

Clinical Characteristics And Outcome of The Treatment of Critically Ill Patients With Abdominal Sepsis

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SUMMARY

Introduction: Abdominal infections are common causes of sepsis and septic shock in the intensive care unit (ICU), which are often associated with negative outcomes.

Aim: To determine the clinical characteristics of patients with abdominal sepsis, as well as the significance of causes thereof, therapeutic procedures in the ICU, and length of hospital stay related with abdominal sepsis treated at the Clinic for Anesthesiology, Intensive Care, and Pain Therapy from January 1, 2022, to December 31, 2022.

Material and Methods: This is a retrospective study conducted at the Intensive Care Unit (ICU), Clinic for Anesthesiology, Intensive Care, and Pain Therapy, University Clinical Center of Vojvodina (UCCV). By reviewing medical records, 60 patients of both genders with abdominal sepsis were analyzed.

Results: Of the 60 patients, 42% were female, while 58% were male, with an average age of 68 years. Of the total number of patients, 38.3% survived, while 61.7% died. Perforation of a hollow organ accounted for 45% of hospitalizations. The mortality rate in the ICU was 65%.

Conclusion: Using multivariate logistic regression, we obtained two independent predictors of fatal outcomes with a constant. Together, in the interaction of age ≥ 65 years and perforations, they increase the probability of a fatal outcomes for about 5.4 times, while vasopressor therapy increases the probability of fatal outcomes about 12 times compared to patients without vasopressor therapy; mortality was statistically higher in patients who required longer mechanical ventilation and in those who were hospitalized longer in the ICU.

Keywords: Abdominal Sepsis, Peritonitis, Cause, Outcome

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INTRODUCTION

Sepsis is defined as a life-threatening organ dysfunction caused by a dysregulated host response to infection. Organ dysfunction is defined as an acute change in the total SOFA (Sequential (Sepsis-Related) Organ Failure Assessment Score) score (increase) of ≥ 2 points in response to infection [1]. The incidence of sepsis ranges from 13.6% to 39.3% in different regions. Mortality rates due to sepsis in the ICU range from 25.8% to 35.3%. The most common cause of sepsis is pneumonia, accounting for half of all cases, followed by intra-abdominal infections and urinary tract infections. Independent risk factors for in-hospital mortality of ICU patients include advanced age, comorbidities (malignancies, chronic heart failure, liver cirrhosis, etc.), use of mechanical ventilation or renal replacement therapy [2]. Intra-abdominal infection is defined as an inflammatory reaction to the presence of bacteria and their toxins in the peritoneum, resulting in purulent exudate in the peritoneal cavity [3]. The most common cause of intra-abdominal infection is secondary peritonitis [4]. Intra-abdominal infections could be particularly challenging for clinicians due to its variety in severity of clinical presentation (ranging from uncomplicated cases to multiple organ dysfunction syndrome-MODS) [5]. The diagnosis of intra-abdominal infections is primarily based on clinical presentation - abdominal pain, fever, tachycardia, and tachypnea. Abdominal rigidity indicates the presence of peritonitis. Hypotension and signs of hypoperfusion such as lactic acidosis, oliguria, and acute changes in mental status suggest the presence of sepsis. Computed tomography (CT), radiography, and abdominal ultrasound can help identify the source of infection and diagnose urgent surgical cases [6]. It is of utmost necessity to surgically resolve the source of infection [7]. In addition to surgical management, the use of appropriate antibiotic therapy is one of the key factors for a good treatment outcome. Every surgical patient with secondary peritonitis requires the implementation of certain key elements of intensive therapy such as prophylaxis of gastric ulcers, lung-protective mechanical ventilation, hemodynamic stabilization (MAP >65 mmHg), administration of inotropic drugs in cases of myocardial dysfunction, invasive hemodynamic monitoring, establishment of

glomerular filtration rate > 0.5 ml/kg body weight, regular measurement of serum lactate, thrombosis prophylaxis, and enteral nutrition [8]. The overall condition of the patient should significantly and progressively improve within 24 to 72 hours of initial treatment (surgical intervention and initiation of antibiotic therapy) [4].

Given the importance of intra-abdominal infections as they are associated with numerous complications, high rates of mortality and morbidity and prolonged hospitalization, this study aimed to present the characteristics and treatment outcomes of critically ill patients with abdominal sepsis at the Clinic for Anesthesiology, Intensive Care, and Pain Therapy, UCCV, over a one-year period.

