

70 Cases of Pulmonary Thromboendarterectomy without Circulatory Arrest

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Abstract

Introduction: For the treatment of patients with chronic thromboembolic pulmonary hypertension (CTEPH) thromboendarterectomy (PTE) is increasingly performing with deep hypothermic circulatory arrest (DHCA). At the last time, there are some publications with describing of the PTE performance without DHCA. **Objective:** To analyze and evaluate the results of surgical treatment of CTEPH under cardiopulmonary bypass (CPB), cardioplegia and without DHCA. **Methods:** Retrospective analysis of the PTE results in 70 patients operated on from January 2018 to February 2023 was conducted. Evaluation pre- and postoperative clinical examinations and invasive pulmonary artery pressure (PAP) measurement in all patients involved were systematically analyzed. **Results:** The average age of the patients was 48.1 ± 10.5 years, including 44.3 % males and 55.7 % females. Due to New York Heart Association (NYHA), 6 (8.6%) patients preoperatively belonged to class II, 48 (68.6%) to class III and 16 (22.9%) to class IV. The thrombotic masses structure according to Jamieson's classification belonged to type I in 42 (60%) patients and to type II in 28 (40%) patients. Postoperatively the systolic PAP (PAPs, mmHg) decreased from 80.8 ± 22.9 to 40.8 ± 13.5 , the mean pressure (mPAP, mmHg)—from 48.5 ± 14.4 to 25.3 ± 7.3 , respectively. Four patients died. The in-hospital mortality rate was 5.7%. According to NYHA, the clinical conditions have also improved: class I was observed in 48 (73%) patients, class II in 15 (23%) and class III in 3 (4%) patients. The postoperative transthoracic echocardiogram (TEE) revealed an improvement of the right ventricle (RV) function and computed tomography (CT) angiogram demonstrated a positive

dynamic and a surgery adequacy. **Conclusion:** PTE under CPB without DHCA can lead to immediate positive results with significant improvements in hemodynamic parameters and life quality without typical DHCA complications in patients with thrombi type I and II according to Jamieson's classification.

Keywords

Chronic Thromboembolic Pulmonary Hypertension, Pulmonary Thromboendarterectomy, Cardiopulmonary Bypass without DHCA, Residual/Recurrent Pulmonary Hypertension

1. Introduction

CTEPH is a rather aggressive disease with an incidence rate from 1% to 3.8% of all pulmonary embolism (PE) cases [1] [2]. CTEPH may be a consequence of one or multiple acute PE cases without complete thrombotic masses' resolution. It leads to the thrombus organization and endothelization [3]. At present, only 65.6% of CTEPH patients proved to have acute PE in anamnesis [4]. As a result, this process eventually leads to increasing of pulmonary vascular resistance (PVR), pulmonary hypertension (PH) and right heart failure (RHF). TEE and computerized tomographic angiogram (CTA) are considered to be diagnostic methods of choice for CTEPH [5]. Moreover, right heart catheterization is a very important method to provide hemodynamic parameters (PAP and PVR) [6].

Nowadays PTE is a radical surgical treatment for CTEPH [7]. The DHCA approach proposed by San-Diego group more than 40 years ago is the preferable method to extract the pulmonary thrombi. However, DHCA is not devoid of certain adverse effects like neurologic deficits [8] [9], renal dysfunction [10] [11] and bleeding [12]. Globally, to avoid DHCA complications several attempts have been made by some groups. Thus, PTE under DHCA with antegrade cerebral perfusion for brain protection by selective axillary or carotid arteries cannulation was performed by Massuda *et al.* [13].

One more approach was proposed by Mikus *et al.*, who performed a PTE with the left heart (atrium and ventricle) double venting using a vacuum device to prevent bronchial back bleeding in a series of eight patients. No neurological complications were notified in this study. One more conclusion was that this method could be applied especially to Jamieson's classification types I and II [14].

Moreover, two papers with successful results of PTE without of DHCA or even on beating heart under CPB and mild hypothermia have appeared recently [15] [16].

Our investigation is an attempt to perform PTE using standard CPB with moderate hypothermia, cardioplegia and without DHCA in patients with thrombotic masses I or II types by Jamieson's classification. The explanation of this is determined by good visualization of thrombi in the main branches of the pulmonary

artery, which in most cases are massive and occlusive, and their separation and extraction up to the subsegmental level is not accompanied by significant blood return.

