

Hemodynamic status of patients with different comorbidities of ischemic heart disease before and after coronary artery bypass grafting

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ABSTRACT

Aim. To assess the hemodynamic status by transpulmonary thermodilution (TPTD) in patients with ischemic heart disease (IHD) with different comorbidities before and after coronary artery bypass grafting (CABG).

Materials and methods. 66 patients with IHD (40 men and 26 women) aged 53 to 77 years who were admitted for planned CABG were examined. The patients were divided into three groups according to the comorbidity: cardiovascular, respiratory, and metabolic. The first comorbidity was represented by a combination of IHD and multifocal atherosclerosis, the second – by IHD and chronic obstructive pulmonary disease (COPD), and the third – by IHD and metabolic syndrome (MS). All patients underwent CABG with the use of cardiopulmonary bypass. Hemodynamic parameters were recorded by the TPTD method using the Pulsion Picco Plus module (Germany) at 3 stages: after the start of mechanical ventilation (stage I), after the completion of cardiopulmonary bypass (stage II), and 24 hours after CABG (stage III).

Results. The patients with IHD with different comorbidities differed in characteristic signs of hemodynamic changes. In IHD with comorbid COPD, after withdrawal from the cardiopulmonary bypass and 24 hours after CABG, the highest index of systemic vascular resistance, the minimum values of the global ejection fraction, and a decrease in the global end-diastolic volume and pulmonary blood volume less noticeable compared with other groups of patients were noted. With comorbid respiratory and metabolic disorders, the maximum values for the indices of extravascular lung water and pulmonary vascular permeability were recorded. In the patients with a comorbid cardiovascular disease, hemodynamic and volume status violations in the dynamic follow-up were less pronounced.

Conclusion. The use of the TPTD method in patients with IHD before and after CABG makes it possible to specify the functional state of the circulatory system in different comorbidities, which increases the effectiveness of risk stratification and the accuracy of predicting possible complications.

Key words: ischemic heart disease, coronary artery bypass grafting, comorbidity, transpulmonary thermodilution.

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Conformity with the principles of ethics. All patients signed an informed consent to participate in the study. The study was approved by the local Ethics Committee at Far Eastern Federal University (Protocol No. 12 of 15.11.2017).

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Гемодинамический статус пациентов с различными вариантами коморбидности ишемической болезни сердца до и после коронарного шунтирования

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РЕЗЮМЕ

Цель – оценить гемодинамический статус методом транспульмональной термодилуции (ТПТД) у больных ишемической болезнью сердца (ИБС) с различными вариантами коморбидности до и после коронарного шунтирования (КШ).

Материалы и методы. Обследованы 66 больных ИБС (40 мужчин и 26 женщин) в возрасте 53–77 лет, поступивших на плановое КШ, которые были разделены на три группы коморбидности: кардиоваскулярную, респираторную и метаболическую. Первая из них представлена сочетанием ИБС и мультифокального атеросклероза, вторая – ИБС и хронической обструктивной болезни легких (ХОБЛ), третья – ИБС и метаболического синдрома (МС). Всем больным проведено КШ в условиях искусственного кровообращения (ИК). Показатели гемодинамики регистрировали методом ТПТД с использованием модуля Pulsion Picco Plus (Германия) на трех этапах: после начала искусственной вентиляции легких (I этап), после завершения ИК (II этап) и через 24 ч после КШ (III этап).

Результаты. Больные ИБС с различными вариантами коморбидности отличались характерными признаками гемодинамических изменений. При сочетании ХОБЛ и ИБС после отхода от ИК и через 24 ч после КШ отмечен наиболее высокий индекс системного сосудистого сопротивления, минимальные значения глобальной фракции изгнания, менее заметное по отношению к другим группам больных снижение глобального конечного диастолического объема и легочного объема крови. При респираторной и метаболической коморбидности фиксировались максимальные значения индексов внесосудистой жидкости в легких и проницаемости легочных сосудов. У больных с кардиоваскулярной коморбидностью нарушения гемодинамического и волеического статуса в динамике наблюдения были менее выраженными.

