Russian Journal of Cardiology 2023;28(S2):5314
doi:10.15829/1560-4071-2023-5314
https://russjcardiol.elpub.ru

ORIGINAL ARTICLES
ISSN 1560-4071 (print)
ISSN 2618-7620 (online)
ISSN 2782-2257 (online)

Assessing the significance of some biomarkers in perioperative period after thoracic aortic reconstruction

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Aim. This study aims to assess the association between levels of biomarkers and postoperative complications in patients after thoracic and thoracoabdominal aortic reconstruction.

Material and methods. This study included 132 patients. The most of them underwent ascending aortic and aortic arch reconstruction (65 and 57, respectively). The concentrations of proadrenomedullin, presepsin, procalcitonin, troponin I and N-terminal brain natriuretic peptide were measured before induction anesthesia, at the end of the surgical operation and in 6 hours after surgery.

Results. 69 patients had postoperative complications. Among them, inflammatory (27,3%) and cardiovascular complications (12,1%) prevailed. At the end of the surgical operation, the levels of the biomarkers in patients without postoperative complications and with postoperative complications were for presepsin 326 [206; 451] и 620 [332; 829] p<0,00001, troponin I 0,77 [0,46; 1,39] and 1,49 [0,59; 3,39], p=0,01, proadrenomedullin 0,894 [0,683; 1,221] and 1,201 [0,944; 1,762], p=0,0002, procalcitonin 0,206 [0,147; 0,452] and 0,563 [0,307; 2,107], p=0,0002, respectively. According to log-linear regression model, the level of prepepsin at the end of the surgical operation >459,5 (odds ratio (OR) 6,84, 95% confidence interval (CI): 3,14-14,87) or proadrenomedullin >0,788 (OR 5,47, 95% CI: 1,52-19,68) are associated with the increased risk of postoperative complications. The level of presepsin >519,5 pg/ml at the end of the surgical operation (OR 4,55, 95% CI: 1,97-10,47) is associated with the increased risk of inflammatory complications. Regarding the prognosis of the risk of prolonged cardiotonic drug infusions, threshold values for troponin were >1,04 at the end of the surgical operation (sensitivity 75%, specificity 71,3%, AUC 0,785), >1,57 in 6 hours after surgery (sensitivity 81,3%, specificity 71,6%, AUC 0,794).

Conclusion. High levels of presepsin at the end of the surgical operation may be useful to predict the postoperative complications in patients who underwent the aortic surgery however, the low levels of presepsin do not exclude the development of postoperative complications. The increased level of troponin I at the end of the surgical operation and in 6 hours after surgery can be a predictor of the need for cardiotonic support in the postoperative period.

Keywords: biomarkers, presepsin, proadrenomedullin, procalcitonin, troponin I, N-terminal brain natriuretic peptide, cardiosurgery, aortic arch, ascending aorta.

Relationships and Activities: none.

Acknowledgements. Thanks to the nurses and doctors of the Department of Anesthesiology and Resuscitation of B.V. Petrovsky II RNCKH, who assisted in the collection of material.

The study ID: NCT04689139 Protocol ID039420200002.

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Received: 16.12.2022
Revision Received: 10.01.2023
Accepted: 15.03.2023

For citation: Axelrod B.A., Dymova O.V., Gubko A.V., Krasnoshchekova A.P., Guskov D.A., Goncharova A.V., Gladysheva V.G., Gubko K.V., Kulinchenko O.S. Assessing the significance of some biomarkers in perioperative period after thoracic aortic reconstruction. *Russian Journal of Cardiology*. 2023;28(2S):5314. doi:10.15829/1560-4071-2023-5314. EDN FPKOHH

Key messages

What is already known about the subject?

- Biomarkers are widely used to predict adverse cardiosurgical outcomes.
- Perioperative dynamics of the biomarker levels may influence the tactics of treatment of cardiosurgical patients.

What might this study add?

- Dynamics of the presepsin levels allows doctors to predict both inflammatory complications and the overall adverse events in postoperative period.
- Troponin I levels may be used to predict cardiovascular insufficiency in postoperative period in patients who underwent thoracic aortic surgery.

How might this impact on clinical practice?

- The parameters of intraoperative biomarker dynamics together with the findings obtained with other methods, allow doctors to determine the ways to correct the postoperative complications. The levels of biochemical parameters in intraoperative period of thoracic aortic reconstruction will become a criterion to correct the tactics of treatment of patients in early postoperative period.

Over the past decade, the level of cardiac surgical care has increased significantly; complex combined surgical interventions are performed in patients with severe cardiovascular and other concomitant diseases. This became possible due to the improvement of preoperative preparation, surgical technique, anesthesiological support and treatment of patients in the postoperative period. Despite the modern achievement in anesthesiology-resuscitation and surgical technique, lethality (during 30 days after operation) in all cardiosurgical patients is still ~3% [1].

