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Prognostic value of sCD14-ST (presepsin) in cardiac surgery

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Abstract

Introduction: Prediction of complications and mortality after cardiac surgery is an important aspect of timely correction of these conditions. One possibility in this case is the use of biomarkers and some prognostic scores.

Aim of the study: To study the prognostic value of presepsin (PSP) as a predictor of postoperative complications development in cardiosurgical patients.

Material and methods: Patients operated for acquired heart diseases with cardiopulmonary bypass (CPB) were included in the study (*n* = 51, age: 58 ± 11 years). Besides routine clinical and laboratory data, PSP and procalcitonin (PCT) levels were monitored perioperatively (before surgery, and on the 1st, 2nd, 3rd and 6th day after surgery).

Results: There were no clinical signs of infection before surgery in any of the studied patients. We found supranormal PSP levels in 6 patients (11.8%) before operations (543 [519-602] pg/ml, max 1597 pg/ml; normal value: 365 pg/ml). Infectious complications developed in 19 patients (37%). Statistically significant differences in PSP levels, APACHE II (Acute Physiology and Chronic Health Evaluation II) and SOFA (Sequential Organ Failure Assessment) scores in groups of patients with and without infection were documented from the 1st and in PCT from the 2nd day after the operation. The cut-off values were 702 pg/ml, 8.5 points, 7.5 points and 3.3 ng/ml, respectively. Hospital mortality was 13.7% (7 patients); all cases of death were in the group of patients with infectious complications. Statistically significant differences in PCT levels, APACHE II and SOFA scores between the groups with favorable and lethal outcomes were observed from the first postoperative day. The same for PSP levels was documented only on the 3rd postoperative day. The cut-off values were 7.42 ng/ml, 11 points, 8.5 points and 683 pg/ml, respectively.

Conclusion: The use of modern biomarkers alongside integral severity-of-disease scores allows prediction of the risk of infectious complications and mortality in cardiosurgical patients.

Key words: cardiac surgery, infection, mortality, procalcitonin, presepsin.

Streszczenie

Wstęp: Przewidywanie powikłań i śmiertelności po operacjach kardiochirurgicznych odgrywa znaczącą rolę we wczesnym podejmowaniu działań mających na celu uniknięcie tych niekorzystnych zdarzeń. Jedną z możliwości jest zastosowanie biomarkerów i niektórych skal prognostycznych.

Cel pracy: Zbadanie prognostycznej wartości presepsyny (PSP) jako predyktora powikłań pooperacyjnych u pacjentów kardiochirurgicznych.

Materiał i metody: Do badania włączono pacjentów poddawanych operacjom wykorzystującym krążenie pozaustrojowe (realizowane przez sztuczne płucoserce) z powodu nabytych chorób serca (*n* = 51, wiek: 58 ± 11 lat). Poza rutynową obserwacją danych klinicznych i laboratoryjnych obserwacja okołooperacyjna objęła stężenie PSP i prokalcytoniny (PCT) (przed operacją oraz w 1., 2., 3. i 6. dniu po operacji).

Wyniki: U żadnego z badanych nie wystąpiły przedoperacyjnie kliniczne oznaki infekcji. Przekraczające normę stężenia PSP wykazano u 6 pacjentów (11,8%) przed operacją [543 (519-602) pg/ml, maks. 1597 pg/ml; norma 365 pg/ml]. Powikłania infekcyjne stwierdzono u 19 pacjentów (37%). Pomiędzy grupami pacjentów z infekcjami i bez nich udokumentowano istotne statystycznie różnice dotyczące stężenia PSP i wyników testów APACHE II (*Acute Physiology and Chronic Health Evaluation II*) i SOFA (*Sequential Organ Failure Assessment*) (od pierwszej doby pooperacyjnej) oraz stężenia prokalcytoniny (od drugiej doby pooperacyjnej). Wartości odcięcia wynosiły odpowiednio: 702 pg/ml, 8,5 pkt, 7,5 pkt oraz 3,3 ng/ml. Śmiertelność szpitalna wyniosła 13,7% (7 pacjentów); wszystkie zgony dotyczyły pacjentów z grupy z powikłaniami infekcyjnymi. Pomiędzy grupami z korzystnymi i śmiertelnymi wynikami leczenia od pierwszej doby pooperacyjnej obserwowano istotne statystycznie różnice w zakresie stężenia PCT oraz wyników testów APACHE II i SOFA. W zakresie stężenia PSP różnice te udokumentowano jedynie w trzeciej dobie pooperacyjnej. Wartości odcięcia wynosiły odpowiednio: 7,42 ng/ml, 11 pkt, 8,5 pkt oraz 683 pg/ml.

