INFECTION AS A RISK FACTOR IN THE OUTCOME OF PATIENTS WITH ACUTE RENAL FAILURE ASSESSED BY SOFA SCORE

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A b s t r a c t: Acute renal failure (ARF) is a complex syndrome, frequently reported with mortality in 20–80% of the patients. Infection, as a cause or a complication of the syndrome, is a risk factor which unfavourably determines the outcome.

A prospective 4-year study was performed of 112 ARF patients in the intensive care unit (ICU), with an evaluation of 68 clinical and laboratory parameters, as risk factors, at admission to the ICU. The scoring system used was SOFA (Sepsis-related Organ Failure Assessment).

The outcome was associated with 27 risk factors among which infection as an acute ARF insult has shown a particularly strong correlation (p < 0.0001). There was no association with infection as an intra-hospital complication. When divided according to the outcome (survivors vs. non-survivors), platelets, hematocrit, total protein and mean arterial pressure were significantly higher, while leucocytes and bilirubin significantly lower in the surviving group of patients. The parameters of the SOFA scoring system, such as the coagulation, liver and cardiovascular code, were statistically significant in relation to the outcome, and also the SOFA score taken as an independent variable (p < 0.0001). The classification matrix of the analyzed SOFA scoring system was successful in the classification of 91.95% of the surviving and 48.00% of the non-surviving patients with ARF and the odds ratio was 41.0.

Mortality rate in patients with ARF is 22.7%. Patients with ARF due to sepsis have a worse prognosis than those with non-septic ARF. Coagulation disorder, liver and cardiovascular dysfunction, as well as the SOFA score itself are independent variable in the outcome prediction. The SOFA score, derived from easily obtained data, is useful for judging survival prognosis in patients with ARF.

Key words: acute renal failure, infection, sepsis, SOFA score.

Introduction

Outcome prediction is important both in clinical and administrative intensive care unit (ICU) management [1]. Recently developed organ failure scores, such as Sepsis-related Organ Failure Assessment (SOFA) [2] can help assess organ dysfunction or failure and are useful in evaluating morbidity. Moreover, the obvious relationship between organ dysfunction and mortality demonstrated in several studies [3, 4], might be helpful in predicting the outcome. This is particularly important in ICU cases of acute renal failure (ARF) with sepsis associated with high mortality and financial cost. Serious infection as a major cause of ARF in hospital patients has been associated with poor patient outcome. Also, it is still uncertain whether infection as a complication during ICU hospitalization of the patients worsens their positive prognosis. The presence of serious infection in patients with ARF is often present as a clinical syndrome of sepsis, characterized by system inflammation, as well as various organ and functional system damage vasodilatation, increased permeability of microcirculation, leucocyte accumulation, etc.) [5–8].

The mechanism with which sepsis or endotoxaemia causes the syndrome of ARF has not yet been elucidated. According to some authors, there is a higher mortality rate in patients with septic ARF (74.5%) than in those whose renal failure did not result from sepsis (45.2%) [9].

The aim of our study was: i) to evaluate infection (presented through various clinical and laboratory parameters) as an associated risk factor in the mortality in ARF patients; ii) to assess the value of the SOFA scoring system as an independent factor in outcome prediction.

Material and methods

We conducted a prospective, randomized clinical trial over a period of four years, at the Department of Nephrology, Renal Intensive Care Unit, Medical Faculty, Skopje. The patient inclusion criteria were: increasing metabolic products: urea (s) and creatinine (s) above normal values (urea > 7.8 mmol/l and creatinine > 109 μmol/l); decreased urine output; assessed morphology and dimension of the ARF kidney by ultrasound examination, and patients over 14 years of age. The exclusion criteria were: pre-existing renal disease, malignant disease, immune deficient syndrome, transplantation, data for elevated metabolic products prior to admission, previous haemodialysis or treatment with other dialysis modalities and post surgical ARF.

Sixty-eight clinical and laboratory parameters, considered as risk factors were collected and analyzed in 112 patients (m = 69, mean age 45.5, SD ± 17.5 years), at their admission to the hospital or within the next 24 hours. The SOFA (Sepsis-related Organ Failure Assessment) score was assessed for each

of the patients at admission to the hospital according to already established criteria (2) (Table 1). Sepsis was defined in the presence of infection and > 2 of the following parameters: temperature $> 38^0$ C or $< 36^0$C; heart rate > 90 beats/min; respiratory rate > 20 breaths/min; partial pressure of carbon dioxide ($PaCO_2$) < 32 mmHg, and white blood cells (WBC) > 12 K/μL or < 4 K/μL or > 10% immature forms [5, 6]. All laboratory and clinical data were registered at admission or within a period of 24 hours.

