Procalcitonin kinetics – prognostic and diagnostic significance in septic patients

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Abstract

Introduction: Severe sepsis and septic shock are advanced clinical conditions representing the patient's response to infection and having a variable but high mortality rate. Early evaluation of sepsis stage and choice of adequate treatment are key factors for survival. Some study results suggest the necessity of daily procalcitonin (PCT) monitoring because of its prognostic and discriminative value.

Material and methods: An observational and prospective study was conducted to evaluate the prognostic and discriminative value of PCT kinetics in comparison to PCT absolute value measurements. In a group of 50 intensive care unit patients with diagnosis of severe sepsis or septic shock, serum PCT measurements were performed on admission, and on the 2nd, 3rd and 5th day of therapy. The level of PCT was determined with a commercially available test according to the manufacturer's protocol.

Results: The kinetics of PCT assessed by ΔPCT was statistically significant in the survivors vs. the non-survivors subgroup ($\Delta PCT_{3/1}$, $p = 0.022$; $\Delta PCT_{5/1}$, $p = 0.021$). ΔPCT has no statistical significance in the severe sepsis and septic shock subgroups for all analyzed days. Only the 5th day PCT level was significantly higher in the non-survivors vs. survivors group ($p = 0.008$). The 1st day PCT level in the severe sepsis vs. septic shock group has a discriminative impact ($p = 0.009$).

Conclusions: According to the results, single serum PCT measurement, regardless of absolute value, has a discriminative impact but no prognostic significance, during the first 2 days of therapy. The PCT kinetics is of prognostic value from the 3rd day and is of earlier prognostic significance in comparison to changes in the patient's clinical condition evaluated by SOFA score kinetics.

Key words: severe sepsis, septic shock, biomarker variation.

Introduction

Procalcitonin (PCT) is a prohormone of calcitonin consisting of 114 to 116 amino acids. The physiological PCT serum level is below 0.5 ng/ml, but the rise to a value higher than 2 ng/ml is indicative of sepsis [1]. The PCT induction period at 4 to 12 h is longer than for cytokines, but it is shorter than for C-reactive protein (CRP) [2]. The half-life of PCT is about 22 to 35 h [3], and in blood samples PCT is a relatively stable protein.

Procalcitonin originates from the calcitonin-I (CALC-I) gene on chromosome 11 [4]. A microbial infection induces a ubiquitous increase in

CALC-I gene expression and a significant release of PCT from various tissues and cell types [5]. Tissues with high levels of PCT-I and PCT-II mRNA expression are potential sources of serum PCT in septic conditions [6, 7]. Whang *et al.* considered that PCT is a secondary mediator, intensifying rather than initiating the septic response [8]. Hoffmann *et al.* stated that PCT is a modulator of the inflammatory cascade [9]. Furthermore, the extent of PCT release is thought to be closely dependent on the extent of host response to microbial challenge [10].

Sepsis is not a single disease, but rather a highly heterogeneous syndrome that is the net result of host and pathogen interactions [11]. Severe sepsis/septic shock remains a leading cause of death in the intensive care unit (ICU), with mortality rates varying from 25% to 80% [12].

The purpose of our study was to assess the predictive and discriminative value of PCT kinetics in comparison to the PCT level in ICU patients with severe sepsis or septic shock during the first 5 days of therapy.

Material and methods

Definition of sepsis, severe sepsis and septic shock

According to the Surviving Sepsis Campaign (SSC) International Guidelines, sepsis is defined as the presence of infection (suspected or documented) in association with systemic manifestation of infection. Severe sepsis is defined as sepsis associated with tissue hypoperfusion or sepsis-induced organ dysfunction (any of the following should result from the infection). Sepsis-induced hypoperfusion is defined as infection-induced hypotension, elevated lactate (> 1 mmol/l), or oliguria. Sepsis-induced hypotension is defined as systolic blood pressure (SBP) < 90 mm Hg or mean arterial pressure (MAP) < 70 mm Hg or SBP decrease > 40 mm Hg or less than two standard deviation below normal for age in the absence of other causes of hypotension. Septic shock is defined as sepsis-induced hypotension persisting despite adequate fluid resuscitation [13].

