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Original Article

Long-term outcomes of hospital- and community-acquired acute kidney injury

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Abstract: Objective: To compare the long-term outcomes of hospital- and community-acquired acute kidney injury (AKI) in Xinjiang and investigate prognostic factors of 3-years all-cause mortality for AKI patients. Methods: Clinical data were screened and collected from the electronic records in the hospital network system of 19528 adult patients admitted to the First Affiliated Hospital of Xinjiang Medical University from January 2013 to July 2016. The study cohort consisted of 352 patients who were reconfirmed according to the Kidney Disease Improving Global Outcomes (KDIGO) guidelines. They were divided into hospital-acquired acute kidney injury (HA-AKI) group and community-acquired AKI (CA-AKI) group in terms of time of onset of AKI. All patients were followed up for 3 years. Clinical data and the results of laboratory examination were collected. Comparison of long-term outcomes between patients with HA-AKI group and those with CA-AKI was performed using the Log rank test, and prognostic factors of 3-years all-cause mortality in AKI patients were analyzed using the Cox regression. Results: The 1-year all-cause mortality was significantly different between patients with CA-AKI (41.8%, 89/213) and HA-AKI (56.8%, 79/139) ($P<0.05$), but the 3-year all-cause mortality showed no significant differences between the two groups (60.1% (128/213) of the CA-AKI group and 64% (89/139) of the HA-AKI group). The multivariate Cox regression model with data from 352 AKI patients indicated that the risk factors related to 3-year outcomes in the AKI patients included increased MODS scores, increased total cholesterol, reduced plasma albumin, decreased ratio of neutrophile granulocyte and leukomonocyte, reduced platelet counts, and low mean arterial pressure. The area under the receiver operator characteristic (ROC) curve in the regression equation Y was 0.795, which is of significance for outcome prediction. Conclusion: There was no difference in 3-year all-cause mortality between HA-AKI group and CA-AKI group. MODS scores, total cholesterol, plasma albumin, ration of neutrophile granulocyte and leukomonocyte, blood platelet and mean arterial pressure is related to prognosis of AKI patients.

Keywords: Acute kidney injury, all-cause mortality, long-term outcomes, cox regression equation

Introduction

Acute kidney injury (AKI) is one of the common critically-ill conditions. Studies have reported the incidence of AKI is 3.38% in the Chinese population. The creatinine level high up to 26.5 umol/L leads to increased risk for death and hospitalization costs of patients, and prolonged hospital stay [1, 2]. With the aging of the world population and widespread of major surgeries, the incidence of AKI is on the rise, frequently accompanied by multiple organ dysfunction syndrome (MODS) and poor prognosis. Hospital acquired acute kidney injury (HA-AKI), opposite to community acquired acute kidney injury (CA-AKI), refers to AKI caused by the iatrogenic factors including medication, infection, surgery, iatrogenic examinations and low perfusion in patients whose creatinine values are normal on admission [3, 4]. Therefore, in clinical practice, clinicians and nurses should attach importance to and guard against the occurrence of AKI, understand the clinical characteristics of HA-AKI and CA-AKI as well as the major factors influencing outcomes, which is conducive to better management and treatment and of important clinical implications. However, few studies in China have reported related outcomes. As a result, in the present study, we performed a retrospective study based on the clinical data collected from the patients with AKI admitted to the First Affiliated Hospital of

Xinjiang Medical University in recent years, with a aim to explore the difference in outcomes between CA-AKI and HA-AKI in Xinjiang regions and the factors behind the differences.

Study subjects and methods

Study subjects

The enrolled subjects were AKI patients diagnosed and screened at the First Affiliated Hospital of Xinjiang Medical University from January 2013 to July 2016 according to the hospital network system. The AKI patients were re-confirmed by the nephrology physicians according to the *Kidney Disease Improving Global Outcomes* (KDIGO) guidelines. The criteria for identifying AKI [5, 6] included (1) an increase in serum creatinine by ≥26.5 umol/L within 48 hours; (2) an increase in serum creatinine to no less than 1.5 times baseline, as inferred or confirmed to occur within the previous 7 days; (3) urine volume ≤0.5 ml/kg/h for 6 hours. The patients were further divided into the HA-AKI group and the CA-AKI group. Patients were identified as having HA-AKI if the presence of AKI was due to iatrogenic treatment or examination during their stay in our hospital, whereas the patients were identified as having CA-AKI if they were measured as having AKL at admission to our hospital. Patients were excluded if they aged younger than 18 years, were pregnant, or had a history of chronic kidney disease and renal transplantation. The general data, basic diseases and clinical manifestations were compared between the two groups. The present study was approved by the hospital ethics committee, and all patients provided written informed consents.