Wnioski: Stosowanie nowoczesnych biomarkerów wraz ze skalami oceniającymi nasilenie choroby umożliwia przewidywanie ryzyka infekcyjnych powikłań i śmiertelności u pacjentów kardiochirurgicznych.

Słowa kluczowe: kardiochirurgia, infekcja, śmiertelność, prokalcytonina, presepsyna.

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Introduction

Systemic inflammation is a practically inevitable state developing after cardiopulmonary bypass procedures [1]. Apart from the impact of surgical trauma and contact activation of leukocytes, the pathogenesis of the inflammatory response is also associated with bacterial translocation from the gastrointestinal tract. Progression of systemic inflammation is connected with the development of numerous complications, the most severe of them being the multiple organ dysfunction syndrome (MODS), which follows only 2-3% of open heart procedures, but is characterized by high mortality, reaching 78% [2, 3].

Today it is evident that the maximum therapeutic effect can be reached only on condition that the treatment is started as early as possible. For example, every hour of delay with the administration of an adequate antibacterial therapy exceeding the 6-hour therapeutic window reduces the chance of a positive outcome in sepsis by 7.6% [4].

In this situation, the use of integral biochemical markers seems to be attractive, as they allow early prediction of a complication's development and the prognosis of the outcome. Alongside the well-studied procalcitonin test (PCT), there is certain interest in the research of other markers' potential and particularly of presepsin (PSP).

Presepsin is a soluble fragment of the CD14 macrophage receptor protein sCD14 (13 kDa), which has recently been put in the focus of investigation for its diagnostic and prognostic value in sepsis. CD14 is a glycoprotein expressed on the membranes of mononuclear cells. It serves as a high-affinity receptor for lipopolysaccharide (LPS) and LPS-binding protein (LBP) complexes. Formation of the LPS-LBP-CD14 complex launches the TLR4-dependant signal transmission mechanism followed by secretion of CD14 into the circulation in its soluble form, sCD14. Further activation of phagocytosis turns sCD14 into sCD14-ST, i.e. presepsin [5, 6].

In vivo experiments in the rabbit sepsis model revealed that in contrast to LPS infusion, which led to the inflammatory response without an increase of blood PSP level, the cecal ligation and puncture sepsis model in turn was associated with a considerable increase of this marker. *In vitro* experiments with rabbit peritoneal cells stimulated with *Escherichia coli* have shown that inhibitors of phagocytosis (cytochalasin D and wortmannin) inhibit the synthesis of PSP. Also, *in vitro* interaction between purified human sCD14 and cathepsin D (lysosomal protease) leads to PSP formation. These data suggest that the mechanism of PSP secretion depends on phagocytosis [6].

Evaluation of PSP levels in the blood of practically healthy subjects allowed normal values of this marker to be determined as within 60.1-365 pg/ml [7]. These limits should be regarded as indicative, and following the manufacturer's instructions each laboratory should set its own reference PSP levels.

Several clinical studies have demonstrated a high diagnostic value of PSP for early diagnosis of sepsis and stratification of its severity, as well as for prognosis of mortality in patients with this serious condition [7-9].

Similarity of the pathogenic mechanisms that take place in sepsis and the inflammatory response after CPB procedures, along with the lack of publications on the results of the clinical use of PSP, constituted the grounds for conducting the present study.

This study aims to investigate the prognostic value of presepsin (PSP) as a predictor of postoperative complications development in cardiosurgical patients.

