

The prognostic factors in sepsis patients after operation of gastrointestinal tumors in ICU

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Research

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Abstract

Objectives: We studied the clinical profiles and the prognostic factors in patients with sepsis after the gastrointestinal tumor surgery in ICU.

Methods: We retrospectively screened patients who underwent the gastrointestinal tumor surgery at the Peking University Cancer Hospital from January 2015 to December 2019. Among them, 181 patients who were diagnosed with sepsis in ICU were enrolled in our study. Cox regression was performed for multivariate adjusted factor analyses.

Results: The 90-day all-cause mortality rate was 11.1% in our study. The univariate analysis showed that BMI, shock within 48h after entering ICU, number of blood leukocytes, the ratio of lymphocytes to neutrophils, INR, creatinine, procalcitonin, lactic acid, oxygenation index, SOFA score within 24h after entering ICU, APACHE II score within 24h after entering ICU were statistically significant. In multiple analysis, we found that BMI ≥ 20 kg/m² was a protective factor, while lactic acid ≥ 3 mmol/L after entering ICU and APACHE II score ≥ 20 within 24h after entering ICU were independent risk factors for the prognosis of sepsis after the gastrointestinal tumor surgery in ICU.

Conclusions: The 90-day all-cause mortality rate was 11.1% in our study. BMI ≥ 20 kg/m² was a protective factor, while lactic acid ≥ 3 mmol/L after entering ICU and APACHE II score ≥ 20 within 24h after entering ICU were independent risk factors for the prognosis of sepsis after the gastrointestinal tumor surgery in ICU.

Background

Sepsis was a worldwide problem. It is estimated that there are 31.5 million patients with sepsis every year in the world, which causes about 5.3 million deaths every year [1]. Sepsis is associated with high mortality. About 14000 people died of its complications every day in the world. Sepsis can be caused by any types of infection. Pathogenic microorganisms include bacteria, fungi, viruses and parasites. As the previous definition of sepsis (infection+SIRS) is too sensitive, the new definition of sepsis is the life-threatening organ dysfunction caused by the host's maladjusted response to infection. Organ dysfunction manifests that sepsis-related organ failure score was no less than two points [2].

The most common postoperative infection of gastrointestinal tumor is abdominal infection. Early identification of infection, control of infection source, proper use of antibiotics and rapid resuscitation of critical patients are the cornerstone of abdominal infection management [3-6]. There are numerous factors affecting the prognosis of sepsis. It has been reported that the prognosis of sepsis is related to lactic acid, interleukin-6, PCT, CRP, HFABP and so on [7-11]. However, as the definition describes, sepsis is a syndrome with extreme heterogeneity. In the past, there were various reports on mortality of sepsis, though, few studies on the prognosis of patients with sepsis after operation. The purpose of this study is to investigate the prognostic factors of patients with sepsis who were admitted to ICU after gastrointestinal operation.

Patients And Methods

Patients

From January 2015 to December 2019, a total of 1636 patients were admitted to ICU after surgery from the gastrointestinal tumor center of Peking University Cancer Hospital. According to the new definition of sepsis, 181 patients diagnosed with sepsis were enrolled in this study. Exclusion criteria: patients were admitted to ICU for other reasons or did not have sepsis during ICU stay, or patients' sepsis occurred out of ICU stay.

Therapeutic method

For sepsis patients, we have active anti-infection treatment, sent etiology examination and tried to find the source of infection. For patients with septic shock, we took the following measures: First, bestowed broad-spectrum antibiotics within one hour, and took the etiological examination before giving antibiotics. Second, 30 ml/kg of crystalloid fluids was used for rapid volume resuscitation within three hours, and the initial target of mean arterial pressure (MAP) was 65 mmHg. If the MAP was not achieved the target within one hour, noradrenaline was used for increasing the blood pressure. Third, we looked for and controlled the source of infection actively. For patients with a definite source of infection, we controlled the source of infection by minimally invasive drainage, surgical debridement, removal of a central venous catheter and sputum aspiration by bronchoscope, etc. To emphasize; we follow the guidelines for other treatment strategies [5, 6].

