# Epidemiology of Sepsis-associated Acute Kidney Injury in Beijing, China : a descriptive analysis

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# Abstract

**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 differences between different time periods, different levels of hospitals, and types of the hospitals (i.e. traditional Chinese medicine hospitals (TCMHs) and Western medicine hospitals (WMHs)) were 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 risk factors for AKI included: age ($P < 0.001$), male ($P < 0.001$), treatment in a level-II hospital ($P < 0.001$) and so on. The overall mortality rate in this cohort was 55%. The risk factors for mortality included: age ($P < 0.001$), female ($P < 0.001$), pre-existing chronic kidney disease (CKD) ($P = 0.023$) and so on. The incidence of S-AKI increased over time, but the mortality rate did not. Compared with level-II hospitals, the incidence of S-AKI was similar in tertiary hospitals, but the mortality rate was significantly higher.

Although patients treated in TCMHs had a shorter hospital stay and a lower cost of care, this cohort had a higher mortality rate when compared with patients treated in WMHs.

**Conclusions** AKI is a common complication in all hospitalized 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.

# Background

Acute Kidney Injury (AKI) is common in critically ill patients. Approximately one out of three patients in intensive care unit (ICU) develop AKI, and its incidence is increasing from 35.8–50.4% [1–5].

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 S-AKI. The largest study to date by Bagshaw et al [10], involving

57 Australian ICUs with > 120,000 critically ill patients, reported a S-AKI incidence of only 11.7%. However, the incidence of S-AKI was reported higher in the Chinese literature, ranging from 45%-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. Furthermore, 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 compares 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.

# Methods

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 hour 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 kidneydisease (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). Because this was a retrospective observational study, an informed consent was exempted by the research ethics committee of Beijing Friendship Hospital.

**Definitions of S-AKI**

Since the publication of the RIFLE consensus classification for AKI, and the modifications by the Acute Kidney Injury Network (AKIN), and Kidney Disease Improving Global Outcomes (KDIGO), these definitions have been used in the majority of studies reporting on AKI [13–15].

Our AKI definition followed the AKIN criteria [15] from the 2005–2011 period and the KIDGO criteria from 2012 onwards [13]. 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 existing knowledge, the following variables: age, age stratification[16], gender, hospital levels, time interval, comorbidities(including diabetes mellitus(DM), hypertension(HT), CKD stage 2 and stage 3, malignancy and cirrhosis) [17–20], ICU admission, types of infection and types of organ function damage [4] were selected and constructed in multivariate analysis to assess the risk factors of S-AKI.

Logistic regression was used to assess the associations of patients characteristics including age, gender, medical insurance patterns, hospital levels, comorbidities, infection sites, presence of organ dysfunction with AKI among patients with sepsis, and with in-hospital death in patients with AKI, respectively.

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).

Participants were divided into four subgroups based on age: 18–39 years old, 40–59 years old, 60–79 years old, 80 years old and above.
Log-rank tests were used to compare hospital survival rates between groups. A p value of < 0.05 was considered statistically significant. All analyses were conducted with SAS 9.4 (SAS Institute Inc., Cary, North Carolina).

## Results

Among 108,848 patients' data obtained from a hospitalised registration system in Beijing, China, 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. Majority of the patients (90.1%) were admitted to a tertiary hospital who were generally admitted from the emergency department (60%).

Compared with septic patients without concurrent AKI, S-AKI patients were older, predominantly male, and have more significant comorbidities (including HT, DM, chronic kidney disease (CKD), cirrhosis and underlying malignancy).

Patients who experienced an episode of shock of any form (i.e. hypovolaemic, 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.

Table 1
Baseline clinical characteristics of sepsis patients with and without AKI

| **Variables** | | **Sepsis with AKI (n = 19579)** | **Sepsis without AKI(n = 21141)** | **P value** |
|---|---|---|---|---|
| Age median [IQR] | | 78(64–84) | 75(59–83) | < 0.001 |
| Age stratification(years) | 18–39 | 949(4.8) | 1703(8) | < 0.001 |
| | 40–59 | 2663(13.6) | 3633(17.2) | |
| | 60–79 | 7304(37.2) | 7761(36.7) | |
| | ≥ 80 | 8693(44.3) | 8059(38.1) | |
| Gender | Female | 7294(37.3) | 8272(39.1) | < 0.001 |
| | Male | 12285(62.7) | 12869(60.9) | |
| Classification of insurance | BMI | 10825(55.3) | 11601(54.9) | < 0.001 |
| | RCMTI | 1485(7.6) | 1612(7.6) | |
| | GMP | 3306(16.9) | 3345(15.8) | |
| | OPP | 1261(6.4) | 1175(5.6) | |
| | Others | 2702(13.8) | 3408(16.1) | |
| Hospital level | Tertiary hospitals | 17519(89.5) | 19151(90.6) | < 0.001 |
| | Second-class hospital | 2060(10.5) | 1990(9.4) | |
| Hospital nature | Western Medicine hospital | 18006(92) | 19412(91.8) | 0.59 |
| | Hospital of TCM | 1573(8) | 1729(8.2) | |
| Time interval(year) | 2005–2011 | 1468(7.5) | 2228(10.5) | < 0.001 |
| | 2012–2017 | 18111(92.4) | 18913(89.4) | |
| Comorbidities(n) | Diabetes | 7024(35.8) | 6571(31.1) | < 0.001 |

