4open 2022, **5**, 12

https://doi.org/10.1051/fopen/2022014

4 Open

Available online at:
www.4open-sciences.org

RESEARCH ARTICLE OPEN ACCESS

Biomarker assessment in urgent surgical pathology of the small bowel: case-control analysis of a retrospective database

Igor A. Kryvoruchko[1,*], Tetiana O. Briukhanova[2], Oksana A. Nakonechna[2], and Olexander S. Olefir[1]

[1] Department of Surgery No. 2, Kharkiv National Medical University, 61022 Kharkiv, Ukraine
[2] Department of Biological Chemistry, Kharkiv National Medical University, 61022 Kharkiv, Ukraine

Received 24 May 2022, Accepted 27 May 2022

Abstract – *Background*: Small bowel obstruction, mesenteric thrombosis, and strangulated ventral hernia area a challenge in emergency abdominal surgery. This study aimed to evaluate biomarkers of damage to the digestive tract in patients with urgent pathology. *Materials and methods:* The study involved 71 patients aged 18 to 80 years who were hospitalized in the intensive care unit in the immediate postoperative period. *Results*: All 71 underwent emergency surgery, 27 with small bowel necrosis. Lactate level area under curve (AUC = 0.964), C-reactive protein (AUC = 0.805) and systolic blood pressure (area under curve, AUC = 0.803) on the context of Sequential Organ Failure Assessment (SOFA) score (AUC = 0.880) showed stratification of patients with complications before surgery. Small bowel necrosis patients revealed an increase in primary thiobarbituric acid (TBA) reactive products (AUC = 0.813) lipid peroxidation products, and a decrease in superoxide dismutase activity (AUC = 0.818) and catalase (AUC = 0.804). Wide variability of intestinal fatty-acid binding protein (I-FABP) from 199.8 to 2189.6 pg/mL were observed in all patients studied, with an AUC = 0.814 in small intestinal necrosis. *Conclusion*: Surgical pathology of the small intestine due to obstruction of various origina, mesenteric thrombosis, and strangulated ventral hernia pronounced revealed disorders of the antioxidant-prooxidant balance. This was expressed by an increase in lipid peroxidation products, and the level of TBA-reactive products, and the activities of superoxide dismutase (SOD), and catalase. Viewed against the background of an increase in I-FABP above 577 pg/mL, these variables were the most significant indicators of small intestinal necrosis.

Keywords: Small bowel obstruction, Mesenteric thrombosis, Strangulated ventral hernia, Ischemia-necrosis of the small intestine, Diagnosis, Prognosis, Results

Introduction

Despite advances in medicine, the diagnosis of morphological changes in the small intestine due to non-ischemic and ischemic injuries in diseases such as acute intestinal obstruction, mesenteric occlusive and non-occlusive ischemia, and strangulated ventral hernia before surgery remains one of the most difficult problems in emergency abdominal surgery. Most studies have shown that the common leading causes of adverse outcomes in most cases in this category of patients is metabolic damage precipitated by an unbalanced response of the body to ischemia/necrosis of the small intestine and infection, which often leads to organ dysfunction, the development of peritonitis, and abdominal sepsis [1, 2]. It should be noted that at least 300,000 operations for small bowel obstruction are performed annually in the United States alone [3], and about 40% of cases are associated with strangulation and necrosis of the small intestine. Asphyxia of the non-viable small intestine is about 16% [4]. In patients with strangulation obstruction of the small intestine, mortality is 2–10 times higher than in patients with obstruction [5].

The severity of the condition of these patients, including at the stages of surgery, is largely determined by the intensity of endogenous intoxication, which contributes to the decompensation of vital body systems. The group of endogenous toxic substances consists of numerous chemical compounds, which include products of proteolysis and lipolysis, circulating immune complexes and humoral regulators, biogenic amines and cytokines, products of lipid peroxidation among others. An important feature of endotoxins is their harmful effects on the vital functions of all systems and organs, they can lead to their functional insufficiency. In urgent pathology of the small intestine, the violation of the barrier function of the small intestine is a factor in the development of endotoxicosis, which provokes systemic disorders.

Currently, the development of oxidative stress in different categories of patients with surgical pathology and endotoxicosis is considered an established fact. Significant

*Corresponding author: ikryvoruchko60@gmail.com

changes in the balance in the prooxidant-antioxidant system associated with the prevalence of prooxidant factors are typical pathophysiological reactions in the human body in various diseases [6, 7]. These phenomena, in turn, mediate many metabolic disorders, in particular, a strong intensification of free radical processes during the suppression of antioxidant defense systems. Undoubtedly, the most important event in the intake of toxins is enteral distress syndrome, which occurs in the early stages of urgent pathology of the small intestine, including non-purulent-inflammatory conditions. And according to recent concepts, an important pathogenic factor responsible for the formation of endogenous intoxication, systemic inflammatory response and multiple organ failure in urgent surgical pathology of the abdominal organs is intestinal insufficiency syndrome, which complicates the course of the postoperative period in 30–50% of patients, despite the elimination of the cause of its development. In patients with urgent pathology of the small intestine, the digestive tract is quite vulnerable, and the occurrence of its dysfunction plays a significant role in the development of complications of the disease [8]. Often, the severity of digestive tract dysfunction indicates the severity of the condition of critical patients since several publications have reported that almost 50% of patients in intensive care units have damage to enterocytes at the initial stage of treatment [9], and among seriously ill patients with digestive tract dysfunction, higher mortality rates are observed [10–12].

This study aimed to evaluate the intensities of some indicators of endogenous intoxication, including the prooxidant-antioxidant system and the biomarker of damage to the digestive tract (I-FABP) in patients with urgent pathology of the small intestine and to determine their prognostic significance.

Material and methods

A two-centre retrospective study was conducted at Kharkiv National Medical University, which involved 71 patients aged 18–80 who were hospitalized in the intensive care unit in the immediate postoperative period. The study was conducted from September 1, 2017, to November 30, 2021, with the consent of the University Ethics Committee (Protocol No. 3 of September 20, 2021).

Medical records were reviewed, including symptoms and signs, laboratory tests, and imaging studies. Written informed consent was obtained from each patient. Initial assessment of patients included: history of abdominal intervention; clinical symptoms (abdominal pain, bloating, nausea, vomiting, shortness of breath and defecation); examination data (bloating with palpated loops of the small intestine, the presence of peristaltic waves, pain or symptoms of peritonitis).

Inclusion criteria

The study included men and women who were hospitalized with small bowel obstruction, pinched abdominal hernias, and mesenteric thrombosis. Based on some clinical data, the inclusion criteria for patients met one of the following conditions: a simple abdominal radiograph or abdominal ultrasound showing multiple levels of air and fluid in the small intestine, but no signs of gas in the colon; radiography and/or computed tomography (CT) of the abdominal cavity; and confirmation of mesenteric occlusion during laparotomy or laparoscopy.

Exclusion criteria

Patients with mechanical obstruction of the colon; patients with early postoperative small bowel obstruction less than 30 days after abdominal surgery; patients with ascites; concomitant disease with acute myocardial infarction and stroke; severe acute pancreatitis with obstruction or necrosis of the small intestine; post-resuscitation disease due to cessation of efficient blood circulation and refractory shock; pregnancy; history of cancer.