2. Methods

2.1. Study Design

Being a retrospective study, ethical approval was waited off. Retrospective data of 70 patients after a CTEPH surgical treatment with CPB, moderate hypothermia, cardioplegia and without DHCA from January 2018 to February 2023 at the Heart Disease with Progressive Pulmonary Hypertension Surgical Treatment Department in the Bakulev National Medical Research Center for Cardiovascular Surgery under the Russian Federation Health Ministry (Moscow, Russian Federation) were collected and thoroughly analyzed. Written and informed consents from the patients were received. All the patients were examined before the surgery, immediately after operations and at the hospital discharge. After the operation the patients were evaluated with clinical assessment, TEE, CTA, invasive PAP measurement; the data received were collected. The inclusion criteria suggested by the American College of Chest Physicians were the following: 1) NYHA class symptomatology; 2) preoperative PVR > 300 dynes-s-cm⁵; 3) surgical accessibility of thrombi in main, lobar, segmental pulmonary arteries (PA) as seen in CTA; 4) no debilitating comorbidities. All the patients with acute pulmonary embolism did not fit CPB undergoing. Demographic variables, PAP (PAPs, mPAP, diastolic pressure (PAPd)), RV dysfunction measured by tricuspid annular peak systolic excursion (TAPSE) on 2D echo, central venous pressure (CVP), oxygen saturation (SatO₂), CPB time, location of thrombi as described by Jamieson's classification as well as the University of California, San Diego (UCSD), surgical classification and any postoperative complications were studied. PAPs were measured by pre- and postoperative TEE. PAPs, mPAP and PAPd, as well as cardiac output (CO), were invasively measured before and after the operation with the subsequent PVR calculation. CVP and SatO₂ were also measured before and after PTE.

2.2. Anesthetic Management

Intraoperative monitoring included electrocardiography (ECG) analysis, SatO₂ due to pulse oximeter data, arterial blood pressure, CVP, PAP, pulmonary capillary wedge pressure (PCWP), blood, rectum and skin temperatures. PAP was measured by Swan-Guns catheter transduced to the main pulmonary artery (MPA) before and after operation in the intensive care unit (ICU). Online neuromonitoring was conducted by determine a bilateral brain oxygen saturation (INVOS, cerebral Oximeter, Somanetics, Troy, Michigan, USA). The gas composition, acid-base and electrolyte balance of arterial and venous blood, clinical and biochemical pattern, coagulogram were discretely analyzed in time. Preoxygenation was performed within 3 - 5 minutes before anesthesia induction. To reduce PVR nitric oxide (NO) had been supplied in the respiratory mixture for all patients. To

prevent CO reduction inotropic support with dobutamine (3 - 5 mcg /kg/min) was carried out in all patients before anesthesia. Infusion therapy was performed under the CVP and PCWP control. Anesthesia induction was conducted with propofol (2 - 3 mg/ kg) and fentanyl (5 - 6 mcg/ kg), myoplegia-pipecurionium bromide (0.1 mg /kg). The proper anesthesia level was maintained by constant sevoflurane (0.8 - 1.0 MAC) inhalation or propofol (3 - 5 mg/kg/h) and fentanyl (2 - 5 mcg/kg) infusion. Pipecurionium bromide—0.05 mg/kg was additionally injected before CPB.

2.3. Cardiopulmonary Bypass

CPB was performed on a Stockert S5 HLM (Munich, Germany) using Skipper (Eurosets, Italy) and Terumo FX-15/30 (Terumo, Japan) oxygenators. The priming volume made up 1500.0 - 1000.0 ml respectively. It consisted of heparin (3 mg/kg), corrective solutions (KCl 2%, NaHCO₃ 4.2%), crystalloid and synthetic colloid solutions, mannitol 15% (0.25 g/kg). The extracorporeal circuit connected the superior and inferior vena cava (SVC, IVC) with ascending aorta. The cannulas and catheter's sizes were selected due to the patient's anthropometric characteristics. When CPB was started and full flow was achieved, the left heart was vented through the right superior pulmonary vein (RSPV) by a 16 FR catheter. CPB was conducted under moderate and superficial hypothermia with temperatures 28°C - 34°C, while maintaining a perfusion flow rate of 2.2 - 2.8 l/min/m² during 130.3 ± 55.5 minutes. The myocardial ischemia time made up 68.4 ± 24.6 minutes. Pharmacologic cardioplegia was carried out with Custodiol solution (Fr. Kohler Chemie, Germany) introduced antegrade to the aortic root in volume of 1.5 - 2.0 liters within 6 - 8 minutes with a 100-mmHg pressure till asystole, then 50 mmHg pressure after it.

