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A focus on abdominal sepsis: The problem of prognostic markers

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ABSTRACT

Background: Determining the prognosis of mortality from abdominal sepsis in patients with one surgical intervention is an urgent problem. *Methods*: It study was based on data from comparing of severity scores in 136 patients with abdominal sepsis who were operated one time with secondary peritonitis and the condition was assessed before surgery and after 72 h using most significant indicators. *Results*: According to the goals and objectives of the study all patients were divided according to the severity of the condition which was determined by the criteria of Sepsis-3: abdominal sepsis was diagnosed in 110 (80.9%), and septic shock in 26 (19.1%) The main finding of this study is that an increase of WBC count, lactate, C-reactive protein levels, and a decrease systolic blood pressure, abdominal perfusion pressure after 72 h from the surgery were prognostic factors for patients with adverse outcome. It should be noted that qSOFA had the optimal cutoff value 2.5 points before surgery by criterion positive outcome/adverse outcome (AUC 0.842) with high sensitivity (93.9%) and low specificity (60.9%); APACHE II score had the optimal cutoff value 15.5 points (AUC 0.808), and SOFA score had the optimal cutoff value 9.5 points (AUC 0.754). In 72 h after surgery, the scores APACHE II (AUC 0.817) and SOFA (AUC 0.892) with the optimal cutoff 21.5 and 11.5 points had a good predictive value for the criterion positive outcome/adverse outcome, respectively. *Conclusions*: The assessment of effective biomarkers has made it possible to personalize surgical tactics and improve outcomes of the treatment.

Keywords: abdominal sepsis, definition of sepsis-3, biomarkers, severity rating scales, prediction of mortality, results.

1. INTRODUCTION

The term intra-abdominal infection (IAI) describes heterogeneity of pathological conditions and it was divided into uncomplicated and complicated (Sartelli, 2010). The urgency of the problem is due to a significant increase in the total number of patients with IAI (the trend is observed in all

developed countries), an increase in the number of patients with fatal complications, the presence of multiple or residual foci of infection and polymicrobial infection, the irrational use of antimicrobial drugs, etc. With complicated IAI, the infectious process goes beyond the organ, causes either localized peritonitis or generalized peritonitis and often leads to multiple organ failure (MOF). The philosophy of treating patients with complex IAI includes both source control and damage control surgery strategy. There is no doubt that the majority of patients with IAI, sepsis/septic shock should urgently undergo the source control procedure, and surgery to manage damage (re-laparotomy on the program) may be an option in a certain proportion of patients with significant physiological disorders and ongoing sepsis (Sartelli et al., 2017; Kryvoruchko et al., 2021).

Recently, thanks to the achievements of basic sciences and clinical medicine, new data have been obtained on the etiology, pathogenesis and tanatogenesis of abdominal sepsis and development of its is determined by the influence of the following main factors (Kryvoruchko et al., 2019):

1. Microbiological factor: type, virulence, quantity, duration of exposure to bacteria that have entered the body.
2. The focus of infection: area, nature and the volume of tissue destruction, the state of blood circulation in the injection site, the place and ways of spreading the infection.
3. Reactivity of the body: the immunological state of the body, the state of various organs and systems, etc.

The aim was to evaluate the prognostic factors of patients hospitalized with abdominal sepsis in both the surgical department and the intensive care unit. We also evaluated the effectiveness of various prognostic scores in predicting mortality among patients diagnosed with abdominal sepsis.

2. MATERIALS AND METHODS

Design of study

We conducted a retrospective and prospective study on patients admitted between January 2011 and June 2021 to Kharkiv Regional Clinical Hospital (Ukraine). The patients were enrolled through a computerized electronic medical record.