All patients were followed up every 2 weeks for 3 years on telephone or clinic appointed visits. The primary follow-up outcome measure was the exact time of the patients' death. AKI was associated with such symptoms as multiple organ dysfunction syndrome (MODS), sepsis, shocks and surgery. The clinicians made assessments based on the clinical data of patients.

Sources of clinical data

Clinical and laboratory data of all patients including age, gender, length of hospital stay, basic medical diseases, routine blood tests and blood biochemical examinations on admission were obtained from the network database system of the First Affiliated Hospital of Xinjiang Medical University. AKI can result from prerenal, renal, or post-renal etiologies. The outcome measures were the cumulative mortality at 30 days, 3 months, and 1, 2, and 3 years, respectively.

Statistical analysis

Statistical analysis was carried out using SPSS software, version17.0. Continuous data were expressed as mean ± standard deviation (SD) and the inter-group comparison was done using the independent t test. Categorical data were expressed as percentages, and the inter-group comparison was done using a chi-squared test. The log Rank test was used to compare cumulative mortality between the two groups and the multivariate Cox regression was used to analyze the risk factors for 3-year outcomes of patients with AKI. The independent variables included age, gender, length of hospital stay, basic medical diseases, routine blood tests and blood biochemical examinations and critically ill conditions. The selected independent variables were variables different in the univariate comparisons of the two groups, as analyzed by the stepwise regression. A p value of <0.05 was considered to be statistically significant.

Results

Demographic characteristics between HA-AKI and CA-AKI patients

Of 19528 patients screened and identified from the network system of our hospital, 352 patients with AKI (139 for HA-AKI and 213 CA-AKI) met the criteria. The mean age of the patients in the CA-AKI group was significantly older than that of those in the HA-AKI group ($P<0.05$). The baseline serum creatinine (Scr) values at diagnosis were not significantly different between the two groups, but the peak Scr values were ($P<0.05$). There was no significant difference between the two groups in the rate of MODS, the proportion of shock or sepsis, but significant differences were observed in the proportions of the mechanical ventilation and operation rate (all $P<0.05$). For the basic medical diseases, the patients in both groups had no significant differences in the incidences of diabetes mellitus, coronary artery disease,

Table 1. Comparison of clinical characteristics between HA-AKI and CA-AKI patients

Items	CA-AKI (n = 213)	HA-AKI (n = 139)	Test value	*P* value
Age (year, $\overline{x}$ ± s)	63.56±16.89	56.06±15.82	-4.170	0.000
Male, % (n)	146 (68.5)	99 (71.2	0.285	0.636
Admission specialties, % (n)				
Internal	84 (39.4)	36 (25.9)	8.143	0.017
Surgical	32 (15)	46 (33.1)		
ICU	52 (24.4)	35 (25.2)		
Other	45 (21.1)	22 (15.8)		
Hospitalization (d)	28.11±26.91	20.18±15.77	1.649	0.102
Comorbidities, % (n)				
Hypertension	88 (41.3)	39 (28.1)	6.410	0.011
DM	48 (22.5)	21 (15.1)	2.944	0.086
CAD	19 (8.9)	11 (7.9)	0.109	0.741
CLD	16 (7.5)	18 (12.9)	2.850	0.091
Chronic lung disease	11 (5.2)	4 (2.9)	1.078	0.299
MT	15 (7.0)	5 (3.6)	1.863	0.172
CKD	14 (6.6)	5 (3.6)	1.458	0.227
Etiological stratification, % (n)				
Prerenal	92 (43.2)	114 (82)	42.213	0.000
Renal	105 (49.3)	23 (16.6)		
Postrenal	16 (7.5)	2 (1.4)		
Critically ill status, % (n)				
MODS	14 (6.6)	11 (7.9)	0.229	0.632
Sepsis	6 (2.8)	1 (0.7)	1.899	0.168
Shock	20 (9.4)	14 (10.1)	0.045	0.832
MV	17 (8.0)	30 (21.6)	13.450	0.000
Surgery, % (n)	45 (21.1)	74 (53.2)	-4.170	0.000
Baseline Scr (μmol/L)	84.561±18.58	88.52±13.23	1.924	0.056
Peak Scr (μmol/L)	208.07±149.09	163.10±127.30	-2.925	
AKI severity, % (n)				0.004
Stage 1	115 (54)	91 (65.5)	4.8824	0.027
Stage 2	54 (25.4)	33 (23.7)		
Stage 3	44 (20.6)	15 (10.8)		

Note: ICU = intensive care units; DM = diabetes mellitus; CAD = Coronary artery disease; CLD = Chronic liver disease; MT = Malignant tumor; CKD = Chronic kidney disease; MODS = multiple organ dysfunction syndrome; MV = mechanical ventilation.

chronic liver disease, chronic lung disease, malignant tumors or chronic kidney disease, but had significant difference in the incidence of hypertension (P<0.05).