Material and methods

The study was approved by the local ethics committee. During March-August 2012, fifty-one adult patients (average age 58 ± 11 years) operated on with CPB for acquired heart diseases and ischemic heart disease were enrolled. Forty-three patients underwent valvular surgery (mitral valve replacement combined with tricuspid valvuloplasty – 19 [37.3%], mitral valve replacement – 7 [13.7%], mitral and aortic valve replacement – 8 [15.7%], aortic valve replacement – 5 [9.8%], mitral valve replacement combined with tricuspid valvuloplasty and coronary artery bypass grafting [CABG] – 4 [7.8%]). Isolated CABG was performed in 7 cases (13.7%); left atrial myxoma resection was performed in 1 patient (2%).

General anesthesia was performed according to a common protocol, based on use of midazolam, fentanyl and isoflurane.

Most patients (93%) were in NYHA class III and IV and had a high risk of developing postoperative complications due to the severe initial condition and comorbidities. Mean expected mortality rate predicted by EuroSCORE was 13.54%. Demographic data, parameters of surgical procedure (CPB duration, time of aortic cross-clamping), APACHE II (Acute Physiology and Chronic Health Evaluation II) score on the 1st day after surgery as well as dynamics (before and on the 1st, 2nd, 3rd and 6th day after the operation) of clinical and laboratory parameters, including body temperature, leucocyte count, SOFA (Sequential Organ Failure Assessment) score, C-reactive protein (CRP, hsCRP, Beckman Coulter, USA), PCT (Vidas BRAHMS PCT, bioMérieux, France) and PSP (PATHFAST Presepsin, Mitsubishi Chemical Medience Corporation, Japan) blood plasma levels were registered.

After discharge from the hospital or death, the respective groups of patients were formed for subsequent analysis: without (group I, n = 32) and with (group II, n = 19) infectious complications as well as groups with a favorable outcome (group A, n = 44) and deceased (group B, n = 7).

Statistical analysis was performed with Statistica 7 (StatSoft Inc., USA) and SPSS, version 20 (SPSS, Inc., Chicago, Ill) software. The data are presented as absolute values, as well as medians and interquartile range. Statistical differences between groups were assessed with the Mann-Whitney *U*-test. Correlations were determined with Spearman's rank method (two-sided). *P*-values less than 0.05 were considered statistically significant.

Results

There were no clinical signs of infection in any patient before the operation. Initial levels of biomarkers revealed

no significant difference in subjects with a smooth postoperative period and patients who afterwards developed infectious complications and/or died. However, in contrast to other investigated parameters, the initial level of PSP in 6/51 (11.8%) patients exceeded the upper normal limit (365 pg/ml) and was 543 (519-602) pg/ml with the maximum of 1597 pg/ml.

Within 7-12 days after the surgery, 19/51 patients (37%) developed infectious complications. One of the most frequently diagnosed complications was ventilator-associated pneumonia (n = 12) combined with superficial surgical site infection (SSI) in 2 subjects and with sepsis in 1 subject. Additionally, 2 cases of superficial surgical site infection and 1 case of sepsis were registered.

For evaluation of the diagnostic value of PSP as a predictor of infectious complications, all patients were divided into two groups: group I (n = 32) without infectious complications and group II with postoperative infection. Baseline characteristics of patients with and without infectious complications are presented in Table I. There were no significant differences between the groups in age, CPB duration, time of aortic cross-clamping, SOFA score or studied laboratory markers. Patients with infectious complications required significantly prolonged ventilator support and longer stay in the ICU.

Comparison of laboratory indices and APACHE II and SOFA scores in groups I and II is presented in Table II. Statistically significant differences in PSP levels and APACHE II and SOFA scores in the analyzed groups were documented from the 1st and in PCT from the 2nd day after the operation. The cutoff values for these markers were 702 pg/ml, 8.5 points, 7.5 points and 3.3 ng/ml respectively. By the 6th day after the operation, statistically significant differences in the axial body temperature were registered. No differences in white blood cell count or in CRP level were documented between the groups during the whole period of investigation.

