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Pulmonary endarterectomy combined with cardiac surgery: A 7-year retrospective analysis

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A B S T R A C T

Background: Pulmonary artery endarterectomy (PEA) is established as a successful method for the treatment of chronic thromboembolic pulmonary hypertension (CTEPH). A significant fraction of patients indicated for the pulmonary endarterectomy has other severe comorbidities that generally increase the risk of cardiac surgery. The aim of our study is to analyze the process of indications and therapeutic procedures at our Cardio-Centre, as well as comparing hemodynamic parameters and long-term results in order to determine the continuation of the treatment.
Method: From September 2004 to August 2012, 192 patients underwent PEA for CTEPH. We carried out a retrospective analysis of patients' data. Patients were divided into two groups: A and B. The group A included patients with PEA only (128 patients), group B consisted of patients with PEA and other cardiac procedure (64 patients, i.e. 33.3% of which 72 cardiac procedures were carried out). Group B was further subdivided into group B1-patients with PEA + CABG, which included 25 patients, and group B2-PEA + suture of PFO, which consisted of 29 patients for more detailed analysis.
Results: Five-year survival rate is 83% in group A, 79.3% in group B, and 63.1% in group B1. Group B1 is statistically significantly different from group A ($P = 0.031$). The cumulative survival rate is comparable for groups A and B2. Cumulative survival rate is very good with annual survival in group A – 94%, group B2 – 90% and group B1 – 82.6%.
Conclusion: Results of combined interventions are comparable with isolated pulmonary endarterectomy. We did not find any differences in hemodynamic effects. All patients indicated for the PEA should be screened for the most common comorbidities regardless of their age. We recommend implementation CryoMAZE for the treatment of atrial fibrillation or atrial flutter.

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Introduction

Pulmonary artery endarterectomy (PEA) is established as a successful method for the treatment of chronic thromboembolic pulmonary hypertension (CTEPH). In a selected group of patients, it can lead to the cure of this disease, which if left untreated has an otherwise very poor prognosis as showed by a number of studies. A significant fraction of patients indicated for the pulmonary endarterectomy have other severe comorbidities that generally increase the risk of cardiac surgery. As a standard, the risk of cardiac surgery is calculated using scoring systems such as the EuroSCORE II, STS score [1,2]. In order to estimate the risk of PEA and PEA combined with other cardiac procedures, we cannot use current scoring systems as they do not take into account the risk factors for CTEPH and PEA. The main risk factors for these procedures are the severity of PH, heart failure, and the significance of deterioration of other organs functions [3]. Nearly 30% of our patients have renal insufficiency, 29% ischemic heart disease, 10% atrial flutter or fibrillation, 12% diabetes mellitus and 5% stroke. Patients with CTEPH combined with cardiac disease account for different portions in various published reports. In the latest report published by the UCSD, PEA combined with CABG, suture of the foramen ovale and valve surgeries is similar to our group of patients, accounting for 30% [3]. Our group of patients contains in addition procedures for atrial fibrillation; all these procedures in our group were performed in 33.3% of patients [4]. Data analysis by the UCSD shows excellent results and comparable mortality in combined procedures as well as in PEA only. However, CABG surgery combined with lung transplantation or resections has significantly worse results [5].

In our report, we will concentrate mainly on the cardiac diseases that can be solved simultaneously with pulmonary hypertension. They are predominantly coronary artery disease, valvular defects, atrial septal defects, and atrial fibrillation. The aim of our study is to analyze the process of indications and therapeutic procedures at our Cardio-Centre, as well as comparing hemodynamic parameters and long-term results in order to determine the continuation of the treatment.

Materials and methods

From September 2004 to August 2012, 192 patients underwent PEA for CTEPH at 2nd Surgical Clinic of Cardiovascular Surgery, General Faculty Hospital and 1st Faculty of Medicine after a complex diagnostic examination at the 2nd Clinic of Internal Medicine – Cardiology and Angiology, General University Hospital and 1st Faculty of Medicine. All operations were performed by one surgeon. Post-operative care was carried out by doctors of both clinics with the addition of The Clinic of Anesthesia, Resuscitation and Intensive Care (KARIM), General Faculty Hospital and 1st Faculty of Medicine.

