



Original Contribution

**WHICH CLINICAL PARAMETERS HAVE IMPACT ON OUTCOME IN
THE EARLY PHASE OF COMPLICATED INTRA-ABDOMINAL
INFECTION? – A PROSPECTIVE STUDY**

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ABSTRACT

Purpose: There is still no comprehensive analysis with Bulgarian patients investigating the association between perioperative clinical parameters and final outcome in the early phase of complicated intra-abdominal infection.

Methods: This single-center prospective study was conducted in the Clinic of Surgical Diseases at the University Hospital Stara-Zagora for the period November 2018 - August 2021. Before surgery and on the 3rd postoperative day (POD) we measured axillary temperature (t), systolic blood pressure (SBP), mean arterial pressure (MAP), respiratory rate (RR), heart rate (HR), mental status and systemic inflammatory response syndrome (SIRS) in 62 patients with complicated intra-abdominal infections (cIAIs).

Results: Of the 62 patients, nine died (14.5%). Preoperatively, only MAP successfully discriminated survivors from non-survivors ($p = 0.027$), which was confirmed by the ROC Curve analysis (AUROC = 0.731). Postoperatively, almost all of the clinical parameters except axillary temperature (AUROC = 0.573) showed prognostic ability – SBP (AUROC = 0.779) and MAP (AUROC = 0.864) for prediction of favorable outcome, HR (AUROC = 0.916) and RR (AUROC = 0.935) for prediction of lethal outcome.

Conclusion: All investigated clinical parameters, except for axillary temperature, demonstrated the ability to predict the final outcome on the 3rd POD in patients with cIAIs.

Key words: clinical parameters, SIRS, intra-abdominal infections, cIAIs, outcome, prognosis

INTRODUCTION

Complicated intra-abdominal infections (cIAIs) represent one of the most common causes for emergency operative intervention in abdominal surgery. They are associated with high mortality rates, in some cases exceeding 30% [1]. The cIAIs often lead to sepsis, which can evolve into septic shock with subsequent multiple organ failure and death.

They affect large and heterogeneous groups of patients, which makes it difficult to create a common treatment algorithm and emphasizes the need for an individual approach for each

patient. Early prognostic assessment of cIAIs is crucial in determining the final outcome [2]. The use of effective routine and easily accessible clinical parameters in the early phase of the disease could provide a very rapid clinical assessment and predict the disease severity. In addition to diagnostic value, each of them also has prognostic capabilities, as the combination of 2 or more indicators usually enhances their ability to predict the risk of intensive care, perioperative complications and death. For this reason, they are used both as single prognostic factors and as part of a number of scoring systems.

To date, their prognostic ability has not been thoroughly investigated in Bulgarian patients with cIAIs, therefore, the aim of this study was to perform a comprehensive analysis regarding the association between perioperative clinical

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parameters and final outcome in the early phase of the disease.

MATERIAL AND METHODS

We performed a single-center prospective study in the Clinic of Surgical Diseases at the University Hospital "Prof. Dr. Stoyan Kirkovich" Stara Zagora. For the period from November 2018 to August 2021, 62 patients with complicated intra-abdominal infections were operated on. Fifty-eight of them were hospitalized from the Emergency Department, 2 from the Clinic of Pulmonology, 1 from the Clinic of Endocrinology, and 1 from the Clinic of General and Operative Surgery.

The preoperative diagnosis was determined stepwise by clinical evaluation, imaging methods, and laboratory tests, and the final diagnosis was made based on the intraoperative finding.

In all patients preoperatively and on the 3rd postoperative day (POD), we analyzed the following clinical parameters: axillary temperature, systolic arterial pressure, mean arterial pressure, respiratory rate, heart rate, mental status and systemic inflammatory response syndrome (SIRS). SIRS includes four criteria – a heart rate >90/min, a tachypnea >20/min, a temperature <36°C or >38°C, and leukocytes count <4000/mm³ or >12,000/mm³.

Positive SIRS is defined as ≥ 2 out of four signs [3].

Clinical parameters were reported in 62 patients, and on the 3rd POD in 60, as 2 patients died before the secondary evaluation.

Sensitivity and specificity analysis and area under receiver operating characteristics (AUROC) for outcome prediction were evaluated for each parameter. Continuous variables were expressed as mean (SD) or median (IQR) and categorical variables were expressed as frequency (%). Comparisons were made by Mann–Whitney U-test or Student's t-test for continuous variables and by Chi-square test or Fisher exact test for categorical variables. For statistical analysis, we used statistical software SPSS version 19 for Windows (IBM, Chicago, Illinois, USA), and p-values < 0.05 were considered statistically significant.