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, MODS = multiple organ dysfunction syndrome, TCM = traditional Chinese medicine. Values are expressed as the median (interquartile range and N (%)).

| Variables | | Sepsis with AKI (n = 19579) | Sepsis without AKI(n = 21141) | P value |
|---|---|---|---|---|
| | Hypertension | 10227(52.2) | 9573(45.2) | < 0.001 |
| | CKD stage 2 and 3 | 2944(15) | 1655(7.8) | < 0.001 |
| | Malignancy | 3750(19.1) | 3832(18.1) | 0.01 |
| | Cirrhosis | 800(4.1) | 592(2.8) | < 0.001 |
| ICU | | 6725(34.3) | 4642(21.9) | < 0.001 |
| Types of shock | No shock | 14617(74.5) | 19233(90.9) | < 0.001 |
| | Septic shock | 3422(17.5) | 1073(5.1) | < 0.001 |
| | Hypovolemic shock | 988(5) | 593(2.8) | < 0.001 |
| | Cardiac shock | 939(4.8) | 357(1.7) | < 0.001 |
| | Two or more kinds of shock | 345(1.8) | 96(0.5) | < 0.001 |
| Types of infection | Pneumonia | 15176(77.4) | 14858(70.2) | < 0.001 |
| | Urinary infection | 1492(7.6) | 1906(9) | < 0.001 |
| | Intra-abdominal infection | 1782(9.1) | 1792(8.5) | 0.03 |
| | CRBSI | 657(3.4) | 472(2.2) | < 0.001 |
| | CNS infection | 47(0.2) | 67(0.3) | 0.14 |
| | Others | 3229(16.5) | 4510(21.3) | < 0.001 |
| Types of organ function damage | Respiratory insufficiency | 11797(60.2) | 8032(38) | < 0.001 |

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, MODS = multiple organ dysfunction syndrome, TCM = traditional Chinese medicine. Values are expressed as the median (interquartile range and N (%)).

| Variables | | Sepsis with AKI (n = 19579) | Sepsis without AKI(n = 21141) | P value |
|---|---|---|---|---|
| | Acute liver injury | 4000(20.4) | 3518(16.6) | < 0.001 |
| | DIC | 680(3.5) | 195(0.9) | < 0.001 |
| | MODS | 3386(17.3) | 1117(5.3) | < 0.001 |
| | Metabolic encephalopathy | 238(1.2) | 124(0.6) | < 0.001 |
| Expenses | Total expense (Yuan) | 60242.42(28580.86-122460.29) | 39853.56(18844.39-81420.71) | < 0.001 |
| | Average daily expense (Yuan) | 5272.18(3190.64-8583.87) | 3224.33(1862.96-5593.4) | < 0.001 |
| | Western medicine expense (Yuan) | 13885.26(5645.02-30424.3) | 9700.77(3298.62-22050.47) | < 0.001 |
| | Chinese medicine expense (Yuan) | 94.74(0-854.43) | 77.75(0-623.56) | < 0.001 |
| Outcome | Length of hospital stay (day) | 13(6–23) | 13(7–22) | < 0.001 |
| | Death(n) | 10647(55) | 6157(29.3) | < 0.001 |
| 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, MODS = multiple organ dysfunction syndrome, TCM = traditional Chinese medicine. Values are expressed as the median (interquartile range and N (%)). | | | | |

### Incidence and risk factors of S-AKI

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 analysis, the following independent risk factors for S-AKI were identified: 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), malignancy (OR = 1.20, 95%CI (1.14–1.26), P < 0.001), cirrhosis (OR = 1.69, 95%CI (1.49–1.91), P < 0.001), emergency admission (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 = 1.2, 95%CI (1.14–1.26), 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), $P < 0.001$), acute respiratory failure (OR = 1.93, 95%CI (1.84–2.03), $P < 0.001$), disseminated intravascular coagulation (OR = 2.15, 95% CI (1.75–2.65), $P < 0.001$).