Заключение. Использование метода ТПТД у больных ИБС до и после КШ позволяет детализировать функциональный статус системы кровообращения при различных вариантах коморбидности, что повышает эффективность риск-стратификации и точность прогнозирования возможных осложнений.

Ключевые слова: ишемическая болезнь сердца, коронарное шунтирование, коморбидность, транспульмональная термодилуция.

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

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INTRODUCTION

Ischemic heart disease (IHD) remains one of the leading causes of death worldwide. Previous research showed that almost 70% of IHD patients have different comorbidities, which often modify clinical presentation of the underlying disease and reduce the effectiveness of pharmacotherapy [1]. The most common types of IHD comorbidity include its combination with other cardiovascular diseases, metabolic syndrome (MS), and chronic obstructive pulmonary disease (COPD). Thus, the combination of IHD with an atherosclerotic occlusion of the carotid and coronary arteries (CA) occurs in 75% of patients, and the combination of IHD with chronic lower limb ischemia accounts for 37–78% of cases [2]. MS is verified in 24% of patients sent for coronary artery bypass grafting (CABG), and COPD – in 35% of patients [3].

According to the American Society of Thoracic Surgeons, IHD patients with comorbid MS have a 1.4-fold increase in the risk of postoperative complications [3]. A study using the SYNTAX Score II scale showed that the likelihood of unfavorable postoperative complications after CABG doubles in IHD patients with comorbid COPD [4]. Depending on the number of arterial basins damaged by atherosclerosis, the risk of postoperative cardiovascular events increases by 1.64–10.5 times in IHD patients with a comorbid vascular disease, compared with isolated coronary artery disease.

High probability of complications and poor prognosis of surgical intervention in patients with IHD with a comorbidity determine the need for more careful monitoring of the functional state of the circulatory system at all stages of the hospital stay [5]. In routine clinical practice, electrocardiography, echocardiography, pulse oximetry, non-invasive and invasive blood pressure measurement, and registration of central venous pressure are used as hemodynamic monitoring methods. However, the generally accepted methods of hemodynamic research do not always provide a personalized approach to assessing the functional state of the circulatory system, which is especially important in cases with a high risk of complications associated with various comorbidities.

A number of studies have shown that the use of modern technologies of volumetric and hemodynamic monitoring significantly increases the efficiency of early diagnosis of adverse cardiovascular events. These technologies include the transpulmonary thermodilution method, which allows for an objective as-

essment of the patient's volume and hemodynamic statuses and their early correction [6].

The aim of the study was to assess the hemodynamic status by transpulmonary thermodilution in patients with coronary artery disease with different comorbidities before and after CABG.

MATERIALS AND METHODS

A prospective observational clinical study included 66 patients with ischemic heart disease (40 men and 26 women) aged 53 to 77 years (the average age was 66 years) who were admitted to the Medical Center of Far Eastern Federal University for planned CABG. Depending on the prevalence of clinical manifestations of comorbid diseases, the IHD patients were divided into 3 groups according to the comorbidity: cardiovascular, respiratory, and metabolic. The first group included 24 patients with IHD and comorbid multifocal atherosclerosis (chronic lower limb ischemia and an atherosclerotic occlusion of the carotid arteries of $\geq 50\%$). The second group included 20 IHD patients with grade II–III COPD without exacerbation. The third group was represented by 22 patients with IHD and comorbid MS, verified according to the clinical guidelines of the Ministry of Health of the Russian Federation.

Among the patients of the third group, the body mass index was in the range of 31–34 kg / m², which indicated class 1 obesity. The patients of all groups were diagnosed with chronic heart failure (CHF) of II–III functional classes according to the NYHA classification and controlled stage 2–3 hypertension with a very high risk. A written informed consent was obtained from each patient to participate in the study. The research protocols were approved by the local Ethics Committee at Far Eastern Federal University (Protocol No. 12 of 15.11.2017) and complied with the Declaration of Helsinki developed by the World Medical Association “Ethical Principles for Scientific Medical Research with Human Participation” as amended in 2000 and “The Rules of Clinical Practice in the Russian Federation” approved by the Order of the Ministry of Health of the Russian Federation of 19.06.2003, No. 266.