After thromboendarterectomy, at the stage of pulmonary artery suturing, the rewarming began, SVC and IVC were released, and the left ventricular drainage catheter was replaced into the PA. The initial drainage rate was equal to 600 ml/min. After the full rewarming and effective hemodynamics recovery at some moderate doses of inotropic support, the rate of PA drainage was gradually decreased to 150 ml/min. When the rectal temperature 34°C was achieved, the SVC catheter was removed. When the T rect. of 36°C was achieved, the perfusion rate was being smoothly reduced under the control of PA pressure. In case of satisfactory hemostasis and the absence of systemic hypoxemia tendency, PA drainage was stopped and the catheter was removed. In case of hemodynamic stabilization, CPB was completed and a full dose of protamine sulfate was administered.

2.4. Surgical Technic

All surgical interventions were performed via median sternotomy. CPB was established following aortic and venous cannulation in a normal fashion by using DLP[®] cannulas (Medtronic Inc, Minneapolis, MN USA). A vent catheter was introduced through the RSPV into the left ventricle. After this, on average all

patients were cooled down to $28.63^{\circ}\text{C} \pm 3.1^{\circ}\text{C}$. The right atrium was opened, and the vent was introduced into the RV via the tricuspid valve (TV). An incision was made on the MPA, which continued to the right or left PA direction, depending on the location of the main thrombi. Another vent (a special Jamieson's catheter) was inserted into the dissected PA branch. Then PTE was started with a smooth separation and detachment of the vessel middle layer. The correct plane provided a structure that can be peeled off under action controlled and without any excessive force. The beginning of thrombi detachment from the inferior PA lobe with subsequent transition to the superior PA lobe is the best way to avoid massive blood inflows and any deterioration in the visual field. Conducting endarterectomy at the level of segmental branches, the excessive traction can lead to thrombi dissection and perforation in the vascular wall. The thrombi should carefully be removed, to the extent of its pointed ends (**Figure 1**). The final results of the intervention were confirmed endoscopically in both PA branches. Then the patient's rewarming was started. The PA incisions were closed in two layers with 5-0 polypropylene sutures. The clamp was removed from the aorta, and the heart-beating was restored. To prevent pulmonary oedema, the vent was moved from the left heart into the MPA. Once normothermia was achieved, the vent was closed and then removed from the PA. If surgical bleeding was not observed, the patient was weaned from CPB. After heparin inactivation and in cause of adequate haemostasis, the chest was closed.



Figure 1. Thrombus extracted with its tapered tails.

2.5. Statistical Analysis

All continuous parameters were checked for the distribution normality due to the Kolmogorov-Smirnov test and presented either as mean with the standard deviation or as median with the interquartile range for the normal and non-normal distribution, accordingly. The statistical data comparison at the different time points were performed through the Wilcoxon Matched Pairs Test or Student's t-

test for some dependent samples. In case of multiple comparisons, Bonferroni's correction was used. Categorical data are presented as numbers and percentages. The software was used to conduct the statistical analysis.

3. Results

The present data analysis included 70 patients, who underwent surgery in the period from January 2018 to February 2023 (average age: 48.1 ± 10.5 years; 31 (44.3%) males and 39 (55.7%) females). The patients had some classical symptoms, i.e. dyspnea on exertion (DOE) (in all 70 patients), palpitations (in 53 patients, 76%), pedal oedema (in 51 patients, 73%), and a cough (in 12 patients, 17%). None of the patients observed had syncope. Severity of DOE was NYHA functional class (FC) II in 6 patients (8.6%), class III in 48 patients (68.6%), and class IV in 16 patients (22.9%). The main CTEPH cause was deep venous thrombosis (DVT) in 60 patients (85.7%), thrombophilia in 4 patients (5.7%) and was unidentified in 6 patients (8.6%). Location and extent of thrombi were evaluated by CTA. According to Jamieson's classification 42 (60%) patients had type I (**Figure 2**) and 28 (40%) patients had type II thrombi. None of the patients had type III or IV thrombi. The baseline demographic and preoperative clinical characteristics of the study population are presented in **Table 1**.