**All-cause mortality and risk factors** (Table 2)

Table 2
Risk factors associated with death of S-AKI

| Variables | | Survivor | Death | P value |
|---|---|---|---|---|
| N (%) | | 8712(45.0) | 10647(55.0)* | |
| Age median [IQR] | | 76(60–84) | 79(68–85) | < 0.001 |
| Age stratification(years) | 18–39 | 575(6.6) | 358(3.4) | < 0.001 |
| | 40–59 | 1487(17.1) | 1134(10.7) | |
| | 60–79 | 3212(36.9) | 3983(37.4) | |
| | ≥ 80 | 3438(39.5) | 5172(48.6) | |
| Gender | Female | 3182(36.5) | 4029(37.8) | 0.06 |
| | Male | 5530(63.5) | 6618(62.2) | |
| Classification of insurance | BMI | 3929(45.1) | 6818(64) | < 0.001 |
| | RCMTI | 958(11) | 483(4.5) | |
| | GMP | 1890(21.7) | 1415(13.3) | |
| | OPP | 622(7.1) | 639(6) | |
| | Others | 1313(15.1) | 1292(12.1) | |
| Hospital level | Tertiary hospitals | 7953(91.3) | 9370(88) | < 0.001 |
| | Second-class hospital | 759(8.7) | 1277(12) | |
| Hospital nature | Western Medicine hospital | 8200(94.1) | 9603(90.2) | 0.59 |
| | Hospital of TCM | 512(5.9) | 1044(9.8) | |
| Time interval(year) | 2005–2011 | 450(5.2) | 798(7.5) | < 0.001 |
| | 2012–2017 | 8262(94.8) | 9849(92.5) | |

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, MODS = multiple organ dysfunction syndrome, TCM = traditional Chinese medicine. Values are expressed as the median (interquartile range and N (%)). * 220 missing values because of lacking of outcome indicators.

| Variables | | Survivor | Death | P value |
|---|---|---|---|---|
| Comorbidities(n) | Diabetes | 3475(39.9) | 3513(33) | < 0.001 |
| | Hypertension | 4785(54.9) | 5394(50.7) | < 0.001 |
| | CKD stage 2 and 3 | 1134(13) | 1804(16.9) | < 0.001 |
| | Malignancy | 1288(14.8) | 2430(22.8) | < 0.001 |
| | Cirrhosis | 305(3.5) | 495(4.6) | < 0.001 |
| ICU | | 3136(36) | 3589(33.7) | < 0.001 |
| Types of shock | No shock | 7179(82.4) | 7400(69.5) | < 0.001 |
| | Septic shock | 1032(11.8) | 2178(20.5) | < 0.001 |
| | Hypovolemic shock | 380(4.4) | 607(5.7) | < 0.001 |
| | Cardiac shock | 190(2.2) | 745(7) | < 0.001 |
| | Two or more kinds of shock | 67(0.8) | 273(2.6) | < 0.001 |
| Types of infection | Pneumonia | 6508(74.7) | 8527(80.1) | < 0.001 |
| | Urinary infection | 898(10.3) | 576(5.4) | < 0.001 |
| | Intra-abdominal infection | 794(9.1) | 967(9.1) | 0.94 |
| | CRBSI | 275(3.2) | 377(3.5) | 0.14 |
| | CNS infection | 20(0.2) | 27(0.3) | 0.74 |
| | Others | 1568(18) | 1580(14.8) | < 0.001 |

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, MODS = multiple organ dysfunction syndrome, TCM = traditional Chinese medicine. Values are expressed as the median (interquartile range and N (%)). * 220 missing values because of lacking of outcome indicators.

| Variables | | Survivor | Death | P value |
|---|---|---|---|---|
| Types of organ function damage | Respiratory insufficiency | 4571(52.5) | 7135(67) | < 0.001 |
| | Acute liver injury | 1780(20.4) | 2199(20.7) | 0.7 |
| | DIC | 205(2.4) | 473(4.4) | < 0.001 |
| | MODS | 1132(13) | 2238(21) | < 0.001 |
| | Metabolic encephalopathy | 112(1.3) | 126(1.2) | 0.52 |
| Expenses | Total expense (Yuan) | 58362.5(29533.66-114864.4) | 62520.49(27564.02-130377.97) | 0.02 |
| | Average daily expense (Yuan) | 4673.41(2681.64-7898.79) | 5823.35(3670.61-9187.57) | < 0.001 |
| | Western medicine expense (Yuan) | 13422.67(5867.98-28107.39) | 14098.64(5414.67-32046.23) | 0.01 |
| | Chinese medicine expense (Yuan) | 142.69(0-1087.74) | 68.98(0-693.93) | < 0.001 |
| Outcome | Length of hospital stay (day) | 14(7–24) | 12(4–22) | < 0.001 |

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, MODS = multiple organ dysfunction syndrome, TCM = traditional Chinese medicine. Values are expressed as the median (interquartile range and N (%)). * 220 missing values because of lacking of outcome indicators.

