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Predictor of Mortality in Complicated Intraabdominal Infection Patients at Dr. Soetomo General Hospital Surabaya

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ABSTRACT

Background: Complicated intraabdominal infection (cIAI) is a surgical emergency reported to be a major contributor to non-traumatic mortality worldwide. Identifying the mortality risk before any operation is important in guiding clinical decision-making and informed patient consent about the risk of complicated intraabdominal infection (cIAI). The study aimed to develop a novel scoring system for predicting postoperative mortality in cIAI.

Methods: Data were collected retrospectively from all consecutive patients 396 patients met the inclusion criteria after excluding missing data undergoing cIAI surgery in Dr. Soetomo Hospital 2020 - 2022. Multivariate logistic regression analysis was performed to correlate the explanatory variable postoperative mortality. Data were analyzed using SPSS version 20.0 for Windows and MedCalc.

Results: Postoperative mortality rate cIAI was 32,2% (128 of 396), and variables identified as the strongest predictors of postoperative mortality were age > 60 y.o (OR 3,196), systolic blood pressure < 100 mmHg (OR 5,894), thrombocyte < 100.000 /uL (OR 5,593), albumin ≤ 2,9 g/dL (OR 6,764), total bilirubin > 1,8 mg/dL (OR 2,180), creatinine serum ≥ 1,58 mg/dL (OR 4,290), cancer comorbidity (OR 3,578), and appendix perforation as negative predictor (OR 5,853). These parameters were included in the prediction model of the novel simplified Airlangga Scoring System.

Conclusion: Despite the relatively low number of risk factors, the Airlangga score has been shown as a good predictor of postoperative mortality after cIAI. External validation is required in hospitals different from those in which the novel scoring system was developed.

Keywords: cIAI, Risk Factors, Post-Operative Mortality.
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INTRODUCTION

Complicated intraabdominal infection (cIAI) is a surgical emergency reported to be a major contributor to non-traumatic mortality worldwide. Intraabdominal infection is broadly divided into uncomplicated intraabdominal infection, where the infection process only occurs in a single organ and does not extend to the peritoneum.[1,2] In contrast, in complicated intraabdominal infection (cIAI), the infection process has expanded beyond a single organ which can cause clinical symptoms in the form of generalized peritonitis, localized peritonitis, and can be an intraabdominal abscess.[1,2]

The high mortality rate makes it crucial to evaluate predictor factors in assessing severity and determining aggressive management in cases of intraabdominal infection. Various score systems have been developed to predict the mortality of cIAI patients. Tolonen et al. compare several predictor scores, such as the CPIRO (Calgary Predisposition Infection Response and Organ Dysfunction) score, WSESSSS (World Society of Emergency Surgery Sepsis Severity Score), APACHE II (Acute Physiology and Chronic Health Evaluation) and SOFA (Sequential Organ Failure Assessment) to consider which one is good enough for a wide population to predict the mortality of intraabdominal infections in the European population.[3]

The high mortality rate and the weakness of the existing prognostic score are the backgrounds to look for factors that further affect the mortality of cIAI patients, so this study aims to produce a formulation of factors that influence the incidence of mortality of cIAI patient care that adapts to the characteristics and conditions in Indonesia, especially at Dr. Soetomo General Hospital which is a national referral health facility that can represent the characteristics and conditions of patients in Indonesia.

MATERIALS AND METHODS

Study Design and Participants

This research is a retrospective cohort study conducted at Dr. Soetomo General Hospital. We examined 396 patients' medical records with cIAI between 2020 and 2022 based on inclusion and exclusion criteria (total sampling). The inclusion criteria were adult age more than 18 years old. Patients could be followed during treatment or up to 30 days after surgery by evaluating clinic medical records or contacting the subject. Followed up to

30 days is a gold standard indicative of overall quality of care mortality.[4] A patient is considered "mortality" if he dies during hospitalization after undergoing any source control operation due to. Patients are treated alive if the treatment exceeds 30 days or the patient is discharged from the hospital in an improved or cured condition and can be followed at the outpatient clinic or by telephone. The exclusion criteria were patients with a history of surgery due to the same diagnosis within the previous month and incomplete medical records.