AIM

To determine the clinical characteristics of patients with abdominal sepsis, as well as the significance of causes thereof, therapeutic procedures in the ICU, and length of hospital stay on the patient's outcome.

MATERIAL AND METHODS

The study represents a clinical academic retrospective study conducted at the Intensive Care Unit (ICU) of the Clinic for Anesthesiology, Intensive Care, and Pain Therapy, University Clinical Center of Vojvodina (UCCV), from January 1, 2022, to December 31, 2022. Approval for the study was obtained from the Ethics Committee of UCCV, approval number 00-213.

The inclusion criteria included critically ill patients over 18 years of age (≥ 18), of both sexes, with abdominal sepsis treated at the Clinic during the specified period. Abdominal sepsis was defined as a SOFA score of ≥ 2 points above the baseline SOFA score (for patients without comorbidities, the baseline value is zero) caused by an abdominal infection. Confirmation of the cause of sepsis was made either macroscopically during laparotomy if the patient underwent surgery and/or based on radiological diagnostics (computed tomography of the abdomen). Abdominal infection was the primary diagnosis upon admission to the Intensive Care Unit. Criteria for exclusion from the study included patients with incomplete data.

During the specified one-year period,

Variable	p	Mean	SD
Age (years)		68.23	14.19
Number of days in the ICU		9.83	11.63
Total hospital stays (days)		16.78	13.51
		Frequency	Percent
Gender	Female	25	41.7
	Male	35	58.3
Age ≥ 65 years	No	19	31.7
	Yes	41	68.3
Survivors	No	37	61.7
	Yes	23	38.3
Survivors after release from ICU	No	24	64.9
	Yes	13	35.1

Table 1. Descriptive statistics for the total number of patients included in the study (N=60)

the total sample comprised of 60 patients, of both sexes, who met the mentioned criteria.

Data for the study were collected from medical records, including:

- medical history (from the clinical information system database)
- temperature-therapy-dietary lists
- laboratory values
- mechanical ventilation lists
- microbiological reports.

Collected and analyzed data included: basic demographic data (gender and age), cause of abdominal sepsis (organ perforation, obstruction/volvulus/incarcerated hernia with consequent ischemia, acute pancreatitis with necrosis/abscess; liver abscess, cholecystitis/cholangitis/gallbladder perforation), number and type of comorbidities, whether eradication of the source of sepsis occurred during the first surgical procedure or if patients were re-operated to control the source of sepsis. Additionally, data on therapeutic procedures within the scope of intensive care measures were collected: use of vasopressor support, corticosteroid therapy (hydrocortisone as part of septic shock therapy), duration of invasive mechanical ventilation (number of days), renal replacement therapy, blood transfusions (number of units of resuspended erythrocytes received in the ICU), insulin therapy, parenteral nutrition,

tracheotomy. Hospital-acquired infections (type and most common causative agents), total length of hospitalization (until discharge from UCCV or death), and number of days hospitalized in the ICU were also recorded. The SAPS II (Simplified Acute Physiology Score II) score was calculated for each patient in the ICU. The SAPS score represents a score for predicting in-hospital mortality, based on 17 parameters, and is calculated within the first 24 hours of patient admission to the ICU. Treatment outcome was defined as survival or death during hospitalization at UCCV, and based on this, patients were divided into two groups.

Descriptive statistics were used, including frequency and percentage (for categorical data), mean and standard deviation, or median with interquartile range (for numerical data). The Mann-Whitney and Chi-square tests or Fisher's exact probability test were used to test hypotheses of differences between groups. The analysis of predictors for no survivors was carried out by multivariate binomial logistic regression. Results were presented in tabular and graphical form. The accepted level of significance was 0.05. Data processing was performed using the IBM SPSS Statistics 20 (NY).