Patient characteristics

When examining patients, the following data were collected: personal data (age, gender, previous operations on the abdominal organs and abdominal trauma); laboratory examination: peripheral blood leukocytes count, platelets, hematocrit, lactate, C-reactive protein; in the dynamics of patient treatment, systolic blood pressure (SBP) was monitored and the following scores were calculated for each patient: Acute Physiology and Chronic Health Evaluation (APACHE) II score, Sequential Organ Failure Assessment (SOFA) score. Evaluation of antioxidant-prooxidant status was performed by determining the content of markers of intensification of free radical oxidation and oxidative damage of cellular structures: compounds reacting with thiobarbituric acid (TBA-AP) and diene conjugates (DC) were performed spectrophotometrically; 8-isoprostane was performed using a set of reagents called "8-isoprostane ELISA" manufactured by "Cayman Chemical" (USA). Assessment of antioxidant status was performed by determining the content of major antioxidant enzymes such as superoxide dismutase (SOD) [13], and catalase with a sandwich enzyme-linked immunosorbent assay using a set of reagents "Human Catalase, ELISA Kit", manufactured in the USA, and glutathione peroxidase (GP) was performed spectrophotometrically. The level of I-FABP was carried out using commercial kits "I-FABP, Human, ELISA kit" manufactured by the Netherlands.

Choice surgery and patient distribution in urgent pathology of the small intestine

The patients underwent urgent surgery with effective source control, supporting appropriate antibiotics, resuscitation, and organ-support therapy. Surgical approaches depended on the specific clinical situation and took into account the existing World Society of Emergency Surgery (WSES) recommendations for these categories of patients, including local conditions and opportunities [14–17].

Statistical analysis

Statistical data processing was performed using the trial version of STATISTICA 13.3 EN. Initially, statistical analysis was performed using descriptive statistics including Tukey for testing differences among samples and the Shapiro–Wilk test to assess the normality of the distributions of the selected indicators. Continuous data were presented as mean and standard deviation (M ± SD). Zero hypotheses (H0) in statistical tests were rejected at a significance level of $p < 0.05$. Prediction of necrosis of the small intestine was carried out with the use of multidimensional statistical methods for all studied indicators. To assess the diagnostic significance of the different biomarkers studied, receiver operating characteristic (ROC) analyses were performed: the sensitivity, specificity, and area under the ROC curve for the biomarkers, and the significance of the differences between them were assessed taking into account its 95% confidence interval. The prognostic effect of the models was assessed based on the area under the curve (AUC) indexes: the efficiency of the model was considered to be restricted to AUC $\geq$ 0.70; was good to AUC $\geq$ 0.80; was excellent to AUC $\geq$ 0.90.

Results

Among the studied patients, 54 had a small bowel obstruction, 9 with a strangulated ventral hernia, and 6 with mesenteric thrombosis. Of the 71 patients examined, 27 had small intestinal necrosis, and all 71 underwent emergency surgery.

It has been established that in the studied diseases there is an increase in the level of toxic products of a hydrophilic nature (peptides of medium molecular weight, $\lambda = 254$ nm), and activation of an acute inflammatory reaction was observed in all patients, which was determined by a significant increase in the level of leukocytes in the blood and C-reactive protein relative to the control ($p < 0.0001$) (Tab. 1) against the background of the development of increased levels of lactate and hematocrit in the blood ($p < 0.05$). The results of the distribution of patients by changes in laboratory data and severity depending on the presence of necrosis of the small intestine are presented in Table 2. Indicators were selected that were reliable and belonged to the category of good and excellent before surgery (Tab. 3): AUC of lactate before surgery was 0.964 ($p < 0.0001$), AUC of C-reactive protein was 0.805 ($p < 0.0001$), and AUC of systolic blood pressure was 0.803 ($p < 0.0001$). The SOFA score was also reliable for assessing the stratification of patients with small bowel necrosis before surgery, and its AUC was 0.880, $p < 0.0001$ (Fig. 1).

It should be noted that lactate level had an optimal cutoff value of 2.19 mmol/L before surgery by the criterion for strangulated/intact small intestine (AUC = 0.964, 95% CI [0.711–0.994]), SOFA score had an optimal cutoff value of 8.5 points (AUC = 0.880, 95% CI [0.682–0.883]), C-reactive protein level had an optimal cutoff value of 195.0 mg/L, and SBP had the optimal cutoff value of 104 mm Hg (AUC = 0.803, 95% CI [0.693–0.851]) (Fig. 1).

In the study of the antioxidant-prooxidant status, a significant probability of an increase in the content of primary (TBA-reactive products, from 1.9 to 2.1 times on average) and secondary (diene conjugates, from 1.9 to 2.3 times on average) products of lipid peroxidation relative to the control group was observed ($p < 0.001$). These changes in prooxidant status were observed in patients without and with the strangulation component of the small intestine and its necrosis, and also in survivors' and non-survivors' patients (Tab. 4). Still, as could be noted in patients with necrosis of the small intestine and non-survivor patients, the average parameters of all these indicators differed considerably and had higher values. Simultaneously with the activation of free radical processes and the formation of oxidative stress, we noted a probable decrease in antioxidant status in all patients (Tab. 5): the activity of SOD decreased on average by 42.6%, 67.9%, 70.9%, and 60.4%, respectively ($p < 0.01$), and GP by 15.1%, 25.9%, 29.2%, and 21.2% relative to control ($p < 0.05$) in patients with small bowel necrosis, and blood catalase content had decreased by 32.7%, 39%, 41.2%, and 39%, respectively, in patients with strangulation and necrosis of the bowel.

Subsequently, indicators were selected, the values of which were reliable and belonged to the category of good before surgery, as shown in Table 6: AUC of TBA-reactive products before surgery was 0.813 ($p < 0.0001$); AUC of SOD activity was 0.818 ($p < 0.0001$), AUC of catalase content was 0.804 ($p < 0.0001$) and the AUC of GP activity was 0.787($p < 0.001$) (Fig. 2).

Structural and morphological changes in the small intestine in the form of non-ischemic and ischemic lesions in diseases such as acute intestinal obstruction, mesenteric occlusion, and strangulated hernia, are common causes of adverse conditions in these diseases both before and after surgery. The patients showed significant changes in I-FABP from 199.8 to 2189.6 pg/mL (911.3 ± 136.3) (Tab. 7) with a significant difference between groups of patients before surgery: strangulation obstruction of the small intestine 881.8 ± 179.3; obstruction of the small intestine 276.2 ± 61.86; mesenteric thrombosis 1232.5 ± 422.6; strangulated ventral hernia 699.5 ± 172.7; the presence of diffuse peritonitis 769.4 ± 214.7; survivors patients 486.2 ± 248.7; non-survivors patients 962.2 ± 270.5. That is, depending on the pathology and the presence of complications, the average level of I-FABP increased in all of them compared to the control, which indicates the influence of the severity of such a sign as ischemia-necrosis of the small intestine on this indicator. And, studies suggested I-FABP as prognostic marker, which had in our study AUC = 0.814, sensitivity 90.9%, but a very low specificity 61.9%) (Fig. 3).

Discussion

The problem of diagnosis and surgical treatment of acute occlusive and neo-occlusive ischemia remains relevant due to the preservation of a fairly high percentage of unsatisfactory treatment results (from 30.0 to 100.0%). Biological markers are evaluated that may be associated with small

Table 1. Baseline endogenous intoxication, inflammatory response and tissue hypoxia, markers of prooxidant status and biochemical parameters of the antioxidant system in patients with small bowel pathology.

