

Original article

Developing a Severity Classification of Complicated Intra-Abdominal Infections

Evgeni Dimitrov^{1,2}, Georgi Minkov^{1,2}, Emil Enchev^{1,2}, Yovcho Yovtchev^{1,2}

¹University Hospital „Prof. Dr. Stoyan Kirkovich“ Stara Zagora, Department of Surgical Diseases,
Stara Zagora, Bulgaria

²Trakia University Stara Zagora, Faculty of Medicine, Department of Surgical Diseases and Anesthesiology,
Stara Zagora, Bulgaria

SUMMARY

Introduction/Aim. Currently, there is no classification reflecting the severity of complicated intra-abdominal infections (cIAIs). Therefore, we aimed to create one and facilitate the prognostic assessment of cIAIs in clinical practice.

Methods. This was a single-center study conducted at a University Hospital Stara Zagora including 140 patients with cIAIs. Retrospectively, for the period January 2017 – October 2018, we divided the patients with cIAIs into three groups according to their sequential organ failure assessment (SOFA) score and World Society of Emergency Surgery Sepsis Severity Score (WSES SSS) – mild cIAIs (SOFA < 2 points), severe cIAIs (SOFA ≥ 2) and severe complicated intra-abdominal sepsis (SCIAs) – WSES SSS ≥ 8 or septic shock. Prospectively, we validated the created classification in 62 patients with cIAIs between November 2018 and August 2021.

Results. For the retrospective and prospective group, respectively, death rate among patients with mild cIAIs was 3.1% and 3.6%, with severe cIAIs – 26.8% and 19%, and with SCIAs we observed the highest mortality – 68.8% and 30.8%. Prognostic scores that differed significantly according to severity for both time periods were SOFA, Mannheim Peritonitis Index, and WSES SSS.

Conclusion. The proposed classification has the potential to be a reliable predictor of severity in patients with cIAIs.

Keywords: intra-abdominal infections, mortality, severity classification, SOFA, WSES SSS

Corresponding author:

Evgeni Dimitrov

e-mail: evgeni_d1984@yahoo.com

INTRODUCTION

Intra-abdominal infections (IAIs) include a wide range of pathological conditions, which according to their spread in the peritoneal cavity are divided into uncomplicated and complicated (1). In uncomplicated IAIs, the infectious process affects only one abdominal organ and does not extend to parietal peritoneum, unlike complicated IAIs (cIAIs), which cause local or diffuse peritonitis (1). Despite the evolution in diagnosis, surgical methods, and intensive care treatment, cIAIs still represent a leading factor in non-traumatic mortality worldwide (2). Any delay in management usually leads to sepsis, septic shock, multiple organ failure, and eventual death. In over 20% of critical patients, the development of sepsis is due to cIAIs (3).

Currently, there is no a global classification which stratifies patients with cIAIs according to their risk of death. In this regard, we decided to propose such severity classification using two of the most reliable prognostic scoring systems so far – the sequential organ failure assessment (SOFA) score and World Society of Emergency Surgery Sepsis Severity Score (WSES SSS). The SOFA score was introduced in 1996 by the Working Group on Sepsis Related Problems of the European Society of Intensive Care Medicine to objectively describe the degree of organ dysfunction over time and to evaluate morbidity and mortality in patients with sepsis in the intensive care unit (ICU) (4). Over the years, the SOFA score had been validated in various patient groups (5, 6), and in 2016, it was included in the last Sepsis-3 definitions (7). In cIAIs, the established sensitivity and specificity of SOFA for prognostication of mortality are within 77.2 – 94.79% and 41.18 – 87.9%, respectively (8 - 10). The World Society of Emergency Surgery (WSES) developed in 2014 a prognostic scoring system specific for cIAIs and called it a WSES SSS (11). Several studies validated this score globally (12 - 14) and found that it can be precise, easy to calculate, and practical for patients with cIAIs. In such patients, the reported sensitivity and specificity for prediction of death vary between 76-92% and 68.2 - 90.48%, respectively (12, 14 - 16). As the WSES SSS mainly reflects the surgical aspect of the patient's condition, SOFA is a surgically independent tool. The two scoring systems can compensate for their disadvantages and differentiate properly an increased risk of death, improving prognostic assessment

and change in inadequate management of each patient.

Therefore, we aimed to introduce a novel severity classification of cIAIs and to compare various parameters and scoring systems between the severity patient groups.

MATERIAL AND METHODS

A single-center study, including retrospective and prospective data, was performed at the University Hospital Stara Zagora. For the period January 2017 – August 2021, a total of 186 patients with cIAIs were admitted in emergency setting to the Department of Surgical Diseases. Non-operative treatment methods like percutaneous drainage were not suitable in the studied group. We found missing data about some clinical parameters in 43 patients, two patients died before surgery, and one was < 18 years old. At the end, 140 participants were involved in the analysis (Figure 1).

Retrospectively, between January 2017 and October 2018, we divided 78 patients according to the severity of the disease into three groups: 1st group – mild cIAIs (mcIAIs), 2nd – severe cIAIs (scIAIs) and 3rd – severe complicated intra-abdominal sepsis (SCIAS). Prospectively, for the period November 2018 – August 2021, the created classification was validated in 62 patients with cIAIs. The protocol for the prospective study was approved by the Ethics Committee of the hospital (№ P4-10-275/05.04.2018). We aimed at screening consecutive eligible patients with cIAIs. Signed informed consent was obtained from patients or the next of kin. All procedures performed in the study involving human participants were in accordance with the ethical standards of the 1964 WMA Helsinki Declaration and its later amendments or comparable ethical standards.

