PREDICTIVE MODEL FOR MORTALITY IN PATIENTS WITH ABDOMINAL SEPSIS

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Mortality among patients with various forms of sepsis is 36.2–47.7%. Predicting the likelihood of death associated with sepsis is critically important for clinical decision-making, stratifying patient risk, and improving overall survival. The study aimed to develop a mathematical model for predicting the outcome of sepsis in patients with abdominal surgical pathology. The study involved 64 patients diagnosed with abdominal sepsis (AS). Based on the AS outcomes, group 1 (n = 46) with favorable outcomes and group 2 (n = 18) with fatal outcomes were allocated. Clinical scales and laboratory testing methods were used to evaluate parameters on days 1, 3, and 7 since the AS diagnosis. On days 3 and 7, SOFA scores of the group with adverse AS outcomes were significantly higher, than that of the group with favorable outcomes. Complete blood counts of patients in group 2 showed the decrease in absolute lymphocyte counts on day 1 compared to group 1. As for blood biochemistry parameters, elevated serum levels of C-reactive protein, urea, creatinine, lactate, procalcitonin, direct bilirubin, as well as aspartate aminotransferase, alanine aminotransferase, and alkaline phosphatase activity were observed. Furthermore, a decrease in respiratory index on days 3 and 7 and venous oxygen saturation on days 1 and 7 was observed. A logistic regression model was constructed, and a software tool "Calculator for Predicting Mortality in AS" was developed. A model to predict the probability of fatal outcome in patients with AS was created. High serum CRP and creatinine levels, as well as the decrease in venous oxygen saturation serve as significant prognostic markers of fatal outcome in patients with AS.

Keywords: abdominal sepsis, mortality, prognosis, model

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МОДЕЛЬ ПРОГНОЗА ВЕРОЯТНОСТИ ЛЕТАЛЬНОГО ИСХОДА У БОЛЬНЫХ С АБДОМИНАЛЬНЫМ СЕПСИСОМ

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Летальность среди пациентов с различными формами сепсиса составляет 36,2–47,7%. Прогнозирование вероятности летального исхода при сепсисе критически важно для принятия клинических решений, стратификации риска пациентов и улучшения общей выживаемости. Целью исследования было разработать математическую модель прогноза исхода сепсиса у пациентов с абдоминальной хирургической патологией. Исследование выполняли на 64 больных с диагностированным абдоминальным сепсисом (АС). В зависимости от исходов АС были выделены группа 1 (n = 46) с благоприятным исходом и группа 2 (n = 18) с летальным исходом. Использовали клинические шкалы и лабораторные методы исследования с оценкой показателей на 1, 3 и 7 сутки с момента диагностирования АС. На 3 и 7 сутки показатели SOFA в группе с неблагоприятным исходом АС были значимо выше, чем в группе с благоприятным исходом. В общем анализе крови у пациентов в группе 2 наблюдалось уменьшение абсолютного количества лимфоцитов на 1 сутки в сравнении с группой 1. Среди биохимических показателей выявлено увеличение концентрации в сыворотке С-реактивного белка, мочевины, креатинина, лактата, прокальцитонина, прямого билирубина, активности аспартатаминотрансферазы, аланинаминотрасферазы и щелочной фосфатазы. Также в группе 2 выявлено снижение респираторного индекса на 3 и 7 сутки, насыщения венозной крови кислородом — на 1 и 7 сутки. Построена модель логистической регрессии и создана программа для ЭВМ «Калькулятор прогноза летальности при АС». Разработана модель вероятности летального исхода у пациентов с АС. Высокий уровень С-РБ, креатинина в сыворотке крови, а также снижение насыщения венозной крови кислородом служат значимыми прогностическими маркерами летального исхода у пациентов с АС.

Ключевые слова: абдоминальный сепсис, летальность, прогноз, модель

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Sepsis is a model disorder underpinned by body's response to infection of various genesis (bacterial, viral, fungal) in the form of generalized (systemic) inflammation resulting in acute multiple organ dysfunction [1]. Mortality among patients with various forms of sepsis admitted to intensive care units all over the world is 36.2–47.7% [2]. In sepsis, the most common sources of infection are lungs (64%), abdominal cavity (20%), circulatory system (15%), and urinary tract (14%) [3].

