Research Article

Predicting of Postoperative Mortality in Cases of Abdominal Sepsis for Two Surgical Strategies Using a New Mathematical Model: Two Centers Review of a 10 Years' Experience with the Same Diagnostic and Tactical Approaches to the Treatment

Kryvoruchko IA*, Boyko VV, Sykal NA and Yevtushenko OV

Department of Surgery, Kharkiv National Medical University of the Ministry of Health of Ukraine, Kharkiv, Ukraine

Corresponding author: Kryvoruchko IA, Department of Surgery, Kharkiv National Medical University of the Ministry of Health of Ukraine, Kharkiv, Ukraine, E-mail: Ikryvoruchko60@gmail.com

Abstract

Background: To determine the prediction of mortality and to develop a mathematical model of abdominal sepsis designed to predict early mortality in severe patients, to be able to select patients for individual surgical treatment that have ongoing infection and require re-laparotomy. **Methods:** It study was based on data from comparing known severity scores for two surgical strategies in 231 patients admitted for sepsis or septic shock. In these patients the severity of the condition was assessed at admission and after 72 hours in accordance with the objectives of the study, including objective laboratory parameters and known severity rating scores. **Results:** One operation was performed in 67.5% of patients; in 20.8% of patients were performed re-laparotomy or re-laparoscopy 'on demand'; in 11.7% of patients surgical interventions were performed according to the 'program'. It well-known scores have shown the ability to predict early mortality: APACHE II scores (AUC 0.939) and SOFA (AUC 0.826). But of all patients who needed re-laparotomy/re-laparoscopy in 28.1% of the control patients identified with these scoring systems had negative results on re-laparotomy, although they had good and excellent AUC values for the APACHE II and SOFA scores. A mathematical model was developed for the early prediction of mortality, taking into account the preliminary values of systolic blood pressure (AUC 0.961), perfusion pressure of the abdominal cavity (AUC 0.893), C-reactive protein level (AUC 0.85) and lactate level (AUC 0.867). The results of this comparison in the whole sample gave a high accuracy of classification by groups: survivors-90.2%, non-survivors-81%, the overall accuracy was 87.6%. **Conclusion:** The severity scoring systems (APACHE II, SOFA), which were used to predict the overall outcome in patients with complicated intra-abdominal disease, did not provide an objective basis for patient stratification when performing re-debridement of the abdominal cavity for abdominal sepsis. A new mathematical model is proposed for calculating the probability of postoperative complications and death, depending on the initial severity of the patient's condition. There is also a need to further develop more specific tools to assist clinicians in the daily follow-up and screening of these patients after an initial emergency laparotomy.

Keywords: Abdominal sepsis; Prediction of early mortality; Mathematical model; Surgical strategies; Results

How to cite this article: Kryvoruchko IA et al. Predicting of Postoperative Mortality in Cases of Abdominal Sepsis for Two Surgical Strategies Using a New Mathematical Model: Two Centers Review of a 10 Years' Experience with the Same Diagnostic and Tactical Approaches to the Treatment AMHSR. 2021;11:383-392

Introduction

Sepsis, in spate of the progress made in its diagnosis and treatment, remains one of the main problems of modern medicine, as it is the leading cause of death in patients of intensive care units around the world, [1,2] occurs in approximately 1.7 million adults in the United States each year and causes the deaths of more than 250,000 of them. According to various studies, 30%-50% of all hospitalized patients who die from sepsis. Sepsis kills as many patients as myocardial infarction.

However, it is not known how to prevent death associated with sepsis, because it disproportionately affects the body of patients, especially the elderly, who have severe comorbidities and functional disorders. [3,4] Patients who have experienced sepsis are at risk of physical and cognitive impairment, and the risk of death in the next 5 years is more than twice as high as in other hospitalized patients. [5,6] According to the Centers for Disease Control and Prevention, in 2008 alone, $14.6 billion was spent on the treatment of hospitalized patients with sepsis in the United States, and from 1997 to 2008, the total costs adjusted taking into account inflation, the number of hospitalized patients with sepsis increased by an average of 11.9% annually.[7]

It is known that sepsis (from the ancient Greek sepsis-rot) is a pathological process, which is based on the body's responsein the form of generalized (systemic) inflammation to infection of various natures (bacterial, viral, fungal). Without using this term, the Greek physician hippocrates (460-370 BC) was probably the first to describe the clinical course of septic shock. Participants in the 1991 American college chest physicians/society critical care medicine conciliation conference, which aimed to identify sepsis based on fundamental developments in inflammation, formulated the concept of SIRS (Systemic Inflammatory Response Syndrome), emphasizing its non-specificity, [8-10] but the criteria of the syndrome itself were published later. [11]

Currently, a number of new provisions have been formulated, the criteria for sepsis and septic shock have been updated, and the final version of the document was published in three separate articles in the journal "JAMA". [12-14] The new document was referred to as the "Third international consensus on the definition of sepsis and septic shock (sepsis-3)". [15] There is a lot of data in the available literature on diagnosis, assessment of patients' severity using different severity scales and different biomarkers to predict the course of abdominal sepsis, choice of treatment tactics in patients, etc.