Indicators	Small bowel obstruction		Mesenteric thrombosis ($n = 6$)	Strangulated hernia ($n = 9$)	Control ($n = 15$)
	Obturation ($n = 44$)	Strangulation ($n = 12$)			
WBC count ($\times 10^9$/L)	15.8 ± 3.63*	21.34 ± 4.13*	23.83 ± 4.56*	17.32 ± 3.92*	7.8 ± 2.1*
PAMW, $\lambda = 254$ нм, (c.u.)	370 ± 12.3*	544 ± 15.2*	582 ± 12.7*	422.6 ± 14.3*	211 ± 18.1
C-reactive protein (mg/L)	93.5 ± 13.3*	187.4 ± 28.3*	201.5 ± 27.8*	142.7 ± 18.6*	6.7 ± 1.8
Lactate (mmol/L)	1.83 ± 0.12*	3.4 ± 0.43*	2.9 ± 0.04*	2.2 ± 0.31*	1.2 ± 0.03*
Hemoglobin (g/L)	150.6 ± 8.09*	156.7 ± 4.37*	151.8 ± 9.56*	146.4 ± 8.11*	134.8 ± 5.4*
Hematocrit (%)	43.55 ± 3.6*	49.58 ± 4.1*	49.24 ± 5.4*	44.6 ± 3.9*	34.12 ± 2.8
TBA-reactive products (μM/g)	6.78 ± 0.71*	7.12 ± 0.66*	7.34 ± 0.87*	6.92 ± 0.74*	3.58 ± 0.44
DC (μM/g of protein)	3.46 ± 0.61*	3.85 ± 0.52*	3.95 ± 0.44*	3.58 ± 0.36	1.74 ± 0.22
8-isoprostane (ng/mL)	4.95 ± 0.78*	4.51 ± 0.71*	4.59 ± 0.66*	4.36 ± 0.68*	2.08 ± 0.48
Activity of SOD (MO/10 mg of protein)	1.52 ± 0.21*	0.85 ± 0.14*	0.77 ± 0.12*	1.05 ± 0.11*	2.65 ± 0.12
Catalase (IU/mg)	256.1 ± 15.93*	231.8 ± 18.02*	223.5 ± 21.02*	231.8 ± 18.02*	380.3 ± 26.85
GP in erythrocytes, (nmol of reduced glutathione/min)	128.7 ± 17.86*	112.4 ± 22.56*	107.4 ± 17.53*	118.4 ± 17.46*	151.6 ± 21.24

WBC – white blood cells; PAMW – peptides of average molecular weight; TBA – thiobarbituric acid; SOD – superoxide dismutase; GP – glutathione peroxidase; Note: *Reliable with control ($p < 0.05$).

bowel necrosis, inflammatory response, the severity of organ dysfunction, and sepsis. Because acute small bowel disease in patients with small bowel obstruction, mesenteric thrombosis, and impaired ventral hernia is life-threatening, timely and accurate diagnosis of ischemia/necrosis and stratification of patients before surgery at risk of local and systemic complications is important. A better understanding of the pathophysiological disorders in the treatment of these patients allows us to determine the moments of favourable prognosis and prevent various complications. The main characteristic of the severity of urgent surgical pathology of the small intestine is endogenous intoxication due to its ischemia-necrosis-reperfusion. These circulatory disorders in the intestine lead to necrosis and perforation [18–20].

An extreme increase in toxic products in the blood is possible with their production or a decrease or loss of the detoxification ability of the organs of the natural detoxification system. In this regard, the question of the causes of this kind of tissue damage at the local level and the organ level of the detoxification system has long been relevant. It is obvious that the destruction and loss of the functional potential of the organ are based on processes at the cellular level that discredit the basic functions of the liver and intestines, but one of the main ones, of course, is those that primarily affect the structural and functional state of the cell membranes. In concept, the universality of agents was recognized as the most important in the pathogenesis of the development of not only catabolic processes – a source of toxins, but also dysfunction of the organs of the detoxification system associated with the development of pathology of cell membranes. A solution to the complex issues in this problem became possible due to an in-depth study of the ongoing pathophysiological processes at the organ, cellular, and molecular levels in various urgent surgical diseases of the abdominal organs. The study aimed to determine the significance of the catabolic process as a whole in the pathogenesis of surgical endotoxicosis by studying the prooxidant-antioxidant system against the background of lesions of the gastrointestinal tract in patients with urgent surgical pathology of the small intestine.

First of all, the results obtained in this study showed that indicators such as lactate (AUC = 0.964), C-reactive protein (AUC = 0.805), and systolic blood pressure (AUC = 0.803) in the background of the severe condition of patients on the SOFA score allow for the diagnosis of developing hypoxia, the assumption of the presence of necrosis of the small intestine before surgery with stratification of patients with this complication, and the prediction of the development of systemic disorders after surgery. It should be noted that numerous studies have examined the relationship between different indicators and prognosis in patients with critical surgical diseases [21–24], but the data were sometimes contradictory. According to the current recommendations, the SOFA score should be used as a prognostic indicator to detect sepsis as well as to stratify the risk of complications in operated patients [25–27]. This approach excludes the influence of one or another dominant diagnostic concept and identifies patients at increased risk of death.

Evaluation of SOFA in our study showed good results in predicting early mortality in patients with urgent surgical pathology of the small intestine and the development of necrosis of the small intestine in the analysis of ROC curves. It should be noted that this indicator had an optimal cutoff of 8.5 points (AUC = 0.880, 95% CI [0.682–0.933]) with a sensitivity of 81.3% and a specificity of 88% for the criterion of patients with necrosis of the small intestine and patients without small intestine intestinal necrosis. It is known that many biomarkers, such as lactate, and C-reactive protein, are powerful predictors of sepsis and adverse outcomes [28, 29]. This study showed within the ROC curve, an AUC, sensitivity and specificity in lactate (9.964, 100%, and 91.7%), C-reactive protein (0.85, 57.5%, and 90.5%), and systolic blood pressure (0.803, 73%, and 76.5%)

Table 2. Laboratory data of patients in the main group depending on their severity and the presence of necrosis of the small intestine.