Results of ROC analysis defining the area under the receiver operating characteristic curve for studied predictors of infectious complications with corresponding values of specificity and sensitivity for optimum cut-off points are shown in Table III.

In-hospital mortality among patients enrolled in the present study was 7/51 (13.7%). All unfavorable outcomes were among patients with infection. Baseline characteristics of patients with different outcomes are presented in Table IV. There were no differences between groups in age or studied laboratory markers, but deceased patients had significantly longer duration of perfusion, ventilator support and stay in the ICU.

APACHE II and SOFA scores as well as dynamics of some routine laboratory indices of patients in groups with favorable (group A) and lethal (group B) outcomes are presented in Table V. Statistically significant differences in PCT levels and APACHE II and SOFA scores between the groups were observed from the first postoperative day. The same for PSP levels was documented only on the 3rd postoperative day. There was no significant difference between the groups in CRP.

The data of ROC analysis for predictors of mortality are presented in Table VI.

To study the interaction between the type of PSP dynamics in the postoperative period and the risk of infectious complications and mortality, 3 groups were formed: with normal PSP levels in the postoperative period (group 1); with PSP levels increased after the operation and then normalized by the 6th postoperative day (group 2); with a persistent increase of PSP level in the postoperative period (group 3) – Figure 1.

It was found that an increase of PSP level in the perioperative period is associated with the risk of infection. The most unfavorable variant is when blood levels of PSP are persistently supranormal as in this case infectious complications are observed in more than 50% of patients. Moreover, elevated PSP level regardless of the type of its subsequent dynamics is associated with higher risk of a negative outcome (Table VII).

It should be underlined that group 3 included 5/6 cases where the PSP level exceeded the normal value before the operation. Infectious complications developed in 3/5 (60%) of these patients, and 1/5 (20%) died.

Tab. I. Baseline characteristics of patients with and without infectious complications

Characteristics	Group I (without infectious complications), n = 32	Group II (with infectious complications), n = 19	p
Age, years	57 (51-65)	62 (60-66)	0.08
CPB duration, min	171 (130-197)	162 (121-296)	0.6
Aortic clamping, min	100 (76-120)	95 (72-156)	0.99
Ventilator support, h	26 (20-35)	95 (29-195)	< 0.001
ICU stay, h	25 (20-36)	96 (28-240)	0.002
Body temperature, °C	36.6 (36.6-36.7)	36.6 (36.5-36.6)	0.4
WBC, 1×10^9/l	6.6 (5.6-7.6)	7.2 (6.2-8.5)	0.23
PCT, ng/ml	0.05 (0.05-0.07)	0.05 (0.05-0.06)	0.69
PSP, pg/ml	140 (122-183)	131 (110-157)	0.47
CRP, mg/dl	0.19 (0.01-0.46)	0.27 (0.01-0.41)	0.8
SOFA	1 (0-1)	1 (0-2)	0.38

CPB – cardiopulmonary bypass, ICU – intensive care unit, WBC – white blood cells, PCT – procalcitonin, PSP – presepsin, CRP – C-reactive protein, SOFA – Sequential Organ Failure Assessment

Tab. II. Postoperative dynamics of laboratory indices in patients with and without infectious complications

