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ORIGINAL RESEARCH

Epidemiology of Sepsis-Associated Acute Kidney Injury in Beijing, China: A Descriptive Analysis

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Background: Sepsis is the most common contributing factor towards development of acute kidney injury (AKI), which is strongly associated to poor prognostic outcomes. There are numerous epidemiological studies about sepsis-associated acute kidney injury (S-AKI), however current literature is limited with the majority of studies being conducted only in the intensive care unit (ICU) setting. The aim of this study was to assess the epidemiology of S-AKI in all hospitalized in-patients.

Methods: This was a retrospective population-based study using a large regional population database in Beijing city from January, 2005 to December, 2017. It included patients with S-AKI. Patients with pre-existing end-stage kidney disease (ESKD), previous history of kidney transplantation, or being pregnant were excluded. Patients' demographic characteristics, incidence, risk factors and outcomes of S-AKI were analyzed. The contrast between different time periods, different levels of hospitals, and types of the hospitals (traditional Chinese medicine hospitals (TCMHs) and western medicine hospitals (WMHs)) was also compared using Mann–Whitney *U*-test.

Results: A total of 19,579 patients were included. The overall incidence of S-AKI in all in-patients was 48.1%. The significant risk factors by multivariate analysis for AKI included: age, male, being treated in a level-II hospital, pre-existing hypertension, chronic kidney disease (CKD), cirrhosis, atrial fibrillation (AF), ischemic heart disease (IHD), being admitted from emergency room, ICU admission, shock, pneumonia, intra-abdominal infection, bloodstream infection, respiratory insufficiency, acute liver injury, disseminated intravascular coagulation (DIC) and metabolic encephalopathy. The overall mortality rate in this cohort was 55%. The multivariate analysis showed that the significant risk factors for mortality included: age, being treated in a level-II hospital and TCMHs, being admitted from emergency room, pre-existing comorbidities (CKD, malignancy, cirrhosis and AF), shock, pneumonia, intra-abdominal infection, bloodstream infection, central nervous system (CNS) infection and respiratory insufficiency.

Conclusion: AKI is a common complication in patients with sepsis, and its incidence increases over time, especially when ICU admission is required. Exploring interventional strategies to address modifiable risk factors will be important to reduce incidence and mortality of S-AKI.

Keywords: epidemiology, sepsis-associated acute kidney injury, traditional Chinese medicine hospitals, western medicine hospitals

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Background

AKI is common in critically ill patients. Approximately one out of three patients in ICU develop AKI, and its incidence is increasing from 35.8% to 50.4%.[1–5]

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Critically ill patients with AKI carries high mortality rates of up to 60%.[6] Survivors following an episode of severe AKI in ICU have an increased risk of developing chronic kidney disease and end-stage kidney disease, cardiovascular disease and are associated with reduced quality of life.[7,8]

Sepsis remains the most common cause of AKI in the critically ill patients.[7,9] There are numerous studies that have evaluated the epidemiology of sepsis-associated acute kidney injury (S-AKI). The largest study to date by Bagshaw et al, involving 57 Australian ICUs with >120,000 critically ill patients, reported a S-AKI incidence of only 11.7%.[10] However, the incidence of S-AKI was reported higher in the Chinese literature, ranging from 45% to 51%.[5,11,12] The difference in incidence could be attributed to differences in ethnic backgrounds and different AKI diagnostic criteria used in different studies. Furthermore, the existing studies on incidence of S-AKI in Chinese population were mainly derived from ICU data, which is not representative of the whole population. There is paucity of information on incidence and outcomes of S-AKI among different levels and types of healthcare system.

Therefore, the objective of this study was to assess the epidemiology of S-AKI in both ICU and non-ICU patients from all the level-II and tertiary hospitals in Beijing, China. The study also compared the differences between the level-II and tertiary level of hospitals as well as between TCMHs and WMHs on the incidence and outcomes of S-AKI, in order to provide greater insight into the burden of this condition in China, which is essential for the planning and assessment of interventional strategies to improve clinical outcomes of AKI patients.

Methods

Data Source

The data in this study was extracted from the Beijing Inpatient Registration System,[13] which contains the diagnostic information of every inpatient in 16 districts and counties in Beijing, China.

According to the number of inpatient beds, it can be divided into three types of hospitals, level-I (20–99 beds), level-II (100–499 beds) and level-III (more than 500 beds). Because the number of level-one hospitals is small and the type of diseases that patients were admitted with are much different from those in the level-II and above hospitals, this study only included the data from the level-II and level-III hospitals for analyses.

Study Population

We conducted this retrospective study including hospitalized patients from 1 January, 2005 to 31 December, 2017 in Beijing, China. Patients with S-AKI were identified using the Primary International Classification of Diseases, 10th revision (ICD-10) codes.

The inclusion criteria consisted of: (1) adult patients (age≥18 years), (2) hospital stay longer than 24 hours in duration and (3) diagnosis consistent with sepsis (A41.9 based on ICD-10 classification). The exclusion criteria consisted of: (1) pre-existing end-stage kidney disease (ESKD), (2) patients who had received kidney transplantation or (3) pregnant patients. All methods in this study were performed in accordance with the relevant guidelines and regulations. This study was approved by the research ethics committee of Beijing Friendship Hospital (Reference Number: 2020-P2-089-01), and an informed consent was exempted by the same research ethics committee.

The reason for the waiver is based on the following statement from National Health Commission of the People's Republic of China, If the subject with identifiable information, whose material or data was used in the study, cannot be reached; and the research project does not involve any personal privacy or commercial interests, informed consent can be exempted by the research ethics committee.

Our study complies with the Declaration of Helsinki and all the patients' data included within our study were protected and maintained with confidentiality.

Definitions of S-AKI

Since the publication of the RIFLE consensus classification for AKI, modifications by the Acute Kidney Injury Network (AKIN), and Kidney Disease Improving Global Outcomes (KDIGO), these definitions have been commonly used in the majority of studies reporting on AKI.[14–16]

Our AKI definition followed the AKIN criteria from the 2005–2011 period and the KIDGO criteria from 2012 onwards.[14,16] Given that the values of serum creatinine level and urine volume could not be obtained, the diagnosis of AKI was extrapolated directly from the database using the ICD-10 code. We used the A41.9 code as the diagnosis of sepsis and the N17.9 code as the diagnosis of AKI.

Statistical Analysis

Patients' demographic characteristics were presented using proportions for categorical variables, mean (standard deviation) or median (interquartile range) as appropriate for continuous variables. Continuous variables were compared using the Student's *t*-test or Mann–Whitney *U*-test according to data distribution, while categorical variables were compared using the chi-square test.

Based on the literature study, variables available from the hospital discharge records and the results of univariate analysis, the following variables including age, age stratification, gender, hospital levels, time interval, comorbidities (including diabetes mellitus (DM), hypertension (HT), CKD stage 2 and stage 3, atrial fibrillation, ischemic heart disease, malignancy and cirrhosis),[17–21] ICU admission, types of infection and types of organ function damage were selected in the logistic regression analysis to assess the risk factors of both the occurrence and mortality of S-AKI.[4]

Pre-specified subgroup analyses included level-II versus tertiary hospitals, TCMHs versus WMHs, and pre-KDIGO guideline era (2005–2011) and post-KDIGO guideline era (2012–2017).

Log rank tests were used to compare hospital survival rates between groups. A p value of < 0.05 was considered statistically significant. Cox regression models were fitted to compare the mortality risk between groups adjusted for age, sex, medical insurance patterns, comorbidities, ICU admission, infection sites, shock and other organ dysfunction.

There were 220 cases (0.54%) with missing hospitalization outcomes and 1 case (0.0025%) with sepsis did not have expense variable. These cases were not included in the corresponding analysis.

All analyses were conducted with SAS 9.4 (SAS Institute Inc., Cary, North Carolina).

Results

A total of 40,720 septic patients were included in the final analysis, of which 19,579 met the criteria for S-AKI. The average age was 78 years old, with 62.7% were male patients. Majority of the patients (90.1%) were admitted to tertiary hospitals generally from the emergency room (60%).

Compared with septic patients without concurrent AKI, S-AKI patients were older, male predominant, and have more significant comorbidities (including HT, DM, CKD, cirrhosis, underlying malignancy, atrial fibrillation and ischemic heart disease).