RESULTS

Basic characteristics

The observed in-hospital mortality was 14.5%. Non-survivors were significantly older than survivors - 79 (61-86) years vs. 65 (47.5-75) years, $p = 0.032$. A diffuse peritonitis was found as unfavorable prognostic factor ($p = 0.024$). No significant differences were established according to gender ($p = 1.000$), comorbidity ($p = 0.423$) and type of exudate ($p = 0.59$) (Table 1).

Table 1. Basic characteristics

Variable	Total population	Survivors(n=53)	Non-Survivors(n=9)	p value
Sex,n(%) <i>male/female</i>	35(56.5)/27(43.5)	30(85.7)/23(85.2)	5(14.3)/4(14.8)	1.000
Age, years (IQR)	65 (49.5-76.25)	65 (47.5-75)	79 (61-86)	0.032
Spread, n(%) <i>Local Peritonitis</i> <i>Diffuse Peritonitis</i>	37 (59.7) 25 (40.3)	35 (66) 18 (34)	2 (22.2) 7 (77.8)	0.024
Exudate, n(%) <i>Clear</i> <i>Purulent</i> <i>Feculent</i>	8 (12.9) 54 (87.1) 0 (0)	8 (15.1) 45 (84.9) 0 (0)	0 (0) 9 (100) 0 (0)	0.59
Comorbidity, n(%) <i>Cardiovascular</i> <i>Endocrine</i> <i>Neurologic</i> <i>Excretory</i> <i>Oncologic</i>	45 (72.6) 38 (61.3) 8 (12.9) 7 (11.3) 5 (8.1) 3 (4.8)	37 (69.8%) 31 (58.5) 8 (15.1) 5 (9.4) 3 (5.7) 3 (5.7)	8 (88.9%) 7 (77.8) 0 (0) 2 (22.2) 2 (22.2) 0 (0)	0.423 0.462 0.59 0.266 0.149 1.000

Systolic blood pressure (SBP)

Although the preoperative median systolic blood pressure (SBP⁰) in the patients, who survived was higher than SBP in non-survivors (130 mmHg vs. 110 mmHg), there was no

significant difference ($p = 0.085$) (Table 2). The performed ROC Curve analysis revealed a low accuracy (AUROC = 0.679) for SBP⁰ in predicting the outcome with a lack of significance ($p = 0.088$) (Table 3).

Table 2. Perioperative values of clinical parameters according to outcome

Clinical parameter	Total	Outcome		p-value
		Survivors	Non-survivors	
SBP ⁰ , mmHg (IQR)	123.5 (110-136.25)	130 (110-140)	110 (100-119)	0.085
SBP ³ , mmHg (IQR)	129.5 (116.25-133.75)	130 (120-137.5)	115 (90-120)	0.016
MAP ⁰ , mmHg (IQR)	91 (83-98.5)	93 (83-100)	82 (78.5-86.5)	0.027
MAP ³ , mmHg (IQR)	93 (90-100)	97 (90-100)	78 (73-87)	0.001
HR ⁰ , beats/min (IQR)	92 (81.5-100)	92 (80-100)	100 (85-105.5)	0.121
HR ³ , beats/min (IQR)	80 (76-83.75)	78 (73.5-82)	110 (85-120)	<0.0001
RR ⁰ , breaths/min (IQR)	20 (18-22)	20 (18-21)	22 (19-23)	0.072
RR ³ , breaths/min (IQR)	16 (16-19)	16 (16-18)	22 (20-25)	<0.0001
t ⁰ , °C (IQR)	36.8 (36.7-37.2)	36.8 (36.7-37.2)	36.8 (36.6-37.35)	0.761
t ³ , °C (IQR)	36.6 (36.5-36.8)	36.6 (36.5-36.9)	36.6 (36.6-36.9)	0.542
AMS ⁰ , n(%)	3 (4.8)	1 (1.9)	2 (22.2)	0.053
AMS ³ , n(%)	7 (11.7)	2 (3.8)	5 (71.4)	<0.0001
SIRS ⁰ , n(%)	36 (58.1)	30 (56.6)	6 (66.7)	0.722
SIRS ³ , n(%)	5 (8.3)	1 (1.9)	4 (57.1)	<0.0001

Table 3. Perioperative Sensitivity, Specificity and AUROCs of clinical parameters as outcome predictors