Characteristics		Group I (without infectious complications), *n* = 32	Group II (with infectious complications), *n* = 19	p
Day 1	Body temp., °C	37 (36.6-37.3)	36.9 (36.6-38)	0.36
	WBC, 1 × 10^9/l	11.2 (8.9-13.8)	11.3 (9.6-13.7)	0.67
	PCT, ng/ml	2.29 (1.28-7.68)	7.59 (2.05-20.64)	0.08
	PSP, pg/ml	568 (363-858)	880.5 (632-1441)	0.005
	CRP, mg/dl	5.68 (2.92-7.5)	5.81 (3.18-7.79)	0.6
	APACHE II	6 (5-9)	12 (9-16)	< 0.001
	SOFA	7 (5-8)	8 (6-10)	0.04
Day 2	Body temp., °C	37 (36.8-37.5)	37.2 (36.7-37.5)	0.7
	WBC, 1 × 10^9/l	16.2 (13.3-21.6)	17.85 (15.6-23.1)	0.24
	PCT, ng/ml	1.8 (0.5-3.13)	4.7 (3.47-34.26)	0.03
	PSP, pg/ml	466 (395-520)	1144 (598-1692)	< 0.001
	CRP, mg/dl	11.1 (6.34-12.5)	7.86 (5.85-11.24)	0.37
	SOFA	6 (4-7)	8 (7-10)	0.01
Day 3	Body temp, °C	37 (36.7-37.5)	37.4 (37-37.9)	0.08
	WBC, 1 × 10^9/l	12.6 (10.1-15.4)	15.8 (12.2-20.8)	0.07
	PCT, ng/ml	0.8 (0.32-2)	4.97 (0.72-8.27)	0.01
	PSP, pg/ml	422 (293-619)	737 (664-1338)	0.005
	CRP, mg/dl	8.75 (7.85-13.37)	7.16 (5.15-11.8)	0.19
	SOFA	4 (3-5)	8 (6-11)	< 0.001
Day 6	Body temp, °C	36.7 (36.6-37)	37.3 (36.8-37.8)	0.001
	WBC, 1 × 10^9/l	10.7 (8.5-12.7)	12.6 (10.9-16.4)	0.06
	PCT, ng/ml	0.18 (0.1-0.44)	0.62 (0.28-3.63)	0.009
	PSP, pg/ml	265 (209-452)	612.5 (325.5-1048)	0.004
	CRP, mg/dl	3.42 (2.16-5.19)	4.96 (1.58-17.2)	0.23
	SOFA	3 (1-4)	5 (4-8)	< 0.001

WBC – white blood cells, PCT – procalcitonin, PSP – presepsin, CRP – C-reactive protein, APACHE II – Acute Physiology and Chronic Health Evaluation II, SOFA – Sequential Organ Failure Assessment

Tab. III. Results of ROC analysis for predictors of infectious complications

Predictor	Cut-off	AUC (95%CI)	Sensitivity, %	Specificity, %	OR (95%CI)
PSP*, pg/ml	702	0.75 (0.6-0.89)	72	66	4.9 (1.37-17.8)
PCT, ng/ml**	3.3	0.75 (0.54-0.96)	82	79	16.5 (2.3-121.2)
APACHE II*	8.5	0.84 (0.73-0.95)	78	74	10.1 (2.6-39.7)
SOFA*	7.5	0.69 (0.47-0.91)	63	65	3.1 (0.95-10.2)

*On the 1st postoperative day, **on the 2nd postoperative day
PSP – presepsin, PCT – procalcitonin, APACHE II – Acute Physiology and Chronic Health Evaluation II, SOFA – Sequential Organ Failure Assessment

There were statistically significant positive correlations of medium strength between PCT and PSP (r = 0.38), PCT and APACHE II (r = 0.53), PCT and SOFA (r = 0.56), PSP and APACHE II (r = 0.43), and PSP and SOFA (r = 0.5) on the 1st postoperative day.

Discussion

The main triggers of systemic inflammation after surgery with cardiopulmonary bypass are tissue damage and endotoxinemia; the leading role in its development and progression is played by monocytes and macrophages.

Tab. IV. Primary comparative characteristic of patients with different outcomes of the postoperative period

Characteristics	Group A (favorable outcome), *n* = 44	Group B (death), *n* = 7	*p*
Age, years	60 (52-65)	63 (60-70)	0.24
CPB duration, min	150 (126-193)	296 (183-334)	0.014
Aortic clamping, min	97 (72-118)	135 (90-190)	0.047
Ventilator support, h	30 (23-51)	183 (48-250)	0.002
ICU stay, h	28 (20-47)	184 (40-240)	0.008
PCT, ng/ml	0.05 (0.05-0.07)	0.06 (0.05-0.06)	0.12
PSP, pg/ml	138 (121-182)	124 (103-154)	0.45
CRP, mg/dl	0.25 (0.01-0.46)	0.2 (0.01-0.48)	0.99
SOFA	1 (0-1)	1 (0-2)	0.74

