Chronic thromboembolic pulmonary hypertension: the impact of advances in perioperative techniques in patient outcomes*

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Table 1S. Baseline characteristics.

	All patients (n = 102)	Group 1 (n = 38)	Group 2 (n = 35)	Group 3 (n = 29)	p
Sex (female), n (%)	64 (62.8%)	20 (52.6%)	25 (71.4%)	19 (65.5%)	0.240*
Age y (mean ± SD)	49.1 ± 14.8	50.8 ± 15.1	46.7 ± 15.5	49.5 ± 13.5	0.486+
Ethnicity (white), n (%)	81 (79.4%)	29 (76.3%)	27 (77.1%)	25 (86.2%)	0.219*
Body mass index, kg/m² (median ± DP)	26.5 ± 5.1	26.4 ± 5.4	26.9 ± 4.7	26.4 ± 5.2	0.912*
NYHA class, n (%)					0.142*
II	34 (33.4%)	13 (34.2%)	13 (37.1%)	8 (27.5%)	
III	56 (54.9%)	21 (55.2%)	20 (57.1%)	15 (51.7%)	
IV	11 (10.8%)	3 (7.8%)	2 (5.7%)	6 (20.6%)	
Dyspnea, n (%)	102 (100%)	38 (100%)	35 (100%)	29 (100%)	-
Edema, n (%)	59 (57.8%)	21 (55.2%)	22 (62.8%)	16 (55.1%)	0.959*
Chest pain, n (%)	34 (33.3%)	10 (26.3%)	14 (40.0%)	10 (34.4%)	0.436*
Syncope, n (%)	24 (23.5%)	7 (18.4%)	12 (34.2%)	5 (17.2%)	0.973*
Fatigue, n (%)	8 (7.8%)	5 (13.1%)	2 (5.7%)	1 (3.4%)	0.134*
Oxygen therapy, n (%)	35 (34.3%)	12 (31.5%)	11 (31.4%)	12 (41.3%)	0.426*
Continuous	20 (19.6)	5 (41.6)	7 (63.6)	8 (72.7)	0.134*
Intermittent	14 (13.7)	7 (58.3)	4 (36.3)	3 (27.2)	
History of confirmed PE, n (%)	91 (89.2%)	33 (86.8%)	34 (97.1%)	24 (82.7%)	0.702*
Diagnosed 1 time	67 (65.6)	24 (72.7)	26 (76.4)	17 (70.8)	0.966*
Diagnosed 2 times	10 (9.8)	3 (9.0)	4 (11.7)	3 (12.5)	
Diagnosed more than 2 times	14 (13.7)	6 (18.1)	4 (11.7)	4 (16.6)	
Comorbidities					
Smoking	21 (20.5)	3 (7.8)	10 (28.5)	8 (27.5)	0.038*
Chronic venous insufficiency	14 (13.7)	6 (15.7)	4 (11.4)	4 (13.7)	0.785*

SD, standard deviation; NYHA, New York Heart Association; DVT, deep vein thrombosis; mPAP, mean pulmonary artery pressure measured by right ventricular catheterization; PVR, pulmonary vascular resistance measured by right ventricular catheterization; CO, cardiac output measured by right ventricular catheterization; PE, pulmonary embolism; PASP, pulmonary artery systolic pressure and pericardial effusion measured by echocardiography; PEA, pulmonary endarterectomy. Values are expressed as means and standard deviations, or medians with interquartile range (IQR) or percentages; n = patients with assessment; $p<0.05$ was considered significant.
*hi-square test (Mantel-Haenszel); +analysis of variance (ANOVA); ++Kruskal-Wallis test.

Table 1S. Continued...