Patients who experienced an episode of shock of any form (ie hypovolemic, cardiogenic or septic) were more susceptible to AKI. Majority of the patients (77.4%) with S-AKI had pneumonia. Approximately, every 1 in 3 patients (34.3%) with S-AKI required an ICU admission. Compared with septic patients without concurrent AKI, patients with S-AKI had longer hospital length of stays and were associated with significantly higher average daily costs (P<0.001) and overall costs (P<0.001). The demographic and clinical characteristics of these patients are presented in Table 1.

Incidence and Risk Factors of S-AKI by Multivariate Analysis

The incidence of S-AKI in all inpatients was 48.1%, which was higher in ICU patients than non-ICU patients (59.2% versus 31.6%, p<0.001).

In multivariate logistic regression analysis, the following independent risk factors for S-AKI were identified (Table 2): age (odds ratio(OR) =1.00, 95% CI (1.00–1.00), P<0.001), male (OR=1.13, 95% CI (1.08–1.19), P<0.001), uninsured (OR=1.33, 95% CI (1.47–1.22), P<0.001), being treated in a level-II hospital (OR=1.18, 95% CI (1.10–1.27), P<0.001), pre-existing hypertension (OR=1.20, 95% CI (1.14–1.26), P<0.001), CKD (OR=1.94, 95% CI (1.80–2.08), P<0.001), cirrhosis (OR=1.69, 95% CI (1.49–1.91), P<0.001), atrial fibrillation (OR=1.28, 95% CI (1.20–1.36), P<0.001), ischemic heart disease (OR=1.25, 95% CI (1.16–1.35), P<0.001), being hospitalized from emergency department (OR=1.69, 95% CI (1.49–1.91), P<0.001), ICU admission (OR=1.2, 95% CI (1.14–1.26), P<0.001), shock (OR=1.29, 95% CI (1.27–1.31), P<0.001), pneumonia (OR=1.33, 95% CI (1.18–1.49), P<0.001), intra-abdominal infection (OR=1.46, 95% CI (1.32–1.61), P<0.001), bloodstream infection (OR=1.51, 95% CI (1.32–1.73), P<0.001), respiratory insufficiency (OR=1.93, 95% CI (1.84–2.03), P<0.001), acute liver injury (OR=1.11, 95% CI (1.05–1.17), P<0.001), DIC (OR=2.15, 95% CI (1.75–2.65), P<0.001) and metabolic encephalopathy (OR=1.93, 95% CI (1.48–2.50), P<0.001).

All-Cause Mortality and Risk Factors by Multivariate Analysis

Overall all-cause mortality in S-AKI patients were 55%. Majority of them (57.9% of non-survivors) were admitted

Table 1 Baseline Clinical Characteristics of Sepsis Patients with and without AKI

Variables		**Sepsis with AKI (n=19,579)**	**Sepsis without AKI(n=21,141)**	***p* value**
Age median [IQR]		78(64–84)	75(59–83)	<0.001
Age stratification(years)	18–39 40–59 60–79 ≥80	949(4.8) 2663(13.6) 7304(37.2) 8693(44.3)	1703(8) 3633(17.2) 7761(36.7) 8059(38.1)	<0.001
Gender	Female Male	7294(37.3) 12,285(62.7)	8272(39.1) 12,869(60.9)	<0.001
Classification of insurance	BMI RCMTI GMP OPP Others	10825(55.3) 1485(7.6) 3306(16.9) 1261(6.4) 2702(13.8)	11,601(54.9) 1612(7.6) 3345(15.8) 1175(5.6) 3408(16.1)	<0.001
Hospital level	Tertiary hospital Level-II hospital	17,519(89.5) 2060(10.5)	19,151(90.6) 1990(9.4)	<0.001
Hospital nature	Western Medicine hospital Hospital of TCM	18,006(92) 1573(8)	19,412(91.8) 1729(8.2)	0.59
Time interval(year)	2005–2011 2012–2017	1468(7.5) 18,111(92.4)	2228(10.5) 18,913(89.4)	<0.001
Comorbidities(n)	Diabetes Hypertension CKD stage 2 and 3 Malignancy Cirrhosis Atrial fibrillation Ischemic heart disease	7024(35.8) 10,227(52.2) 2944(15) 3750(19.1) 800(4.1) 3991 (20.4) 2710(13.8)	6571(31.1) 9573(45.2) 1655(7.8) 3832(18.1) 592(2.8) 2846 (13.5) 1764(8.3)	<0.001 <0.001 <0.001 0.01 <0.001 <0.001 <0.001
ICU		6725(34.3)	4642(21.9)	<0.001
Types of shock	No shock Septic shock Hypovolemic shock Cardiac shock Two or more kinds of shock	14,617(74.5) 3422(17.5) 988(5) 939(4.8) 345(1.8)	19,233(90.9) 1073(5.1) 593(2.8) 357(1.7) 96(0.5)	<0.001 <0.001 <0.001 <0.001 <0.001
Types of infection	Pneumonia Urinary infection Intra-abdominal infection CRBSI CNS infection Others	15,176(77.4) 1492(7.6) 1782(9.1) 657(3.4) 47(0.2) 3229(16.5)	14,858(70.2) 1906(9) 1792(8.5) 472(2.2) 67(0.3) 4510(21.3)	<0.001 <0.001 0.03 <0.001 0.14 <0.001
Types of organ function damage	Respiratory insufficiency Acute liver injury DIC Metabolic encephalopathy	11,797(60.2) 4000(20.4) 680(3.5) 238(1.2)	8032(38) 3518(16.6) 195(0.9) 124(0.6)	<0.001 <0.001 <0.001 <0.001
Expenses (Yuan)	Total expense Average daily expense Western medicine expense Chinese medicine expense	60,242.42(28,580.86–122,460.29) 5272.18(3190.64–8583.87) 13,885.26(5645.02–30,424.3) 94.74(0–854.43)	39,853.56(18,844.39–81,420.71) 3224.33(1862.96–5593.4) 9700.77(3298.62–22,050.47) 77.75(0–623.56)	<0.001 <0.001 <0.001 <0.001

(*Continued*)

Table 1 (Continued).

Variables		Sepsis with AKI (n=19,579)	Sepsis without AKI(n=21,141)	*p* value
Outcome	Length of hospital stay (day) Death(n)	13(6–23) 10,647(55)	13(7–22) 6157(29.3)	<0.001 <0.001

Note: Values are expressed as the median (interquartile range and N (%)).
Abbreviations: BMI, basic medical insurance; RCMTI, rural cooperative medical treatment insurance; GMP, governmental medical payment; OPP, out-of-pocket payments; ER, emergency room; CRBSI, Catheter Related Blood Stream Infection; CNS, central nervous system; DIC, disseminated intravascular coagulation; TCM, traditional Chinese medicine.

Table 2 Risk Factors of Occurrence of S-AKI by Logistic Regression Analysis

Variable	OR	Lower 95% CI	Higher 95% CI	*p* value
Age, years	1.00	1.00	1.00	<0.001
Male	1.13	1.08	1.19	<0.001
Uninsured	1.33	1.47	1.22	<0.001
Level-II hospital	1.18	1.10	1.27	<0.001
Treated in Western Medicine hospitals	0.97	0.89	1.05	0.465
Diabetes	1.03	0.98	1.08	0.263
Hypertension	1.20	1.14	1.26	<0.001
CKD stage 2 and 3	1.94	1.80	2.08	<0.001
Malignancy	1.06	1.00	1.12	0.058
Cirrhosis	1.69	1.49	1.91	<0.001
Atrial fibrillation	1.28	1.2	1.36	<0.001
Ischemic heart disease	1.25	1.16	1.35	<0.001
Admission from emergency department	1.69	1.49	1.91	<0.001
ICU admission	1.20	1.14	1.26	<0.001
Shock	1.29	1.27	1.31	<0.001
Pneumonia	1.33	1.18	1.49	<0.001
Urinary infection	0.77	0.70	0.84	<0.001
Intra-abdominal infection	1.46	1.32	1.61	<0.001
Bloodstream infection	1.51	1.32	1.73	<0.001
CNS infection	1.19	0.79	1.79	0.403
Respiratory insufficiency	1.93	1.84	2.03	<0.001
Acute liver injury	1.11	1.05	1.17	<0.001
DIC	2.15	1.75	2.65	<0.001
Metabolic encephalopathy	1.93	1.48	2.50	<0.001

Abbreviations: CKD, chronic kidney disease; CNS, central nervous system; DIC, disseminated intravascular coagulation.

to ICU. The mortality of patients admitted to ICU was lower than those who were not (53.4% versus 54.8%, P<0.001).