However, many researchers agree that despite the elucidation of the mechanisms of postoperative complications, mortality in the development of septic shock remains at a fairly high level and will be able to reach 80%. Therefore, the study of early laboratory criteria and biomarkers for severity in patients with sepsis is relevant the pathophysiological processes of this disease are well accepted. It involves not only the complex effects of systemic inflammation and immune dysfunction, but also acute failure of multiple organ systems in the body. [16] The immune response to infective agents may trigger a cascade of cytokines, causing cells impairment, organs failure, and ultimately result in the coagulopathy, which is significantly correlated to the prognosis of sepsis patients. [17] As the condition deteriorates, hypotension and tachycardia can occur due to cardiovascular disorders, and often associated with a poor prognosis. [18]

There are still a lot of ambiguity surrounding the risks stratification and prognostic evaluations of comprehensive indicators for sepsis nowadays. Consequently, it can be of great importance for patients with sepsis, as it establishes an accurate multi-index system for stratification of patients according to the strategy of surgical treatment.

The severity of infection and reversibility of organ dysfunction strongly affect the outcomes of sepsis patients. It has been shown that serum levels of lactate and pro-calcitonin, Sequential Organ Failure Assessment (SOFA), and Acute Physiology and Chronic Health Evaluation II (APACHE II) scores are predictive of fatal outcomes in patients with critical illness. [19] Although in other studies have assessed the predictive value of biomarkers [20,21] but most of these studies have focused only on inflammation or organ failure, complex biomarker evaluations have been rare. It also current research results were largely controversial [22] including studies that assess the diagnostic value of various scores of severity in the choice of surgical strategy in the treatment of this category of patients. [23]

The aim of study was to determine the prediction of mortality and to develop a mathematical model of abdominal sepsis designed to predict early mortality in severe patients, to be able to select patients for individual surgical treatment of abdominal sepsis that had ongoing infection and require reoperations.

Materials and Methods

231 adult patients of both sexes, aged 18-70 years, were hospitalized for sepsis or septic shock within 24 hours of admission to intensive care for sepsis-3 criteria and after preparation all patients were operated. Excluded criteria were: comorbidity with acute myocardial infarction and stroke; AS caused by 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 subjects were given initial surgery with effective «source control», supporting appropriate antibiotics, resuscitation, and organ support therapy using protective mechanical ventilation according to the Surviving Sepsis Campaign (SSC) 2016 guideline recommendations. All patients were divided into two groups: The first group was a comparison group (110 patients), who had been on treatment from January 2010 to April 2014, and in whom a treatment analysis was retrospectively conducted; the second-the main

(121 patients), who were treated from May 2014 to December 2020, and who prospectively studied the effectiveness of the proposed surgical approach, the basis of which was a revised approach to the implementation of surgery of the abdominal cavity, and the vector of the treatment was displaced in favor of performing re-laparotomy/re-laparoscopy on-demand if there were indications for repeated sanation of the abdominal cavity.

Evaluation of important results was compared to the use of modern systems to determine the predictive criteria for early mortality: qSOFA (upon admission to the hospital), APACHE-II score, and SOFA score (upon admission to the hospital, and 72 hours after surgery, as well as during the entire treatment period). Patients were evaluated level of endogenous intoxication, severity of the condition, Systolic Blood Pressure (SBP), Intra-Abdominal Pressure (IAP), Abdominal Perfusion Pressure (APP), Charlson Comorbidity Index (CCI), WBC count, blood hematocrit, platelets, lactate, Procalcitonin (PCT), C-Reactive Protein (CRP), blood creatinine, total bilirubin levels. Upon admission of the patients to the hospital a mathematical model investigations was developed and it was checked of the discriminant function after 72 hours after surgery in the course of complex treatment.

Subgroups of patients

Surgical treatment of the analyzed patients included two main components: Control of the source of infection (source control) and control of function of the affected organ and systemic protective mechanisms (damage control). Taking into account the surgical tactics of all patients, it was divided into three subgroups: 1 subgroup: 156 (67.5%) patients who underwent only one operation during which the source of infection was removed and there was no need to perform a re-laparotomy/re-laparoscopy; 2 subgroups: 48 (20.8%) patients who underwent on demand re-laparotomy (30) or re-laparoscopy (18); 3 subgroups: 27 (11.7%) patients, managed through surgical interventions on the program.

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-Wilkie test) of the selected indicators was assessed. Continuous data was presented as me (Q1; Q3), where me is the median, Q1 and Q3 is the Interquartile Range (IQR). The Spearman correlation coefficient and criterion X^2 were used for all patients; the nonparametric Mann-Whitney test was used for pairwise comparisons of means in independent groups, and the Wilcoxon test was used for dependent samples. Zero hypotheses (H0) in statistical tests were rejected at a significance level of p>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 AS: 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 ROC curve were determined for each scale 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 AUC index. The efficacy of the model was considered limited at AUC ≥ 0.70; good-at AUC ≥ 0.80; excellent-at AUC ≥ 0.90.

Results

In each groups, patients were divided according to the severity of the condition which was determined by the criteria of sepsis-3: [15] AS was diagnosed in 186 (80.5%), and septic shock in 45 (19.5%) patients.