Hemodynamic and volumetric parameters were recorded by transpulmonary thermodilution using the Dreger Delta XL monitor and the Pulsion PiCCO Plus module (Germany) after a catheter from the PV2015L20 kit was inserted into the brachial artery. The duration of its presence in the arterial bed was no more than three days. Arterial line lavage was carried

out with boluses of 0.9% NaCl with the addition of heparin 1 U / ml. When calibrating the module, three consecutive thermodilutions were performed. Hemodynamic and volumetric parameters were analyzed at three stages of the study: immediately after tracheal intubation and the beginning of mechanical ventilation (stage I); after completion of the cardiopulmonary bypass (stage II); and 24 hours after the surgery (stage III).

The following parameters were recorded: stroke index (SI), cardiac index (CI), pulse pressure variability (PPV), stroke volume variability (SVV), systemic vascular resistance index (SVRI), global end-diastolic volume index (GEDI), global ejection fraction (GEF), cardiac function index (CFI), extravascular lung water (EVLW), and extravascular lung water index (EVLWI). In addition, the following parameters were calculated: pulmonary blood volume (PBV) = GEDI – EVLW, pulmonary vascular permeability index (PVPI) = EVLW / PBV, and dynamic arterial elastance (Ea_{dyn}) = PPV / SVV.

Statistical data processing was performed using the STATISTICA 10 software (StatSoft, Inc., USA) and Excel (Microsoft Office 2018) in the Microsoft Windows 10 operating system. The hypothesis of normal distribution of quantitative parameters in the analyzed groups was tested using the Shapiro – Wilk test. Data analysis was performed using descriptive statistics: medians (*Me*) and their 95% confidence intervals (CI). CI was calculated by the bootstrap method. Intergroup differences were assessed using the Kruskal – Wallis test. The differences were considered statistically significant at $p < 0.05$.

RESULTS

The obtained data showed that at the first stage of the study, the SI and CI indices in the IHD patients with comorbid cardiovascular and metabolic disorders corresponded to the standard values (40–60 ml / m² and 3–5 l / min / m²). After cardiopulmonary bypass withdrawal in the IHD patients with comorbid lesions of other arterial regions, a decrease in SI by 18% was recorded against the background of a stable CI level. At stage III, SI reached the initial values in this group, and CI exceeded them by 8.6%. With comorbid metabolic diseases at stage II of the study, the SI and CI indices decreased more significantly (by 37% and 18%, respectively), and a tendency to their increase was noted one day after the surgery. In the IHD patients with comorbid COPD, withdrawal from the cardiopulmonary bypass was accompanied by similar changes

in hemodynamics: a decrease in SI by 34% and in CI – by 9%. At the same time, 24 hours after CABG, this tendency was increasing, which was illustrated by a further decrease in the values of these parameters.

Before the surgery, in the patients of all groups, an increase in GEDI and a decrease in GEF were recorded, compared with their normal values, which indicated systolic and diastolic myocardial dysfunction (Table). 24 hours after CABG, in the IHD patients with a comorbid cardiovascular disease, GEDI decreased by 12.7%, while GEF increased by 2%. In IHD with comorbid MS, the dynamics of these parameters was more pronounced and amounted to 33% and 13.6%, respectively, which indicated a more significant decrease in preload and improvement in the cardiac pump function [5]. In patients with comorbid cardiorespiratory disorders, after withdrawal from the cardiopulmonary bypass, GEDI decreased by only 5%, compared with the initial level, and 24 hours after CABG – by 11%. At the same time, GEF had minimal values at all stages of the study, compared with other groups of the examined, which indicated decreased cardiac reserve in this category of patients.

