POSSIBILITIES AND PERSPECTIVES OF RETROGRADE PULMONARY ARTERY PERFUSION AS A COMPONENT OF SURGICAL TREATMENT OF PULMONARY EMBOLISM

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Abstract. Aim of the study: to analyze the results of performing retrograde perfusion of the pulmonary artery during an open thromboembolectomy from the pulmonary artery. Materials and methods: the experience of performing retrograde perfusion of the pulmonary artery in 10 patients operated in our clinic for massive pulmonary embolism is presented. Retrograde perfusion was performed after the stage of embolectomy from the pulmonary artery. For the latter, we used a disposable cardioplegic solution delivery system and 2 cardioplegic pumps of the heart-lung machine: the first for taking blood perfusate from the oxygenator, the second for supplying the combined solution. The blood perfusate and solution were mixed in a 3:1 ratio and injected selectively into the orifices of the pulmonary veins under a pressure of up to 20 mm Hg. (volume perfusion rate 200–250 ml/min) for 4 minutes. Results: despite the initial severity of the patients' condition, as well as the amount of surgical intervention performed, the hospital survival rate was 100%. Along with this, we did not note the development of specific complications, as well as the aggravation of the course of the intraoperative and early postoperative periods. Conclusion: retrograde pulmonary artery perfusion is a very encouraging and promising technique that provides effective and safe removal of small thromboembolism from the peripheral parts of the pulmonary arterial bed, as well as preventing the development of residual pulmonary hypertension as a result of developing intraoperative air embolism.

Keywords: pulmonary embolism, retrograde pulmonary artery perfusion.

List of Abbreviations

ACS – acute coronary syndrome
ALV – artificial lung ventilation
COPD – chronic obstructive pulmonary disease
CPB – cardiopulmonary bypass
ECG – electrocardiography
Echo – transthoracic echocardiography
IHD – ischemic heart disease
MIP – maximal intensity projection
PE – pulmonary embolism
TLT – thrombolytic therapy
WHO – World Health Organization

Introduction

Pulmonary embolism (PE) is recognized by the World Health Organization (WHO) as one of the most common and dangerous cardiovascular diseases, diagnosed in 0.5-2 people per 1000 of the adult population, and among people over 75 years old, reaching up to 10 cases per 1000 people per year (ESC, 2008). In industrialized countries, PE ranks third in the incidence of sudden cardiac death, where it is second only to coronary heart disease (CHD) and stroke. And if we take into account the number of asymptomatic forms diagnosed on sectional material, the true frequency of PE increases by 3-4 times (Spampinato *et al.*, 2020). In particular, up to 100,000 cases of pulmonary embolism per year are registered in France, up to 65,000 patients with pulmonary embolism are admitted to multidisciplinary hospitals in England and Scotland, and up to 60,000 patients annually in

Italy (Medvedev et al, 2021). In the United States, up to 65,000 patients with PE are diagnosed per year and about 99,000 patients with relapses of this disease. The difficulty of compiling a reliable epidemiological picture of the disease is associated not only with the presence of asymptomatic and unverifiable forms of PE, but also with the formation of post-thromboembolic pulmonary hypertension that occurs after the disappearance of symptoms of acute pulmonary artery occlusion and is observed in 0.01% of the studied patients (Wells *et al.*, 2000). Such an epidemiological situation has quite explainable physiological mechanisms. On the one hand, physiological autolysis or the consequences of thrombolysis lead to the fragmentation of large thromboembolic agents, which lead to microembolization of the peripheral pulmonary arterial bed. On the other hand, the remaining microemboli interact with the endothelial lining of the microvasculature, which determines the reflex spasm of the latter and initiates the processes of secondary thrombosis (Medvedev et al, 2021; Martinez et al, 2020). During therapy, most patients experience a decrease in pressure in the pulmonary arteries and afterload on the right ventricle with clinical improvement, however, in almost a quarter of the considered patients, 3-4 months after the initial episode of PE, a persistent perfusion disorder is detected on lung scintigraphy (Fedorov *et al.*, 2021).