The results of the distribution of patients by tactical approach by severity and mortality are presented in the Table 1.

Table 1: Demographic, clinical and laboratory characteristics of patients with AS.

Indicators	Before surgery		After 72 hours	
	Survivors	Non-survivors	Survivors	Non-survivors
Ages, Me (IQR)	52 (18-70)	51 (23-69)	-	-
	P=0.133			
Sex				
Male	89 (47.8%)	21 (46.7%)		
Female	97 (52.2%)	24 (53.3%)		
	NA		NA	
CCI , Me (IQR)	1	3	-	-

	(1-4) P=0.016	(1-5)		
WBC count (´109/ l), Me (IQR)	15.7 (12.2-17.3) P=0.000	16.8 (12.8-22.2)	15.6 (12.8-24.1) P=0.000	24.3 (16.4-28.6)
Platelets (´103/l), Me (IQR) (n=231)	294.5 (212.8-322.6) P=0.056	270.4 (236.5-309.7)	254.5 (234.6-281.3) P=0.000	170.6 (138.9-210.1)
Hematocrit (%), Me (IQR) (n=231)	38.2 (35.8-42.1) P=0.068	39.1 (36.4-43.8)	33.6 (29.4-36.5) P=0.003	39.8 (35.4-42.6)
Creatinine (mg/dl), Me (IQR) (n=231)	0.97 (0.86-1.109) P=0.104	0.99 (0.92-0.114)	0.93 (0.88-1.101) P=0.004	1.82 (1.46-2.21)
Total bilirubin (μmol/l), Me (IQR) (n=231)	24.5 (16.8-62.4) P=0.121	24.4 (21.2-74.6)	26.5 (14.5-44.7) P=0.000	57.5 (18.3-101.6)
Lactate (mmol/l), Me (IQR) (n=95)	2.1 (1.8-2.6) P=0.000	2.7 (2.1-6.9)	2.2 (1.9-4.6) P=0.000	4.9 (2.9-7.3)
PCT (pg/ml), Me (IQR) (n=84)	1.825 (0.123-72.242) P=0.358	1.934 (0.116-82.543)	2.783 (1.917-86.021) P=0.000	5.245 (2.456-154.873)
CRP (mg/l), Me (IQR) (n=76)	143 (121-166) P=0.000	175 (130-201)	153 (148-176) P=0.000	204 (160-213)
SBP (mm Hg), Me (IQR) (n=231)	115 (90-130) P=0.000	85 (70-100)	130 (90-155) P=0.000	130 (90-155)
APP (mm Hg), Me (IQR) (n=63)	70 (64-76) P=0.000	64 (58-70)	72 (64-78) P=0.000	62 (56-68)
qSOFA score (points), Me (IQR) (n=87)	2 (1-3) P=0.000	3 (2-3)	-	-
APACHE II score (points), Me (IQR) (n=231)	14 (8-21) P=0.000	24 (12-28)	11 (4-21) P=0.000	26 (15-32)
SOFA score (points), Me (IQR) (n=231)	9 (7-11)	12 (8-14)	8 (6-11)	14 (9-16)

	P=0.000		P=0.000
Shock	30 (16.1%)	29 (64.4%)	NA
Inotropic support	34 (18.3%)	38 (84.4%)	NA
Ventilation support	12 (6.5%)	45 (100%)	NA

P: Mann-Whitney test; NA: Not Applicable.

Understanding the pathophysiological essence of multiple dysfunctions of organs in AS as a result of the study showed the multifactorial nature of these critical processes that lead to damage to the cellular structures of organs and tissues and blood lactate will be able to an objective criterion for diagnosing of perfusion tissues disorders including in sepsis and septic shock. [15] At the same time, we revealed the presence of statistically significant differences according to Wilcoxon's and Spearman's criteria for APACHE II score, SOFA score, APP and lactate level upon admission of patients to the hospital and 78 hours after surgery and intensive care [Table 2].

Table 2: Statistical data between the studied parameters in patients with AS.

Indicators	Initial data (n=63)	Data after 72 hours (n=63)	Wilcoxon's test	Spearman's criterion
APACHE II score, Me (IQR)	14 (8-28)	11 (4-34)	W=158.0, z=1.941, p=0.052	r=0.824, p=0.000
SOFA score, Me (IQR)	11 (7-14)	9 (6-16)	W=126.0, z=1.924, p<0.002	r=0.683, p=0.000
APP (ммHg), Me (IQR)	68 (58-70)	66 (56-78)	W=382.0, z=4.523, p=0.000	r=0.917, p=0.000
Lactate (mmol/l), Me (IQR)	2.2 (1.8-6.9)	2.7 (1.9-7.3)	W= -306.0, z=3.884, p=0.000	r=0.786, p=0.000

The ability of selected scores SOFA and APACHE II scores to predict the early mortality in patients with AS according to ROC curves analysis was shown in Figures 1-3. It should be noted that qSOFA had the optimal cutoff value 2.5 points before surgery by criterion survivors/non-survivors (AUC 0.805, 95% CI 0.699-0.841), APACHE II score had the optimal cutoff value 12.5 points (AUC 0.939, 95% CI 0.809-0.945), and SOFA score had the optimal cutoff value 11.5 points (AUC 0.826, 95% CI 0.728-0.841). In 72 hours after surgery, the scores APACHE II (AUC 0.985, 95% CI 0.812-1.0) and SOFA (AUC 0.957, 95% CI 0.726-0.983) with the optimal cutoff 21.5 and 11.5 points had a good predictive value for the criterion 'survivors/non-survivors', respectively [Figure 1]. But of all patients requiring re-laparotomy, 28.1% of the control patients identified with these scoring systems had negative reoperation outcomes although they had good and excellent AUC values for the APACHE II and SOFA scores.