Data collection and follow-up

The clinical data and laboratory examination of the patients were collected as follows: age, body mass index (BMI), underlying diseases, the length of the first operation, pathogen susceptibility test, antibiotics used, whether shock occurred within 48 hours after entering ICU, the number of blood leukocytes, lymphocyte percentage, neutrophil percentage, international standardized ratio (INR), activated partial thromboplastin time (APTT), albumin, creatinine, cardiac troponin I (TNI), procalcitonin (PCT), lactic acid (Lac), base excess (BE), oxygenation index (PaO₂ / FiO₂) after entering ICU, sequential organ failure (SOFA) score and acute physiological function and chronic health evaluation (APACHE) II score within 24h after entering ICU. Unless otherwise stated, the first test after entering ICU was used for analysis. They were followed up to 90 days in the clinic or by phone call.

Statistical analyses

The data of continuous variables were statistically described by mean \pm standard deviation. The non-continuous variables were described by median (quartile 1 [Q1], quartile 3 [Q3]). The counting variables were described by numerical value (percentage). The Kaplan-Meier method was used to calculate the survival rate of patients and log-rank test was used for the univariate analysis. Cox regression was used for the multivariate adjusted analyses with forward LR method. Statistical analyses were carried out using SPSS version 24.0 and *P* values less than 0.05 (two-tailed) were considered significant.

Results

Patient characteristics

According to the new definition of sepsis, a total of 181 patients were diagnosed with sepsis and 86 of them were diagnosed with septic shock within 48 hours after entering ICU. There were 13 patients complicated by abdominal bleeding or gastrointestinal bleeding, 16 cases by deep-vein thrombosis, one case by cerebral infarction and one case by myocardial infarction. See Table 1 for baseline characteristics of patients.

The Univariate and multiple survival analyses

The univariate analysis is shown in Table 2. All the sepsis patients were followed up for 90 days; 20 patients died, and the 90-day all-cause mortality rate was 11.1%. Univariate analysis showed that there were statistically significant differences in BMI, shock within 48h after entering ICU, the number of blood leukocytes, the ratio of lymphocyte to neutrophil, INR, creatinine, PCT, Lac, BE, oxygenation index after entering ICU, SOFA score and APACHE II score within 24h after entering ICU. Among them, BMI more than 20 kg/m² was a protective factor; the others were risk factors. Especially, shock within 48h after entering ICU, INR, creatinine, Lac, oxygenation index after entering ICU, SOFA score and APACHE II score within 24h after entering ICU had P values less than 0.01.

See Table 3 for multiple analyses. Those factors with P values less than 0.05 were enrolled in the Cox regression analysis. The results showed that BMI, lactic acid after entering ICU and APACHE II score within 24h after entering ICU were independent prognostic factors. The BMI ≥ 20 kg/m² was a protective factor, while lactic acid ≥ 3 mmol/L after entering ICU and APACHE II score ≥ 20 within 24 hours after entering ICU were risk factors. The survival curves of these three factors are shown in Figure 1, figure 2 and figure 3.

Discussion

Sepsis is one of the most common causes of death in critically ill patients. At present, there are only a few studies focused on postoperative sepsis. This study focuses on sepsis after operation of gastrointestinal tumor. In this study, the mortality rate is lower than that of sepsis reported in the literature [12], which may be related to the fact that most of the infection sources of the patients we selected are abdominal infection, and we can actively control the infection sources by multidisciplinary cooperation. In this study, 181 patients with sepsis who were admitted to ICU after operation of gastrointestinal tumor were analyzed retrospectively and we found that BMI ≥ 20 kg/m², lactic acid ≥ 3 mmol/L after entering ICU and APACHE II score ≥ 20 within 24h after entering ICU were independent prognostic factors.

