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Research Article

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Features of Hospital Period in Patients Who Underwent Surgical Treatment for Chronic Thromboembolic Pulmonary Hypertension in Combination With Myocardial Revascularization

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AIM OF THE STUDY To study the features of hospital period after pulmonary endarterectomy (PEA) and coronary artery bypass grafting (CABG) in patients with chronic thromboembolic pulmonary hypertension (CTEPH) and surgically significant coronary artery (CA) stenosis, and to conduct a comparative analysis with hospital period after PEA in patients with CTEPH without CA lesions.

MATERIAL AND METHODS An analysis of 141 patients with CTEPH was carried out. The average age is 53.5 (42.7-68.9) years. The 1st group (38 people) consisted of patients with CTEPH and surgically significant CA lesions, the 2nd group (103 people) — without surgically significant CA lesions. An intergroup analysis of clinical and functional data and the course of the early postoperative period was carried out.

RESULTS According to clinical data, the 1st group of patients with CTEPH was characterized by older age (p=0.003), a larger proportion of patients with concomitant type 2 diabetes (p=0.004), arterial hypertension (p<0.001), atherosclerosis of the brachiocephalic arteries ⩽ 50% (p<0.001), a history of myocardial infarction (p=0.008), and a higher comorbidity index (p=0.03) compared to the 2nd group of patients. The early postoperative period was more severe in the 1st group of patients with CTEPH, where a higher proportion of patients with the development of neurological disorders (p=0.02), newly diagnosed atrial fibrillation (p=0.04), and a higher proportion of patients with prolonged artificial ventilation (p=0.03) were identified. No intergroup differences were found in hospital mortality (p=0.74).

CONCLUSIONS 1. In patients who underwent PEA in combination with myocardial revascularization, the hospital period is characterized by a more severe course in comparison with patients with CTEPH but without coronary artery disease. This is reflected in a higher incidence of neurological disorders, rhythm disturbances, and prolonged mechanical ventilation. 2. In-hospital mortality between the group of patients who underwent combined intervention and isolated PEA did not differ, despite the impact of concomitant pathology.

Keywords: chronic thromboembolic pulmonary hypertension, hospital period, myocardial revascularization

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CA – coronary arteries
CABG – coronary artery bypass grafting
CHD – coronary heart disease
CTEPH – chronic thromboembolic pulmonary hypertension
ECG – electrocardiographyя
PA – pulmonary artery
PEA – pulmonary endarterectomy
TTE – transthoracic echocardiography

INTRODUCTION

Pulmonary endarterectomy (PEA) is the method of choice in the treatment of such a severe pathology as chronic thromboembolic pulmonary hypertension (CTEPH) [1]. Despite the achievements of modern cardiac surgery and anesthesiology in PEA, the problem of postoperative complications still remains in this group of patients [2].

In patients with CTEPH, a number of concomitant diseases may develop with age, the most common of which is coronary heart disease (CHD) with surgically significant atherosclerotic lesions of the coronary arteries (CA) [3]. Russian medical centers already have experience with a hybrid approach to surgical treatment of this category of patients [3]. At the same time, the literature contains very limited data on the nature of the course of the hospital period in the early stages after PEA and coronary artery bypass grafting (CABG).

Based on the above, **the aim of this study** was to examine the characteristics of the hospital period after PEA and CABG in patients with CTEPH with surgically significant coronary stenosis, and to conduct a comparative analysis with the course of the hospital period after PEA in patients with CTEPH without coronary artery disease.

MATERIAL AND METHODS

The study included 141 patients with CTEPH, of whom 38 patients had concomitant CHD with surgically significant coronary artery disease. The mean age of patients in the general group was 53.5 (42.7–68.9) years. All the patients were divided into two groups: Group 1 (38 people) included patients with CTEPH and CHD who underwent surgical treatment in the form of PEA and CABG. Group 2 (103 patients) included patients with CTEPH without concomitant CHD who underwent PEA. The study was conducted in accordance with Good Clinical

Practice standards and the principles of the Declaration of Helsinki. The study protocol was approved by the local Ethics Committee. Written informed consent was obtained from all the patients prior to inclusion in the study.