Among 139 HA-AKI patients, 25.9% (n = 36) were medical patients and 33.1% (n = 46) surgical ones; of 213 CA-AKI patients, 39.4% (n = 84) were medical patients and 15% (n = 32) surgical ones. The differences between the two groups were statistically significant (P<0.05). 25.2% (n = 35) of HA-AKI were admitted to intensive care unit (ICU) and 15.8% (n = 22) to other divisions; 24.4% (n = 52) of CA-AKI were admitted to ICU and 21.1% (n = 45) to other departments, and the differences between the two groups were statistically significant (P< 0.05).

The proportions for pre-renal renal and post-renal CA-AKI were 43.2% (n = 92), 49.3% (n = 105) and 7.5% (n = 16), respectively; whereas the proportions for HA-AKI were 82% (n = 114), 16.6% (n = 23) and 1.4% (n = 2), and the inter-group differences were statistically significant (P<0.05).

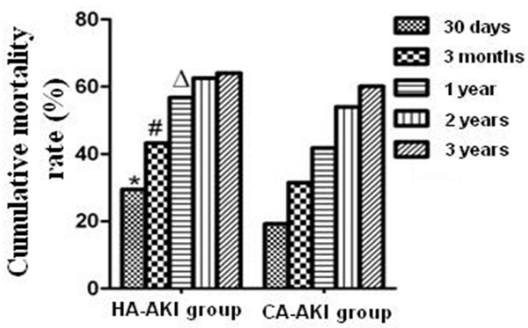

Figure 1. Comparison of cumulative mortality between the two groups, *for the comparison with patients in the CA-AKI group, χ^2 = 4.943, P = 0.026; #for the comparison with patients in the CA-AKI group, χ^2 = 5.001, P = 0.025; Δfor the comparison with patients in the CA-AKI, χ^2 = 7637, P = 0.006.

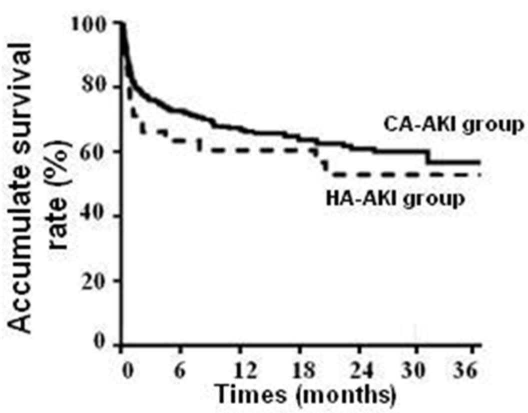

Figure 2. Comparison of cumulative survival rates between the two groups.

The proportions of AKI Stage 1 and Stage 3 in patients with CA-AKI were 54% (n = 115) and 20.6% (n = 44), respectively; whereas the proportions of AKI Stage 1 and Stage 3 in patients with HA-AKI were 65.5% (n = 91) and 10.8% (n = 15), respectively. No significant difference was found in the proportions of AKI II demonstrated between groups (**Table 1**).

Comparison of prognosis in patients with HA-AKI to those with CA-AKI

The cumulative mortality at 30 days, 3 months, 1, 2 and 3 years were 19.2%, 31.5%, 41.8%, 54% and 60.1% respectively in the patients of the CA-AKI group and 29.5%, 43.2%, 56.8%, 62.6% and 64%, respectively in the patients of the HA-AKI group. There was a significant difference between the two groups in terms of cumulative mortality at 30 days, 3 months, and 1 year (all P<0.05, **Figure 1**). The log Rank test demonstrated the 1-year-all-cause mortality differed significantly between the two study groups (P<0.05), but the 3-year-all-cause mortality was not significantly different (**Figure 2**).

The multivariate Cox regression model

The multivariate Cox regression model indicated that the risk factors related to 3-year outcomes in the AKI patients included increased MODS scores, increased total cholesterol, decreased plasma albumin, reduced ratio of neutrophile granulocyte and leukomonocyte, decreased platelet counts, and low mean arterial pressure (**Table 2**).