In our study, the CFI level, which is an integral parameter of myocardial performance, was significantly lower than the standard values in all the patients before surgical treatment. One day after CABG, the patients in groups 1 and 3 showed an increase in this parameter to the reference range, while in the IHD patients with a comorbid respiratory disease, it did not reach it. The SVRI value before the surgery in the patients of all groups significantly exceeded the standard level, but did not have intergroup differences. After CABG, in the patients with comorbid vascular and metabolic diseases, SVRI decreased by 46–48%, and in the IHD patients with comorbid COPD, this parameter did not differ from the initial values.

SVV, PPV, and Ea_{dyn} belong to predictors of the hemodynamic response of patients to infusion load and are indicators of cardiorespiratory interaction during mechanical ventilation [6]. The levels of SVV and PPV depend on the filling of the vascular bed and on the ability of the heart to respond to a sudden increase in preload. At the same time, an increase in the values of these parameters is associated with hypovolemia, and a decrease – with progressing heart failure.

It was found that after withdrawal from the cardiopulmonary bypass, statistically significant changes in SVV and PPV were observed only among the patients with comorbid respiratory diseases, which was manifested through an increase in the values of these

parameters by 28% and 22%, respectively. A day after CABG, a significant increase in these parameters was recorded among the patients of all groups, but with a maximum level in IHD with comorbid COPD. Dynamic arterial elastance in the patients with comorbid vascular and metabolic diseases before CABG was above the threshold value, and after surgery, it reached it. At the same time, in the patients with COPD, a reversed tendency was observed, which was manifested through an increase in this parameter at stages II and III of the study.

EVLWI before surgery exceeded the standard values (3.0–7.0 ml/kg) in the patients of all groups, but was the highest among people with MS and COPD (Table). After withdrawal from the cardiopulmonary bypass, the EVLWI level did not change significantly. One day after the surgery, it decreased, but did not reach the reference values. In the patients with MS, the EVLWI level was the highest, which was associated with the effect of excessive intra-abdominal pressure on pulmonary blood flow [7]. Before the surgery, the PBV index in the patients with COPD was significantly lower than in the comparison groups. After withdrawal from the cardiopulmonary bypass, all the examined patients showed a tendency to its decrease, which persisted 24 hours after CABG. At the first stage of the study, in the patients with a comorbid respiratory disorder, PVPI was significantly higher than in other groups. After withdrawal from the cardiopulmonary bypass, in the patients with comorbid COPD and MS, the increase in PVPI was more noticeable, which could indicate an increasing likelihood of acute lung injury [8].

DISCUSSION

The authors attempted to perform a comprehensive assessment of the hemodynamic and volume status of the IHD patients in order to clarify the phenotypic features of blood circulation in different clinical comorbidities. It was found that initially decreased GEF and CFI levels in patients with comorbid cardiovascular and metabolic diseases and their subsequent growth to the reference level demonstrate significant improvement in the functional state of the myocardium already one day after its surgical revascularization. In the patients with comorbid cardiorespiratory diseases, the absence of positive dynamics of these indicators may be due to the systemic effects of chronic arterial hypoxemia and persistent inflammation, which prevent restoration of myocardial contractile function even with resumed coronary blood flow [1].

The results of SVRI measurement with continuous monitoring significantly complement the hemodynamic “portrait” of IHD patients. Thus, at the first stage of the study, most of them showed an increase in this indicator against the background of normal or decreased CI values, which is typical of elderly people with hypertension [5]. After withdrawal from the cardiopulmonary bypass in individuals with comorbid vascular and metabolic diseases, a decrease in SVRI indicated a decrease in left ventricular (LV) afterload and improvement in the cardiac pump function. In the patients with a comorbid respiratory disorder, the SVRI value in the early postoperative period exceeded the upper limit of the normal values, which may be due to a more noticeable limitation of the dilatation potential of the peripheral arterial bed in a combination of IHD and COPD.

Currently, measurement of GEDI is considered to be one of the most accurate technologies for assessing static cardiac preload [6]. In our study, before transitioning to the cardiopulmonary bypass, this parameter in the IHD patients with COPD was statistically significantly lower than in other groups. In these cases, a decrease in the volume of diastolic filling of the heart chambers may be a consequence of a more noticeable limitation of venous return and an increase in pulmonary vascular resistance induced by remodeling of the lung tissue. This was confirmed by the results of assessing the dynamic cardiac preload using SVV and PPV.