In the mcIAIs group, we assigned the patients with absence of preoperative sepsis (SOFA < 2), SCIAS (WSES SSS ≤ 8) or septic shock; the scIAIs group included the patients with diagnosed sepsis (SOFA ≥ 2) and no signs of SCIAS (WSES SSS ≤ 8) or septic shock before surgery; the SCIAS group involved patients with the score ≥ 8 of the WSES SSS or present septic shock (Figure 2). The chosen cut-off values for group discrimination were defined from the concept of "sepsis" and "septic shock" according to the SEPSIS-3 definitions (7), and "severe compli-

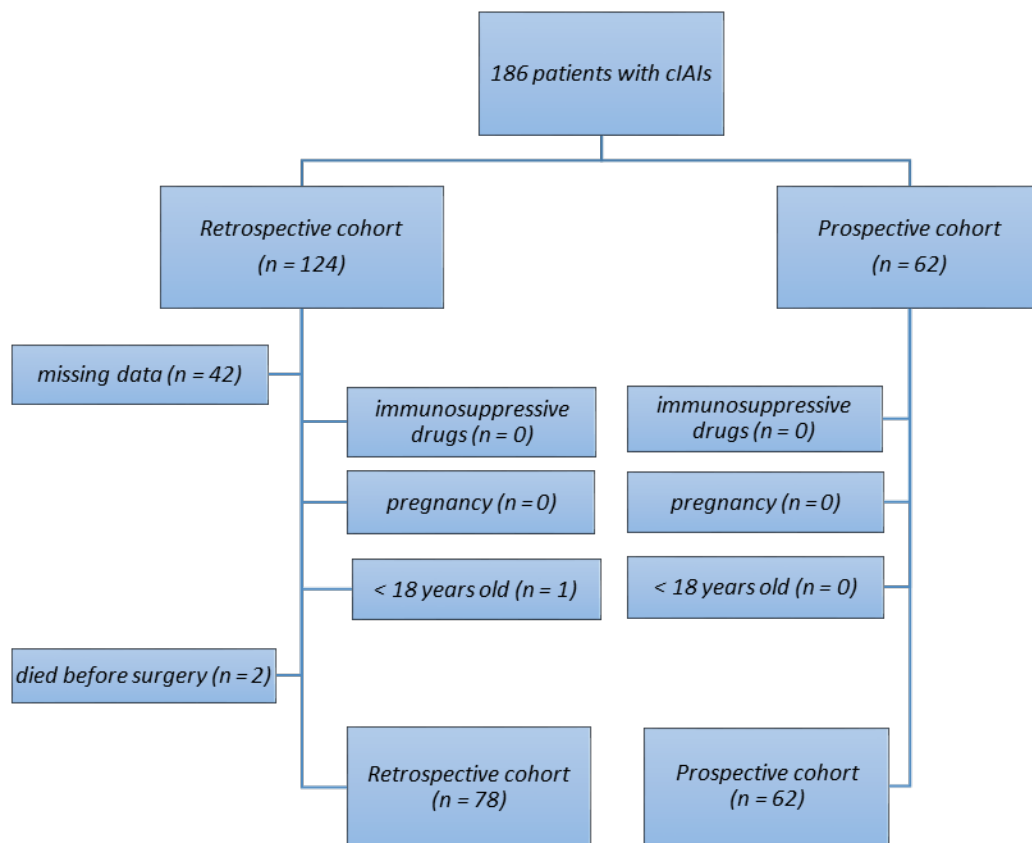


Figure 1. Flowchart of the study

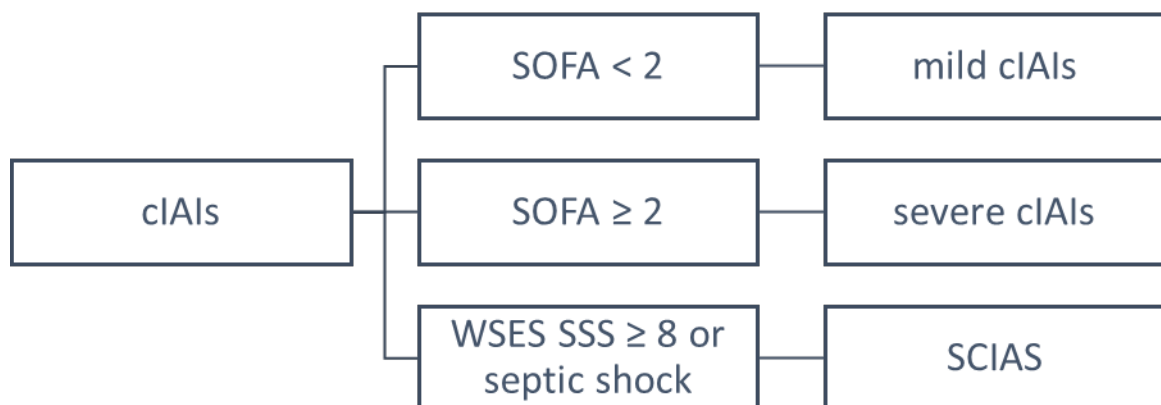


Figure 2. Severity classification of cIAs using SOFA and WSES SSS

cated intra-abdominal sepsis” according to Kirkpatrick et al. (17) The Third International Consensus Definitions for Sepsis and Septic Shock (7) state the following: sepsis is a life-threatening organ dysfunction (an increase of two or more points on the SOFA score) due to a dysregulated host response to infec-

tion. Septic shock was defined clinically as the presence of sepsis (despite adequate volume resuscitation) plus persistent hypotension requiring vasopressors to maintain SBP ≥ 65 mm Hg and serum lactate ≥ 2 mmol/L. In 2018, Kirkpatrick et al. (17) proposed the term “Severe Complicated Intra-Abdomi-

nal Sepsis" and defined it as the presence of septic shock according to SEPSIS-3 definitions, WSES SSS score ≥ 8 or Calgary Predisposition, Infection, Response, and Organ dysfunction (CPIRO) score ≥ 3 . According to the criteria we determined, the distribution by severity was as follows: retrospective group – mIAIs – 32 (41%), scIAIs – 30 (38.5%), and SCIAS – 16 (20.5%) patients; prospective group – mIAIs – 28 (45.2%), scIAIs – 21 (33.9%), and SCIAS – 13 (21%) patients.