Abdominal sepsis (AS) is a syndrome underpinned by body's systemic inflammatory response to intra-abdominal infection resulting in acute organ dysfunction [4]. Intra-abdominal infections rank second among the causes of sepsis after pulmonary lesions [4]. Complicated intra-abdominal infections lead to the development of local or diffuse peritonitis, thereby causing organ failure and eventually AS [4]. The AS-associated mortality varies between 7.6 and 36% [4].

Many clinical and laboratory markers are not sensitive and specific enough for predition of sepsis outcomes due to complex pathophysiological mechanisms. Today, the WSES (World Society of Emergency Surgery) sepsis severity score is used to predict the course of AS in patients with complicated intra-abdominal infections, and the PIPAS severity score is used in patiens with acute peritonitis to determine treatment efficacy and mortality rate [5, 6]. A multi-marker approach will make it possible to construct a mathematical model of a patient depending on the disease outcome, as well as to characterize a personal forecast. In recent years, the algorithms for predicting AS outcomes involving the use of the Akaike information criterion (AIC) for linear regression models were superior to conventional statistical methods [7]. The mathematical model for predicting the probability of fatal outcome in patients with AS will make it possible to change surgical treatment tactics, ensure timely determination of indications for extracorporeal methods of treatment (selective cytokine hemoadsorption combined with adsorption of lipopolysaccharides, hemodiafiltration, plasma exchange, selective plasma filtration) and intensify therapy.

The study aimed to develop a mathematical model for predicting fatal outcome of sepsis in patients with abdominal surgical pathology.

METHODS

We conducted a cross-sectional study by the continuous sampling methods as patients with abdominal surgical pathology were admitted to the intensive care unit of the Chelyabinsk City Clinical Hospital No. 8, who earlier underwent surgery involving debridement of primary lesion within the first 24 h of hospital stay. All patients of the sample were diagnosed with sepsis in accordance with the current Sepsis-3 concept. The sample was represented by 64 patients aged 32–82 years. Inclusion criteria: age over 18 years; availability of written informed consent, abdominal surgery within the first 24 h of ongoing hospital stay; verified focus of intra-abdominal infection (bacterial culture test and / or direct monitoring of the site of infection); organ dysfunction (SOFA score > 2 points). Exclusion criteria: developing intra-abdominal infection during the hospital stay; preceding immunotropic, antibacterial therapy, taking anticoagulants within 90 days; malignant neoplasms; history of autoimmune disorder, allergy, immunodeficit; earlier disgnosed hereditary disorders of hemostasis; pregnancy.

Dependence on the disease outcome was chosen as a criterion for patient division: group 1 was formed 1 (n = 46) with beneficial AS outcomes and group 2 (n = 18) with fatal AS outcomes. In accordance with the Sepsis-3 concept the patient condition severity was assessed using the Sequential Organ Failure Assessment (SOFA) Score [8, 9]. Thrombohemorrhagic disorders were assessed using the International Society on Thrombosis and Haemostasis ISTH/SSC score, criteria for sepsis-induced coagulopathy (SIC) [10].

Whole peripheral blood, its plasma and serum were used for laboratory testing. Partial pressure of arterial oxygen (PaO_2) for calculation of respiratory index (PaO_2/FiO_2), acid-base balance of venous blood (blood pH), bicarbonate ion concentration (SB), base excess or deficit (BE), venous oxygen saturation (SvO_2) were tested using the ABL 800 FLEX radiometer (Radiometer Medical ApS, Denmark). Serum biochemistry indicators (α-amylase, total and direct bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), urea, creatinine, alkaline phosphatase, blood glucose, lactate) were tested using the Mindray BS — 800 M biochemical analyzer (Mindray, China). Complete blood counts were determined using the Sysmex XT — 1800i / XT – 2000i analyzer (Sysmex, Japan). Prothrombin time (PT), prothrombin index (PI), international normalized ratio (INR), activated partial thromboplastin time (aPTT), plasma fibrinogen concentration were assessed using the Technology Solution coagulometer (Technology Solution, Japan). Serum concentrations of procalcitonin and standard C-reactive protein (CRP) were determined by enzyme immunoassay using the Personal Lab analyzer (Adaltis, Italy).