Indications for pulmonary endarterectomy included:

1. Symptomatic patients usually NYHA III or IV.
2. PVR greater than 320 dyn (4 Wj).
3. Pulmonary lesion manifested on angiography or CT-AG.
4. Effective anticoagulation for at least 3 weeks.

Patients where combined etiology of PH was not dominant to the CTEPH were contraindicated. Furthermore, we contraindicated patients with severe disease that significantly limited patient's survival (malignancy) and patients with irreversible multi-organ dysfunction. We did not indicated any uncooperative patients and patients in which a psychiatrist or neurologist did not recommend the procedure.

We carried out a retrospective analysis of patient data. Patients were divided into two groups: A and B. These groups of patients were mutually analyzed. The group A included patients with PEA only (128 patients), group B consisted of patients with PEA and other cardiac procedure (64 patients, i.e. 33.3% of which 72 cardiac procedures were carried out). Table 1 shows the number of individual procedures in group B.

For detailed analysis of this group, we have dedicated group B1-patients with PEA + CABG, which included 25 patients, group B2-PEA + suture of PFO, which consisted of 29 patients. The remaining 10 patients with combined procedure were not subjected to a separate analysis due to its statistical insignificance. The overall mortality was 5.2%, 3.9% in group A and 7.8% in group B.

Statistical analysis

All continuous variables were tested for normality using Kolmogorov–Smirnov test. All normal variables were expressed as mean ± standard error of mean (SEM) and the differences between groups were assessed by the one-way ANOVA (for 3 groups) or independent samples *t*-test (for 2 groups). Analogically, all non-normal variables were represented by median (Min – Max) and the between-group comparisons were performed using Kruskal–Wallis test or Mann–Whitney test. Chi-square test was used for comparisons of frequencies between groups in the case of categorical variables. The variables measured pre- and post-operation were analyzed using one-way ANCOVA with repeated measures. Survival distribution was estimated by the Kaplan–Meier method. Significant differences in the probability of surviving between the groups were evaluated by the Gehan–Wilcoxon test. Cox proportional hazard models were used to identify risk factors for survival. All tests were performed in Statistica 12 (StatSoft, Inc, Tulsa, OK, USA).

Operating procedures

All operations were performed through median sternotomy. After cannulation, extracorporeal circulation was started.

Table 1 – Overview of cardiac procedures carried out simultaneously with the PEA.

Suture DSS (PFO)	29
Coronary artery bypass graft	25
MAZE	13
AVR	2
MVP	1
Pacemaker	2

Venting of left atrium and pulmonary artery was performed in a standard manner; patient was cooled down to a 20° C. During the cooling procedure superior vena cava was dissected in order to access the right pulmonary artery, and if myocardial revascularization was planned, than Great Saphenous Vein and LIMA was harvested.

After cooling to 20 °C, the ascending aorta was cross-clamped, 1000 ml of crystalloid cardioplegia was infused through the aortic root into the coronary circulation (Custodiol, Kohler Pharma). We open the right branch of the pulmonary artery between the aorta and the superior vena cava. The incision was extended into the intermediate trunk if necessary. Endarterium was dissected with Jamieson dissector after cutting the wall with thin dissector in the correct part of media. We were trying to dissect the appropriate layer circularly. Due to the retrograde bleeding the dissection is performed in circulatory arrest during which each segment is completely freed from the endarterium. In peripheral segments, it is very important to ensure the proper spacing layer in each segment separately.

After completing the desobliteration of all segments, the extracorporeal circulation was started and suture of arteriotomy of the right pulmonary artery was performed in two layers. On the left pulmonary artery, we proceed in above described manner. Due to the short accessibility of left branch, we perform the incision in the trunk of the left pulmonary artery, and the incision was extended to the left branch. Desobliteration was performed after extracorporeal circulation was stopped. After the completion of endarterectomy extracorporeal circulation and heating process of the patient were started. In the case of combined procedures we performed peripheral anastomosis of coronary bypasses, valve surgery or CRYOMAZE. Central coronary bypass anastomosis was performed after releasing clamp from the ascending aorta.