Mortality in the group of patients with high and intermediate-high risk PE is about 70%, while when using an active surgical approach, it does not exceed 10-15% (Howard, 2019). However, despite the achieved results of treatment, the implementation of open surgical interventions has not become widespread, which is determined by the high incidence of intra- and postoperative complications. Currently, thrombolytic therapy (TLT) is the “gold standard” for restoring blood flow in the pulmonary artery (Claeys *et al.*, 2019; Fedorov *et al.*, 2021). However, the impossibility of performing the latter or its inefficiency shifts the scales towards open surgery, which is also consistent with current clinical guidelines. In addition, the accumulation of experience in TLT showed the presence of conflicting results, reflecting the percentage of developing complications.

Thus, the results of the MAPPET (Management Strategies and Prognosis in Patients with Pulmonary Embolism) study showed that more than 40% of patients who underwent TLT for PE had at least one relative contraindication to its conduct, and in a third of cases there were absolute contraindications, which were reflected in the treatment outcomes (Konstantinides *et al.*, 2002; Sharifi *et al.*, 1999). Subsequently, data from the ICOPER register demonstrated the development of major bleeding in 21.7% of the subjects, and intracranial bleeding in 3% (Goldhaber *et al.*, 1999). This trend has revived the interest of researchers in performing a surgical method of treatment (Andriyashkin *et al.*, 2015). At the same time, the lack of large multicenter studies on the comprehensive assessment of surgical intervention in PE, as well as the unsatisfactory results of the available, single, publications, leave a large number of unresolved issues, the discussions and intensity of which are second only to the issues of primary verification in the group of urgent patients (Patel & Bergl, 2020). All of the above motivates researchers to modify both the indications for open surgery and its techniques.

Aim of the study: to analyze the results of performing retrograde perfusion of the pulmonary artery during open thromboembolectomy from the pulmonary artery in a group of patients with high and intermediate-high risk.

Materials and Methods

This manuscript was based on the experience of performing retrograde pulmonary artery perfusion in 10 patients operated on in our clinic for massive high- and intermediate-high-risk PE. In the general group of patients, women predominated (6 people). The mean age of the examined patients was 54.6 ± 4.12 years. It should be noted that all the subjects were hospitalized in a serious condition, within 8 to 125 hours from the episode of thromboembolism. Such a time spread was determined by the difficulties of primary verification of PE and, in some cases, false diagnosis of acute coronary syndrome (ACS). Upon admission to inpatients, a comprehensive laboratory and instrumental examination was carried out in terms of determining the nature and severity of competitive insufficiency, the severity of right ventricular failure, the nature of pulmonary hypertension, and assessing the risks of recurrent pulmonary embolism. According to the results of laboratory methods of additional examination, all patients showed signs of multiple organ failure, namely, increased levels of creatinine in 4 patients (162 ± 9.21 mmol/l), hepatic transaminases in 6 cases (63 ± 5.2 U/l), blood glucose levels in 3 patients (6.9 ± 1.12 mmol/l), as well as anemia of moderate severity (88 ± 1.14 g/l). In all cases, the D-dimer test turned out to be positive and averaged 2.10 ± 0.85. All patients had high risks of PE according to the Geneva and Wells scales and belonged to the group of high and intermediate-high risk of early cardiac death according to the classification of the European Society of Cardiology. The severity of PE was calculated using the PESI scale, which in all cases belonged to classes IV and V of mortality risk and averaged 128 ± 8.4 points.

The considered group of patients was represented by persons of high morbid status, which was determined both by the severity of the underlying pathology and the nature of concomitant diseases (Table 1). At the time of admission to the emergency room, patients underwent complex cardioprotective, respiratory therapy aimed at stabilizing the general clinical condition.