Patients

The observational and prospective study was conducted in the Department of Anesthesiology and Intensive Therapy of Wroclaw Medical University, Poland. The research was approved by the Medical Ethics Committee of Wroclaw Medical University and was performed in accordance with Helsinki Declaration of 1975, as revised in 1983. Informed consent was obtained from the patients or their legal representatives.

Fifty critically ill patients were consecutively enrolled in the study starting from admission when they met SSC criteria for severe sepsis or septic shock. On admission to the ICU, patients exhibited different phases of severe sepsis or septic shock. The former antibiotic treatment (ineffective or delayed) and/or the type of experienced surgery influenced the admission PCT concentrations. Patients were divided into the following subgroups: survivors (52%) and non-survivors (48%); severe sepsis (38%) and septic shock (62%). For all patients the following data were reported: age, gender, source of infection, type of causative microorganisms, the Acute Physiology and Chronic Health Evaluation (APACHE) II score [14] on admission, and the Sequential Organ Failure Assessment (SOFA) score [15] and PCT level on admission and on the 2nd, 3rd and 5th day of therapy (Table I). The treatment of all patients with severe sepsis or septic shock was performed according to established standards, including antimicrobial treatment, fluid resuscitation, vasopressor therapy and mechanical ventilation.

Blood samples were taken in relation to the time of admission to the ICU rather than the onset of sepsis, and were collected on admission (1st day), and on the 2nd, 3rd and 5th day. The obtained serum was aliquoted and stored at –80°C until further analysis. The PCT level measurements were executed with a commercially available test (LUMItest PCT, BRAHMS Diagnostica GMBH, Germany), according to the manufacturer's instructions. The detection limit of the test was 0.08 ng/ml.

Statistical analysis

All statistical analyses were performed with StatSoft. Inc. (2010) Statistica (data analysis software system), version 9.1. www.statsoft.com. The normality of the distribution was estimated by the Kolmogorov-Smirnov test. The data were analyzed with a nonparametric test (Mann-Whitney *U*-test) to compare the two groups. APACHE II and SOFA score values are presented as the mean ± SD. *P*-value ≤ 0.05 was considered statistically significant.

Results

All patients enrolled in the study were classified according to the International Sepsis Definitions Conference guidelines [16]. The patients' status was assessed by APACHE II and SOFA scores. The APACHE II score on the 1st day in survivors and non-survivors was 18.3 and 27.0, respectively, and in the severe sepsis and septic shock subgroups it was 19.5 and 24.3, respectively. In the non-survivors and septic shock subgroups the most common source of infection was the lung (n = 10 and n = 13, respectively) and abdomen (n = 10 and n = 12, respectively). The mortality rate in the studied critically ill patient group was 48%.

Table I. Demographic and clinical characteristics of the critically ill patients in severe sepsis vs. septic shock and survivors vs. non-survivors subgroups

Parameter	Severe sepsis (*n* = 19)	Septic shock (*n* = 31)	Survivors (*n* = 26)	Non-survivors (*n* = 24)
Age [years][a]	47.8 (18–80)	60.7 (21–91)	51 (18–88)	60.6 (19–91)
Sex (female/male)[b]	9/10	14/17	14/12	9/15
APACHE II 1st day[a]	19.5 (8–35)	24.3 (13–44)	18.3 (8–32)	27 (11–44)
SOFA 1st day[a]	6.3 (0–16)	10.4 (5–18)	6.6 (0–14)	11.2 (4–18)
SOFA 5th day[a]	5.6 (0–12)	9.6 (2–20)	4.2 (0–14)	11.5 (3–19)
WBC 1st day[a] [×10³/mm³]	10.4 (0–24.2)	16.3 (0.04–74)	15.1 (2.9–74)	13.2 (0–37.2)
WBC 5th day[a] [×10³/mm³]	6.9 (0.1–12.2)	13.1 (0.1–51.6)	9.7 (2.7–32.9)	12.9 (0.1–51.6)
CRP 1st day[a] [mg/l]	259.4 (49.3–737)	290.1 (3.5–603.7)	295.5 (49.3–737)	258.3 (3.5–515.1)
CRP 5th day[a] [mg/l]	142.2 (19.2–347.9)	116.5 (15.7–452)	71.5 (15.7–287.2)	175.2 (24.2–452)
Source of infection[b]:				
Respiratory	8	13	11	10
Abdominal	6	12	8	10
Other	5	6	7	4
Pathogens[b]:				
Gram-positive	1	7	3	5
Gram-negative	3	7	5	5
Fungi	0	1	0	1
Mixed	4	6	4	6
Unknown	11	10	14	7