There were 220 missing values because of lack of in-hospital outcomes. Overall all-cause mortality in S-AKI patients were 55%. Majority of them (57.9% of non-survivors) were admitted to ICU. The mortality in ICU patients was lower at 53.4%, compared to 54.8% in non-ICU patients (P < 0.001).

Patients with pneumonia had significantly higher mortality rates than those without (P<0.001). Patients with more severe 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).

A multivariate regression analysis revealed that risk factors for mortality included age (OR = 1.02, 95%CI (1.02–1.03), P < 0.001), female (OR = 1.15, 95%CI (1.08–1.24), P < 0.001), pre-existing comorbidities (CKD (OR = 1.12, 95%CI (1.02–1.24), P = 0.023), malignancy (OR = 2.03, 95%CI (1.86–2.23, P < 0.001), and cirrhosis (OR = 1.75, 95%CI (1.45–2.11), P < 0.001)), ICU admission (OR = 1.15, 95%CI (1.05–1.27), P =

0.005),pulmonary infection (OR = 1.47, 95%CI (1.23–1.76),P < 0.001)respiratory failure (OR = 2.02, 95%CI (1.87–2.17), P < 0.001), DIC (OR = 1.8, 95%CI (1.41–2.29), P < 0.001) and MODS (OR = 2.07, 95%CI (1.86–2.29), P < 0.001).We tested collinearity for relevant variables model 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)

**S-AKI before and after the KDIGO guideline era** (Table 3)

Table 3
Comparison of the epidemiology of S-AKI between pre and post KDIGO guideline for AKI definition

| **Variables** | | **2005–2011** | **2012–2017** | **P value** |
|---|---|---|---|---|
| N (%) | | 1468(100) | 18111(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) | 11370(62.8) | |
| Classification of insurance | BMI | 750(51.1) | 10082(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) | 16163(89.2) | < 0.001 |
| | Second-class hospital | 111(7.6) | 1948(10.8) | |
| Hospital nature | Western Medicine hospital | 1352(92.1) | 16656(92) | 0.86 |
| | Hospital of TCM | 116(7.9) | 1455(8) | |
| Comorbidities(n) | Diabetes | 257(17.5) | 6763(37.3) | < 0.001 |

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, MODS = multiple organ dysfunction syndrome, TCM = traditional Chinese medicine. Values are expressed as the median (interquartile range and N (%)).

| Variables | | 2005–2011 | 2012–2017 | P value |
|---|---|---|---|---|
| | 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) | 13937(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) | 14320(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) | 11123(61.4) | < 0.001 |
| | Acute liver injury | 131(8.9) | 3865(21.3) | < 0.001 |

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, MODS = multiple organ dysfunction syndrome, TCM = traditional Chinese medicine. Values are expressed as the median (interquartile range and N (%)).

| Variables | | 2005–2011 | 2012–2017 | P value |
|---|---|---|---|---|
| | DIC | 199(13.6) | 481(2.7) | < 0.001 |
| | MODS | 585(39.9) | 2800(15.5) | < 0.001 |
| | Metabolic encephalopathy | 17(1.2) | 221(1.2) | 0.83 |
| Expenses | Total expense (Yuan) | 62115.33(24502.22-134419.29) | 60158.84(28824.21-121703.84) | 0.88 |
| | Average daily expense (Yuan) | 3859.29(2200.42-6547.85) | 5406.94(3280.57-8719.52) | < 0.001 |
| | Western medicine expense (Yuan) | 25847.1(9208.77-58538.56) | 13329.13(5430.34-28760.24) | < 0.001 |
| | Chinese medicine expense (Yuan) | 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 |
| 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, MODS = multiple organ dysfunction syndrome, TCM = traditional Chinese medicine. Values are expressed as the median (interquartile range and N (%)). | | | | |

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, Fig. 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). In these two time periods, there were significant differences in the distribution of patients visiting 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 89.2%. (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. 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 second 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).