Variable

The dependent variable in this study is the outcome of patient care, namely mortality 30 days after receiving surgery (source control). Patients are categorized as "dead" if they have died during hospitalization after undergoing source control surgery. Patients were classified as alive if the treatment exceeded 30 days or the patient was discharged from the hospital in an improved or recovered condition and could be followed at the clinic or by telephone. While the independent variables in this study consisted of 22 variables which included agent, host, and environment.

Statistical Analysis

The data analysis used in this study was bivariate analysis and simple logistic regression. Each independent variable was tested against mortality. If significant, it will continue to the multivariate logistic regression test. Furthermore, multivariate analysis is done with multiple logistic regression. The bivariate logistic regression test will be tested with multivariate logistic regression for significant variables. The p-value used is 0.05, and the confidence interval is 95%. Factors with a significant relationship will be used as a formula to form a new score system. Furthermore, the cut-off value is assessed with the Receiver Operating Characteristic (ROC) test and the new score system's sensitivity and specificity test. The software used to perform the analysis are SPSS version 20.0 for Windows and MedCalc.

RESULTS

In this study, we included a total of 396 subjects, consisting of 255 men (255/396; 64.40%) and women (141/396; 35.60%). The mean age of the study subjects was 44.8 ± 18.651 years. During treatment and followed up to 30 days after surgery, 268 patients lived (67.68%), and 128 patients died (32.32%) (Table 1). At the cut-off value, age > 60 years has an influence on the incidence of mortality in the treatment of cIAI patients (P < 0.0001) with an OR value of 3.196 (CI 95% 1.987 - 5.142).

In this study, 381 patients (96.2%) had generalized peritonitis and 15 patients (3.8%) had localized peritonitis. Patients with appendiceal perforation had a high survival rate of 86.98% (147 of 168 patients diagnosed with appendiceal perforation). The diagnosis of appendiceal perforation had a significant association with patient survival (P < 0.0001; OR: 5.853; CI 95% 3.486 - 9.830). Meanwhile, patients with perforation due to ulcerative colitis/ Crohn's disease had a low survival rate of 5 patients (83.3% of the total 6 patients diagnosed with perforation due to ulcerative colitis/Crohn's disease). The complete data is shown in Table 2.

Data collection of comorbid diseases in this study was based on history taking, physical examination, and support when the patient was diagnosed with cIAI. Comorbid cancer significantly influences the incidence of mortality in the treatment of cIAI patients (P = 0.002) with an OR value of 3.578 (CI 95% 1.623 - 7.887). The data is shown in Table 3.

Vital signs and laboratory examinations were conducted when the patient was first diagnosed with cIAI. Systolic blood pressure has a significant influence on the occurrence of mortality in cIAI patients (P < 0.0001) with OR 5.894 (95% CI 3.646 - 9.529) (Table 4). There were also significant laboratory examination results, namely haemoglobin (P < 0.0001), haemoglobin cut-off value <8 g/dL (P = 0.007), platelet cut-off value 100,000/uL (P = 0.003), platelet cut-off value 150,000 /uL (P = 0.003), neutrophil-to-lymphocyte ratio cut-off value 31.99 (P = 0.041), albumin (P < 0.0001), albumin cut-off value 2.9 g/dL (P < 0.0001), total bilirubin cut-off value 1.8; 1.9; 5.9 respectively (p=0.008; p=0.049; p=0.043), and serum creatine (P < 0.0001). Platelet examination with a cut-off value of <100,000 /uL significantly influenced the incidence of mortality of cIAI patient care with an OR value of 5.593 (CI 95% 1.719 - 18.196). Albumin levels also significantly influenced the incidence of morbidity at a cut-off value of 2.9 g/dL albumin with an OR value of 6.764 (CI 95% 4.246-10.773). Likewise, serum creatinine significantly influenced mortality at a cut-off value of serum creatinine > 1.58 g/dL with an OR value of 4.290 (CI 95% 2.721 - 6.764). The data are presented in Table 5.