Currently, forecasting of intensive care unit length of stay and outcome after cardiosurgical operations is based on the clinical parameters and concomitant diseases of different organs and systems and their severity (Parsonnet model, EuroSCORE II etc). Cardiosurgical operations include the use of artificial blood circulation which activates the different ways of systemic inflammatory response of body, and extensive surgical trauma also contributes to this. Systemic inflammatory response is characterized by systemic disorders of a number of bodies`s natural defense mechanisms from traumas and infections: fibrinolysis, coagulation, complement activation, immune cell activation, and oxidative stress in addition to inflammation. The damage to target organs arises as a result of the interaction between patient`s activated defense systems and the lesion of a regional vessel wall due to either physical trauma or ischemia/reperfusion [2].

With the aim to improve clinical results and to decrease mortality in cardiosurgical patient population, new biomarkers are being investigated for the improvement of the quality of prognostic models. In particular, presepsin (PSP) and procalcitonin have a comparable prognostic value in regard to unfavorable renal, cardiovascular and respiratory outcomes in cardiosurgical patients. Besides, PSP has a prognostic value in relation to intrahospital, 30-day and 6-month mortality [3], and it also highly effective for early diagnostics of sepsis in intensive care and resuscitation unit patients [4]. Some biomarkers are routinely used in cardiosurgery including preoperative assessment, such as troponins and cerebral natriuretic peptides [5, 6], while others are still under investigation.

Currently, cardiospecific troponins (cTnI, cTnT) localized mainly in the myocardium, are widely used as a marker of cardiovascular lesion [7]. The markers can reflect the damage to cardiomyocytes not only in the occurrence of irreversible pathological conditions (myocardial infarction) but also in the potentially reversible pathophysiological mechanisms (myocardial ischemia-reperfusion injury, mechanical impact during surgical operation, sepsis, acute renal failure and other processes) [8].

Adrenomedullin (ADM) is expressed in many organ systems including cardiovascular, renal, pulmonary, cerebrovascular, gastrointestinal and endocrine [9]. ADM affects the cardiovascular system causing vasodilation, natriuresis and inhibition of aldosterone production thereby, providing a general optimization of cardiac pre-load [10]. It was found that ADM provides prognostic information in cardiac failure (CF) [9]. Unfortunately, the ADM peptide is unstable and not suitable for use in clinical practice. But MR-proADM, a protein fragment reflecting the ADM levels in the bloodstream, was stable and suitable for use in clinical practice [11].

The study aims to assess the relationship between the level of biomarkers and development of postope-

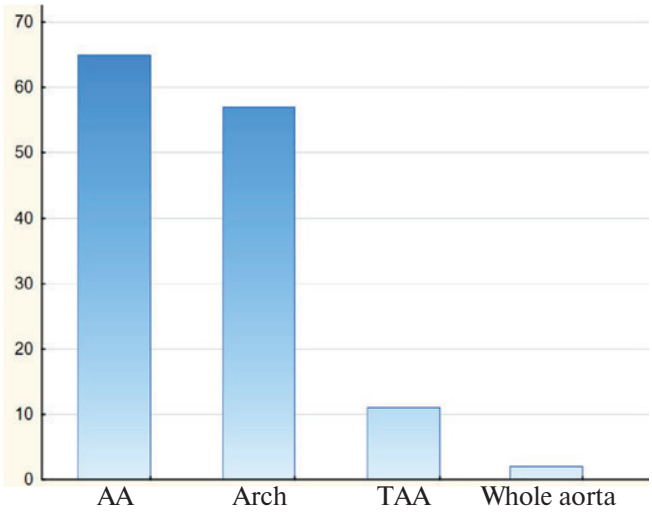

Figure 1. Types of surgical interventions.
Abbreviations: AA — ascending aorta, TAA — thoracoabdominal aorta.

Table 1

Initial pathology

Pathology	All patients (n=132)
Aortic insufficiency of the 3rd degree, n (%)	32 (24%)
Aortic insufficiency of the 4th degree, n (%)	8 (6%)
Aortic valve stenosis of the 3rd degree, n (%)	15 (11%)
Aortic valve stenosis of the 4th degree, n (%)	5 (4%)
Mitral insufficiency of the 3rd degree, n (%)	5 (4%)
Mitral insufficiency of the 4th degree, n (%)	1 (1%)
Ascending aortic aneurysm, n (%)	66 (50%)
Aortic arch aneurysm, n (%)	21 (16%)
Aortic root aneurysm, n (%)	44 (33%)
Connective tissue dysplasia syndrome, n (%)	17 (13%)
Thoracoabdominal aortic aneurysm, n (%)	27 (20%)
Aortic dissection type 1, n (%)	20 (15%)
Aortic dissection type 2, n (%)	6 (5%)
Aortic dissection type 3, n (%)	13 (10%)
Aortic dissection neither A nor B type, n (%)	3 (2%)
Thrombosis of the ascending aorta, aortic arch, n (%)	1 (1%)

Table 2

Anthropometric patient data, M±SD

Parameter	Value (n=132)
Women, n (%)	45 (34%)
Men, n (%)	87 (66%)
Age, years	56±13
Height, cm	174±14
Weight, kg	86±20
Body surface area, m^2	2±0,22

