MEDICAL SCIENCE MONITOR

CLINICAL RESEARCH

e-ISSN 1643-3750
© Med Sci Monit, 2016; 22: 3755-3763
DOI: 10.12659/MSM.895875

Received: 2015.09.05
Accepted: 2016.01.21
Published: 2016.10.17

Early and Late Acute Kidney Injury in Severely Burned Patients

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ACDEFG 1 **Wojciech Witkowski**
ACDFG 2,3 **Marek Kawecki**
BCDEF 1 **Agnieszka Surowiecka-Pastewka**
BCDEF 4 **Wojciech Klimm**
CDE 5 **Katarzyna Szamotulska**
ACDEFG 4 **Stanisław Niemczyk**

1 Department of Burns, Plastic and Reconstructive Surgery, Military Institute of Medicine, Warsaw, Poland
2 Centre for the Treatment of Burns, Siemianowice Śląskie, Poland
3 Department of Emergency Medicine, Faculty of Health Sciences, Academy of Technology and Humanities, Bielsko-Biała, Poland
4 Department of Internal Medicine, Nephrology and Dialysotherapy, Military Institute of Medicine, Warsaw, Poland
5 Department of Epidemiology and Biostatistics, Institute of Mother and Child, Warsaw, Poland

Corresponding Author: Agnieszka Surowiecka-Pastewka, e-mail: agnieszkasurowiecka@op.pl
Source of support: Departmental sources

Background: This study evaluated factors influencing early and late occurrence of AKI in severely burned patients and assessed the relationship between time of occurrence of AKI and mortality of AKI patients.

Material/Methods: Renal function was evaluated at 3 time points: at admission, at the critical point or middle point of hospitalization, and at the endpoint for which death or a discharge from the center was considered. AKI criteria were: decrease in GFR of less than 60 ml/min at admission, decrease in GFR of more than 75% compared to baseline, and decrease in the daily diuresis of less than 500 ml/24 h.

Results: At admission, 15.1% of the patients had eGFR <60 ml/min. AKI occurred in 38.5% of cases. The occurrence of AKI was associated with: elderly age (p<0.001), female sex (p=0.017), overweight and obesity (p=0.055); extent and depth of burns, respiratory failure, low protein concentration (for all p<0.001), low blood pressure (p=0.014), and high WBC (p=0.010). Early AKI was detected in 28% of patients. Mortality was 100% with the initial GFR ≥60, 100% with the initial GFR <60 and early deterioration of renal function, 80% with the initial GFR <60 and late worsening, and 60% with the initial GFR <60 and no worsening. Late AKI was observed in 10% of patients and mortality in this group was 79.2%. Mortality in the entire group with AKI was 88.0% versus 24.5%.

Conclusions: The frequent occurrence of AKI, especially early, worsens the prognosis for survival. Assessment of renal function should be included in the prognostic scales for burned patients.

MeSH Keywords: **Acute Kidney Injury • Burns • Renal Replacement Therapy • Respiratory System Abnormalities • Sepsis**

Full-text PDF: http://www.medscimonit.com/abstract/index/idArt/895875

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Background

Treatment of severe burns is still a major multidisciplinary clinical problem. Burn disease proceeds with rapid devastation of the body, dehydration or overhydration, multiple organ failure, and inflammation and is burdened with high mortality [1–5]. Noninflammatory acute kidney injury (AKI) is one of the most important complications decreasing the chances of survival in patients with extensive burns covering over 15–20% of the total body surface area (TBSA). The criteria for the diagnosis of AKI are still being modified. In 3–5% of patients, biochemical parameters of renal damage reach life-threatening values, which requires the implementation of renal replacement therapy (RRT). Despite the development of increasingly effective dialysis techniques and optimization of intensive care, AKI requiring urgent RRT is fraught with high mortality [6–9].

On average, AKI occurs in approximately 30% of patients with severe burns, thereby increasing the risk of death and mortality in this group to more than 80% [1,5,12,13]. This applies especially to patients with respiratory tract burns [1,14]. The pathogenesis of AKI in patients with burns is complex and not fully understood; therefore, it is very difficult to distinguish septic from non-septic AKI. It is currently unclear whether the time of occurrence of AKI is important for the survival of a burned patient.