The dynamics of their changes during mechanical ventilation indicated that in the patients with a respiratory comorbidity, a more significant increase in intrathoracic pressure and a decrease in venous return to the heart were observed, compared with other groups. High level of Ea_{dyn} confirmed excessive arterial stiffness in the patients with COPD [5]. According to a number of authors, EVLWI is one of the most accurate parameters characterizing the volume of extravascular lung water. According to the literature, an increase in this parameter of more than 10 ml / kg is a predictor of subclinical pulmonary edema [8, 9].

In our study, the highest values of this parameter were recorded for respiratory and metabolic comorbidity groups, which may be due to more pronounced pulmonary circulatory disorders in this category of patients. Earlier, it was shown that an increase in the pressure in the pulmonary circulation leads to the “sieve effect” of pulmonary capillaries and provokes extravasation of fluid into the interstitial tissue [7]. Important factors in the pathogenesis of extravascular lung water include lung reperfusion.

Table

Parameters of systemic and pulmonary hemodynamics in patients with ischemic heart disease with different comorbidities (Me, 95% CI)										
Parameters	Research stages									p-value
	I			II			III			
	IHD + PAD (n = 24)	IHD + COPD (n = 20)	IHD + MS (n = 22)	IHD + PAD (n = 24)	IHD + COPD (n = 20)	IHD + MS (n = 22)	IHD + PAD (n = 24)	IHD + COPD (n = 20)	IHD + MS (n = 22)	
GEDI, ml (680–800)	989.35 ¹ [911.1; 1,067.5]	948.5 ² [786.2; 1,110.8]	1,193.56 ³ [993.4; 1,393.7]	902.82 ⁴ [824.6; 981.1]	895.2 ⁵ [810.7; 979.7]	917.89 ⁶ [759.2; 1,076.5]	899.06 ⁷ [806.94;991.17]	847.33 ⁸ [745.8; 948.8]	897.56 ⁹ [707.01; 1,088.11]	$p_{1-4} = 0.01$; $p_{4-7} = 0.47$; $p_{1-7} = 0.02$; $p_{2-5} = 0.06$; $p_{5-8} = 0.06$; $p_{2-8} = 0.024$; $p_{3-6} = 0.02$; $p_{6-9} = 0.07$; $p_{3-9} = 0.037$; $p_{2-3} = 0.02$;
GEF, % (25–35)	22 ¹ [20;25]	19 ² [18;22]	22 ³ [20;24]	21 ⁴ [19;24]	18 ⁵ [15;22]	21 ⁶ [18;25]	26 ⁷ [23;30]	19 ⁸ [16;21]	25 ⁹ [22;28]	$p_{1-4} = 0.06$; $p_{4-7} = 0.053$; $p_{1-7} = 0.03$; $p_{2-5} = 0.452$; $p_{5-8} = 0.07$; $p_{2-8} = 0.73$; $p_{3-6} = 0.65$; $p_{6-9} = 0.073$; $p_{3-9} = 0.01$
CFI, l/min (4.5–6.5)	3.9 ¹ [3.2;4.6]	3.98 ² [3.4;4.6]	3.25 ³ [3.1;3.42]	4.32 ⁴ [3.9;4.7]	3.94 ⁵ [3.66;4.23]	4.44 ⁶ [3.62;5.25]	4.75 ⁷ [4.4;5.1]	3.83 ⁸ [3.6;4.09]	5 ⁹ [4.2;5.8]	$p_{1-4} = 0.06$; $p_{4-7} = 0.03$; $p_{1-7} = 0.001$; $p_{2-5} = 0.08$; $p_{5-8} = 0.07$; $p_{2-8} = 0.06$; $p_{3-6} = 0.007$; $p_{6-9} = 0.078$; $p_{3-9} = 0.0056$
SVRI, dyn/sec/ sm ⁻⁵ /m ² (1200–2000)	2,345.6 ¹ [1,942.76; 2,748.41]	2,320.8 ² [1,910.3; 2,731.36]	2,355.89 ³ [1,973.08; 2,739.4]	1,791.5 ⁴ [1,499.1; 2,084.2]	2,359.67 ⁵ [2,125.91; 2,593.42]	1,788.4 ⁶ [1,600.28; 1,976.83]	1,646.4 ⁷ [1,466.4; 1,826.3]	2,294 ⁸ [2,070.7; 2,517.3]	1,589.33 ⁹ [1,383.18; 1,795.48]	$p_{1-4} = 0.02$; $p_{4-7} = 0.07$; $p_{1-7} = 0.002$; $p_{2-5} = 0.45$; $p_{5-8} = 0.09$; $p_{2-8} = 0.06$; $p_{3-6} = 0.005$; $p_{6-9} = 0.07$; $p_{3-9} = 0.015$
SVV, % (< 10)	7.71 ¹ [4.63;10.8]	9.5 ² [7.93;11.1]	7.22 ³ [4.13;10.3]	8.75 ⁴ [5.23;12.3]	11.5 ⁵ [6.57;16.4]	6.33 ⁶ [3.38; 9.39]	12.13 ⁷ [9.4;14.9]	16.8 ⁸ [12.2; 21.5]	14.22 ⁹ [9.8; 18.6]	$p_{1-4} = 0.06$; $p_{4-7} = 0.043$; $p_{1-7} = 0.03$; $p_{2-5} = 0.06$;