Table 3

Concomitant diseases and transthoracic echocardiography data, M±SD

Parameter	All patients (n=132)
LV EF, %	57±7,6
LV EDV, ml	171±88
CHF 3 FC according to NYHA, n (%)	9 (7%)
CHF 4 FC according to NYHA, n (%)	2 (2%)
COPD, n (%)	14 (11%)
CVD, n (%)	18 (14%)
DM, n (%)	7 (5%)
CKD C2, n (%)	16 (12%)
CKD C3, n (%)	21 (16%)
CKD C4, n (%)	2 (2%)
Constant form of AF, n (%)	9 (7%)
Paroxysmal form of AF, n (%)	17 (13%)
ACVA in the anamnesis, n (%)	9 (7%)
Leriche syndrome, n (%)	6 (5%)
Hypertensive disease stage 3, n (%)	64 (48%)
IHD, n (%)	27 (20%)
VDLE, n (%)	15 (11%)
Repeated cardiac surgery, n (%)	16 (12%)
Hereditary thrombophilia, n (%)	1 (1%)
Multiple organ failure, n (%)	5 (4%)
IDA, n (%)	5 (4%)
Obesity degree 1, n (%)	13 (10%)
Obesity degree 2, n (%)	7 (5%)
Obesity degree 3, n (%)	3 (2%)

Abbreviations: VDLE — varicose disease of lower extremities, IDA — iron deficiency anemia, IHD — ischemic heart disease, LV EDV — left ventricular end-diastolic volume, ACVA — acute cerebrovascular accident, DM — diabetes mellitus, LV EF — left ventricular ejection fraction, AF — atrial fibrillation, CKD — chronic kidney disease, COPD — chronic obstructive pulmonary disease, CHF FC according to NYHA — chronic heart failure according to functional classification of New York Heart Association, CVD — cerebrovascular disease.

rative complications in patients after thoracic and thoracoabdominal aortic reconstruction.

Material and methods

The study was performed in accordance with the standards of Good Clinical Practice and the principles of the Declaration of Helsinki. The study protocol was approved by the Ethic committee of B.V. Petrovsky Russian scientific center of surgery. We obtained written informed consent from all participants prior to inclusion into the study. The study is registered on ClinicalTrials.gov. NCT04689139 Protocol ID039420200002.

The prospective non-randomized cohort study included 132 patients who underwent surgical interventions aimed to restore and reconstruct the thoracic aorta (Figure 1). In the spectrum of surgical interventions, the reconstruction of the ascending aorta prevails.

The inclusion criteria: 18-75 years of age, reconstruction surgery in aneurysms of thoracic and/or thoracoabdominal aorta.

The exclusion criteria: impossibility to analyze at least one of three patient samples due to pre-analytic errors (hemolysis).

Blood sampling aiming to determine the biomarker concentrations was performed in three consecutive stages:

1. Before induction anesthesia;
2. At the end of surgical operation;
3. In 6 hours after surgery.

The patients included into the study underwent surgical interventions for aneurysm/dissection of ascending aorta, aortic arch and/or thoracoabdominal aorta (Table 1). Anthropometric data are given in the Table 2. Initially, most of patients had preserved left ventricular ejection fraction and increased left ventricular end-diastolic volume. Among concomitant pathology, arterial hypertension, chronic kidney disease, ischemic heart disease, rhythm disturbances in the form of atrial fibrillation and other nosology prevailed (Table 3).

To collect intraoperative data, we used a unique scientific system "Collection of electronic anesthesia cards of cardiosurgery patients of the B.V. Petrovsky Russian scientific center of surgery"[1].

Before surgery, patients received premedication with drugs from the benzodiazepine group (sibazone 10 mg/m or alprazolam 0,25-0,5 mg orally) on the eve of surgery and opioids (trimeperidine 20 mg/m), H_1-histamine receptor blockers (chloropyramine hydrochloride 20 mg/m). Introduction anesthesia was performed using propofol 2,0-2,5 mg/kg, fentanyl 2-3 mcg/kg and cisatracurium bezilate 0,15 mg/kg. Anesthesia was maintained by inhalation of sevoflurane 0,7-1,0 MAC and fentanyl using a perfuser at a dosage of 2-3 mcg/kg×h. Myoplegia was maintained by continuous infusion of cisatracurium bezilate at a rate of 0,06-0,1 mg/kg×h. Monitoring included: electrocardiography of 7 leads (I, II, III, avL, avR, avF, V5), invasive arterial pressure, central venous pressure, pulse oximetry and capnography. Surgical interventions on the aortic arch were performed under circulatory arrest with a target temperature of 27° C, selective mono- and/or bihemispheral antegrade cerebral perfusion with control of the volumetric perfusion rate (8-12 ml/kg) according to transcranial dopplerography and cerebral oximetry. Surgical interventions on the thoracoabdominal aorta were performed in the conditions of selective perfusion of the renal arteries, superior mesenteric artery and coeliac trunk. During intra- and postoperative periods, the cerebrospinal fluid pressure with target values 8-12 mm Hg was constantly monitored.