CPB – cardiopulmonary bypass, ICU – intensive care unit, PCT – procalcitonin, PSP – presepsin, CRP – C-reactive protein, SOFA – Sequential Organ Failure Assessment

Tab. V. Postoperative dynamics of clinical characteristics of patients in groups with favorable and lethal outcomes

Characteristics		Group A (favorable outcome), *n* = 44	Group B (lethal outcome), *n* = 7	*p*
Day 1	PCT, ng/ml	2.29 (1.28-7.6)	12.69 (7.59-33)	0.003
	PSP, pg/ml	649.5 (389.5-968.5)	795 (464-1365)	0.24
	CRP, mg/dl	5.67 (2.99-7.46)	7.7 (2.22-9.03)	0.34
	APACHE II	7 (5-10)	14 (12-18)	0.001
	SOFA	7 (6-9)	9 (8-11)	0.02
Day 2	PCT, ng/ml	2.34 (0.5-4.7)	11.37 (4.53-44.63)	0.008
	PSP, pg/ml	506 (426-754)	1029 (598-1692)	0.05
	CRP, mg/dl	8.67 (5.89-11.36)	10.8 (7.5-11.74)	0.69
	SOFA	6 (4-7)	10 (7-11)	0.004
Day 3	PCT, ng/ml	1.08 (0.32-2.11)	7.73 (4.05-12.11)	0.006
	PSP, pg/ml	500 (324-776)	830 (694-1294)	0.04
	CRP, mg/dl	8.71 (5.92-13.1)	8.71 (8.38-11.85)	0.93
	SOFA	5 (3-6)	11 (8-15)	0.006
Day 6	PCT, ng/ml	0.24 (0.11-0.59)	3.34 (0.5-6.28)	0.014
	PSP, pg/ml	321 (213.5-615.5)	325 (319-932)	0.31
	CRP, mg/dl	3.47 (1.98-5.57)	20.25 (80.7-20.62)	0.025
	SOFA	3 (1-5)	8 (4-8)	0.03

PCT – procalcitonin, PSP – presepsin, CRP – C-reactive protein, APACHE II – Acute Physiology and Chronic Health Evaluation II, SOFA – Sequential Organ Failure Assessment

Tab. VI. Results of ROC analysis for predictors of a lethal outcome

Marker	Cut-off	AUC (95%CI)	Sensitivity, %	Specificity, %	OR (95%CI)
PSP, pg/ml**	683	0.79 (0.63-0.95)	80	68	8.4 (0.8-83.9)
PCT, ng/ml*	7.42	0.88 (0.78-0.97)	86	77	16.2 (1.7-151.9)
APACHE II*	11	0.89 (0.78-0.99)	86	80	22.2 (2.3-207)
SOFA*	8.5	0.77 (0.56-0.98)	71	74	7.3 (1.3-43)

*On the 1st postoperative day, **on the 3rd postoperative day
PSP – presepsin, PCT – procalcitonin, APACHE II – Acute Physiology and Chronic Health Evaluation II, SOFA – Sequential Organ Failure Assessment

Moderate CPB-associated injury did not significantly disturb the balance between pro- and anti-inflammatory cytokine patterns, and the inflammatory response quickly attenuated. In contrast, excessive surgical trauma leads to systemic inflammation with an immunoreactivity imbalance. Phagocytic system overload with progressive accumulation of inflammatory mediators ("cytokine storm"), accompanied by the phenomenon of endotoxin tolerance, is observed. Hyperactivation of proinflammatory reactions with the reduction of synthesis of anti-inflammatory cytokines and phagocytosis depression predisposes to infection, multiorgan dysfunction and negative outcome [10].