Results

The main characteristics of group A and B and subgroups B1 and B2 are summarized in Table 2.

This list shows the basic demographic data of patients, as well as clinical disease based on NYHA severity, operation data, degree and type of disability of pulmonary artery, hemodynamic parameters, total duration of hospitalization, hospitalization in the intensive care unit (ICU) in days, and duration of mechanical ventilation in hours (extubation). All these parameters are statistically analyzed and the results of these comparisons are summarized in Table 3. Table 3 also shows the expected differences in the length of simple and combined procedure, where the total duration of surgery and duration of the extracorporeal circulation is greater in combined procedures in group B. Our analysis also shows that patients who underwent combined procedure are longer artificially ventilated, and the time leading to their extubation is significantly longer than in patients who had undergone only PEA.

It is well known that the length of mechanical ventilation is a major risk factor for post-operative pulmonary inflammatory complications, as its length increases the number of lung infections. In contrast, a statistically significant difference was observed in gender and age distribution in the groups B1 and B2. When compared with group A, the difference in the age of women in group B1-patients with revascularization and patients in group B2 were significantly younger.

If we follow the hemodynamic improvements compared with the preoperative condition, all groups showed a statistically significant improvement in both a decrease in the pulmonary vascular resistance (PVR), increase in the cardiac index (CI) and a decrease in the mean pulmonary artery pressure (MPa).

The effect's summary and comparison of pulmonary vascular resistance are presented in Graphs 1 and 2 for CI

Table 2 – Patients characteristics.

	Total	Group A	Group B	Group B1	Group B2
Age	59.98 ± 0.87	59.69 ± 1.06	60.61 ± 1.54	65 ± 1.73	56.34 ± 2.51
Sex (male/female) [a]	119/73	77/55	42/18	20/3	17/12
NYHA (I./II./III./IV.) [a]	0/34/133/25	0/25/93/16	0/11/40/9	0/2/17/4	0/7/17/5
Type of disability (I./II./III./IV.) [a]	18/85/87/2	11/60/59/2	7/25/28/0	3/14/6/0	3/9/17/0
Surgery duration (min)	398.2 ± 4.2	391.8 ± 4.5	412.2 ± 8.8	420.5 ± 17.3	400.3 ± 9.8
Time of EC (min)	299.5 ± 3.1	294.8 ± 3.3	309.7 ± 6.5	300.8 ± 10.9	306.7 ± 8.7
EC arrest (min)	33.6 ± 0.78	33.6 ± 0.93	33.6 ± 1.46	29.6 ± 1.88	36.8 ± 2.13
Extubation [b]	22 (0–212)	18 (7–212)	30 (0–202)	29 (0–192)	32 (7–202)
ICU time [b]	7 (0–42)	7 (2–41)	7 (0–42)	10 (0–42)	7 (4–32)
Hospitalization time [b]	12 (2–59)	12 (3–42)	12 (2–59)	12 (2–59)	11.5 (3–40)
Pre MPA (mmHg)	53.53 ± 0.75	53.27 ± 0.87	54.09 ± 1.47	57.59 ± 2.56	54.24 ± 1.76
Post MPA (mmHg)	24.72 ± 0.67	25.05 ± 0.84	23.93 ± 1.09	22.48 ± 1.20	24.52 ± 1.80
Difference of MPA	26.8 ± 1.34	25.8 ± 1.61	29.05 ± 2.43	34.57 ± 3.42	28.73 ± 3.23
Pre PVR (dyn s cm^{-5})	873.8 ± 23.6	873.8 ± 27.5	889.7 ± 45.3	1039.3 ± 91.8	815.5 ± 44.0
Post PVR (dyn s cm^{-5})	160 ± 7.7	151.6 ± 9.0	149.5 ± 15.1	124.8 ± 21.0	163.7 ± 24.0
Difference of PVR	705.8 ± 25.5	690.9 ± 30.0	738.5 ± 48.5	925.1 ± 96.8	639.1 ± 48.9
Pre CI (l/min gm)	2.09 ± 0.04	2.11 ± 0.05	2.05 ± 0.05	1.99 ± 0.07	2.10 ± 0.08
Post CI (l/min gm)	2.9 ± 0.05	2.89 ± 0.06	2.9 ± 0.08	3.04 ± 0.15	2.88 ± 0.10
Difference of CI	−0.98 ± 0.08	−1.02 ± 0.09	−0.90 ± 0.15	−1.05 ± 0.24	−0.87 ± 0.23

Note: Data are expressed as mean ± SEM.