The aim of the present study was to evaluate the factors influencing early and late occurrence of AKI in severely burned patients and to assess the relationship between the time of occurrence of AKI and the mortality rate.

Material and Methods

We performed a retrospective analysis of burn patients admitted to the Clinical Department of Burns, Plastic and Reconstructive Surgery, Military Institute of Medicine (MIM) in Warsaw and to the Centre for the Treatment of Burns (CTB) in Siemianowice Slaskie in 2012 and 2013. From the population of all burn patients (947 people) we selected a group of severely burned patients (241 people), of which we included into the study 225 patients that met the established criteria of analysis. As the main criterion for the assignment to the group of severely burned patients, we established thermal burns exceeding 30% of TBSA.

The group of severely burned patients was analyzed in terms of time from burn to the admission to MIM or CTB, sex, age, BMI, burn surface area, surface of full-thickness third-degree skin burns, the presence of the respiratory tract burns, respiratory failure, and renal function failure.

Mean arterial pressure (MAP) was calculated using the formula MAP=[(2 × diastolic) + systolic]/3. In addition, we analyzed laboratory results taking into account morphology (number of erythrocytes, leukocytes, platelets, hemoglobin, and hematocrit), coagulation profile (APTT and INR), and selected biochemical parameters (sodium, potassium, glucose, creatinine, urea, total protein, and albumin). For further analysis, we used only those laboratory test variables which in univariate analysis affect the survival of severely burned patients: total protein, albumin, creatinine level, and leukocytosis. Due to the missing data we decided to analyze albumin or/and total protein as a single variable, not eliminating cases lacking both of these values. The results of microbiological testing of cultures of wounds, bronchi, blood, and central venous access were also evaluated. The presence of pathogens in the blood culture was considered to be bacteremia.

The results of laboratory tests were collected at 3 time points: at admission, at the critical or middle point of hospitalization for which a moment of the deterioration of a patient was chosen, and at the end point for which death or a discharge from the center was considered.

Respiratory failure in patients with respiratory tract burns was defined as the need for intubation or symptoms of acute respiratory failure confirmed by arterial blood gas analysis.

Glomerular filtration rate (GFR) was calculated at admission and at the selected point according to the simplified MDRD formula, based on knowledge of the creatinine level, age, and sex using the equation:

$$eGFR=186.3 \times creatinine^{-1.154} \times age^{-0.203} \times (0.742 \text{ for women}).$$

The failure of renal functions was assessed in accordance with the previously existing classifications (RIFLE, KDIGO, and AKIN) [7–10] forming the authors' definition of AKI for the study, based on the analysis of the applied classifications and modified for the needs of the retrospective evaluation of routine clinical practice:

- decrease in GFR of less than 60 ml/min at admission;
- decrease in GFR of more than 75% compared to baseline or
- decrease in the daily diuresis of less than 500 ml for at least 24 h.

The first-line AKI therapy was a conservative treatment in the form of fluid resuscitation. Parkland formula was adopted as the optimal method. Following the recommendations, we transfused 4 ml of fluid per 1 kg of body weight for every 1% of burned TBSA during the first day after injury. Fifty percent of fluid was administered during the first 8 h and the second 50% during the next 16 h.

Burn surface area was assessed using the Lund and Browder charts. The depth of a burn was assessed by multiple clinical inspection of wounds. In the case of deterioration of diuresis despite proper hydration, infusions of loop diuretics (Furosemide) were administered. In case of an unfavorable increase of renal parameters (creatinine clearance, and urea), ions (refractory hypernatremia), or symptoms of renal excretory failure (persistent oliguria or anuria) as the principle we used a nephrologist consultation in the context of multidisciplinary cooperation.

The statistical analysis used descriptive statistics and chi-square test (for 2 categorical variables), the *t* test and ANOVA (for a categorical variable and a continuous variable with normal distribution), and the Mann-Whitney and Kruskal-Wallis tests (for a categorical variable and a continuous variable with non-normal distribution). We also estimated parameters of the logistic regression model and the Cox proportional hazards model with a time-dependent covariate. We set the level of statistical significance at α=0.05. Calculations were performed using SPSS software v. 18.0.