	Cut-off	Sensitivity, %	Specificity, %	AURO C	Std. Error	95% CI		p-value
						Lower bound	Upper bound	
SBP ⁰	> 114	64.2	66.6	0.679	0.092	0.498	0.860	0.088
SBP ³	> 122	64.2	85.7	0.779	0.105	0.573	0.985	0.017
MAP ⁰	> 83.5	67.9	78.8	0.731	0.096	0.543	0.918	0.028
MAP ³	> 87.5	88.7	85.7	0.864	0.100	0.668	1.000	0.002
HR ⁰	> 98	66.7	67.9	0.661	0.089	0.4878	0.836	0.124
HR ³	> 84	85.7	86.8	0.916	0.054	0.811	1.000	<0.0001
RR ⁰	> 21	66.7	77.4	0.687	0.101	0.490	0.884	0.075
RR ³	> 19	85.7	86.8	0.935	0.044	0.849	1.000	<0.0001
t ⁰	36.85	44.4	56.6	0.469	0.106	0.260	0.677	0.764
t ³	36.85	42.9	88.7	0.573	0.141	0.297	0.849	0.534

When the same indicator was evaluated on the 3rd postoperative day in the group of deceased patients, there was a tendency for a permanent decrease reported with a lower SBP (SBP³) compared to the group of survivors (130 mmHg vs. 115 mmHg, $p = 0.016$). We found a good ability of SBP³ to predict favorable outcome (AUROC = 0.779, $p = 0.017$) (Figure 1). A threshold value of SBP³ >122 mmHg with a sensitivity of 64.2% and a specificity of 85.7% allowed the discrimination of patients with a higher chance of survival.

Mean arterial pressure (MAP)

Preoperative MAP values (MAP⁰) in non-survivors were significantly lower than those in survivors (82 mmHg vs. 93 mmHg, $p = 0.027$) (Table 2). The good prognostic value was also

confirmed by the performed ROC Curve analysis (AUROC = 0.731) (Figure 1). We found that a threshold of MAP⁰ >83.5 mmHg allows the prediction of a favorable outcome with a sensitivity of 67.9% and a specificity of 78.8% (Table 3).

We had the same observation on the 3rd POD, where MAP³ remained significantly higher in patients with favorable outcome compared to those who died (97 mmHg vs. 78 mmHg, $p = 0.001$). MAP³ demonstrated a better ability to predict outcomes than MAP⁰ (AUROC = 0.864 vs. AUROC = 0.731) (Figure 1). As a predictor of survival, for MAP³ >87.5 mmHg we found high sensitivity of 88.7% and specificity of 85.7% (Table 3).