[illegible]

Note: PAD – peripheral arterial disease; GEDI – global end-diastolic volume index; GEF – global ejection fraction; CFI – cardiac function index; SVRI – systemic vascular resistance index; SVV – stroke volume variability; PPV – pulse pressure variability; EVLWI – extravascular lung water index; PBV – pulmonary blood volume; PVPV – pulmonary vascular permeability index; p^{1-9} – the level of statistical significance of differences between similar comorbidities at the research stage.

According to randomized clinical trials, its main cause is previous lung hypoperfusion, which develops against the background of the cardiopulmonary bypass [2]. The accumulation of extravascular fluid in the lungs is also facilitated by opening of the pleural cavities, systemic inflammatory response to the cardiopulmonary bypass, excessive transfusion therapy, atelectasis of the basal segments of the lungs, and microangiopathy associated with MS and diabetes mellitus [3]. For early recognition of cardiogenic and non-cardiogenic pulmonary edema, PVPI assessment is important. The latter can significantly increase in acute respiratory distress syndrome, but remain within the reference values in cardiogenic pulmonary edema.

An increase in PVPI indicates capillary leakage of the lungs, which requires timely limitation of infusion therapy and prescription of loop diuretics. Before the surgery, in the IHD patients with comorbid cardiorespiratory diseases, PVPI was significantly higher than in the comparison groups, which indicated initially higher pulmonary capillary permeability due to the influence of the pathogenetic factors of COPD. After withdrawal from the cardiopulmonary bypass in the groups of IHD patients with comorbid COPD and MS, an increase in the value of this parameter was noted. The results obtained indicate that stress factors related to cardiac surgery, including cardiopulmonary bypass, are triggers of pathophysiological reactions that contribute to an increase in pulmonary vascular permeability and the likelihood of respiratory complications in this category of patients.

CONCLUSION

Detailing the circulatory and volume status following TPTD increases the effectiveness of risk stratification and the accuracy of predicting possible complications. The role of these studies increases in IHD with a comorbidity associated with phenotypic features of

blood circulation, which was manifested through a more noticeable increase in extravascular lung water and permeability of pulmonary capillaries in IHD with comorbid respiratory and metabolic diseases.

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Authors contribution

Geltser B.I. – conception of the study, drafting of the manuscript. Karpov R.S., Kotelnikov V.N. – design of the study, analysis of data, drafting of the manuscript. Sergeev E.A., Silaev – collection of data, interpretation of results, drafting of the manuscript.

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