Patients with pneumonia had significantly higher mortality rates than those without (P<0.001). Patients with multi-functional organ dysfunction syndrome was also associated with increased mortality, and had significantly higher overall costs (p=0.02) and average daily costs (P < 0.001) (Table 3).

A multivariate regression analysis revealed that risk factors for mortality included (Table 4): age (OR=1.02, 95% CI (1.02–1.02), P < 0.001), being treated in a level-II hospital (OR=1.57, 95% CI (1.42–1.74), P < 0.001), being hospitalized from emergency department (OR=1.14, 95% CI (1.07–1.22), P < 0.001), pre-existing comorbidities CKD (OR=1.24, 95% CI (1.14–1.36), P < 0.001), malignancy (OR=2.03, 95% CI (1.86–2.23), P < 0.001), cirrhosis (OR=1.75, 95% CI (1.45–2.11), P < 0.001), atrial fibrillation (OR=1.21, 95% CI (1.12–1.31), P < 0.001), shock (OR=1.45, 95% CI (1.42–1.49), P < 0.001), pneumonia (OR=1.56, 95% CI (1.33–1.83), P < 0.001), intra-abdominal infection (OR=1.61, 95% CI (1.41–1.83), P < 0.001), bloodstream infection (OR=1.34, 95% CI (1.12–1.59), P < 0.001), CNS infection (OR=2.27, 95% CI (1.20–4.30), P = 0.012), and respiratory insufficiency (OR=1.87, 95% CI (1.75–2.0), P < 0.001).

We tested collinearity for relevant variables models and there was no collinearity among the included variables.

The development of AKI strongly influenced hospital survival rates in patients with sepsis (45.0% versus 70.7% in patients with and without AKI, respectively; p < 0.001; Figure 1).

After adjusting for the confounding factors mentioned in the statistical analysis section, the results from the Cox proportional hazards model showed that septic patients with AKI had a significantly higher risk of death than those without (HR=1.47, 95% CI (1.42–1.53), P < 0.001).

S-AKI Before and After the KDIGO Guideline Era (Table 5)

The incidence of S-AKI post the KDIGO guideline era was higher than pre-KDIGO (48.9% versus 39.7%, P < 0.001), but the mortality rate was significantly lower after the KDIGO guideline era (54.4% versus 63.9%, p < 0.001, Figure 2). Comparing with the patients before the KDIGO guideline era (period 2005–2011), patients after the KDIGO guideline era (2012–2017) were older (p < 0.001), but no gender difference was observed (p=0.69).

Table 3 Baseline Clinical Characteristics of Survivors and Non-Survivors of S-AKI Patients

Variables		Survivors	Non-Survivors	*p* value
N (%)		8712(45.0)	10,647(55.0)*	
Age median [IQR]		76(60–84)	79(68–85)	<0.001
Age stratification(years)	18–39 40–59 60–79 ≥80	575(6.6) 1487(17.1) 3212(36.9) 3438(39.5)	358(3.4) 1134(10.7) 3983(37.4) 5172(48.6)	<0.001
Gender	Female Male	3182(36.5) 5530(63.5)	4029(37.8) 6618(62.2)	0.06
Classification of insurance	BMI RCMTI GMP OPP Others	3929(45.1) 958(11) 1890(21.7) 622(7.1) 1313(15.1)	6818(64) 483(4.5) 1415(13.3) 639(6) 1292(12.1)	<0.001
Hospital level	Tertiary hospitals Second-class hospital	7953(91.3) 759(8.7)	9370(88) 1277(12)	<0.001
Hospital nature	Western Medicine hospital Hospital of TCM	8200(94.1) 512(5.9)	9603(90.2) 1044(9.8)	0.59
Time interval(year)	2005–2011 2012–2017	450(5.2) 8262(94.8)	798(7.5) 9849(92.5)	<0.001
Comorbidities(n)	Diabetes Hypertension CKD stage 2 and 3 Malignancy Cirrhosis Atrial fibrillation Ischemic heart disease	3475(39.9) 4785(54.9) 1134(13) 1288(14.8) 305(3.5) 2406(22.6) 1183(13.6)	3513(33) 5394(50.7) 1804(16.9) 2430(22.8) 495(4.6) 1584(18.2) 1518(14.3)	<0.001 <0.001 <0.001 <0.001 <0.001 <0.001 0.18
ICU		3136(36)	3589(33.7)	<0.001
Types of shock	No shock Septic shock Hypovolemic shock Cardiac shock Two or more kinds of shock	7179(82.4) 1032(11.8) 380(4.4) 190(2.2) 67(0.8)	7400(69.5) 2178(20.5) 607(5.7) 745(7) 273(2.6)	<0.001 <0.001 <0.001 <0.001 <0.001
Types of infection	Pneumonia Urinary infection Intra-abdominal infection CRBSI CNS infection Others	6508(74.7) 898(10.3) 794(9.1) 275(3.2) 20(0.2) 1568(18)	8527(80.1) 576(5.4) 967(9.1) 377(3.5) 27(0.3) 1580(14.8)	<0.001 <0.001 0.94 0.14 0.74 <0.001
Types of organ function damage	Respiratory insufficiency Acute liver injury DIC Metabolic encephalopathy	4571(52.5) 1780(20.4) 205(2.4) 112(1.3)	7135(67) 2199(20.7) 473(4.4) 126(1.2)	<0.001 0.7 <0.001 0.52

(*Continued*)

Table 3 (Continued).

Variables		Survivors	Non-Survivors	*p* value
Expenses (Yuan)	Total expense Average daily expense Western medicine expense Chinese medicine expense	58,362.5(29,533.66–114,864.4) 4673.41(2681.64–7898.79) 13,422.67(5867.98–28,107.39) 142.69(0–1087.74)	62,520.49(27,564.02–130,377.97) 5823.35(3670.61–9187.57) 14,098.64(5414.67–32,046.23) 68.98(0–693.93)	0.02 <0.001 0.01 <0.001
Outcome	Length of hospital stay (day)	14(7–24)	12(4–22)	<0.001

Notes: *220 missing values because of lacking of outcome indicators. Values are expressed as the median (interquartile range and N (%)).
Abbreviations: BMI, basic medical insurance; RCMTI, rural cooperative medical treatment insurance; GMP, governmental medical payment; OPP, out-of-pocket payments; ER, emergency room; CRBSI, Catheter Related Blood Stream Infection; CNS, central nervous system; DIC, disseminated intravascular coagulation; TCM, traditional Chinese medicine.

Table 4 Risk Factors of Mortality of S-AKI by Logistic Regression Analysis

Variable	OR	Lower 95% CI	Higher 95% CI	*p* value
Age, years	1.02	1.02	1.02	<0.001
Male gender	0.96	0.90	1.02	0.207
Insured	1.03	0.90	1.17	0.678
Level-II hospital	1.57	1.42	1.74	<0.001
Western Medicine hospital	0.56	0.50	0.64	<0.001
Admission from emergency department	1.14	1.07	1.22	<0.001
Diabetes	0.94	0.87	1.01	0.097
Hypertension	1.07	0.94	1.22	0.276
CKD stage 2 and 3	1.24	1.14	1.36	<0.001
Malignancy	2.03	1.86	2.23	<0.001
Cirrhosis	1.75	1.45	2.11	<0.001
Atrial fibrillation	1.21	1.12	1.31	<0.001
Ischemic heart disease	0.94	0.88	1.01	0.087
ICU admission	0.81	0.76	0.87	<0.001
Shock	1.45	1.42	1.49	<0.001
Pneumonia	1.56	1.33	1.83	<0.001
Intra-abdominal infection	1.61	1.41	1.83	<0.001
Bloodstream infection	1.34	1.12	1.59	0.001
CNS infection	2.27	1.20	4.30	0.012
Respiratory insufficiency	1.87	1.75	2.00	<0.001
Acute liver injury	1.01	0.94	1.09	0.728
DIC	1.21	0.98	1.50	0.074

In these two time periods, there were significant differences in the patients allocation between tertiary and level-II hospitals ($p < 0.001$): more patients started to attend level-II hospitals although the vast majority of patients still went to tertiary hospitals (10.75% versus 89.20%, $p < 0.001$). There were more S-AKI diagnosed in patients with underlying comorbidities (hypertension, CKD, cirrhosis and malignant tumors) in the post-KDIGO guideline era, and more patients were also more likely to be admitted in ICU ($p < 0.001$). Pneumonia ($p < 0.001$) and abdominal infection ($p = 0.002$) appeared to be more commonly complicated by S-AKI patients in the post KDIGO era. Although the average daily cost of patients in the latest period was higher ($p < 0.001$), the hospital stays were shorter ($p < 0.001$), making no difference in the total cost related to the hospitalization (p=0.88).