From the results of the multivariate logistic regression analysis test, 8 statistically significant variables were obtained, namely: age > 60 years, systolic blood pressure < 100 mmHg, preoperative platelet count < 100,000 /uL, albumin level ≤ 2.9 gr/dL, total bilirubin > 1.8 mg/dL, serum creatinine ≥ 1.58 mg/dL, and comorbid cancer. There was also a negative risk factor, namely appendiceal perforation. A probability score was calculated by adding a constant to each variable based on differences in the regression coefficients. The multiple regression equation for mortality is: exp [-5.493 + (0.950 x **Age**) + (1.734 x **systolic** < 100 mHg) + (1.380 x **platelets** < 100. 000 /uL) + (1.586 x **albumin** ≤ 2.9 gr/dL) + (1.036 x **total bilirubin** > 1.8 mg/dL) + (1.267 x **serum creatinine** ≥ 1.58 mg/dL) + (1.080 x **comorbid cancer**) - (0.698 x **appendiceal perforation**)]

The formula is simplified by weighting using a different number of points on each variable, according to the calculation of the regression coefficient, as shown in Table 6. From the existing score data, an analysis using the receiver operating characteristic (ROC) graph explains that the score has a fairly good AUC of 0.875 with a sensitivity value of 77.61% and a specificity of 82.03% (Figure 1). From the AUC graph, the cut-off value that determines low and high risk is ≤3 (Tables 7 and 8).

DISCUSSION

The mortality rate of cIAI patient care is crucial to evaluate predictor factors in assessing severity and determining aggressive management. The high mortality of cIAI patients depends on several holistic factors, including the host, agent, and environment. Early identification of cIAI patients with an increased risk of postoperative mortality is an important first step for identifying

the need for early intervention and more appropriate management (source control) or referring patients to higher-level health facilities.[5]

The Airlangga score system has a cut-off value of ≤3, which has a low mortality risk. In this study, cIAI patients who underwent source control measures had a low mortality risk of around 9.96%, while patients with high risk had a higher mortality risk. The AUC value of the Airlangga score system was 0.875, with a sensitivity value of 77.61 and a specificity of 82.03. The results of the external validation of the CPIRO and WSESSSS scores are presented in Table 8. The strength of a mortality predictor score system is its ability to distinguish study subjects who experience mortality from study subjects who do not experience mortality. The Airlangga score system performs better in predicting 30-day mortality after cIAI surgery than the CPIRO and WSESSSS.

In addition, there are some weaknesses in the variables assessed in the CPIRO score, such as the type of comorbidity that is not explained in detail, the limitations related to organ dysfunction are still unclear, besides the weighting of each gets the point value of 1 indicating that the variables included in the CPIRO score are equivalent, even though several studies have different odds ratios. Meanwhile, the WSESSS score only nominally explains whether the patient has organ failure, not stratifying sepsis's severity. The above describes the weakness of the WSESSS score system parameters, which resulted in false negative values in the study subjects even though the number was insignificant.

The mortality rate in this study was 32.2% of 396 subjects who met the criteria for this study. This figure is not much different from the research conducted by Nugraha, who examined cIAI patients at Dr. Soetomo Hospital in 2020-2021 with a mortality rate of 34.7%.[6] In contrast to other studies, the WISS (World Society of Emergency Surgery cIAIs Score Study) study involving 132 medical institutions

Table 1. Sample Demography Data

Variable	Outcome (n=396)		Total	p
	Alive (n=268)	Deceased (n=128)		
Gender, n (%)				
Male	175 (65.30)	80 (62.50)	255 (64.40)	0.666
Female	93 (34.70)	48 (37.50)	141 (35.60)	
Age (Years), n (%)				
<50	176 (65.67)	50 (39.06)	226 (57.07)	0.000*
50-59	41 (15.30)	27 (21.09)	68 (17.17)	
60-69	34 (12.69)	27 (21.09)	61 (15.40)	
70-79	16 (5.97)	18 (14.06)	34 (8.59)	
>79	1 (0.37)	6 (4.70)	7 (1.77)	

*Statistically significant if p-value less than 0.05

Table 2. Characteristics of etiological diagnosis of cIAI patients at Dr. Soetomo Hospital in 2020-2022.