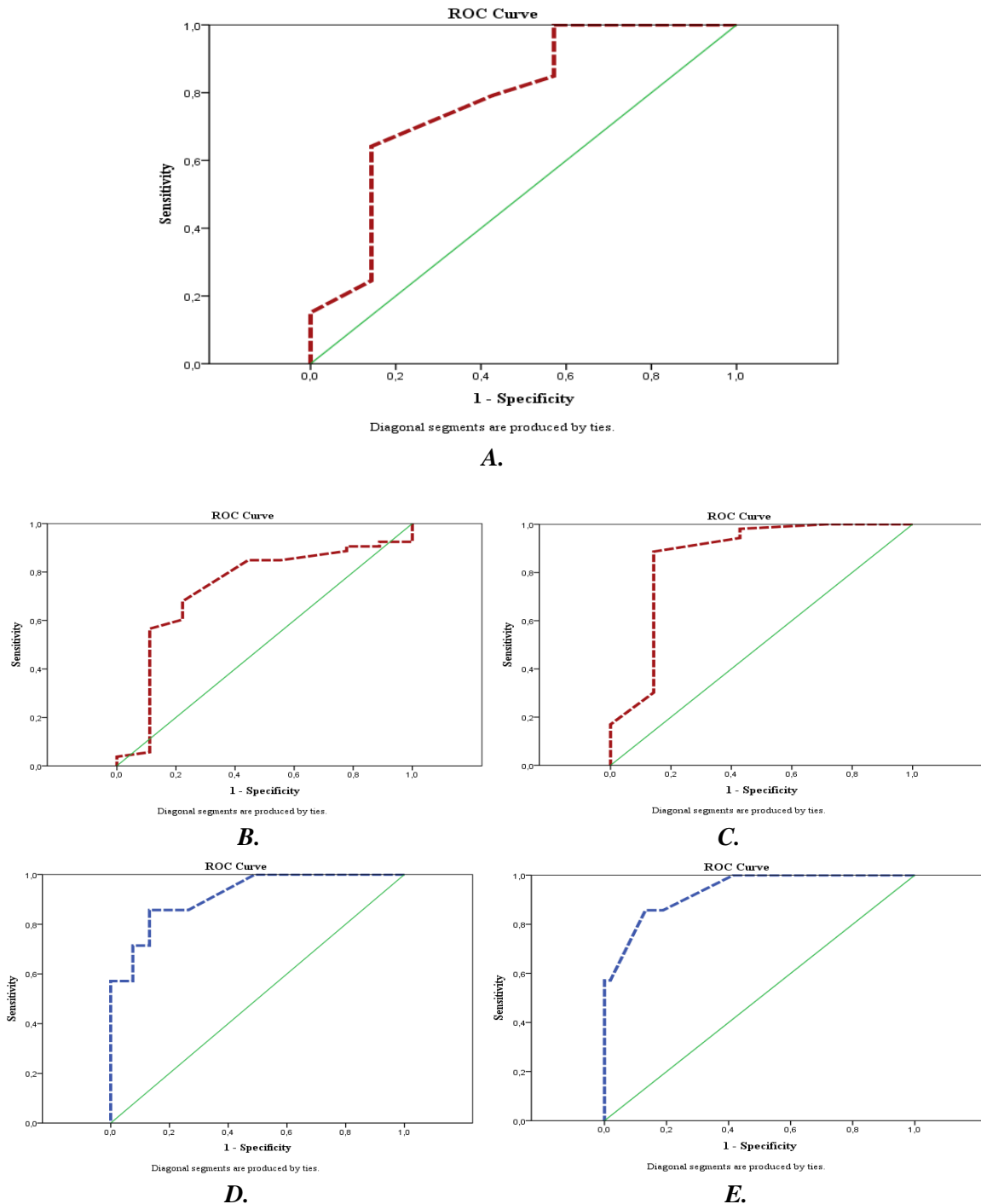


Figure 1. ROC Curves for: A. postoperative systolic blood pressure (SBP³) in prediction of favorable outcome; B. preoperative mean arterial pressure (MAP⁰) in prediction of favorable outcome; C. postoperative mean arterial pressure (MAP³) in prediction of favorable outcome; D. postoperative heart rate (HR³) in prediction of fatal outcome; E. postoperative respiratory rate (RR³) in prediction of fatal outcome;

Heart rate (HR)

Median preoperative heart rate (HR⁰) did not differ according to outcome ($p = 0.121$), which was confirmed by ROC Curve analysis (AUROC = 0.661, $p = 0.124$) (Table 3).

However, the secondary evaluation of HR on the 3rd POD (HR³) revealed a better accuracy for

outcome prediction, whereat non-survivors had significantly higher HR than survivors - 110 beats/min vs 78 beats/min, $p < 0.0001$. Excellent ability for prognostication of fatal outcome (AUROC = 0.916) was observed for a threshold value of HR³ >84 beats/min (Figure 1). The established sensitivity and specificity were 85.7% and 86.8%, respectively.

Respiratory rate (RR)

Preoperatively measured respiratory rate (RR⁰) did not show the ability to differentiating survivors from non-survivors (20/min vs. 22/min, $p = 0.072$). The prognostic value of RR⁰ was not established (AUROC = 0.687, $p = 0.075$) (**Table 3**).

On the 3rd POD, however, patients who died had a significantly higher RR³ than survivors (22/min vs. 16/min, $p < 0.0001$) (**Table 2**). RR³ showed excellent ability for prognostication of adverse outcome (AUROC = 0.935, $p < 0.0001$) (**Figure 1**). The optimal threshold value >19 /min allowed predicting mortality with a sensitivity of 85.7% and a specificity of 86.8%.

Axillary temperature (t)

When analyzing the measured axillary temperature preoperatively (t⁰), no significance was found according to the outcome ($p = 0.761$) (**Table 2**). Ability of t⁰ as a predictor of outcome was not observed (AUROC = 0.469).

The lack of statistical significance of this indicator was also preserved in the postoperative period. On the 3rd POD, t³ showed no predictive performance (AUROC = 0.573) (**Table 3**).

Altered mental status (AMS)

When analyzing the alteration of mental status before the operative treatment (AMS⁰) we observed that 22.2% of the non-survivors and 1.9% of the survivors had a Glasgow Coma Score (GCS) <15 points and the difference was very close to statistical significance ($p = 0.053$) (**Table 2**).

AMS recorded at 3rd POD (AMS³) showed a significant association with outcome. We observed a highly significant difference between non-survivors and survivors with a GCS score <15 points (71.4% vs. 3.8%, $p < 0.0001$).

Systemic Inflammatory Response (SIRS)

More than half of the patients (58.1%) had SIRS preoperatively, but it did not show prognostic qualities - we registered SIRS in 56.6% of the survivors and in 66.7% of non-survivors ($p = 0.722$) (**Table 2**).

Although only 5 (8.3%) patients had clinical evidence of SIRS at 3rd POD, the fatal outcome was predicted with excellent ability. SIRS occurred in 57.1% of those who died and only in 1.9% of those who survived ($p < 0.0001$).