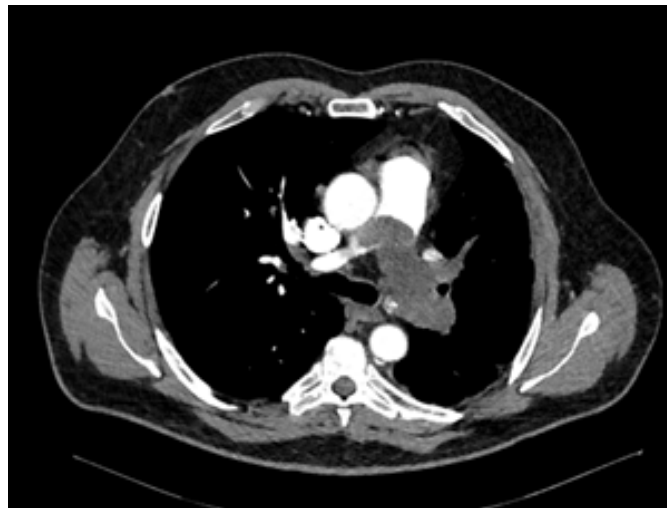


Figure 2. Type I thrombus according to Jamieson's classification.

Table 1. Baseline demographic and preoperative clinical characteristics.

Parameters	Values
Gender, n (%)	
Male	31 (44.3)
Female	39 (55.7)
Age, years	48.1 ± 10.5
BSA, m ²	1.98 ± 0.63
BMI, kg/m ²	25.5 ± 1.7

Continued

Symptoms, n (%)	
DOE	70 (100)
Palpitation	53 (76)
Pedal oedema	51 (73)
Cough	12 (17)
Syncope	Nil
NYHA FC, n (%)	
I	Nil
II	6 (8.6%)
III	48 (68.6%)
IV	16 (22.9%)
Causes of CTEPH, n (%)	
DVT history	60 (85.7)
Thrombophilia	4 (5.7)
Unknown	6 (8.6)
Thrombus type by Jamieson's classification, n (%)	
I	42 (60)
II	28 (40)

BSA—Body Surface Area. BMI—Body Mass Index.

The mean CPB duration was 130.7 ± 55.5 min, and the mean aortic cross-clamp time was 68.4 ± 24.6 min. Patients were cooled down to $28.63^\circ\text{C} \pm 3.1^\circ\text{C}$. CPB provided an adequate oxygen delivery ($\text{DO}_2 > 270$ mL/m²/min), with adequate hemodynamic (average arterial pressure ≥ 50 mm Hg) and metabolic characteristics (the maximum lactate level was 1.7 [1.28; 2.1] mmol/L). In 68 patients (97.1%), the spontaneous restoration of cardiac activity was observed. CPB was completed with moderate doses of inotropic agents (inotropic score— $5.0 \pm 4.85^*$). In 80% of the patients observed, norepinephrine was required to maintain an adequate total peripheral vascular resistance. The PaO₂/FiO₂ ratio (264 ± 94 mmHg) significantly increased compared to preoperative values (119 ± 110 mm Hg). Some other peri- and postoperative parameters are presented in **Table 2**.

Table 2. Cardiopulmonary bypass parameters, clinical and hemodynamic data, intra- and postoperative complications.

Parameters	Values**
CPB duration (min)	130.3 ± 55.5
Cross-clamp time (min)	68.4 ± 24.6
Average patient's temperature during CPB, °C	28.63 ± 3.1
Lactate, mmol/L	
post-CPB	1.7 [1.28; 2.1]
max (the 1st day after surgery)	2.0 [1.4; 3.5]