According to the protocol, the period of observation and collection of the information within the present study was 10 days or until discharge from hospital, depending on which event occurs earlier.

The inclusion criteria of these or those biomarkers into the study were: the availability of technical capability to determine the biomarker concentration and the turnaround time not more than 40 min. Thus, the following parameters were included into the study:

- procalcitonin, PSP — biomarkers of inflammation,
- proadrenomedullin — marker of organ dysfunction,
- troponin I TnI-hs — marker of myocardial injury,
- N-terminal pro-brain natriuretic peptide (NT-proBNP) — marker of HF.

The determination of procalcitonin and proadrenomedullin concentrations was performed using the analyzer Kryptor Compact Plus (Thermo Fisher Scientific), troponin I, NT-proBNP, PSP — using the analyzer PATHFAST (LSI Medience Corporation).

Statistical processing of the obtained data was carried out using a software package "Statistica 10 for Windows". The parameters were checked for the normality of the distribution considering the chi-square criterion. The comparative analysis was performed using the Student's t-test or Mann-Whitney U test, depending on the results of the previous normality test. In $p<0,05$ the difference between the groups were considered statistically significant. The search for predictors of the development of complications in the postoperative period was carried out using log-linear regression, ROC analysis; logistic regression coefficients were used to estimate the odds ratio (OR) for each dependent variable of the model. To identify the influence of a set of nominal and non-nominal values on the quantitative response of biomarkers, the regression analysis was performed.

[1] A unique scientific installation "Collection of electronic anesthesia cards of cardiac surgery patients of the B.V. Petrovsky Russian National Research Center" B.V. Petrovsky Russian Scientific Center of Surgery (Moscow), Head of UNU: Axelrod B.A., MD, Professor of the Russian Academy of Sciences, https://med.ru/ru/unikalnaa-naucnaa-ustanovka.

- Lethal outcomes — 2 patients (2,9%)
- Extracorporeal detoxification — 7 (10,1%)
- Inflammatory complications — 36 patients (27,3%)
  - Pneumonia — 29 (22,0%)
  - Wound infection — 7 (5,3%)
  - Mediastinitis — 3 (2,3%) Sepsis — 5 (3,8%)
- Myocardial infarction — 5 (3,8%)
- Cardiac rhythm disturbances — 24 (18,2%)
- Acute renal failure — 11 (8,3%)
- Need in cardiotonic support — 16 (12,1%)
- Need in vasopressor support — 14 (10,6%)

Figure 2. Spectrum of complications (n=69).

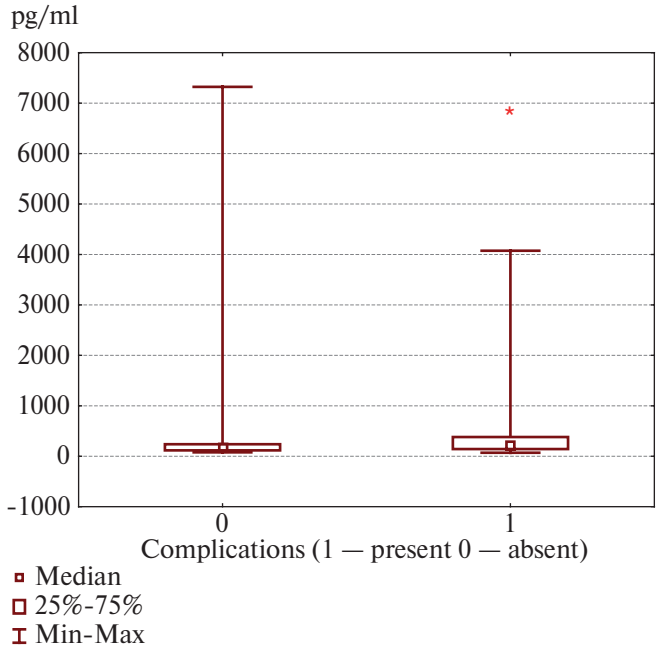

Figure 3. Initial values of PSP.
Note: * — p<0,01.

Results

A complicated course (the presence of at least one of the complications given below) of the postoperative period was observed in 69 patients of 132 (Figure 2).

The criterion of the increased need in cardiotonic support — the need for dopamine/dobutrex infusion >3 mcg/kg×min and/or duration >24 hours from the moment of surgery. The criterion of vascular insufficiency is the need for norepinephrine infusion >150 ng/kg×min and/or the duration of administration >24 hours from the moment of surgery, acute renal failure — an increase in serum creatinine level ⩾26,5 mmol/l during 48 hours, an increase in serum creatinine by ⩾1,5 times compared to the previous 7 days, urine volume <0,5 ml/kg×h during 6 hours.

According to the results of comparative analysis between the groups with non-complicated and complicated postoperative periods at the stage "before induction anesthesia", statistically significant differences were revealed only for PSP concentrations (Figure 3), and at the same time, the group of the patients with complicated postoperative period course had statistically higher PSP levels.

At the stages "at the end of surgical operation" and "in 6 hours after surgery", the patients with complicated postoperative period course had higher values of PSP, troponin I, procalcitonin and proadrenomedullin (Figure 4).