Inclusion criteria: 1) patients with CTEPH who underwent elective PEA, as well as patients with CTEPH and CHD with surgically significant coronary artery disease who underwent elective simultaneous surgery in the form of PEA and CABG; 2) age over 18 years. The exclusion criterion was emergency surgery. The diagnosis of CTEPH was established based on the data of angiopulmonography with catheterization of the right heart: the average pressure in the pulmonary artery (PA) at rest is not lower than 25 mm Hg, the wedge pressure in the PA is not higher than 15 mm Hg, the resistance of the vessels of the pulmonary circulation is more than

300 dyn*s*cm-5. Surgically significant stenoses of the main branches of the coronary arteries were recorded based on the results of coronary angiography.

Surgical treatment in all the patients was performed under artificial circulation. In patients with CTEPH and CHD with surgically significant coronary artery disease, the first stage was PEA with circulatory arrest, perfusion cooling of the body to 18°C and craniocerebral hypothermia. The second stage was CABG. Myocardial revascularization was performed using the internal thoracic artery or autovenous shunt as grafts.

In all examined patients, clinical and anamnestic data, transthoracic echocardiography (TTE) parameters [4], and 24-hour Holter electrocardiography (ECG) monitoring data [5] were analyzed. Various complications and mortality were recorded in the early postoperative period.

Statistical analysis of the results was performed using the Statistica 6.1 statistical software package (USA). Nonparametric statistical methods were used with calculation of the median (Me) with interquartile range (25% and 75% percentiles), as well as in numerical values and percentages. The Mann–Whitney U test was used to compare independent variables. The $\chi 2$ test was used for categorical variables. Values were considered statistically significant at $p<0.05$ for all types of analysis.

RESULTS

The study included 141 patients with CTEPH. The mean age was 53.5 (42.7–68.9) years. In the general group of patients with CTEPH, surgically significant atherosclerotic lesions of the coronary arteries were detected in 27% of cases.

All patients with CTEPH were divided into two groups: Group 1 (38 people) - patients with CTEPH who underwent PEA in combination with CABG; Group 2 (103 people) - patients with CTEPH without surgically significant coronary artery disease.

Clinical characteristics of patients in both groups are presented in Table 1.

As can be seen from the table 1, due to the presence of CHD with surgically significant atherosclerotic lesions of the CA, Group 1 patients were naturally characterized by an older age, a higher proportion of patients with concomitant arterial hypertension, type 2 diabetes mellitus, atherosclerosis of the brachiocephalic arteries under 50%, a history of myocardial infarction, and a higher comorbidity index compared to patients of Group 2.

There were no statistically significant differences in the characteristics of the pulmonary hypertension level between the groups. High pulmonary hypertension was detected in both groups of patients. At the same time, the angiopulmonography data had no intergroup differences. Pulmonary vascular resistance in groups 1 and 2 was 868.4 (461.5–1102.7) and 871.2 (482.8–1116.1) dyn*s*cm-5 ($p=0.55$), the average pressure in the PA was 50.8 (36.4–60.5) and 49.3 (35.7–57.6) mmHg ($p=0.64$), the wedge pressure in the PA was 11.4 (8.7–12.9) and 12.3 (9.7–12.2) mmHg, respectively ($p=0.77$).

The parameters of transthoracic echocardiography (TTE) in patients with CTEPH of both groups are given in Table 2.

As can be seen from the table 2, in both groups of patients the sizes of both atria are increased, while the longitudinal axis and left atrial area in patients of Group 1 are larger compared to patients of Group 2.

The thickness of the right ventricular myocardial wall and its area are increased in both groups without statistically significant differences. At the same time, in the 1st Group of patients, hypertrophy of the interventricular septum and the posterior wall of the left ventricle are more pronounced compared to the 2nd Group, which is a consequence of concomitant CHD.