Variable	Outcome (n=396)		Total n (%)
	Alive (n=268)	Deceased (n=128)	
Diagnosis, n (%)			
Gastric perforation	47	45	92 (23.2)
Duodenal perforation	5	3	8 (2)
Jejunal perforation	4	3	7 (1.8)
Ileal perforation	12	8	20 (5.1)
Appendiceal perforation	147	22	169 (42.4)
Caecal perforation	9	8	17 (4.3)
Ascending colon perforation	2	1	3 (0.8)
Transverse colon perforation	1	4	5 (1.3)
Descending colon perforation	1	1	2 (0.5)
Sigmoid colon perforation	9	4	13 (3.3)
Rectal perforation	0	1	1 (0.3)
Hepatic abscess rupture	8	6	14 (3.5)
Spleen abscess rupture	2	0	2 (0.5)
Necrotic pancreas	2	2	4 (1.0)
Gallbladder perforation	3	2	5 (1.3)
Bile duct injury	1	1	2 (0.5)
An intraabdominal abscess (psoas. retroperitoneal)	6	3	9 (2.3)
Ileal diverticle perforation	1	0	1 (0.3)
Sigmoid diverticle perforation	1	4	5 (1.3)
Perforation of abdominal tuberculosis	5	5	10 (2.6)
Colon perforation (ulcerative colitis. *Crohn's disease*)	1	5	6 (1.6)
Primary Peritonitis (VP shunt. CAPD. PID)	2	1	3 (0.8)
Peritonitis Type			
Generalized	255	126	381 (96.2)
Local	13	2	15 (3.8)

Table 3. Comorbidities of cIAI patients at Dr. Soetomo Hospital in 2020-2022

Comorbid	Outcome (n=396)		Total n (%)
	Alive (n=268)	Deceased (n=128)	
Cancer, n (%)	12	20	32 (8.08)
AIDS, n (%)	3	6	9 (2.27)
Liver disease, n (%)	8	12	20 (5.05)
Renal disease, n (%)	6	9	15 (3.78)
Chronic pulmonary disease, n (%)	20	14	34 (8.58)
Heart disease, n (%)	19	9	28 (7.07)
Cerebral vascular disease, n (%)	15	4	19 (4.79)
Peripheral vascular disease, n (%)	56	38	97 (24.49)
Diabetes mellitus, n (%)	62	26	88 (22.22)
Covid-19, n (%)	31	11	42 (10.60)
Others, n (%)	8	3	11 (2.28)

Table 4. Vital Signs of cIAI patients at Dr. Soetomo Hospital in 2020-2022

Variable	Outcome (n=396)		Total n (%)	P
	Alive (n=268)	Deceased (n=128)		
Vital Sign				
Heart rate (times/minutes)				0.176
>100	139	78	217 (54.8)	
60-100	126	49	175 (44.2)	
<60	3	1	4 (1.0)	
SBP (mmHg)				0.000
≥100	234	6	240 (60.6)	
<100	34	122	156 (39.4)	
Temperature (Celcius)				
<36.5	31	14	45 (11.4)	1.000
Normal	135	77	212 (53.5)	0.085
Hyperthermia	102	37	139 (35.1)	0.091
GCS				0.733
15	262	124	386 (97.5)	
<15	6	4	10 (2.5)	

SBP: Systolic Blood Pressure; GCS: Glasgow Coma Scale

over a 4-month observation period reported 4533 cIAI patients over 18 years old had a mortality rate of 9.2%.[2] Likewise, another study in Indonesia found that the prevalence of cIAI in six tertiary hospitals in Indonesia in 2017 was around 10%, with a mortality rate of 16.6%.[1] The higher mortality rate in Dr. Soetomo Hospital than the results of other studies may be due to the high incidence of sepsis and sepsis shock when the subject arrives at Dr. Soetomo Hospital. Dr Soetomo Hospital, a referral centre, especially in the East Java region and even eastern Indonesia, which is geographically far apart, results in longer patient handling time, so the patient's condition worsens before therapy.