To search for possible predictors, we used the analysis of log-linear regression, according to results of which we found that at the end of surgical operation only the increased levels of proadrenomedullin are associated with the increased risk of complicated postoperative period course (OR 6,23, 95% CI: 1,78-21,86).

To determine the level of proadrenomedullin, the ROC-analysis was the most effective (with the maximum possible simultaneously sensitivity and specificity) allowing us to separate groups of patients with complicated and non-complicated postoperative period. It was found that the optimal cut-off level for proadrenomedullin at the end of surgical operation is 0,788 (sensitivity 43,75%, specificity 88,89%). The proadrenomedullin concentrations at the end of surgical operation >0,788 are associated with the increased risk of the complicated postoperative period course (OR 5,47, 95% CI: 1,52-19,68).

When analyzing the results of the determination of PSP, it was noted that despite statistically higher PSP levels in patients with complicated postoperative period course, the low values of PSP do not allow us to exclude the development of complications with sufficient confidence. Most likely, this feature of the distribution of PSP concentrations in the groups of patients with normal and complicated postoperative periods was a reason why, according to the log-linear regression results, the increase in the PSP level at the end of surgical operation is not associated with the increased risk of the development of complications in postoperative period.

At the same time, according to the nature of the distribution of PSP concentrations at the end of surgical operations, it was noticed that the complicated postoperative period course is characterized by such high values of this biomarker, which were not

Parameter	Stage	Non-complicated course of p/o period (M (Q1-Q3); minimum-maximum values)	Complicated course of p/o period (M (Q1-Q3); minimum-maximum values)	P
Presepsin pg/ml	Before surgical operation	171 (117-239) 78,8-7323	216 (143-381) 70,4-4074	0,0072
	At the end of surgical operation	326 (206-451) 119-1263	620 (332-829) 145-2531	0,000007
	In 6 hours after surgery	450,5 (269-716) 151-3337	627,0 (382-1015) 132-3480	0,0147
Troponin I ng/ml	At the end of surgical operation	0,4510 (0,202-0,957) 0,006-17,6	0,755 (0,345-1,81) 0,009-23,9	0,0133
	In 6 hours after surgery	0,77 (0,46-1,39) 0,008-17,9	1,49 (0,59-3,39) 0,008-23,5	0,0278
Proadrenomedullin nmol/l	At the end of surgical operation	0,894 (0,683-1,221) 0,234-2,098	1,201 (0,944-1,762) 0,484-3,254	0,0018
	In 6 hours after surgery	1,009 (0,772-1,235) 0,351-2,682	1,475 (1,135-1,894) 0,484-3,534	0,0002
Procalcitonin ng/ml	At the end of surgical operation	0,094 (0,064-0,131) 0,027-0,98	0,137 (0,102-0,234) 0,057-4,523	0,0033
	In 6 hours after surgery	0,206 (0,147-0,452) 0,080-6,278	0,563 (0,307-2,107) 0,112-17,33	0,0002

Figure 4. Dynamics of markers and course of p/o period.
Abbreviation: p/o — postoperative.

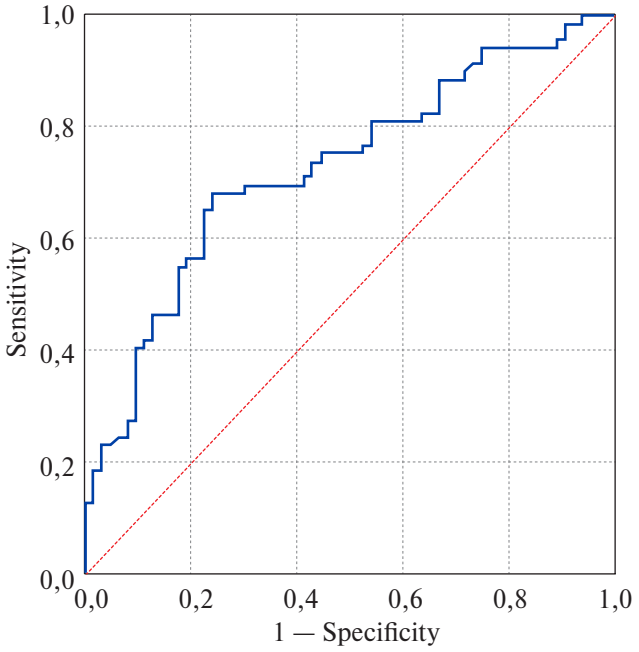

Figure 5. ROC-analysis of PSP at the end of surgical operation and risk of complications.

