ± 12	4.9 ± 1.1	2.6 ± 0.5	317 ± 226	579 ± 393	34 ± 8
p	A vs B: NS A vs C, D, and E: < 0.000001 B vs C, D and E: < 0.05	A vs B, C, D and E: < 0.000001	A vs B, C, D and E: < 0.000001	A vs B, C, D and E: < 0.000001	A vs B, C, D and E: < 0.000001	A vs B, C, D and E: < 0.000001	A vs B, C, D and E: < 0.000001

CI = cardiac index; CO = cardiac output; CVP = central venous pressure; mPAP = mean pulmonary artery pressure; PVR = pulmonary vascular resistance; PVRI = pulmonary vascular resistance index; RV-EF = right ventricular ejection fraction.

Table III. Echocardiographic data (40 patients with complete 3-year follow-up).

	RV-EDD (mm)	RV-FAS (%)	RV-WT (mm)	LV-EDD (mm)	LV-EDV (ml)	TI (absent/mild/ moderate/severe)	ASM (yes/no)
A: Before-PEA	39 ± 9	21 ± 10	7.3 ± 1.7	41 ± 8	74 ± 32	5/13/13/9	33/7
B: Before discharge	30 ± 8	28 ± 12	6.9 ± 1.5	46 ± 5	99 ± 33	18/17/5/0	4/36
C: 3 months	27 ± 6	28 ± 10	5.9 ± 1.5	48 ± 5	108 ± 30	20/16/4/0	3/37
D: 1 year	27 ± 6	33 ± 9	5.9 ± 1.6	48 ± 5	105 ± 29	16/18/6/0	4/36
E: 3 years	29 ± 6	37 ± 7	5.6 ± 1.1	48 ± 6	111 ± 32	15/17/6/2	5/35
p	A vs B, C, D and E: < 0.000001	A vs B, C, D, and E: < 0.01 B and C vs E: < 0.001	A vs B: NS A vs C, D, and E: < 0.000005 B vs C, D and E: < 0.05	A vs B, C, D, and E: < 0.000001	A vs B, C, D and E: < 0.000001	A vs B, C, D and E: < 0.0001	A vs B, C, D and E: < 0.0001

ASM = abnormal septal motion; LV-EDD = left ventricular end-diastolic diameter; LV-EDV = left ventricular end-diastolic volume; RV-EDD = right ventricular end-diastolic diameter; RV-FAS = right ventricular fractional area shrinkage; RV-WT = right ventricular wall thickness; TI = tricuspid insufficiency.

Table IV. Lung function indices, gas exchanges and modified Bruce test (35 patients with complete 3-year follow-up).

	FEV_1 (%)	FVC (%)	DL_{CO} (%)	PaO_2 (mmHg)	$PaCO_2$ (mmHg)	O_2-sat (%)	DBT (m)
A: Before PEA	94 ± 18	87 ± 17	68 ± 14	68 ± 9	31 ± 4	94 ± 3	137 ± 176
B: Before discharge	Not done	Not done	Not done	Not done	Not done	Not done	Not done
C: 3 months	94 ± 15	89 ± 17	73 ± 18	81 ± 9	34 ± 4	97 ± 1	373 ± 271
D: 1 year	99 ± 16	92 ± 14	74 ± 17	84 ± 9	34 ± 4	97 ± 1	483 ± 247
E: 3 years	98 ± 16	91 ± 17	74 ± 13	79 ± 9	35 ± 4	97 ± 1	555 ± 382
p	NS	NS	NS	A vs C, D and E: < 0.000001	A vs C, D and E: < 0.0005	A vs C, D and E: < 0.00001	A vs C, D and E: < 0.0001 C vs E: < 0.01

DBT = distance with modified Bruce test; DL_{CO} = diffusing lung capacity for carbon monoxide; FEV_1 = forced expiratory volume in 1 s; FVC = forced vital capacity; O_2-sat = oxygen saturation; PaO_2 = arterial oxygen tension; $PaCO_2$ = arterial carbon dioxide tension.

Table V. Cardiopulmonary exercise testing data (17 patients with complete 3-year follow-up).

	pPre (mmHg)	pDP (mmHg*b/min)	pVO_2 (ml/kg/min)	pExe (W)
A: Before PEA	130 ± 25	157 92 ± 4673	9.4 ± 2.6	49 ± 14
B: Before discharge	Not done	Not done	Not done	Not done
C: 3 months	176 ± 29	20 612 ± 5459	14.2 ± 4.4	75 ± 25
D: 1 year	179 ± 29	21 913 ± 5334	16.5 ± 5.6	89 ± 37
E: 3 years	180 ± 28	23 212 ± 6337	17.3 ± 5.8	98 ± 37
p	A vs C, D and E: < 0.00005	A vs C, D and E: < 0.05	A vs C, D and E: < 0.005	A vs C, D and E: < 0.05

pDP = peak double product; pExe = peak exercise; pPre = peak pressure; pVO_2 = peak oxygen consumption.

of medically treated patients, low operative mortality after PEA, and good mid- and long-term outcomes make PEA itself the procedure of choice in the treatment of CTEPH. After a successful procedure, life expectancy is identical to the general age matched population.

Advantages of PEA over lung transplantation are several and important: no waiting list, intervention usually on an elective basis, lower operative mortality, neither acute or chronic rejection, no complications related to chronic immunosuppression, better functional status and quality of life after surgery.

The functional improvement is consequent to the hemodynamic changes right after the procedure. This is shown by the correlation between mPAP and peak oxygen consumption. Besides, the major cause of immediate postoperative morbidity and mortality is the incomplete dissolution of the obstruction. PEA is a complex procedure and there is undoubtedly a learning curve. This is mainly due to the difficulty in properly recognizing the embolic lesions. Only an experienced surgical team can guarantee optimal operative results in terms of survival and functional outcomes.

As surgical and clinical experience accrued, criteria for surgery may be expanded without affecting the outcomes. Thus, a handful of patients have been successfully shifted from our lung transplantation waiting list to the PEA program. This also allowed a better allocation of lung grafts.

A timely diagnosis of CTEPH and an increasing awareness about the efficacy and safety of PEA among the medical community will allow specialists in CTEPH to provide the optimal treatment to a growing number of patients.

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