Presented data are expressed as mean values with ranges ([a]) or actual number of patients ([b]). APACHE II – Acute Physiology and Chronic Health Evaluation II, SOFA – Sequential Organ Failure Assessment, WBC – white blood cell count, CRP – C-reactive protein.

Kinetics of serum procalcitonin in patient subgroups

Procalcitonin kinetics was expressed as delta PCT (ΔPCT) and calculated as the difference between PCT level on admission day (1st) and the consecutive days (2nd, 3rd, 5th) in relation to the 1st day value (chain index). The kinetics of PCT level for survivors vs. non-survivors subgroups was presented in Table II and for severe sepsis vs. septic shock subgroup in Table III. The PCT level on the 5th day was significantly higher in the non-survivors than survivors (p = 0.008). In survivors vs. non-survivors subgroups the differences between PCT levels on the 3rd and 1st day ($\Delta PCT_{3/1}$), and the differences between PCT levels on the 5th and 1st day (ΔPCT5/1) were statistically significant (p = 0.022 and p = 0.021, respectively) (Table II). In severe sepsis vs. septic shock subgroups the PCT level was statistically significant on the 1st (p = 0.009) and 3rd day (p = 0.047), but there was no statistically significant difference in ΔPCT for all analyzed days (Table III).

Sequential Organ Failure Assessment score changes in patient subgroups

The SOFA score value was significantly different in survivors vs. non-survivors subgroups for all analyzed days, and in contrast to the absolute value, only $\Delta SOFA_{5/1}$ was significantly different in this subgroup (Table IV).

In severe sepsis vs. septic shock subgroups the SOFA score value was statistically significant in the course of the study, except for the 5th day, and there were no statistically significant differences in ΔSOFA in the study (Table V).

Procalcitonin and receiver operating curve analysis in patient subgroups

In the receiver operating curve (ROC) analysis of the survival on the day of admission the cut-off value for PCT was 16.26 µg/l and area under the curve (AUC) = 0.567, the sensitivity was 0.46, and the specificity was 0.27. On the 2nd day of therapy the cut-off value was 16.65 µg/l and AUC = 0.567, the sensitiv-

Table II. Comparison of significance of changes in the PCT absolute value and its kinetics (ΔPCT) in survivors and non-survivors subgroups during the first 5 days following ICU admission

PCT [µg/l]	Survivors (n = 26)	Non-survivors (n = 24)	P-value*	ΔPCT	Survivors (n = 26)	Non-survivors (n = 24)	P-value*
$PCT_{1st\ day}$	7.38 (0.92–18.5)	11.1 (1.03–29.5)	0.42	$\Delta PCT_{2/1}$	0.353 (–0.30–0.54)	0.198 (–0.36–0.47)	0.35
$PCT_{2nd\ day}$	5.84 (0.51–16.6)	7.13 (0.63–26.3)	0.42	$\Delta PCT_{3/1}$	0.752 (0.40–0.90)	0.292 (0.03–0.72)	0.022
$PCT_{3rd\ day}$	1.03 (0.33–4.25)	10.1 (0.75–21.0)	0.08	$\Delta PCT_{5/1}$	0.890 (0.74–0.98)	0.752 (–0.66–0.94)	0.021
$PCT_{5th\ day}$	1.01 (0.17–3.25)	3.91 (1.28–20.7)	0.008				

*Data are presented as median values and interquartile range (IQR) (25^{th} to 75^{th} percentiles). PCT kinetics is expressed as delta PCT (ΔPCT) concentrations. ΔPCT was calculated as the difference between concentrations on admission day (1^{st}) and the consecutive days (2^{nd}, 3^{rd} and 5^{th}) in relation to the 1^{st} day value. PCT – procalcitonin; *p-value for difference between survivors and non-survivors.*