Inclusion criterias: The study included 136 men and women over 18 and under 70 years of age were admitted to hospital for sepsis or septic shock within 24 hours of admission to the surgery or intensive care unit. Prognostic scores in predicting mortality among patients diagnosed with abdominal sepsis. The study included 136 men and women over 18 and under 70 years of age were admitted to hospital for sepsis or septic shock to the surgery or intensive care unit (ICU). All patients had the Sepsis-3 criteria (Rhodes et al., 2017), they were operated on urgently and all patients underwent one operation.

Exclusion criterias: Comorbidity with acute myocardial infarction and stroke; IAI caused by the cancer of the hollow organ; post-resuscitation illness due to stopping effective blood circulation; pregnancy; cancer in anamnesis, and useless resuscitation status due to refractory shock.

All patients were done surgery with effective source control, supporting appropriate antibiotics, resuscitation, and organ support therapy. Patients were divided in two groups: in the 1st included those with positive outcome (discharged) and in the 2nd those with adverse outcomes (died). For each enrolled patient were collected: personal data, admission data; comorbidity (Charlson Comorbidity Index (CCI), laboratory analysis (WBC count, platelets, total bilirubin, creatinine, lactate, C-reactive protein (CRP), procalcitonin, hematocrit) on the first admission day and after 72 h, antibiotics and fluid therapy during hospitalization and after surgery including organs' support. In the dynamics of the treatment of patients after surgery, studies were carried out systolic blood pressure (SBP), intra-abdominal pressure (IAP), abdominal perfusion pressure (APP). We also computed for each patient the following scores, validated for abdominal sepsis: qSOFA, Acute Physiology and Chronic Health Evaluation II (APACHE II) and The Sequential Organ Failure Assessment SOFA.

Statistical analyses

Statistical data processing was performed using the trial version of STATISTICA 13.3 EN. Initially, statistical analysis was performed using descriptive statistics. Using the Tukey test, the presence of emissions was checked and the normality of the distributions (Shapiro-Wilk test) of the selected indicators was assessed. Continuous data was presented as Me (Q_1; Q_3), where Me is the median, Q_1 and Q_3 is the interquartile range (IQR). The nonparametric Mann-Whitney test was used for pairwise comparisons of means in independent groups. Zero hypotheses (H0) in statistical tests were rejected at a significance level of $p \geq 0.05$.When predicting the outcome of treatment, the greatest accuracy and adequacy in terms of a posteriori classification was obtained by discriminant analysis. Prediction of treatment was carried out not only with the use of multidimensional statistical methods, but also with the help of various scores of the severity of the condition or disorders of the physiological condition of the patient in abdominal sepsis: Quick SOFA (qSOFA) score on admission, APACHE II score and SOFA score in the dynamics of treatment. To

assess the diagnostic significance of the studied scales and biomarkers, an ROC analysis was performed: the sensitivity, specificity, and area under the receiver operating characteristic curve (ROC curve) were determined for each scores and each biomarker, and the significance of the differences between them was assessed and taking into account its 95% confidence interval. The prognostic efficacy of the models was assessed by discrimination based on the area under ROC curve (AUC) index. The efficacy of the model was considered limited at AUC≥0.70; good - at AUC≥0.80; excellent - at AUC≥0.90.

3. RESULTS

In each groups, patients were divided according to the severity of the condition which was determined by the criteria of Sepsis-3: abdominal sepsis was diagnosed in 110 (80.9%), and septic shock in 26 (19.1%) (Figure 1). The causes of abdominal sepsis were secondary peritonitis with perforated peptic ulcer, perforation of the vermiform appendix, failure of intra-intestinal and gastrointestinal anastomoses (Figure 2). The study was dominated by men (65.4%).