The laboratory and clinical measurements necessary for calculating the scoring systems, as well as demographic data and clinical outcomes, were collected from patients' medical records. The SOFA score was calculated based on six different scores – each for the neurological, cardiovascular, respiratory, hepatobiliary, renal and coagulation systems (4) (Table 1). The WSES SSS was calculated after surgery according to six criteria (12) (Table 2).

We assessed the severity of cIAIs also using the quick-SOFA (qSOFA) score, Systemic Inflammatory Response Syndrome (SIRS), and Mannheim Peritonitis Index (MPI). A positive SIRS (18) was defined as ≥ 2 of the following four signs: heart rate $> 90/\text{min}$, respiratory rate $> 20/\text{min}$, body temperature $< 36^\circ\text{C}$ or $> 38^\circ\text{C}$ and, leucocytes count $< 4 \times 10^9/\text{L}$ or $> 12 \times 10^9/\text{L}$. The qSOFA score was calculated according to values of systolic blood pressure ≤ 100 mmHg, respiratory rate $\geq 22/\text{minute}$, and a Glasgow Coma Scale < 15 points (1 point for each criterion to yield a score value between 0 and 3). A positive score was identified as ≥ 2 points (7).

SIRS, qSOFA and SOFA were calculated based on patients' clinical data on admission; MPI and WSES SSS were calculated postoperatively based on eight (19) (Table 3) and six (12) (Table 2) risk factors, respectively.

The primary endpoint of the study was to assess the significance of proposed severity classification in predicting of the fatal outcome. Twenty-eight-day mortality was considered for the study.

SPSS Statistics 19.0 (IBM, Chicago, Illinois, USA) was used for data analysis. Prognostic performance of each scoring system was compared performing Receiver Operating Characteristics (AUROC) Curve analysis. Continuous variables were expressed as mean ($\pm$ SD) or median (IQR) for normally or non-normally distributed data, respectively. Group differences for continuous variables were established using Student's t-test and One-Way ANOVA test or Mann-Whitney U test and Kruskal-Wallis test. Categorical variables were presented as frequency (%) and compared by Fisher exact test or Chi-square test. A p-value was considered significant at < 0.05 .

Table 1. Sequential Organ Failure Assessment (0 – 24 score)

Organ system	0	1	2	3	4
Respiratory					
PaO ₂ /FiO ₂ (mmHg)	> 400	< 400	< 300	< 200	< 100
Coagulation					
Platelets, $10^3/\text{mm}^3$	> 150	< 150	< 100	< 50	< 20
Liver					
Bilirubin ($\mu\text{mol/L}$)	< 20	20 - 32	33 - 101	102 - 204	> 204
Cardiovascular					
Hypotension (mmHg)	MAP ≥ 70	MAP < 70	Dopamine ≤ 5 or dobutamine (any dose)	Dopamine > 5 or norepinephrine ≤ 0.1	Dopamine > 15 or norepinephrine > 0.1
Nervous					
Glasgow Coma Scale	15	13 - 14	10 - 12	6 - 9	< 6
Renal					
Creatinine ($\mu\text{mol/L}$) or urine output (mL/day)	< 110	110 - 170	171 - 299	300 - 440 or $< 500\text{mL/day}$	> 440 or $< 200\text{ mL/day}$

Table 2. WSES Sepsis Severity Score (0–18 score)

Risk factor	Points
<i>Age > 70 years</i>	2
<i>Immunosuppression</i>	3
<i>Setting of acquisition</i>	
Healthcare-associated infection	2
<i>Clinical condition on admission</i>	
Severe sepsis	3
Septic shock	5
<i>Origin of cIAIs</i>	
Colonic non-diverticular perforation peritonitis	2
Diverticular diffuse peritonitis	2
Postoperative diffuse peritonitis	2
Small bowel perforation peritonitis	3
<i>Delay in source control</i>	
Delayed initial intervention > 24 hours	3

Table 3. Mannheim peritonitis index (0 - 47 score)

Risk factor	Points
Age > 50 years	5
Female	5
Organ failure	7
Malignancy	4
Preoperatively duration of peritonitis > 24 hours	4
Origin of sepsis, non-colonic	4
Diffuse peritonitis	6
Exudate	
- Clear	0
- Purulent	6
- Fecal	12

RESULTS

Patient characteristics

Both in the retrospective and prospective cohorts (RC and PC), average age between severity groups differs significantly ($p < 0.0001$ and $p = 0.005$, respectively), whereas patients with mCIAIs were the youngest and those with SCIAS were the oldest.

Statistically significant differences emerged for the source ($p = 0.043$) of infection in RC, however,

this observation was not present in PC ($p = 0.177$). As the severity increased, we observed the presence of cardiovascular comorbidity more frequently in both cohorts ($p = 0.019$). Sex and type of exudate demonstrated no significance in RC ($p = 0.728$ and $p = 0.548$) and PC ($p = 0.978$ and $p = 0.616$) (Table 4).