DISCUSSION

Despite advances in surgical techniques, antimicrobial therapy, and intensive care, treatment of cIAIs remains a challenging task [4]. An early prognostic assessment can provide an objective classification of the severity of the infection and differentiation of high-risk patients to whom more aggressive therapeutic measures can be applied [5, 6]. Unfortunately, most patients with cIAIs do not seek help in time and are hospitalized with a significant delay, which further complicates effective treatment [7]. All these facts indicate the need for meaningful methods that could contribute to an early prognosis, and an early assessment of the aggressiveness of the treatment regimen.

The hallmarks reflecting the transition of the local immune response to a systemic inflammatory response include changes that occur at the microvascular and cellular level with massive activation of inflammatory and coagulation cascades leading to vasodilation and vascular volume redistribution, capillary endothelial dysfunction, impaired cellular metabolism, and impaired absorption of oxygen. An objective examination of the patient should detect these changes by assessing the basic clinical parameters, which include blood pressure, pulse, respiratory rate, body temperature and mental status.

Hypotension is usually reflected as a decreased systolic blood pressure or as a decreased mean arterial pressure. Lower values of systolic blood pressure have the ability to predict the adverse outcome, which is why they are included as an independent prognostic factor in a number of scoring systems - quick-SOFA (qSOFA), National Early Warning Score (NEWS) Confusion, Blood Urea Nitrogen, Respiratory rate, Blood Pressure, Age ≥ 65 (CURB-65), SAPS 2. A Dutch study examining 8204 patients with suspected sepsis found that lower SBP values were associated with a higher risk of death (119.6 \pm 36.2 mmHg vs 132.3 \pm 25.4 mmHg, $p < 0.0001$). A number of studies based on large databases from North America and Europe have found that typically at SBP <110 mmHg, mortality rate begins to increase dramatically on the order of 5% for each $\downarrow 10$ mmHg. At SBP <60 mmHg, it is reported that between 1/3 and 2/3 of patients are likely to have lethal outcomes [8, 9].

In the present study, we found that preoperative SBP had no prognostic value ($p = 0.085$), in contrast to SBP measured on the 3rd POD, which

was able to discriminate survivors from deceased patients (130 mmHg vs. 115 mmHg, $p = 0.016$). With successful SBP compensation above 122 mmHg on the 3rd POD, we reported an increased chance of survival (AUROC = 0.779, $p = 0.017$).

In surgical patients with sepsis, non-survivors had a significantly lower preoperative SBP than the survivors (116 mmHg vs. 125 mmHg, $p < 0.001$) and a SBP value < 111 mmHg was associated with mortality rates $>20\%$ [10]. In patients with cIAIs, Yamamoto et al. [11], Jung et al. [12], our retrospective analysis from 2020 [13], as well as the World Society of Emergency Surgery "PIPAS" study [2] demonstrate that lower SBP levels are also in positive correlation with fatal outcome. Yamamoto et al. [11] reported that non-survivors had lower median SBP values than survivors (96 mmHg vs. 130 mmHg, $p = 0.004$). Preoperative SBP values ≤ 100 mmHg were observed 2 times more often in the deceased than in the survivors in the study by Jung et al. [12] (72% vs. 35.4%, $p < 0.001$) and 2.5 times more often in our 2020 retrospective analysis (36% vs. 14.1%, $p = 0.021$). Sartelli et al. [2] registered in "PIPAS" that the decrease in SBP is associated with an increased risk of death - values above 100 mmHg were observed in 85.7% of survivors and 57.5% of those who died ($p < 0.001$), values in the range 90-100 mmHg in 11.15% of the survivors and 25% of the deceased ($p < 0.001$) and values < 90 mmHg in 3.1% of the survivors and 17.5% of the deceased ($p < 0.001$). Luo et al. [14] reported higher than us postoperative SBP levels in non-survivors (109 mmHg in deceased vs. 120.5 mmHg in survivors, $p < 0.001$).

Mean arterial pressure is an important parameter that can adequately assess organ perfusion [15]. MAP is included as an indicator in the SOFA score, reflecting organ dysfunction and the risk of fatal outcomes [16]. When MAP is below a certain threshold, the blood flow to the organs begins to decrease in a linear progression. In patients with septic shock, even a relatively short period of organ hypoperfusion is associated with a fatal outcome [17], which is also the reason for the 2016 sepsis treatment recommendations [18] to require maintenance of $MAP \geq 65$ mmHg.