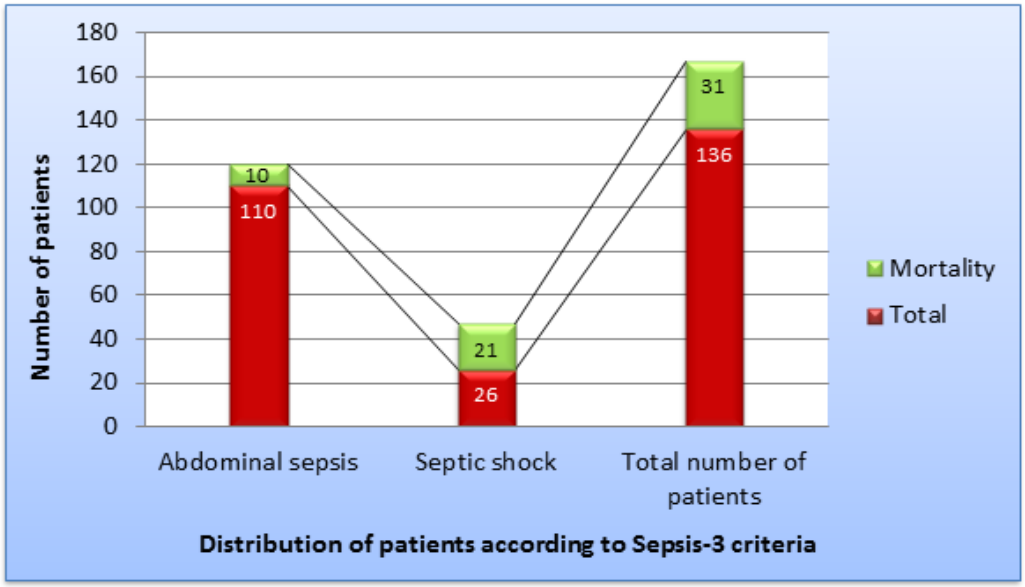

Figure 1 Distribution of patients according to the Sepsis-3 criteria.

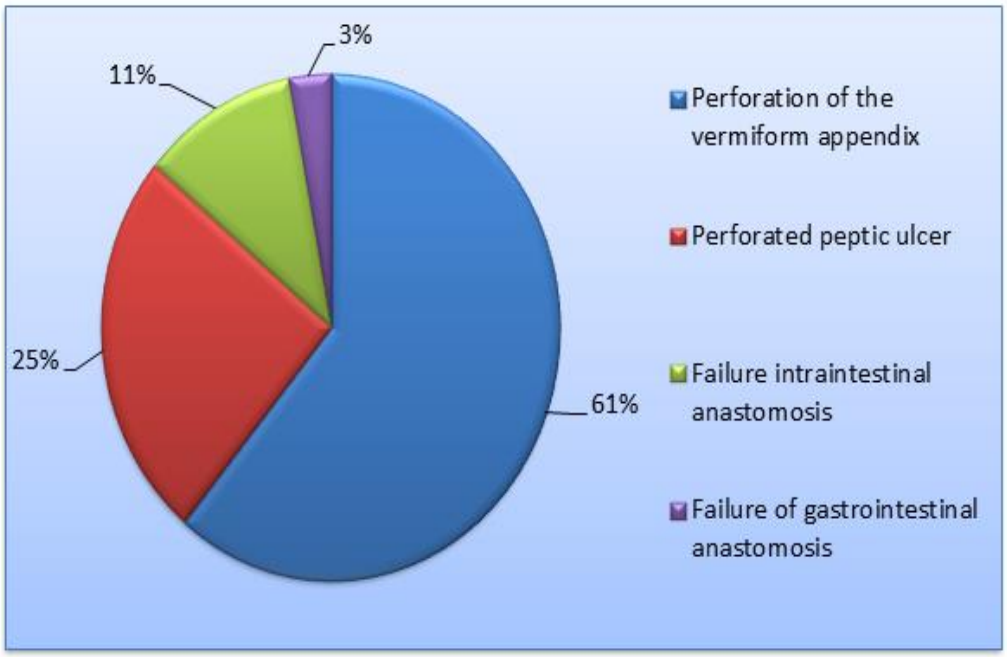

Figure 2 The causes of abdominal sepsis.