A university analysis was performed for the analysis of the relationship between various variables and the outcome of ARF. To establish the individual risk factors that might be associated with the outcome in ARF patients a multivariate analysis was performed. *P* value (p < 0.05) was considered significant at a two-tailed level. Low *p* value in the multivariate analysis was assumed as greater certainty that that particular risk factor was important for the model of discrimination. STATISTICA 5 statistical soft-ware was used for the statistical analysis of the data.

Table 1 – Табела 1

The SOFA (Sepsis-related Organ Failure Assessment) score

СОФА систем за проценка (процена на системска слабост во однос на сепса)

SOFA score	1	2	3	4
Breathing				
PaO2/FiO2 mmHg	< 400	< 300	< 200	< 100
			-With respiratory support -	
Coagulation				
Platelets x10^3/mm^3	< 150	< 100	< 50	< 20
Liver				
Bilirubin mg/dl(μmol/l)	1,2–1,9 (20–32)	2.0–5.9 (33–101)	6.0–11.9 (102–204)	> 12 (> 204)
Cardiovascular				
Hypotension	MAP < 70 mmHg	Dopamine≤5 or dobutamine (any dose)*	Dopamin e > 5 or epinephrine ≤ 0.1 or norepinephrine ≤ 0.1	Dopamine > 15 Or epihephrine > 0.1 or norepinephrine 0.1
Central nervous system				
Glasgow Coma Score(GCS)	13–14	10–12	6–9	< 6
Renal				
Creatine, mg/dl (μmol/l) or urine output	1.2–1.9 110–170	2.0–3.4 171–299	3.5–4.9 300–440 or < 500ml/day	> 5.0 > 440 < 200 ml/day

* Adrenergic agents administered for at least 1h (doses given are in μg/kg/min).

Results

　　Sepsis/infection was the most frequently present individual acute insult in 90/112 (80%) of patients with ARF, followed by volume depletion, i.e. dehydratation, in 80/112 patients (71%) (Figure 1). When related to the outcome, a significant correlation was shown in the patients with ARF influenced by sepsis (p = 0.004) and toxicity (p = 0.003). The mortality rate in patients with ARF was assessed at as much as 22.7%.
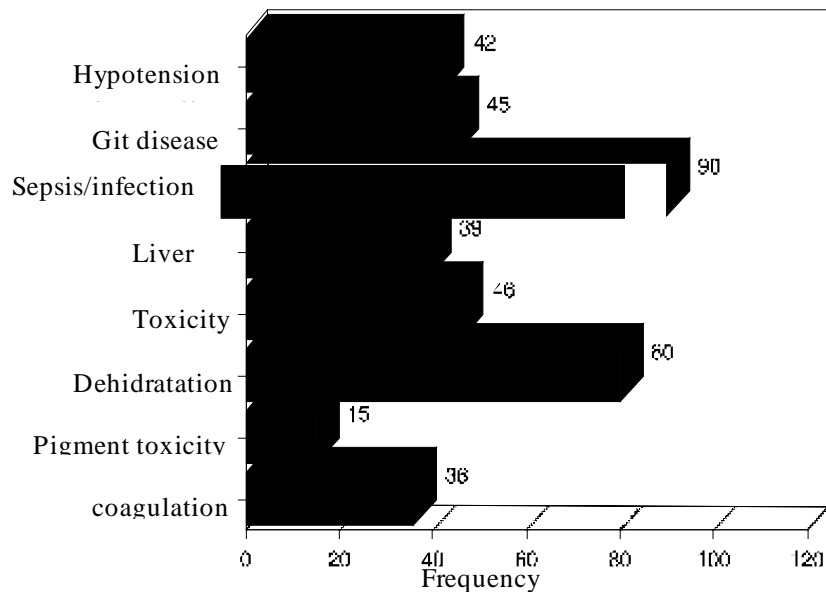
DISTRIBUTION OF ACUTE INSULTS IN Pts WITH ARF

Figure 1– Distribution of acute insults
Фигура 1 − Застапеност на акутни инсулти одделно

