RESEARCH ARTICLE

Predictors in-hospital mortality of septic vs non-septic acute kidney injury patients: an observational cohort study [version 1; peer review: awaiting peer review]

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Abstract

Background: To compare the predictors In-hospital mortality of patients with septic Acute Kidney Injury (S-AKI) and non-septic AKI (NS-AKI).

Methods: a cohort study of critically ill patients with AKI admitted to the emergency room at a tertiary hospital from January to June 2019. The primary outcome was hospital mortality.

Results: There were 116 patients who met the inclusion criteria. Compared with NS-AKI, patients with S-AKI had significantly lower mean MAP, median eGFR, and urine output. (UO). S-AKI had higher mortality and vasopressor requirements and had a lower renal recovery than NS-AKI (63.2% vs 31.4%, $p=0.001$; 30.8% vs 13.7%, $p=0.031$, and 36.9% vs 60.8%, $p=0.011$, respectively). AKI stage 3 and vasopressor requirements were dependent risk factors for both S-AKI and NS-AKI mortality. Meanwhile, SOFA score > 7 and the need for dialysis are dependent and independent risk factors for mortality in S-AKI. Worsening and/or persistence in UO, serum urea and creatinine levels at 48 h after admission were predictors of mortality in S-AKI and NS-AKI. Improvement in UO in surviving patients was more pronounced in S-AKI than in NS-AKI (50% vs 17.1%, $p=0.007$). The surviving S-AKI patients had a longer hospital stay than surviving NS-AKI [8 (6-14.5) vs 5 (4 - 8), $p=0.004$]. S-AKI have higher mortality and vasopressor requirements and have lower renal recovery than NS-AKI.

Conclusion: S-AKI have higher mortality and vasopressor requirements and a lower renal recovery than NS-AKI. Independent predictors of mortality in S-AKI were high SOFA scores and the need for dialysis.

Keywords

acute kidney injury, length of stay, mortality, predictors, septic

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Introduction

Acute kidney injury (AKI) is a disorder that occurs in the kidneys with a sudden onset characterized by a decrease in kidney function and/or a decrease in urine output.¹ AKI is a common disorder worldwide which affects 7–18% of hospital inpatients and 30–70% of critically ill patients.² Sepsis is a frequent cause of AKI, especially in critically ill patients in the intensive care unit (ICU) with an incidence of 11 to 70%.^{1,3,4} Sepsis-associated AKI (S-AKI) is also associated with a significant disease burden with poor clinical outcome.⁵ The mortality rate of septic patients with complicated AKI is significantly higher than that of non-AKI patients⁶ and is an independent contributor to mortality.⁷ Among critically ill patients with AKI, S-AKI is correlated with higher risk of in-hospital death, longer duration of hospital stay^{3,8,9} and increased chances for progression to chronic kidney disease (CKD)^{1,3,4} compared with AKI caused by other reasons. Although there have been significant advances in treatment and care, the morbidity associated with this condition remains rather high.⁵ This condition is partly the result of the pathophysiology of S-AKI itself, which remains only partially understood.¹⁰ AKI caused by sepsis has a complex and multifactorial pathophysiology which will certainly have different impacts and need for different interventions when compared to AKI due to non-sepsis.^{11,12} There are also difficulties in early diagnosis and treatment of S-AKI that need to be resolved.⁵ Treatment options with adequate antibiotics and maintaining hemodynamic stability still have limitations. Based on the paper of Murugan *et al*, it turns out that up to 25% of patients with hemodynamically stable non-severe pneumonia can develop AKI.¹³ This indicates that hemodynamic instability is not a prerequisite for the occurrence of AKI in these patients. So, information on S-AKI is still limited. This study aims to compare the outcomes of S-AKI and NS-AKI patients and identify predictive factors to the outcomes by analyzing the demographic, clinical and laboratory characteristics of these patients during their stay in the hospital.

