

Incidence, Risk Factors, and Outcomes of Acute Kidney Injury in Major Burn Patients: A 7-Year Experience in Ramathibodi Hospital

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Objective: To identify the incidence of acute kidney injury (AKI) in patients with major burn injuries within the first week of intensive care unit (ICU) admission at Ramathibodi Hospital and to identify risk factors associated with AKI.

Materials and Methods: The present study was a retrospective observational study of the patients with major burn injuries in the burn intensive care unit (BICU) at Ramathibodi Hospital. All data were retrieved from the scanned medical records of the patients admitted to the BICU between January 1, 2016 and December 31, 2022. The patients were diagnosed and graded according to the Kidney Disease Improving Global Outcomes (KDIGO) recommendation. Independent risk factors associated with AKI were identified by multivariable logistic regression.

Results: Eight of the 50 patients (16%) had AKI within the first week of admission. The baseline international normalized ratio (INR) level of 1.5 or greater was independently associated with AKI with an odds ratio (OR) of 32.42 (95% confidence interval [CI] 2.194 to 478.608). No independent risk factor was identified for 28-day mortality. Fluid balance in the first week had an area under receiver operating characteristics (ROC) of 0.856 (95% CI 0.747 to 0.964) to diagnose 28-day mortality. A cutoff point of 22,761 mL or more provided a sensitivity of 90.91% and a specificity of 61.54%.

Conclusion: The incidence of AKI in the first seven days of BICU admission was 16%. Coagulopathy, defined as INR of 1.5 or greater, was identified as an independent risk factor associated with early AKI in patients with major burns. Utilizing a simple value of INR could be a practical way to identify patients with major burns that may require further workup. Furthermore, the fluid balance cutoff point could be used as a warning signal of high risk for mortality during a weekly review of patients' clinical rounds.

Keywords: Acute kidney injury; Burn; Mortality; Critically ill patients; Intensive care; ICU

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Major burn injury introduces hemodynamic disturbances⁽¹⁾ to patients, leading to acute kidney injury (AKI)⁽²⁻⁴⁾. The disturbances, from under-resuscitation to excessive fluid balance, lead to renal vasoconstriction, tissue hypoxia, and cardiac dysfunction. All of these are the underlying pathophysiological mechanisms of AKI in burn

injuries⁽⁵⁾.

Previous studies have shown that older age, increased burn total body surface area (TBSA) percentage, increased burn depth, diabetes mellitus (DM), hypertension, high absolute burn surface index, presence of inhalation injury, mechanical ventilation use, surgery, high Acute Physiology and Chronic Health Evaluation II (APACHE II) scores, and high Sequential Organ Failure Assessment (SOFA) score were identified as risk factors of AKI in patients with burn injury⁽²⁻⁶⁾.

However, those data were from an older period, earlier than 2015. There has been an evolution in medical practice in treating patients with major burn injuries. The Kidney Disease Improving Global Outcomes (KDIGO) publication of AKI definition and treatment in 2012⁽⁷⁾ and the Advanced Trauma Life Support (ATLS) updated material in 2018⁽⁸⁾ were two of the most crucial improvements in the

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innovation of burn injury treatment. Therefore, the present study aimed to determine the incidence of AKI and associated risk factors during the first week of burn intensive care unit (BICU) admission for burn patients.

Materials and Methods

The present study was a retrospective cohort study conducted at Ramathibodi Hospital, Bangkok, Thailand. After obtaining approval from the Ethics Committee of the Faculty of Medicine Ramathibodi Hospital, Mahidol University (approval number MURA2023/213), the authors collected data using scanned medical records. The authors retrieved patients' laboratory results from the hospital's electronic medical record system. The Faculty of Medicine Ramathibodi Hospital, Mahidol University, sponsored and funded this study. Patients admitted to the BICU were screened between January 1, 2015 and December 31, 2022. All patients were then followed to either at least 28 days after admission or expiration. As Ramathibodi Hospital is a tertiary referral center, all patients in the present study were referred from other hospitals. The authors recorded all collected data in an Excel spreadsheet.