Indicators	Before surgery		*P*	Before surgery		*P* value
	Survivors ($n = 59$)	Non-survivors ($n = 12$)		Without necrosis small intestine ($n = 44$)	With necrosis small intestine ($n = 27$)	
WBC count ($\times 10^9$/L)	17.56 ± 2.92	20.95 ± 4.09	0.007	16.78 ± 4.15	22.74 ± 5.77	0.000
	95% CI [−5.804 to −0.9789]			95% CI [−8.313 to −3.607]		
PAMW, $\lambda = 254$ нм, (c.u.)	0.37 ± 0.02	0.54 ± 0.02	0.000	0.41 ± 0.03	0.52 ± 0.03	0.000
	95% CI [−0.1859 to −0.1541]			95% CI [−0.1246 to −0.09537]		
TBA-reactive products (μM/g)	6.37 ± 0.71	7.39 ± 0.99	0.000	6.78 ± 0.71	7.12 ± 0.87	0.029
	95% CI [−1.607 to −0.4344]			95% CI [−0.6447 to −0.03535]		
DC (μM/g of protein)	4.2 ± 0.26	3.53 ± 0.43	0.000	3.46 ± 0.61	3.95 ± 0.52	0.000
	95% CI [0.4485 to 0.8915]			95% CI [−0.7718 to −0.2082]		
8-isoprostane (ng/mL)	4.42 ± 0.52	4.88 ± 0.77	0.038	4.95 ± 0.78	4.51 ± 0.67	0.018
	95% CI [−0.893 to −0.02614]			95% CI [0.07887 to −0.1541]		
Activity of SOD (MO/10 mg of protein)	1.59 ± 0.19	0.92 ± 0.16	0.000	1.52 ± 0.21	0.85 ± 0.14	0.000
	95% CI [0.521 to 0.819]			95% CI [0.5789 to 0.7611]		
Catalase, (IU/mg)	268.5 ± 14.8	228.6 ± 19.3	0.000	256.1 ± 15.93	231.8 ± 18.02	0.000
	95% CI [27.74 to 52.06]			95% CI [16.13 to 32.47]		
The activity of GP in erythrocytes, nmol of reduced glutathione/min * g Hb	126.6 ± 21.11	109.5 ± 18.3	0.043	128.7 ± 17.26	112.4 ± 22.19	0.000
	95% CI [0.5157 to 33.38]			95% CI [6.904 to 25.7]		
Lactate (mmol/L)	1.6 ± 0.04	2.9 ± 0.3	0.000	1.8 ± 0.12	3.8 ± 0.43	0.000
	95% CI [−1.377 to −1.223]			95% [CI −2.113 to −1.887]		
C-reactive protein (mg/L)	86.7 ± 15.8	193.9 ± 25.2	0.000	92.7 ± 18.6	198.5 ± 24.3	0.000
	95% CI [−120.6 to −93.84]			95% CI [−114.1 to −97.47]		
SBP (mm Hg)	115.3 ± 12.9	88.5 ± 9.8	0.000	130.8 ± 16.4	81.2 ± 6.8	0.000
	95% CI [16.75 to 36.85]			95% CI [42.97 to 56.23]		
APP (mm Hg)	75.7 ± 2.2	62.1 ± 1.9	0.000	70.4 ± 1.83	65.2 ± 1.48	0.000
	95% CI [11.87 to 15.33]			95% CI [4.368 to 6.032]		
APACHE II score	11.3 ± 1.5	16.7 ± 1.4	0.000	13.7 ± 1.9	14.6 ± 2.09	0.066
	95% CI [−6.589 to −4.215]			95% CI [−1.863 to 0.06259]		
SOFA score	4.3 ± 1.4	8.1 ± 1.2	0.000	9.3 ± 1.1	12.8 ± 1.3	0.000
	95% CI [−5.099 to −2.901]			95% CI [−4.075 to −2.925]		

WBC – white blood cells; PAMW – peptides of average molecular weight; TBA – thiobarbituric acid; DC – diene conjugates; SOD – superoxide dismutase; GP – glutathione peroxidase; SBP – systolic blood pressure; APP – abdominal perfusion pressure; Note: *P*-Student's criterion; 95% CI – 95% confidence interval for difference; APP – abdominal perfusion pressure.

Table 3. Diagnostic value of hypoxia, inflammation and systemic disturbances for the small intestine necrosis before surgery.

Indicators	AUC	Cut-off	SE	95% CI	Sensitivity	Specificity
WBC	0.712	18.05	0.0897	0.612–0.815	0.357	1.0
PAMW	0.757	0.495	0.912	0.624–0.846	0.407	1.0
Lactate	0.964	2.175	0.0643	0.711–0.994	1.0	0.917
C-reactive protein	0.805	195.0	0.0512	0.714–0.877	0.577	0.905
SBP	0.803	104.0	0.0667	0.693–0.851	0.730	0.765
APP	0.756	62.5	0.0932	0.624–0.882	0.489	0.676
APACHE II score	0.785	13.0	0.0543	0.667–0.821	0.697	0.542
SOFA score	0.880	8.5	0.0812	0.682–0.933	0.813	0.880

AUC – area under the curve; SE = Standard error; CI – confidence interval; PAMW – peptides of average molecular weight; SBP – systolic blood pressure; APP – abdominal perfusion pressure; APACHE – Acute Physiology and Chronic Health Evaluation score; SOFA = Sequential Organ Failure Assessment score.

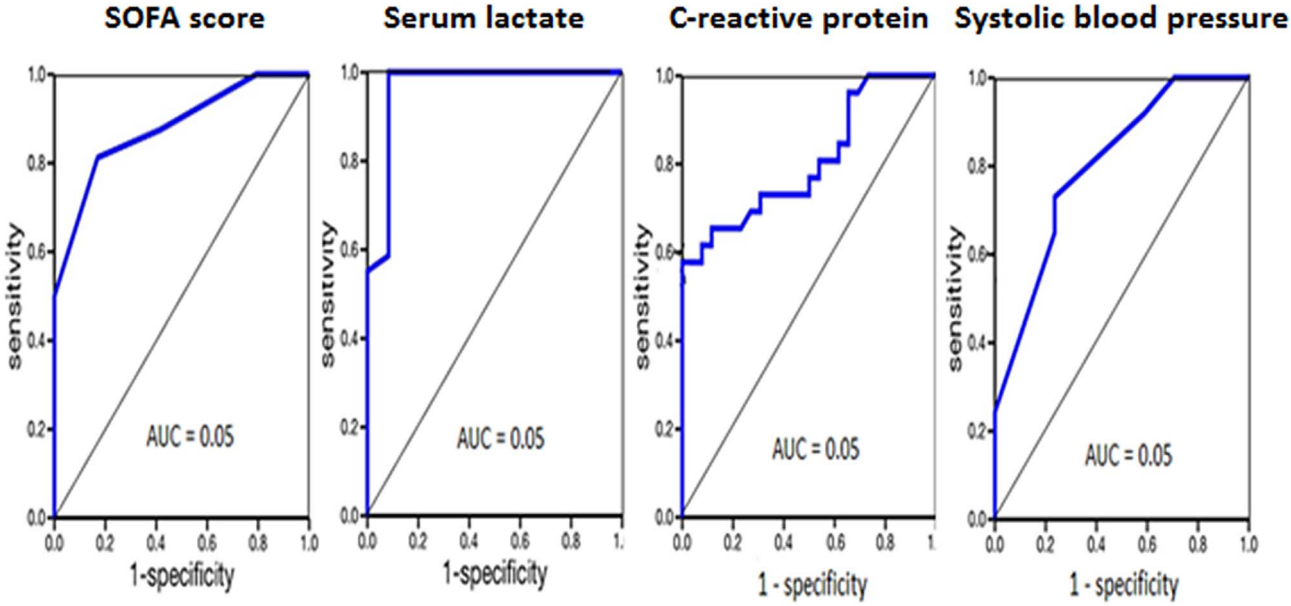

Fig. 1. Efficacy of AUC prediction models for suspected small bowel necrosis for score SOFA, lactate, C-reactive protein, and systolic blood pressure. AUC – area under the curve; SOFA – Sequential Organ Failure Assessment score.

associated with early mortality. However, the low sensitivity in valuing these findings needs to be taken into account.

The data presented in the study indicate that in surgical pathology of the small intestine as a result of its obstruction, mesenteric thrombosis, and strangulated ventral hernia, pronounced disorders of the antioxidant-prooxidant balance were revealed, expressed in a particularly likely increase in primary (TBA-reactive products) and secondary (diene conjugates) products of lipid peroxidation. These changes in the prooxidant status were observed in patients of both study groups with both strangulation and obstructive genesis of pathology, and more pronounced changes were recorded in patients with necrotic changes in the small intestine, which, in our opinion, are due to pathogenetic mechanisms associated not only with obstruction of the intestinal lumen, but also with impaired blood flow in its wall, which creates additional conditions for tissue damage with the formation of local and systemic hypoxia and, accordingly, leads to a more massive formation of toxic metabolic products and their entry into the bloodstream.