Continued

Inotropic score post-CPB	5.0 ± 4.85
Norepinephrine, n (%)	56 (80)
NO, n (%)	24 (34.3)
paO ₂ /FiO ₂ , mm Hg	
preoperatively	119.0 ± 110.0
post-CPB	264.0 ± 94.0
Ventilation time, hours	14 [8.0; 20.25] (6 - 362)
Mean ICU length of stay, days	1.0 [1.0; 2.0] (1 - 28)
Mean length of hospital stay, days	9.0 [8.0; 12.0]
Patients without complications, n (%)	48 (68.6)
Reperfusion pulmonary oedema, n (%)	16 (23)
VA-ECMO, n (%)	4 (5.7)
Transient brain oedema, n (%)	3 (4.2)
Stroke n, (%)	1 (1.42)
Bleeding n, (%)	2 (3)
Blood loss, mL	300.0 [200.0; 300.0] (100.0 - 8500.0)
Kidney injury, n (%)	2 (3)
Multiorgan failure, n (%)	1 (1.42)
Mortality, n (%)	4 (5.7)
NYHA FC, n (%)	66 (100)
I	48 (73)
II	15 (23)
III	3 (5)
IV	Nil
Residual pulmonary hypertension (mPAP >35 mm Hg), n (%)	11 (16)

*Inotropic score: epinephrine 0.1 µg/kg/min is 10 points; dopamine, dobutamine 1 µg/kg/min is 1 point each). **Values are presented as mean ± standard deviation, median [1st quartile; 3rd quartile], range (min-max), or number with percentage (n (%)), accordingly. VA-ECMO—veno-arterial ECMO.

The mean duration of mechanical ventilation was 14.0 [8.0; 20.25] (range from 6 to 362 hours). The mean ICU length of stay was 1.0 [1.0; 2.0] days (range from 1 to 28 days). Most patients required one inotropic agent, and 24 (34.28%) patients required one vasodilator (NO insufflation) to reduce mPAP and PVR and improve the right ventricular function. In 48 (68.6%) patients, the postoperative period was uncomplicated. Reperfusion pulmonary oedema developed in 16 patients (23%), and it was only in 4 of them severe. In one case, ECMO was effectively used in combination with massive diuretic therapy. Four patients died of the right ventricular dysfunction due to PH. All of them had high initial PA pressure values (Table 3). In 2 patients, the PVR exceeded 1400 dyn/sec/cm⁻⁵, and in 2 patients—1700 dyn/sec/cm⁻⁵. After the surgery, all 4 patients had residual PH. The mPAP

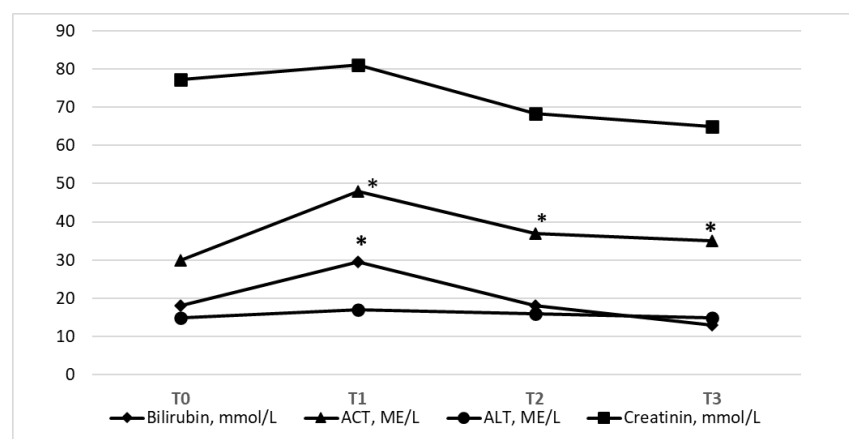
value ranged from 52 to 78 (68.7 ± 14.0) mm Hg, and the PVR values ranged from 640 to 1310 (963.2 ± 341.4) dyn/sec/cm⁻⁵, which caused their death. In 3 cases, the patients were placed on VA-ECMO without any beneficial effect.

Table 3. Baseline hemodynamic parameters in fatal cases.

No.	Age, years	PAPs, mm Hg	mPAP, mm Hg	PVR, dyn/sec/cm ⁻⁵	NT-proBNP, pg/mL
1	28	127	76	1710	1142.0
2	64	90	52	1780	685.7
3	50	117	66	1460	1055.0
4	56	92	48	1420	710.0

NT-proBNP—terminal part of the brain natriuretic peptide.