Statistical processing of the results was performed using the SPSS 17.0 software package (IBM, USA). To describe quantitative traits, the median (Me), lower and upper quartiles (LQ; UQ) were calculated. A distribution was tested for normality using the Kolmogorov–Smirnov test. Based on quantitative traits the groups of patients were compared using the Kruskal–Wallis test and Mann–Whitney U test. The confidence level was $p < 0.05$. The data obtained were used when developing a software tool for predicting sepsis outcomes in patients with abdominal surgical pathology by the logistic regression method.

RESULTS

Among patients with AS, fatal outcomes were reported in 18 individuals (28.1%) during the follow-up period. The analysis of clinical prognostic scores showed that SOFA scores reported on days 3 and 7 in the group with adverse AS outcomes were significantly higher, than in the group with beneficial outcomes (Table 1).

In the group of patients with adverse AS outcomes, complete blood counts reported on days 1 and 3 showed anemia with the red blood cell counts, hemoglobin concentration, hematocrit decreased relative to the generally accepted reference values, as well as with thrombocytopenia, leukocytosis and neutrophilia, lymphocytopenia. During follow-up absolute basophil and eosinophil counts were elevated on day 7, and monocyte counts were elevated on days 3 and 7 (Table 2). In the group of patients with beneficial outcomes, there was a significant increase in absolute eosinophil counts on day 7 relative to the indicators reported on days 1 and 3. In patients with adverse AS outcomes, a significant decrease in absolute lymphocyte and monocyte counts relative to the group with beneficial AS outcomes was observed on day 1.

In patients with AS of both groups, high CRP, procalcitonin and direct bilirubin levels relative to reference values were reported on days 1, 3, and 7 (Table 3). The group of patients wuth adverse AS outcomes also showed growth of serum urea, creatinine, lactate and alkaline phosphatase levels. During follow-up of the group of patients with adverse AS outcomes there was a significant decrease in concentrations of α-amylase, direct and total bilirubin on day 7 relative to the indicators

Table 1. Clinical and prognostic scores of patients with beneficial and adverse AS outcomes, Me (LQ; UQ)

Indicators	Group 1 — patients with beneficial AS outcomes (n = 46)			Group 2 — patients with adverse AS outcomes (n = 18)		
	Day 1 (n = 46)	Day 3 (n = 46)	Day 7 (n = 46)	Day 1 (n = 18)	Day 3 (n = 14)	Day 3 (n = 10)
SOFA, points	6.0 [5.0; 9.0]	5.0 [3.0; 8.0]	5.0 [2.5; 10.0]	8.0 [5.0; 14.0]	12.0 [8.0; 14.0]*	10.0 [10.0; 10.0]*
SIC score, points	4.00 [4.00; 5.00]	4.00 [4.00; 5.00]	4.5 [4.00; 5.00]	4.00 [4.00; 5.00]	4.00 [4.00; 5.00]	5.00 [4.00; 5.00]
DIC 1 score, points	4.00 [4.00; 5.00]	4.00 [4.00; 5.00]	4.00 [4.00; 5.50]	4.00 [4.00; 4.00]	5.00 [4.00; 6.00]	5.00 [5.00; 5.00]

Note: * — significant ($p < 0.05$) differences from group 1 on appropriate day.

reported on days 1 and 3. In contrast, ALT activity significantly increased on days 3 and 7, and AST activity increased on day 7 relative to day 1. Serum lactate concentration significantly decreased on days 3 and 7 relative to day 1. Procalcitonin levels significantly increased on day 3 and decreased on day 7 relative to days 1 and 3, respectively. In the group of patients with beneficial AS outcomes there was a significant decrease in serum concentrations of total bilirubin on day 3, as well as of direct bilirubin and procalcitonin levels on days 3 and 7 relative to day 1. In the group of patients with adverse AS outcomes, a significant increase in serum CRP, urea, creatinine, and lactate levels was reported on day 1 relative to the group with beneficial AS outcomes. During follow-up, concentrations of procalcitonin, urea, creatinine, AST, ALT, direct bilirubin and alkaline phosphatase increased on day 3, and concentrations of procalcitonin, creatinine, urea, ALT, alkaline phosphatase and C-reactive protein increased on day 7. In patients with adverse outcomes, GFR was significantly lower on days 3 and 7.