Methods

Study design and participants

This is a prospective cohort of AKI patients admitted to the emergency unit of Saiful Anwar General Hospital, a tertiary hospital in Malang, East Java, Indonesia. Patients in critical condition and diagnosed with AKI with or without sepsis, age > 40 years, who were admitted to the hospital from January to June 2019 were included as inclusion criteria. While the exclusion criteria included patients with CKD stages 3-5, kidney transplant patients, pregnant conditions, tumor history, anaphylactic shock, hospital stay <48 hours and denied research authorization. This study has obtained written informed consent from all patients or close relatives and has been approved by the Ethics Committee of the Faculty of Medicine, Universitas Brawijaya, with number 400/02/K.3/302/2018. Collecting data, including demographic data, personal history, including history of disease and treatment. Blood samples were taken at admission and subsequently, urine production was monitored within the first 0-12 hours. The management of AKI patients follows the standard guidelines in hospitals for patients with critical conditions. Subsequently, patients were followed closely and patient data, including urine output, serum urea and creatinine (sCr) levels were evaluated and recorded during hospitalization until discharge.

The diagnosis of AKI was based on the KDIGO criteria, based on an increase in sCr levels compared to the reference value or the previous baseline sCr value if recorded on medical records and/or based on a decrease in urine production.¹⁴ Stage 1, sCr level increased 1.5-1.9 times or urine output (UO) <0.5 mL/kg/h for 6–12 h, stage 2, sCr level increased 2.0-2.9 times or UO <0.5 mL/kg/h for 12 h; and stage 3, sCr increased > 3.0 times or UO <0.3 mL/kg/h for 24 h or anuria for 12 h.

The UO, urea and serum sCr level was evaluated at 48 hours after admission. The criteria for improved kidney function if there is a decrease in sCr levels $\geq 20\%$ compared to baseline. Likewise, for UO and serum urea levels; improves or worsens if there is a change of $\geq 20\%$ compared to the baseline level, and persists if the change is < 20%. The criteria for sepsis are based on The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3).¹⁵ The Sequential Organ Failure Assessment (SOFA) score is used to determine the extent of a person's organ function or the degree of failure. Sepsis is identified when a SOFA score > 2 points is obtained in a patient with suspected infection.¹⁶ Meanwhile, septic AKI is defined as AKI in the presence of sepsis without other significant contributing factors explaining AKI or characterized by the simultaneous presence of both Sepsis-3 and KDIGO criteria.¹⁷

Outcomes

The primary outcome was mortality during hospitalization. The secondary outcomes were need for dialysis, recovery of kidney function at 48 h after admission, and hospital length of stay.

Statistical analysis

To assess the frequency, measurement of central tendency and measurement of dispersion related to clinical, demographic, and laboratory characteristics of patients using descriptive statistics. Categorical variables are expressed as absolute numbers (n) and relative frequencies (%), and quantitative variables are expressed as mean and standard

deviation for data with normal distribution. Quantitative variables with non-Gaussian distributions are expressed as medians and interquartile ranges. Independent t-test, chi-square test or Fisher and Mann-Whitney were used to compare the mean, frequency and median between the S-AKI versus NS-AKI groups. Bivariate analysis was performed to compare groups. Logistic regression was used to determine the independent predictor of mortality, using the $p < 0.10$ criteria in bivariate analysis to select the variables that make up the multivariate logistic regression model. A $p < 0.05$ indicates a significant relationship or difference. Statistical analysis using SPSS 25.0 software.

Results

This study assessed the subjects of 116 patients with a diagnosis of AKI in critically ill. Patients with S-AKI had comorbid diabetes ($p = 0.002$), while heart failure was the most prevalent in patients with NS-AKI ($p < 0.001$). At admission, patients with S-AKI had higher sCr and urea levels, and significantly lower UO and mean of MAP than NS-AKI. There was a history of higher use of RAS blocker drugs in NS-AKI than S-AKI patients which was in line with the higher proportion of heart failure in this group (Table 1).