Table 4. Patient characteristics

Variable	Retrospective group					Prospective group				
	Total (78)	mcIAIs (32)	scIAIs (30)	SCIAs (16)	p value	Total (62)	mcIAIs (28)	scIAIs (21)	SCIAs (13)	p value
Age, years (±SD)	59.09±18.8	47.8±16.1	63.17±18.5	74±8.7	<0.0001	65 (49.5-76.25)	52.5 (41.25-71.5)	68 (58.5-76)	75 (68-80.5)	0.005
Sex, n (%) male/female	43(55.1)/35 (44.9)	16(37.2)/16 (45.7)	18(41.9)/12 (34.3)	9(20.9)/7 (20)	0.728	35(56.5)/27 (43.5)	16(45.7)/12 (44.4)	12(34.3)/9 (33.3)	7(20)/6 (22.2)	0.978
Source, n (%)										
Appendix	19 (24.4)	13 (40.6)	6 (20)	0 (0)	0.043	15 (24.2)	11 (39.3)	3 (14.3)	1 (7.7)	0.177
Hepatobiliary system	16 (20.5)	5 (15.6)	8 (26.7)	3 (18.8)		22 (35.5)	6 (21.4)	9 (42.9)	7 (53.8)	
Stomach/duodenum	17 (21.8)	6 (18.8)	7 (23.3)	4 (25)		12 (19.4)	7 (25)	3 (14.3)	2 (15.4)	
Large bowel	14 (17.9)	4 (12.5)	4 (13.3)	6 (37.5)		7 (11.3)	2 (7.1)	3 (14.3)	2 (15.4)	
Small bowel	2 (2.6)	0 (0)	0 (0)	2 (12.5)		2 (3.2)	0 (0)	1 (4.8)	1 (7.7)	
Gynecological	4 (5.1)	2 (6.3)	2 (6.7)	0 (0)		4 (6.5)	2 (7.1)	2 (9.5)	0 (0)	
Other	6 (7.7)	2 (6.3)	3 (10)	1 (6.3)		0 (0)	0 (0)	0 (0)	0 (0)	
Exudate, n (%)										
Clear	12 (15.4)	6 (18.8)	5 (16.7)	1 (6.3)	0.548	8 (12.9)	3 (10.7)	4 (19)	1 (7.7)	0.616
Purulent	62 (79.5)	25 (78.1)	24 (80)	13 (81.2)		54 (87.1)	25 (89.3)	17 (81)	12 (92.3)	
Feculent	4 (5.1)	1 (3.1)	1 (3.3)	2 (12.5)		0 (0)	0 (0)	0 (0)	0 (0)	
Preoperative duration of peritonitis > 24 h, n (%)	36 (46.2)	10 (31.3)	13 (43.3)	13 (81.3)	0.004	41 (66.1)	16 (57.1)	12 (57.1)	13 (100)	0.007
Comorbidity, n(%)										
Cardiovascular	30 (38.5)	7 (21.9)	13 (43.3)	10 (62.5)	0.019	38 (61.3)	12 (42.9)	15 (71.4)	11 (84.6)	0.019
Endocrine	9 (11.5)	1 (3.1)	4 (13.3)	4 (25)	0.059	8 (12.9)	2 (7.1)	5 (23.8)	1 (7.7)	0.199
Oncological	15 (19.2)	4 (12.5)	3 (10)	8 (50)	0.002	3 (4.8)	1 (3.6)	1 (4.8)	1 (7.7)	0.79

*statistical significance at p-value < 0.05

Scoring systems

We found a high significance of SOFA in evaluating our severity classification ($p < 0.0001$ both in RC and PC). We had the same observation for the WSES SSS ($p < 0.0001$ both in RC and PC), whereas median SOFA and WSES SSS scores were lower in mcIAIs, higher in scIAIs, and the highest in SCIAs. These results are explained in part by the fact that $\text{SOFA} < 2$ and $\text{WSES SSS} \geq 8$ are criteria for the differentiation of scIAIs and SCIAs, respectively. The qSOFA showed significant differences in median values among severity groups in RC ($p = 0.025$),

however, in PC, this pattern disappeared ($p = 0.101$). SIRS had no ability to discriminate the severity of cIAIs ($p = 0.844$ in RC and $p = 0.408$ in PC). MPI showed great ability to discriminate severity both in RC and PC ($p < 0.0001$), whereas higher scores were associated with more severe course of cIAIs (mcIAIs vs. scIAIs vs. SCIAs = 19 IQR 15-21 vs. 21 IQR 18.75-26 vs. 32 IQR 32.25-37 in RC and mcIAIs vs. scIAIs vs. SCIAs = 20 IQR 14.25-25 vs. 26 IQR 20-32 vs. 28 IQR 25.5-32 in PC) (Table 5).

Table 5. Scoring systems

Variable	Retrospective group					Prospective group				
	Total (78)	mcIAIs (32)	scIAIs (30)	SCIAs (16)	p value	Total (62)	mcIAIs (28)	scIAIs (21)	SCIAs (13)	p value
SOFA, points (IQR)	2 (1-4)	1 (0-1)	3 (2-4)	5 (3-6)	<0.0001	2 (1-3)	1 (0-1)	3 (2-3)	4 (2.5-5.5)	<0.0001
qSOFA, points (IQR)	0 (0-1)	0 (0-0)	0 (0-1)	0.5 (0-1.75)	0.025	0 (0-1)	0 (0-1)	0 (0-1)	1 (0-1.5)	0.101
SIRS, points (IQR)	1 (0-2)	1 (1-1)	1 (0-2)	1 (0-2)	0.844	2 (1-2)	2 (1-2)	2 (1-2.5)	1 (1-2)	0.408
MPI, points (IQR)	21 (18-28)	19 (15-21)	21 (18.75-26)	32 (30.25-37)	<0.0001	25 (19-30)	20 (14.25-25)	26 (20-32)	28 (25.5-32)	<0.0001
WSES SSS, points (IQR)	3 (0-6.25)	0 (0-3)	2 (0-5)	8 (8-9.5)	<0.0001	5 (3-6.25)	3 (0-5)	6 (5-6)	8 (8-8)	<0.0001

*statistical significance at p-value < 0.05

Mortality

Death rate among severity groups in both cohorts progressively increased (Table 6). In RC, participants with mcIAIs had mortality rate of 3.1% and those with scIAIs – 26.7%. More than the half of the patients (68.8%) with SCIAs died, which was notable (Figure 3A). In PC, the overall in-hospital mortality

was significantly lower (14.5% vs 25.6%). According to the severity classification, the established death rate in PC showed the following distribution: patients with mcIAIs – 3.6%, those with scIAIs – 19%, and SCIAs – 30.8%. (Figure 3B).