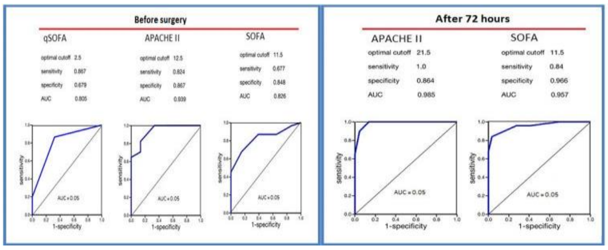

Figure 1: ROC curves of measured values in survivors and non-survivors patients with AS: Before surgery and in 72 hours after surgery.

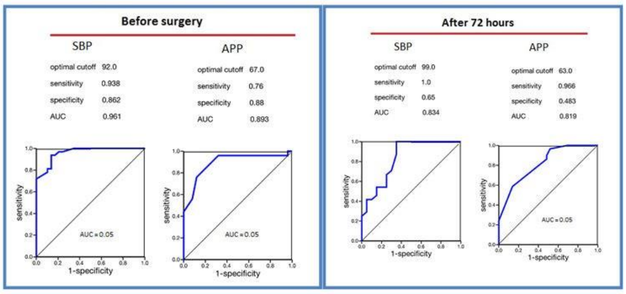

Figure 2: ROC curves of measured values in survivors and non-survivors patients with AS: before surgery and in 72 hours after surgery.

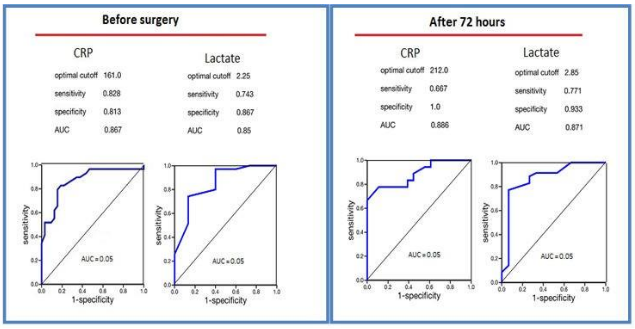

Figure 3: ROC curves of measured values in survivors and non-survivors patients with AS: before surgery and in 72 hours after surgery.

At the next stage all parameters the changes of which were most different in survivors and in non-survivors patients upon admission to the clinic were determined: SBP and APP, lactate and CRP levels [Table 1]. ROC curves for these values in patients on admission are shown in Figures 2 and 3.

These studies have shown that before surgery the most pronounced changes were to SPB (AUC 0.961, 95% CI 0.797-0.988) with optimal cutoff 92.0 mmHg and APP (AUC 0.893, 95% CI 0.749-0.923) with optimal cutoff 67.0 mmHg. The same trend of changes in these parameters was established 72 hours after surgery with optimal cutoff for SPB 99.0 mmHg and for APP 63.0 mmHg. Several classifications was worse for CRP (AUC 0.867, 95% CI 0.778-0.898) and lactate levels (AUC 0.85, 95% CI 0.742-0.881) with optimal cutoff 161.0 mg/l and 2.25 mmol/l before surgery and 212.0 mg/l (AUC 0.886) and 2.85 mmol/l (AUC 0.871) after 72 hours, respectively.

An analysis of the matrix of factor structure showing the values of the canonical correlation coefficient for the outcome predictors and standardized coefficients of the discriminant function was held. These analyses of the factor structure has showed how the selected indicators correlate with the discriminant function and have made to determine the contribution of each indicators to discrimination and to divide patients into groups and the matrix of factor structure. As can be seen from the matrix of factor structure [Table 3], the main role in discrimination is played by SBP (-0,555).

Table 3: A factor structure matrix.

Indicators	Value
SBP, mmHg	-0.555
CRP, mg/L	0.4
APP, mmHg	-0.47
Lactate, mmol/L	0.51

Table 4: Standardized coefficients of discriminant function.

Indicators	Value
SBP, mmHg	-0.735
CRP, mg/L	0.307
APP, mmHg	-0.532
Lactate, mmol/L	0.426

The contribution of variables to discrimination was measured by the value of standardized coefficients for variables in the discriminant function. Determination of standardized coefficients of the discriminant function showed that SPB (-0.735) and APP (-0.532) have played the most major role in discrimination and the following were lactate level (0.426) and CRP (0.307) and these data by two groups (survivor/non-survivor) are presented in Tables 4 and 5.

Table 5: Characteristic classification function coefficients for patients with AS.