Patients aged at least 18 years with major burns, defined by combined second and third-degree burn wounds of at least 20% of TBSA, were included. Those with underlying end-stage renal disease, pre-diagnosed AKI, pregnancy, or those who died within 24 hours after admission were excluded from the study.

Patient's data, namely, age, gender, body weight, height, underlying disease, current medication, details of burn wound injury including degrees, percentages, and mechanism, vital signs, fluid balance, type of fluid details, vasopressor use, and mechanical ventilation status were extracted through scanned medical records. Blood count, blood chemistry, and arterial blood gas results were retrieved through the electronic health information reporting system. Missing data were presumed to be similar to the latest available previous data.

AKI, the primary outcome, was defined according to the KDIGO criteria⁽⁷⁾. The patients were classified as having AKI if they met those criteria on any day within the first seven days of BICU admission. The patient's living status was deemed alive if the patient survived for more than 28 days after BICU admission.

The authors included all adult patients with major burn injuries since the inception of the authors' BICU, which was equipped with scanned medical

records. These numbers became the sample size of the present study.

Continuous data were expressed as mean with standard deviation (SD) when they were normally distributed and otherwise, as median with interquartile ranges at 25th and 75th percentiles (IQR25, IQR75). The normality of data distribution was assessed by comparing means and standard deviations. Categorical data were presented as counts with percentages. Between-group comparisons of continuous data were done using independent t-tests or Mann-Whitney tests as appropriate. In contrast, comparisons of categorical data were performed using the chi-square test or Fisher's exact test. A p-value of less than 0.05 was considered statistically significant. There was no loss in follow-up in the present study as it relied on retrieving digital medical records.

Univariable logistic regression initially identified risk factors for AKI in the first week and 28-day mortality. Then, all risk factors with p-values of less than 0.1 were selected to be included in multivariable logistic regression analyses. Risk factors with p-values of less than 0.05 in multivariable logistic regression analysis were considered independently associated with those outcomes. A receiver operating characteristic (ROC) analysis was used to determine an appropriate cutoff point to predict a 28-day survival status. The authors performed all analyses using Stata Statistical Software, version 18 (StataCorp LLC, College Station, TX, USA).

Results

The present study included 50 patients admitted during the study period. Among them, there were eight out of 50 patients (16%) who developed AKI in the first week of BICU admission. During the 28 days after admission, eleven patients (22%) died. The demographic data, baseline laboratory values, and initial hemodynamic variables of patients are depicted in Table 1. Comparing the AKI and non-AKI groups, only age, and APACHE II scores differed statistically with p-values of 0.026, and 0.079, respectively.

In Table 2, comparing patients who developed AKI to those who did not, fluid intake during the first week did not differ significantly in all periods listed. Urine output in the first three days differed significantly between the two groups ($p < 0.001$). Fluid balances (intake – output) during days 4 to 7 and 1 to 7 were statistically different, with a p-value of 0.007 and 0.019, respectively. Blood components given to patients during days 4 to 7 were statistically different, with a p-value of 0.034. Fluid intake in