Patients with S-AKI had a higher mortality, a lower proportion of renal function improvement, and a higher need for vasopressors. There was no difference in terms of dialysis need and hospital length of stay (LOS) between S-AKI and NS-AKI (Table 2). However, surviving S-AKI patients had a significantly longer hospital LOS compared to those who died [8 (6-14.5) vs 3 (2-5.5), $p < 0.001$] and surviving NS-AKI patients [8 (6-14.5) vs 5 (4-8), $p = 0.004$] (Figure 1).

Table 1. Characteristic of demographic, clinical and laboratory of all AKI patients who were admitted to emergency unit in our hospital.

Variable	S-AKI, n = 65 (56%)	NS-AKI, n = 51 (44%)	P value
Age, years, mean (SD)	65.1 (11.1)	63.5 (12.6)	0.538
Age > 65 years, n (%)	27 (41.5)	24 (47.1)	0.552
Male gender, n (%)	31 (47.7)	29 (56.9)	0.327
Female gender, n (%)	34 (52.3)	22 (43.1)	
BMI, kg/m ² , mean (SD)	22.8 (3.1)	22.2 (2.1)	0.298
MAP, mmHg, mean (SD)	80.5 (19.2)	88.4 (19.0)	0.030
Ureum, mg/dL, median (IQR)	122.5 (73.7-177.8)	93.5 (67.2-133.4)	0.058
Creatinine, mg/dL, median (IQR)	2.8 (1.8-3.9)	2.0 (1.6-2.8)	0.010
eGFR, mL/min, median (IQR)	20.00 (14.0-30.5)	28.0 (18.0-38.0)	0.037
UO, mL/kg/h, median (IQR)	0.83 (0.45-1.25)	1.07 (0.8-1.72)	0.003
Comorbidities:			
• Diabetes, n (%)	30 (46.2)	13 (25.5)	0.022
• Heart failure, n (%)	18 (27.7)	32 (62.7)	<0.001
• Hypertension, n (%)	25 (38.5)	21 (41.2)	0.767
• CKD, n (%)	6 (9.2)	3 (5.9)	0.503
AKI stage:			
• 1, n (%)	33 (50.8)	31 (60.8)	0.282
• 2, n (%)	15 (23.1)	11 (21.6)	0.847
• 3, n (%)	17 (26.2)	9 (17.6)	0.275
Antihypertensive drug:			
• ACEi/ARB, n (%)	6 (9.2)	13 (25.5)	0.019
• CCB, n (%)	9 (13.8)	4 (7.8)	0.309
• ACEi/ARB + CCB, n (%)	2 (3.0)	8 (15.7)	0.067
• Others	1 (1.5)	2 (3.9)	0.581

Note: Data were presented in mean (SD), median (IQR), or n (%). n, number; eGFR, estimated Glomerular filtration rate; UO, urine output; AKI, acute kidney injury; S-AKI, septic-AKI; NS-AKI, non-septic-AKI; MAP, mean arterial pressure; BMI, body mass index; SD, standard deviation; IQR, interquartile range; CKD, chronic kidney disease; ACEi, angiotensin converting enzyme; ARB, angiotensin receptor blocker; CCB, calcium channel blockers.

Table 2. Specific treatment and outcome between S-AKI vs NS-AKI patients.

Outcome	S-AKI, n = 65 (56%)	NS-AKI, n = 51 (44%)	P value
Need for dialysis, n (%)	24 (36.9)	15 (29.4)	0.395
Vasopressor use, n (%)	20 (30.8)	7 (13.7)	0.031
Hospital mortality, n (%)	41 (63.1)	16 (31.4)	0.001
Recovery of renal function, n (%) *	24 (36.9)	31 (60.8)	0.011
Hospital LOS, days, median (IQR)	5 (3-10)	5 (4-7)	0.722

Note: Data were presented in median (IQR), or n (%). n, number; AKI, acute kidney injury; S-AKI, septic-AKI; NS-AKI, non-septic-AKI; IQR, interquartile range; LOS, length of stay.