Comorbidities	Total number of patients (N)	Frequency	Percent
CVS	60	42	70
DM		15	25
COPD		5	8,3
Malignancy		9	15
CKD		16	26.6
Others		15	25

Table 2. Types and frequency of comorbidities

CVS - cardiovascular system
 DM - diabetes mellitus
 COPD - chronic obstructive pulmonary disease
 CKD - chronic kidney disease
 Others - diseases of the central nervous system and endocrine system

Table 3. The cause of abdominal sepsis

The cause of abdominal sepsis	Frequency	Percent
Organ perforation	27	45
Others	33	55
Total	60	100

Other - obstruction/volvulus/incarcerated hernia with resulting ischemia, acute pancreatitis with necrosis/abscess; liver abscess, cholecystitis/cholangitis/gallbladder perforation

Table 4. Frequently applied intensive care measures

	Frequency	Percent
Vasopressor support	43	71.7
Blood transfusion	42	70.0
Insulin therapy	26	43.3
Hydrocortisone	23	38.3
Parenteral nutrition	14	23.3
Renal replacement therapy	13	21.6
Mechanical ventilation	46	76.7

Vasopressor Support - administration of noradrenaline and vasopressin

RESULTS

The total number of patients included in the study was 60 (N=60).

Percentage prevalence of comorbidities: patients with cardiovascular system diseases (CVS) 70%; followed by chronic kidney disease (CKD) 26.6%; diabetes mellitus (DM) 25%; other associated diseases 25%; previous malignancies 15%; chronic obstructive pulmonary disease (COPD) 8.3% (Table 2).

Perforation of a hollow organ was the cause of sepsis in 45% of patients, while other causes of sepsis were present in 55% of patients (Table 3).

Vasopressor support was utilized in 71.7% of patients, blood transfusion in 70.0% of patients, insulin therapy in 43.3% of patients, administration of hydrocortisone in 38.3% of

patients, parenteral nutrition in 23.3% of patients, and renal replacement therapy in 21.6% of patients and mechanical ventilation in 76.7% (Table 4).

Patients with age ≥ 65 years and perforations and patients with vasopressor therapy, compared to patients without these characteristics, had a fatal outcome more often (37.8% vs 13% and 89.2% vs 43.5%) (Table 5).

Using multivariate logistic regression, we obtained two independent predictors of fatal outcomes with a constant. Together, in the interaction of age ≥ 65 years and perforations, they increase the probability of a fatal outcomes for about 5.4 times (Table 6), while vasopressor therapy increases the probability of a fatal outcomes about 12 times compared to patients without vasopressor therapy (Table 6). Multivariate binomial logistic regres-

Table 5. Differences in the frequency distribution between groups No / Yes fatal outcome in characteristics Age ≥ 65 years and perforations and Vasopressor therapy

		Fatal outcome		P
		No	Yes	
Age ≥ 65 years and perforations	No	20 (87.0%)	23 (62.2%)	0.045
	Yes	3 (13.0%)	14 (37.8%)	
Vasopressor therapy	No	13 (56.5%)	4 (10.8%)	0.000
	Yes	10 (43.5%)	33 (89.2%)	

Table 6. Logistic regression parameters for predictors of fatal outcomes

	B	SE	Wald	df	p	Odds ratio	95% Confidence interval for odds ratio	
							Lower	Upper
Age ≥ 65 years (Yes) and perforations (Yes)	1.694	0.837	4.102	1	0.043	5.444	1.056	28.057
Vasopressor therapy (Yes)	2.498	0.743	11.305	1	0.001	12.163	13 (56.5%)	4 (10.8%)
Constant	1.701	0.683	6.194	1	0.013	0.183		

B - unstandardized beta

SE - standard error

Wald - Wald Chi-Squared Test

df - degree in freedom

	Duration of mechanical ventilation (days)		Length of stay in the ICU (days)	
	Survivors	Non survivors	Survivors	Non survivors
Mean	2.65	10.97	5.57	12.49
SD	3.42	13.50	5.55	13.56
IQR	5	12	8	12
Min	0	0	3	0
Max	11	54	20	54
p	<0.001 ^b		0.023 ^b	

Table 7. Impact of duration of mechanical ventilation and the length of stay in ICU on mortality

SD - standard deviation
IQR - interquartile range

sion model showed good construct validity (Nagelkerke R² = 0.377) and excellent adequacy by the Hosmer-Lemesh test (Chi-square = 0.000; p = 1.000).

There was a statistically significant difference in mortality depending on the duration of mechanical ventilation of the lungs. In patients with fatal outcomes, mechanical ventilation was applied significantly longer (p<0.001). There is a statistically significant difference in mortality relative to the length of hospitalization in the ICU (number of days spent in the ICU). Mortality was significantly higher in patients who were hospitalized longer in the ICU, P <0.05 (p = 0.023) (Table 7).