Table 1

Structure of comorbidities

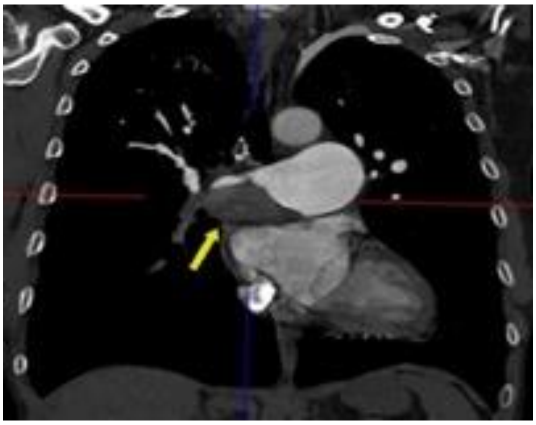
Characteristics of patients	n
Deep vein thrombosis	10
Hypertension	7
Obesity III > degree	6
Diabetes	5
Oncopathology	3
COPD	3
Recent surgery	2
Arteriosclerosis obliterans	2

In terms of determining the nature of the lesion of the pulmonary arterial bed, we used the results of magnetic computed angiography with ECG synchronization and bolus contrast enhancement. It should be noted that in all cases we diagnosed the central form of PE, with localization of thromboembolism in the trunk and bifurcation of the lobar branches of the pulmonary artery (Fig. 1 A, B, C)

According to the results of transthoracic echocardiography (Echo), in all cases, acute systolic overload of the right ventricle, dilatation of the right heart, signs of high pulmonary hypertension with the formation of obstructive biphasic blood flow in the pulmonary artery were observed (Fig. 2 A, B). The peak pressure in the pulmonary artery was 63 ± 1.23 mmHg, while the mean pressure was 47 ± 2.56 mmHg.

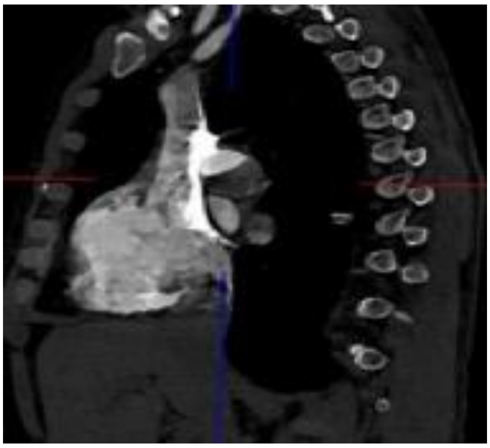
To verify the source of the thromboembolic substrate, as well as to assess the risk of PE recurrence, all patients underwent duplex scanning of the lower extremity veins. According to the results of the latter, in all patients, the occlusive form of deep vein thrombosis of the lower extremities was verified, without signs of significant free-floating thrombi. The study of the peripheral venous bed, in our opinion, is a mandatory component of the preoperative additional examination, which makes it possible to determine the extent of the surgical intervention to be performed.

At the end of the diagnostic stage, all patients were transferred to the operating room for surgical intervention. In all cases, a standard median sternotomy was used as a surgical approach, followed by a T-shaped opening of the pericardium. After the latter was completed, the cardiopulmonary bypass (CPB) was connected by cannulation of the ascending aorta and selective catheterization of the orifices of both vena cava with 32F and 36F cannulas, respectively. For CPB, a Jostra HL20 Maquet apparatus was used; the initial filling volume was 1400–1500 ml depending on the patient's body weight (hematocrit 25–28%). CPB was performed with a perfusion index of 2.4–2.8 l/min m^2 and an average perfusion arterial pressure of 60–80 mm Hg. Art. under conditions of normothermia with a temperature of 36°C in the esophagus.