There is a significant difference in age with the incidence of mortality in treating patients with intra-abdominal infections. In this study, the cut-off value of age > 60 significantly influenced the incidence of mortality in surgery for patients with intra-abdominal infections. Our result concordance with the research conducted by Arvaniti examining the relationship between age and mortality in patients with intra-abdominal infections and reported that age over 60 correlates with a higher incidence of mortality. Older age is often accompanied by comorbidities that make it vulnerable to complications.[7] Elderly patients are also often accompanied by decreased organ function, cognitive function, nutritional status, daily activities, multi-comorbidities, psychological disorders, increased ASA status, and reduced socio-economic status, which are at high risk of postoperative morbidity and mortality.[7]

Based on the cause of infection, the most common diagnosis in this study was appendiceal perforation. Appendicitis is the most common cause of cIAI cases in the world. As researchers found in this study, the prevalence rate of appendicitis is around 34% as the cause of cIAI.[2] Likewise, another study mentioned that the appendiceal mortality rate is around 2.3 - 10%, mostly related to the patient's comorbid diseases.[8] The high mortality rate in cases of peptic ulcer perforation is related to preoperative patients who are in sepsis to sepsis shock. External drainage often carries out source control measures in cases of peptic ulcer perforation in shock conditions. Approximately 40 - 80% of peptic ulcer perforations are expected to close spontaneously with conservative therapy (Taylor's Method) and not require laparotomy. Non-operative treatment with external drainage combined with conservative management (Taylor's Method) in Boey score 3 peptic ulcer perforation (history of shock, onset >24 hours, comorbidities) can have a success

Table 5. Laboratory parameters of cIAI patients at Dr. Soetomo Hospital in 2020-2022

Variable	Outcome (n=396)		p
	Alive (n=268)	Deceased (n=128)	
Haemoglobin (Mean±SD)	12.700±2.900	11.000±3.200	0.000*
< 8 g/dL	19	21	0.007*
≥ 8 g/dL	249	107	
Platelet (Mean±SD)	325.391±149.064	322.801±160.628	0.875
< 50.000	2	4	0.089
< 100.000	4	10	0.003*
< 150.000	14	19	0.003*
Leucocyte (Mean±SD)	16.189±12.302	15.241±11.020	0.459
< 4000	4	6	0.083
≥ 4000	264	122	
Neutrophil (Mean±SD)	13.498±7.041	13.340±10.094	0.857
Lymphocyte (Mean±SD)	1.110±0.689	1.113±1.851	0.980
NLR (Mean±SD)	16.6±13.74	20.400±26.700	0.059
< 31.99	244	107	0.041*
≥ 31.99	24	21	
Albumin (Mean±SD)	3.300±0.500	2.800±0.500	0.000*
> 2.9	64	87	0.000*
≤ 2.9	204	41	
Total Bilirubin (Mean±SD)	1.300±1.400	1.500±1.700	0.102
< 1.2	201	86	0.118
≤ 1.8	235	98	0.008*
< 1.9	235	102	0.049*
< 5.9	264	121	0.043*
Creatinin Serum (Mean±SD)	1.400±1.300	2.200±2.400	0.000*
< 1.2	172	52	0.000*
≤ 1.58	212	60	0.000*
< 1.9	226	70	0.000*
< 3.4	250	103	0.000*
< 4.9	262	121	0.129

*Statistically significant if p-value less than 0.05

rate of up to 47% compared to laparotomy, which is 20%.[8]