　　When divided according to the outcome (survivors vs. non-survivors), there were no significant differences in gender, but the surviving group of patients was significantly younger (p < 0.01). However, platelets, hematocrit (Htc), total protein and mean arterial pressure (MAP) were significantly higher, while WBC and bilirubin significantly lower in the surviving group of patients. All these parameters were included in the multiple regression analysis as independent variables influencing the outcome of ARF (Figure 2–5), while some of the parameters did not show any statistical significance, such as RENAL_SOFA code, i.e. serum creatinine values (Figure 6). Some of them (except WBC and Htc) were also included as a parameter for measurement in the SOFA score as an independent variable (Figure 7).
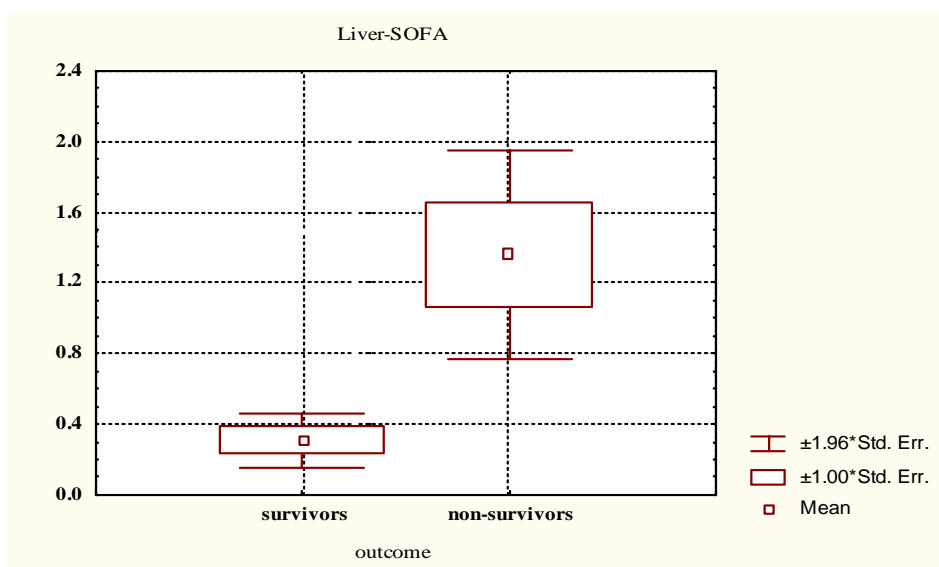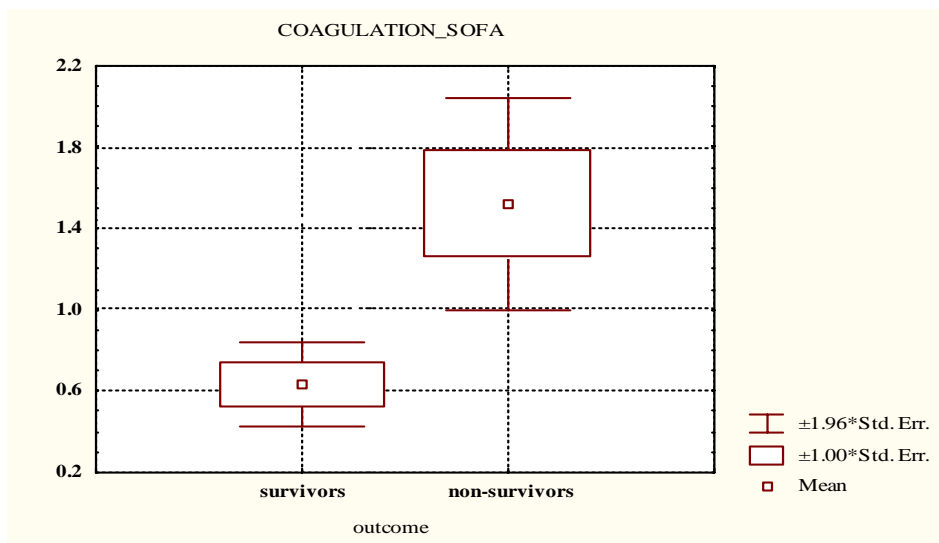
Figure 2 and 3 – Mean values of the Coagulation and Liver codes
of SOFA with a 95% Confidence Interval