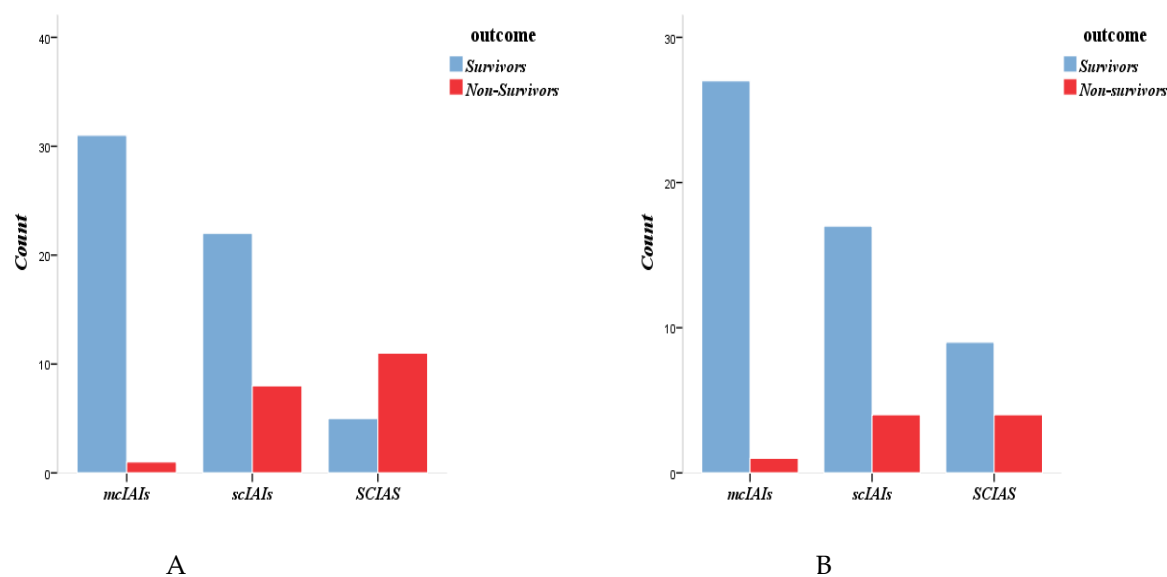


Figure 3. Death rate in A. retrospective and B. prospective cohort

Table 6. Mortality rate

Mortality, n (%)	Retrospective group				Prospective group			
	Total (78)	mcIAIs (32)	scIAIs (30)	SCIAS (16)	Total (62)	mcIAIs (28)	scIAIs (21)	SCIAS (13)
	20 (25.6)	1 (3.1)	8 (26.7)	11 (68.8)	9 (14.5)	1 (3.6)	4 (19)	4 (30.8)

DISCUSSION

Globally, complicated intra-abdominal infections rank among the first cause of non-traumatic mortality and often lead to sepsis and septic shock (20). Despite advances in conservative treatment and surgical techniques over the past decade, the cIAIs remain an important factor of adverse outcome, regardless of age, race, or social status. Early prognosis helps to identify high-risk patients, facilitating assessment of the adequacy of the therapeutic approach and the possibilities for treatment adjustment (20). The search for new prognostic methods which could correctly evaluate the severity of cIAIs is still a topic of high interest.

Due to the lack of a classification reflecting the severity of cIAIs at the moment, which is accepted in everyday practice, we decided to propose a new one. Retrospectively, we created such severity classification and then prospectively tried to validate it. Two scoring systems (SOFA and WSES SSS) were used to differentiate three groups of severity - mild cIAIs (no sepsis), severe cIAIs (sepsis), and SCIAS (severe complicated sepsis). Several prognostic factors successfully predicted the developed severity classification.

The patient's age is one of the easiest prognostic factors to establish. Ageing is accompanied by a loss of physiological reserve, which makes older patients significantly more vulnerable to various diseases. Elderly patients constitute a very large proportion of the general population in intensive care units, and for them sepsis appears to be significantly more dangerous (21). Compared with younger patients, both the incidence and mortality of sepsis are increased (22). Our severity classification confirmed these findings. Age was found as a significant factor for prognostication of severity both in retrospective ($p < 0.0001$) and prospective ($p = 0.005$) cohorts,

whereas advanced age was associated with higher severity (RC: mcIAIs - 47.8 years, scIAIs - 63.17

years, and SCIAS - 74 years and PC: mcIAIs - 52.5 years, scIAIs - 68 years, and SCIAS - 75 years).

An international multicenter study analyzing the epidemiology of patients with cIAIs and sepsis found that mortality increases with age - 20.9% in patients aged 40 - 59 years, 30.5% aged 60 - 69 years, 31.2% aged 70 - 79 years, and 44.7% > 80 years ($p < 0.001$) (23). The age was assessed as a significant predictor of severity and death in patients with cIAIs by Maseda et al. (24), Jung et al. (10), Pan et al. (25) and the WSES studies "CIAOW" (11) and "PIPAS" (20).