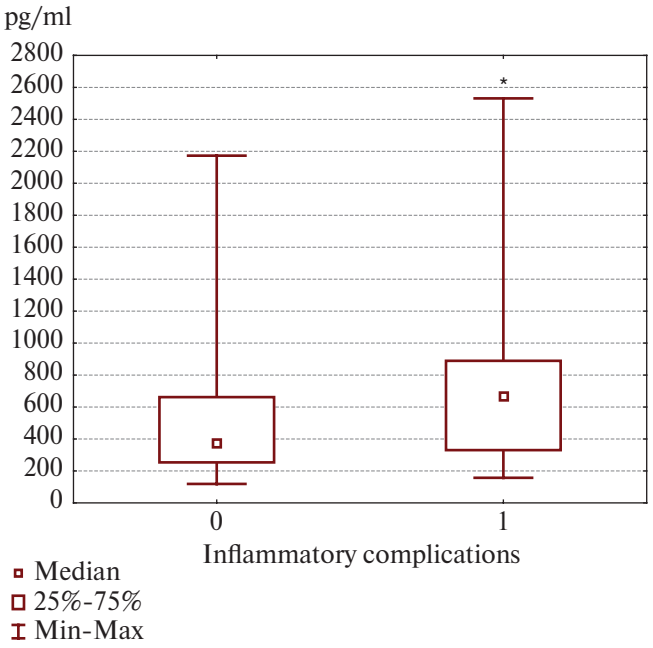

Figure 6. PSP level at the end of surgical operation in patients with inflammatory complications.
Note: * — p<0,01, 1 — complicated postoperative period, 2 — non-complicated postoperative period.

found in patients with non-complicated postoperative period. This fact allowed us to assume that probably the increased PSP levels can be associated with the increased risk of complications in postoperative period, however, low or slightly raised PSP levels do not allow us to exclude the development of complications.

According to the ROC-analysis results, the most acceptable cut-off level for PCP at the end of surgical operation is 459,5 (sensitivity 68,1%, specificity 76,2%). The PSP levels at the end of surgical operation >459,5 are associated with the increased risk of

Parameter	Stage	Non-complicated course of p/o period (M (Q1-Q3); minimum-maximum values)	Complicated course of p/o period (M (Q1-Q3); minimum-maximum values)	P
N-terminal pro-brain natriuretic peptide, pg/ml	Before surgical operation	229 (123-871) 13-30001	1160 (280-7054) 39-11871	0,0025
	At the end of surgical operation	213 (86-668) 11-23734	684 (351-3971) 51-10803	0,0014
	In 6 hours after surgery	421 (203-1270) 26-14616	1305 (626-7159) 224-27346	0,0011
Troponin I ng/ml	At the end of surgical operation	0,548 (0,202-1,29) 0,006-7,58	1,74 (0,833-5,41) 0,317-23,9	0,0001
	In 6 hours after surgery	0,858 (0,453-1,825) 0,008-23,5	2,275 (0,317-23,9) 0,833-5,410	0,0001

Figure 7. Markers and prolonged infusion of cardiotonic drugs in postoperative period.
Abbreviation: p/o — postoperative.

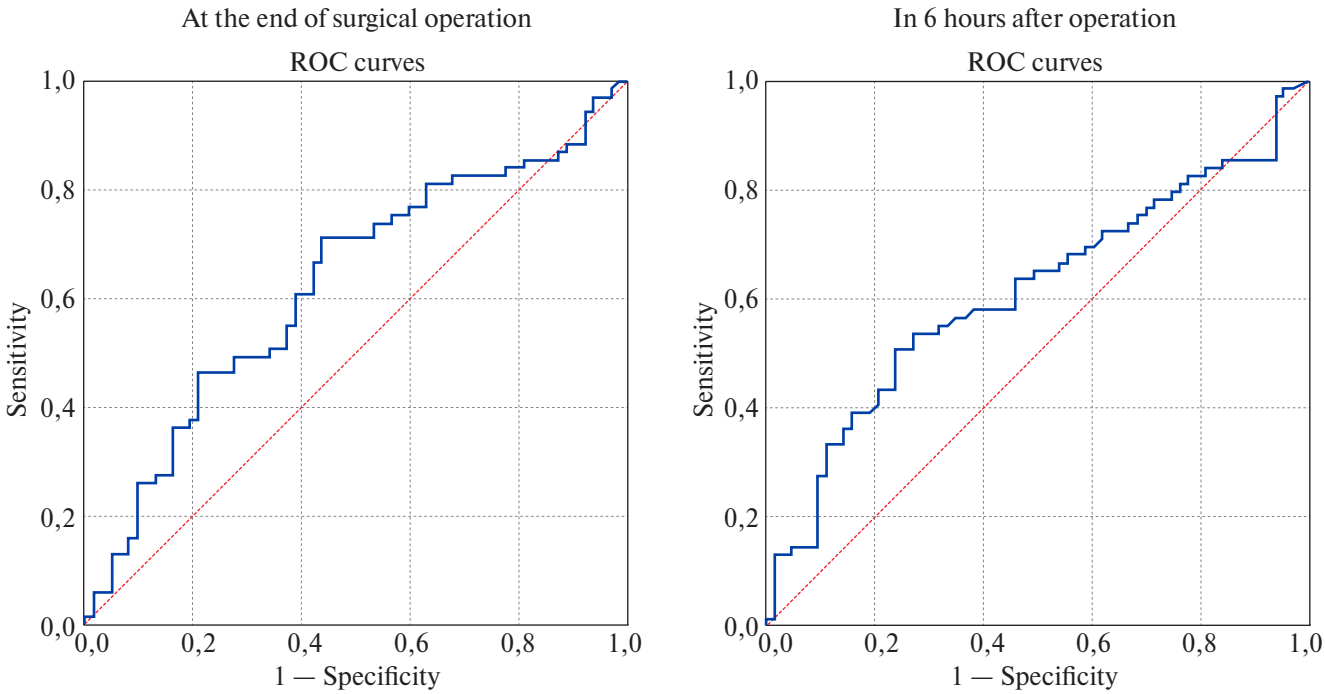

Figure 8. ROC-analysis for Troponin I.

the complicated postoperative period course (OR 6,84, 95% CI: 3,14-14,87) (Figure 5).