Table 1. Characteristics of patients

Characteristics	Total (n=50)	AKI (n=8)	Non-AKI (n=42)	p-value
Age (years); mean±SD**	39.64±13.81	49.5±15.89	37.76±12.73	0.026
Female sex; n (%) ^b	15 (30.00)	4 (50.00)	11 (26.19)	0.220
BMI (kg/m ²); n (%) ^b				0.472
<18.5	1 (2.00)	-	1 (2.38)	
18.5 to 22.9	13 (26.00)	1 (12.50)	12 (28.57)	
23 to 27.5	22 (44.00)	3 (37.50)	19 (45.24)	
>27.5	14 (28.00)	4 (50.00)	10 (23.81)	
APACHE II; mean±SD**	10.36±4.76	14.38±4.93	9.6±4.38	0.079
Percentage of B-BSA (%); mean±SD ^a	48.99±21.5	57.06±14.33	47.45±22.42	0.251
Mechanism of burn; n (%) ^b				0.618
Flame	31 (62.00)	4 (50.00)	27 (64.29)	
Explosion	10 (20.00)	2 (25.00)	8 (19.05)	
Electrical	3 (6.00)	1 (12.50)	2 (4.76)	
Chemical	5 (10.00)	1 (12.50)	4 (9.52)	
Thermal	1 (2.00)	-	1 (2.38)	
28-day mortality; n (%) ^b	11 (22.00)	3 (37.50)	8 (19.05)	0.351
Baseline laboratory values; mean±SD ^a				
Na (mmol/L)	137.79±4.33	140.38±4.27	137.28±4.2	0.064
K (mmol/L)	4.39±0.61	4.43±0.76	4.39±0.59	0.844
Cl (mmol/L)	106.02±5.11	107.38±3.2	105.75±5.4	0.417
HCO ₃ (mmol/L)	19.44±3.91	20.46±5.27	19.24±3.62	0.424
Blood urea nitrogen (mg/dL)	14.65±7	18±9.61	13.98±6.31	0.140
Creatinine (mg/dL)	0.99±0.54	1.22±0.75	0.94±0.49	0.185
Albumin (g/dL)	2.34±0.82	2.04±0.88	2.4±0.8	0.262
PaO ₂ (mmHg); median [P25, P75] ^c	155.2 [99.5, 199.9]	127.35 [84.35, 179.9]	155.3 [120.6, 202.7]	0.223
Hemoglobin (g/dL)	15.52±3.44	14.74±4.88	15.7±3.08	0.480
Hematocrit (%)	46.18±10.78	45.01±15.46	46.41±9.87	0.742
White blood cell (×10 ³ /mCL)	15.72±8.91	15.91±9.04	15.69±8.99	0.949
Platelet (×10 ³ /mCL); median [P25, P75] ^c	176 [150, 253]	218.5 [174, 290.5]	174 [142, 249]	0.301
INR level	1.24±0.27	1.56±0.47	1.19±0.16	0.108
Initial hemodynamic parameters; mean±SD ^a				
MAP (mmHg)	100.97±17.24	97.92±22.98	101.55±16.21	0.590
Pulse rate (bpm)	103.16±21.63	96.75±25.5	104.38±20.94	0.366
Respiratory rate (/minute)	20.1±4.65	22.38±8.88	19.67±3.34	0.421
Temperature (°C)	37.45±1.21	36.7±2.19	37.59±0.89	0.294

SD=standard deviation; APACHE=Acute Physiology and Chronic Health Evaluation; AKI=acute kidney injury; BMI=body mass index; B-BSA=burned body surface area; INR=international normalized ratio; MAP=mean arterial pressure

Statistically tested by ^a Student's t-test, ^b Fisher's exact test, ^c Mann-Whitney test

* Statistically different comparing the AKI with the Non-AKI group by t-test

the present study consisted of balanced crystalloids such as Ringer's acetate solution, glucose-containing crystalloids, human albumin solution, and blood components.

Of the patients who had AKI in the first week, three of them had AKI for more than a day, and all three died within 28 days after BICU admission. Overall, the median BICU length of stay was 1,364 (IQR 813, 3,046) hours, with a rate of death of 22%. Patients with AKI had a median length of stay of

2,230.5 (IQR 1,038.5, 4,385) hours, while those who did not have AKI had a median length of stay of 1,278 (IQR 740, 2,811) hours. The two groups' length of stay did not differ statistically ($p=0.29$). Three of eight patients (37.5%) with AKI died within 28 days, and eight of 42 patients (19.05%) without AKI died. There was also no statistical significance in the death rate ($p=0.351$). All patients with AKI had the onset day of day 1 with a median duration of 1 (IQR 1, 1.75) day. Their median fluid intake before AKI onset was