The research was approved by the Bioethics Commission of the Military Institute of Medicine in Warsaw (34/WIM.2013; 19.06.2013).

Results

The group consisted of 176 men with a mean age of 48 years (SD 16, range 18–90) and 49 women with a mean age of 59 (SD 19, range 19–92) (Table 1).

Table 1. Characteristics of the studied group (n=239).

	N	Studied group
Sex: (%)		
Males	176	78.2%
Females	49	21.8%
Age (mean ±SD)	225	50.3±17.0
TBSA% (median, 25-75 percentile)	225	46% (35–61%)
III% (median, 25-75 percentile)	225	20% (6–40%)
Superficial burns (%)	225	5.8%
Respiratory tract burn (%)	225	70.7%
Endotracheal intubation (%)	225	39.1%
Diseases in the medical history (%)		
Diabetes	7	3.1%
Vascular events	16	7.1%
Diabetic vascular complications	9	4.0%
Chronic kidney disease	2	0.9%
Admission after one day since the injury (%)	222	22.1%
Admission from other centres (%)	225	26.7%
eGFR at admission <60 (%)	225	16.0%

The median percentage of burned TBSA was 46%, and the median percentage of severe partial thickness burns was 20%.

In 13 patients we found a superficial burn of IIa/IIb type, with no evidence of deep thermal injury. In 159 cases we diagnosed respiratory tract burns in which 46% of patients required endotracheal intubation.

Most patients were accepted directly to the centers on day 1 after the event (73%). Twenty-seven percent of patients were directed from other centers, usually also on day 1 after the event (range 0–31 days after the burn occurrence).

From the interviews at admission we obtained information on chronic diseases in only 32 burn patients. Seven patients had diabetes, 16 had a vascular event (hemorrhagic and ischemic stroke, myocardial infarction, ischemic heart disease, and chronic limb ischemia), 9 had diabetic vascular complications in the past, and 2 had previous chronic kidney disease (2 women: the first was age 55, eGFR at admission 48 ml/min, TBSA 50%, III 47%, respiratory tract burns with respiratory failure, after 3 days eGFR 13 ml/min, and death after 5 days; the second was age 73, eGFR at admission 25 ml/min, TBSA 40%, III 31%, no respiratory tract burns with respiratory failure, after 20 days eGFR 22 ml/min, oliguria, bacteremia, and death after 23 days).

At admission 16.0% of the patients had eGFR <60 ml/min and AKI (as defined above) in the entire group occurred in 40.0% of cases. Renal failure occurred in 28.6% of patients with normal baseline eGFR. In our study, 9 burned patients underwent RRT. In 6 patients we administered continuous renal replacement therapy (CRRT), in 2 intermittent renal replacement therapy, and in 1 case we used both methods. In all of these patients, during the hospitalization we performed on average 2 dialyses (range 1–10). Sixty-seven percent of the dialyzed group were males and the average age of dialyzed patients was 52 years (SD 13, range 22–68). The mortality rate in this group was 100% and in the entire studied group mortality was 50.7%.

HD was performed as a conventional treatment every day or every second day using bicarbonate buffer. In the study we

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Table 2. The occurrence of AKI in severely burned patients depending on the parameters assessed at admission.