[a] Absolute frequencies describe categorical variables.

[b] Non-normal variables are represented by Median (Min – Max).

Table 3 – *P*-values of the between-group comparisons.

	Group A vs. group B	Group A vs. group B1 vs. group B2			
	P-value	Global P	A vs. B1	A vs. B2	B1 vs. B2
Age	0.628	0.044*	0.107	0.945	0.047*
Sex	0.123	0.031*	0.009**	0.977	0.025*
NYHA	0.832	0.546	0.502	0.463	0.329
Type of disability	0.732	0.194	0.193	0.364	0.057
Surgery duration	0.041*	0.062	0.057	1.000	0.433
Time of EC	0.042*	0.456	1.000	0.703	1.000
Total EC arrest	0.998	0.061	0.213	0.672	0.057
Pre MPA	0.617	0.178	0.191	1.000	0.656
Pre PVR	0.658	0.032*	0.056	1.000	0.042
PRE CI	0.453	0.606	0.960	1.000	1.000
Extubation	0.003**	0.018*	0.731	0.018*	0.797
ICU time	0.335	0.335	0.467	1.000	1.000
Hospitalization time	0.861	0.525	0.937	1.000	0.868

Note: Global P-values are based on the one-way ANOVA and Kruskal–Wallis test for normal and non-normal variables, respectively. Bonferroni post-hoc test was used for pairwise comparisons. *P*-values of the categorical variables were derived from the chi-square tests.

* $P < 0.05$.

** $P < 0.01$.

and for the MPA Graph 3. Statistical analysis shows comparable results for all groups.

The long-term effect of surgery (PEA) is shown in Graph 4; cumulative survival rate is comparable for groups A and B2.

Cumulative survival rate is very good with annual survival in group A – 94%, group B2 – 90% and group B1 – 82.6%. Five-year survival rate is 83% in group A, 79.3% in group B1, and 63.1% in group B1. Group B1 is statistically significantly different from group A (P = 0.031).

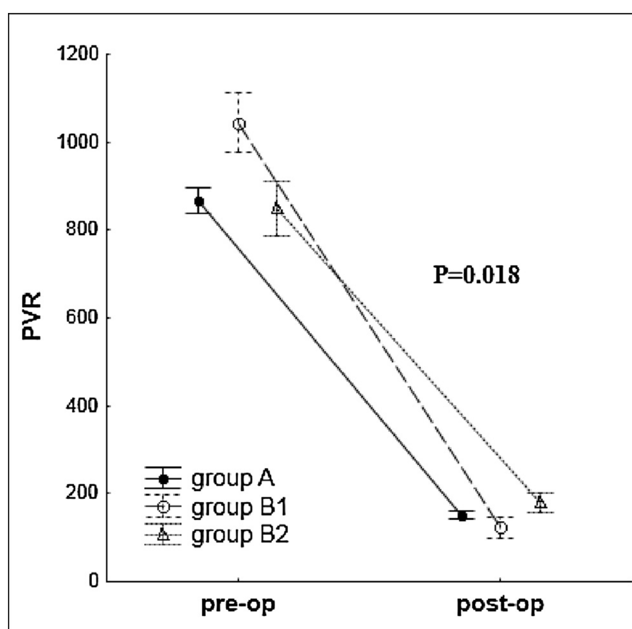
Graph 5 shows the cumulative survival rate of the entire database.