Фигура 2 и 3 – Средни вредности на кодот за коагулација и хепар
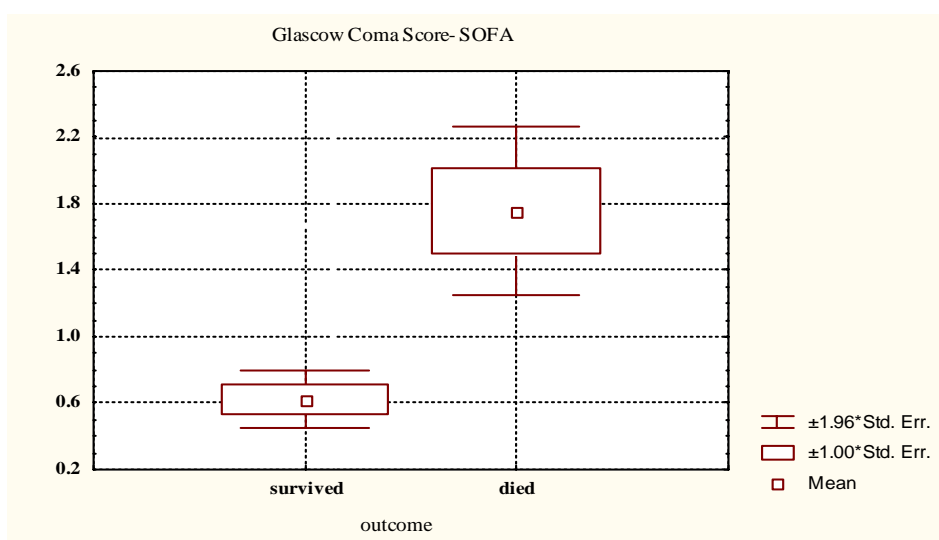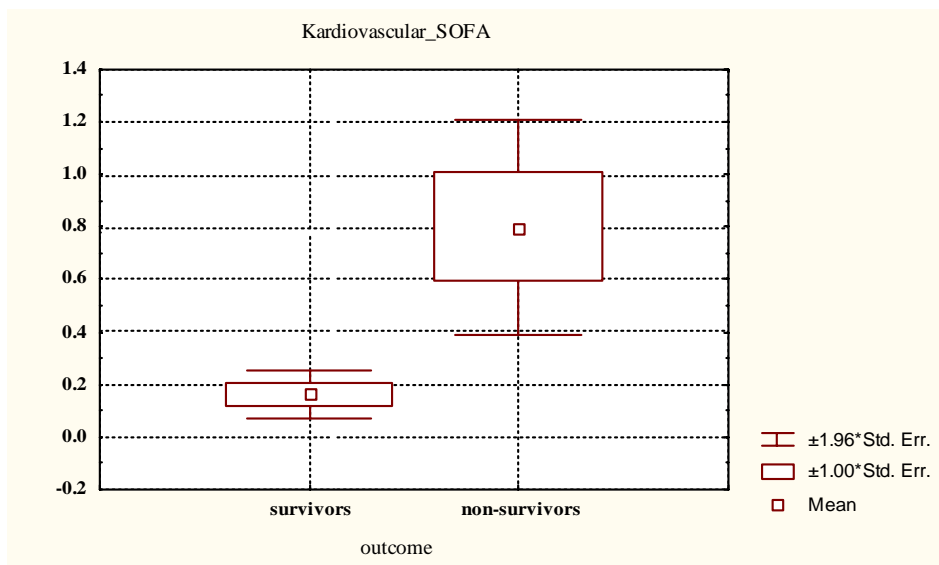*од СОФА со 95% интервал на сигурност*

Figure 4 and 5 – Mean values of the Cardiovascular and GCS codes of SOFA with a 95% Confidence Interval+