In 3 patients (4.2%), the transient cerebral oedema was identified. In one patient, who was on ECMO for 13 days and died, the brainstem stroke was diagnosed. Two patients (2.85%) were diagnosed with postoperative bleeding. The volume of postoperative blood loss was 300.0 mL [200.0; 300.0] (ranged from 100.0 to 8500.0 mL). In 16 patients (23%), the signs of the right ventricular failure and respiratory failure were detected. Two patients (2.9%) on ECMO were diagnosed with renal failure (one them died). In one patient, who was on ECMO for 13 days and died, the signs of multiple organ dysfunction were observed. Of the tissue damage markers, the aspartate transaminase (AST) and total bilirubin levels had increased significantly, with peaks of 48.0 [40.0; 62.75] U/L and 29.5 [12.95; 45.0] mmol/L, accordingly, by the first postoperative day, with the following gradual decrease (**Figure 3**). Simultaneously, peak lactate values (2.0 [1.4; 3.5] mmol/L) were noted. All patients were assessed for the right ventricular function, tricuspid regurgitation, and PAP through TEE, CTA, and right heart catheterization. Clinical and hemodynamic changes after the procedure described are presented in **Table 4**.



T0—before surgery, T1-3—the 1st, 2nd, 3rd days after surgery; *p < 0.017.

Figure 3. Changes in the tissue damage markers.

Table 4. Clinical and hemodynamic parameters before and after surgery.

Parameters	Before	After	P value
RAD (cm ²)	33.0 ± 3.0	24.0 ± 6.0	<0.0000001
RVD (cm ²)	32.0 ± 3.0	25.0 ± 6.0	<0.0000001
TV incompetence (+)	3.0 [2.0;3.0]	1.0 [1.0; 1.0]	<0.0000001
RV EDV (mL)	149.2 ± 44.1	112.1 ± 30.1	<0.0000001
RV EF (%)	40.0 [36.0; 44.0]	50.0 [47.0; 54.0]	<0.0000001
TAPSE (mm)	14.1 ± 1.7	18.3 ± 2.2	<0.0001
6MWT (m)	231.6 ± 90.3	420.4 ± 52.5	<0.0001
NT-pro BNP (pg/mL)	206.2 ± 105.4	50.9 ± 35.7	<0.0001
Sat O ₂ (%)	90.1 ± 1.8	96.6 ± 1.7	<0.05
NYHA Class	3 (2 - 4)	2 (1 - 3)	<0.05
PAPs (mm Hg)	80.8 ± 22.9	40.8 ± 13.5	<0.0000001
PAPd (mm Hg)	31.1 ± 11.1	14.4 ± 11.2	<0.0000001
mPAP (mm Hg)	48.5 ± 14.4	25.3 ± 7.3	<0.0000001
PVR (dynes·s·cm ⁻⁵)	931.2 ± 384.3	354.2 ± 184.2	<0.0001
CVP (mm Hg)	19.6 ± 4.4	12.1 ± 2.4	<0.05

RAD—right atrial dimension; RVD—right ventricular dimension; RV EDV—right ventricular end-diastolic volume; RV EF—right ventricular ejection fraction; 6MWT—6 minute-walking test.

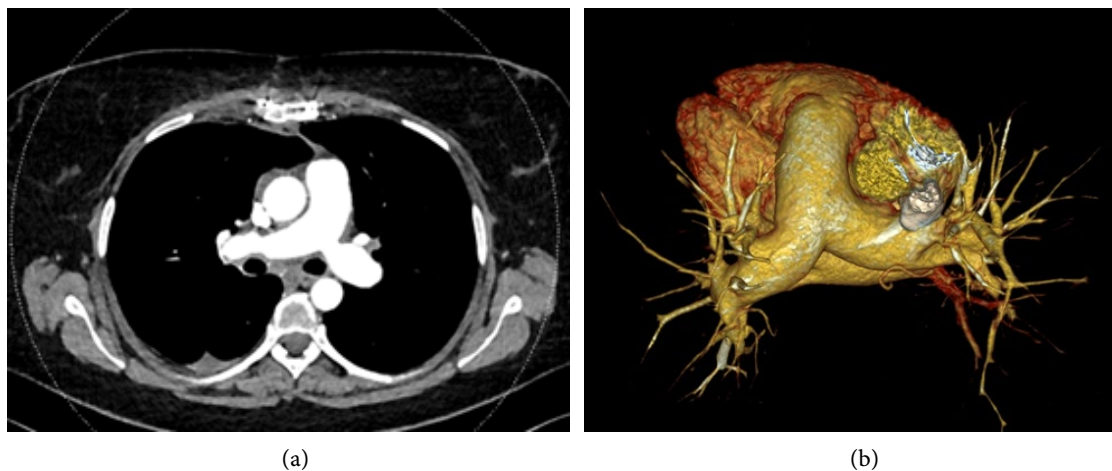


Figure 4. Postoperative CTA (a) and three-dimensional computed tomography (3D CT) (b). Contrast filling in all branches including segmental and subsegmental levels.