As for the PSP concentrations in 6 hours after surgery, the noted tendency was no longer observed in this period. For this period, despite statistically reliably higher PSP values in the group of patients with complicated postoperative period, the PSP values in general were so heterogeneous that it was not possible to identify the predictor.

Thus, the high PSP levels (>459,5) at the end of surgical operation can be useful regarding the prognosis of the development of complications in postoperative period in patients after aortic surgery but at the same time, the low PSP levels cannot exclude the development of complications in postoperative period in such patients, that is important to take into account while interpreting the results of this biomarker in postoperative period.

The inflammatory complications in postoperative period were observed in 36 patients of 132. Of them:

- pneumonia — 29;
- wound infection — 7;
- mediastinitis — 3;
- sepsis — 5.

According to the comparative analysis results, the most suitable biomarker for forecasting the development of inflammatory complications in postoperative period is the level of PSP at the end of surgical operation (Figure 6). The group with inflammatory complications in postoperative period had higher values of PSP (the median of the values in the group with normal postoperative period course was 372,5, range 119-2173 the median of the values in the group with complicated postoperative period course — 668,5, range 157-2531, p=0,0029). Using the ROC-analysis, we found that the most acceptable threshold value of the biomarker is the level of 519,5 pg/ml (sensitivity 69,4%, specificity 66,7%, area under ROC-curve (AUC) 0,669, 95% CI: 0,563-0,775), above which the risk of inflammatory complications is increased (OR 4,55, 95% CI: 1,97-10,47) with the same statement that low or slightly raised PSP levels do not allow us to exclude the development of complications.

High need in the infusion of cardiotonic drugs, indirectly indicating HF, was observed in 16 patients of 132. The comparative analysis outlined the range of possible predictors — the levels of NT-proBNP before surgical operation, at the end of surgical operation and in 6 hours after surgery, and the levels of troponin I at the end of operation and in 6 hours after surgery (Figure 7). But the log-linear regression results showed that only increase in the troponin levels directly after operation and in 6 hours after operation can be the predictors of prolonged infusion of cardiotonic drugs in postoperative period (OR 1,53, 95% CI: 1,15-2,04 and OR 1,23, 95% CI: 1,08-1,40, respectively).

Using the ROC-analysis, we determined the optimal cut-off levels for troponin I (Figure 8):

- at the end of surgical operation >1,04 (sensitivity 75%, specificity 71,3%, AUC 0,785),
- in 6 hours after surgery >1,565 (sensitivity 81,3%, specificity 71,6%, AUC 0,794).

According to the long-linear regression analysis results, the risk of high need in prolonged infusion of cardiotonic drugs in postoperative period is associated with the raised troponin levels >1,04 at the end of surgical operation (OR 7,45, 95%, CI: 2,22-25,07) and the troponin level >1,565 (OR 10,90, 95%, CI: 2,88-41,25) in 6 hours after surgery.

Discussion

The ideal indicator of biological processes in the modern clinical conditions should have sufficient sensitivity and specificity, be informative, accessible, reproducible and timely, since the dynamics of an indicator may be used not only to forecast unfavorable events in postoperative period but also to control treatment. In this study, we used both the biomarkers which have been used in routine practice for a long time and relatively new peptides, the use of which can be quite perspective (PSP) in forecasting postoperative complications. We used proadrenomedullin as a marker of organ dysfunction, PSP, procalcitonin as the markers of inflammation, troponin I as an indicator of myocardial injury, and NT-proBNP as an indicator of HF. The concept of the complex evaluation of biomarkers, which was used in the present study, coincide with the studies of other authors. For example, Vershinina MG, et al. [4] showed the advantages of using a combination of biomarkers (the model of the use of the PSP and proadrenomedullin combination is the most effective) for early diagnostics of sepsis in intensive care and resuscitation unit patients in critical state.

It should be noted that most of the studies dedicated to the prognostic significance of the biomarkers in cardiosurgery were performed in valvular pathology surgery and/or in myocardial revascularization. The study performed by Clementi A, et al. showed a high prognostic value of PSP and procalcitonin for the estimation of postoperative renal, cardiovascular and respiratory complications. PSP was also effective for forecasting intrahospital, 30-day and 6-month lethality [3].

Despite the significance of the problem of thoracic and thoracoabdominal aortic reconstructive surgery, the publications dedicated to the use of biomarkers for forecasting postoperative complications are sporadic.