Cardiovascular comorbidities seem to be a significant prognostic factor in cIAIs. Xue et al. (26) and Pan et al. (25) found an association between hypertension and mortality in patients with IAI ($p = 0.013$; $p = 0.018$). Blot et al. (27) established in critically ill patients with IAI and sepsis that congestive heart failure was an independent predictor of fatal outcome with OR = 1.86. In patients with secondary peritonitis, Ohmann et al. (28) observed that cardiovascular comorbidity was associated with a high risk of death ($p = 0.001$). Jung et al. (10) in cIAIs reported a predictive value of hypertension ($p = 0.011$). Sartelli et al. (20) found cardiovascular comorbidity as an independent predictor of death in patients with cIAIs ($p < 0.001$). In our RC, we found significantly more frequent cardiovascular comorbidities with a more severe course of the infection (mcIAIs - 21.9% vs scIAIs - 43.3% vs SCIAS - 62.5%, $p = 0.019$). This observation was validated in the PC - 42.9% in mcIAIs, 71.4% in scIAIs, and 84.6% in SCIAS, $p = 0.019$.

Considering the source of infection as a prognostic factor, we determined its significant association with severity in RC ($p = 0.043$). Analyzing this

association in PC, however, we established that it was no longer present ($p = 0.177$). Despite the lack of statistical significance in PC, we should still note that most of cIAIs of appendicular origin occurred as mCIAIs – 73.3% in PC and 68.4% in RC, and only one patient from both cohorts had SCIAS. Infections of gynecological origin occurred also as less severe – no patient had SCIAS. Mortality due to appendicular and gynecological origin in general is low, which was also reported in the "WISS" study (12), with mortality rate for appendicular and gynecological peritonitis 4.1% and 0%, respectively. Opposite to this, we observed the small bowel origin as unfavorable prognostic factor – in RC 100% of patients had SCIAS and in PC 50% had sCIAIs and 50% had SCIAS. Small bowel perforation has been shown to be an independent predictor of fatal outcome in the CIAOW study (11), therefore, it is included in the WSES SSS as the least favorable source of infection. The source of infection itself undoubtedly contributes to the severity of cIAIs, and thus some intra-abdominal infections are more severe and are associated with higher mortality rates than others. This is perhaps also one of the reasons for the differences in mortality in SCIAS between RC and PC that we observed (68.8% vs 30.8%).

Early and effective source control should be performed as soon as possible to reduce morbidity and mortality rates (20). Preoperative duration of peritonitis over 24 hours is a proven prognostic factor according to a number of authors and was even included as an independent predictor of death in the scoring systems MPI (19) and WSES SSS (11). In our study, we had a similar observation – both in RC and PC, this prognostic factor showed an unfavorable impact on disease severity ($p = 0.004$ and $p = 0.007$, respectively). Unfortunately, nearly half (46.2%) of the patients in the RC and 2/3 (66.1%) of the patients in PC were present with an ongoing peritonitis >24 h before surgery, which also affected survival rates.

In 1900s, the cIAIs have been associated with nearly 90% mortality due to predominantly conservative behavior (29). At the end of the 20th century, owing to more aggressive surgical methods, the development of intensive care and the availability of a wide variety of antimicrobials, a significant reduction in mortality to < 25% was reported (30). Recent global multicenter studies established even lower mortality rates of 8.9-10.5% (11, 12, 20). However, other authors reported higher death rates in the range of 10.9-29.1% (10, 25, 27, 28, 31). In RC, we ob-

served in-hospital mortality of 25% and a significant reduction in PC – 14.5%. Both in RC and PC, death rates were successfully predicted by our severity classification – 3.1% and 3.6% in patients with mCIAIs, 19% and 26.75% in sCIAIs, 68.8% and 30.8% in SCIAS, respectively. The lower mortality in PC both in general and in SCIAS could also be due to the fact that in no patient we detected feculent exudate (in RC there were four patients and two of them were classified as SCIAS), which is a proven independent predictor of fatal outcome and is included in the MPI scoring system rated with 12 points (the most severe parameter) (14).

The qSOFA showed prognostic value for prediction of severity in RC ($p = 0.025$). In validation cohort, however, the significance was lost ($p = 0.101$) and we believe that this might be due the smaller sample size of PC. The SOFA and WSES SSS scoring systems successfully predicted not only the specific severity group for which they were used, but the entire classification we created. Both in RC and PC, SOFA increased in association with severity (RC = 1 in mCIAIs vs. 3 in sCIAIs vs. 5 in SCIAS, $p < 0.0001$ and RC = 1 in mCIAIs vs. 3 in sCIAIs vs. 4 in SCIAS, $p < 0.0001$). The same observation applied to the WSES SSS – for RC ($p < 0.0001$) and PC ($p < 0.0001$) we found the lowest median value in patients with mCIAIs (0 and 3, respectively), higher in sCIAIs (2 and 6, respectively) and the highest in SCIAS (8 and 8, respectively). The other analyzed surgical score MPI demonstrated a great ability to prognosticate the severity in RC ($p < 0.0001$) and PC ($p < 0.0001$) and validated our classification, whereat higher score was associated with higher severity (mCIAIs vs sCIAIs vs SCIAS = 19 vs 21 vs 32 in RC and mCIAIs vs sCIAIs vs SCIAS = 20 vs 26 vs 28 in PC).

We believe that our proposed severity classification of cIAIs can be easily adopted in clinical practice, as it correctly predicts the course of the disease and the increased risk of poor outcome. Stratification of patients according to the risk of fatal outcome of mild cIAIs, severe cIAIs, and severe complicated intra-abdominal sepsis provides an early chance of prognostic evaluation. This further enables the adoption of a timely and suitable change in the therapeutic strategy, creating conditions for a favorable outcome of the treatment and reducing the mortality.

As limitations of our study, we can highlight the single-center experience and the small sample size. Further larger multicenter prospective studies

could assess the accuracy of this classification in patients with cIAs.