DISCUSSION

The results obtained from our retrospective one-year analysis of 60 critically ill patients was as follows: 38.3% survived, while 61.7% died during hospitalization at UKCV, which includes both the mortality in the ICU and at the surgical department (in-hospital mortality). Sakr et al. included 10,069 subjects from Europe (54.1%), Asia (19.2%), America (17.1%), and other continents (9.6%). The incidence rates of sepsis ranged from 13.6% to 39.3% in different regions. The mortality of patients with abdominal sepsis in the ICU and in-hospital was 25.8% and 35.3%, respectively. These percentages varied depending on the region [2]. Prest et al. obtained results showing that from 2004 to 2018, the mortality rate from abdominal sepsis was 46.7/1,000,000 people, and there was an increase in mortality rate [10]. Blot et al. presented results in their study where the overall mortality rate of 2621 patients was 29.1% [5]. Compared to these results, the mortality rate in the ICU of our patients was twice as high. Jan De Waele et al. analyzed 1392 patients in their study and found that the mortality from abdominal sepsis in

the ICU was 29.4%. Furthermore, the mortality of these patients was higher compared to the mortality from other infections in the ICU [7]. The limitation of our research is the significantly smaller number of patients compared to these studies. Morar (Morar) et al. found that out of 55 examined patients, the mortality rate in the ICU was 74.1%, indicating that the majority of patients died in the ICU [11]. We obtained similar results in our study.

The burden of comorbidities is an important factor in the mortality of most critically ill patients. The most common comorbidities in patients in our study were cardiovascular diseases and diabetes mellitus. Xingzheng et al. concluded that the highest percentage of patients had cancer and chronic obstructive pulmonary disease among comorbidities [12]. Differences in this comparison may be due to demographic and geographical specificities. The limitation of our research is the significantly smaller number of patients compared to the study by Xingzheng et al. whose clinical study included 476 patients. Morar et al. observed a mutual association between comorbidities and mortality, stating that the comorbid condition hindered the surgical management of the source of abdominal infection and thus led to a fatal outcome [11].

When discussing the cause of abdominal sepsis in our patients, perforation of a hollow organ was the cause in 45% of our patients. Other causes such as obstruction, volvulus, incarcerated hernia with resulting ischemia, acute pancreatitis with necrosis and/or abscess, liver abscess, cholecystitis with/without gallbladder perforation, and cholangitis were present in 55% of patients. Morar et al. state that out of their 55 patients, perforation was present in 40 clinical cases, indicating that organ perforation was the most common cause of fatal outcome [11]. The discrepancy of our result compared to Morar et al. may lie in the

fact that in the mentioned study, firearm organ injury caused most of organ perforation, while such a cause was not present among our patients. The study conducted by Blot et al. mentions that diffuse peritonitis is associated with a higher mortality rate compared to all other causes, which differs from our results [5]. Despite noticing that organ perforation as a cause of abdominal sepsis occurred less than other causes, we have concluded, using logistic regression, that organ perforation is a significant cause of fatality and is one of determinants of the patient outcome amongst our patient study group. One mustn't neglect age as another contributing factor, which in association with organ perfusion, increased the probability of fatal outcome 5,4 times more often than other causes, and can, therefore, be another determinant for patient outcome (alongside the cause of intra - abdominal infection).

Commonly applied therapy (besides antibiotics) within the intensive care measures included vasopressor drugs, blood transfusions, insulin therapy, and the administration of hydrocortisone as part of the treatment for severe septic shock. Vasopressor support of our patients mostly involved the use of norepinephrine, and in some cases, vasopressin for patients with refractory septic shock. Vasopressor support was administered in over 70% of patients. Sartelli et al. in their work cite a large multicenter retrospective analysis of 2849 patients with septic shock where researchers found that mortality was lowest when vasopressors were administered within the first six hours of shock onset. Norepinephrine is the first-choice vasopressor used to correct hypotension and hypoperfusion in states of septic shock [6]. In our study vasopressor therapy increased the probability of fatal outcome about 12 times compared to patients without vasopressor therapy. This result cannot be used as a single determination factor in terms of patient outcome, but the result was indicative of the severity of patient's status and the likely development of septic shock.