Characteristics at admission		N=100%	AKI Yes (n=135)	AKI No (n=90)	p-value*
Age (mean ±SD)		225	45.7±15.0	57.2±17.6	<0.001**
Sex (%)	Male	49	44.9%	55.1%	0.015
	Female	176	64.2%	35.8%	
TBSA% (median; 25–75 percentile)		225	40; 32–54	57; 40–79	<0.001***
III% (median; 25–75 percentile)		225	10; 4–22	34; 16–64	<0.001***
Respiratory tract burns (%)	No	66	66.7%	33.3%	0.188
	Yes	159	57.2%	42.8%	
Respiratory failure (%)	No	123	78.0%	22.0%	<0.001
	Yes	101	37.6%	62.4%	
BMI (%)	<20.0 kg/m^2	16	81.3%	18.8%	0.024
	20.0–25.0 kg/m^2	87	69.0%	31.0%	
	25.0–30.0 kg/m^2	70	51.4%	48.6%	
	≥30.0 kg/m^2	41	51.2%	48.8%	
Day of admission since the event (%)	0	173	60.7%	39.3%	0.482
	1 and more	49	55.1%	44.9%	
Hematocrit (%)	≤45.9%	128	60.2%	39.8%	0.805
	>45.9%	94	58.5%	41.5%	
WBC (%)	3.0–14.9×10^9/l	96	67.7%	32.3%	0.029
	>14.9×10^9/l	126	53.2%	46.8%	
Protein or albumin (%)	<6.00 lub <3.50 g/dL	125	50.4%	49.6%	0.001
	≥6.0 and ≥3.5 g/dL	54	79.6%	20.4%	
	No data	46	63.0%	37.0%	
MAP (%)	<70 mmHg	39	43.6%	56.4%	0.038
	70–109 mmHg	141	63.1%	36.9%	
	>109 mmHg	37	70.3%	29.7%	

* In chi-square test, unless otherwise stated; ** in Student's t-test; *** in Mann-Whitney test.

performed 1 to 11 (4 on average) treatments in individual patients, 40 procedures in total. Total time of hemodialyses was 119 h, with an average of 11.9 h for each patient. HD treatments lasted from 2.5 to 3.25 h (2.93 h on average). Blood flow was between 150 and 260 ml (average of about 190 ml/min). We used dialyzers made of highly biocompatible polysulfone membranes ranging from 1.3 to 1.7 m^2 adapted to the size and weight of the patients. Heparinization was used in the form of low-molecular-weight heparin (Fragmin at doses from 1250 to 2500 IU) except for 4 patients presenting clinical signs of bleeding diathesis. The potassium concentration in the dialysis liquid concentrate varied from 1.0 to 4.0 mmol/L and was adjusted according to the actual kalemia (Table 1).

CVVHDF was performed in a system of 2 successive 3-day treatments using Prismaflex equipment. HDF dose was constant at 35 ml/kg body weight/h of treatment. Due to the accompanying coagulation disorders, anticoagulation with the use of citrates was performed. Ultrafiltration ranged from 50 to 75 ml/h.

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Table 3. The occurrence of AKI in severely burned patients depending on the parameters assessed at admission – multivariate analysis.

		Odds ratio	p-value	95% confidence interval for odds ratio
Age		1.081	<0.001	1.050; 1.113
III%		1.042	0.001	1.018; 1.067
Respiratory failure	No	ref.	<0.001	–
	Yes	5.250		2.156; 12.784
Protein or albumin	<6.00 or <3.50 g/dL	4.517	0.003	1.501; 13.599
	≥6.0 and ≥3.5 g/dL	ref.		–
	No data	1.010		0.254; 4.008
BMI	<25.0 kg/m²	ref.	<0.001	–
	≥25.0 kg/m²	4.589		2.014; 10.454

Table 4. Analysis of the time of AKI occurrence depending on the variables assessed at admission and during hospitalization.