The World Health Organization classified BMI as follows: BMI < 18.5 kg/m² was underweight, $18.5 \leq \text{BMI} < 25$ kg/m² was normal weight, $25 \leq \text{BMI} < 30$ kg/m² was overweight and BMI ≥ 30 kg/m² was obesity [13]. In this study, we found that patients with BMI ≥ 20 kg/m² had a better prognosis than those with BMI ≤ 20 kg/m²,

so we guessed that $BMI \geq 20 \text{ kg/m}^2$ might be a protective factor. However, the number of patients in this study was limited, and we did not conduct a more detailed stratified study. There were numerous reports about the relationship between BMI and the prognosis of sepsis, though the results were still controversial [14, 15]. Matthaios PO et al. [16] found that the mortality of obese patients with sepsis increased significantly. But one recent meta-analysis divided sepsis patients into three groups: overweight ($25 \leq BMI < 30 \text{ kg/m}^2$), obesity ($30 \leq BMI < 40 \text{ kg/m}^2$) and morbid obesity ($BMI \geq 40 \text{ kg/m}^2$). The results showed that the death risk of overweight patients with sepsis was reduced, while obesity and morbid obesity patients with sepsis did not increase the death risk. The reason for this controversy might be related to the distribution of adipose tissue. It was reported that the visceral fat (VAT) accumulation detected by CT scan was a risk factor for poor prognosis of sepsis. Sepsis patients with a high ratio of VAT area to the subcutaneous fat (SAT) area had an increased risk of death and organ damage [17]. In future, more detailed and rigorous studies should be designed to clarify the relationship between sepsis and BMI.

Lactic acid was constantly produced in metabolism and exercise, but its concentration generally did not rise. Only when the production of lactic acid was accelerated and lactate could not be removed in time, its concentration would increase. Generally speaking, when the energy of the tissue could not be satisfied by aerobic respiration, the tissue could not get enough oxygen or could not deal with oxygen fast enough, the concentration of lactic acid would rise. Hence, sepsis and septic shock guidelines used lactic acid as an indicator of tissue hypoperfusion and as a target for fluid resuscitation [5, 6]. Many studies had shown that lactate was an independent risk factor for sepsis prognosis [18-20]. In our study, it was also confirmed that the lactic acid $\geq 3 \text{ mmol/L}$ after entering ICU was an independent risk factor for sepsis patients after the gastrointestinal tumor surgery.

There were many scoring systems for evaluating the severity of critical patients, such as SOFA score and APACHE II score [21-23]. APACHE II score was considered as the gold standard for risk assessment of critical patients in the past. Several studies confirmed that APACHE II score is an independent risk factor for the prognosis of sepsis patients [24, 25]. In our study, we found that the SOFA score and APACHE II score within 24 hours after entering ICU were statistically significant in the univariate analysis, while the multivariate analysis showed that only APACHE II score ≥ 20 was an independent risk factor in this group. However, there was evidence that APACHE II score might provide inaccurate information in some patients, for example, in patients with unconsciousness, the score might be too high [26]. Therefore, we need to increase the sample size to confirm this result in the future.

The limitations of this study should be referred. First, this study was a retrospective study and the subjects of this study were patients with sepsis who were admitted to ICU after operation of gastrointestinal tumor, so, whether the results could be extended to all sepsis populations remains to be confirmed. Second, patients with sepsis in the general ward were not included in this study, and most of these patients improved in our hospital. Therefore, the mortality of patients with sepsis after gastrointestinal surgery might be overestimated in our study. In the future, we will design prospective research to verify it. Third, there were several missing data, especially BNP, echocardiography, etc. So we

could not accurately evaluate their impact on the prognosis of sepsis patients. Finally, the small sample size of this study increased the risk of type two error which made the study power limited. We hope that there will be more large-scale researches to confirm these results in the future.

Conclusions

The 90-day all-cause mortality rate was 11.1% in our study. BMI ≥ 20 kg/m² was a protective factor, while lactic acid ≥ 3 mmol/L after entering ICU and APACHE II score ≥ 20 within 24 hours after entering ICU were independent risk factors for the prognosis of sepsis after the gastrointestinal tumor surgery in ICU.

Declarations

Ethics approval and consent to participate

We received the approval of the Medical Ethical Committee of Peking University Cancer Hospital. All patients or their near kin in our study provided informed consent.

Consent for publication

Not applicable.

Availability of data and materials

Data will be shared after this study is published.

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Authors' contributions

Ren-Xiong Chen designed the study and drafted the manuscript. Hong-Zhi Wang and Jia-Fu Ji critically revised the manuscript. Zhou-Qiao Wu participated in the study design and helped to perform statistical analysis. Zhou-Qiao Wu and Zi-Yu Li helped draft the manuscript. All authors read and approved the final manuscript.