Discussion

AKI consists of subtypes of CA-AKI and HA-AKI. The incidence of HA-AKI is increasing on a yearly basis, affecting the lives and prognosis of the patients, which may be related to a large number of organ transplantation, invasive examinations, and application of a sea of antibiotics and other new drugs in recent years [7, 8]. Studies have suggested that the incidence of HA-AKI was approximately 1.9%, 7.5% of whom were required to receive blood purification treatment associated with a mortality of 2.6%, which was approximately nine-folds higher than that of the patients without HA-AKI [9, 10]. Another study noted that the mortality rate of HA-AKI was 62.7%, and the cure rate of renal function was about 20.5% [11, 12].

The differences in the clinically reported mortality and morbidity in patients with HA-AKI may be attributed to the differences in inclusion criteria, diagnostic criteria, patient distribution, hospital levels, as well as the proportions of patients accessible to intensive care [13, 14]. In fact, the incidence of CA-AKI was significantly higher than that of HA-AKI. A study reported after 8-year follow ups for 50204 patients, 79.4% of the patients with AKI suffered CA-AKI [15].

In the present study, we found that the mean age for onset of CA-AKI was 63 years or so, which was significantly older than that of HA-AKI. This might be due to the facts that the elderly's renal physiological reserve function decreases gradually with the increase in age,

Table 2. Multivariate Cox regression analysis for 3-year outcomes in patients with AKI

Variable	Wald	*P* Value	RR	95% CI
MODS scores	3.898	0.049	2.521	1.007-6.265
TC	7.585	0.006	4.735	1.567-14.318
PA	18.426	0.000	3.920	1.095-7.751
RONG	4.578	0.032		
PC	6.078	0.014	5.026	1.393-18.142
MAP	18.594	0.000	11.573	3.803-15.217

Notes: MODS = Multiple organ dysfunction syndrome; TC = Total cholesterol; PA = Plasma albumin; PONG = Ratio of neutrophile granulocyte; PC = Platelet counts; MAP = Mean arterial pressure.

and elderly patients are often associated with chronic complications like diabetes and hypertension, which gives rise to their sensitivity to acute renal injury caused by changes in renal toxicity and hemodynamics. The majority of patients with CA-AKI are medical patients whereas most of HA-AKI ones are surgical. HA-AKI is mainly derived from the surgical system, which may be related to the recent development of surgeries involved in complex procedures including the coronary artery bypass surgeries and liver transplantation, as well as invasive examination and treatment [16, 17]. Surgery is another important cause for AKI, especially for HA-AKI. One study reported approximately 60% of patients developed AKI after liver transplantation [18]. The present study found that more than half of the HA-AKI patients had postoperative complications, and the proportions of pre-renal, renal and post-renal HA-AKI were significantly higher than those of CA-AKI, implying that attempts to avoid preoperative inadequate fluid intake, reduce introperative fluid loss or loss of blood, improve the perioperative treatment, prevent postoperative infection, and not to administer nephrotoxic drugs may be beneficial to reductions in the incidence of HA-AKI.

For the prognosis of patients, the 1-year all-cause mortality was significantly higher in the patients with HA-AKI than those with CA-AKI ($P<0.05$), but the 3-year all-cause mortality was insignificantly different. The cumulative mortality rate of HA-AKI was significantly higher at 30 days and 3 months, respectively. This may be associated with the complicated and serious conditions in patients with HA-AKI. The analyses on the critically ill status of patients revealed that patients with HA-AKI were more likely to have mechanical ventilation than CA-AKI patients.

The multivariate Cox regression model indicated that the risk factors related to 3-year outcomes in the AKI patients included increased MODS scores, increased total cholesterol, decreased plasma albumin, decreased ratio of neutrophile granulocyte and leukomonocyte, reduced platelet counts, and low mean arterial pressure. These results are similar to those reported in previous studies [19]. Therefore, attempts to avoid the presence of multiple organ failure syndromes like respiratory failure or heart failure in patients, value supportive treatment of important organs in patients, and improve renal perfusion pressure and nutritional support are likely to create favorable conditions for renal function recovery in AKI and also conducive to improvement in the survival of patients [20].

In conclusion, the patients with CA-AKI and HA-AKI had different clinical characteristics, but their 3-year long-term outcomes were insignificantly different. Increased MODS scores, increased total cholesterol, reduced plasma albumin, decreased ratio of neutrophile granulocyte and leukomonocyte, reduced platelet counts, and low mean arterial pressure are independent risk predictors for 3-year outcomes in the AKI patients. However, the present study is single-centered, with a small sample size, so additional studies are required to validate the above conclusions. Multi-department and multi-center cooperative studies in the future are required to improve the clinical diagnosis and treatment of acute renal injury.

Disclosure of conflict of interest

None.

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