Table 2. Fluid balance and blood component volume given

Characteristics	Total (n=50)	AKI (n=8)	Non-AKI (n=42)	p-value
Fluid balance (L)				
Fluid intake day 1 to 3	23.02±9.27	24.32±10.64	22.76±9.11	0.595
Fluid intake day 4 to 7 ^a	20.74±9.17	25.71±4.06	19.79±9.59	0.008
Fluid intake day 1 to 7	43.4±15.68	50.03±10.88	42.14±16.23	0.195
Urine output day 1 to 3 ^a	8.7±3.2	5.08±2.73	9.39±2.81	<0.001
Urine output day 4 to 7	12.07±5.5	11.26±6.98	12.23±5.26	0.653
Urine output day 1 to 7	20.77±7.32	16.34±9.36	21.62±6.67	0.061
Positive balance day 1 to 3; median [P25, P75]	12.28 [5.79, 20.98]	19.28 [8.91, 29.15]	11.41 [5.63, 19.5]	0.169
Positive balance day 4 to 7; median [P25, P75] ^b	6.66 [3.85, 13.44]	12.83 [10.9, 19.46]	5.09 [3.27, 11.56]	0.007
Positive balance day 1 to 7; median [P25, P75] ^b	22.76 [11.7, 33.64]	35.24 [23.08, 38.7]	15.86 [10.16, 29.67]	0.019
Blood components (mL); median [P25, P75]				
Day 1 to 3	0 [0, 1,000]	120 [0, 1,605]	0 [0, 960]	0.631
Day 4 to 7 ^b	1,090 [0, 2,120]	2,045 [1,180, 3,097.5]	640 [0, 1,995]	0.034
Day 1 to 7	1,765 [0, 3,095]	2,380 [1,605, 4,950]	1,023.5 [0, 2,880]	0.081

SD=standard deviation; AKI=acute kidney injury

Statistically different comparing the AKI with the non-AKI group by ^a t-test, ^b Mann-Whitney test**Table 3.** Univariable and multivariable analysis for AKI in the first 7 days

Characteristics	Univariable analysis		Multivariable analysis	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age ≥60 years old	3.17 (0.47 to 21.24)	0.235		
Female sex	2.82 (0.6 to 13.24)	0.189		
BMI ≥27.5 kg/m ²	3.2 (0.67 to 15.19)	0.143		
B-BSA ≥40%	6.36 (0.72 to 56.35)	0.096	6.14 (0.29 to 132.41)	0.247
APACHE II score >10	7 (0.79 to 61.98)	0.08	2.35 (0.18 to 31.37)	0.518
Fluid balance in the first week ≥22,761 mL	3.63 (0.66 to 20.12)	0.14	0.74 (0.06 to 8.49)	0.806
Norepinephrine use in the first week	1.86 (0.17 to 20.51)	0.613		
Hct <30%	4.33 (0.6 to 31.54)	0.148		
INR ≥1.5	41 (3.65 to 461.03)	0.003	32.4 (2.19 to 478.61)	0.011
Albumin <3 g/dL	2.8 (0.31 to 25.26)	0.359		
Creatinine ≥1.9 mg/dL	3.17 (0.47 to 21.24)	0.235		

APACHE=Acute Physiology and Chronic Health Evaluation; AKI=acute kidney injury; BMI=body mass index; B-BSA=burned body surface area; Hct=hematocrit; INR=international normalized ratio; OR=odds ratio; CI=confidence interval

6,897.5 mL (IQR 4,675.5, 12,159.5) with a median fluid balance of 6,441.5 (IQR 4,115.5, 10,652.5). After AKI was resolved, the median fluid intake was 38,362 (IQR 27,988, 47,025.25), accompanying a median fluid balance of 20,372 (IQR 14,417.25, 23816.5).

Univariable analysis to identify risk factors related to AKI in the first seven days of BICU admission is shown in Table 3. There were three factors with p-values less than 0.1 that were selected to be included in subsequent multivariable analysis, namely, burn body surface area (B-BSA) of at least 40%, high APACHE II score, and international normalized ratio (INR) level of 1.5 or greater. Additionally, a fluid balance higher than the median

of this cohort (22,761 mL) was forced into the multivariable analysis. After controlling other factors in multivariable model analysis, only a high INR level was associated with AKI in the first week of BICU admission (p=0.011).