In patients with AS of both groups on all days of follow-up there was growth of D-dimer, fibrinogen and INR relative to reference values. Growth of aPTT and PT was reported for the group with adverse outcomes on day 1 (Table 4). In the group of patients with adverse AS outcomes, there was a significant decrease in PT, INR, and D-dimer levels on day 3 relative to day 1. During follow-up, there was also a significant decrease in D-dimer levels, aPTT, and PT on day 7 relative to that reported on day 1, along with PI relative to days 1 and 3. A significant decrease in PI on day 7 relative to the values reported on days 1 and 3 was revealed in patients of the group with beneficial outcomes. Patients with adverse AS outcomes showed a significant PI decrease on days 3 and 7, along with the increase in aPTT and PT on day 1 relative to the group with beneficial AS outcomes.

In patients with AS of groups 1 and 2, low respiratory index (PaO_2/FiO_2), venous oxygen saturation (SvO_2) relative to the generally accepted reference values had been reported throughout all days of follow-up. When interpreting the acid-base balance of patients with adverse AS outcomes, decompensated metabolic acidosis was reported on day 1 of follow-up, and in the group of patients with beneficial AS outcomes there was compensated metabolic acidosis on days 1 and 3 (Table 5). In the group of patients with adverse AS outcomes, there was a significant increase in bicarbonate ion levels (SB) relative to the values reported on day 3, as well as the decrease in PaO_2/FiO_2 on day 7 relative to days 1 and 3. In the group of patients with adverse outcomes there was a significant decrease in PaO_2/FiO_2 on days 3 and 7 and the decrease in SvO_2 on days 1 and 7 relative to the group of patients with beneficial AS outcomes. Similar alterations were reported for venous blood pH and SB concentration on day 1.

Table 2. Complete blood counts of patients with AS, Me (LQ; UQ)

Indicators/reference values	Group 1 — beneficial AS outcome (n = 46)			Group 2 — adverse AS outcome (n = 18)		
	Day 1 (n = 46)	Day 3 (n = 46)	Day 7 (n = 46)	Day 1 (n = 18)	Day 3 (n = 14)	Day 7 (n = 10)
Red blood cells / 3.5–6 × 10^{12}/L	4.10 [3.16; 4.87]	3.67 [3.56; 4.05]	3.67 [3.48; 4.16]	3.50 [2.93; 3.85]	3.65 [3.54; 3.84]	4.23 [3.18; 4.45]
Hemoglobin / 120–160 r/n	113.00 [95.00; 135.00]	105.00 [99.00; 117.00]	109.50 [102.00; 118.50]	101.50 [83.00; 130.00]	109.00 [89.00; 125.00]	118.00 [102.00; 128.00]
Hematocrit / 32–52%	32.70 [28.90; 40.10]	31.15 [29.30; 33.90]	32.10 [30.50; 35.15]	29.25 [24.00; 36.40]	31.20 [26.00; 35.70]	35.90 [29.80; 37.00]
Platelets / 150–400 × 10^9/L	184.00 [135.00; 320.00]	252.00 [156.00; 346.00]	194.50 [142.50; 307.50]	147.00 [92.00; 190.00]	122.00 [36.00; 292.00]	132.00 [116.00; 356.00]
White blood cells / 3.5–11 × 10^9/L	16.88 [9.39; 24.20]	12.64 [9.62; 15.14]	10.76 [8.37; 13.84]	16.29 [13.86; 18.56]	13.37 [6.46; 20.59]	12.29 [11.41; 17.87]
Neutrophils / 1.5–7.5 × 10^9/L	15.25 [7.77; 22.77]	10.81 [7.65; 13.32]	9.04 [6.21; 12.41]	15.23 [12.41; 18.93]	10.71 [4.84; 17.93]	10.72 [8.49; 15.98]
Lymphocytes / 1–4 × 10^9/L	1.59 [0.51; 3.77]	0.84 [0.53; 1.87]	0.76 [0.39; 2.13]	0.71 [0.31; 0.96]*	0.86 [0.18; 2.55]	0.72 [0.49; 1.28]
Basophils / 0–0.1 × 10^9/L	0.02 [0.01; 0.14]	0.03 [0.02; 0.04]	0.02 [0.01; 0.06]	0.01 [0; 0.01]*	0.01 [0; 0.06]	0.02 [0.01; 0.05]#
Eosinophils / 0–0.4 × 10^9/L	0.01 [0.01; 0.27]	0.03 [0.01; 0.13]	0.38 [0.11; 0.66]#$	0.01 [0; 0.29]	0.01 [0; 0.16]	0.44 [0.41; 0.64]#$
Monocytes / 0–0.7 × 10^9/L	0.59 [0.06; 1.4]	0.51 [0.31; 0.94]	0.60 [0.28; 1.27]	0.11 [0.06; 0.18]*	0.70 [0.45; 2.19]#	0.73 [0.46; 1.66]#

Note: * — significant ($p < 0.05$) differences from group 1 on appropriate day; # — differences from indicators reported on day 1 for appropriate group; $ — differences from indicators reported on day 3 for appropriate group.