After adjusting for other confounders, the results from the Cox proportional hazards model showed that the risk of death was significantly higher in patients hospitalized from 2005 to 2011 than those from 2012 to 2017 (HR=1.32, 95% CI (1.22–1.43), $P < 0.001$).

AKI Patients in Both Level-II and Tertiary Hospitals (Table 6)

The majority of S-AKI patients (89.5%) presented and were admitted to tertiary hospitals, despite an overall increase in presentation to level-II hospitals over the observed time period. The proportion rose from 7.56% in the pre KDIGO guideline era to 10.75% in the post KDIGO guideline era ($P < 0.001$). Patients over 80 years old were mostly in level-II hospitals ($p < 0.001$) whilst tertiary hospitals had younger patients ($p < 0.001$). Patients were predominantly male in both levels of the hospitals.

The ICU admission rate of S-AKI patients in level-II hospitals was significantly lower than that in tertiary hospitals (29.77% versus 34.89%, $p < 0.001$). Compared with level-II hospitals, the proportion of patients with septic shock (p=0.006), abdominal infection ($p < 0.001$), bloodstream infection ($p < 0.001$), respiratory failure ($p < 0.001$) and MODS ($p < 0.001$) was higher in tertiary hospitals. Despite similar length of stay was seen in both hospitals (p=0.15), the total cost, and average daily cost for patients being treated in tertiary hospitals were all higher ($p < 0.001$).

Both the incidence (50.8% versus 47.7%, $p < 0.001$) and the mortality rate (62.1% versus 54.1%, $p < 0.001$,

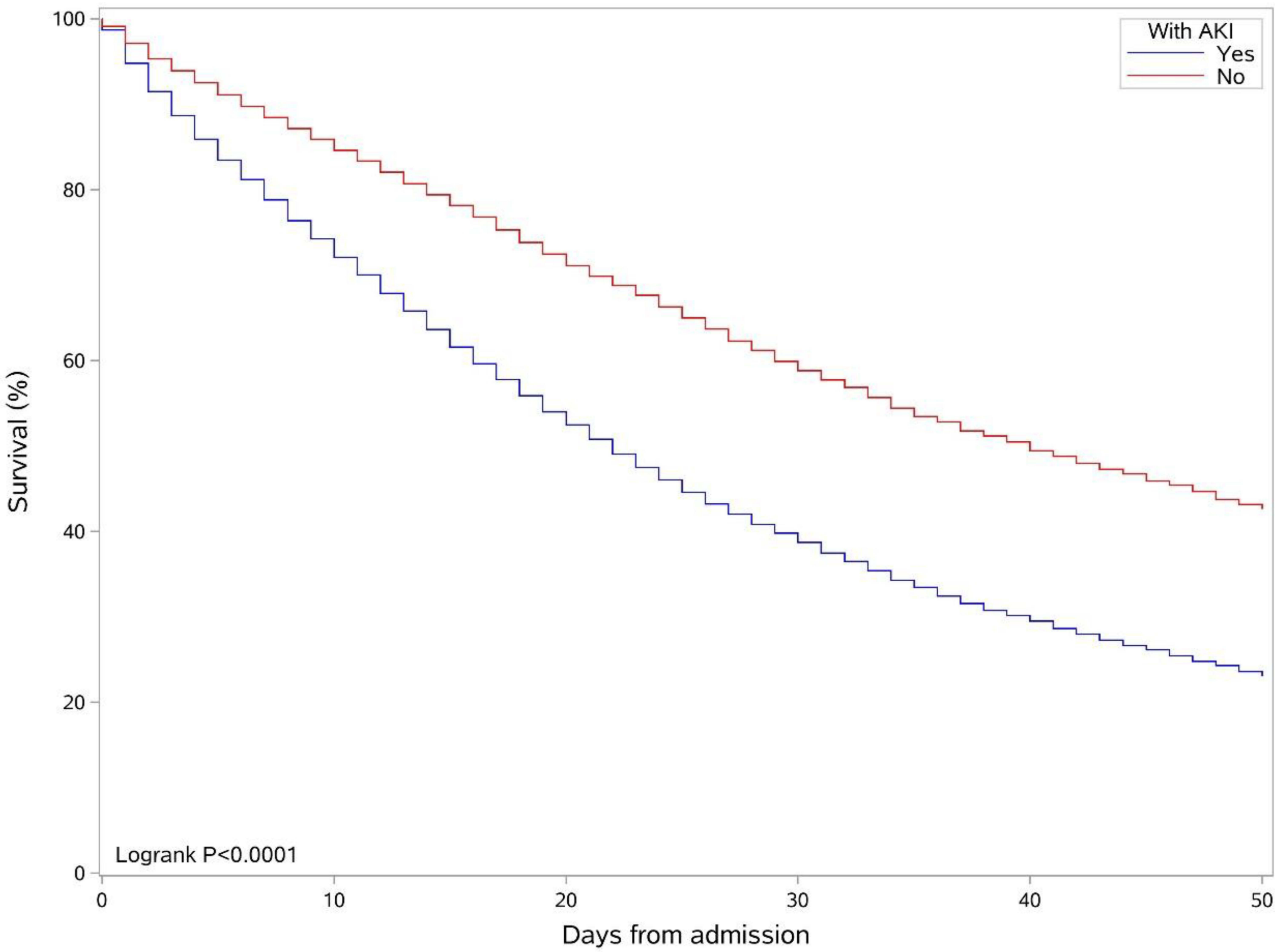

Figure 1 Different hospital survival probability curves of all septic patients with or without AKI.
Notes: The blue line represents the hospital survival curve of patients with AKI; the red line represents the hospital survival curve of patients without AKI.
Abbreviation: AKI, acute kidney injury.

Figure 3) of S-AKI were significantly higher in level-II hospitals than those in tertiary hospitals.

After adjusting for other confounding factors, the results from the Cox proportional hazards model showed that the risk of death was significantly higher for patients in level-II hospitals than patients in tertiary hospitals (HR=1.14, 95% CI (1.07–1.22), P < 0.001).

S-AKI Patients in Traditional Chinese Medicine Hospitals and Western Medicine Hospitals (Table 7)

The vast majority (92%) of S-AKI patients were treated in WMHs rather than in TCMHs. The survival rate of patients treated in the WMHs was significantly higher than patients treated in TCMHs (45.5% versus 32.5%, P < 0.001, Figure 4). Patients from WMHs was younger than those from TCMHs (P < 0.001).

The proportion of S-AKI patients admitted in ICU in WMHs was also higher than in TCMHs (36.4% versus 10.1%, p < 0.001). The proportion of S-AKI patients with septic shock and abdominal infections in WMHs was higher than in TCMHs hospital (p < 0.001). In contrast, there were less patients with lung infections in TCMHs than in WMHs (P=0.01). The proportion of MODS patients admitted in TCMHs was higher than in WMHs (19.4% versus 17.1%, p=0.02).

The total cost, and the average daily cost were all higher in patients of WMHs (p < 0.001). S-AKI patients from WMHs had longer length of hospitalization than patients from TCMHs (P = 0.03).

After adjusting for other confounding factors, the results from the Cox proportional hazards model showed that the risk of death of patients in WMHs was significantly lower than that of patients in TCMHs (HR=0.70, 95% CI (0.65–0.75), P < 0.001).