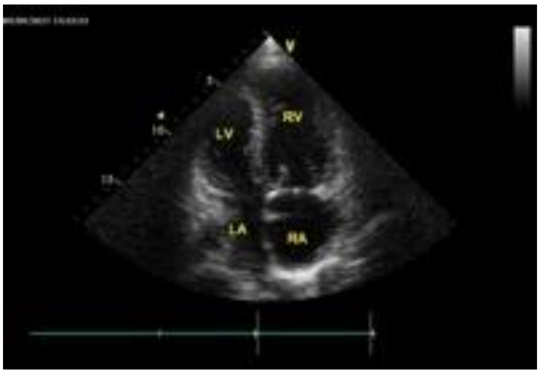
A

B

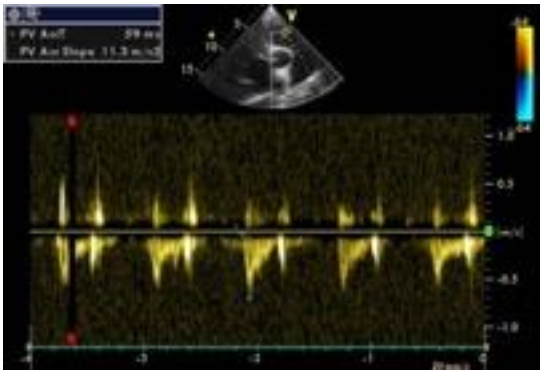


C

Fig. 1. Fragments of MSCT angiopulmonography in projections of MIP reconstruction of the coronal (1A), axial (1B), sagittal (1C) projections
Note: thromboembolic masses are determined in the trunk and main branches of the pulmonary artery



A



B

Fig. 2. Results of transthoracic echocardiography
Note: 2A - signs of dilatation of the right parts of the heart with the phenomena of paradoxical movement of the interventricular septum, 2B - signs of high pulmonary hypertension

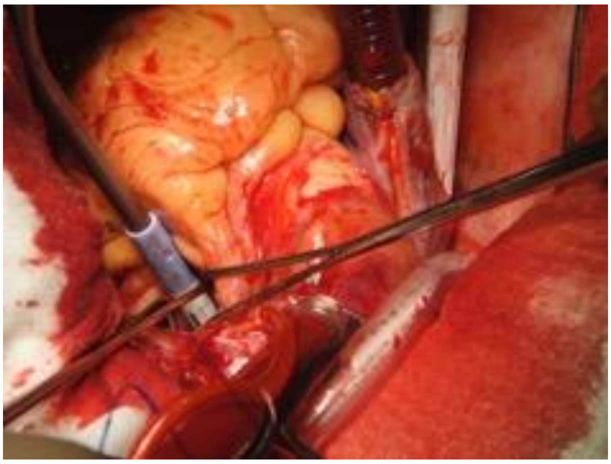


Fig. 3. Pulmonary arteriotomy

Fig. 4. Fragments of removed thromboembolism

After reaching the calculated performance of CPB, aortic clamping was performed, followed by antegrade pharmaco-cold cardioplegia by introducing the Consol solution into the aortic root. After complete electromechanical cardiac arrest, an arteriotomy approach to the pulmonary artery was performed starting from the pulmonary valve with a transition to its left main branch (Fig. 3).

To assess the state of the segmental and subsegmental branches of the pulmonary artery, the trifurcation of its right branch was isolated and opened, as well as the original incision was continued to the bifurcation of the trunk of the left branch. Under direct optical control, thromboembolectomy was performed from the trunk, main and lobar branches of the pulmonary artery using a set of straight and curved foreceps, as well as using a 2F-4F Fogarty catheter in two patients (Fig. 4).

After the end of the embolectomy stage, we proceeded to the stage of retrograde perfusion of the pulmonary artery. For this, biatrial access to the left atrium was performed. For retrograde perfusion of the lungs, we used a disposable system for the delivery of cardioplegic solution and 2 cardioplegic pumps of the CBP apparatus: the first one for taking blood perfusate from the oxygenator, the second one for supplying the combined solution. The composition of the protective solution included: sodium chloride solution 0.9% – 800 ml, dexamethasone 16 ml, actovegin – 400 ml and mannitol 15% – 100 ml. The blood perfusate and solution were mixed in a 3:1 ratio and injected selectively into the orifices of the pulmonary veins under a pressure of up to 20 mm Hg. (volume perfusion rate 200–250 ml/min) for 4 minutes. For sequential cannulation of the latter, an endotracheal tube with a size of 6.0–6.5 with an inflatable cuff was used, which was connected to a system for retrograde perfusion of the lungs. Against the background of retrograde perfusion, peripheral thromboembolism was removed from the peripheral parts of the pulmonary arterial bed using vacuum aspiration of the blood flowing from the arteriotomy access.