Table 3. Biochemistry indicators of patients with AS, Me (LQ; UQ)

Indicators/reference values	Group 1 — beneficial AS outcomes (n = 46)			Group 2 — adverse AS outcome (n = 18)		
	Day 1 (n = 46)	Day 3 (n = 46)	Day 7 (n = 46)	Day 1 (n = 18)	Day 3 (n = 14)	Day 7 (n = 10)
α-Amylase / 28–100 U/L	27.91 [22.52; 90.67]	36.51 [16.74; 69.18]	47.39 [26.14; 68.51]	57.33 [43.50; 75.61]	52.20 [29.97; 74.42]	25.28 [20.74; 29.59]#$
Total bilirubin / 0–20.5 μmol/L	23.89 [11.72; 57.93]	9.75 [8.45; 17.89]#	14.78 [7.61; 23.14]	17.80 [13.46; 66.86]	15.30 [9.97; 32.96]	10.99 [9.55; 12.96]#$
Direct bilirubin / 0–5.1 μmol/L	20.38 [8.12; 48.55]	6.53 [4.20; 8.99]#	9.81 [4.53; 14.73]#	11.80 [10.45; 61.36]	15.30 [9.97; 32.96]*	9.25 [5.26; 9.96]#$
ALT / 0–40 U/L	20.00 [15.00; 29.00]	18.50 [15.00; 23.00]	15.00 [11.50; 21.00]	16.00 [13.00; 22.00]	29.00 [22.00; 196.00]#*	27.00 [21.00; 39.00]#*
AST / 0–40 U/L	33.00 [27.00; 49.00]	30.00 [20.00; 37.00]	29.50 [18.50; 41.50]	24.00 [20.00; 44.00]	48.00 [32.00; 1070.00]*	33.00 [28.00; 35.00]#
C-reactive protein / 0–6 mg/L	152.68 [128.18; 249.62]	171.15 [111.79; 203.17]	115.17 [64.71; 193.28]	326.89 [252.93; 361.27]*	224.76 [163.83; 369.78]	274.27 [269.26; 308.39]*
Procalcitonin, ng/mL	19.40 [5.10; 22.90]	2.80 [1.10; 4.50]#	1.50 [0.80; 4.10]#	19.10 [17.00; 28.20]	21.10 [19.80; 22.40]#*	10.00 [1.20; 12.00]#$*
Urea / 1,7–8.3 mmol/L	8.70 [7.80; 15.70]	7.90 [4.80; 12.80]	7.30 [4.50; 14.00]	15.90 [13.40; 23.60]*	18.30 [11.80; 25.10]*	19.80 [11.00; 21.00]*
Creatinine / 62–106 μmol/L	102.67 [74.83; 118.85]	70.28 [58.11; 112.52]	66.55 [57.03; 110.43]	170.29 [102.00; 316.08]*	263.52 [146.36; 345.00]*	215.72 [116.97; 217.10]*
GFR / 90–150 mL/min	55.0 [50.0; 60.0]	55.0 [50.0; 60.0]	60.0 [52.5; 65.0]	40.0 [40.0; 55.0]	40.0 [35.0; 50.0]*	45.0 [40.0; 50.0]*
Alkaline phosphatase / 40–130 U/L	90.88 [67.25; 98.86]	86.56 [69.21; 98.90]	87.30 [68.45; 104.33]	94.90 [84.88; 144.34]	175.50 [102.81; 305.24]*	133.70 [103.84; 151.96]*
Blood glucose / 3.3–6.1 mmol/L	7.40 [4.80; 8.90]	6.40 [5.80; 9.10]	6.90 [5.60; 9.00]	5.90 [4.50; 19.10]	6.60 [4.70; 16.70]	8.30 [7.70; 9.40]
Venous lactate /0.5–1.6 mmol/L	1.70 [1.50; 2.00]	1.70 [1.30; 2.10]	1.80 [1.50; 2.50]	4.150 [3.90; 20.00]*	1.60 [1.30; 3.20]#	2.50 [2.20; 3.00]#

Note: * — significant ($p < 0.05$) differences from group 1 on appropriate day; # — differences from indicators reported on day 1 for appropriate group; $ — differences from indicators reported on day 3 for appropriate group.