The search for reliable predictors of postoperative complications and mortality remains a crucial task of scientific research. Traditionally used methods, including body temperature measurement, white blood cell count and estimation of CRP level, do not allow one to predict the development of infectious complications in cardiac surgery patients due to the insufficient sensitivity and specificity of these parameters, which are influenced by a considerable number of different factors. In our previous studies we identified an opportunity to use PCT as a predictor of infectious complications after open heart procedures [11]. This marker serves as an indicator of systemic inflammation with bacterial etiology, i.e. the substrate on which background infectious complications after CPB operations develop. It was found that from the 1st postoperative day, a statistically significant increase of PCT level was observed in the group of patients who developed infectious complications in the early postoperative period. An optimal prognostic level of PCT in plasma was determined as 3 ng/ml, of which the sensitivity and specificity were 71% and 72%, respectively [11]. The results obtained in the present study are consistent with earlier conclusions: there is a tendency to a higher PCT level on the 1st postoperative day in the group of patients who afterwards developed infectious complications compared to the group with an uncomplicated postoperative period. On the 2nd postoperative day these differences became statistically significant. Presepsin levels, APACHE II and SOFA scores were characterized by statistical significance already on the 1st postoperative day, which was maintained afterwards. Results of ROC analysis revealed that among studied parameters maximum prognostic value was shown by the APACHE II score on the 1st day after the operation.

An important point of application of biomarkers is their use for risk stratification of negative outcome of a disease and particularly for prognosis of the course of the postoperative period. In a previous study it was demonstrated in a group of 60 adult patients that normal PCT levels on the 1st postoperative day correlated with positive outcome, while a considerable increase of PCT level (> 10 ng/ml) was associated with mortality of 29% [11]. In this study we also observed statistically significant differences in PCT levels, APACHE II and SOFA scores between the groups, with positive and lethal outcomes already on the 1st postoperative day (on the 3rd day in the case of PSP levels). The highest prognostic value was shown by PCT levels and APACHE II scores.

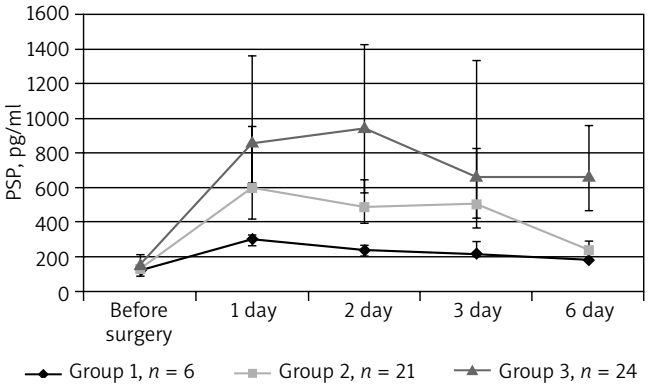

Fig. 1. Types of presepsin levels' dynamics in the perioperative period, pg/ml (median and interquartile range)

Tab. VII. Frequency of infectious complications and mortality depending on the type of presepsin dynamics

Group	Infectious complications	Mortality
Group 1, *n* = 6	0	0
Group 2, *n* = 21	4 (19%)	3 (14.3%)
Group 3, *n* = 24	14 (58.3%)*	4 (16.7%)**

*p_{2-3} = 0.017, **p_{2-3} = 0.85

One component of anesthesia in patients included in this study was isoflurane. This drug as well as some other modern volatile anesthetics (e.g. sevoflurane) has immunomodulatory effects, in part by attenuating (NF)-κB signal transduction, which leads to downregulation of proinflammatory cytokine synthesis [12]. This fact should be considered when interpreting the levels of inflammatory mediators in the perioperative period; this issue needs further study.

Of great interest is the fact that PSP levels were high in patients with acute heart failure and acute coronary syndrom with no signs of infection [13]. It may serve as a basis for further investigation of PSP potential as a cardiac marker.

Conclusions

The use of modern biomarkers alongside integral severity-of-disease scales allows identification of patients with an increased risk of infectious complications and negative outcomes. In our study the most optimal way to predict the risk of infectious complications and mortality in patients after open-heart procedures was the APACHE II scoring on the 1st postoperative day. Presepsin in combination with other biomarkers represents a perspective object of scientific research aimed at specification of sepsis pathogenesis and identification of factors influencing phagocytosis in different diseases. It is also a promising tool in the search for and assessment of the effectiveness of different sepsis treatment methods, including extracorporeal ones.

Disclosure

Authors report no conflict of interest.