As an adequate prevention of air embolism and the formation of residual pulmonary hypertension, the trunk and main branches of the pulmonary artery were sutured at the height of the flow of retrograde incoming blood. The retrograde perfusion of the lungs was completed only at the end of the sealing of the arteriotomy access. In one patient, pulmonary artery sealing was performed using a xenopericardial patch to prevent iatrogenic stenosis. After decannulation of the pulmonary veins, the left and right heart chambers were sutured. Prevention of air embolism was carried out with the help of left ventricular drainage, carried out through the orifice of the upper right pulmonary vein. After the end of the main stage of the operation, decannulation of the aorta and vena cava, sealing of heart wounds, and restoration of the integrity of the chest frame using wire cerclages were per-

Table 2

Parameters of transthoracic echocardiography

Transthoracic echocardiogram index	Before operation ($M \pm \delta$)	After operation ($M \pm \delta$)
Right atrium	53 ± 3.14 / 46 ± 1.14 (mm)	41 ± 3.74 / 37 ± 1.25 (mm)
Right ventricle	63.2 ± 3.11 / 43.1 ± 2.21 (mm)	56.2 ± 1.01 / 38.7 ± 3.51 (mm)
Ejection fraction of the left ventricle	45.3 ± 2.17 (%)	44.2 ± 2.19 (%)
Mean pressure in the pulmonary artery	47 ± 2.56 (mm Hg.)	34 ± 2.02 (mm Hg.)
Peak pressure in the pulmonary artery	63 ± 1.23 (mm Hg.)	34 ± 2.23 (mm Hg.)

formed. By the time of skin sutures, in all cases, the appearance of electrical activity of the brain was noted (BIS-index at the time of transfer was 17). The mean blood loss was 368 ± 58.4 ml.

The study was carried out in accordance with the standards of good clinical practice (Good Clinical Practice) and the principles of the Declaration of Helsinki 1975. and its revised version of 2000. Prior to inclusion in the study, written informed consent was obtained from all participants, and the study itself was approved by the Local Ethics Committee.

Statistical processing of the studied material was carried out using the licensed software package "Statistica 10.0". Quantitative features are presented in the work as $M \pm \delta$, where M is the arithmetic mean, δ is the standard deviation. When assessing the severity of the condition and the degree of risk of developing PE, we used generally recognized classifications in accordance with current clinical guidelines.

Results

After the completion of the surgery, the patients were transferred to the ICU, where they received an extended course of conservative therapy, namely: antibiotic therapy, anticoagulant, infusion therapy, cardioprotective therapy, as well as therapy aimed at restoring the acid-base balance of the body. In order to stop the residual effects of acute right ventricular failure, patients underwent two-component inotropic myocardial stimulation (maximum dose of noradrenaline 0.11 ± 0.04 µg/kg/min, duration up to 18.6 ± 4.3 hours; maximum dose of adrenaline 0.09 ± 0.04 µg/kg/min, lasting up to 12.1 ± 3.2 hours). Despite the initial degree of respiratory disorders, as well as the duration of CPB, we did not reveal a single episode of neurological disorders: all patients showed signs of adequate awakening within 5 to 9 hours after surgery. The average time of artificial lung ventilation (ALV) was 15.2 ± 4.31 hours. In addition to the quite predictable phenomena of cardiovascular and respiratory failure, one of the postoperative complications we recorded was the syndrome of multiple organ failure with a predominance of hepatic and renal failure, leveled at the time of transfer of patients from the ICU.

Subsequently, the patients were transferred to a cardiological hospital, where they completed a course of complex conservative therapy. The hospital survival rate was 100%. When assessing the objective status of patients, there was an increase in exercise tolerance, leveling the phenomena of stagnation in both circles of blood circulation, which was in harmony with the subjective improvement in the general somatic status.