A logistic regression model was constructed and a software tool "Calculator for Predicting Mortality in Abdominal Sepsis" was developed based on the data obtained to determine the probability of fatal outcomes in patients with AS [11]. Indicators were selected by constructing logistic regression models and step-by-step elimination of traits. The resulting model included three indicators: SvO_2, SRP concentration, and serum creatinine levels. ROC curve was selected as a metrics for the model for predicting fatal outcomes in AS (see Figure).

Considering the SvO_2, serum SRP and creatinine level values, the tool estimates the AS-associated mortality forecast expressed as a percentage. The relationship observed is described by the following equation:

$$P = 1/(1 + \exp(-3.192989 - 0.081246 \times SvO_2 + 0.016764 \times CRP + 0.014123 \times \text{creatinine})),$$

where P is the likelihood of fatal outcome (%), SvO_2 is venous oxygen saturation (%), CRP is serum concentration of C-reactive protein (mg/L), creatinine is serum creatinine level (μmol/L).

According to our data and the model constructed, fatal outcomes of AS are more common in patients with high serum concentrations of CRP (above 30 mg/L), creatinine (above 70 μmol/L), as well as with low SvO_2 values (below 65%). Validation of the model involving the data used yielded the following: accuracy — 89.8%, sensitivity — 92.11%, specificity — 81.82%, area under the ROC curve — 96%.

The forecast of the likelihood of fatal outcome in patients with AS can be calculated daily. On the one hand, the result can be considered as static to determine surgical tactics, establish indications for on-demand relaparotomy. Patients may have indications for repeated debridement relaparotomy in case of growing likelihood of fatal outcome. On the other hand, the results of calculating the probability of fatal outcome can be used as a dynamic indicator to assess efficacy of the ongoing therapy, including surgical treatment and expensive extracorporeal detoxification methods. In this situation, when we see growing likelihood of fatal outcome, it is necessary to change the ongoing therapy and use other extracorporeal detoxification methods.

DISCUSSION

The analysis of the assessment results using the SOFA clinical score has revealed significant changes in AS patients in two groups, which makes it possible to use the score to assess AS outcomes. This is due to the fact that the SOFA score reflects the function of many organs and systems (respiratory, cardiovascular, nervous, renal, liver, hemostasis systems). Assessment using this score involves quantitative data, which ensures higher objectivity and reproducibility of the results [12]. In patients with adverse AS outcomes, leukocytosis, neutrophilia, anemia with reduced red blood cell counts, hemoglobin concentration, hematocrit, and thrombocytopenia have been reported. Such alterations are associated with activation of innate and adaptive immunity, plasma and platelet components of hemostasis, vascular endothelium with subsequent immunosuppression manifested by lymphopenia, monocytopenia increasing the likelihood of secondary infection

Table 4. Hemostasis indicators of patients with AS, Me (LQ; UQ)

Indicators/reference values	Group 1 — beneficial AS outcomes (n = 46)			Group 2 — adverse AS outcomes (n = 18)		
	Day 1 (n = 46)	Day 3 (n = 46)	Day 7 (n = 46)	Day 1 (n = 18)	Day 3 (n = 14)	Day 7 (n = 10)
Prothrombin index, %	56.60 [51.20; 73.30]	67.41 [52.50; 78.90]	42.65 [21.90; 48.50]#$	55.20 [48.50; 67.10]	45.90 [25.10; 51.30]*	21.90 [20.90; 21.90]#$*
Prothrombin time / 11–17 s	17.00 [15.50; 19.20]	16.50 [15.70; 19.10]	17.95 [16.65; 20.15]	19.95 [17.20; 39.60]*	15.80 [15.40; 18.70]#	16.10 [15.50; 16.50]#
aPTT / 22–38 s	35.85 [32.65; 36.25]	37.45 [34.80; 43.00]	42.75 [36.25; 48.90]	41.30 [38.60; 69.70]*	32.70 [17.00; 43.00]	33.80 [30.60; 42.00]#
Fibrinogen / 2–4 g/L	4.97 [4.33; 6.23]	5.68 [4.97; 6.82]	5.53 [4.59; 6.49]	6.58 [4.30; 8.47]	6.57 [3.65; 8.23]	6.42 [4.68; 8.60]
INR / 0.8–1.2 U	1.31 [1.22; 1.86]	1.28 [1.20; 1.45]	1.37 [1.27; 1.53]	1.53 [1.36; 3.43]	1.22 [1.18; 1.44]#	1.24 [1.19; 1.27]
D-dimer / 0–250 ng/mL	2085.00 [965.00; 2595.00]	565.00 [226.00; 2472.00]	1284.50 [631.50; 3382.00]	2488.50 [926.00; 4325.00]	2078.00 [990.00; 3118.00]#	2146.00 [1046.00; 3310.00]#