References

1. Warren O, Smith A, Alexiou C, Rogers P, Jawad N, Vincent C, Darzi A, Athanasiou T. The inflammatory response to cardiopulmonary bypass: part 1 – mechanisms of pathogenesis. J Cardiothorac Vasc Anesth 2009; 23: 223-231.
2. Rossi M, Sganga G, Mazzone M, Valenza V, Guarneri S, Portale G, Carbone L, Gatta L, Pioli C, Sanguinetti M, Montalto M, Glieca F, Fadda G, Schiavello R, Silveri NG. Cardiopulmonary bypass in man: role of the intestine in a self-limiting inflammatory response with demonstrable bacterial translocation. Ann Thorac Surg 2004; 77: 612-618.
3. Wan S, LeClerc J, Vincent J. Inflammatory response to cardiopulmonary bypass: mechanisms involved and possible therapeutic strategies. Chest 1997; 112: 676-692.
4. Kumar A, Roberts D, Wood K, Light B, Parrillo J, Sharma S, Suppes R, Feinstein D, Zanotti S, Taiberg L, Gurka D, Kumar A, Cheang M. Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. Crit Care Med 2006; 34: 1589-1596.
5. Yaegashi Y, Shirakawa K, Sato N, Suzuki Y, Kojika M, Imai S, Takahashi G, Miyata M, Furusako S, Endo S. Evaluation of a newly identified soluble CD14 subtype as a marker for sepsis. J Infect Chemother 2005; 11: 234-238.
6. Naitoh K, Shirakawa K, Hirose J, Nakamura M, Takeuchi T, Hosaka Y, Furusako S. The new sepsis marker, sCD14-ST (PRESEPSIN), induction mechanism in the rabbit sepsis models. SEPSIS 2010; p. 19.
7. Spanuth E, Ebelt H, Ivandic B, Werdan K. Diagnostic and prognostic value of soluble CD14 subtype (sCD14-ST) in emergency patients with early sepsis using the new assay PATHFAST Presepsin. 21st International Congress of Clinical Chemistry and Laboratory Medicine, IFCC-WorldLab – EuroMedLab, Berlin, 15-19 May 2011: P. 0333
8. Endo S, Suzuki Y, Takahashi G, Shozushima T, Ishikura H, Murai A, Nishida T, Irie Y, Miura M, Iguchi H, Fukui Y, Tanaka K, Nojima T, Okamura Y. Usefulness of presepsin in the diagnosis of sepsis in a multicenter prospective study. J Infect Chemother 2012; 18: 891-897.
9. Shozushima T, Takahashi G, Matsumoto N, Kojika M, Okamura Y, Endo S. Usefulness of presepsin (sCD14-ST) measurements as a marker for the diagnosis and severity of sepsis that satisfied diagnostic criteria of systemic inflammatory response syndrome. J Infect Chemother 2011; 17: 764-769.
10. de Jong PR, Schadenberg AW, van den Broek T, Beekman JM, van Wijk F, Coffer PJ, Prakken BJ, Jansen NJ. STAT3 regulates monocyte TNF-alpha production in systemic inflammation caused by cardiac surgery with cardiopulmonary bypass. PLoS One 2012; 7: e35070.
11. Beloborodova N, Popov D. Diagnostic Value of Some Markers of Infection in the Early Postoperative Period in Cardiac Surgery Patients. Anesthesiology and Intensive Care 2005; 3: 45-49.
12. Wang H, Wang L, Li NL, Li JT, Yu F, Zhao YL, Wang L, Yi J, Wang L, Bian JF, Chen JH, Yuan SF, Wang T, Lv YG, Liu NN, Zhu XS, Ling R, Yun J. Subanesthetic isoflurane reduces zymosan-induced inflammation in murine Kupffer cells by inhibiting ROS-activated p38 MAPK/NF-κB signaling. Oxid Med Cell Longev 2014; 2014: 851692.
13. Spanuth E, Thomae R, Giannitsis E. Presepsin (sCD14-ST) in Acute Coronary Syndromes and Heart Failure. Clinical Chemistry (Supplement) 2014; 60: B-343.