In the studied patients, we found that mean arterial pressure was a highly significant predictor of a favorable outcome. Higher MAP values, measured both preoperatively and on the

3rd POD, were able to distinguish survivors from non-survivors ($p = 0.027$ and $p = 0.001$ respectively). Postoperative MAP demonstrated even better prognostic ability than preoperatively measured (AUROC = 0.864 vs. 0.731), as its threshold value was higher than the preoperative one ($MAP^3 > 87.5$ mmHg vs. $MAP^0 > 83.5$ mmHg).

Unfortunately, we couldn't find any source in the literature investigating the prognostic abilities of MAP as a single indicator in patients with cIAIs, which prevented us from comparing our results.

Tachycardia is an indicative marker of the body's systemic response to stress and is a common sign in patients with cIAIs. It is a universal compensatory physiological mechanism by which the cardiac output and oxygen delivery to the tissues are increased. Tachycardia is usually associated with hypovolemia and the need for volume replacement with fluids. In sepsis, despite adequate volume replacement, tachycardia often persists. Low pulse pressure and increased heart rate are considered the earliest signs of shock. Tachycardia can also be the result of a febrile state. Heart rate > 90 /min is one of the criteria for systemic inflammatory response syndrome (SIRS), and its various values are included in the Acute Physiology and Chronic Health Evaluation II (APACHE II) score, Simplified Acute Physiology Score II (SAPS II), and NEWS.

Preoperative heart rate values in the present study failed to predict outcome ($p = 0.121$). Like us, Yamamoto et al. [11] and Shin et al. [19] found no prognostic value in preoperatively measured heart rate ($p = 0.074$ and $p = 0.206$, respectively). In contrast, our retrospective analysis [13], as well as the World Society of Emergency Surgery "PIPAS" study [2] found HR as a predictor of adverse outcome. In "PIPAS", Sartelli et al. observed a threshold value >100 /min in significantly more deceased patients than survivors (57.9% vs. 36.7%, $p < 0.001$). In our retrospective analysis, HR > 90 /min was also found more often in those who died (48% vs. 25.9%, $p = 0.035$). In patients with suspected sepsis, Brink et al. [20] reported that non-survivors had a higher HR than the survivors (103.7/min vs. 97.5/min, $p < 0.0001$).

In contrast to the preoperative HR, the measured on the 3rd POD showed a significant prognostic ability. Patients who died had a higher median

HR than those who survived – 110/min versus 78/min, and the reported difference was of a very high degree of significance ($p < 0.0001$). The excellent ability of HR³ to predict adverse outcomes (AUROC = 0.916) was reported at a threshold value >84 /min.

Tachypnea is common in patients with sepsis and is a clear indicator of metabolic acidosis caused by tissue hypoperfusion. Elevated RR is also an indicator of possible pulmonary dysfunction. Usually, RR in patients with cIAIs and sepsis increases along with the heart rate as a compensatory mechanism of the body for hypotension and acidosis. RR >22 /min was included in the qSOFA score as an independent predictor of the need for intensive care and in-hospital mortality.

In the group studied by us, we did not find the abilities of the preoperatively measured RR to predict the outcomes ($p = 0.072$).

Jung et al. [12], our retrospective analysis [13] and Satelli et al. [2] established a prognostic value of RR in patients with cIAIs. Tachypnea ≥ 22 /min in the study by Jung et al. occurs about 2 times more often in deceased patients (48% vs. 26.7%, $p < 0.001$), and in our retrospective analysis even three times more often (36% vs. 11.8%, $p = 0.013$). In "PIPAS" RR <22 /min occurred more often in survived patients (74.2% vs. 44.3%, $p < 0.001$), and tachypnea conversely more often in deceased patients (45.6% vs. 25.7%, $p < 0.001$).

However, RR at 3rd POD demonstrated significant prognostic ability, whereat non-survivors had higher RR than survivors (22/min vs. 16/min, $p < 0.0001$). The threshold value > 19 /min showed an excellent value for prognostication of fatal outcomes (AUROC = 0.935).

Luo et al. [14] found no prognostic performance of postoperative RR ≥ 22 /min ($p = 0.06$).

The systemic inflammatory response is usually accompanied by two types of changes in body temperature: fever $>38^\circ\text{C}$ and hypothermia $<36^\circ\text{C}$. While elevated temperature is generally considered beneficial to patients, hypothermia is associated with increased mortality [21,22]. In septic patients with $t >38^\circ\text{C}$, the estimated mortality rates are approximately 22%, while at $t <36^\circ\text{C}$ they reach 47% [23].