Table 1

Clinical characteristics of patients with chronic thromboembolic pulmonary hypertension

Indicators		Group 1 (n=38)	Group 2 (n=103)	p
Men, n (%)		23 (61.0)	60 (58.0)	0.80
Age, years (Me, 25–75%)		61.5 (57.0–68.5)	52.0 (43.0–62.0)	0.003
Functional class of chronic heart failure according to NYHA, n (%)	II	6 (16.0)	31 (30.0)	0.08
	III	32 (84.0)	72 (70.0)	0.08
	IV	0	2 (2.0)	0.38
History of myocardial infarction, n (%)		8 (21.0)	6 (6.0)	0.008
History of stroke, n (%)		3 (8.0)	5 (5.0)	0.48
Obesity, n (%)		10 (26.0)	32 (31.0)	0.58
Arterial hypertension, n (%)		24 (63.0)	33 (32.0)	<0.001
Type 2 diabetes mellitus, n (%)		10 (26.0)	8 (8.0)	0.004
Atherosclerosis of the brachiocephalic arteries under 50%, n (%)		22 (58.0)	16 (16.0)	<0.001
Atherosclerosis of the brachiocephalic arteries over 50%, n (%)		1 (3.0)	2 (2.0)	0.80
Chronic obstructive pulmonary disease, n (%)		6 (16.0)	14 (14.0)	0.74
Atrial fibrillation, n (%)		5 (13.0)	10 (10.0)	0.55
Ventricular extrasystole, n (%)		1 (3.0)	2 (2.0)	0.80
Sinus tachycardia, n (%)		4 (11.0)	10 (10.0)	0.88
All rhythm disturbances, n (%)		10 (26.0)	22 (21.0)	0.53
Chronic kidney disease, n (%)		3 (8.0)	14 (14.0)	0.35
Age-adjusted Charlson Comorbidity Index (scores), (Me, 25–75%)		4.0 (4.0–5.0)	3.5 (2.0–4.0)	0.03

Table 3 provides characteristics of intraoperative parameters and the course of the early postoperative period in patients with CTEPH in both groups.

As can be seen from the table 3, according to intraoperative parameters, a longer aortic occlusion was noted in the 1st Group of patients (p<0.001), associated with an increase in the volume of surgical intervention. A more severe course of the early postoperative period was also observed in the 1st Group of patients compared to the 2nd Group due to a higher proportion of patients with the development of neurological disorders (p=0.02), AF (p=0.04), and duration of mechanical ventilation over 24 hours (p=0.03). In-hospital mortality did not differ between the groups.

Table 2

Transthoracic echocardiography indicators of patients with chronic thromboembolic pulmonary hypertension

Indicators	Group 1 (n=38)	Group 2 (n=103)	p
Right atrium longitudinal axis, cm	6.0 (5.4–7.0)	6.1 (5.5–6.7)	0.38
Right atrium area, cm^2	29.8 (23.5–35.9)	30.3 (22.1–37.2)	0.53
Left atrium longitudinal axis, cm	5.8 (5.3–6.4)	5.2 (4.7–5.6)	0.03
Left atrium area, cm^2	25.9 (19.8–28.3)	18.9 (15.1–21.5)	0.04
Right ventricular end-diastolic volume/Body surface area, ml/m^2	47.2 (39.4–63.5)	51.7 (40.1–64.3)	0.67
End-diastolic area of the right ventricle, cm^2	29.1 (22.0–35.5)	30.3(23.5–34.2)	0.88
Thickness of the right ventricular free wall in diastole, cm	0.8 (0.6–1.3)	0.9 (0.7–1.1)	0.86
Right ventricular fractional area change (%)	29.5 (25.0–33.0)	30.5 (25.0–34.0)	0.65
Left ventricular end-diastolic volume/Body surface area, ml/m^2	36.7 (30.5–39.1)	33.8 (29.5–40.2)	0.85
Left ventricular end-systolic volume/Body surface area, ml/m^2	14.7 (10.5–16.2)	12.9 (8.7–15.3)	0.13
Interventricular septum thickness in diastole, cm	1.3 (1.1–1.3)	1.1 (0.8–1.2)	0.01
Left ventricular posterior wall thickness in diastole, cm	1.2 (1.0–1.2)	1.0 (0.8–1.1)	0.04
Left ventricular ejection fraction (Simpson method), %	61.2 (58.5–66.0)	64.0 (60.0–72.0)	0.07