At the same time, it was found that only TBA-reactive products have predictive capabilities in relation to the diagnosis of small intestine necrosis since for this indicator the AUC was 0.813 with a sensitivity of 63.2% and a specificity of 89.3%. Undoubtedly, in conditions of acute damage to the intestinal wall, the presence in the blood of molecules that are degradation products of cell membranes and other macromolecules is a prognostically unfavourable indicator of deep structural and metabolic disorders in patients with membrane pathology. In addition, a significant increase in 8-isoprostane from 2.2 to 2.4 times before surgery ($p < 0.01$) confirms the presence of oxidative stress in all cases of surgical pathology, since this compound is a metabolite of the arachidonic acid cascade, and its presence signals a strong release of highly reactive compounds that can damage cells and extracellular formations, which under

Table 4. Biochemical parameters of prooxidant status in patients before surgery.

Indicators/Groups	TBA-reactive products	*P*	Diene conjugates	*P*	8-isoprostane	*P* value
Control ($n = 20$)	3.58 ± 0.44	$P_1 = 0.000$	1.74 ± 0.22	$P_1 = 0.000$	2.08 ± 0.48	$P_1 = 0.000$
With necrosis of the small intestine ($n = 27$)	7.12 ± 0.87	$P_2 = 0.000$	3.95 ± 0.52	$P_2 = 0.000$	4.95 ± 0.67	$P_2 = 0.000$
Without necrosis of the small intestine ($n = 44$)	6.78 ± 0.71	$P_3 = 0.078$	3.46 ± 0.61	$P_3 = 0.005$	4.51 ± 0.78	$P_3 = 0.004$
Survivors ($n = 59$)	6.37 ± 0.71	$P_4 = 0.001$	3.53 ± 0.43	$P_4 = 0.000$	4.42 ± 0.52	$P_4 = 0.013$
Non-survivors ($n = 12$)	7.39 ± 0.99		4.2 ± 0.26		4.88 ± 0.77	

TBA = thiobarbituric acid; DC = diene conjugates; Note: P_1 – reliable between control and strangulation; P_2 – reliable between control and obturation; P_3 – reliable between strangulation and obturation; P_4 – reliable between survivors and non-survivors.

Table 5. Biochemical parameters of the antioxidant system in patients before surgery.

Indicators/groups	Superoxide dismutase	*P* value	Catalase	*P* value	Glutathione peroxidase	*P* value
Control ($n = 20$)	2.65 ± 0.12	$P_1 = 0.000$	380.1 ± 26.85	$P_1 = 0.000$	151.6 ± 21.24	$P_1 = 0.000$
With necrosis of the small intestine ($n = 27$)	0.85 ± 0.14	$P_2 = 0.000$	231.8 ± 18.02	$P_2 = 0.000$	112.4 ± 22.56	$P_2 = 0.003$
Without necrosis of the small intestine ($n = 44$)	1.52 ± 0.21	$P_3 = 0.000$	256.1 ± 15.93	$P_3 = 0.000$	128.7 ± 17.86	$P_3 = 0.031$
Survivors ($n = 59$)	1.59 ± 0.19	$P_4 = 0.000$	268.5 ± 14.8	$P_4 = 0.000$	126.6 ± 21.11	$P_4 = 0.027$
Non-survivors ($n = 12$)	0.92 ± 0.11		228.6 ± 19.3		109.5 ± 18.32	

SOD – superoxoid dismutase; GP – glutathione peroxidase; Note: P_1 – reliable between control and strangulation; P_2 – reliable between control and obturation; P_3 – reliable between strangulation and obturation; P_4 – reliable between survivors and non-survivors.

Table 6. Diagnostic value of antioxidant-prooxidant status and intestinal fatty-acid binding protein to assess the probability of necrotic changes in the small intestine before surgery.

Indicators	AUC	Cutoff	SE	95% CI	Sensitivity	Specificity
TBA-reactive products	0.813	6.66	0.0693	0.712–0.895	0.632	0.893
Diene conjugates	0.680	3.565	0.0812	0.524–0.746	0.750	0.684
8-isoprostane	0.780	5.05	0.0743	0.641–0.854	0.786	0.789
Superoxide dismutase	0.818	1.1	0.0618	0.734–0.917	0.750	1.0
Catalase	0.804	225.2	0.0667	0.702–0.891	0.714	1.0
Glutathione peroxidase	0.787	111.1	0.0332	0.634–0.835	0.679	0.787
Intestinal fatty-acid binding protein	0.814	577.25	0.0712	0.714–0.895	0.909	0.619

AUC – area under the curve; CI – confidence interval.

such conditions significantly complicate the course of the pathological process and create additional conditions for deepening the severity of endogenous intoxication. In this study, it was found that the 8-isoprostane level had no significant predictive value for the diagnosis of small bowel necrosis (AUC = 0.780 with a sensitivity of 78.6% and a specificity of 78.9%) because it was known that the performance of the prediction model is considered limited at AUC = 0.70–0.80.

Hydrogen peroxide (H_2O_2) is the end product of the SOD reaction can react in vivo to form the hydroxyl free radical, but H_2O_2 can only be detoxified by the selenoenzyme, glutathione peroxidase (GP), but not by catalase as the Michaelis constant, which is an inverse measure of enzyme affinity, Km (affinity) of GP, for H_2O_2 is orders of magnitude lower than for catalase [30–32]. Data from the scientific literature on the severity of changes not only in biochemical parameters but also in histomorphological changes of hepatocytes in endotoxicosis of various origins were reported [33, 34]. Some authors noted that under such conditions, disruption of superoxide dismutase synthesis may be due to reduced production of transport proteins, in particular ceruloplasmin, but these data certainly require a more detailed study [35].

The GP activity in our study decreased in patients with surgical pathology of the small intestine of various origins which then itself will result into less detoxification of free radicals [32]. GP requires the presence of NADPH (H+), which is formed in the pentose phosphate cycle, and under conditions of endogenous intoxication. It seems that inhibition of enzyme protection in patients significantly exacerbated endogenous intoxication. According to our research,

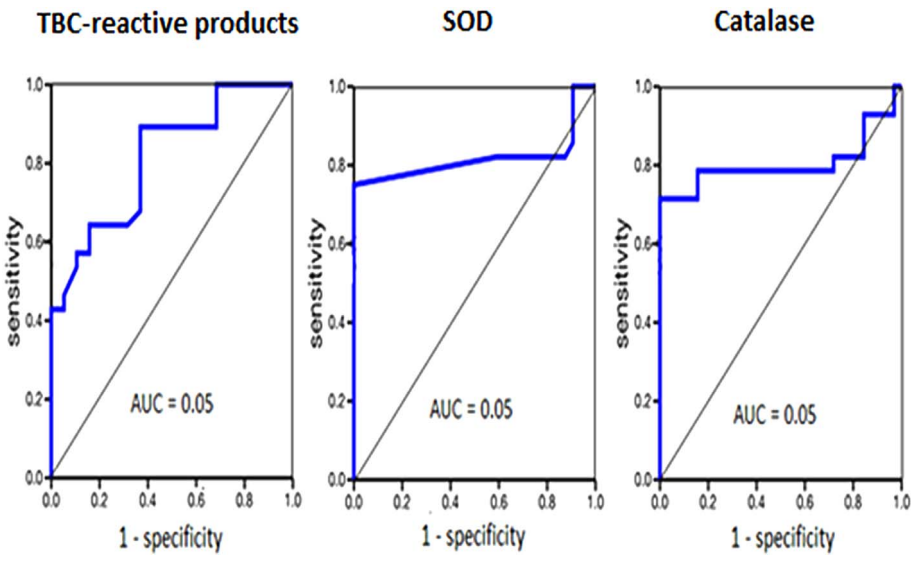

Fig. 2. Efficacy of AUC prediction models for suspected small bowel necrosis for TBA-reactive products, the activity of SOD, and catalase level. AUC – area under the curve; TBA – thiobarbituric acid; SOD – superoxide dismutase.