Discussion

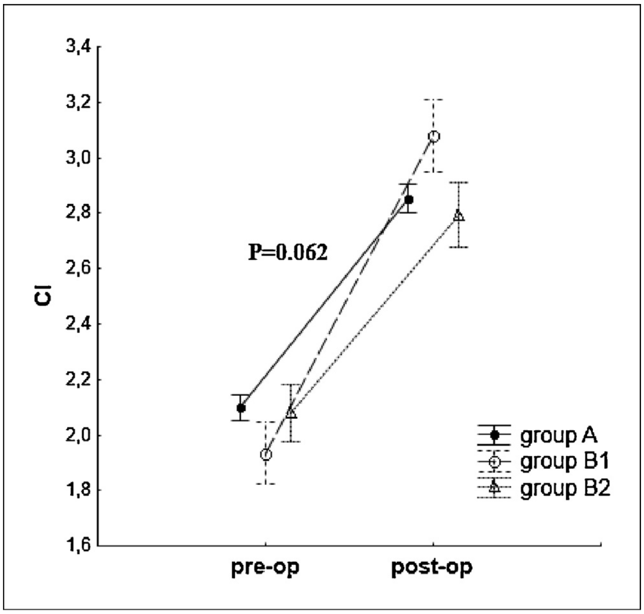
CTEPH is a disease with poor prognosis if not in time indicated for surgical treatment. Medically treated patients with CTEPH have a poor prognosis for long-term survival [6]. Surgical treatment of PEA is a recognized treatment of choice with good long-term results and with capability of curing this disease [7,8]. Results of combined interventions are comparable with isolated pulmonary endarterectomy. We did not find any differences in hemodynamic effects. The only difference found was in the length of intubation, number of complications and longer hospitalization. However, early mortality was comparable in both our groups and the large group published by the UCSD [3].

In our center, we introduced surgical treatment of patients with diagnosed fibrillation or atrial flutter with CryoMAZE [9,10]. This combination of procedures was for the first time performed in 2005, and since then we have operated on the total of 13 patients, 8 of the 11 living patients (i.e. 72%) have sinus rhythm after the surgery with an average of 26 months. Indications for MAZE simultaneously with PEA seem to be highly beneficial. Sinus rhythm is very important for an uncomplicated post-operative course and the hemodynamic stability of the patient. Hemodynamically stable patients require smaller catecholamine support and even treatment of right ventricular dysfunction is much faster [11].

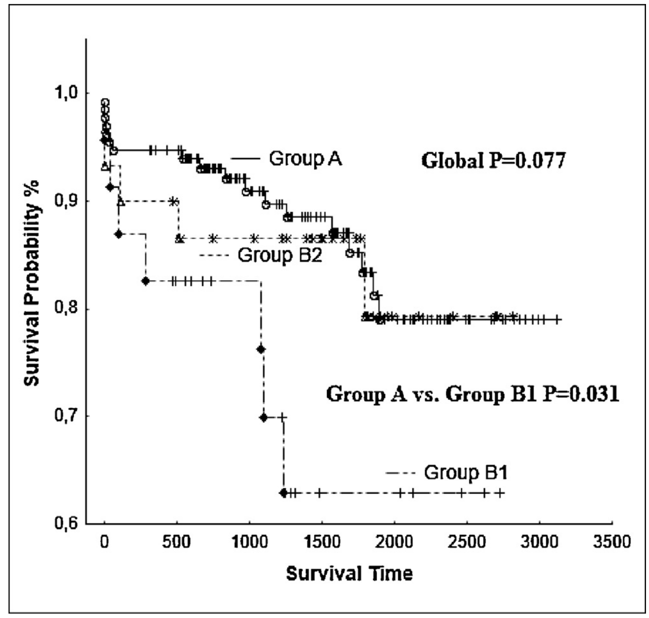
The differences between patients' samples can also be caused by a targeted investigation of comorbidities. In particular, the search for atrial septal defect preoperatively and intraoperatively, continuous implementation of coronary angiography in all patients indicated for PEA without any age limitation carried out in some centers [3,12]. We currently do not have an age limits, and we simultaneously perform right-sided catheterization with the injection of bronchopulmonary collaterals. We do not search just after stenotic lesions caused by atherosclerosis, but we also search for stenosis caused by dilatation of the pulmonary artery and oppression that is rather dependent on the amount of pressure in the pulmonary artery and the anatomical arrangement rather than absolute age.



Graph 1 – Pulmonary vascular resistance before and after operation.