Table 5 Comparison of the Epidemiology of S-AKI Between Pre and Post KDIGO Guideline for AKI Definition

Variables		2005–2011 (Year)	2012–2017 (Year)	*p* value
N (%)		1468(100)	18,111(100)	
Death		798(63.9)	9849(54.4)	<0.001
Age median [IQR]		75(60.5–82)	78(65–85)	<0.001
Age stratification(years)	18–39	111(7.6)	838(4.6)	<0.001
	40–59	238(16.2)	2419(13.4)	
	60–79	623(42.4)	6666(36.8)	
	≥80	496(33.8)	8188(45.2)	
Gender	Female	554(37.7)	6741(37.2)	0.69
	Male	914(62.3)	11,370(62.8)	
Classification of insurance	BMI	750(51.1)	10,082(55.7)	<0.001
	RCMTI	222(15.1)	1260(7)	
	GMP	96(6.5)	3215(17.8)	
	OPP	41(2.8)	1222(6.7)	
	Others	359(24.5)	2332(12.9)	
Hospital level	Tertiary hospitals	1357(92.4)	16,163(89.2)	<0.001
	Second-class hospital	111(7.6)	1948(10.8)	
Hospital nature	Western Medicine hospital	1352(92.1)	16,656(92)	0.86
	Hospital of TCM	116(7.9)	1455(8)	
Comorbidities(n)	Diabetes	257(17.5)	6763(37.3)	<0.001
	Hypertension	422(28.7)	9799(54.1)	<0.001
	CKD stage 2 and 3	72(4.9)	2872(15.9)	<0.001
	Malignancy	182(12.4)	3560(19.7)	<0.001
	Cirrhosis	21(1.4)	779(4.3)	<0.001
ICU		99(6.7)	6626(36.6)	<0.001
Types of Shock	No shock	677(46.1)	13,937(77)	<0.001
	Septic shock	721(49.1)	2674(14.8)	<0.001
	Hypovolemic shock	68(4.6)	920(5.1)	0.45
	Cardiac shock	41(2.8)	897(5)	<0.001
	Two or more kinds of shock	39(2.7)	305(1.7)	0.01
Types of infection	Pneumonia	842(57.4)	14,320(79.1)	<0.001
	Urinary infection	144(9.8)	1347(7.4)	0.001
	Intra-abdominal infection	100(6.8)	1681(9.3)	0.002
	CRBSI	29(2)	628(3.5)	0.002
	CNS infection	3(0.2)	44(0.2)	0.77
	Others	495(33.7)	2720(15)	<0.001
Types of organ function damage	Respiratory insufficiency	661(45)	11,123(61.4)	<0.001
	Acute liver injury	131(8.9)	3865(21.3)	<0.001
	DIC	199(13.6)	481(2.7)	<0.001
	Metabolic encephalopathy	17(1.2)	221(1.2)	0.83

(*Continued*)

Table 5 (Continued).

Variables		2005–2011 (Year)	2012–2017 (Year)	p value
Expenses (Yuan)	Total expense	62,115.33(24,502.22–134,419.29)	60,158.84(28,824.21–121,703.84)	0.88
	Average daily expense	3859.29(2200.42–6547.85)	5406.94(3280.57–8719.52)	<0.001
	Western medicine expense	25,847.1(9208.77–58,538.56)	13,329.13(5430.34–28,760.24)	<0.001
	Chinese medicine expense	31.06(0–305.98)	107.58(0–917.56)	<0.001
Length of hospital stay (day)		16(7–35)	12(6–23)	<0.001

Note: Values are expressed as the median (interquartile range and N (%)).
Abbreviations: BMI, basic medical insurance; RCMTI, rural cooperative medical treatment insurance; GMP, governmental medical payment; OPP, out-of-pocket payments; ER, emergency room; CRBSI, Catheter Related Blood Stream Infection; CNS, central nervous system; DIC, disseminated intravascular coagulation; TCM, traditional Chinese medicine.

Discussion

In this study, we analyzed the epidemiology of S-AKI in all inpatients, including ICU and non-ICU patients from 158 hospitals in Beijing, China from January 2005 to December 2017. We found the overall incidence of S-AKI was 48.1%, with 59.2% in ICU patients and 31.6% in non-ICU patients, respectively; and overall mortality rate of 55% among the S-AKI patients. Pneumonia was the most likely source of sepsis in this cohort. The reported incidence of S-AKI was higher after KDIGO

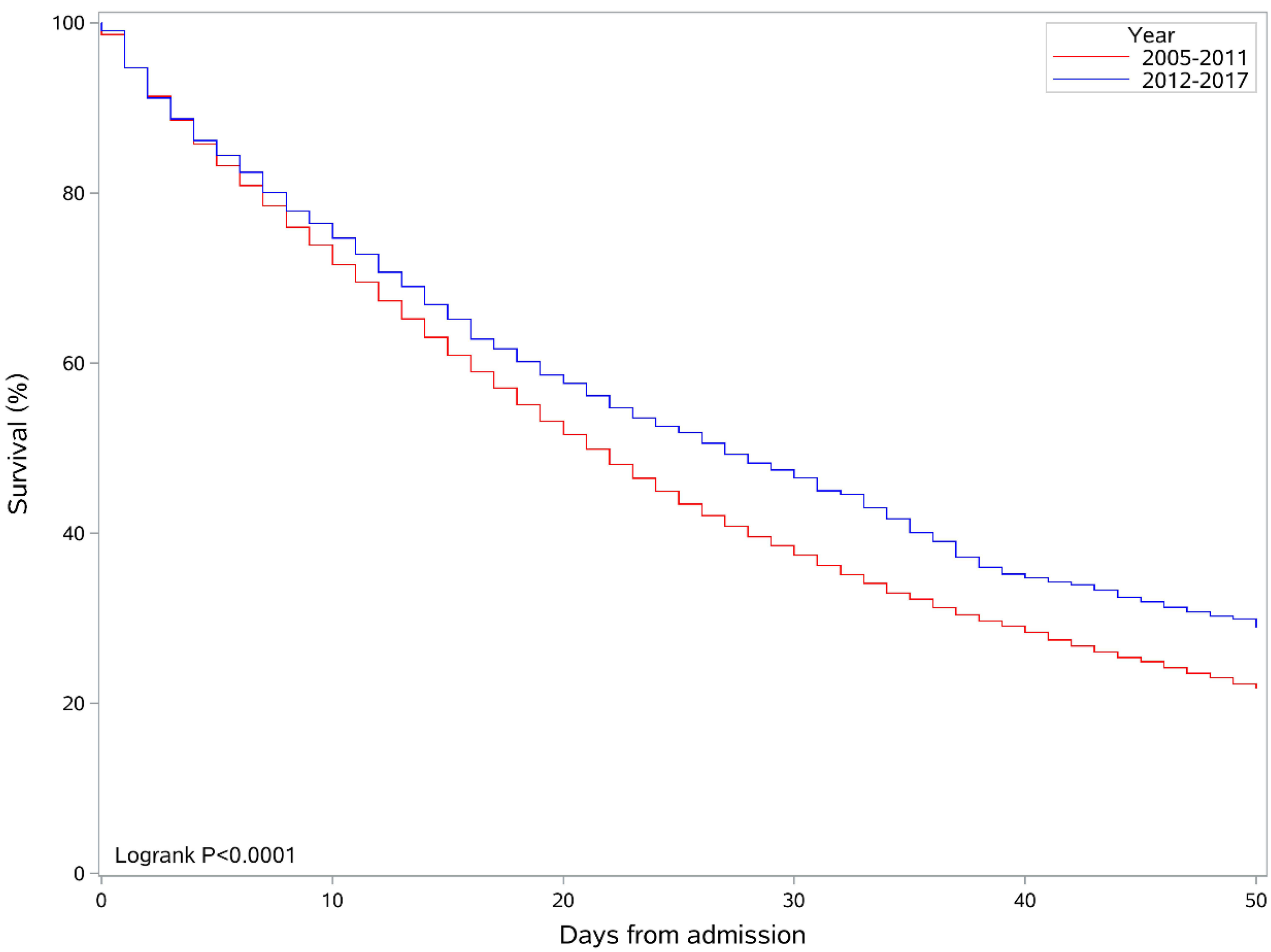

Figure 2 The hospital survival probability curves of patients with S-AKI classified according to admission date.
Notes: The blue line represents the hospital survival curve of S-AKI patients hospitalized from the year of 2005 to 2011; the red line represents the hospital survival curve of S-AKI patients hospitalized from the year of 2012 to 2017.
Abbreviation: S-AKI, sepsis-associated acute kidney injury.