Table 3

Intraoperative parameters and the course of the early postoperative period in patients with chronic thromboembolic pulmonary hypertension

Indicators, units of measurement	Group 1 (n=38)	Group 2 (n=103)	p
Artificial circulation time, min	267.0 (232.0–293.0)	256.5 (228.3–281.5)	0.59
Aortic occlusion time, min	150.5 (129.5–168.0)	114.0 (97.1–125.3)	<0.001
Time of circulatory arrest, min	41.0 (33.0–51.0)	39.0 (30.5–47.0)	0.54
Mechnical ventilation for more than 24 hours, n (%)	19 (50.0)	32 (31.0)	0.03
Acute cerebrovascular accident, n (%)	2 (5.0)	1 (1.0)	0.11
Encephalopathy, n (%)	14 (37.0)	22 (21.0)	0.06
All neurological disorders, n (%)	16 (42.0)	23 (22.0)	0.02
Newly diagnosed atrial fibrillation, n (%)	13 (34.0)	19 (18.0)	0.04
Heart failure, n (%)	10 (26.0)	30 (29.0)	0.74
Pulmonary heart disease, n (%)	6 (16.0)	22 (21.0)	0.46
Acute renal failure, n (%)	7 (18.0)	22 (21.0)	0.70
Multiple organ dysfunction syndrome, n (%)	7 (18.0)	17 (17.0)	0.78
Rethoracotomy (hemostasis), n (%)	2 (5.0)	6 (6.0)	0.89
Duration of hospital stay after surgery (days), (Me, 25–75%)	26.4 (16.0–31.0)	22.5 (13.0–27.5)	0.24
Hospital mortality, n (%)	2 (5.0)	7 (7.0)	0.74

DISCUSSION

This study examined the features of the hospital period after carotid endarterectomy and CABG in patients with CTEPH with surgically significant coronary stenosis, and conducted a comparative analysis with the course of the hospital period after PEA in patients with CTEPH without coronary stenosis.

The results of the study showed that the group of patients with CTEPH and surgically significant coronary stenosis initially differed from patients with CTEPH without coronary artery disease by older age, a higher proportion of patients with concomitant arterial hypertension, type 2 diabetes mellitus, atherosclerosis of the brachiocephalic arteries of no more than 50%, a history of myocardial infarction, and a higher comorbidity index. According to TTECG data, patients with CTEPH and concomitant CA stenosis were found to have larger left atriums, and more pronounced hypertrophy of the interventricular septum and posterior wall of the left ventricle compared to the values of these parameters in patients without CA stenosis, which is a manifestation of long-standing concomitant cardiovascular pathology. The intraoperative period in the group of patients with CTEPH and CA stenosis was characterized by a longer period of aortic occlusion compared to the group of patients without CA stenosis, which is associated with an increase in the volume of surgical treatment.

The presence of concomitant CHD with surgically significant CA disease, an increase in the volume of surgical intervention (PEA in combination with CABG) determine a more severe course of the early postoperative period in the group of patients with CTEPH and CA stenosis, which was expressed by a higher incidence of neurological disorders, newly diagnosed AF, and duration of mechanical ventilation over 24 hours. At the same time, despite the described features of the hospital period, combined surgical treatment of CTEPH with myocardial revascularization does not lead to an increase in mortality compared to isolated treatment of CTEPH.