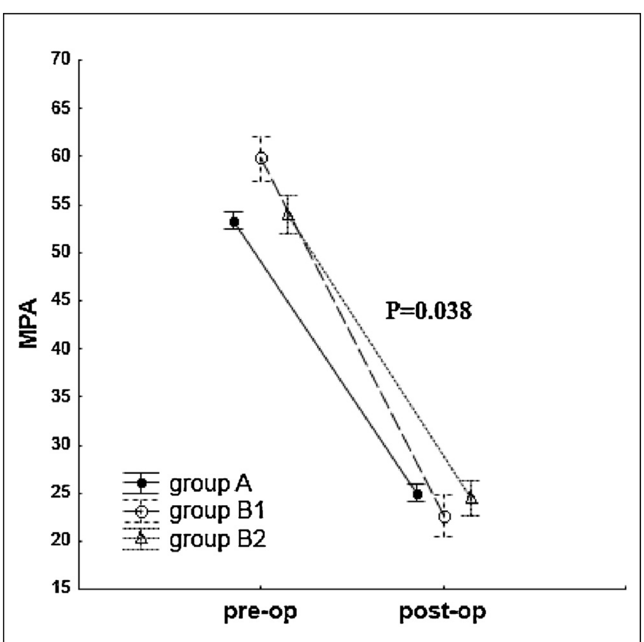
Graph 2 – Cardiac index before and after operation.



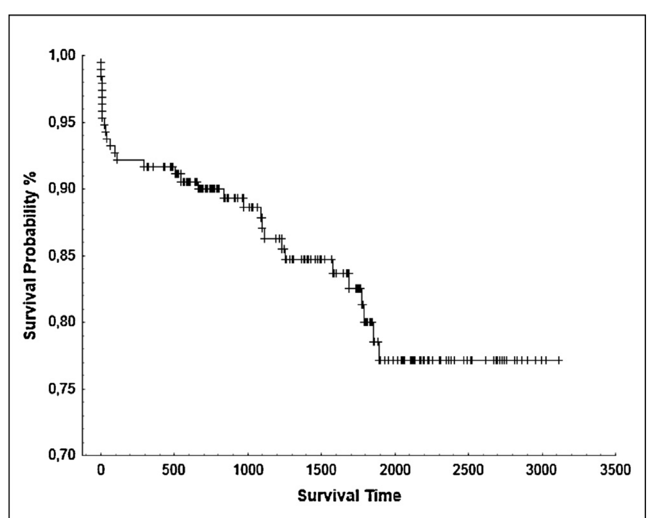
Graph 4 – Cumulative survival by group.

Valvular surgeries combined with PEA are rare and occur in about 1–2% of PEA procedures in the largest database from the UCSD. Aortic valve replacement is the most common procedure followed by a mitral valve repair. Our patients' database follows the same pattern as shown in Table 1. The most affected valve is the tricuspid valve. Valves incompetence is most of the time functional; therefore the resolution of pulmonary hypertension by pulmonary endarterectomy resolves the tricuspid valve insufficiency and the procedure is therefore not indicated [13,14]. These results are also confirmed from our experience. Japanese authors suggest that tricuspid valve procedure should be performed due to the fact that in the most severe patients with right-sided cardiac insufficiency this eases the post-operative course [15]. In their database analysis they have the largest number of heart supports for right-sided heart failure [16].

Accurate CTEPH diagnosis and characterization of its extent and distribution are imperative to allow the prompt initiation of treatment, particularly surgical pulmonary endarterectomy in eligible patients [17].



Graph 3 – Mean pulmonary artery pressure before and after operation.



Graph 5 – Cumulative survival of the entire patient database.

Conclusion

Results of combined interventions are comparable with isolated pulmonary endarterectomy. We did not find any differences in hemodynamic effects. The only difference found was the length of intubation, number of complications and longer hospitalization. However, early mortality was comparable in both our group and the large data analysis performed by the UCSD All patients indicated for the PEA should be screened for the most common comorbidities regardless of their age. We recommend implementation CryoMAZE for the treatment of atrial fibrillation or atrial flutter.

Informed consent

Patients provided informed written consent with collections anonymous data.

Ethical statement

Research was done according to ethical standards.

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Conflict of interest

The authors declare that there is no conflict of interest.

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