Comorbid cancer has a significant influence on the mortality of cIAI patients. This result is in line with previous research by Luo, which states that comorbid chronic diseases are associated with increased mortality.[9] Some of these chronic diseases can be chronic obstructive pulmonary disease, chronic heart disease (NYHA level III-IV), cancer with metastases, haematological malignancies (lymphoma, acute leukemia, or multiple myeloma), liver cirrhosis, chronic kidney disease (renal failure requiring hemodialysis or serum creatinine > 300 umol/L), immunosuppressive status, chemotherapy/radiotherapy status, human immunodeficiency virus infection, and diabetes.[9]

The systolic blood pressure of patients in shock with systolic blood pressure < 100 mmHg has a significant relationship with the incidence of mortality in patients with intra-abdominal infections. Venkatesan et al.'s study on 251,567 adult patients who underwent elective non-cardiac surgery found that a decrease in systolic blood pressure significantly increased postoperative 30-day mortality, especially in the elderly patient group.[10] Systolic blood pressure is one of the indicators to assess the occurrence of shock sepsis or not. The diagnosis of shock sepsis is made when sepsis is accompanied by hypotension that requires vasopressors to reach a target MAP of 65 mmHg or more and serum lactate of more than 2 mmol/L that requires fluid resuscitation.[11] In addition, resuscitation fluids given because the patient is in shock will increase tissue oedema, which inhibits oxygen metabolism in the tissue, so excessive fluid administration in resuscitation increases patient mortality. Besides, the EGDT program provides more fluids and more expensive treatment costs. Fluid resuscitation in intra-abdominal infections and surgical trauma can also increase tissue exudation in the abdominal cavity, causing abdominal hypertension or even causing compartment syndrome in severe cases, eventually leading to reduced perfusion of the abdominal organs.[8]

Serum creatinine has a significant effect on the incidence of mortality. Serum creatinine can reflect the level of damage to glomerular filtration function caused by factors external to the kidney. Likewise, elevated BUN often indicates pathological conditions, which often occur in gastrointestinal bleeding. Gastrointestinal bleeding causes more red blood cells, which converts plasma protein into a source of nitrogen that is absorbed into the blood (increased catabolism

Table 6. Airlangga score system as a predictor of cIAI patient care mortality

Variable	Point
Age > 60 y.o	1
Systolic Blood Pressure < 100 mmHg	4
Thrombocyte < 100.000 /uL	3
Albumin ≤ 2,9 gr/dL	3
Total bilirubin > 1,8 mg/dL	2
Creatinine Serum ≥ 1,58 mg/dL	2
Cancer Comorbid/*immunodeficiency syndrome*	2
Appendiceal Perforation	-1