In our study, we found significant differences before the main stage of the surgical intervention in PSP only. However, even in the presence of statistically reliable differences, the values of this biomarker concentrations were so overlapping both in the region of high values and in the region of normal values, that it was not possible to use this indicator to forecast the development of inflammatory complications.

A revealed regularity that the high values of this biomarker are typical of complicated postoperative period course and were not observed in patients with non-complicated postoperative period course, also seems interesting. This fact allowed us to assume and then to prove that the increased PSP levels at the end of surgical operation are associated with the increased risk of the postoperative complications but low or slightly raised PSP levels do not allow us to exclude the development of complications. It is necessary to consider the revealed characteristic when interpreting the PSP determination results: high PSP levels (>459,5 pg/ml) at the end of surgical opera-

tion can be useful for forecasting the development of complications in postoperative period in patients who underwent aortic surgery, but at the same time low PSP levels at the end of operation cannot exclude the development of complications.

Regarding to forecasting inflammatory complications, it was found that according to the comparative analysis results, the most suitable biomarker for forecasting inflammatory complications in postoperative period is the PSP level at the end of surgical operation. But the pattern of distribution of PSP values in the analyzed groups also showed that even in statistically reliable differences, the values overlapped both in the region of high values and in the region of normal values, and according to the log-linear regression analysis results, the increased PSP level is not associated with the increased risk of complicated postoperative period course.

We found that the most acceptable threshold value of the biomarker is the level of 519,5 pg/ml (sensitivity 69,4%, specificity 66,7%, AUC 0,669, 95% CI: 0,563-0,775), above which the risk of inflammatory complications is increased (OR 6,84, 95% CI: 3,14-14,87), but at the same time the low PSP levels at the end of surgical operation (<519,5 pg/ml) cannot exclude the development of complications.

When investigating the dynamics of the changes in the levels of the analyzed biomarkers, we found that the auxiliary calculated parameters reflecting the dynamics of the changes in PSP levels can be also attributed to the predictors of inflammatory complications.

The 2-times and more increase in PSP level during time of surgical operation is associated with the increased risk of the development of complicated postoperative period course (OR 3,05, 95% CI: 1,34-6,95). The absence of the increase in PSP level during first 6 hours after surgery is associated with the increased risk of the development of complicated postoperative period course (OR 4,15, 95% CI: 1,83-9,41). And the combination of these two risk factors — PSP level at the end of surgical operation >519,5 pg/ml and the absence of the increase in PSP level during first 6 hours after surgery — is associated with the increased risk of the development of complicated postoperative period course (OR 5,80, 95% CI: 2,19-15,35).

Thus, for forecasting the development of inflammatory complications in postoperative period it is appropriate to use not only absolute PSP values at the end of surgical operation but also the monitoring of the dynamics of this indicator.

Highly sensitive troponin I has proven itself well in the diagnostics of not so much myocardial infarction as cardiovascular lesion [12]. It is an independent predictor of postoperative complications and lethality in patients with acute aortic dissection, and patients with initially elevated value of the marker had a greater number of cardiovascular complications [13]. In this regard, troponin I has some advantage over classical assessment scales (EuroSCORE, VA) in cardiosurgical patients [14].

In aortic surgery, the diagnostics of myocardial lesion is especially important because myocardial infarction in postoperative period is diagnosed quite rare. Our study revealed it in just 5 (3,8%) patients, while the need in cardiotonic and vasopressor support in 16 (12,1%) and 14 (10,6%), respectively. The evaluation of troponin I level will speed up the start of inotropic support because the myocardial damage during surgical operations on the thoracic aorta more often has a subclinical character and its causes are indirect (circulatory arrest, ischemia-reperfusion syndrome and other factors).

It should be also noted that the publications dedicated to the dynamics of highly sensitive troponin I in cardiosurgical patients emphasize a great role of a type of surgical intervention. In the study performed by Mastro F, et al., patients underwent mitral and aortic valve surgery, thoracic aortic surgery, myocardial revascularization and combined operations were examined. The maximum growth of the indicator was found in patients underwent mitral valve surgery as well as after combined operations [15]. These facts may be important in interpreting the laboratory results and making clinical decisions in postoperative period.

The limitation of our study is that its results cover the patients who underwent reconstructive surgery on the thoracic and thoracoabdominal aorta. The study included 132 patients that is also one of its limitations. To extend the use of these biomarkers as the predictors of complications in other categories of patients, further investigations will be required.

Conclusion

- High PSP levels at the end of surgical operation can be useful for forecasting the development of complications in postoperative period in patients underwent aortic surgery however, low PSP levels do not exclude the possibility of the development of complications.
- PSP showed greater informativity in forecasting of complications in general than precisely inflammatory complications.
- The increased troponin I level immediately after surgical operation and in 6 hours after operation can be a predictor of the need in cardiotonic support in postoperative period.

Acknowledgements. Thanks to the nurses and doctors of the Department of Anesthesiology and Resuscitation of B.V. Petrovsky II RNCKH, who assisted in the collection of material.

Relationships and Activities: none.

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