Variables	Non-survivors	Survivors
SBP, mmHg	0.85	1.04
CRP, mg/L	0.56	0.5
APP, mmHg	5.96	6.44
Lactate, mmol/L	20.32	16.83
Constant	-301.9	-335.7

The next step for the patients were calculated the group whose qualification function was the highest and thus, the groups were predicted in a particular patient on admission to the hospital and its are listed below:

$$F_{\text{non-survivors}} = -301.9 + 0.85 \times X1 + 0.56 \times X2 + 5.96 \times X3 + 20.32 \times X4$$

$$F_{\text{survivors}} = -335.8 + 1.04 \times X1 + 0.5 \times X2 + 6.44 \times X3 + 16.8 \times X4,$$

Note: X1: SBP (mm/Hg); X2: CRP (mg/L); X3: APP (mm/Hg); X4: Serum lactate (mmol/L).

Since there were only two groups in our classification (survivors/non S survivors), the calculations can be significantly simplified if we consider not the functions themselves but their differences:

$$F\ survivors - F\ non\text{-}survivors = \Delta F = \geq 0\ survivors / < 0\ non\text{-}survivors$$

$$\Delta F = F\ survivors - F\ non\text{-}survivors = -33.8 + 0.19 \times X1 - 0.06 \times X2 + 0.48 \times X3 - 3.5 \times X4$$

Table 6: A matrix of a posteriori classification.

Groups of patients	Columns-the predicted groups	Series-the observed groups	
	The percentage of true matching	Non-survivors	Survivors
Non-survivors	81%	17	4
Survivors	90.20%	6	54
Totally	87.60%	23	58

Verification of the obtained discriminant model was performed using a posteriori classification, when it was assumed that the outcome of treatment was unknown and it has predicted on the basis of the obtained classification functions. Comparing the results of forecasting with the results of treatment allowed us to assess the adequacy of the discriminant model. The results of this comparison in the whole sample (81 patients) gave a high accuracy of classification by groups: Survivors: 90.2%, non-survivors: 81%, the overall accuracy was 87.6% [Table 6].

In the comparison group semi-open re-laparotomy procedures were performed on average 3.5 (1-7) for 6 days (1-9), and open methods in the amount of 4 (2-7) for 6.5 days (1-12). In the main group, re-laparoscopy procedures were performed on average 3 (1-5) were performed for 4 days (2-7), and open methods of re-laparotomy in the amount of 3 (1-4) for 5 days (4-7). These results are presented in Table 7. In Table 8 was showed the postoperative complications that caused the death of patients: in the comparison group postoperative complications (n=67) were occurred in 47 patients (56%) and 27 patients were died (32.1%); in the main group postoperative complications (n=37) were occurred in 34 patients (29.1%) and 31 patients (26.5%) were died [Table 7]. The main causes of mortality among the patients under consideration were the following: postoperative multiple organ dysfunction was in 19.9% (40 patients), persistent AS was in 5% (10 patients), intestinal fistulas due to suppuration of the wound and surgery was in 1.5% (3 patients), myocardial infarction was in 1% (2 patients) and pulmonary artery thromboembolism was in 1.5% (3 patients). The rest of the complications were managed by complex medical measures.

Table 7: The results of the distribution of subgroups of patients by severity, types of surgery procedures and mortality.

Subgroups of patients	AS	Septic shock	Died	%	Totally
The patients who have used closed surgery	142	14	28	17.9	156
The patients who have used 'on demand' re-laparotomy/re-laparoscopy	32	16	16	33.3	48
The patients who have used 'programmed' re-laparotomy/re-laparoscopy	12	15	14	51.9	27
Totally	186	45	58	25.1	231

X2=47.165, P=0.000

Table 8: Postoperative complications in patients with AS.

The postoperative complications	Comparison group, n=110	Main group, n=121
Postoperative MODS	26 (23.6%)	14 (11.6%)
Persistent AS	3 (2.7%)	3 (2.3%)
Suppuration of the wound and atmospheric intestinalfistula	3 (2.7%)	1 (0.8%)
Pulmonary artery thromboembolism	1(0.9%)	4(3.3%)

Myocardial infarction	1(0.9%)	5(4.1%)
Other	14(12.7%)	11(9.1%)
Died	31(28.2%)	27(22.3%)

X2=8.377, P=0.05

Discussion

The problem of diagnosis and surgical treatment of abdominal sepsis remains relevant due to the preservation of a fairly high percentage of unsatisfactory treatment results (from 30.0% to 50.0%). The search continues for biological markers that may be associated with the presence of infection in the body, the level of the inflammatory response and sepsis. In addition, when studying the epidemiology of sepsis from the perspective of the Sepsis-3 criteria, it is important to understand whether the new diagnostic concept will lead to a change in the number of reported cases of sepsis. Considering that a necessary criterion for the diagnosis of sepsis is the mandatory presence of organ dysfunction, it is logical to assume that the reported incidence will decrease. Nevertheless, in the study by Mellhammar, when comparing the incidence of sepsis according to the sepsis-1 and sepsis-3 criteria in the same population, the following indicators: 687 cases and 780 cases per 100 thousand population, respectively, but the actual coincidence of the diagnosis was obtained only in approximately 50% of patients. [24]