*Improvement of creatinine serum level $\geq 20\%$ at 48 hours compared with baseline value.

Figure 1. Bar chart showing the comparison of median length of stay in S-AKI vs NS-AKI patients. The hospital LOS surviving S-AKI patients longer than NS-AKI patients [8 (6-14.5) vs 5 (4-8), p = 0.004]. AKI, acute kidney injury; S-AKI, septic-AKI; NS-AKI, non-septic-AKI.

Based on bivariate analysis, there was a significantly higher mortality in patients with lower mean MAP, septic condition, requiring dialysis, SOFA score > 7, stage 3 AKI, use of vasopressors, and UO < 0.5 ml/kg/h, and sCr level > 3 mg/dL in the first 0-12 hours admissions (Table 3). In patients with S-AKI the use of vasopressors, stage 3 AKI and SOFA score > 7 were significant predictors of mortality. In addition, the SOFA score was also an independent predictor of mortality in S-AKI patients (OR: 8.9; 95% CI: 2.37-33.9, p = 0.001) (Table 4). In NS-AKI patients, in addition to the use

Table 3. Risk factors for dead in all AKI patients (n = 116).

Variable	Bivariate analysis			Multivariate analysis [#]		
	OR	95%CI	P value	OR	95%CI	P value
Sepsis	3.7	1.7-8.1	0.001			
Vasopressor use	6.8	2.4-19.6	<0.001			
SOFA score >7	15.3	4.9-47.8	<0.001	13.0	4.0-48.7	<0.001
HD	4.2	1.8-9.7	0.001	5.2	1.3-21.1	0.019
MAP < 65 mmHg	4.4	1.6-12.1	0.002			
UO < 0.5 ml/kg/h*	4.0	1.6-10.0	0.002			
Creatinine > 3 mg/dL*	3.1	1.4-6.9	0.004			
AKI stage 1	0.5	0.2-0.9	0.042			
AKI stage 3	8.6	2.8-27.2	<0.001	6.4	1.3-30.8	0.012

Note: Data were presented in n (%). SOFA, Sequential Organ Failure Assessment; HD, haemodialysis; UO, urine output; AKI, acute kidney injury; MAP, mean arterial pressure; OR, odd ratio, CI, confident interval.

*Based on the results at admission.

[#]Determinant value (R square): 0.499.

Table 4. Risk factors for dead in S-AKI patients (n = 65).

Variable	Bivariate analysis			Multivariate analysis [#]		
	OR	95%CI	P value	OR	95%CI	P value
Vasopressor use	4.9	1.3-19.3	0.015			
SOFA score > 7	10.8	3.1-37.9	<0.001	8.96	2.37-33.9	0.001
AKI stage 3	6.3	1.3-30.8	0.001			

Note: Data were presented in n (%). SOFA, Sequential Organ Failure Assessment; AKI, acute kidney injury; S-AKI, septic-AKI; OR, odd ratio, CI, confident interval.

[#]Determinant value (R square): 0.416.

Table 5. Risk factors for dead in NS-AKI patients (n = 51).

Variable	OR	95%CI	P value
Vasopressor use	7.5	1.3-44.3	0.025
HD	17.1	3.9-75.2	<0.001
MAP < 65 mmHg	20.4	2.2-189.9	0.003
UOP < 0.5 ml/kg/h*	-	-	<0.001
AKI stage 1	0.2	0.04-0.58	0.003
AKI stage 3	12.8	2.3-72.8	0.002

Note: Data were presented in n (%). HD, haemodialysis; UO, urine output; AKI, acute kidney injury; NS-AKI, non-septic-AKI; MAP, mean arterial pressure; OR, odd ratio, CI, confident interval.

*Based on the result at admission.

Table 6. Source of infection in S-AKI patients between dead and alive.