Table 7. The level of fatty intestine acid-binding protein in patients with small bowel pathology.

Patients with the pathology of the small intestine	Min/max	M ± SD	*P*
All groups	199.8–2189.6	911.3 ± 136.3	$P < 0.0001$
Strangulation obstruction of the small intestine ($n = 12$)	567.7–1240.4	881.8 ± 179.3	$P < 0.0001$ $P_1 < 0.0001$ $P_2 < 0.0001$ $P_3 < 0.01$
Obstructive obstruction of the small intestine ($n = 44$)	199.8–409.4	276.2 ± 61.86	$P < 0.001$
Mesenteric thrombosis ($n = 6$)	734.6–2189.6	1232.5 ± 422.6	$P < 0.0001$
Strangulated hernia ($n = 9$)	412.5–986.3	699.5 ± 172.7	$P < 0.0001$
Complicated by diffuse peritonitis ($n = 25$)	323.4–1104.6	769.4 ± 214.7	$P < 0.0001$
Survivors ($n = 59$)	199.8–654.7	486.2 ± 248.7	$P < 0.001$ $P_4 < 0.0001$
Non-survivors ($n = 12$)	567.7–2189.6	962.2 ± 270.5	$P < 0.0001$
Control ($n = 15$)	74.5–172.2	80.86 ± 40.3	

Note: P – reliable with control; P_1 – reliable strangulation and obturation; P_2 – reliable between strangulation of small bowel obstruction and mesenteric thrombosis; P_3 – reliable between strangulation of small bowel obstruction and strangulated hernia; P_4 – reliable between survivors and non-survivors.

the level of TBA-reactive products (AUC = 0.813), superoxide dismutase activity (AUC = 0.818), and catalase (AUC = 0.804) in patients analyzed before surgery was the most significant indicators of the necrosis of the small intestine. Otherwise it is of importance that catalase is only active where hydrogen peroxide concentrations are very high in peroxisomes and here catalase is key but everywhere else, GP is the key enzyme.

There are many risk factors for mortality in this category of patients analyzed in this study, which include the development of multiple organ failure, the use of vasopressors, mechanical ventilation, etc., and the role of the intestine as a "motor" of systemic disorders has been established [36]. Since the function of the gastrointestinal tract is known to be very complex, many researchers have tried to develop different scoring systems to assess its severity in the intensive care unit. The AGI score proposed by the European Society of Intensive Medicine (ESICM) Working Group [12], which includes abdominal signs and symptoms, IAP score, and organ function, is considered an important indicator of GI function in ICU patients. This classification is now considered classical and accepted by various medical societies. Reduced intestinal perfusion and loss of integrity of the enterocyte cell membrane contribute to the rapid release of I-FABP into the bloodstream and subsequent excretion by the kidneys [37].

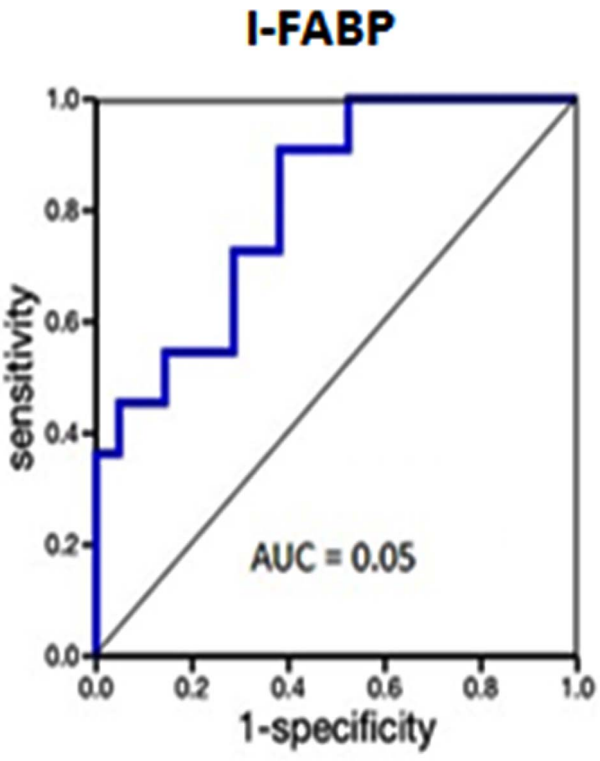

Fig. 3. Efficacy of AUC prediction models for suspected small bowel necrosis for I-FABP level. AUC – area under the curve; I-FABP – intestinal fatty-acid binding protein.

As our studies have shown, the concentration of I-FABP in the plasma of healthy volunteers was low and ranged from 74.5 to 172.2 pg/mL. According to the data obtained by other authors, its value significantly increases in the blood within 60 min after ischemia, which indicates that the release of this biomarker occurs in parallel with ischemia of the small intestine [38]. The highest mean I-FABPs were observed in patients with mesenteric thrombosis and in patients with strangulated small bowel obstruction. Also, this figure was significantly lower in patients with obstructive obstruction ($p = 0.000$) compared with the strangulated form of the disease, but in the presence of peritonitis, its mean values were lower than in strangulated intestinal obstruction without peritonitis ($p = 0.008$) and significantly higher than in obstructive obstruction ($p = 0.000$). Characteristic differences in the value of I-FABP were also found in living and deceased patients: in patients before surgery, its mean value was 49.5% lower than in the deceased. Understanding the pathophysiological basis of digestive tract dysfunction in abdominal surgical urgencies as a result of previous studies has shown that this may be the result of many factors that lead to damage to enterocytes, and an objective biomarker of enterocyte damage, which is I-FABP, can be used to predict the consequences of many critical conditions, including acute decompensated heart failure and cardiac arrest [39], septic shock, severe acute pancreatitis [40–42], and so on.

To sum up, for this category of patients, rapid diagnosis and effective treatment are of decisive importance, which is based on the etiology, severity, duration of delay in diagnosis, prognosis, etc. Over the past three decades, the management of these patients has evolved using two main principles, such as "source control" and "damage control", using various sophisticated and highly accurate non-invasive imaging techniques at the disposal of the surgeon. Early mortality in these patients, which is usually associated with septic shock and multiple organ failure, currently remains quite high. In our opinion, the use of early diagnosis, the choice of adequate surgical methods for surgical treatment, and personalized treatment of complications after surgery are factors that reduce the mortality of patients. This study showed that preoperative diagnosis and prognosis of small bowel necrosis for the choice of appropriate treatment for patients are the most correctly for assessing postoperative complications and mortality.

Research limitations

Our study had several limitations. First, this was a retrospective study, and our data was based on the medical records of patients who were being treated. Secondly, this study did not include all patients, but only those who had a complete set of biomarkers in the study profile. Of course, in the ignoring group, some patients died after surgery. Thus, we have not been able to completely avoid selection bias, and all of the results obtained require further validation in a much larger number of patients with urgent surgical pathology of the small intestine.