		eGFR at admission						p-value*
		≥60			<60			
		No deterioration (n=135, 100%)	Deterioration 0-6 days (n=31, 100%)	Deterioration 7+ days (n=23, 100%)	No deterioration (n=10, 100%)	Deterioration 0-6 days (n=14, 100%)	Deterioration 7+ days (n=10, 100%)	
Age (mean ±SD)		45.7±15.0	52.6±16.9	55.6±16.9	55.3±20.3	64.3±20.2	63.9±10.8	<0.001**
Sex (%)	Female	16.3%	19.4%	34.8%	20.0%	35.7%	50.0%	0.041
	Male	83.7%	80.6%	65.2%	80.0%	64.3%	50.0%	
TBSA% (median; 25–75 percentile)		40; 32–54	65; 50–90	45; 40–60	55;35–77	78;64–90	39;34–53	<0.001***
III% (median; 25–75 percentile)		10; 4–22	44; 30–80	20; 10–30	33;13–54	58;40–73	23;6–33	<0.001***
Respiratory tract burns (%)	No	32.6%	16.1%	39.1%	40.0%	0.0%	30.0%	0.028
	Yes	67.4%	83.9%	60.9%	60.0%	100.0%	70.0%	
Respiratory failure (%)	No	71.6%	19.4%	47,8%	60.0%	0.0%	30.0%	<0.001
	Yes	28.4%	80.6%	52.2%	40.0%	100.0%	70.0%	
BMI (%)	<25.0 kg/m²	56.2%	50.0%	38.1%	20.0%	23.1%	30.0%	0.035
	≥25.0 kg/m²	43.8%	50.0%	61.9%	80.0%	76.9%	70.0%	
Day of admission since the event (%)	0	79.5%	90.3%	69.6%	50.0%	85.7%	50.0%	0.020
	1 and more	20.5%	9.7%	30.4%	50.0%	14.3%	50.0%	
Hematocrit (%)	≤45.9%	58.3%	58.1%	60.9%	50.0%	57.1%	50.0%	0.987
	>45.9%	41.7%	41.9%	39.1%	50.0%	42.9%	50.0%	
WBC (%)	3.0–14.9×10⁹/l	49.2%	29.0%	56.5%	40.0%	0.0%	40.0%	0.001
	>14.99×10⁹/l	50.8%	71.0%	43.5%	60.0%	100.0%	60.0%	
Protein or albumin (%)	<6.00 or <3.50 g/dL	59.4%	82.6%	76.2%	90.0%	100.0%	90.0%	0.015
	≥6.0 and ≥3.5 g/dL	40.6%	17.4%	23.8%	10.0%	0.0%	10.0%	
MAP (%)	<70 mmHg	12.9%	46.4%	13.6%	10.0%	23.1%	20.0%	0.056
	70–109 mmHg	67.4%	42.9%	72.7%	70.0%	69.7%	70.0%	
	>109 mmHg	19.7%	10.7%	13.6%	20.0%	7.7%	10.0%	
Bacteremia (%)	No	83.7%	100.0%	52.2%	80.0%	100.0%	60.0%	<0.001
	Yes	16.3%	0.0%	47.8%	20.0%	0.0%	40.0%	
Dialysis (%)	No	100.0%	90.3%	81.8%	100.0%	91.7%	90.0%	<0.001
	Yes	0.0%	9.7%	18.2%	0.0%	8.3%	10.0%	

* In Fisher test, unless otherwise stated; ** in analysis of variance; *** in Kruskal-Wallis test

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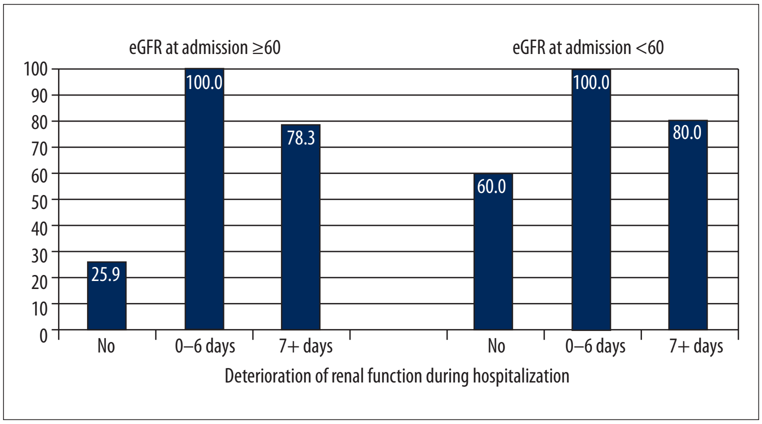

Figure 1. The incidence of deaths (per 100) by eGFR at admission and time of deterioration of renal function during hospitalization.

Table 5. Analysis of survival depending on the occurrence of AKI after eliminating the effect of selected variables predictive for death.