Source of infection	Dead, n = 41 (63%)	Alive, n = 24 (37%)	P value
Lung, n (%)	23 (56.1)	13 (54.2)	0.880
Skin and soft tissue, n (%)	4 (9.8)	6 (25.0)	0.154
Urinary tract, n (%)	4 (9.8)	2 (8.3)	0.100
Gastrointestinal tract, n (%)	2 (4.9)	1 (4.2)	0.100
Unknown source, n (%)	8 (19.5)	2 (8.3)	0.228

Note: Data were presented in n (%). n, number; AKI, acute kidney injury; S-AKI, septic-AKI.

of vasopressors and stage 3 AKI as in S-AKI patients; dialysis need, lower mean MAP and UO were also predictors of mortality, whereas stage 1 AKI was predictor of survival (Table 5). However, in multivariate analysis the effect of these risk factors on mortality was not seen.

The most common source of infection was the lungs (55.4%), but there was no difference between the source of infection and the incidence of mortality (Table 6). The median UO at 0-12 h admission to NS-AKI between patients who died vs. alive was significantly different, while that to S-AKI was not significantly different (Figure 2A). The median serum urea and sCr levels at the time of admission between the dead vs. alive on S-AKI and NS-AKI were not significantly different (Figure 2B and 2C). However, at the 48-h after admission, the median UO, serum urea and sCr levels were significantly different between those who died vs. alive, in both S-AKI and NS-AKI patients (Figure 2).

Improvement in UO was associated with a lower proportion of death in S-AKI (2.4% vs 50%, (OR: 0.03, 95% CI: 0.01-0.21; p < 0.001), but not in NS -AKI (6.3% vs 17.1%; p = 0.293). On the other hand, the presence of worsening or persistence of UO was associated with a higher proportion of deaths in S-AKI and NS-AKI (Figure 3A). Furthermore, the improvement or worsening of serum urea and sCr levels between deceased and living patients was significantly different (p < 0.001), whereas in the persistent one there was no difference (Figure 3B and 3C). Further analysis of the comparison of the improvement in the proportion of patients who survived, only the UO differed significantly (17.1% vs 50%, p = 0.007) (Figure 3A).

Figure 2. Bar chart showing the comparison of median on: A: Urine output; B: serum urea level, and C: serum creatinine level. I: S-AKI (a) vs. NS-AKI (b); II: NS-AKI: dead (a) vs alive (b); III: S-AKI: dead (a) vs alive (b).

Discussion

AKI is a common condition in critically ill patients.⁸ One of the important factors causing AKI is sepsis.^{3,18,19} This study showed that S-AKI accounted for approximately 56% of AKI patients admitted to the emergency unit at our hospital (Table 1). This result is slightly higher than previous studies.^{3,19} Our higher results may be related to our study subjects involving patients >40 years of age. It has been proven that sepsis is more common at an older age.²⁰ The expanding elderly population suffering from extensive comorbidity burden, physiological frailty and immune senescence²¹ leads to predict an increased mortality rate for sepsis over the next couple of decades.²²

Compared with NS-AKI, patients with S-AKI had a higher hospital mortality (Table 2). These results are similar to several previous studies.^{3,19,23} These results may be related to the lower proportion of S-AKI patients who experience recovery of renal function (Table 2). Forni *et al* showed that the degree of recovery of kidney function is significantly associated with the risk of short- and long-term mortality.²⁴ The course of the disease, with progression or improvement, consequently represents both the nature and extent of injury and repair, the associated comorbidities, and the management.²⁵ The lower proportion of renal function recovery in S-AKI patients was in line with the higher need for vasopressor (Table 2), the lower mean MAP at admission, and a higher proportion of diabetes in S-AKI than in NS-AKI (Table 1). There appears to be a close association between comorbid diabetes and the incidence of S-AKI, with slower recovery rates, higher vasopressor needs, and higher hospital mortality. Sepsis increased the risk of death in all AKI patients 3.7 times compared to non-sepsis (Table 3). However, based on multivariate analysis, sepsis was not an independent predictor of death in all AKI patients (Table 3), which was different from the results of previous studies.¹⁹