In the present study, we found no benefit in measuring axillary temperature before and after

surgery. Its perioperative values showed no ability to predict outcome ($p = 0.761$ preoperatively and $p = 0.542$ at 3rd POD). Our results confirmed the observations of Yamamoto et al. [11] and Luo et al. [14] for their lack of prognostic qualities ($p > 0.05$ and $p = 0.172$, respectively). In "PIPAS", Sartelli et al. [2], like us, did not report prognostic ability in febrile patients' $t >38^\circ\text{C}$ (deceased 25.7% vs survivors 24.1%, $p = 0.54$), but found qualities as a predictor of death for $t = 36-38^\circ\text{C}$ (deceased 66.1% vs survivors 73.7%, $p < 0.05$) and for $t < 36^\circ\text{C}$ (died 8.2% vs. survived 2.2%, $p < 0.001$). The WSES study "CIAO" [24] registered excellent ability of $t >38^\circ\text{C}$ or $t <36^\circ\text{C}$, measured on the 3rd POD to predict adverse outcome (OR = 3.3, $p < 0.0001$). In patients with suspected sepsis, Brink et al. [20] observed a significantly higher body temperature in patients who died (37.7°C vs. 36.9°C , $p < 0.0001$).

Altered mental status is a common feature of systemic inflammatory response and sepsis. It is considered as a sign of organ dysfunction and is associated with increased mortality. The cause of alteration is not fully understood, as it is believed that, in addition to brain hypoperfusion, an important role is also played by altered amino acid metabolism.

Preoperatively, we found no influence of impaired consciousness on the outcome ($p = 0.053$). Similarly, Jung et al. [12] did not observe an association between AMS and fatal outcome (2.7% in survivors vs. 8% in non-survivors, $p = 0.07$). Other studies that investigated AMS as a predictor of death in patients with cIAIs found a high prognostic value of this indicator. Luo et al. [14] reported a significant difference in GCS values between survivors and non-survivors - 15 (15-15) pts vs. 15 (13-15), $p < 0.001$. Our retrospective analysis from 2020 [13] also reported excellent performance of GCS <15 for mortality prediction (1.2% in survivors vs. 40% in non-survivors, $p < 0.0001$). In the "PIPAS" study [2] Sartelli et al. used the simplified AVPU scale and reported its excellent ability to discriminate deceased patients ($p < 0.001$).

In contrast to our preoperative results, we found that the presence of AMS at the 3rd POD demonstrated excellent qualities for the prediction of death ($p < 0.0001$). GCS <15 points was found in 71.4% of the deceased and only in 3.8% of the survived patients. We attributed the observed postoperative results to

the persistent septic condition and/or incomplete eradication of the infectious source. Only one clinical parameter measured preoperatively (mean arterial pressure) demonstrated predictive qualities. Since these indicators are an expression and consequence of the systemic pro-inflammatory response, we decided that the latter had no influence on mortality before the surgical intervention in the studied group. We also confirmed this through a comparative analysis of SIRS related to outcome. Preoperatively, we recorded SIRS in a similar number of survivors and non-survivors (56.6% vs. 66.7%, respectively, $p = 0.722$). The lack of preoperative prognostic ability can be explained by the adequate treatment approach and the successful removal of the infectious source. The correct therapeutic strategy can also be judged by a reduction in the frequency of the systemic inflammatory reaction postoperatively. Before the operative intervention, SIRS was reported in more than half of the patients (58.1%), while on the 3rd POD was found in only five (8.3%).

Almost all measured clinical parameters (except axillary temperature) demonstrated prognostic ability as single indicators postoperatively and with a high degree of significance. This leads us to consider that the presence of a systemic pro-inflammatory reaction postoperatively is the main reason for the occurrence of the fatal outcome in the studied patient population. We also confirmed this by the perfect ability ($p < 0.0001$) of postoperative SIRS to differentiate patients according to outcome (its presence was found in 57.1% of the deceased and only in 1.9% of the survivors).

CONCLUSION

Since clinical parameters measured after surgery showed prognostic performance, it is in this period that these data should be taken into account in order to make a simple and quick prognostic assessment, through which we could influence the final outcome in an early phase of the complicated intra-abdominal infection.

REFERENCES

1. Tridente A, Clarke GM, Walden A, et al. Patients with faecal peritonitis admitted to European intensive care units: an epidemiological survey of the GenOSept cohort. *Intensive Care Med.* 2014;40(2):202-210
2. Sartelli M, Abu-Zidan FM, Labricciosa FM, et al. Physiological parameters for prognosis in abdominal sepsis (PIPAS)