The most frequent postoperative complications in patients with CTEPH are neurological disorders, which is associated with cerebral hypoperfusion during circulatory arrest in PEA [6]. In the studied group of patients with concomitant atherosclerotic lesions of the CA, the pathophysiological mechanisms of development of postoperative neurological disorders, in addition to the specifics of conducting PEA, may also be associated with concomitant cerebrovascular disorders. These factors contribute to the reduction of adaptive regulatory mechanisms of the cardiovascular and other systems during surgical intervention [2]. The authors found that bilateral stenosis of the internal carotid artery of any degree, indicating a tendency to a systemic atherosclerotic process, increases the risk of neurological complications after cardiac surgery [7]. The above is consistent with the results of the current study: the group of patients with CTEPH and

surgically significant CA disease differed from patients with CTEPH without CA disease by older age and high comorbidity due to the presence of atherosclerosis of the brachiocephalic arteries, arterial hypertension, and diabetes mellitus. In the hospital period after PEA and CABG, a large proportion of patients with the development of neurological disorders were identified in this group.

The development of AF is often associated with age and cardiovascular diseases (CHD, arterial hypertension, diabetes mellitus, chronic kidney disease, etc.), which contribute to structural and functional remodeling of the left heart (dilation), and disorders of the autonomic innervation of the myocardium [8]. These data confirm the results of our study. In the group of patients with CTEPH and surgically significant coronary stenosis after PEA and CABG, a higher proportion of patients with newly developed AF was found compared to patients with CTEPH without coronary stenosis. In addition to greater comorbidity in patients with CTEPH and CA disease, TTECG data initially showed larger sizes of the left atrium, and more pronounced hypertrophy of the interventricular septum and posterior wall of the left ventricle compared to patients without CA stenosis.

In-hospital mortality with combined surgical intervention (PEA in combination with myocardial revascularization) in the study group of patients with CTEPH and surgically significant CA stenosis was 5%, which is comparable to mortality with isolated PEA [9].

Limitations of the study: further data collection is required to analyze the long-term outcomes of surgical treatment of patients with CTEPH and surgically significant coronary stenosis.

Thus, despite the high risk of combined surgical intervention in patients with CTEPH and surgically significant CA disease, and a more severe course of the early postoperative period, the results of our study demonstrate the high efficiency of PEA in combination with CABG. Combined surgical treatment for CTEPH and CHD is an alternative to conventional surgical treatment, and the method of choice in patients with concomitant pathology.

CONCLUSIONS

1. The presence of chronic thromboembolic pulmonary hypertension and concomitant ischemic heart disease with surgically significant coronary artery disease in patients compared to patients with chronic thromboembolic pulmonary hypertension without coronary artery disease is accompanied by an older age — 62.5 (57.0–68.5) and 52.0 (43.0–62.0) years, p=0.003. Patients with CTEPH and coronary artery stenosis compared to patients with chronic thromboembolic pulmonary hypertension without coronary artery disease are distinguished by statistically significantly higher comorbidity: the proportion of concomitant arterial hypertension was 63% and 32%, respectively (p<0.001); the proportion of type 2 diabetes mellitus was 26% and 8%, respectively (p=0.004); the proportion of atherosclerosis of the brachiocephalic arteries was 58% and 16%, respectively (p<0.001); the presence of a history of myocardial infarction was 21% and 6%, respectively (p=0.008); the comorbidity index was 4.0 (4.0–5.0) and 3.5 (2.0–4.0), respectively, p=0.03. These patients also had statistically significantly more pronounced dilation of the left atrium (p=0.03), hypertrophy of the interventricular septum (p=0.01) and the posterior wall of the left ventricle (p=0.04).

2. In patients who underwent surgical treatment of chronic thromboembolic pulmonary hypertension in combination with myocardial revascularization, the hospital period is characterized by a more severe course compared to patients who underwent isolated pulmonary endarterectomy. This is expressed in statistically significantly higher incidence of development of neurological disorders (42% and 22%, respectively (p=0.06)), rhythm disturbances (34% and 18%, respectively (p=0.04)), and prolonged mechanical ventilation (50% and 31%, respectively (p=0.03)).

3. In-hospital mortality in combined surgical treatment for chronic thromboembolic pulmonary hypertension with myocardial revascularization does not have statistically significant differences compared to that in isolated pulmonary endarterectomy (5% and 7%, respectively, p=0.74).

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