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Abbreviations

BMI: body mass index; INR: International standardized ratio; APTT: activated partial thromboplastin time; TNI: cardiac troponin I; PCT: procalcitonin ; Lac; lactic acid; BE: base excess; SOFA score: sequential organ failure and acute score; APACHE II score: Acute Physiology and Chronic Health Evaluation II score.

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Tables

Table 1
Baseline characteristics of sepsis patients

Baseline characteristics	Number (%)
Age, median (Q1, Q3)	65 (59,71)
Sex	
Male	145 (80.1)
Female	36 (19.9)
BMI, Mean (SD), kg/m ²	23.5 (0.3)
Tumor type	91 (50.3)
Gastric cancer	
Colorectal cancer	84 (46.4)
Other abdominal tumors	6 (3.3)
Coexisting conditions ^a	
Hypertension	64 (35.4)
Diabetes	32 (17.7)
Coronary heart disease	17 (9.4)
Chronic obstructive pulmonary disease	11 (6.1)
Arrhythmia	9 (5.0)
Chronic renal insufficiency	2 (1.1)
Location of infection ^b	
Abdominal infection	134 (74.0)
Enterogenous infection	12 (6.6)
Intrathoracic infection	17 (9.4)
Pulmonary infection	31 (17.1)
Skin and soft tissue infection	6 (3.3)
^a 27 patients had two or more chronic diseases.	
^b 31 patients were infected with two or more locations.	

Baseline characteristics	Number (%)
Surgical wound infection	4 (2.2)
Central line-associated bloodstream infection	3 (1.7)
Urinary tract infection	2 (1.1)
Length of first operation, median(Q1,Q3), min	195 (140,246)
^a 27 patients had two or more chronic diseases.	
^b 31 patients were infected with two or more locations.	

Table 2
The univariate analysis of sepsis patients

Items	Number (%)	Survival rate at 90-day	P value
Age, years			0.840
≤ 65	96 (53.0)	0.885	
> 65	85 (47.0)	0.894	
Sex			0.254
Male	145 (80.1)	0.876	
Female	36 (19.9)	0.944	
BMI, kg/m ²			0.018
≤ 20	37 (20.4)	0.784	
> 20	144 (79.6)	0.917	
Charlson score			0.356
≤ 3	142 (78.5)	0.901	
> 3	39 (21.5)	0.846	
Length of first operation, min			0.361
≤ 240	129 (71.3)	0.876	
> 240	52 (28.7)	0.923	
Empirical anti infection evaluation			0.729
Sensitive	132 (72.9)	0.894	
Resistance	18 (10.0)	0.833	
No pathogen detected	31 (17.1)	0.903	
Shock within 48 h after entering ICU			0.001
No	95 (52.5)	0.979	
Yes	86 (47.5)	0.791	
Number of blood leukocytes, 10 ⁹ /L			0.010

Items	Number (%)	Survival rate at 90-day	P value
≤ 4	31 (17.1)	0.774	
$4 < WBC \leq 12$	77 (42.6)	0.963	
> 12	73 (40.3)	0.863	
Ratio of lymphocyte to neutrophil			0.035
≤ 0.15	148 (81.8)	0.912	
> 0.15	33 (18.2)	0.788	
International standardized ratio			0.001
≤ 1.5	127 (70.2)	0.937	
> 1.5	54 (29.8)	0.778	
Activated partial thromboplastin time, S			0.064
≤ 50	138 (76.2)	0.913	
> 50	43 (23.8)	0.814	
Albumin, g/L			0.058
≤ 30	99 (54.7)	0.848	
> 30	82 (45.3)	0.939	
Creatinine, $\mu\text{mol/L}$			0.001
≤ 120	150 (82.9)	0.927	
> 120	31 (17.1)	0.710	
Cardiac troponin I, ng/ml			0.063
≤ 0.05	138 (76.2)	0.913	
> 0.05	43 (23.8)	0.814	
Procalcitonin, ng/ml			0.011
≤ 5	93 (51.4)	0.946	
> 5	88 (48.6)	0.830	
Lactic acid, mmol/L			0.001