The analysis of predictors of early mortality remains relevant, especially when it is necessary to perform repeated surgical interventions due to the ineffectiveness of the primary surgical intervention in the abdominal cavity. We would like to point out that multiple studies have explored the association between different indicators and prognosis in critically surgical ill patients. [25-28]

In accordance with the currentrecommendations 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 [29-31] andat the same time, the several meta-analyzes have showed that qSOFA, which was recommended in the new recommendations sepsis-3, was poorly sensitive and moderately specific for the risk of death [32] or had of moderate predictive value in both septic and non-septic patients. [33] Due to the lack of a gold standard for determining the diagnosis of sepsis, the most large-scale studies are focused on determining the prognostic rather than diagnostic significance of various scales and biomarkers in patients with infections. [34] This approach allows one to get rid of the influence of one or another dominant diagnostic concept and to identify patients with an increased risk of death.

In two Meta-analyzes published to date it is the predictive value of the qSOFA score that has been studied. [35,36] In a study by Maitra, the combined sensitivity and specificity for qSOFA ≥ 2 points in predicting death in ICU and out-of-ICU patients were 56 (95% CI 47–65%) and 78 (95% CI 71–83%), respectively. [37] A meta-analysis by Song et al. (2018), including the non-ICU patient population, compared the predictive value of the qSOFA score and the SIRS criteria. For the qSOFA score and SIRS criteria in the prognosis of death the combined sensitivity was 51 (95% CI 39-62%) and 86 (95% CI 79-92%), specificity: 83 (95% CI 74-89 %) and 29 (95% CI 17–45%), respectively. [38] In our study, it was shown that the qSOFA scale has high sensitivity (86.7%), but low specificity (67.9%) with an area under the ROC curve of 0.805 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 and excellent prediction results the early mortality in patients with AS when analyzing ROC curves. It should be noted that APACHE II score had the optimal cutoff value 12.5 points (AUC 0.939, 95% CI 0.809-0.945) before surgery by criterion survivors/non- survivors, and SOFA score had the optimal cutoff value 11.5 points (AUC 0.826, 95% CI 0.728-0.841). In 72 hours after surgery, the scores APACHE II (AUC 0.985, 95% CI 0.812-1.0) and SOFA (AUC 0.957, 95% CI 0.726-0.983) with the optimal cutoff 21.5 and 11.5 points had a good predictive value for the criterion 'survivors/non-survivors', respectively. But of all patients requiring re-laparotomy, 28.1% of the control patients identified with these scoring systems had negative reoperation outcomes although they had good and excellent AUC values for the APACHE II and SOFA scores.

It is known that many biomarkers, such as lactate, procalcitonin and C-reactive protein, are powerful predictors of sepsis and adverse outcomes. [33,39,40] This study has showed that only lactate (sensitivity 82.8%, specificity 81.3%, area under the ROC curve 0.867 before surgery) and C-reactive protein (sensitivity 74.3%, specificity 86.7% area under the ROC curve 0.85 preoperative) in assessing systolic blood pressure (sensitivity 93.8%, specificity 86.2%, area under the ROC curve 0.961 before surgery) and perfusion pressure in the abdominal cavity (sensitivity 76%, specificity 88%, area under the ROC curve 0.893 before surgery) and showed the significance of these indicators for predicting early mortality which was confirmed by the definition of standardized coefficients of the discriminant function: SPB (0.735), APP (0.532), lactate (0.426) and CRP (0.307) levels have made the most important contribution to prediction. This have made it possible to divide patients into two groups according to the "survivors/non-survivors" criterion, and multivariate analysis of variance for express diagnostics of early mortality made it possible to create a mathematical model with an overall accuracy of 87.6%. [41]

It is well known that rapid diagnosis and effective treatment of AS are crucial for this category of patients, and it based on the etiology, severity, the duration of the delay in diagnosis, prognosis, etc. There are three main points in the treatment of the patients with AS: 1) The timing of the operation and decision-making; 2) Intraoperative findings; 3) Postoperative treatment. During the past three decades, there has been changed for management of these patients with used two main principles such as source control and damage control with using the various sophisticated and highly accurate noninvasive imaging modalities at surgeon's disposal. Early mortality in these patients, which is usually associated with septic shock and MOF due to severe intra-abdominal infection, currently remains high enough. In our opinion, the use of early diagnosis, the choice of appropriate surgical methods to identify and eliminate the source of infection and personalized treatment of complications after surgery was factors that reduced mortality in patients. This study showed that the prognosis of treatment of patients with AS and septic shock is the most appropriate for assessment in terms of postoperative complications and mortality. The proposed system allows predicting the development of complications and mortality. The probability of death when using re-laparotomy on the program was in 2.3 times higher than when using re-laparotomy on demand.

Conclusion

The severity scoring systems (APACHE II, SOFA), which were used to predict the overall outcome in patients with complicated intra-abdominal disease, did not provide an objective basis for patient stratification when performing re-debridement of the abdominal cavity for abdominal sepsis. A new mathematical model is proposed for calculating the probability of postoperative complications and death, depending on the initial severity of the patient's condition. There is also a need to further develop more specific tools to assist clinicians in the daily follow-up and screening of these patients after an initial emergency laparotomy. A new mathematical model was proposed for calculating the probability of postoperative complications and death, depending on the initial severity of the patient's condition. There is a need to develop more specific tools to assist clinicians in the daily follow-up and screening of these patients after initial emergency laparotomy. In patients with AS and septic shock, the most appropriate in terms of reducing the number of cases of postoperative complications and mortality was a tactical approach using re-laparotomy «on demand».