Note: * — significant (p < 0.05) differences from group 1 on appropriate day; # — differences from indicators reported on day 1 for appropriate group; $ — differences from indicators reported on day 3 for appropriate group.

[13, 14]. High serum levels of procalcitonin and CRP in the group with adverse AS outcomes reflect severity of the AS-associated inflammatory response. Growth of these indicators can suggest adverse outcome when predicting the course of AS [15–18]. Among biochemistry indicators of patients with adverse AS outcomes, we should mention growth of serum creatinine, urea, direct bilirubin concentrations, ALT, AST activity, along with the decrease in GFR compared to the group with beneficial AS outcomes. These alterations are associated with organ dysfunction in AS, the development of multiple organ dysfunction syndrome (MODS) due to damage caused by pathogens and endotoxins, activation of innate and adaptive immunity. Mitochondrial dysfunction caused by sepsis is a major cause of the cell metabolism disturbances, insufficient energy supply and oxidative stress, which lead to apoptosis, dysfunction of multiple organs, MODS, thereby increasing patient mortality rate [19–21].

In terms of the hemostasis system, high plasma levels of fibrinogen, D-dimer, increased aPPT, PT, and decreased PI are typical for patients with adverse AS outcomes. These alterations are associated with the hypercoagulable and hypofibrinolytic hemostasis alteration phenotype, activation of extrinsic and intrinsic coagulation pathways, suppression of anticoagulant processes, disturbed fibrinolysis, liver dysfunction with impaired clotting factor synthesis, development of sepsis-induced coagulopathy, DIC syndrome [22–25]. In terms of the acid-base balance and blood gases, patients with adverse AS outcomes showed more severe metabolic acidosis accompanied by high lactate levels, as well as the decreased PaO_2/FiO_2 and SvO_2 values, which was due to disturbed central and peripheral hemodynamics, microcirculation, impaired oxygen delivery, consumption and utilization in the tissues, acute kidney damage. Serum lactate levels represent an important biomarker of sepsis that is positively correlated to morbidity and mortality in sepsis or septic shock [26–28].

According to our data and the model constructed, high serum concentrations of CRP and creatinine, as well as low SvO_2 values can serve as valuable clinical tools for prediction of AS outcomes. The laboratory indicators used in the "Calculator for Predicting Mortality in Abdominal Sepsis" are available for all medical institutions providing care to patients with AS, inclusing the non-ICU departments, which makes it possible to timely estimate the likelihood of fatal disease outcome and determine further patient management tactics at any stage.

CONCLUSIONS

The study has shown that the prognostic model based on serum C-reactive protein, creatinine concentrations and venous oxugen saturation is an effective tool for prediction of AS outcomes. The value of these three markers reported emphasizes the key role of renal dysfunction, inflammatory

Table 5. Blood acid-base balance and blood gases in patients with AS, Me (LQ; UQ)