Conclusion

The development of endogenous intoxication in patients with urgent surgical pathology of the small intestine is accompanied by a significant increase in the number of reactive molecules that can damage such macromolecules as proteins, nucleic acids, cell membranes, and intracellular organelles, as well as an increase in the number of substrates of endogenous intoxication in the blood, which are active forms of oxygen, products of lipid peroxidation and oxidative modification of proteins: peroxides, hydroperoxides, diene conjugates, etc. The established metabolic disorders against the background of an increase in peptides of average molecular weight may indicate an increase in endogenous intoxication and the formation of membrane pathology in these patients, and tissue hypoxia and inhibition of the antioxidant system, leading to uncoupling of oxidative phosphorylation and tissue respiration, activation of oxidative stress, inhibition of bioenergy, and possibly the development of mitochondrial dysfunction, were the most expressed in patients with the presence of necrosis of the small intestine.

This study demonstrated that plasma I-FABP positively correlates with the necrotic changes of the small intestine presented in urgent surgical diseases. I-FABP was increased in plasma, probably in order to signal early indigestion in the small intestine due to its ischemic damage. The research for biomarkers needs to continue to

anticipate the progression of gut-necrotic associated damage and, thus, allow the prevention and monitoring of the therapeutic strategies used.

Nomenclature of abbreviations

APACHE II	Acute Physiology and Chronic Health Evaluation II score
APP	Abdominal perfusion pressure
AUC	Area under the curve
CI	Confidence interval
CT	Computed tomography
CU	Conventional units
DC	Diene conjugates
ESICM	European Society of Intensive Medicine
GP	Glutathione peroxidase
I-FABP	Intestinal fatty-acid binding protein
PAMW	Peptides of average molecular weight
ROC	Receiver operating characteristic
SBO	Small bowel obstruction
SBP	Systolic blood pressure
SOD	Superoxide dismutase
SOFA	SEQUENTIAL Organ Failure Assessment score
TBA	Thiobarbituric acid
WBC	White blood cells
WSES	World Society of Emergency Surgery

Compliance with ethical standards

The work has cleared by the Ethics Committee of Kharkiv National Medical University, Ukraine (protocol №3, September 20, 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. The content of this manuscript contain original material which has not been published before.

Informed consent process

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

Funding sources

This research was part of the research work of the Kharkiv National Medical University "Improvement and development of methods for diagnosis and surgical treatment of diseases and injuries of the abdominal cavity and chest, vessels of the upper and lower extremities using mini invasive techniques in patients at high risk of postoperative complications" The number of state registration is 0116u00499. Funding source is from the state budget.

References

1. Paulson EK, Thompson WM (2015), Review of small-bowel obstruction: the diagnosis and when to worry. Radiology 275, 2, 332–342. https://doi.org/10.1148/radiol.15131519.
2. Taydaş O, Ünal E, Onur MR, Akpınar E (2018), Role of computed tomography in intestinal obstruction. İstanbul Med J 19, 105–112. https://doi.org/10.5152/imj.2018.81084.
3. Sakari T, Christersson M, Karlbom U (2020), Mechanisms of adhesive small bowel obstruction and outcome of surgery; a population-based study. BMC Surg 20, 62. https://doi.org/10.1186/s12893.
4. Fevang BT, Fevang J, Stangeland L, Soreide O, Svanes K, Viste A (2000), Complications and death after surgical treatment of small bowel obstruction: a 35-year institutional experience. Ann Surg 231, 4, 529–537. https://doi.org/10.1097/00000658-200004000-00012.
5. Amara Y, Leppaniemi A, Catena F, Ansaloni L, Sugrue M, Fraga GP, et al. (2021), Diagnosis and management of small bowel obstruction in virgin abdomen: a WSES position paper. World J Emerg Surg 16, 1, 36. https://doi.org/10.1186/s13017-021-00379-8.
6. Gutteridge J, Hallewell B (2000), Free radicals and antioxidants in the year 2000. A historical look to the future. Ann NY Acad Sci 899, 136–147. https://doi.org/10.1111/j.1749-6632.2000.tb06182.x.
7. Ames BN, Shigenaga MK, Hagen TM (1993), Oxidants, antioxidants, and the degenerative diseases of aging. Proc Natl Acad Sci USA 90, 17, 7915–7922. https://doi.org/10.1073/pnas.90.17.7915.
8. Reintam A, Parm P, Kitus R, Kern H, Starkopf J (2009), Gastrointestinal symptoms in intensive care patients. Acta Anaesthesiol Scand 53, 318–324. https://doi.org/10.1111/j.1399-6576.2008.01860.x.
9. Li H, Chen Y, Huo F, Wang Y, Zhang D (2017), Association between acute gastrointestinal injury and biomarkers of intestinal barrier function in critically ill patients. BMC Gastroenterol 17, 45. https://doi.org/10.1186/s12876-017-0603-z.
10. Piton G, Belon F, Cypriani B, Regnard J, Puyraveau M, Manzon C, et al. (2013), Enterocyte damage in critically Ill patients is associated with shock condition and 28-Day mortality. Crit Care Med 41, 2169–2176. https://doi.org/10.1097/CCM.0b013e31828c26b5.
11. Reintam A, Parm P, Kitus R, Starkopf J, Kern H (2008), Gastrointestinal failure score in critically ill patients: a prospective observational study. Crit Care 12, R90. https://doi.org/10.1186/cc6958.
12. Reintam Blaser A, Malbrain ML, Starkopf J, Fruhwald S, Jakob SM, De Waele J, et al. (2012), Gastrointestinal function in intensive care patients: terminology, definitions and management. Recommendations of the ESICM Working Group on Abdominal Problems. Intensive Care Med 38, 384–394. https://doi.org/10.1007/s00134-011-2459-y.