Items	Number (%)	Survival rate at 90-day	P value
≤ 3	128 (70.7)	0.938	
> 3	53 (29.3)	0.774	
Base excess, mmol/L			0.011
≤ -3	101 (55.8)	0.941	
> -3	80 (44.2)	0.825	
Oxygenation index, mmHg			0.003
≤ 200	97 (53.6)	0.825	
> 200	84 (46.4)	0.964	
SOFA score			0.001
≤ 8	124 (68.5)	0.968	
> 8	57 (31.5)	0.719	
APACHE II score			0.001
≤ 20	124 (68.5)	0.976	
> 20	57 (31.5)	0.702	

Table 3
Multiple analysis of sepsis patients

Factors	RR	95% interval		P value
		Lower limit	Upper limit	
BMI	0.199	0.076	0.522	0.001
Lactic acid	3.333	1.290	8.610	0.013
APACHE II score	14.479	4.145	50.580	0.001

Figures

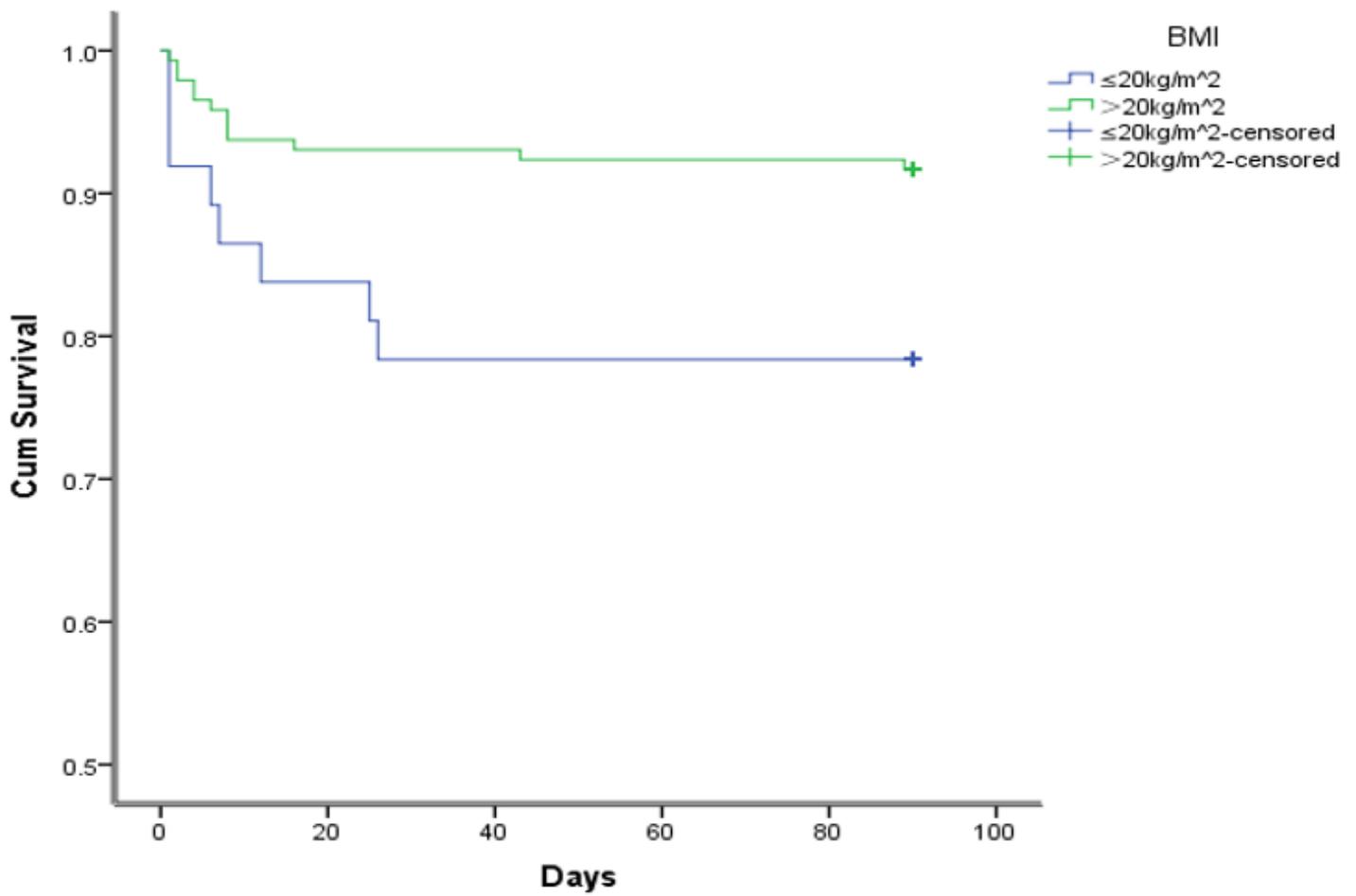


Figure 1