	All patients (n = 102)	Group 1 (n = 38)	Group 2 (n = 35)	Group 3 (n = 29)	p
Family history of DVT or PE	11 (10.8)	4 (10.5)	4 (11.4)	3 (10.3)	0.990*
Hypothyroidism	10 (9.8)	2 (5.2)	4 (11.4)	4 (13.7)	0.235*
DVT, n (%)	43 (42.1%)	16 (48.4%)	17 (50.0%)	10 (41.6%)	0.642*
Thrombophilic disorder, n (%)	45 (44.1%)	20 (52.6%)	16 (45.7%)	9 (31.0%)	0.083*
Pulmonary vasodilator therapy, n (%)	34 (34.0%)	11 (28.9%)	11 (31.4%)	12 (41.3%)	0.299*
Anticoagulant therapy, n (%)	94 (92.1)	32 (84.1)	33 (94.2)	29 (100)	0.016*
Time from last PE to PEA (mo), median (IQR)	36.0 [21-60]	36 (24-48)	34.5 (21-66)	24 (21-60)	0.750⁺⁺
mPAP mmHg (mean ± SD)	53.2 ± 13.1	52.9 ± 14.45	53.2 ± 12.4	53.3 ± 12.5	0.992⁺
PVR dyn.s. cm^{-5} (mean ± SD)	869.5 ± 380.2	828.4 ± 295.13	838.9 ±428.4	969 ± 417.3	0.313⁺
CO, l/min	3.9 ± 1.1	4.14 ± 1.03	4.46 ± 1.42	3.68 ± 1.04	0.065⁺
Estimated PASP mmHg (mean ± SD)	81.0 ± 23.3	83.3 ± 20.7	77.6 ± 26.6	82.3 ± 22	0.574⁺
Pericardial effusion, n (%)	18 (17.4)	6 (17.1)	4 (12.1)	8 (30.7)	0.225*

SD, standard deviation; NYHA, New York Heart Association; DVT, deep vein thrombosis; mPAP, mean pulmonary artery pressure measured by right ventricular catheterization; PVR, pulmonary vascular resistance measured by right ventricular catheterization; CO, cardiac output measured by right ventricular catheterization; PE, pulmonary embolism; PASP, pulmonary artery systolic pressure and pericardial effusion measured by echocardiography; PEA, pulmonary endarterectomy. Values are expressed as means and standard deviations, or medians with interquartile range (IQR) or percentages; n = patients with assessment; p<0.05 was considered significant.
*hi-square test (Mantel-Haenszel); ⁺analysis of variance (ANOVA); ⁺⁺Kruskal-Wallis test.

Table 2S. Intraoperative characteristics.

Variable	Group 1 (n = 38)	Group 2 (n = 35)	Group 3 (n = 29)	p
CPB time (min), mean ± SD	192.3 ± 39.4	251.7 ± 33.4	298.2 ± 40.2	<0.001⁺
Cooling time (min), mean ± SD	47.9 ± 18.5	66.9 ± 5.9	70.6 ± 3.7	<0.001⁺
Warming time (min), mean ± SD	66.8 ± 17.7	87.2 ± 8.1	107.7 ± 23.5	<0.001⁺
Reperfusion time (min), mean ± SD	25.5 ± 7.6	20.7 ± 8.4	18.6 ± 9.4	0.007⁺
DHCA time (min), mean ± SD	51.0 ± 11.8	48.3 ± 12.6	51.1 ± 16.5	0.620⁺
Up to 2 DHCA, n (%)	4 (10.8%)	14 (40.0%)	13 (44.8%)	0.002*
More than 2 DHCA, n (%)	33 (89.2%)	21 (60.0%)	16 (55.2%)	
Mean time of each DHCA (min), mean ± SD	15.5 ± 2.9	17.8 ± 1.7	19.2 ± 2.0	<0.001⁺

CPB, cardiopulmonary bypass; DHCA, deep hypothermic circulatory arrest; n, patients with assessment. Values are expressed as means with percentages and/or standard deviation.
* P value from the chi-square test (Mantel-Haenszel);
⁺P value from the analysis of variance;
p<0.05 was considered significant.

VARIABLES EVALUATED IN THE UNIVARIATE MODEL

The variables evaluated were as follows: sex, age, chest pain, study group, hemoptysis, syncope, New York Heart Association class, use of oxygen therapy, time from last pulmonary embolism (PE) to pulmonary endarterectomy, deep vein thrombosis, thrombophilic disorder, smoking, family history of confirmed PE, pulmonary hypertension-specific therapy, hemodynamic measurements of right cardiac catheterization (mean pulmonary artery pressure, pulmonary artery systolic pressure [PASP], pulmonary vascular resistance [PVR], cardiac output), functional evaluation by an echocardiogram (estimated PASP, right ventricular[RV] dilation, abnormal RV contractility), warming, reperfusion, deep hypothermic circulatory arrest [DHCA], mean time of each DHCA, and number of DHCAs.