Table 6 Comparison of the Epidemiology of S-AKI Between Level-II and Tertiary Hospitals

Variables		Level-II Hospital	Tertiary Hospitals	*p* value
N (%)		2059(100)	17,520(100)	
Death		1277(62.7)	9370(54.1)	<0.001
Age median [IQR]		80(70–85)	78(64–84)	<0.001
Age stratification(years)	18–39 40–59 60–79 ≥80	45(2.2) 213(10.3) 737(35.8) 1064(51.7)	904(5.2) 2444(13.9) 6552(37.4) 7620(43.5)	<0.001
Gender	Female Male	817(39.7) 1242(60.3)	6478(37) 11,042(63)	0.02
Classification of insurance	BMI RCMTI GMP OPP Others	1384(67.2) 263(12.8) 193(9.4) 96(4.7) 123(6)	9448(53.9) 1219(7) 3118(17.8) 1167(6.7) 2568(14.7)	<0.001
Hospital nature	Western Medicine hospital Hospital of TCM	1967(95.5) 92(4.5)	16,041(91.6) 1479(8.4)	<0.001
Time Period	2005–2011 2012–2017	111(5.4) 1948(94.6)	1357(7.7) 16,163(92.3)	<0.001
Comorbidities(n)	Diabetes Hypertension CKD stage 2 and 3 Malignancy Cirrhosis	719(34.9) 1085(52.7) 403(19.6) 258(12.5) 40(1.9)	6301(36) 9136(52.1) 2541(14.5) 3484(19.9) 760(4.3)	0.35 0.64 <0.001 <0.001 <0.001
ICU		613(29.8)	6112(34.9)	<0.001
Types of shock	No shock Septic shock Hypovolemic shock Cardiac shock Two or more kinds of shock	1593(77.4) 312(15.2) 108(5.2) 78(3.8) 31(1.5)	13,021(74.3) 3083(17.6) 880(5) 860(4.9) 313(1.8)	0.003 0.006 0.66 0.02 0.36
Types of infection	Pneumonia Urinary infection Intra-abdominal infection CRBSI CNS infection Others	1582(76.8) 122(5.9) 131(6.4) 22(1.1) 3(0.1) 382(18.6)	13,580(77.5) 1369(7.8) 1650(9.4) 635(3.6) 44(0.3) 2833(16.2)	0.49 0.002 <0.001 <0.001 0.36 0.006
Types of organ function damage	Respiratory insufficiency Acute liver injury DIC Metabolic encephalopathy	1064(51.7) 286(13.9) 37(1.8) 28(1.4)	10,720(61.2) 3710(21.2) 643(3.7) 210(1.2)	<0.001 <0.001 <0.001 0.53

(*Continued*)

Table 6 (Continued).

Variables		Level-II Hospital	Tertiary Hospitals	*p* value
Expenses (Yuan)	Total expense	41,047.75(17,598.47–92,271.23)	62,702.87(30,227.13–125,862.83)	<0.001
	Average daily expense	3822.54(2297.78–6014.34)	5499.86(3329.52–8886.23)	<0.001
	Western medicine expense	9085.04(3349.65–22,224.82)	14,510.38(5984.67–31,314.93)	<0.001
	Chinese medicine expense	78.04(0–650.52)	98.49(0–869.4)	0.19
Length of hospital stay (day)		13(4–25)	13(6–23)	0.15

Note: Values are expressed as the median (interquartile range and N (%)).
Abbreviations: BMI, basic medical insurance; RCMTI, rural cooperative medical treatment insurance; GMP, governmental medical payment; OPP, out-of-pocket payments; ER, emergency room; CRBSI, Catheter Related Blood Stream Infection; CNS, central nervous system; DIC, disseminated intravascular coagulation; TCM, traditional Chinese medicine.

guideline being used to define AKI. The majority of AKI patients in this study was admitted to tertiary teaching hospitals and western Medicine hospitals.

There is an increasing incidence of AKI worldwide.[1–5] The current literature reported incidence of S-AKI is from 39.4% to 60.7% in ICU, which is consistent with our finding (48%).[22,23]

According to the nationwide survey regarding AKI across Mainland China, 72% of AKI episodes occurred in the non-ICU setting, which reminds us that the occurrence of AKI outside the ICU requires more attention.[17]

Our study showed that certain demographic characteristics, including advanced age, male and the presence of comorbidities such as hypertension, CKD and liver cirrhosis, and severity of the diseases as assessed by requirements for ICU admission and shock status were significantly associated with the incidence of AKI. These results were consistent with previous studies.[14,24] However, an Australian S-AKI study revealed female patients had increased risk to develop AKI,[2] whereas some other studies showed no significant difference in age or sex.[4,13] These inconsistent findings may be due to different population and demographic characteristics in each study.

The overall in-hospital mortality among S-AKI in this cohort was 55%, which was higher than the results from previous studies.[4,25] The healthcare system in China is different from some developed countries where patients can have free access to certain procedures such as dialysis therapy,[22] which may be a potential factor contributing to higher mortality rates.

Our study shows that hypertension is a risk factor for S-AKI, and 52.2% of S-AKI patients have hypertension, which are consistent with previous studies.[26,27] Approximately, 244.5 million of the Chinese adult population ≥18 years of age have been diagnosed with hypertension, which contributes to a significant burden of disease.[27]

Hypertension is both a cause and effect of CKD and contributes to its progression. RAAS-induced injury is associated with lower glomerular filtration rate (GFR), lower renal blood flow, kidney fibrosis, up-regulation of sodium transporters, which results in both the structural and functional changes of the kidney.[28–31] In the course of blood pressure intervention, some medications used can also increase the incidence of AKI. A nested case-control study showed that a triple therapy combination consisting of diuretics with angiotensin converting enzyme inhibitors or angiotensin receptor blockers and NSAIDs (Nonsteroidal anti-inflammatory drugs) was associated with an increased risk of AKI. Although antihypertensive drugs have cardiovascular benefits, vigilance may be warranted when they are used concurrently.[32]

Hepatitis B virus (HBV) infection is a serious problem in China, contributing to more than one-third of the world's HBV-infected people (approximately 93 million).[33] Liver cirrhosis is a progressive condition in chronic hepatitis B. AKI occurs in approximately 19% of hospitalized patients with cirrhosis from previous research.[34–36]

Almost all the causes of AKI in patients with cirrhosis are prerenal and intrarenal, accounting for approximately 68% and 32% of the cases.[37,38] Cirrhosis is characterized by reduced systemic vascular resistance due to splanchnic arterial vasodilation.[39] In early stages of the disease, splanchnic vasodilation is moderate and reduced systemic vascular resistance is balanced by increased cardiac output. In advanced stages, vasodilation is more pronounced because of increased synthesis of vasodilator factors which cannot be balanced by an increase in cardiac output.[40] Eventually, changes in hemodynamics in the kidney and altered autoregulation of kidney blood flow contribute to decreased glomerular filtration rate (GFR) leading to acute