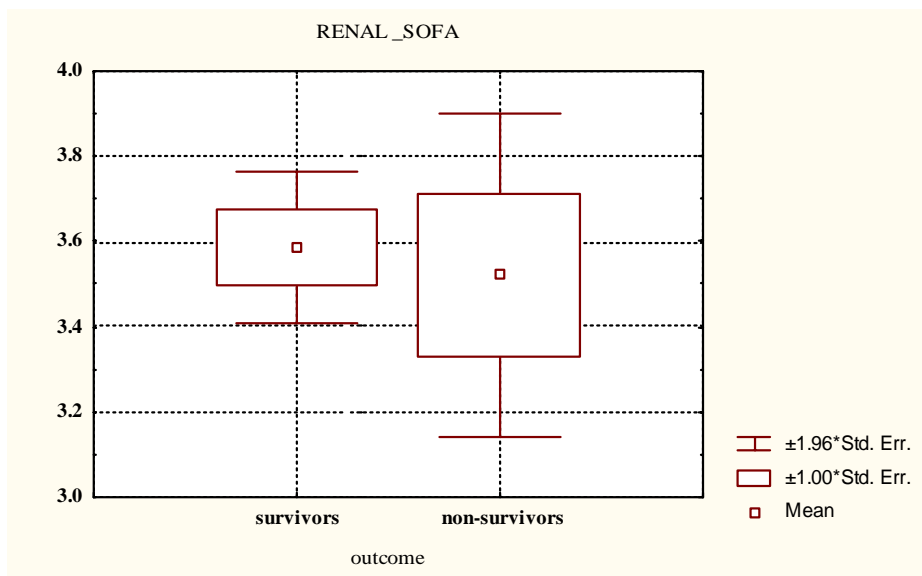*Фигура 4 и 5 – Средни вредности за кардиоваскуларните и ГКС кодови од СОФА процена*

Figure 6 – Mean values of Renal code SOFA score with 95% Confidence Interval
Фигура 6 – Средни вредности на реналниот код на СОФА проценаша
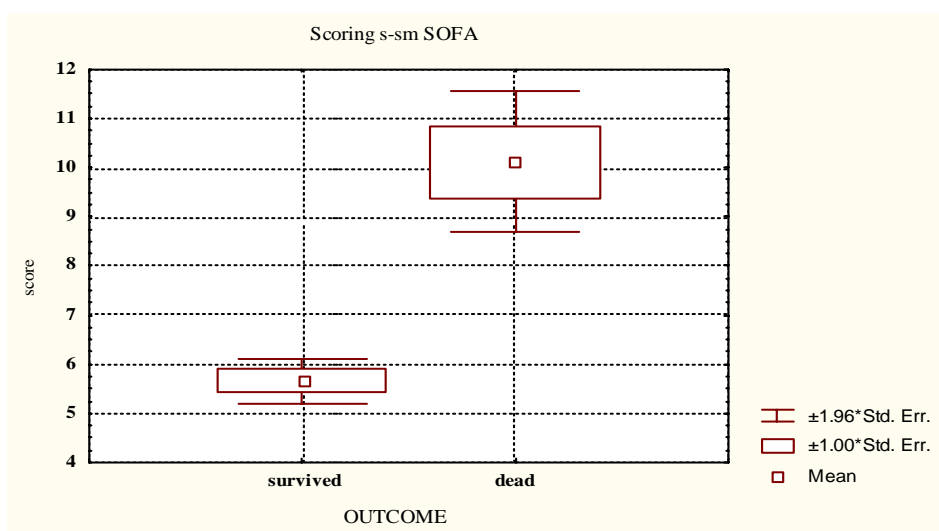со 95% иншервал на сигурносш

Figure 7 – Mean values of the SOFA Scoring System with a 95% Confidence Interval
Фигура 7 – Средни вредности на сисшемош за процена СОФА
со 95% иншервал на сигурносш

Classification matrix of analyzed SOFA scoring system determined with probability function (logistic regression) was successful in the classification of 91.95% of the surviving and 48.00% of the non-surviving patients with ARF and the odds ratio was 41.0 (Table 2).

Table 2 – Табела 2

Classification matrix of analyzed scoring system determined with probability function (logistic regression)

Класификациона матрица на анализираниот систем за процена определена со функција на веројатности (логистичка регресија)

Scoring system	Determined situation	Predictive situation		Successful in classification (%)	Odds ratio
		Survivors	Non-survivors		
SOFA	Survivors	80	7	91,95	
	Non-survivors	13	12	48,00	*41*

Discussion

Our study results confirmed previously reported findings of sepsis and toxicity as the most frequent individual acute insult in patients with ARF. Indeed, these two mechanisms in reality have a strong influence on the outcome of the disease. It was shown that patients with ARF conditioned with sepsis have a much worse outcome than those with non-septic ARF [2, 10, 11]. In fact, this observation is in line with the statistically significant influence of sepsis/infection as an acute insult on the patients' mortality.