Acknowledgements

The authors are thanked the Rector of the Kharkiv National Medical University, Professor Kapustnyk VA and the Head of Academic Council, Professor Lisovyi VM for supporting this study. The authors are very grateful to the Municipal non-commercial enterprise of Kharkiv regional council, regional clinical hospital and the Zaitcev Institute of General and Emergency Surgery NAMS of Ukraine for providing all the diagnostic and surgical equipment used in this study.

References

1. Vincent JL, Marshall JC, Namendys-Silva SA, François B, Martin-Loeches I, pickers P, et al. Assessment of the worldwide burden of critical illness: TheIntensive Care Over Nations (ICON) audit. Lancet Respir Med. 2014; 2(5): 380-386.
2. Rhee C, Dantes R, Epstein L, Murphy DJ, Seymour CW, Wang R, et al. Incidence and trends of sepsis in US hospitals using clinical *vs.* claims data, 2009-2014. JAMA. 2017;318(13):1241-1249.
3. Liu V, Escobar GJ, Greene JD, Soule J, Whippy A, Angus DC, et al. Hospital deaths in patients with sepsis from 2 independent cohorts. JAMA. 2014; 312(1): 90-92.
4. Quartin AA, Schein RM, Kett DH, Peduzzi PN. Magnitude and duration of the effect of sepsis on survival. Department of veterans affairs systemic sepsis cooperative studies group. JAMA. 1997; 277(13):1058-1063.
5. Heffner AC, Horton JM, Marchick MR, Jones AE. Etiology of illness in patients with severe sepsis admitted to the hospital from the emergency department. Clin Infect Dis. 2010;50(6):814-820.
6. Nathan C. Points of control in inflammation. Nature. 2002; 420(6917): 846-852.
7. Bone RC.Toward an epidemiology and natural history of SIRS (Systemic Inflammatory Response Syndrome). JAMA. 1992; 268(24):3452–3455.
8. Bone RC. Sir Isaac Newton, sepsis, SIRS, and CARS. Crit Care Med. 1996; 24(7): 1125-1128.
9. Bone RC. Toward a theory regarding the pathogenesis of the systemic inflammatory response syndrome: What we do and do not know about cytokine regulation. Crit Care Med. 1996(1); 24:163-172.
10. Marshall JR, Aarts MA. From celsus to galen to bone: The illnesses, syndromes and diseases of acute inflammation. Year of intensive care and emergency medicine. 2001.
11. Seymour CW, Liu VX, Iwashyna TJ, Brunkhorst FM, Rea TD, Scherag A, et al. Assessment of clinical criteria for sepsis: For the third international consensus definitions for sepsis and septic shock (Sepsis-3). JAMA. 2016; 315(8): 762-774.
12. Shankar HM, Phillips G, Levy M, Seymour CW, Liu VX, Angus DC et al. Developing a new definition and assessing new clinical criteria for septic shock for the third international consensus definitions for sepsis and septic shock (Sepsis-3). JAMA. 2016; 315(8):775-787.
13. Singer M, Deuschman CS, Seymour CW, Shankar-Hari M, Bauer M, Angus DCet al. The third international consensus definitions for sepsis and septic shock (Sepsis-3). JAMA. 2016; 315(8): 801-810.
14. Kryvoruchko IA, Boyko VV, Ivanova YV, Andreieshchev SA. Sepsis–3: Renewed determinations, potential problems and further practical footsteps. Klinichnakhirurhiia. 2019; 86(6):60-72.
15. Liu Y, Han N, Li Q, Li Z. Regulatory mechanisms underlying sepsis progression in patients with tumor necrosis factor-alpha genetic variations. ExpTher Med. 2016; 12(1): 323-328.
16. Costa RT, de Araújo OR, Brunialti MKB, Assunção MCS, Azevedo LCP, FlávioFreitas F, et al. T helper type cytokines in sepsis: Time-shared variance and correlation with organ dysfunction and hospital mortality. Braz J Infect Dis. 2019; 23(2): 79-85.
17. Guarracino F, Bertini P, Pinsky MR. Cardiovascular determinants of resuscitation from sepsis and septic shock. Crit Care. 2019; 23(1):118.
18. Liu Z, Meng Z, Li Y, Zhao J, Wu S, Gou S, et al. Prognostic accuracy of the serum lactate level, the SOFA score and the

qSOFA score for mortality among adults with sepsis. Scand J Trauma ResuscEmerg Med 2019; 27(1):51.