The results of the distribution of patients by tactical approach by severity and mortality are presented in the Table 1. Patients with positive outcome had significantly lower CCI than patients with adverse outcome (p=0.011) (Table 1). Regarding the laboratory analysis, there were the differences between the two groups at admission to the hospital were significant in terms of such indicators as WBC count (p= 0.000), lactate (p= 0.000), CRP (p= 0.000), SBP(p= 0.000) and APP (p= 0.000) both before surgery and after 72 h after its and increased significantly in patients with an adverse outcome. Procalcitonin is an important biomarker in various infections, however, as our studies showed the value of this parameter before surgery was insignificant (P = 0.358) and only 72 hours after surgery a PCT changes in patients with positive and negative outcomes were highly significant (P = 0.000).

Table 1 Demographic, clinical and laboratory characteristics of patients with abdominal sepsis

Indicators	Before surgery		After 72 hours	
	Positive outcome	Adverse outcome	Positive outcome	Adverse outcome
Ages, Me [IQR]	58 [18-70]	61 [23-69]	–	–
	P=0.112			
CCI , Me [IQR]	1 [1-4]	5 [2-5]	–	–
	P=0.011			
WBC count ($\times10^9$/l), Me [IQR]	14.7 [12.4-21.3]	19.8 [13.2-22.2]	14.6 [12.3-24.1]	24.8 [17.4-28.2]
	P=0.000		P=0.000	
Platelets ($\times10^3$/l), Me [IQR] (n=231)	292.22 [232.8-329.6]	282.4 [256.2-359.7]	264.8 [224.4-311.3]	187.5 [158.2-215.1]
	P=0.056		P=0.000	
Hematocrit (%), Me [IQR]	38.2 [35.8-46.1]	39.1 [36.4-46.3]	38.6 [35.4-49.5]	44.8 [36.4-46.6]
	P=0.168		P=0.004	
Creatinine (mg/dl), Me [IQR]	0.87 [0.76-1.109]	0.89 [0.72-0.94]	0.113 [0.88-1.543]	1.92 [1.46-2.21]
	P=0.104		P=0.000	
Total bilirubin (μmol/l), Me [IQR]	24.5 [16.8-52.4]	24.4 [21.2-64.6]	26.5 [14.5-58.2]	59.5 [28.3-108.2]
	P=0.121		P=0.000	
Lactate (mmol/l), Me [IQR]	2.1 [1.6-2.8]	2.6 [1.8-6.9]	3.4 [1.9-7.6]	9.9 [5.2-12.3]
	P=0.000		P=0.000	
PCT (pg/ml), Me [IQR]	2.125 [0.125-71.212]	2.234 [0.116-80.143]	5.881 [2.117-86.021]	10.115 [3.426-151.113]
	P=0.358		P=0.000	
CRP (mg/l), Me [IQR]	134 [121-166]	185 [130-201]	151 [148-176]	201 [160-213]
	P=0.000		P=0.000	
SBP (mm Hg), Me [IQR]	115 [90-130]	85 [70-100]	130 [90-155]	70 [70-100]
	P=0.000		P=0.000	
APP	72	60	70	60

(mm Hg), Me [IQR]	[64-76]	[58-70]	[64-78]	[56-68]
	P=0.000		P=0.000	
qSOFA score (points), Me [IQR]	2 [1-3]	3 [2-3]	–	–
	P=0.000			
APACHE II score (points), Me [IQR]	13 [10-22]	21 [14-28]	14 [12-22]	26 [16-36]
	P=0.000		P=0.000	
SOFA score (points), Me [IQR]	9 [7-11]	12 [8-14]	9 [8-12]	14 [9-16]
	P=0.000		P=0.000	

Note: P - Mann-Whitney test.