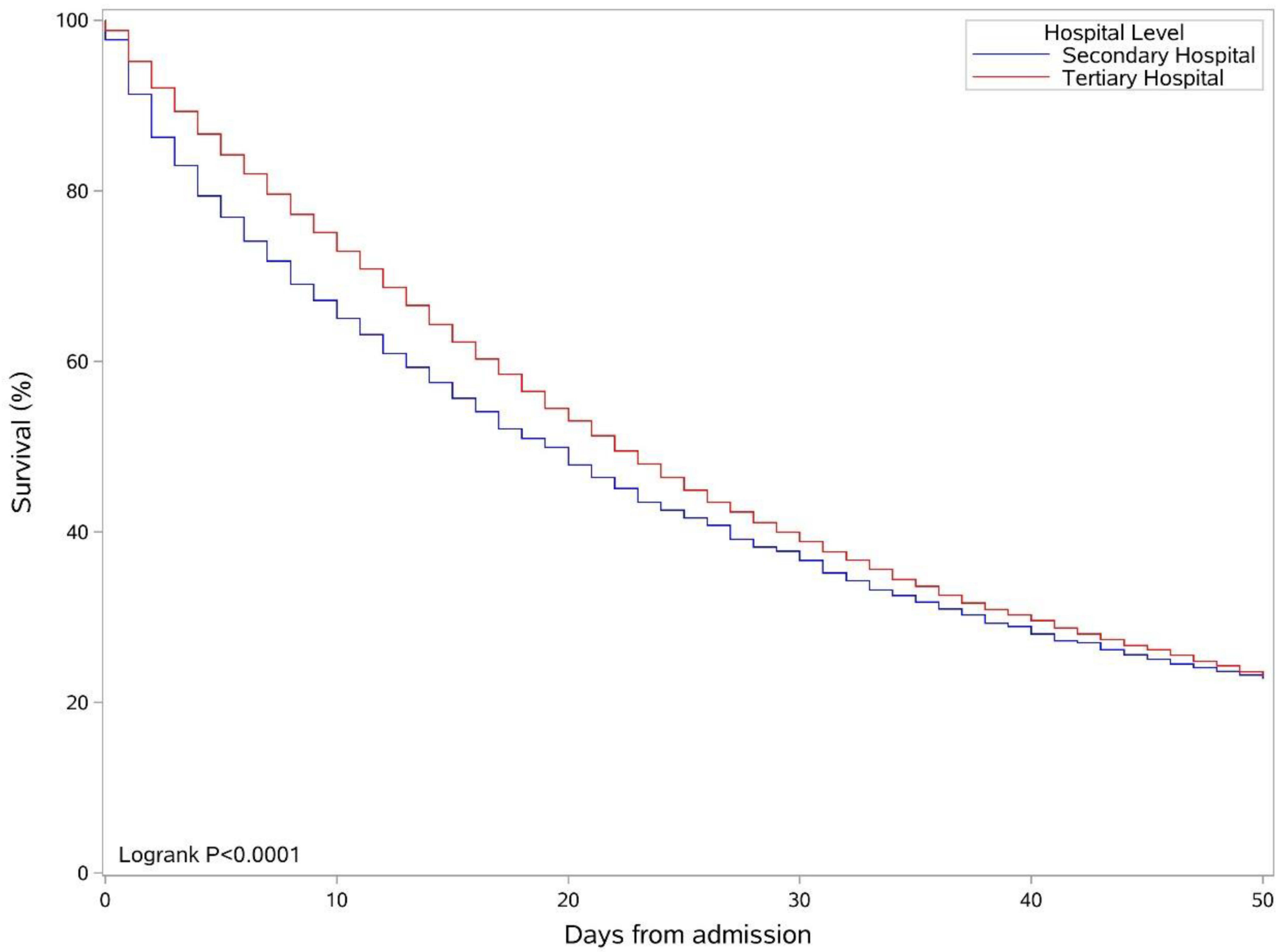

Figure 3 The hospital survival probability curves of patients with S-AKI classified according to hospital levels.
Notes: The blue line represents the hospital survival curve of S-AKI patients treated in the secondary hospital; the red line represents the hospital survival curve of S-AKI patients treated in the tertiary hospital.
Abbreviation: S-AKI, sepsis-associated acute kidney injury.

kidney injury. Moreover, these patients are often exposed to nephrotoxic agents such as nonsteroidal anti-inflammatory drugs, contrast agents, and aminoglycosides,[41] which are directly toxic to renal tubules, eventually leading to acute tubular necrosis. Vasoconstrictive agents (terlipressin in particular) are the first-line treatment option. Liver transplantation is the only curative treatment of AKI due to cirrhosis.[42,43]

Comparison of the Incidence of S-AKI Between Pre and Post KDIGO Guideline for AKI Definition

There have been multiple attempts to universally standardize the classification and definition of AKI to enable consistent diagnosis and treatment across different healthcare systems. These classifications include the RIFLE (Risk, Injury, Failure, Loss, End Stage), AKIN (Acute Kidney Injury Network) and KDIGO (Kidney Disease: Improving Global Outcomes) which have been good predictors of mortality in critically ill patients.[44] Despite slight variations in the definitions, A systematic review performed by Thomas et al has found that these definitions do not significantly differ in their predictive outcomes.[45]

The introduction of new AKI definition in the KDIGO guideline attempted to unify the definition of AKI of both the RIFLE and AKIN criteria. In our study, we found that the change in definitions used may have attributed to an increase in incidence of AKI. According to the AKIN criteria, the incidence of S-AKI in our cohort of patients was 39.7% from the period of 2005–2011. When the updated KDIGO criteria was used, the incidence was higher (48.9%) from the period of 2012–2017. This

Table 7 Comparison Between Traditional Chinese Medicine Hospitals and Western Medicine Hospitals

Variables		TCMHs	WMHs	*p* value
N (%)		1573(8.0)	18,006(92.0)	
Survivors(n)		512(32.9)	8200(46.1)	<0.001
Age median [IQR]		80(71–85)	78(64–84)	<0.001
Age stratification(years)	18–39 40–59 60–79 ≥80	24(1.5) 133(8.4) 590(37.5) 826(52.5)	924(5.1) 2526(14) 6703(37.2) 7853(43.6)	<0.001
Gender	Female Male	653(41.5) 920(58.5)	6642(36.9) 11,364(63.1)	<0.001
Classification of insurance	BMI RCMTI GMP OPP Others	1166(74.2) 109(6.9) 133(8.4) 113(7.2) 52(3.3)	9659(53.6) 1376(7.6) 3173(17.6) 1148(6.4) 2650(14.7)	<0.001
Hospital level	Tertiary hospitals Second-class hospital	1481(94.2) 92(5.8)	16,038(89.1) 1968(10.9)	<0.001
Time interval(year)	2005–2011 2012–2017	117(7.4) 1456(92.6)	1351(7.5) 16,655(92.5)	
Comorbidities(n)	Diabetes Hypertension CKD stage 2 and 3 Malignancy Cirrhosis	521(33.1) 828(52.6) 299(19) 240(15.2) 22(1.4)	6503(36.1) 9399(52.1) 2645(14.7) 3510(19.5) 778(4.3)	0.02 0.73 <0.001 <0.001 <0.001
ICU		159(10.1)	6566(36.4)	<0.001
Types of shock	No shock Septic shock Hypovolemic shock Cardiac shock Two or more kinds of shock	1294(82.2) 182(11.6) 58(3.7) 60(3.8) 18(1.1)	13,323(73.9) 3240(18) 930(5.2) 879(4.9) 327(1.8)	<0.001 <0.001 0.01 0.06 0.05
Types of infection	Pneumonia Urinary infection Intra-abdominal infection CRBSI CNS infection Others	1260(80) 106(6.7) 86(5.5) 55(3.5) 3(0.2) 256(16.3)	13,916(77.2) 1386(7.7) 1696(9.4) 602(3.3) 44(0.2) 2973(16.5)	0.01 0.17 <0.001 0.74 0.68 0.81
Types of organ function damage	Respiratory insufficiency Acute liver injury DIC Metabolic encephalopathy	850(54) 359(22.8) 54(3.4) 34(2.2)	10,947(60.7) 3641(20.2) 626(3.5) 204(1.1)	<0.001 0.01 0.93 <0.001
Expenses (Yuan)	Total expense Average daily expense Western medicine expense Chinese medicine expense	46,013.3(20,515.42–94,055.27) 4166.6(2721.57–6398.43) 9744.02(3425.73–21,786.67) 995.2(182.92–3489.11)	61,667.38(29,297.85–125,052.5) 5413.71(3248.88–8781.84) 14,285.38(5896.72–31,166.39) 73.09(0–686.88)	<0.001 <0.001 <0.001 <0.001
Length of hospital stay (day)		13(5–22)	13(6–23)	0.03

Note: Values are expressed as the median (interquartile range and N (%)).
Abbreviations: BMI, basic medical insurance; RCMTI, rural cooperative medical treatment insurance; GMP, governmental medical payment; OPP, out-of-pocket payments; ER, emergency room; CRBSI, Catheter Related Blood Stream Infection; CNS, central nervous system; DIC, disseminated intravascular coagulation; TCM, traditional Chinese medicine.