19. Innocenti F, Meo F, Giacomelli I, Tozzi C, Ralli ML, DonniniCC, et al. Prognostic value of serial lactate levels in septic patients with and without shock. Intern Emerg Med. (2019); 14(8): 1321-1330.
20. Yu G, Yoo SJ, Lee SH, Kim JS, Jung S. Utility of the early lactate area score as a prognostic marker for septic shock patients in the emergency department. Acute Crit Care. 2019; 34(2), 126-132.
21. Liu J, Bai C, Li B, Aijun SA, Shi F, Yao C, et al. Mortality prediction using a novel combination of biomarkers in the first day of sepsis in intensive care units. Scientific Reports. 2021;11:1275.
22. Van Ruler O, Kiewiet JJS, Boer KR, Lamme B, Gouma DJ,Reitsma JB, et al. Failure of available scoring systems to predict ongoing infection in patients with abdominal sepsis after their initial emergency laparotomy. BMC Surg. 2011; 11: 38.
23. Mellhammar L, Wullt S, Lindberg A. Sepsis incidence: a population-based study. Open forum infectious diseases. Open Forum Infect Dis. 2016; 3(4).
24. Lee ChW, Kou HW, Chou HS, Chou HH, Huang SF, Wu CH, et al. A combination of SOFA score and biomarkers gives a better prediction of septic AKI and in-hospital mortality in critically ill surgical patients: A pilot study. World J Emerg Surg. 2018; 13: 41.
25. Faix JD. Biomarkers of sepsis. Crit Rev Clin Lab Sci. 2013; 50(1): 23-36.
26. PawełMajewski P, Zegan-Barańska M, Karolak I, Kaim K, Żukowski M, Kotfis K. Current evidence regarding biomarkers used to aid postoperative delirium diagnosis in the field of cardiac surgery:Review. Medicina (Kaunas). 2020; 56(10): 493.
27. Kelly BJ, Lautenbach E, Irving NI, Coffin SE, Gerber JS, Fuchs BD, et al. Combined biomarkers predict acute mortality among critically ill patients with suspected sepsis. Crit Care Med. 2018; 46(7): 1106-1113.
28. Koch C, Edinger F, Fischer T, Brenck F, Hecker A, Katzer K, et al. Comparison of qSOFA score, SOFA score, and SIRS criteria for the prediction of infection and mortality among surgical intermediate and intensive care patients. World J Emerg Surg. 2020; 15(1):63.
29. Seymour CW, Liu VX, Iwashyna TJ, Brunkhorst FM, Rea TD, Scherag A, et al. Assessment of clinical criteria for sepsis: For the third international consensus definitions for sepsis and septic shock(Sepsis-3). JAMA. 2016; 315: 762-774.
30. Kovach CP, Fletcher GS, Rudd KE, Grant RM, Carlbom DJ. Comparative prognostic accuracy of sepsis scores for hospital mortality in adults with suspected infection in non-ICU and ICU at an academic public hospital. PLoS One. 2019; 14(9).
31. Fernando SM, Tran A, Taljaard M, Cheng W, Rochwerg B, Seely AJE, et al. Prognostic accuracy of the quick sequential organ failure assessment for mortality in patients with suspected infection: A systematic review and meta-analysis. Ann Intern Med. 2018; 168(4): 266-275.
32. Ho KM, Lan NS. Combining quick sequential organ failure assessment with plasma lactate concentration is comparable to standard sequential organ failure assessment score in predicting mortality of patients with and without suspected infection. J Crit Care. 2017; 38:1-5.
33. Wacharasint P, Nakada TA, Boyd JH, Russell JA, Walley KR. Normal-range blood lactate concentration in septic shock is prognostic and predictive. Shock. 2012; 38(1): 4-10.
34. Vincent JL, Opal SM, Marshall JC, Tracey KJ. Sepsis definitions: Time for change. Lancet. 2013; 381: 774-775.
35. Jawad I, Lukšić I, Rafnsson SB. Assessing available information on the burden of sepsis: global estimates of incidence, prevalence and mortality. J Global Health. 2012; 2(1): 010404.
36. Shankar-Hari M, Phillips GS, Levy ML,Singer M, Angus DC, Rubenfeld GD, et al. Developing a new definition and assessing new clinical criteria for septic shock: for the third international consensus definitions for sepsis and septic shock (Sepsis-3). JAMA. 2016; 315(8): 775-787.
37. Maitra S, Som A, Bhattacharjee S. Accuracy of quick Sequential Organ Failure Assessment (qSOFA) score and systemic inflammatory response syndrome (SIRS) criteria for predicting mortality in hospitalized patients with suspected infection: a meta-analysis of observational studies. ClinMicrobiol Infection. 2018; 24(11): 1123-1129.
38. Song JU, Sin CK, Park HK, Shim SR, Lee J.. Performance of the quick Sequential (sepsis-related) organ failure assessment score as a prognostic tool in infected patients outside the intensive care unit: A systematic review and meta-analysis. Crit Care. 2018; 22(1): 28.
39. Chu DC, Mehta AB, Walkey AJ. Practice patterns and outcomes associated with procalcitonin use in critically ill patients with sepsis. Clin Infect Diseases. 2017; 64(11):1509-1515.
40. Simon L, Gauvin F, Amre DK,saint-Louis P, Lacroix J. Serum procalcitonin and C-reactive protein levels as markers of bacterial infection: A systematic review and meta-analysis. Clin Infect Diseases. 2004; 39(2):206-217.