Comparison of ROC curves between the two groups was used, which showed that high cut-offs APACHE II and SOFA scores had been associated with negative prognosis after surgery (Figures 3 & 4). It should be noted that qSOFA had the optimal cutoff value 2.5 points before surgery by criterion positive outcome/adverse outcome (AUC 0.842, 95% CI 0.672-0.911) with high sensitivity (93.9%) and low specificity (60.9%). The APACHE II score had the optimal cutoff value 15.5 points (AUC 0.808, 95% CI 0.699-0.845) with low sensitivity (49.2%) and high specificity (95.2%), and SOFA score had the optimal cutoff value 9.5 points (AUC 0.754, 95% CI 0.628-0.811) with sensitivity 67.4% and specificity 72.7%. In 72 hours after surgery, the scores APACHE II (AUC 0.817, 95% CI 0.706-0.890) and SOFA (AUC 0.892, 95% CI 0.686-0.943) with the optimal cutoff 21.5 and 11.5 points had a good predictive value for the criterion positive outcome/adverse outcome, respectively.

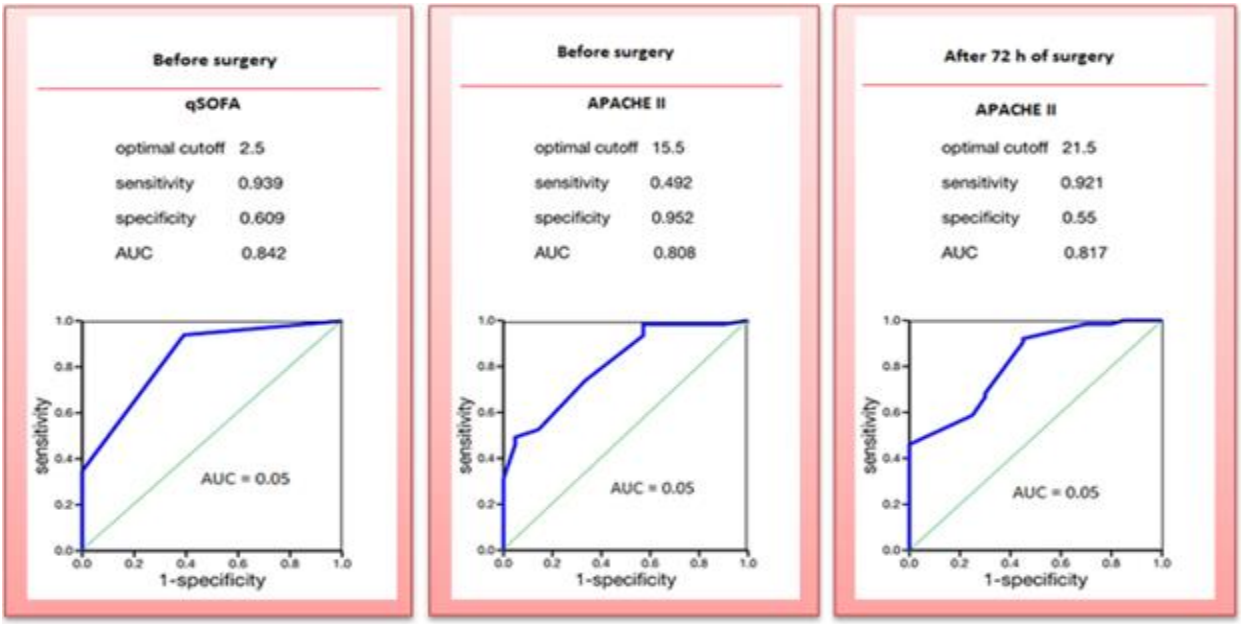

Figure 3 ROC curves qSOFA and APACHE II scores of measured values in positive outcome and adverse outcome patients.