Table III. Comparison of significance of changes in the PCT absolute value and PCT kinetics (ΔPCT) in severe sepsis and septic shock subgroups during the first 5 days following ICU admission

PCT [µg/l]	Severe sepsis (n = 19)	Septic shock (n = 31)	P-value*	ΔPCT	Severe sepsis (n = 19)	Septic shock (n = 31)	P-value*
$PCT_{1st\ day}$	2.69 (0.34–9.71)	16.3 (1.55–31.9)	0.009	$\Delta PCT_{2/1}$	0.33 (–1.53–0.59)	0.278 (–0.18–0.52)	0.63
$PCT_{2nd\ day}$	2.04 (0.57–14.9)	9.05 (0.67–28.1)	0.12	$\Delta PCT_{3/1}$	0.793 (–0.65–0.94)	0.355 (0.18–0.79)	0.84
$PCT_{3rd\ day}$	0.56 (0.23–4.06)	5.12 (0.92–19.9)	0.047	$\Delta PCT_{5/1}$	0.877 (0.14–1.00)	0.88 (0.03–0.95)	0.35
$PCT_{5th\ day}$	1.01 (0.26–7.22)	1.73 (0.95–8.74)	0.41				

*Data are presented as median values and interquartile range (IQR) (25^{th} to 75^{th} percentiles). PCT kinetics is expressed as delta PCT (ΔPCT) concentrations. ΔPCT was calculated as the difference between concentrations on admission day (1^{st}) and the consecutive days (2^{nd}, 3^{rd} and 5^{th}) in relation to the 1^{st} day value. PCT – procalcitonin; *p-value for difference between severe sepsis and septic shock.*

Table IV. Comparison of significance of changes in SOFA score absolute value and its kinetics (ΔSOFA) in survivors vs. non-survivors subgroups during the first 5 days following ICU admission

SOFA	*P*-value*	ΔSOFA	*P*-value*
$SOFA_{1st\ day}$	0.00016	$\Delta SOFA_{2/1}$	0.56
$SOFA_{2nd\ day}$	0.00013	$\Delta SOFA_{3/1}$	0.57
$SOFA_{3rd\ day}$	0.0023	$\Delta SOFA_{5/1}$	0.05
$SOFA_{5th\ day}$	0.00089		

*SOFA kinetics is expressed as delta SOFA (ΔSOFA). ΔSOFA was calculated as the difference between value on admission day (1st) and the consecutive days (2nd, 3rd and 5th) in relation to the 1st day value. SOFA – Sequential Organ Failure Assessment; *p-value for difference between survivors and non-survivors.*

Table V. Comparison of significance of changes in SOFA score absolute value and its kinetics (ΔSOFA) in severe sepsis vs. septic shock subgroups during the first 5 days following ICU admission

SOFA	*P*-value*	ΔSOFA	*P*-value*
$SOFA_{1st\ day}$	0.0026	$\Delta SOFA_{2/1}$	0.89
$SOFA_{2nd\ day}$	0.0074	$\Delta SOFA_{3/1}$	0.44
$SOFA_{3rd\ day}$	0.032	$\Delta SOFA_{5/1}$	0.32
$SOFA_{5th\ day}$	0.13		

*SOFA kinetics is expressed as delta SOFA (ΔSOFA). ΔSOFA was calculated as the difference between value on admission day (1st) and the consecutive days (2nd, 3rd and 5th) in relation to the 1st day value. SOFA – Sequential Organ Failure Assessment; *p-value for difference between severe sepsis and septic shock.*

ity was 0.42, and the specificity was 0.23. On the 3rd day of therapy the cut-off value was 5.99 µg/l and AUC = 0.649, the sensitivity was 0.59, and the specificity was 0.24. On the 5th day of therapy the cut-off value was 0.32 µg/l and AUC = 0.737, the sensitivity was 1.0, and the specificity was 0.567 (Figure 1 A).