		Hazard ratio	p-value	95% confidence interval for hazard ratio
Age		1.017	0.007	1.005; 1.030
TBSA%		1.009	0.311	0.991; 1.027
III%		1.020	0.003	1.007; 1.034
Respiratory tract burns	No	Ref.	0.029	–
	Yes	1.877		1.067; 3.302
AKI*	No	Ref.	<0.001	–
	Yes	8.224		5.259; 12.862

* Time-dependent variable.

The data collected at admission were subjected to univariate analysis to determine the parameters influencing the occurrence of AKI in a group of severely burned patients. Parameters significantly influencing AKI at admission (p<0.05) were: age, burn surface area, deep burn surface area, respiratory failure co-existing with respiratory tract burns, and low protein level and/or albumin. Further variables predisposing to the occurrence of AKI were low mean arterial pressure (MAP), female sex, overweight or obesity (p=0.024), and leukocytosis above 14.9×10×/1. Days elapsed from the burn event to admission to the MIM or CTB proved to have no statistical significance as a parameter influencing the occurrence of AKI (Table 2).

Next, we analyzed the results by stepwise logistic regression with AKI as the outcome variable and predictors in Table 2 (p<0.1). Statistically significant association with the occurrence of renal failure in the studied group of severely burned patients showed (Table 3): age (OR=1.081, p<0.001), full-thickness body surface area burns (OR=1.042, p=0.001), respiratory tract burns and co-existing respiratory failure (OR=5.250, p<0.001), low protein and/or albumin levels (OR=4.517, p=0.003), and obesity or overweight (OR=4.589, p<0.001).

Due to the heterogeneity of the AKI group, we analyzed in detail the time of occurrence and changes in renal function during hospitalization (Table 4).

In the entire group, early AKI, defined as having been diagnosed by the end of the sixth day since the event, was detected in 20% of patients and late AKI in 15% of the entire group.

Older age, a large burned body surface area, extensive deep injury, the presence of respiratory failure with co-existing respiratory tract burns, low protein and/or albumin level, high WBC, and low MAP clearly predisposed to an early form of AKI. Variables predicting late occurrence of renal failure were bacteremia, protein disorders, late admission to the center, and older age. The occurrence of AKI after 7 days was an indication for renal replacement therapy more often than earlier occurrence of AKI.

Eighty-eight percent of burned patients with diagnosed AKI died while in patients without AKI mortality was 25.9% (p<0.001). The relative risk of death depending on AKI was 3.353 (95% confidence interval 2.502; 4.494).

The highest mortality was observed in patients with early deterioration of renal function, with both normal baseline renal parameters and reduced eGFR at admission (p<0.001, Figure 1).

The risk of death due to the occurrence of AKI (treated as an independent variable, but depending on time) was 8.224 in the Cox model adjusted for age, TBSA%, burned surface area III%, and respiratory tract burns (Table 5).

Discussion

Recent studies have shown a huge increase in the number of AKI in the United States, also requiring dialyses in patients with AKI for various reasons, with a doubled number of dialyzed and dying patients [17]. More frequent occurrence of the problem results from the prolonged life of patients and increased survival in numerous severe cases [16].

The definition of AKI has been evolving for several years. RIFLE criteria recognize AKI to a lesser extent than KDIGO guidelines, and AKIN detect AKI better than RIFLE classification [8–11,16,18,19]. KDIGO introduced criteria to systematize the definition of AKI but also increased the number diagnoses [10]. In the present study we used our own criteria which resulted from the analysis of the employed methods and allow for evaluation of routine clinical practice (see Methods).

AKI in burned patients can take 2 forms: early and late. The early AKI occurs in the first few days to a week after the injury and results from insufficient filling of the vascular bed caused by a rapid loss of fluid through the damaged skin and respiratory system. The other reason for the occurrence of the early AKI is a patient's severe condition, with hypotension. These results are also presented in our work. The incidence of AKI was reduced by implementing standard fluid resuscitation [3]. In our work, the early occurrence of AKI was dependent on the burn surface area, respiratory tract burns and respiratory failure, hypotension, and hypoproteinemia. Transfusion of large fluid volumes, mainly crystalloids, reaching several liters per day in the initial period of treatment, can largely prevent hypovolemia and early renal complications [3]. The late AKI is characteristic for the weeks following the injury and is mainly due to septic complications and nephrotoxicity of the drugs used [2]. We proved in our work that the early occurrence of AKI had the worst prognosis, especially if observed at the time of admission (Figure 1). Mosier et al., in a study of 221 patients evaluated by RIFLE classification every 24 h, demonstrated that early development of AKI in patients with severe burns was associated with multiple organ failure and increased mortality. AKI developed in 28% of patients, of which 29% developed renal dysfunction by RIFLE classification [14]. We obtained similar results using the proposed classification of AKI assessment.