Regarding risk factors for 28-day mortality, the univariable analysis revealed seven factors with p<0.1, which are age at least 60 years old, high B-BSA, high APACHE II score, high fluid balance in the first week, any norepinephrine used in the first seven days of admission, high INR level and high serum creatinine level (Table 4). Older age and high creatinine levels were ignored in the subsequent multivariable regression analysis due to these two factors being already included in the APACHE II

Table 4. Univariable and multivariable analysis for 28-day mortality

Characteristics	Univariable analysis		Multivariable analysis	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age ≥ 60 years old	10.57 (1.61 to 69.27)	0.014		
Female sex	1.46 (0.35 to 5.97)	0.603		
BMI ≥ 27.5 kg/m ²	1.66 (0.4 to 6.88)	0.487		
B-BSA $\geq 40\%$	10.53 (1.23 to 90.31)	0.032	4.41 (0.25 to 76.55)	0.308
APACHE II score >10	11.67 (1.36 to 100.14)	0.025	7.81 (0.37 to 166.15)	0.188
Fluid balance in the first week $\geq 22,761$ mL	16 (1.86 to 137.94)	0.012	5.61 (0.35 to 90.95)	0.225
Norepinephrine use in the first week	14.25 (1.31 to 155.23)	0.029	20.22 (0.78 to 521.98)	0.07
Hct $<30\%$	2.67 (0.39 to 18.42)	0.32		
INR ≥ 1.5	6.94 (0.99 to 48.55)	0.051	1.61 (0.16 to 16.35)	0.685
Albumin <3 g/dL	1.77 (0.33 to 9.52)	0.507		
Creatinine ≥ 1.9 mg/dL	4.5 (0.76 to 26.53)	0.097		
AKI in the first week	2.55 (0.5 to 12.96)	0.259		

APACHE=Acute Physiology and Chronic Health Evaluation; AKI=acute kidney injury; BMI=body mass index; B-BSA=burned body surface area; Hct=hematocrit; INR=international normalized ratio; OR=odds ratio; CI=confidence interval

score. The multivariable logistic regression analysis resulted in no statistically independent risk factor.

A further look into the data regarding fluid balance in the first week and 28-day mortality showed that such fluid balance had an area under ROC of 0.856 (95% CI 0.747 to 0.964) to diagnose the 28-day death status. Using a cutoff point of 22,761 mL or greater, the median fluid balance of this cohort yielded a sensitivity of 90.91% (95% CI 58.7 to 99.8) and a specificity of 61.54% (95% CI 44.6 to 76.6) and correctly identified 68% of the actual results, as shown in Figure 1.

Discussion

The authors found that a high INR level was an independent risk factor for developing AKI within the first week of BICU admission. Still, the authors could not identify an independent risk factor for 28-day death status. A fluid balance of more than 22,761 mL served as a good cutoff point to determine this status.

The incidence of AKI in the present study differed from the recent meta-analysis published by Folkestad et al., which determined an overall incidence of 38%⁽⁹⁾. The data from the review were collected from studies published between 2007 and 2019, in which different criteria to diagnose AKI were used. The difference in the definition of AKI and an evolution in practice could explain the difference. Compared to a more recent study published by Tsai et al. in 2020, which also focused on early AKI similar to the present study, more patients in their cohort (61.2%) suffered from AKI despite having similar B-BSA⁽¹⁰⁾. This incongruence could be due to the

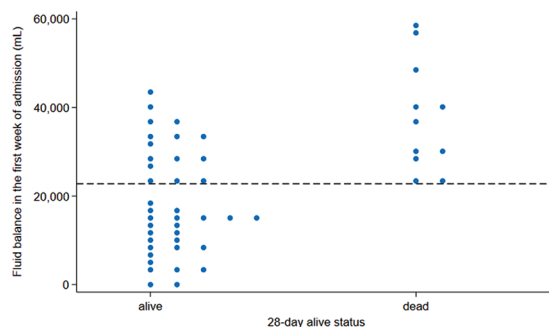


Figure 1. Fluid balance in the first week of admission with 28-day death status.