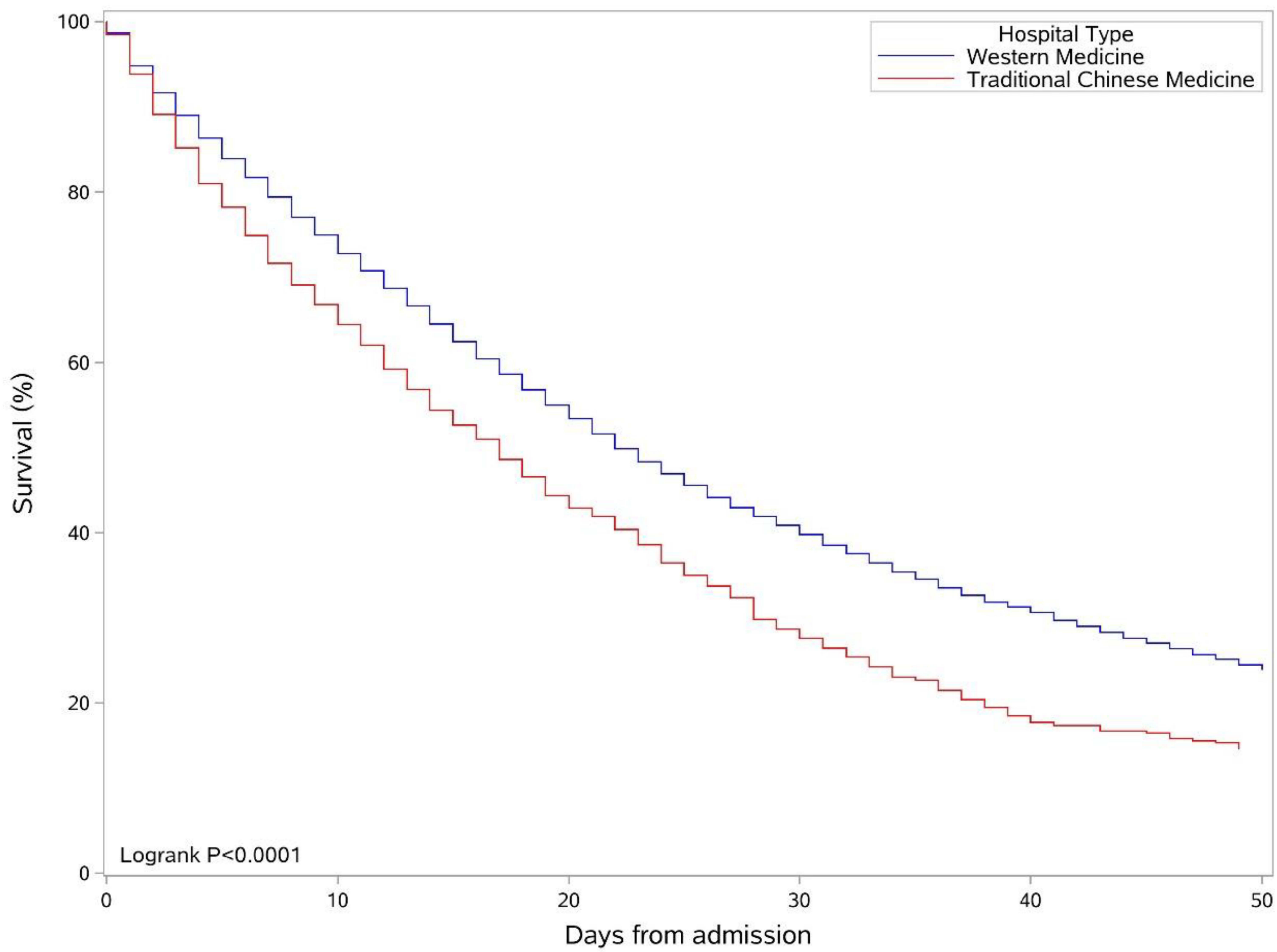

Figure 4 The hospital survival probability curves of patients with S-AKI classified according to different hospital types.
Notes: The blue line represents the hospital survival curve of S-AKI patients treated in Western Medicine hospitals; the red line represents the hospital survival curve of S-AKI patients treated in Traditional Chinese Medicine hospitals.
Abbreviation: S-AKI, sepsis-associated acute kidney injury.

finding is similar to previous studies,[46,47] which compared utilization of different classifications and found that the AKIN classification had consistently reported lower incidence levels when compared with KDIGO and RIFLE classifications. However, the higher incidence in our study in the later time period may also be attributed to aging population and the increased incidence of multiple chronic illnesses. Despite the increase in incidence, the mortality rates declined from pre (63.9%) to post (54.4%) KDIGO guideline era.

The declining mortality rates post the KDOGO guideline era may be due to multiple factors including standardized classifications of AKI leading to early recognition and treatment by clinicians;[48–50] significant advances in supportive medical technologies such as continuous renal replacement therapy (CRRT) and other measures for treating sepsis, such as early appropriate antibiotic administration and fluid resuscitation;[50,51] as well as more patients seeking treatment in tertiary hospital centers where they have access to the highest level of medical staff and equipment.[52]

Outcomes Between Level-II and Tertiary Hospitals

To the best of our knowledge, there are limited literature that provide direct comparisons of the mortality rates between tertiary hospitals and those with limited healthcare resources such as level-II, rural or peripheral hospitals. The incidence of S-AKI in level-II and tertiary hospitals in this study were similar, 50.8% and 47.7%, respectively. The mortality rate in level-II hospitals was 9% higher than that in tertiary hospitals.

The higher mortality rates in level-II hospitals in our cohort could be attributed to two main reasons. Firstly, the proportion of patients over 80-year-old in level-II hospitals was higher than that in tertiary hospitals (51.7% versus 43.5%). Secondly, there is a limited access to interventional management strategies in level-II hospitals such as renal replacement therapy. For those who had clinical indications for being transferred to a tertiary hospital for advanced treatment but were unable to be transferred in a timely fashion (eg due to bed block or change of the treatment goal to conservative treatments), they would only be able to receive limited treatment based on the hospital resource.

Traditional Chinese Medicine Hospitals (TCMHs) versus Western Medical Hospitals (WMHs)

In China, the health care system is uniquely divided into the western and traditional Chinese medical system.[53] The Chinese cultural heritage has traditionally focused on the administration of traditional Chinese service and products (such as medicinal herbs, acupuncture and dietary therapy), however, there has been a shift by the Chinese government to "integrate both Chinese and Western medicine" through the implementation of modern medicine and technologies within TCMHs since the 1970's.[54]

A distinct aspect of this study is the comparison of the patient outcomes between TCMHs and WMHs. In our study, the majority of the patients (92%) were diagnosed and treated with S-AKI in WMHs. Furthermore, the number of patients admitted to WMHs was 5.6 times that of the TCMHs in 2018 alone. This can be explained by fewer availability of TCMHs when compared to WMHs. However, in both categories of hospitals, the incidence of AKI is increasing annually. The mortality rate of S-AKI patients in WMHs is lower than that of patients in TCMHs. This can be explained by more sufficient means of supporting and treating patients in WMHs. This is likely to explain higher costs for patients receiving treatment in WMHs compared to patients in TCMHs.

In addition, many Chinese patients, especially the elderly, take Chinese herbal medicine as the first choice for treating diseases. However, some herbal medicines are also known to cause nephrotoxicity, which is often overlooked by the treating physicians and patients.[55] The incidence of acute kidney injury induced by Chinese herbal medicines is difficult to assess. One cross-sectional survey of AKI in China found that Chinese patients (71.6%) were more likely to be exposed to traditional Chinese medicine before and during AKI than patients from developed countries (20–50%).[16] This high proportion of exposure to nephrotoxic agents is probably consistent with the increasing incidence of drug-induced disease in China.[56] Therefore, the use of Chinese herbal medicine may be a double-edged sword in the treatment of AKI patients.

Strengths and Limitations

This large retrospective cohort study assessed epidemiological features of S-AKI at the municipal level, in China, consisting 40,720 patients and 158 hospitals. To our knowledge, this is the first study investigated the impact of levels (level-II versus tertiary teaching hospitals) and types of hospitals (TCMHs versus western medicine hospitals) as well as definition of AKI on incidence, and risk factors of S-AKI.

Our study has several limitations. Firstly, our study used a large administrative dataset with insufficient information in the stages of AKI, use of renal replacement therapy (RRT) and the long-term prognosis of renal function, which may impact on morbidity and hospital mortality. Secondly, even though a number of statistical analyses were conducted in our study, potential confounders still exist, which may have an impact on the study finding. Thirdly, due to the nature of the study using an administrative dataset, a diagnosis of S-AKI in this study was made when based upon a septic patient developed an episode of AKI at the same time. This may overestimate the incidence of S-AKI. Fourthly, the use of different definitions of AKI during our study can lead to variations in overall incidence. From an epidemiologic standpoint it may be difficult to compare results of future studies which highlights the necessity for a standardized and comprehensive AKI classification system. Finally, there were large differences in the patients' numbers in different time periods and different levels and categories of hospitals, so the results of the comparisons may have a certain deviation.

Conclusions

AKI is a common complication in all hospitalized patients with sepsis, and its incidence increases over time, especially when ICU admission is required. Our findings provide valuable information about the epidemiology of hospitalized patients with S-AKI in Beijing, China. Exploring interventional strategies to address modifiable risk factors will be important to reduce incidence and mortality of S-AKI.

Abbreviations

AKI, Acute kidney injury; S-AKI, Sepsis-associated acute kidney injury; ICU, Intensive care unit; ESKD, End-stage kidney disease; TCMHs, Traditional Chinese medicine hospitals; WMHs, Western medicine hospitals; CKD, Chronic kidney disease; AKIN, Acute Kidney Injury Network; KDIGO, Kidney Disease Improving Global Outcomes; RIFLE, Risk, Injury, Failure, Loss, End Stage; CRRT, Continuous renal replacement therapy; DM, Diabetes mellitus; HT, Hypertension.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available on reasonable request from the corresponding author, Dr. Meili Duan (Email: dmeili@ccmu.edu.cn).

Ethics Approval and Consent to Participate

The study was approved by the research ethics committee of Beijing Friendship Hospital (Reference Number: 2020-P2-089-01).

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

Dr Amanda Ying Wang is supported by RACP Jacquot Research Establishment Fellowship, Australia. The authors report no other conflicts of interest in this work.

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