Kaplan-Meier survival curves of BMI on overall survival at 90 days

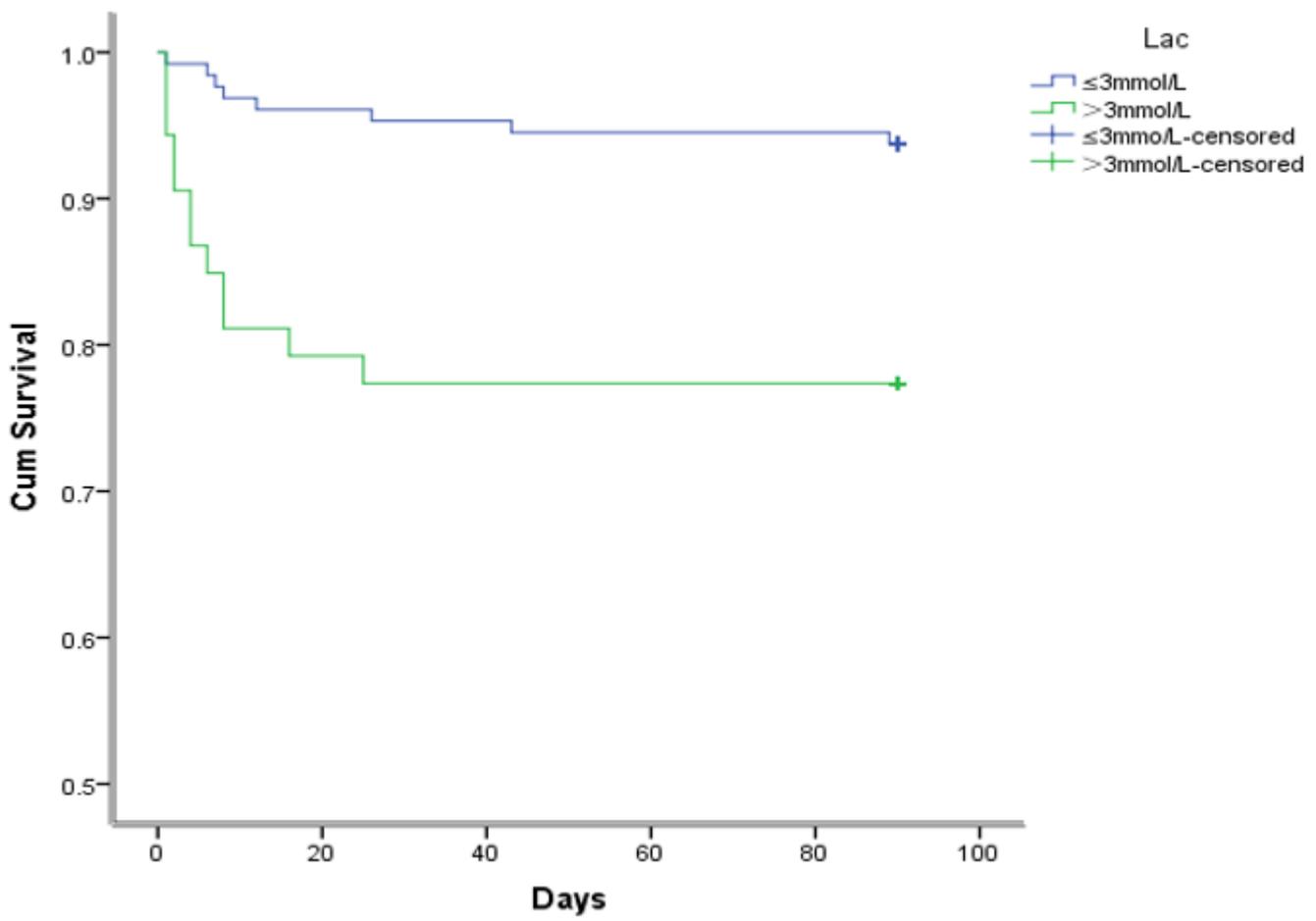


Figure 2

Kaplan-Meier survival curves of Lac on overall survival at 90 days

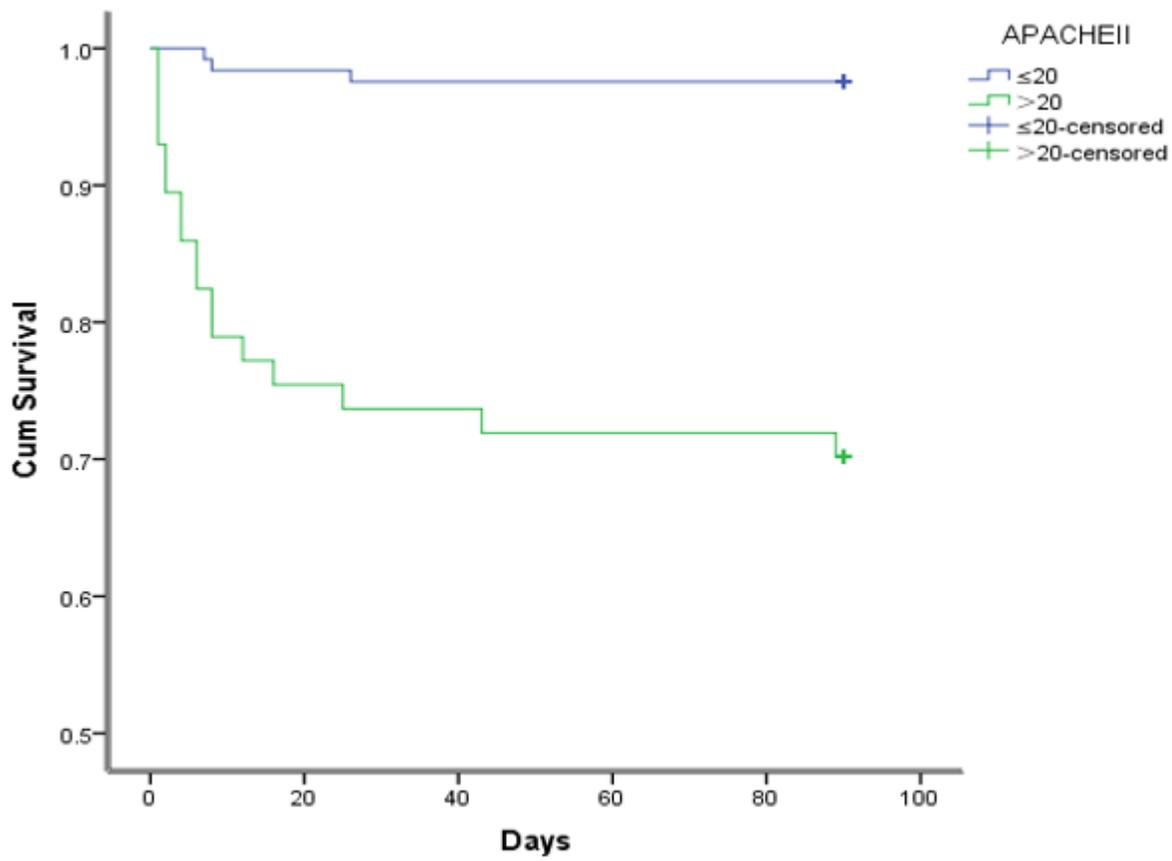


Figure 3

Kaplan-Meier survival curves of APACHE II score on overall survival at 90 days