Numerous studies confirm the high incidence of AKI in severely burned patients [13]. In our study we found AKI in as many as 40% of patients, and the occurrence of AKI worsened the prognosis (mortality of patients with AKI is up to 88.0%, but without AKI it is 25.9%).

What factors contribute to the development of AKI in severely burned patients? In our work we demonstrated the influence of age, negative effects of female sex, a larger surface area and depth of burns, respiratory failure, high BMI, high WBC, low total protein and/or albumin levels, and low blood pressure. Sex of the patients and blood pressure values were irrelevant when using stepwise logistic regression (see Results). Many works confirm our results [1–3,15,20–22], although there is no information that higher BMI is unfavorable. The negative effect of high BMI can be explained by high catabolism rate and difficulties in wound healing.

Influence of burned surface area, deep burns, age, and respiratory tract burns on the prognosis of burned patients is well documented and used in prognostic scales. Renal function is taken into account as one of the factors affecting mortality of burned patients only in the scales generally used in Intensive Care Units based on the APACHE II system. FLAME and BEAMS scales are examples of the scales used in patients with burns [23,24]. None of the scales directly takes into account the strong relationship between the occurrence of renal failure and increased risk of death, which is shown in our analysis. In our work, deaths in patients with AKI are related to the time of its occurrence, and patients with early AKI have a much higher mortality rate (Figure 1).

In a very interesting work, Schneider et al. examined which factors cause kidney damage at different times in a group of 220 patients with burns [25]. Early renal failure developed in 22.2% of the patients, late renal failure developed in 17.7%, and 7.2% had progressive renal failure. Patients in the third group were older, had more comorbidities, and worse survival.

In the analysis by Classification and Regression Tree (CART), as many as 33 different variables, including clinical and pharmacological parameters, were used. In the method used, the occurrence of late AKI could have been predicted with 80% confidence, accuracy verified on less amount of data (their own research) was 73% (25). We did not analyze the occurrence of progressive renal failure after AKI. However, we confirmed a higher incidence of AKI in elderly patients, and the prognosis for survival of these patients is poor (see Results).

The work by Noshad showed the occurrence of AKI in up to 75% of patients with severe burns. The most important factors favoring the occurrence of AKI were sepsis, burned surface area, length of hospitalization, and nephrotoxic drugs.

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Concomitant diabetes, heart failure, and other kidney diseases were important as well [26]. A study by Steinvall et al. showed that the depth of burns increases the incidence of AKI by 2.25-fold [20]. In our work, bacteremia, which favored the development of late AKI, was associated with intubation of patients (data not shown).

Bagshaw et al. reported a very high incidence of AKI (in almost 80% of patients) using the RIFLE criteria [22]. A study by Yang et al. showed that AKI developed in 81 patients out of 304 patients with burn surface area greater than 10%. Respiratory tract burns, catheter-related infections, and sepsis favored the development of AKI [15]. Patients with severe burns (more than 30% of body TBSA) and co-existing proteinuria have a high risk of developing AKI [27]. Coca et al. reported that AKI occurred in 26.6% of patients, also using RIFLE classification [1].

The RIFLE classification has been used most frequently to evaluate the occurrence of AKI in patients with severe burns [8]. The usefulness of the RIFLE classification was observed in a study by Palmieri et al., which demonstrated a high percentage of patients with AKI with severe burns. The severity of burns (area and depth), sepsis, surgeries performed, the cumulative amount of administered fluids, and the use of nephrotoxic drugs were confirmed as factors contributory to AKI. The study was conducted in 60 patients [21].