DETAILED DESCRIPTION OF THE CLINICAL OUTCOMES

Pulmonary reperfusion syndrome was defined as the presence of new pulmonary infiltrates on chest radiography, hypoxemia calculated using the ratio of arterial oxygen

partial pressure to fractional inspired oxygen, positive end-expiratory pressure, and pulmonary complacency, if on mechanical ventilation (17, 18). Acute kidney injury was defined according to Acute Kidney Injury Network ≥2, based on creatinine ≥2 mg/dL, or the need for renal replacement therapy (19). Surgical complications were defined as bleeding, pericardial effusion, and/or reoperation. Bleeding was defined as blood loss exceeding 100–300 ml/h after admission to the intensive care unit (ICU) (20). Pericardial effusion was diagnosed as fluid accumulation in the pericardium, with signs of compromised cardiac output (CO), diagnosed by echocardiography (21). Reoperation was indicated for bleeding refractory to clinical measures, with associated hemodynamic instability or evidence of acute or subacute cardiac tamponade (22). Infectious complications included mediastinitis, as deep infection of the operative wound with positive culture obtained from the sternum (23), and septic shock, defined as the most severe form of infection, characterized by metabolic and perfusion abnormalities (24). Neurological complications included delirium, diagnosed using the confusion assessment method scale for the ICU (25), and stroke, defined as a focal neurological deficit with duration ≥24 h with a computed tomography finding compatible with acute ischemic or hemorrhagic infarction (26, 27). Residual PH was defined as mPAP ≥25 mmHg (15).

DETAILED DESCRIPTION OF THE ANESTHETIC TECHNIQUES PERFORMED AFTER APRIL 2015 (GROUP 3)

During anesthesia induction, a central venous catheter and a pulmonary artery catheter were inserted into the internal jugular vein. A femoral artery catheter was inserted to avoid underestimated measures of arterial pressure through the radial artery in cases of prolonged CPB with excessive vasoconstriction or vasodilation. Transoesophageal echocardiography was used during surgery to assess ventricular function and filling pressures, to evaluate the pericardium, and to help with fluid management. The bispectral index (BIS) monitor was used during surgery to evaluate the depth of anesthesia, avoiding excessive drugs and aiding neuroprotection. During the pre-CPB period, the head was wrapped in a cooling jacket, and the temperature was maintained at 4°C.

Before DHCA, mannitol (12.5 g), methylprednisolone sodium succinate (20 mg/kg), phenytoin sodium (15 mg/kg), and sodium thiopental (6 mg/kg) were administered. Warming and cooling were carried out slowly to avoid reperfusion complications. To wean from CPB, low-dose inotropic support was often needed because of previous right ventricular failure or because of long hypothermia and long aortic cross-clamp duration. Under these conditions, we used dopamine 5–10 mg/kg or epinephrine 0.04–0.15 mg/Kg/min.

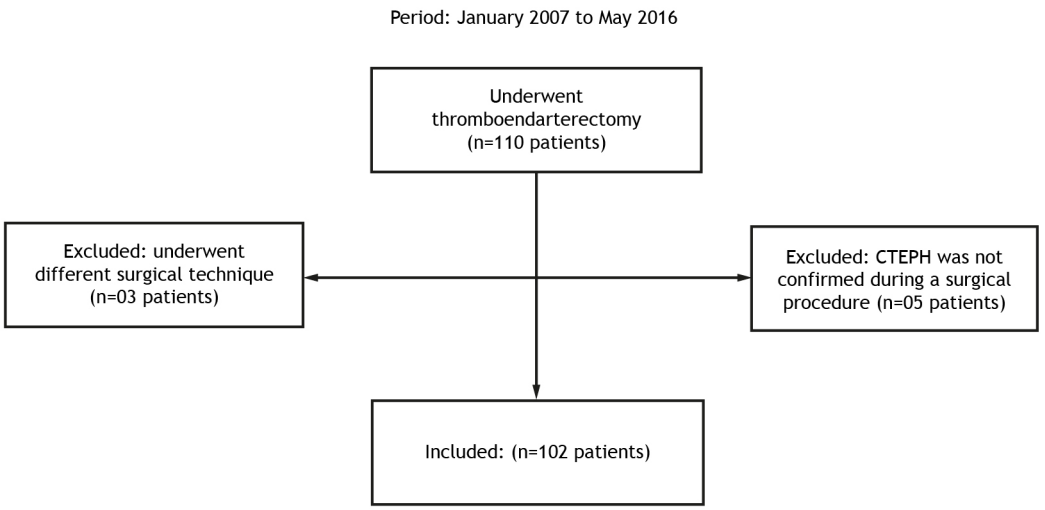

Figure 1S. All patients included in this study.