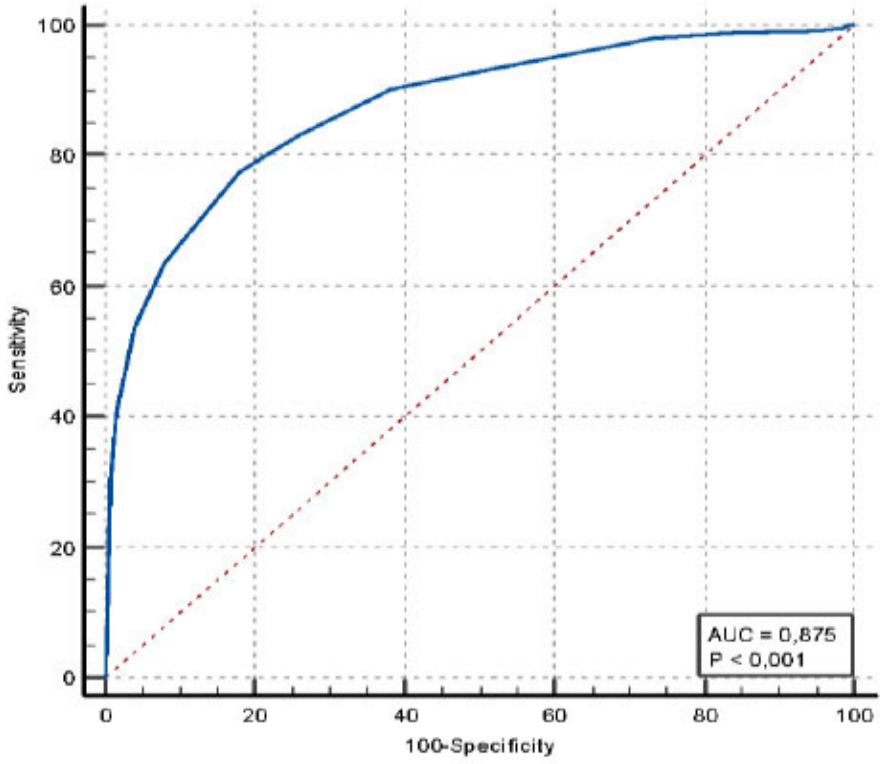

Figure 1. ROC graph of Airlangga Intraabdominal Infection Mortality score system.

Table 7. Score system with point ranges for each risk factor

Mortality Risk	Score	Alive n (%)	Deceased n (%)
Low Risk	-1 to 3	208 (90.04)	23 (9.96)
High Risk	4 to 15	60 (36.36)	105 (63.64)

Table 8. Prediction performance of Airlangga, CPIRO, and WSESSSS score system of ROC

Score system	AUC	Sensitivity (%)	Specificity (%)
CPIRO	0.697	75.75	53.91
WSESSSS	0.701	88.06	44.53
Airlangga Score	0.875	77.61	82.03

resulting in increased urea absorption by the intestine).

Serum albumin significantly influences mortality. Similarly, research conducted by Rungsakulkij reported that serum albumin has a significant relationship with the incidence of mortality in patients with intra-abdominal infections with a cut-off value of <3.5 g/dL.[8] Another study by Neumayer et al. also explained that low serum albumin levels < 3.5 mg/dL are an independent risk factor significantly related to surgical site infection (SSI) incidence.[12] Bendersky's research also reported that preoperative serum albumin is associated with mortality in gastrointestinal, pancreatic, and colorectal surgery.[13] Albumin is also a transport protein with multiple ligand binding, cellular receptor engagement, and a long half-life so that albumin can bind drug substances that can affect the healing process.[14-17] In postoperative care, albumin also has a role in wound healing.[14]

The sepsis severity score system is commonly used to calculate the degree of sepsis. A higher score indicates a more severe disease status and a greater likelihood of complications. This will certainly have an impact on the length of hospitalization. Tolonen et al. mentioned that conducting a score system analysis on cIAI cases like this is necessary to identify and classify patients at risk of treatment mortality.[3] By knowing the risk stratification of cIAI patients, clinicians can determine the appropriate source control surgery for patients.

This study's limitations were conducted in a tertiary referral hospital, which may not reflect the population and the quality or standard of health services in Indonesia. The second was a retrospective study which has the potential to cause bias when collecting data. The third was that some preoperative risk factors or variables are not included because these data are not routinely recorded and/or checked. Suggestion need for external validation of this scoring system in populations and hospitals that differ from the population and hospitals.

CONCLUSION

Despite the relatively low number of risk factors, the Airlangga scoring system has been shown as a good predictor of postoperative mortality after cIAI. External validation is required in hospitals different from those in which the novel scoring system was developed.

CONFLICTS OF INTEREST

No competing interests were declared.

ETHICAL CLEARANCE

This study was reviewed and approved by the Medical Ethical Committee of Dr. Soetomo General Hospital, Surabaya, Indonesia (Ref. No.: 1179/LOE/301.4.2/I/2023) following the guidelines of The Office for Human Research Protection (OHRP) the US Departement of Health and Human Services (HHS).

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AUTHOR CONTRIBUTIONS

All authors equally contribute to the study from the conceptual framework, data acquisition, and data analysis until reporting the study results through publication.

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