The present postoperative clinical data, such as right atrial and ventricular dimensions, and NT-pro BNP level significantly decreased (**Table 4**). Simultaneously, the 6MWT, RV EF values and TAPSE showed a substantial increase with a certain statistical improvement of the NYHA class. Some positive results were obtained for postoperative PAP (PAPs, mPAP, PAPd) and CVP, which showed a significant reduction compared to preoperative values, and even with SatO₂ normalization. **Figure 4(a)** and **Figure 4(b)** present the postoperative CTA and three-

dimensional CT where the contrast filling is seen in all the branches including segmental and subsegmental levels. In the early postoperative period, the life quality became better than before the intervention. The NYHA classes I, II and III were identified in 48 (73%), 15 (23%) and 3 (4%) patients, accordingly. Residual pulmonary hypertension (mPAP > 35 mmHg) developed in 11 patients.

4. Discussion

PTE has become the standard treatment for CTEPH since it was described for the first time in the San-Diego University College publication in late 1980s. Though, PTE is still the definitive surgical approach [7], but it has always been recognized as a difficult procedure often burdened by a high mortality [17]. Starting from the initial embolectomy till now there has been no doubt that a complete thrombotic masses extraction is vital for the best outcome [18]. Utley with colleagues emphasized that DHCA is absolutely essential for the thrombi extraction from distal segmental vessels because of the increased bronchial circulation [19]. The surgical technique has also considerably been improved by the use of specific surgical instruments. At present, the surgical mortality rate has decreased from 24% to 2.2% [7] [20].

Since the DHCA use and its adverse effects were extensively described in literature [9]-[11], now different strategies to avoid its complications, as well as bloodless field obtaining and operating time decreasing have appeared. Besides, a number of techniques like antegrade cerebral perfusion with the left and right heart double venting, descending aorta occlusion by inflatable balloon catheter were also described [8] [21] [22]. Moreover, several papers with successful results of PTE without DHCA or even on beating heart under CPB and mild hypothermia were published recently [15] [16]. Our study demonstrates the technical feasibility of PTE performing without DHCA in 70 patients with types I and II according to Jamieson's classification. Our technique allows to perform a continues dissection for more than 20 min, which is generally an accepted and recognized time limit for DHCA in PTE. Using any other method than DHCA, its necessary to be confident that DHCA can be easily and promptly applied. Our PTE method considerably differs from the method described by Mikus *et al.* [14]. We use an extensive left atrium venting through RSPV, a contra lateral PA and venting of the main or left PA during rewarming until the end of CPB. What is more, it is crucial to start the thrombus peeling from the inferior lobar pulmonary artery. It allows to avoid massive bleedings and provide a bloodless operative field.

Reperfusion pulmonary edema is a specific immediate complication following PTE under DHCA. In a large European registry [23], the frequency of this complication is around 9.6%, but it may also range from 7% to 26% [8] [24]. In our experience, the complication, mentioned above was detected in 23%. It develops within the first postoperative hours and should be treated with a deep sedation, aggressive diuretic therapy, controlled intermittent positive pressure ventilation with high positive expiratory pressure, and even ECMO performing. Most patients