Indicators/reference values	Group 1 — beneficial AS outcomes (n = 46)			Group 2 — adverse AS outcomes (n = 18)		
	Day 1 (n = 46)	Day 3 (n = 46)	Day 7 (n = 46)	Day 1 (n = 18)	Day 3 (n = 14)	Day 7 (n = 10)
PaO_2/FiO_2 / above 300 U	220.00 [210.00; 280.00]	230.00 [210.00; 280.00]	240.00 [200.00; 300.00]	246.70 [200.00; 280.00]	214.00 [190.00; 240.00]*	170.00 [160.00; 180.00]#$*
SvO_2, % / above 70%	73.50 [67.30; 86.40]	69.40 [56.40; 77.50]	71.70 [65.60; 73.60]	70.70 [53.40; 91.10]*	75.00 [65.00; 82.00]	66.60 [64.60; 72.90]*
Venous blood pH / 7.31–7.41	7.38 [7.33; 7.41]	7.38 [7.32; 7.40]	7.34 [7.34; 7.35]	7.27 [7.23; 7.31]*	7.34 [7.24; 7.38]	7.34 [7.34; 7.35]
Venous blood SB / 21–28 mmol/L	20.80 [18.60; 25.80]	22.95 [21.10; 25.20]	20.90 [19.30; 21.60]$	15.50 [15.40; 19.10]*	19.30 [17.20; 23.80]	20.90 [19.30; 21.60]$
Venous blood BB / 0–2 mmol/L	–3.50 [–6.90; 2.00]	–1.40 [–3.50; 1.40]	–3.70 [–5.80; –2.80]	–8.40 [–10.80; –3.00]	–6.00 [–8.60; –0.40]	–3.70 [–5.80; –2.80]
Venous blood BE / 0–2 mmol/L	–3.50 [–7.20; 1.80]	–1.40 [–3.60; 1.60]	–3.60 [–5.70; –2.70]	–8.30 [–10.90; 22.80]	–6.20 [–8.60; –0.10]	–3.60 [–5.70; –2.70]

Note: * — significant (p < 0.05) differences from group 1 on appropriate day; # — differences from indicators reported on day 1 for appropriate group; $ — differences from indicators reported on day 3 for appropriate group.

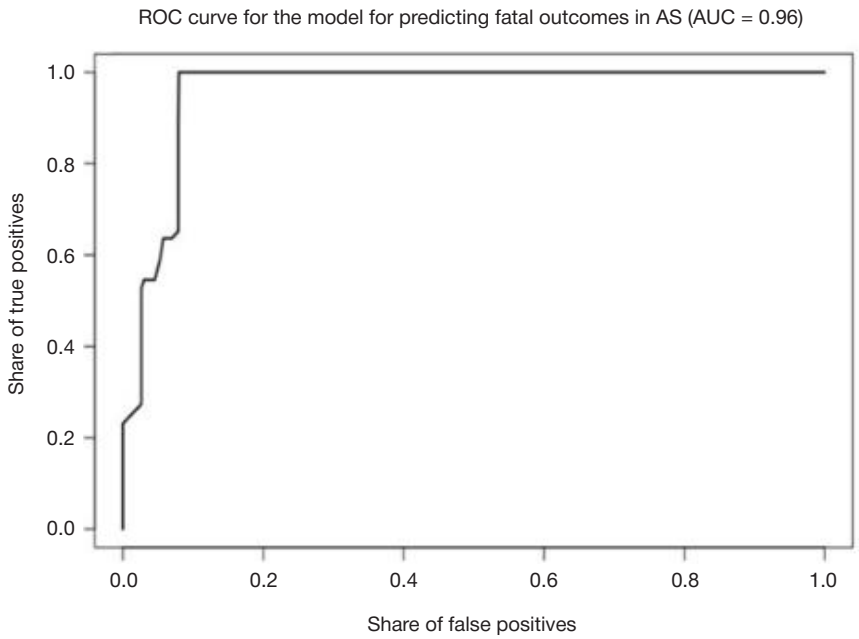

Fig. The metrics used for the model for predicting fatal outcomes in AS

response, and tissue hypoxia in the AS pathogenesis and outcome. The mathematical model for predicting outcome of sepsis in patients with abdominal surgical pathology has been constructed. The software tool "Calculator for Predicting Mortality in Abdominal Sepsis" has been developed. The model constructed represents a valuable tool for clinical practice and further research in the field of pathophysiology of septic conditions. Timely identification of patients with high probability of fatal AS outcome will make it possible to promptly intensify treatment, including early targeted hemodynamic support, ensure antibacterial therapy adjustment, and repeated surgery in case of the need for repeated lesion debridement. This will allow one to improve treatment outcomes and reduce AS-associated mortality. Improvement of the model for predicting the likelihood of fatal outcome in AS presented through inclusion of other clinical and laboratory markers aimed to increase its prognostic accuracy and feasibility remains promising.

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