In contrast to the results of several previous studies, that S-AKI were associated with a longer duration of hospitalization than NS-AKI patients,^{3,8,9,23} our study showed that there was no difference in hospital LOS between S-AKI and NS-AKI (Table 2). These results may relate to our study subjects who were over 40 years old, with diabetes being the predominant comorbidity in S-AKI and, on the other hand, heart failure predominant in NS-AKI, both of which contribute to poor patient outcomes (Table 1). However, on further analysis, it appears that surviving S-AKI have a longer hospital LOS compared to surviving NS-AKI [8 (6-14.5) vs 5 (4-8), $p = 0.004$] (Figure 1).

Persistent or worsening of UO and/or elevated of serum urea and sCr levels at 48 hours after admission were associated with a higher risk of mortality in both S-AKI and NS-AKI (Figure 3). Compared to NS-AKI, patients with S-AKI had

Figure 3. Stacked bar chart showing the comparison of the proportion of patients who died vs. alive between NS-AKI and S-AKI based on changes in: A: Urine output; B: Serum urea level and C: serum creatinine level at admission and 48 hours admission. Note: The criteria for improving or worsening are based on changes of 20% compared to the baseline value, while persistent if the change is < 20% from the baseline value. AKI, acute kidney injury; S-AKI, septic-AKI; NS-AKI, non-septic-AKI.

lower UO (Figure 2A). In contrast, the proportion of surviving patients associated with improved UO was significantly higher in S-AKI than in NS-AKI (50% vs 17.1%, $p = 0.007$) (Figure 3A). This condition may be related to the occurrence of acute tubular necrosis (ATN) due to prolonged renal hypoperfusion and patient with S-AKI, with proper treatment provides a better improvement response than NS-AKI. Previous studies have found that patients with S-AKI are more likely to develop oliguric than AKI due to other causes.^{3,8} Oliguria is a key marker of the sepsis process,²⁶ and intensive monitoring of UO is associated with improved survival in patients developing AKI, more specifically in S-AKI.²⁷ This data is in accordance with the results of research by Uhel *et al* that early interventions could improve kidney function and prevent persistence of AKI.¹⁰ The problem in the proper management of S-AKI patients lies in the sepsis itself, which has a complex and unique pathophysiology, which makes S-AKI a distinct syndrome from any other phenotype of AKI. Identifying the exact onset of injury in sepsis is nearly impossible, leading to difficulty in timely intervention for prevention of renal injury.²⁸

The more severe the stage of AKI is associated with the higher specificity of renal impairment. Stage 1 AKI is more sensitive related to transient impaired renal perfusion as the body's compensatory mechanism for conditions relative to fluid deficits. In this study, AKI stage 1 was found to be associated with a good prognosis in all AKI and NS-AKI (Tables 3 and 5). In contrast, stage 3 AKI was a dependent predictor of mortality in S-AKI and NS-AKI (Tables 4 and 5), and an independent predictor of mortality in all AKI patients (Table 3). This is consistent with previous studies, which showed that increased severity of AKI is associated with a greater risk for death.^{29,30} Patients who reach maximum AKI stage by both serum creatinine and UO criteria have the highest rates of in-hospital renal replacement therapy (RRT), longer ICU and hospital stays, and increased mortality.³¹

Among the many risk factors, diabetes and hypertension are associated with a high risk of AKI.^{5,32} Our study shows that diabetes is an important comorbid factor in S-AKI (Table 1), on the other hand, HF is a comorbid factor in NS-AKI. Diabetes conditions increase the risk of infection, even in those with optimal glucose control³³, and a 2 to 6 times higher risk of sepsis compared to the age-matched non-diabetic people,³⁴ and higher sepsis-related morbidity and mortality compared to non-diabetic individuals.^{34,35} Diabetic patients with sepsis had a higher risk of developing AKI (RR, 1.54; 95% CI, 1.44–1.63) and were more likely to be undergoing haemodialysis in the ICU (15.55% vs. 7.24%).³⁶