CONCLUSION

The severity classification we created reflects the course of the disease and correctly assesses the increased risk of an adverse outcome. Therefore, we believe that it can be applied in everyday practice

and fill the current lack of such a classification, ensuring a significant reduction in morbidity and mortality in the future.

Conflict of interest

All authors have no conflicts of interest to report and have received no financial support in relation to this manuscript.

References

1. Menichetti F. and Sganga G. Definition and Classification of Intra-abdominal Infections, J. Chemother 2009;21(sup1), 3-4.
<https://doi.org/10.1179/joc.2009.21.Supplement-1.3>
2. Tochie JN, Agbor NV, Frank Leonel TT, et al. Global epidemiology of acute generalised peritonitis: a protocol for a systematic review and meta-analysis. BMJ Open 2020;10:e034326.
<https://doi.org/10.1136/bmjopen-2019-034326>
3. Vincent JL, Rello J, Marshall J, et al. International study of the prevalence and outcomes of infection in intensive care units. JAMA 2009; 302: 2323-9.
<https://doi.org/10.1001/jama.2009.1754>
4. Vincent JL, Moreno R, Takala J. et al. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. Intensive Care Med 1996; 22: 707-10.
<https://doi.org/10.1007/BF01709751>
5. Lorente JA, Vallejo A, Galeiras R, et al. Organ dysfunction as estimated by the SOFA score is related to outcome in critically ill burned patients. Shock 2009;31:125-31.
<https://doi.org/10.1097/SHK.0b013e31817fc3ef>
6. Lopes Ferreira F, Peres Bota D, Bross A, et al. Serial evaluation of the SOFA score to predict outcome. JAMA 2001;286:1754-58.
<https://doi.org/10.1001/jama.286.14.1754>
7. Singer M, Deutschman CS, Seymour CW, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA 2016;315(8):801-10.
<https://doi.org/10.1001/jama.2016.0287>
8. Jobin SP, Maitra S, Baidya DK. et al. Role of serial lactate measurement to predict 28-day mortality in patients undergoing emergency laparotomy for perforation peritonitis: prospective observational study. J intensive care 2019; 7 : 58

<https://doi.org/10.1186/s40560-019-0418-9>

9. Nugraha GL, Septarendra D, Lesmana, T. Comparative study of SOFA, WSES, and CPRO scoring systems as mortality predictors in a patient with complicated intra-abdominal infection. *Bali Med J* 2022; 11(3): 1397-403. <https://doi.org/10.15562/bmj.v11i3.3523>
10. Jung YT, Jeon J, Park JY, et al. Addition of lactic acid levels improves the accuracy of quick sequential organ failure assessment in predicting mortality in surgical patients with complicated intra-abdominal infections: a retrospective study. *World J Emerg Surg* 2018;13:14. <https://doi.org/10.1186/s13017-018-0173-6>
11. Sartelli M, Catena F, Ansaloni L, et al. Complicated intra-abdominal infections worldwide: the definitive data of the CIAOW Study. *World J Emerg Surg* 2014; 9:37. <https://doi.org/10.1186/1749-7922-9-37>
12. Sartelli M, Abu-Zidan FM, Catena F. et al. Global validation of the WSES Sepsis Severity Score for patients with complicated intra-abdominal infections: a prospective multicentre study (WISS Study). *World J Emerg Surg* 2015; 10 : 61. <https://doi.org/10.1186/s13017-015-0055-0>
13. Mwenda KI, Ojuka DK, Awori MN. Utility of World Society of Emergency Surgery Sepsis Severity Score in Predicting Outcomes of Intra-abdominal Infections. *Ann Afr Surg* 2020; 17(2):65-68 <https://doi.org/10.4314/aas.v17i2.5>
14. Dimitrov E, Minkov G, Enchev E, Yovtchev Y. Prognostic performance of world society of emergency surgery sepsis severity score in bulgarian patients with complicated intra-abdominal infections. *Trakia J Sci* 2021; 3:253-8. <https://doi.org/10.15547/tjs.2021.03.009>
15. Godínez-Vidal AR, Vázquez-Rentería R, Guerrero-Ponce AE, et al. Use of the WSES scale to predict mortality in patients with intra-abdominal infection. *Rev Mex de Cirugía del Aparato Digestivo* 2020;9(2): 65-70.
16. Tolonen, M., Coccolini, F., Ansaloni, L. et al. Getting the invite list right: a discussion of sepsis severity scoring systems in severe complicated intra-abdominal sepsis and randomized trial inclusion criteria. *World J Emerg Surg* 13, 17 (2018). <https://doi.org/10.1186/s13017-018-0177-2>
17. Kirkpatrick AW, Coccolini F, Ansaloni L. et al. Closed Or Open after Source Control Laparotomy for Severe Complicated Intra-Abdominal Sepsis (the COOL trial): study protocol for a randomized controlled trial. *World J Emerg Surg* 2018; 13 : 26. <https://doi.org/10.1186/s13017-018-0183-4>
18. Bone RC, Balk RA, Cerra FB, et al. Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. *Chest* 1992;101:1644-55. <https://doi.org/10.1378/chest.101.6.1644>
19. Wacha H, Linder MM, Feldman U, et al. Mannheim peritonitis index - prediction of risk of death from peritonitis: construction of a statistical and validation of an empirically based index. *Theoretical Surg* 1987; 1:169-77.
20. Sartelli M, Abu-Zidan FM, Labricciosa FM. et al. Physiological parameters for Prognosis in Abdominal Sepsis (PIPAS) Study: a WSES observational study. *World J Emerg Surg* 2019; 14 : 34. <https://doi.org/10.1186/s13017-019-0253-2>
21. Pisani MA. (). Considerations in caring for the critically ill older patient. *J Intensive Care Med* 2009; 24(2) 83-95. <https://doi.org/10.1177/0885066608329942>
22. Starr ME, Saito M, Evers BM, Saito H. Age-Associated Increase in Cytokine Production During Systemic Inflammation-II: The Role of IL-1 β in Age-Dependent IL-6 Upregulation in Adipose Tissue. *J Gerontol A Biol Sci Med Sci*. 2015;70(12):1508-15. <https://doi.org/10.1093/gerona/glu197>
23. Arvaniti K, Dimopoulos G, Antonelli M, et al. Epidemiology and age-related mortality in critically ill patients with intra-abdominal infection or sepsis: an international cohort study. *Int J Antimicrob Agents* 2022;60(1):106591