Brusselaers et al. examined the incidence of AKI in burn patients based on 57 articles. AKI occurred in more than one-quarter of the patients (average mortality of these patients was 34.9%) and in 3% AKI required renal replacement therapy, which had an 80% mortality rate. AKI increased mortality in burned patients [5]. In the work by Noshad, AKI occurred in 75% of patients [26]. In our study, all 10 patients treated with RRT died.

In the study by Steinvall et al., 24% of patients (31 of 127) with burned surface area of more than 20% developed AKI. In the entire group, mortality was 14% and in patients with AKI the mortality rate was 83%, similarly to our results. In 55% of cases, AKI occurred within the first 7 days and disappeared in all surviving patients. Respiratory failure and sepsis were observed in all patients before the occurrence of AKI, and systemic inflammatory response syndrome (SIRS) intensified AKI in 48% [20]. In our study, the incidence of AKI was 38.5% and the mortality rate in the entire group was 49%; as we have shown, the mortality rate of patients with AKI was nearly 4 times higher than in patients without AKI (88.0% *vs.* 24.5%).

Patients with AKI (using RIFLE classification) have a higher mortality, greater need for mechanical ventilation, longer stays in the ICU, and longer hospitalizations. Mortality increases with age, TBSA of burns, and damage to the respiratory tract (as in our study). The usefulness of the RIFLE classification is confirmed in predicting the mortality rate in patients with moderate AKI [1,17,27,28].

Mortality of patients with burns is high and does not change despite the improvement in intensive care [17]. Our study confirms the relationship between mortality rate and burned surface area, its depth, and occurrence of AKI. These events coexist, particularly in patients with early AKI (Table 5). AKI is a very common phase in development of multiple organ failure in severely burned patients [13]. Rhabdomyolysis can be significant in the development and course of AKI in burned patients [29], but this aspect was not examined in the present study.

Our study demonstrates that late AKI, unlike early AKI, is more common in the presence of bacteriemia. Early AKI is associated with larger and deeper burns, lower average blood pressure, and respiratory failure resulting from bronchial burns. Higher BMI favored the development of AKI in both early and late periods. In our work, bacteriemia was associated with intubation of burned patients, and patients with late AKI were dialyzed more frequently.

AKI treatment in burn patients is very difficult. In the ICU at the hospital, where early RRT was implemented in a group of 234 patients, RIFLE classification showed that 76.9% of patients had renal failure, 85% had mechanical ventilation, mean creatinine level was 331 umol/L, patients had oliguria, and mean diuresis was 265 ml (maximum 860 ml/d) [22]. Seventy-four percent of patients on RRT had no classic indications for the implementation of the method. Early implementation in a patient in relatively good condition was associated with better survival, indicating that time of implementation can modify the survival of patients. However, most studies show poor results of RRT [11,18,20,36]. In our study, RRT was ineffective. The early implementation of CVVHD in burn patients is recommended in patients with acute lung injury (ALI) as the standard of care. The implementation of this method reduced the mortality on day 28 and hospital mortality, in contrast with the results of other studies [19].

Other studies [37–39] indicate that there are no benefits of hemofiltration compared to intermittent hemodialysis in the treatment of AKI in burn patients. Therapeutic plasma exchange (TPE) may be effective in the treatment of burn shock, as demonstrated by a study of 40 patients [40]. Gille et al. demonstrated that citrate anticoagulation is a safe and effective method to treat severe burn patients who have bleeding risk, electrolyte disturbances, and acid-base imbalance [41].

Our work confirms that the occurrence of AKI, especially early, in patients with severe burns decreases patient survival. Our classification used to assess the incidence of AKI is useful. The occurrence of AKI should be included in the classifications used to assess the severity and prognosis in patients with severe burns.

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Conclusions

1. AKI is a common problem in severely burned patients. It is favored by older age, female sex, overweight and obesity, extent and depth of burns, respiratory tract burns with respiratory failure, low protein and/or albumin concentration, low-medium blood pressure, and high WBC at admission.
2. The occurrence of AKI, especially early, worsened the prognosis for survival in our study.
3. Assessment of renal function is a valuable prognostic factor and should be included in the prognostic scales used in burn patients.

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