In our study, mechanical ventilation of the lungs was applied in 76.7% of patients. We also found that there was a statistically significant difference in mortality depending on the duration of mechanical ventilation of the lungs. In patients with fatal outcomes, mechanical ventilation was applied significantly longer. Mechanical ventilation is carried out in critically ill patients who are respiratory

insufficient, which is often part of the clinical picture of patients with abdominal sepsis and speaks to the severity of the disease [13]. Xingzheng et al. found in their study that the number of days of mechanical ventilation was similar in survivors and non-survivors and that there was no correlation between the duration of mechanical ventilation and the fatal outcome [12]. The results of our study indicated the opposite. The reason for such outcome may lie in the occurrence of pneumonia as a nosocomial infection, which indirectly or directly plays an important role in morbidity and length of hospital stay, and which was one of the common treatment complications among our patients.

We found that another contributing factor to mortality outcome was the length of stay in the ICU. The length of stay in the ICU was determined by the severity of the clinical condition and the application of various treatment modalities, primarily mechanical ventilation of the lungs, invasive monitoring, which lead to a higher risk of nosocomial infections and therefore, to a higher mortality proportionate to the length of hospitalization in the ICU. Similar findings were reached by Xingzheng et al. as well as Jiaqi et al. who discovered a higher mortality in patients who required intensive care modalities - mechanical ventilation, renal replacement therapy, vasopressor support and glucocorticoid therapy [12,13].

In summary, we have identified an important interaction between gastrointestinal perforation and age 65 and older. This interaction is a predictor of mortality outcome. In line with this finding, these patients must immediately undergo emergency abdominal surgery and empiric broad-spectrum antibiotic therapy covering both Gram positive and Gram-negative pathogens, including anaerobes and fungi.

CONCLUSION

This scientific research aimed to determine the characteristics and treatment outcomes of critically ill patients with abdominal sepsis hospitalized at the Clinic for Anesthesiology, Intensive Care, and Pain Therapy of the University Clinical Center of Vojvodina over a one-year period. We have identified an important interaction between perforation and age 65 or older. This interaction is a predictor of

mortality outcome.

From our study, it is evident that the mortality rate in the studied patient population is high, emphasizing the need to implement all measures for timely recognition and treatment of patients whose critical condition is due to abdominal sepsis.

CONFLICT OF INTEREST

All authors declare no conflict of interest.

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Karakteristike i ishod lečenja kritično obolelih pacijenata sa abdominalnom sepsom

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KRATAK SADRŽAJ

Uvod: Abdominalne infekcije su česti uzroci sepse i septičkog šoka u jedinici intenzivne nege (JIN) i povezane su sa negativnim ishodima.

Cilj: Odrediti kliničke karakteristike pacijenata sa abdominalnom sepsom, kao i značaj uzroka abdominalne sepse, terapijskih procedura u JIN-u i dužine bolničkog boravka pacijenata sa abdominalnom sepsom lečenih na Klinici za anestezilogiju, intenzivnu negu i terapiju bola od 1. januara 2022. do 31. decembra 2022.

Materijali i metode: Ovo je retrospektivna studija sprovedena na Odeljenju intenzivne nege (ICU), Klinike za anestezilogiju, intenzivnu negu i terapiju bola, Univerzitetskog kliničkog centra Vojvodine (UKCV). Pregledom medicinske dokumentacije analizirano je 60 pacijenata oba pola sa abdominalnom sepsom.

Rezultati: Od 60 pacijenata, 42% su bile žene, dok je 58% bilo muškaraca, sa prosečnom starošću od 68 godina. Od ukupnog broja pacijenata, 38,3% je preživelo, dok je 61,7% umrlo. Perforacija šupljeg organa činila je 45% hospitalizacija. Stopa smrtnosti u JIN-u bila je 65%.

Zaključak: Korišćenjem multivarijantne logističke regresije, dobili smo dva nezavisna prediktora smrtnog ishoda sa konstantom. Zajedno, u interakciji starosti ≥ 65 godina i perforacija, povećavaju verovatnoću smrtnog ishoda za oko 5,4 puta, dok terapija vazopresorima povećava verovatnoću smrtnog ishoda za oko 12 puta u poređenju sa pacijentima bez terapije vazopresorima; smrtnost je statistički viša kod pacijenata koji su zahtevali dužu mehaničku ventilaciju pluća; smrtnost je statistički viša kod pacijenata koji su duže bili hospitalizovani u JIN-u.

Ključne reči: abdominalna sepsa, peritonitis, uzrok, ishod

Received: June 17, 2024

Accepted: July 17, 2024