study: a WSES observational study. *World J Emerg Surg* 2019;14:34

3. Bone RC, Balk RA, Cerra FB, et al. American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference: Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. *Chest* 1992, 101:1644–1655.
4. Malangoni MA, Inui T. Peritonitis - the Western experience. *World J Emerg Surg.* 2006;1:25
5. Ranju S, Nishant K, Abhijit B, Homay V. Preoperative predictors of mortality in adult patients with perforation peritonitis. *Indian Journal of Critical care Medicine.* 2011;15(3):157–63;
6. Billing A, Fröhlich D, Schildberg FW. Prediction of outcome using the Mannheim peritonitis index in 2003 patients. Peritonitis Study Group. *Br J Surg.* 1994;81(2):209-213
7. Ersumo T, WM Y, Kotisso B. Perforated peptic ulcer in Tikur Anbessa Hospital: a review of 74 cases. *Ethiop Med J.* 2005;43(1):9–13.
8. Convertino, Victor A.; Hasler RM, Nuesch E, et al. Systolic blood pressure below 110 mm Hg is associated with increased mortality in blunt major trauma patients: multicenter cohort study. *Resuscitation.* 2011 Sep;82(9):1202-7. doi:10.1016/j.resuscitation.2011.04.021;
9. Russel JA. The current management of septic shock. *Minerva Med.* 2008 Oct;99(5):431-58.;
10. Clarke DL, Chipps JA, Sartorius B, Bruce J, Laing GL, Brysiewicz P. Mortality rates increase dramatically below a systolic blood pressure of 105-mm Hg in septic surgical patients. *Am J Surg.* 2016;212(5):941-945
11. Yamamoto T, Kita R, Masui H, et al. Prediction of mortality in patients with colorectal perforation based on routinely available parameters: a retrospective study. *World J Emerg Surg.* 2015;10:24. doi:10.1186/s13017-015-0020-y;
12. Yun Tae Jung, Jiyeon Jeon, Jung Yun Park et al. Addition of lactic acid levels improves the accuracy of quick sequential organ failure assessment in predicting mortality in surgical patients with complicated intra-abdominal infections: a retrospective study. *World Journal of Emergency Surgery* (2018) 13:14

13. Dimitrov, E., Minkov, G., Enchev, E., et al. 2020. The Quick Sequential Organ Failure Assessment (qSOFA) Score is a Poor Mortality Predictor in Patients with Complicated Intra-abdominal Infections. *Open Access Macedonian Journal of Medical Sciences*. 8, B (May 2020), 221–225.
DOI:<https://doi.org/10.3889/oamjms.2020.3869>.
14. Luo X, Li L, Ou S, et al. Risk Factors for Mortality in Abdominal Infection Patients in ICU: A Retrospective Study From 2011 to 2018. *Front Med (Lausanne)*. 2022;9:839284
15. Lamia B, Chemla D, Richard C, et al: Clinical review: Interpretation of arterial pressure wave in shock states. *Crit Care* 2005; 9:601–606
16. Vincent JL, Moreno R, Takala J, et al: The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. *Intensive Care Med* 1996, 22:707-710
17. Waechter J, Kumar A, Lapinsky SE, et al. Interaction between fluids and vasoactive agents on mortality in septic shock: a multicenter, observational study. *Crit Care Med*. 2014;42:2158–68
18. Rhodes A, Evans LE, Alhazzani W, et al. Surviving Sepsis Campaign: international guidelines for management of sepsis and septic shock: 2016. *Crit Care Med*. 2017;45:486–552
19. Shin R, Lee SM, Sohn B, et al. Predictors of Morbidity and Mortality After Surgery for Intestinal Perforation. *Ann Coloproctol*. 2016;32(6):221-227
20. Brink A, Alsma J, Verdonshot RJCG, et al. Predicting mortality in patients with suspected sepsis at the Emergency Department; A retrospective cohort study comparing qSOFA, SIRS and National Early Warning Score. *PLoS One*. 2019;14(1):e0211133
21. Kushimoto S, Gando S, Saitoh D, et al. The impact of body temperature abnormalities on the disease severity and outcome in patients with severe sepsis: an analysis from a multicenter, prospective survey of severe sepsis. *Crit Care*. 2013;17(6):R271;
22. Clemmer TP, Fisher Jr CJ, Bone RC, et al. Hypothermia in the sepsis syndrome and clinical outcome. The Methylprednisolone Severe Sepsis Study Group. *Crit Care Med*. 1992;20(10):1395–401.;
23. Rumbus Z, Matics R, Hegyi P, et al. Fever is associated with reduced, hypothermia with increased mortality in septic patients: a meta-analysis of clinical trials. *PLoS One*. 2017;12(1):e0170152
24. Sartelli M, Catena F, Ansaloni L, et al. Complicated intra-abdominal infections in Europe: a comprehensive review of the CIAO study. *World J Emerg Surg*. 2012;7(1):36. Published 2012 Nov 29. doi:10.1186/1749-7922-7-36