In the ROC curve analysis of the septic shock diagnosis on the day of admission, the cut-off value for PCT was 8.01 µg/l and AUC = 0.72, the sensitivity was 0.70, and the specificity was 0.26. On the 2nd day of therapy the cut-off value was 5.55 µg/l and AUC = 0.634, the sensitivity was 0.67, and the specificity was 0.37. On the 3rd day of therapy the cut-off value was 0.6 µg/l and AUC = 0.68, the sensitivity was 0.83, and the specificity was 0.47. On the 5th day of therapy the cut-off value was 1.13 µg/l and AUC = 0.582, the sensitivity was 0.75, and the specificity was 0.46 (Figure 1 B).

White blood cell and C-reactive protein in patient subgroups

There was no statistically significant difference in the WBC level between the subgroups (Table VI

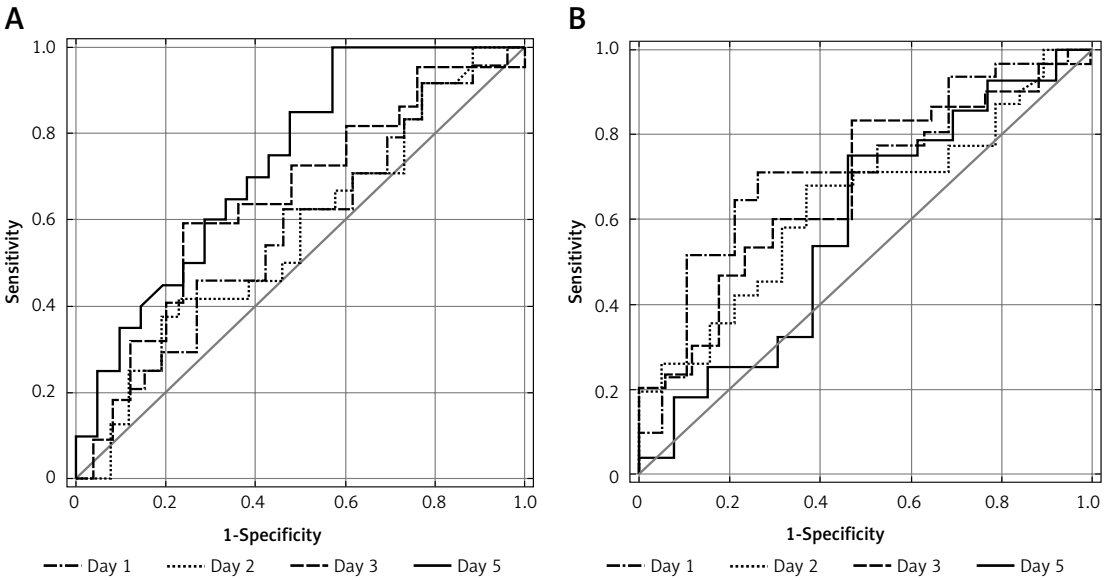

Figure 1. ROC curve of PCT analysis for survival (**A**) on all analyzed days: 1st day (blue line) with the cut-off value of 16.26 µg/l (AUC = 0.567, sensitivity 0.46, and specificity 0.27); 2nd day (red line) with the cut-off value of 16.65 µg/l (AUC = 0.567, sensitivity 0.42, and specificity 0.23); 3rd day (green line) with the cut-off value of 5.99 µg/l (AUC = 0.649, sensitivity 0.59, and specificity 0.24); 5th day (pink line) with the cut-off value of 0.32 µg/l (AUC = 0.737, sensitivity 1.0, and specificity 0.567). ROC curve of PCT analysis for septic shock diagnosis (**B**) on all analyzed days: 1st day (blue line) with the cut-off value of 8.01 µg/l (AUC = 0.72, sensitivity 0.70, and specificity 0.26); 2nd day (red line) with the cut-off value of 5.55 µg/l (AUC = 0.634, sensitivity 0.67, and specificity 0.37); 3rd day (green line) with the cut-off value of 0.6 µg/l (AUC = 0.68, sensitivity 0.83, and specificity 0.47); 5th day (pink line) with the cut-off value of 1.13 µg/l (AUC = 0.582, sensitivity 0.75, and specificity 0.46)

ROC – receiver operating curve, AUC – area under curve, PCT – procalcitonin.

and VII) and the differences in the C-reactive protein (CRP) value were not statistically significant in the course of the study, except for the 5th day in the survivors vs. non-survivors subgroup (Table VII).