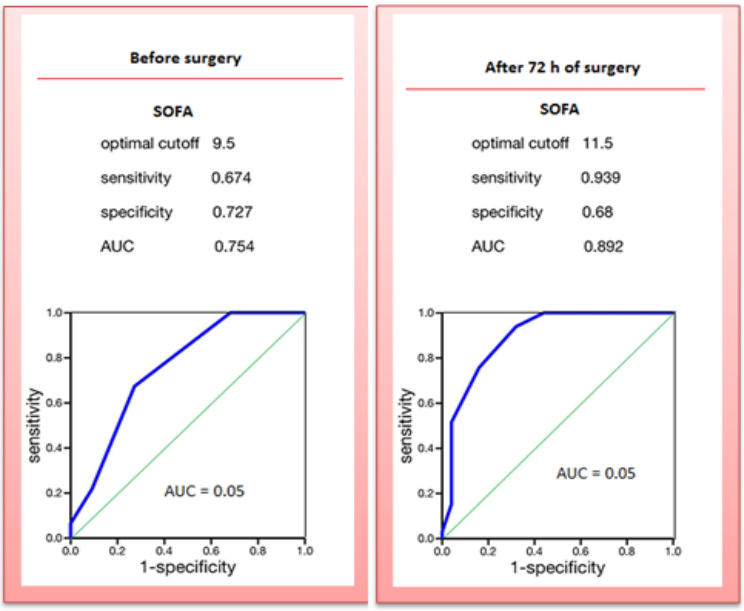

Figure 4 ROC curves SOFA score of measured values in positive outcome and adverse outcome patients.

4. DISCUSSION

According to the Sepsis-3 classification, we stratified 110 abdominal sepsis and 26 septic shocks. In the CIAO study, the overall mortality rate was 7.7% (Sartelli et al., 2012), but in the analysis of a subgroup of patients with severe sepsis or septic shock upon admission to the hospital, the mortality rate reached 32.4%, and in the immediate postoperative period, the mortality rate was 42.3%. Septic shock was observed in patients of different ages and in our observations, we did not note the importance of old age as an important predictor of the development of organ failure in elderly patients, as noted in other studies as important prognostic factor (Angus & van der Poll, 2013; Sartelli et al., 2013). Indeed, older patients have more frequently organ failure during abdominal sepsis.

The first aim of our study was to estimate Charlson Comorbidity Index and it was found that the patients with positive outcome had significantly lower CCI than patients with adverse outcome. It has also been shown that such indicators as WBC count, lactate level, CRP, SBP and APP both before surgery and 72 h after it's and increased significantly in patients with an adverse outcomend. It was also shown that such indicators as WBC count, lactate level, CRP, SBP and APP both before surgery and 72 h after its and increased significantly in patients with an adverse outcomend.It should be noted that similar violations have been noted in other studies (Boyko et al., 2020; Para et al., 2021; Kryvoruchko et al., 2021). As is already known, early prediction of mortality in abdominal sepsis is an important component for assessing the severity and prognosis of the disease. As is already known, early prediction of mortality in abdominal sepsis is an important component of the treatment of this severe category of patients. At the same time, factors influencing the prognosis of patients with abdominal sepsis include old age, poor nutrition, pre-existing diseases, immunosuppression, widespread peritonitis, poor source control, organ failure, prolonged hospitalization before therapy, and infection with nosocomial pathogens, etc. (Mulari & Leppäniemi, 2004; Horiuchi et al., 2007; Ohmann et al., 1997; Inui et al., 2009; Sartelli, 2010). De Waele et al., (2014) performed a review of the literature to identify factors independently associated with outcome in patients of abdominal sepsis. Risk factors associated with mortality had been categorized into three major classes: 1) severity of comorbidity, 2) the adequacy of treatment and the timing of its initiation, and 3) severity of the disease before surgery (Sartelli et al., 2017).