13. Arthur JR, Boyne R (1985), Superoxide dismutase and glutathione peroxidase activities in neutrophils from selenium deficient and copper deficient cattle. Life Sci 36, 1569–1575. https://doi.org/10.1016/0024-3205(85)90381-9.
14. Di Saverio S, Coccolini F, Galati M, Smerieri N, Biffl WL, Ansaloniet L, et al. (2013), Bologna guidelines for diagnosis and management of adhesive small bowel obstruction (ASBO): 2013 update of the evidence-based guidelines from the world society of emergency surgery ASBO working group. World J Emerg Surg 8, 42. https://doi.org/10.1186/1749-7922-8-42.
15. Ten Broek RPG, Krielen P, Di Saverio S, Coccolini F, Biffl W, Ansaloni L, et al. (2018), Bologna guidelines for diagnosis and management of adhesive small bowel obstruction (ASBO): 2017 update of the evidence-based guidelines from the world society of emergency surgery ASBO working group. World J Emerg Surg 13, 1, 24. https://doi.org/10.1186/s13017-018-0185-2.
16. Birindelli A, Sartelli M, Di Saverio S, Coccolini F, Ansaloni L, van Ramshorst GH (2017), 2017 update of the WSES guidelines for emergency repair of complicated abdominal wall hernias. World J Emerg Surg 12, 37. https://doi.org/10.1186/s13017-017-0149-y.
17. Bala M, Kashuk J, Moore EE, Kluger Y, Biffl W, Gomes CA, et al. (2017), Acute mesenteric ischemia: guidelines of the World Society of Emergency Surgery. World J Emerg Surg 12, 38. https://doi.org/10.1186/s13017-017-0150-5.
18. Long B, Robertson J, Koyfman A (2019), Emergency medicine evaluation and management of small bowel obstruction: evidence-based recommendations. J Emerg Med 56, 2, 166–176. https://doi.org/10.1016/j.jemermed.2018.10.024.
19. Amara Y, Leppaniemi A, Catena F, Ansaloni L, Sugrue M, Gustavo GP, et al. (2021), Diagnosis and management of small bowel obstruction in virgin abdomen: a WSES position paper. World J Emerg Surg 16, 36. https://doi.org/10.1186/s13017-021-00379-8.
20. Khurshid Alam ABM, Jahan KI, Ali M (2019), Intestinal obstruction: an overview of aetiology, evaluation and management. J Surg Sci 17, 2, 89–95. https://doi.org/10.3329/jss.v17i2.43783.
21. Lee Ch-W, Kou H-W, Chou H-S, Chou H, Huang S-F, Chang C-H, Wu C-H, Yu M-C, Tsai H-I (2018), 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 13, 41. https://doi.org/10.1186/s13017-018-0202-5.
22. Faix JD (2013), Biomarkers of sepsis. Crit Rev Clin Lab Sci 50, 1, 23–36. https://doi.org/10.3109/10408363.2013.764490.
23. Majewski P, Zegan-Barańska M, Karolak I, Kaim K, Żukowski M, Kotfis K (2020), Current evidence regarding biomarkers used to aid postoperative delirium diagnosis in the field of cardiac surgery-review. Medicina (Kaunas) 56, 10, 493. https://doi.org/10.3390/medicina56100493.
24. Kelly BJ, Lautenbach E, Nachamkin I, Coffin SE, Gerber JS, Fuchs BD, et al. (2018), Combined biomarkers predict acute mortality among critically ill patients with suspected sepsis. Crit Care Med 46, 7, 1106–1113. https://doi.org/10.1097/CCM.0000000000003137.
25. Koch C, Edinger F, Fischer T, Brenck F, Hecker A, Katzer K, et al. (2020), 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 15, 63. https://wjes.biomedcentral.com/articles/10.1186/s13017-020-00343-y#citeas.
26. Seymour CW, Liu VX, Iwashyna TJ, Brunkhorst FM, Rea TD, Scherag A, et al. (2016), Assessment of clinical criteria for sepsis: for the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA 315, 762–774. https://doi.org/10.1001/jama.2016.0288.
27. Kovach CP, Fletcher GS, Rudd KE, Grant RM, Carlbom DJ (2019), 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 14, e0222563. https://doi.org/doi.org/10.1371/journal.pone.0222563.
28. Wacharasint P, Nakada TA, Boyd JH, Russell JA, Walley KR (2012), Normal-range blood lactate concentration in septic shock is prognostic and predictive. Shock 38, 1, 4–10. https://doi.org/10.1097/SHK.0b013e318254d41a.
29. Chu DC, Mehta AB, Walkey AJ (2017), Practice patterns and outcomes associated with procalcitonin use in critically ill patients with sepsis. Clin Infect Diseases 64, 11, 1509–1515. https://doi.org/10.1093/cid/cix179.
30. Simmons TW, Jamall IS (1989), Relative importance of intracellular glutathione peroxidase and catalase in vivo for prevention of peroxidation to the heart. Cardiovasc Res 23, 9, 774–779. https://doi.org/10.1093/cvr/23.9.774.
31. Jamall IS, Smith JC (1985), Effects of Cadmium on Glutathione peroxidase, superoxide dismutase, and lipid peroxidation in the rat heart: a possible mechanism of cadmium cardiotoxicity. Toxicol Appl Pharmacol 80, 1, 33–42. https://doi.org/10.1016/0041-008x(85)90098-5.
32. Simmons TW, Jamall IS (1988), Significance of alterations in hepatic antioxidant enzymes. Biochem J 251, 3, 913–917. https://doi.org/10.1042/bj2510913.
33. Bhattacharyya A, Chattopadhyay R, Mitra S, Crowe SE (2014), Oxidative stress: an essential factor in the pathogenesis of gastrointestinal mucosal diseases. Physiol Rev 94, 2, 329–354. https://doi.org/10.1152/physrev.00040.2012.
34. Vlasov AP, Kamkina OV, Trofimov VA, Vlasova TI, Abramova SV, Bolotskikh VA (2017), Metabolic restructuring in the liver under conditions of endogenous intoxication. Bull Exp Biol Med 163, 3, 317–320. https://doi.org/10.1007/s10517-017-3793-z.
35. Skrypko VD, Deltsova OI, Klymenko AO, Gonchar MH, Sheviak PI (2016), The use of antihypoxant and antioxidant therapy in comprehensive treatment of acute small intestinal obstruction. Galician Med J 23, 3. https://doi.org/10.21802/gmj.2016.3.52.
36. Clark JA, Coopersmith CM (2007), Intestinal crosstalk: a new paradigm for understanding the gut as the "motor" of critical illness. Shock 28, 384–393. https://doi.org/10.1097/shk.0b013e31805569df.
37. Kanda T, Fujii H, Tani T, Murakami H, Suda T, Sakai Y, et al. (1996), Intestinal fatty acid-binding protein is a useful diagnostic marker for mesenteric infarction in humans. Gastroenterology 110, 339–343. https://doi.org/10.1053/gast.1996.v110.pm8566578.
38. Schellekens DH, Grootjans J, Dello SA, Dello SA, van Dam RM, Dejong CHC, et al. (2014), Plasma intestinal fatty acid binding protein levels correlate with morphologic epithelial intestinal damage in a human translational ischemia-reperfusion model. J Clin Gastroenterol 48, 253–260. https://doi.org/10.1097/MCG.0b013e3182a87e3e.
39. Kitai T, Kim YH, Kiefer K, Morales R, Borowski AG, Grodin JL, Tang WHW (2017), Circulating intestinal fatty acid-binding protein (I-FABP) levels in acute decompensated heart failure. Clin Biochem 50, 491–495. https://doi.org/10.1016/j.clinbiochem.2017.02.014.
40. Grimaldi D, Guivarch E, Neveux N, Fichet J, Pène F, Marx JS, et al. (2013), Markers of intestinal injury are associated with endotoxemia in successfully resuscitated patients. Resuscitation 84, 60–65. https://doi.org/10.1016/j.resuscitation.2012.06.010.

41. Sekino M, Funaoka H, Sato S, Okada K, Inoue H, Yano R, et al. (2017), Intestinal fatty acid-binding protein level as a predictor of 28-day mortality and bowel ischemia in patients with septic shock: a preliminary study. J Crit Care 42, 92–100. https://doi.org/10.1016/j.jcrc.2017.07.012.

42. Kryvoruchko IA, Boyko VV, Honcharova NN, Taraban IA, Arsenyev OV, Ivanova JuV, Smetskov DA, Drozdova AG (2019), Evaluation of intestinal barrier biomarker I-FABP and severity of patients in acute pancreatitis. Novosti Khirurgii 27, 6, 640–649. https://doi.org/10.18484/2305-0047.2019.6.640.

Cite this article as: Kryvoruchko IA, Briukhanova TO, Nakonechna OA & Olefir OS 2022. Biomarker assessment in urgent surgical pathology of the small bowel: case-control analysis of a retrospective database. 4open, **5**, 12.