There was a strong correlation between PCT and WBC on all analyzed days in the survivors subgroup: $r_{1st\ day} = 0.93$, $p = 0.00002$; $r_{2nd\ day} = 0.91$, $p = 0.0001$; $r_{3rd\ day} = 0.92$, $p = 0.00004$; $r_{5th\ day} = 0.91$, $p = 0.0001$.

In the septic shock subgroup there was a strong correlation between PCT and WBC on all analyzed days except for the 5th day ($r_{1st\ day} = 0.79$, $p = 0.0001$; $r_{2nd\ day} = 0.64$, $p = 0.003$; $r_{3rd\ day} = 0.55$, $p = 0.02$) and a correlation between PCT and CRP on admission day ($r_{1st\ day} = 0.53$, $p = 0.021$).

Discussion

Procalcitonin is elevated in patients with severe infections complicated by severe sepsis or septic shock [10]. Monitoring of the PCT concentration is used as an indicator of effectiveness of applied therapy in everyday clinical use. It has been confirmed that the implementation of a PCT-guided algorithm to discontinue antibiotic treatment was associated with a reduced duration of antibiotic therapy in septic ICU patients without negative effects on the final clinical outcome [17]. The usefulness of PCT assessment in sepsis confirmation is well established, but for prediction of survival in septic patients it is still being extensively studied, with conflicting results [18–20]. In the opinion of some authors the admission PCT level in patients with septic shock is a better prognostic biomarker than CRP, but PCT sensitivity is too low to establish an admission cut-off value for distinguishing survivors from non-survivors [21, 22]. According to Herrmann *et al.*, during the first 5 days of therapy single PCT measurements do not differentiate survivors from non-survivors and significant differences in PCT levels are observed in the second week of the severe sepsis/septic shock course [23]. In our results in the ROC curve analysis for survival the 5th day of therapy PCT cut-off value represented the best prognostic properties and in the ROC curve analysis for the septic shock diagnosis the 1st day of therapy PCT cut-off value had the best diagnostic properties.

Currently the discriminative and prognostic significance of PCT level kinetics has started to be an object of clinical research. Karlsson *et al.* reported that PCT concentrations did not differ between survivors and non-survivors at day 0 and 72 h [24]. In the study by Charles *et al.* neither 1st nor 2nd day PCT level was associated with death in the study population. In Charles' and Sakran's results, like in ours, there was a trend toward higher PCT values in the non-survivors group [25, 26]. In contrast to absolute values, the PCT kinetics ($\Delta PCT_{3/1}$, $\Delta PCT_{5/1}$)

Table VI. Evaluation of WBC and CRP levels in severe sepsis vs. septic shock subgroups during the first 5 days following ICU admission

WBC [×10³/mm³]	Severe sepsis (*n* = 19)	Septic shock (*n* = 31)	*P*-value *	CRP [mg/l]	Severe sepsis (*n* = 19)	Septic shock (*n* = 31)	*P*-value *
$WBC_{1st\ day}$	10.0 (0.0–24.2)	14.7 (0.04–74.0)	0.21	$CRP_{1st\ day}$	190.5 (49.3–737.0)	302.1 (3.50–603.7)	0.63
$WBC_{2nd\ day}$	9.3 (0.10–17.4)	14.8 (0.10–48.9)	0.06	$CRP_{2nd\ day}$	221.5 (41.7–473.0)	243.0 (12.6–451.2)	0.56
$WBC_{3rd\ day}$	6.9 (0.0–16.6)	11.1 (0.10–40.7)	0.07	$CRP_{3rd\ day}$	98.7 (28.2–589.5)	118.4 (9.80–420.0)	0.89
$WBC_{5th\ day}$	7.3 (0.10–12.2)	9.2 (0.10–51.6)	0.15	$CRP_{5th\ day}$	85.6 (19.2–347.9)	72.8 (15.7–462.0)	0.60