The next study objective was characterized in assessing various severity indicators in predicting mortality during resuscitation after surgery, and for this we calculated three main scores. Scoring systems can be broadly divided into two groups: disease-independent scores for evaluation of serious patients requiring care in the ICU such as Acute Physiology and Chronic Health Evaluation II and Simplified Acute Physiology scores II and peritonitis-specific scores such as Mannheim Peritonitis Index (Horiuchi et al., 2007). All scoring systems for the severity of patients with intra-abdominal infections Horiuchi et al., (2007) divided into several groups: disease-independent scores for patients as Acute Physiology and Chronic Health Evaluation II and Simplified Acute Physiology scores II, and peritonitis-specific such as the Mannheim Peritonitis Index.

Currently, to assess the course of various intra-abdominal infections, prognostic indicators are used in order to identify patients with complications and intra-abdominal sepsis using a system of objective assessments to select the optimal methods of their treatment and the objective early identification of patients with a unfavorable prognosis, as well as to enable the comparison of treatment results. Unfortunately, none of the current scoring systems satisfies all prerequisites (Levy et al., 2003; Sartelli, 2010; Jaffe et al., 2004; Agresta et al., 2006; Lamme et al., 2006). Although, qSOFA, APACHE II and SOFA scores were validated in different setting, their application in the surgical department and in the ICU demonstrated the most accurate relationship with patients' outcome. In accordance with the current recommendations of the Sepsis Survival Campaign, SOFA should be used as a prognostic indicator for detecting sepsis as well as for risk stratification of critically ill patients (Koch et al., 2020; Seymour et al., 2016; Kovach et al., 2019). Nevertheless, the several meta-analyzes have showed that the qSOFA recommended in the new 'Sepsis-3' guidelines was insensitive and moderately specific for assessing the risk of poor outcome in sepsis (Fernando et al., 2018) or had a moderate predictive value for all patients with generalized IAI (Ho & Lan, 2017).

In our study it was shown that the qSOFA had high sensitivity (93.9%) but low specificity (60.9%) with AUC = 0.842 in the diagnosis of abdominal sepsis in a population of patients requiring urgent surgery. An optimal combination of sensitivity and specificity on the qSOFA scale was obtained for the number of point's ≥ 2, while this model is low-specific, which can lead to a large number of false-positive diagnoses and to an increase in the aggressiveness of therapy including repeated surgical interventions which were done. SOFA and APACHE II scores have also showed good prediction results the early mortality in patients with abdominal sepsis when ROC curves were analyzed. Nevertheless that APACHE II score had low sensitivity and high specificity, and SOFA score had with moderate specificity and sensitivity. This study was some limitations, as it was conducted in one department of one hospital center, and the number of clinical observations had limited to 136 patients. Further studies in multicenter system should be conducted to assess prognostic factors in patients recovered in surgical wards. This is due to the fact that of the rapidly evolving MOF after surgery which makes stratification of patients at the onset of symptoms a real challenge.

5. CONCLUSIONS

In the setting postoperative period in abdominal sepsis causes significant mortality rate. Stratifying patients according to prognosis is essential to optimize therapy and establish correct care setting. Our study showed that an increase of WBC count, lactate, C-reactive protein, and decrease systolic blood pressure and abdominal perfusion pressure after 72 h from the surgery are prognostic factors for patients with adverse outcome. Moreover, the main scores such as qSOFA, APACHE II and SOFA validated in different settings demonstrated a good correlationship with our patients' outcome.

Compliance with ethical standards

The work has cleared by the Ethics Committee of Kharkiv National Medical University, Ukraine (the protocol №2, March, 12, 2021).The number of state registration is 0116u00499.

Competing interests

The authors declare that they have no competing interests. All authors have contributed equally to this work. All authors have read and approved the final manuscript.

Informed consent process

Informed consent was obtained from all participants included in the study.

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Authors' contribution

A – Study design;
B – Data collection;
C – Statistical analysis;
D – Data interpretation;
E – Manuscript preparation;
F – Literature search;

Data and materials availability

All data associated with this study are present in the paper.

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