<https://doi.org/10.1016/j.ijantimicag.2022.106591>

24. Maseda E, Ramírez S, Picatto P, et al. Critically ill patients with community-onset intraabdominal infections: Influence of healthcare exposure on resistance rates and mortality. *PLoS One* 2019;14(9):e0223092
<https://doi.org/10.1371/journal.pone.0223092>
25. Pan J, Zhu Q, Zhang X, et al. Factors Influencing the Prognosis of Patients with Intra-Abdominal Infection and Its Value in Assessing Prognosis. *Infect Drug Resist* 2021;14:3425-32.
<https://doi.org/10.2147/IDR.S325386>
26. Xue G, Liang H, Ye J, et al. Development and Validation of a Predictive Scoring System for In-hospital Death in Patients With Intra-Abdominal Infection: A Single-Center 10-Year Retrospective Study. *Front Med* 2021;8:741914
<https://doi.org/10.3389/fmed.2021.741914>
27. Blot S, Antonelli M, Arvaniti K, et al. Epidemiology of intra-abdominal infection and sepsis in critically ill patients: "AbSeS", a multinational observational cohort study and ESICM Trials Group Project. *Intensive Care Med* 2019;45(12):1703-17.
28. Ohmann C, Wittmann DH, Wacha H. Prospective evaluation of prognostic scoring systems in peritonitis. Peritonitis Study Group. *Eur J Surg* 1993;159(5):267-74.
<https://doi.org/10.1007/s00134-019-05819-3>
29. Barie Ps, Hydo IJ, Eachempati sR. Longitudinal outcomes of intra-abdominal infection complicated by critical illness. *Surg Infect (larchmt)* 2004; 5(4):365-73.
<https://doi.org/10.1089/sur.2004.5.365>
30. Dellinger EP, Wertz MJ, Meakins JL, et al. surgical infection stratification system for intra-abdominal infection. *Multicenter Trial Arch Surg* 1985;120(1):21-9.
<https://doi.org/10.1001/archsurg.1985.01390250015003>
31. Tridente A, Clarke GM, Walden A, et al. Association between trends in clinical variables and outcome in intensive care patients with faecal peritonitis: analysis of the GenOSept cohort. *Crit Care* 2015;19(1):210.
<https://doi.org/10.1186/s13054-015-0931-8>

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Uvođenje klasifikacije ozbiljnosti komplikovanih intraabdominalnih infekcija

Evgeni Dimitrov^{1,2}, Georgi Minkov^{1,2}, Emil Enčev^{1,2}, Jovčo Jovčev^{1,2}

¹Univerzitetska bolnica Stara Zagora, Departman za hirurške bolesti, Stara Zagora, Bugarska

²Univerzitetska bolnica „Prof. dr Stojan Kirkovič“ Stara Zagora, Departman za hirurške bolesti, Stara Zagora, Bugarska
Trakijski univerzitet Stara Zagora, Medicinski fakultet, Departman za hirurške bolesti i anesteziologiju, Stara Zagora, Bugarska

SAŽETAK

Uvod/cilj. Budući da trenutno ne postoji klasifikacija koja prikazuje ozbiljnost komplikovanih intraabdominalnih infekcija (engl. *complicated intra-abdominal infections* – cIAIs), cilj ovog rada bio je da uvede novu klasifikaciju koja bi olakšala prognostičku procenu cIAIs-a u kliničkoj praksi.

Metode. Reč je o studiji jednog centra sprovedenoj u Univerzitetškoj bolnici Stara Zagora, koja je obuhvatila 140 bolesnika sa cIAIs-om. Retrospektivno, uzimajući u obzir period od januara 2017. do oktobra 2018. godine, na osnovu SOFA (engl. *Sequential organ failure assessment*) skora i WSES SSS skora, bolesnike sa cIAIs-om podelili smo u tri grupe: grupu sa blagim cIAIs-om (SOFA < 2 boda), grupu sa teškim cIAIs-om (SOFA ≥ 2) i grupu sa teškom komplikovanom intraabdominalnom sepsom (engl. *complicated intra-abdominal sepsis* – SCIAS), u kojoj je zabeležen WSES SSS ≥ 8 ili septički šok. Prospektivno smo potvrdili izrađenu klasifikaciju kod 62 bolesnika sa cIAIs-om između novembra 2018. i avgusta 2021. godine.

Rezultati. U retrospektivnoj i prospektivnoj grupi stopa smrtnosti kod bolesnika sa blagim cIAIs-om iznosila je 3,1% i 3,6%, a kod bolesnika sa teškim cIAIs-om 26,8% i 19%, redom. Najveća stopa smrtnosti uočena je u grupi sa SCIAS-om: 68,8% i 30,8%. Prognostički skorovi koji su se značajno razlikovali u zavisnosti od težine infekcije i u jednom i u drugom ispitanom periodu bili su SOFA, Mannheim Peritonitis Index, kao i WSES SSS.

Zaključak. Predložena klasifikacija može biti pouzdan prediktor ozbiljnosti kod bolesnika sa intraabdominalnim infekcijama.

Ključne reči: intraabdominalne infekcije, smrtnost, klasifikacija ozbiljnosti, SOFA skor, WSES SSS skor