The most common source of infection was lung (55.4%), followed by skin and soft tissue (15.4%) and urinary tract (9.2%) and there was no difference between the source of infection and mortality in septic AKI patients (Table 6). Previous research has also shown that the lungs are the main source of S-AKI.^{37,38} In contrast to our data, the research by Fan *et al*, also shows that sources of lung infection are associated with worse outcomes and poorer kidney recovery than those infected by another source.³⁸ Possibility related to the common occurrence of ALI/ARDS in severe lung infections.³⁹ Close relationship and interaction between ALI/ARDS and AKI can lead to a worse outcome among patients.⁴⁰

In this study, the need for dialysis in S-AKI patients compared to NS-AKI was not significantly different (Table 2). This result is different from some previous studies; where between 47% to 71% of S-AKI patients require dialysis.^{3,8,18} This difference may be related to the differences in the criteria for indications for RRT, especially in S-AKI patients. However, the need for dialysis was a predictor of mortality in all AKI (OR: 4.2; 95%CI: 1.8–9.7; $p = 0.001$) and NS-AKI patients (OR: 17.1; 95%CI: 3.87–75.2; $P < 0.001$) (Tables 3 and 5). The need for dialysis indicates a more severe clinical and laboratory AKI patient's condition and the indications for dialysis do not appear to be related to the etiologic AKI (Table 2). The appropriate timing of the initiation of RRT remains unclear. KDIGO leaves this to the opinion of the treating doctor taking into account the clinical and biological context,¹⁴ while the Surviving Sepsis Campaign Guidelines suggest not using RRT for increased sCr or oliguria alone without other definitive indications for dialysis.⁴¹

Another predictor of mortality in AKI patients is a high SOFA score. SOFA score > 7 was a dependent and independent predictor of mortality in all AKI and S-AKI patients (Tables 3 and 4). The limit value of the SOFA 7 score in predicting mortality is in accordance with several previous studies.^{42,43}

Our study has several limitations that should be considered. First, the sample size is relatively small and only involves subjects with age > 40 years, so it may affect the outcome. Second, very few patients had prior data, so the diagnosis of AKI was based on variations in serum creatinine, not on baseline creatinine levels. Third, the duration of follow-up in this study was short, so the long-term outcome of these AKI patients is unclear. However, this study is a prospective cohort, which has the advantage of more accurate data collection (less bias), especially in measuring urine output.

Conclusion

AKI associated with sepsis had the worst outcome compared to NS-AKI. Compared with NS-AKI patients, S-AKI patients had more severe disease and higher vasopressor requirements and hospital mortality. Vasopressor requirement

and AKI stage 3 were dependent predictors of mortality in S-AKI and NS-AKI patients, while a high SOFA score was an independent predictor of mortality in all AKI and S-AKI patients. Compared with worsening or persistent, all AKI patients who had improvement in UO, serum urea and creatinine levels at 48 h after admission had a lower incidence of mortality. In surviving patients, UO improvement was more pronounced in S-AKI than in NS-AKI patients. Our study demonstrates the importance of adopting a more aggressive therapeutic strategy for the prevention and management of AKI patients, especially S-AKI with the goal of rapid improvement in UO. Further research is needed to find a tool or biomarker that can distinguish S-AKI patients from NS-AKI early, so that they can describe appropriate therapeutic strategies.

Data availability

Figshare. Supplementary File: Predictors in-hospital Mortality of Septic vs Non-septic Acute Kidney Injury Patients: An Observational Cohort Study.xlsx. DOI: <https://doi.org/10.6084/m9.figshare.16782415.v1>.⁴⁴

Data are available under the terms of the [Creative Commons Zero “No rights reserved” data waiver](#) (CC0 1.0 Public domain dedication).

Author contributions

NRS: study design, data collection, data analysis, writing; MJR, ICP, RAD: data collection, data analysis; AR: data analysis, writing; MA: study design, writing, language retouching. All authors have read and approved the final manuscript.

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