with CTEPH, who underwent PEA postoperatively enhanced the functional class and are considered to be cured of PH [7] [25] [26]. However, residual or persistent PH after PEA is rather common [27]-[29]. A meta-analysis indicated that a residual PH was found in 25% [30]. Currently, there is no consensus on a persistent or residual PH after PEA determination, and there are no threshold values for these phenomena [28] [29]. Residual PH rates ranged from 8.2% [31] to 41.9% [24]. Some previous studies provided solid evidence that patients with persistent or residual PH immediately after PEA have an increased risk of in-hospital death [7] [23]. These studies showed that early mPAP > 30 mmHg was relevant for the prognosis. In a bi-national study, Kallonen *et al.* also defined similar criteria of residual PH in patients with worse long-term survival [32]. On the other hand, the United Kingdom National Cohort showed that mPAP > 38 mmHg measured 3 - 6 months postoperatively correlated with a poor long-term survival and a higher risk of CTEPH related death [25]. In our study invasive PAP measurements were performed during 5 days after the surgery. We decided, that it would be rational to use 35 mmHg as the cut-off value, which is a mean data between 30 mmHg and 38 mmHg, as it was mentioned above. Postoperatively, in all patients some obtained sustained clinical and functional benefits were observed. The in-hospital mortality was 5.7%. The main causes of mortality were residual PH in association with reperfusion pulmonary oedema. Thomson *et al.* reported about 15% of mortality with the same reason [8]. The recent European Respiratory Society Statement on CTEPH considers a significant residual PH to be a challenge for an early postoperative treatment and the most common cause of in-hospital mortality [29]. Ineligible for surgery patients may take a treatment with a balloon pulmonary angioplasty usage [33] or a targeted medical therapy for the symptom's improvement [27].

The high mortality probability is likely to be determined by the thrombi of distal localization in the PA, what, in some cases, may affect the effectiveness of the operation [24]. Studying patients with distal pulmonary embolism was beyond this research as we adhere endovascular treatment tactics with transluminal balloon angioplasty, especially in patients with high PH. The current endovascular CTEPH treatment has positive results in the world practice and can significantly improve clinical outcomes [34]-[37]. Besides, such experience accumulation will make certain adjustments to the multimodal approach in CTEPH treatments. From our point of view, the accumulation of such experience can make certain adjustments for the CTEPH treatment.

In our research three patients (4.3%) were diagnosed with posthypoxic cerebral oedema in the early postoperative period with the subsequent regress in neurological symptoms including one patient, who was successfully disconnected from VA-ECMO after the expiration of 21 days. The brain stem stroke was detected at the autopsy in one patient, who died after 14 days being connected to VA-ECMO. Complications observed can hardly be associated with CPB, hence during the whole perfusion period the parameters of cerebral oxygenation were within the

appropriate limits (rSO₂ were equal to 60% - 80%). Moderate changes in dependent homeostasis parameters, such as lactate and tissue damage markers levels, indicate in favor of the present procedure adequacy. Moreover, the neurological complication frequency (5.7%) in the group observed was considerably lower than the indicators (29%) received with DHCA (9). Our results concerning to pulmonary hypertension regression after operation don't distinguish from the data obtained after circulatory arrest method of surgery. The absence of arrest-specific neurological complications makes it possible to advocate this method of surgery. In addition, the use of this approach can significantly reduce the time duration of the operation, as well as financial expense, which are significantly higher while using circulatory arrest.

The positive initial results received have encouraged us to apply systematically our technique, although further investigations to prove this approach are likely to be taken in the future.

5. Conclusion

PTE under CPB, moderate hypothermia without DHCA can lead to immediate positive results with significant improvements in hemodynamic parameters and life quality without typical DHCA complications. Using this technique, it's necessary to take into account the volume and location of the thrombotic masses. The comparison with similar interventions under DHCA in III-IV types thrombi localization according to Jamieson's classification was not within the framework of the study, where we stick to the endovascular treatment approach.

Limitations

The major limitations of the study are a retrospective analysis and a lack of long-term follow-ups. However, we believe that this study may provide some useful information for the surgical management of CTEPH patients.

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Authors' Roles & Responsibilities

Sergey Gorbachevsky: suggested and designed the study, approved the final version to be published.

Leo Bockeria: drafted the work or revised it critically for important intellectual final approval of the version to be published.

Tatiana Averina: analyzed the statistical data, described the CPB procedure and its results.

Komoliddin Rakhmonov and Amir Sabitov: acquired the data, contributed to the data interpretation.

Kakhaber Diasamidze: worked out and described the anesthetic management.
Elena Golukhova: approved the final version to be published.

What Is Already Known?

PTE under DHCA is considered to be the gold standard for CTEPH surgical treatment.

What Does This Study Adds?

PTE under CPB, moderate hypothermia without DHCA can be successfully performed in patients with I-II types CTEPH according to Jamieson's classification without DHCA adverse effects.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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