We found a number of statistically determined significant risk factors that correlate with the outcome of ARF: hematocrit, leukocytes, platelets, bilirubin, total protein, liver and coagulation disorders as acute insults causing ARF. In addition, these basic laboratory findings can easily be assessed immediately after the admission of patients to the ICU. On the other hand, a group of selected significant risk factors was used for the determination of the existing system of prediction; such are the SOFA score, the coagulation code, liver code and cardiovascular code. The SOFA coagulation code of was presented by coded values of platelets, the liver code by coded values of bilirubin and the cardiovascular code by coded values of mean arterial pressure and a dose of Dopamine treatment. Importantly, each of them is very easily measured and assessed in routine clinical practice. Although included in the model of the SOFA scoring

system, the renal code, represented by serum creatinine values, has appeared to be a more than poor prognostic risk factor in the outcome of patients with ARF, a result that differs from the other findings [6].

In contrast to previous reports [12], our study data did not show intra-hospital infection to be an independent risk factor in the outcome of patients with ARF, but sepsis as a significant prognostic index on admission to the ICU was.

Finally, we have shown that the SOFA score (with its basic parameters) might have been an independent variable in the outcome prediction. Hence, the application of this scoring system might also help the predictability of patients with post-surgical ARF.

Conclusions

The mortality rate in patients with ARF was 22.7 %. According to the mechanism and origin in this group of patients haemodynamic and septic ARF is more frequent. Patients with ARF due to sepsis have a worse prognosis than those with non-septic ARF. Lower platelets, hematocrit, total protein and mean arterial pressure as well as higher WBC and bilirubin are associated with a poor outcome of patients with ARF. The most important risk factors for mortality in ARF patients are often present on admission to the ICU. Coagulation disorder, liver and cardiovascular dysfunction, as well as the SOFA score itself are independent variables in the outcome prediction. The SOFA score, derived from easily obtained data, is useful for judging the survival prognosis in patients with ARF.

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Резиме

ИНФЕКЦИЈАТА КАКО РИЗИК ФАКТОР ВО ИСХОДОТ НА ПАЦИЕНТИ СО АКУТНА БУБРЕЖНА СЛАБОСТ ОЦЕНЕТИ СО СОФА-СИСТЕМОТ ЗА ПРОЦЕНКА

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Акутната бубрежна слабост (АБС) е комплексен синдром, многу често со смртен исход кај 20–80%. Постоење на инфекцијата, како причина или компликација за текот на синдромот, е ризик фактор кој го одредува неповолниот исход.

Студијата претставува проспективно, четиригодишно клиничко истражување кај 112 пациенти од одделот за интензивна нега со синдром на АБС. Анализирани беа 68 клинички и лабораториски параметри, насловени како ризик фактори, при приемот во институцијата. Употребен беше системот за процена СОФА (оцена на органската слабост во однос на сепсата).

Исходот беше асоциран со 27 ризик фактори, меѓу кои инфекцијата како акутен инсулт беше со најсилна корелација (p < 0.0001). Инфекцијата пак како интрахоспитална компликација немаше статистичка значајност. При поделбата според исходот (преживеани vs. починати), тромбоцитите, хема-

токритот, вкупните протеини и средниот артериски притисок беа сигнификантно повисоки, а леукоцитите и билирубинот сигнификантно пониски кај групата на преживеани пациенти. Одделните параметри вклучени во системот за процена СОФА, како код за коагулација, црнодробна и кардиоваскуларна процена, беа статистички значајни во однос на исходот, како и самиот систем за процена СОФА, земен како поединечна варијабла (p < 0.0001). Класификационата матрица на анализираната процена со СОФА беше успешна во класификацијата 91,95 преживеани и 48% починати пациенти со АБС, со "odds ratio" или индекс на ризик од 41.

Морталитетот на пациентите со АБС е 22,7%. Пациентите со сепса како причинител за АБС имаат полоша прогноза од оние кои немаат сепса и АБС. Нарушувањата во коагулацијата, црнодробната и кардиоваскуларната дисфункција, како и СОФА-системот за процена како целина се независни варијабли кои го предвидуваат исходот. Процената со СОФА, која се добива преку лесно добивање на податоци, е корисна во прогнозата за преживување на пациентите со АБС.

Клучни зборови: акутна бубрежна слабост, инфекција, сепса, систем за процена – СОФА.

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Dehydratuion
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