Each dot represents a patient, and the dashed reference line represents a fluid balance of 22,761 mL, corresponding to the median value of patients' fluid balance in the first week.

difference in mechanisms of burn, as all patients in Tsai's cohort suffered from explosion-based injury. In contrast, the majority of patients in the present study had flame burn injuries.

The authors did not find AKI in the first week to be correlated with mortality statistically despite the difference in mortality rate of 37.5% in patients with AKI versus 19.05% in patients without AKI. This could be due to the small sample rate of AKI and the overall sample size. However, the authors found that three of the patients who sustained AKI for longer than a day died. This could potentially signify the importance of AKI in affecting the mortality of patients with major burn injuries. The trend towards affecting mortality of AKI in patients with major burn was consistent with previous reports from Putra et al. and Sánchez-Sánchez et al., which reported

increase in mortality in patients with AKI of more than four-fold⁽¹¹⁾ and ten-fold⁽¹²⁾ compared with non-AKI groups, respectively.

In the present study multivariable analysis to identify risk factors for AKI, the authors found that a high INR level was an independent risk factor. This correlated with patients in the AKI group receiving more blood components during days 4 to 7. In contrast to Tsai's cohort⁽¹⁰⁾, the only study found to have reported the volume of blood components given in patients with major burn injuries, the authors did not detect the difference in blood components given between the AKI and non-AKI groups. The authors also found a high INR level led to this difference but could not find any previous study reporting INR levels in patients with major burn injuries. The higher INR levels, which signify coagulopathy in critically ill patients, could result from major inflammation impacting the clot formation process. Another explanation for the high INR levels would be the high volume of resuscitation fluid, which could dilute coagulation factors, leading to coagulopathy^(13,14). Regarding the burned surface area, a very high B-BSA of 40% or more would mean that the patients with high burn areas are more critically ill, warranting more care and attention. This severity bias could be the mechanism behind the non-significance of a very high B-BSA as an independent risk factor for AKI. Additionally, the discrepancy in results regarding the B-BSA issue could be due to the difference in the population characteristics. The study by Yoldaş et al. consisted of 35.4% of patients with 0% to 20% B-BSA⁽¹⁵⁾, while the present study only included patients with at least 20% B-BSA.

Regarding risk factors for 28-day mortality, the authors did not find any independent risk factors through a multivariable analysis. This could be due to the small sample size of the present study cohort. However, the authors found a positive fluid balance of at least 22,761 mL in the first week, which was the median of this cohort, was a good predictor for 28-day mortality in this cohort. This cutoff point had a high sensitivity of 90.91% with an acceptable specificity of 61.54% to predict death within 28 days. This finding could provide insight into managing fluid in patients with major burn injuries.

The present study has limitations. First, the small sample size of the cohort could affect outcomes and explain the disparity of risk factors identified by the present study and others' studies. Another limitation was the present study was a single-center study. This could be viewed as a limitation in interpreting the

present study because the present study institute is a tertiary referral center. Thus, the selection of the patients by the institute should be acknowledged when interpreting the present study.

Further research efforts should focus on including more patients from different settings to represent a more generalized group of patients and increase the sample size of the study, which, in turn, would improve the power of the study to detect risk factors associated with AKI and mortality in patients with major burn injuries.

In conclusion, high INR level was an independent risk factor increasing the risk of developing AKI in the first week of patients with major burn injuries. No risk factor was identified to be independently associated with higher 28-day mortality. The authors also propose a cutoff point of 22,761 mL or greater as a positive fluid balance in the first week to predict death within 28 days of admission.

What is already known on this topic?

Major burn injury triggers a severe inflammation cascade, leading to AKI. Multiple factors were shown to be risk factors for AKI, such as increased burn total surface area, but those studies were from an older period.

What does this study add?

Coagulopathy, defined as INR of 1.5 or greater, was an independent risk factor for developing AKI in the first week of patients with major burns. A positive fluid balance of 22,761 mL or greater in the first week may predict 28-day mortality.

Conflicts of interest

The authors declare no conflict of interest.

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