To assess the hemodynamic efficiency of the surgical intervention, we focused on the data of transthoracic echocardiography (Table 2).

As can be seen from the presented data, already at the time of discharge from the hospital, reverse remodeling of the right heart chambers, restoration of their normal kinetics, and a decrease in pressure in the pulmonary artery were noted. Despite the fact that the first experience of retrograde perfusion of the pulmonary artery, proposed in this article, was in the status of "mastering the technique", we did not note technical intraoperative difficulties, as well as the development of specific postoperative complications.

Discussion

Despite a comprehensive study of the issue of venous thromboembolic complications, and in particular PE, many aspects related to early diagnosis, as well as the preference for choosing the method of reperfusion of the pulmonary arterial bed, are ambiguous and require further study (Medvedev et al, 2021). The first disappointing experience of surgical treatment of PE, just like the dizzying results of using TLT, determined the place of the latter as the "gold standard" of treatment (Rivera-Lebron et al, 2019). However, the accumulation of experience in surgical treatment, the modification of surgical and anesthesiology-perfusion aids gave a rapid impetus to the development of the surgical direction, while determining an increase in survival rates. Thus, the first attempt at surgical treatment of PE was proposed by Trendelenburg in 1908, and subsequently implemented by Kirchner in 1924. (Mkalaluh *et al.*, 2019). The lack of specialized equipment, perfusion support, and a well-coordinated team approach led to disappointing clinical results, which required the search for new solutions. Of the variety of proposed options for surgical treatment, the most widely used method was D. Cooley, proposed by the author in 1961. (Fedorov *et al.*, 2021). The main significant disadvantage of the known method is the impossibility of performing radical thromboembolectomy from the peripheral branches of the pulmonary arterial bed, which may contain both primary thrombotic masses and fragments of thromboembolism formed during their traction removal from the proximal sections. Embolization of the microcirculatory bed determines the violation of perfusion of a significant segment of the lung tissue, which determines the persistence of not only respiratory failure after surgery, but also leads to the formation of chronic pulmonary hypertension, which reduces the effectiveness of interventions. In addition, the air that inevitably enters and remains in the pulmonary artery after its opening, with the onset of blood flow in the pulmonary circulation, is deployed to the peripheral regions and causes air embolism of the branches of the pulmonary artery. These pathophysiological mechanisms lead to damage to the alveolar membranes, as a result, patients develop severe respiratory disorders, which increase the length of stay of patients in the hospital and increase mortality rates (Fanola *et al.*, 2020). Attempts to mechanically evacuate thromboembolic masses from small branches of the pulmonary artery by compressing the lungs and repeatedly using Fogarty catheters significantly increase the risk of injury to the endothelial lining of the pulmonary artery, which can lead to fatal pulmonary hemorrhage. Thus, the use of the technique of retrograde pulmonary artery perfusion allows leveling possible hemodynamic disturbances in the system of the microcirculatory pulmonary bed, and in parallel with this determines the possibility of performing a surgical intervention that meets the criteria of precision and radicality. The absence of specific complications and the technical simplicity of execution allow us to speak of a good reproducibility of the technique (Fedorov *et al.*, 2021). If we talk about practical implementation, then this technique is certainly effective in terms of preventing air embolism and the development of residual pulmonary hypertension. If we talk about passive washing out of the microembolic substrate from the peripheral parts of the arterial bed, then it should be noted that the effectiveness and expediency of performing the latter will be determined by the time interval elapsed from the moment of the PE episode. Based on the available data, it can be noted that the best performance is achieved within 3 days, which is determined by the pathophysiological mechanisms of peripheral thromboembolism retraction and their fixation to the endothelial surface.

Conclusion

Retrograde pulmonary artery perfusion is a very encouraging and promising technique that provides effective and safe removal of small thromboembolism from the peripheral parts of the pulmonary arterial bed, as well as preventing the development of residual pulmonary hypertension as a result of developing intraoperative air embolism.

The technical simplicity of execution, as well as the absence of the need for expensive consumables, determines the high reproducibility of the technique.

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