*Data are presented as median values and interquartile range (IQR) (25th to 75th percentiles). WBC – white blood cell count, CRP – C-reactive protein, *p-value for difference between severe sepsis and septic shock.*

Table VII. Evaluation of WBC and CRP in survivors and non-survivors subgroups during the first 5 days following ICU admission

WBC [×10³/mm³]	Survivors (*n* = 26)	Non-survivors (*n* = 24)	*P*-value *	CRP [mg/l]	Survivors (*n* = 26)	Non-survivors (*n* = 24)	*P*-value *
$WBC_{1st\ day}$	10.7 (2.9–74.0)	13.5 (0.0–37.2)	0.68	$CRP_{1st\ day}$	242.2 (49.3–737.0)	290.9 (3.5–515.1)	0.55
$WBC_{2nd\ day}$	11.4 (2.8–48.9)	14.1 (0.10–34.7)	0.91	$CRP_{2nd\ day}$	249.9 (41.7–473.0)	233.3 (12.6–451.2)	0.76
$WBC_{3rd\ day}$	9.15 (2.3–40.7)	10.9 (0.0–36.5)	0.80	$CRP_{3rd\ day}$	88.6 (28.2–589.5)	170.4 (9.8–454.1)	0.29
$WBC_{5th\ day}$	8.45 (2.7–32.9)	8.30 (0.10–51.6)	0.40	$CRP_{5th\ day}$	46.6 (15.7–287.2)	126.9 (24.2–462.0)	0.01

*Data are presented as median values and interquartile range (IQR) (25th to 75th percentiles). WBC – white blood cell count, CRP – C-reactive protein, *p-value for difference between survivors and non-survivors.*

was significantly different for the 3rd and 5th day of therapy in the survivors vs. non-survivors subgroup. Weak or no decline of PCT level noted on the 3rd and 5th day compared to admission was associated with unfavorable outcome, similarly to the results of Guan *et al.* [27] and Georgopoulou *et al.* [28]. In Karlsson's study the effect on hospital survival was connected with a decrease in PCT concentrations of greater than 50% between the 1st and 3rd study day [24]. ΔPCT 2nd day – 3rd day was an independent predictor of death in Charles' study group [25]. In Seligman's study the decrease of PCT on the 5th day vs. 1st day predicts favorable outcome [29]. In contrast to our results Bousseкey *et al.* stated that PCT decline during the first 2 days of ICU stay was a good indicator of outcome, and PCT increase was an independent risk factor of mortality, with an odds ratio greater than 4 [30]. The PCT level, which was significant only on the 5th day for survivors vs. non-survivors subgroups, did not reflect statistical significance in SOFA score results observed on all analyzed days. These findings are similar to those of de Oliveira *et al.* [31], where not the PCT level but the SOFA score value was highly associated with mortality in ICU patients with severe sepsis and septic shock. In our study in severe sepsis and septic shock subgroups the values of PCT and SOFA score were significantly different on the 1st day of therapy, similarly to Lavrentieva's study [32]. According to our results in this subgroup the absolute SOFA score value was a better differentiating factor than absolute values of PCT. Kinetics of both elements did not reach statistical significance on any of the study days.

In conclusion, according to our results the PCT absolute values obtained on the 1st day of therapy significantly differ between severe sepsis and septic shock. Single PCT level measurements during the first 2 days of therapy have no prognostic impact, and the 5th day of PCT cut-off value represents the best prognostic properties. The PCT kinetics reflecting its level time course is of prognostic value from the 3rd day of therapy. The significant PCT level decrease reflecting therapy effectiveness might result in a good outcome. The kinetics of PCT achieves prognostic significance earlier than the changes of the patient's clinical condition reflected by kinetics of SOFA score. These results indicate that PCT measurement is needed on an everyday basis because it provides a wide range of patient's evaluation. According to our results the WBC and CRP measurements, though used for everyday septic patient's assessment, have no diagnostic, prognostic or discriminative value. These elements should be taken into consideration in terms of individualization of septic patients' clinical status monitoring and treatment. The question why there is a strong correlation between PCT and WBC in patient groups with an extremely different septic response (survivors and septic shock subgroups) is open to further study.

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Conflicts of interest

The authors report no conflicts of interest.

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