**AKI patients in both level-II and tertiary hospitals** (Table 4)

Table 4
Comparison between level II and tertiary hospitals

| Variables | | Level-II hospital | Tertiary hospitals | P value |
|---|---|---|---|---|
| N (%) | | 2059(100) | 17520(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 | 45(2.2) | 904(5.2) | < 0.001 |
| | 40–59 | 213(10.3) | 2444(13.9) | |
| | 60–79 | 737(35.8) | 6552(37.4) | |
| | ≥ 80 | 1064(51.7) | 7620(43.5) | |
| Gender | Female | 817(39.7) | 6478(37) | 0.02 |
| | Male | 1242(60.3) | 11042(63) | |
| Classification of insurance | BMI | 1384(67.2) | 9448(53.9) | < 0.001 |
| | RCMTI | 263(12.8) | 1219(7) | |
| | GMP | 193(9.4) | 3118(17.8) | |
| | OPP | 96(4.7) | 1167(6.7) | |
| | Others | 123(6) | 2568(14.7) | |
| Hospital nature | Western Medicine hospital | 1967(95.5) | 16041(91.6) | < 0.001 |
| | Hospital of TCM | 92(4.5) | 1479(8.4) | |
| Time Period | 2005–2011 | 111(5.4) | 1357(7.7) | < 0.001 |
| | 2012–2017 | 1948(94.6) | 16163(92.3) | |
| Comorbidities(n) | Diabetes | 719(34.9) | 6301(36) | 0.35 |
| | Hypertension | 1085(52.7) | 9136(52.1) | 0.64 |

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, MODS = multiple organ dysfunction syndrome, TCM = traditional Chinese medicine. Values are expressed as the median (interquartile range and N (%)).

| Variables | | Level-II hospital | Tertiary hospitals | P value |
|---|---|---|---|---|
| | CKD stage 2 and 3 | 403(19.6) | 2541(14.5) | < 0.001 |
| | Malignancy | 258(12.5) | 3484(19.9) | < 0.001 |
| | Cirrhosis | 40(1.9) | 760(4.3) | < 0.001 |
| ICU | | 613(29.8) | 6112(34.9) | < 0.001 |
| Types of shock | No shock | 1593(77.4) | 13021(74.3) | 0.003 |
| | Septic shock | 312(15.2) | 3083(17.6) | 0.006 |
| | Hypovolemic shock | 108(5.2) | 880(5) | 0.66 |
| | Cardiac shock | 78(3.8) | 860(4.9) | 0.02 |
| | Two or more kinds of shock | 31(1.5) | 313(1.8) | 0.36 |
| Types of infection | Pneumonia | 1582(76.8) | 13580(77.5) | 0.49 |
| | Urinary infection | 122(5.9) | 1369(7.8) | 0.002 |
| | Intra-abdominal infection | 131(6.4) | 1650(9.4) | < 0.001 |
| | CRBSI | 22(1.1) | 635(3.6) | < 0.001 |
| | CNS infection | 3(0.1) | 44(0.3) | 0.36 |
| | Others | 382(18.6) | 2833(16.2) | 0.006 |
| Types of organ function damage | Respiratory insufficiency | 1064(51.7) | 10720(61.2) | < 0.001 |
| | Acute liver injury | 286(13.9) | 3710(21.2) | < 0.001 |
| | DIC | 37(1.8) | 643(3.7) | < 0.001 |
| | MODS | 300(14.6) | 3085(17.6) | < 0.001 |

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, MODS = multiple organ dysfunction syndrome, TCM = traditional Chinese medicine. Values are expressed as the median (interquartile range and N (%)).

| Variables | | Level-II hospital | Tertiary hospitals | P value |
|---|---|---|---|---|
| | Metabolic encephalopathy | 28(1.4) | 210(1.2) | 0.53 |
| Expenses | Total expense (Yuan) | 41047.75(17598.47-92271.23) | 62702.87(30227.13-125862.83) | < 0.001 |
| | Average daily expense (Yuan) | 3822.54(2297.78-6014.34) | 5499.86(3329.52-8886.23) | < 0.001 |
| | Western medicine expense (Yuan) | 9085.04(3349.65-22224.82) | 14510.38(5984.67-31314.93) | < 0.001 |
| | Chinese medicine expense (Yuan) | 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 |

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, MODS = multiple organ dysfunction syndrome, TCM = traditional Chinese medicine. Values are expressed as the median (interquartile range and N (%)).

The majority of S-AKI patients (89.5%) were presented and 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%, $p < 0.001$, Fig. 3) of S-AKI were significantly higher in level II hospitals than those in tertiary hospitals.

**S-AKI patients in Traditional Chinese Medicine hospitals and Western Medicine hospitals** (Table 5)

Table 5
Comparison between Traditional Chinese Medicine hospitals and Western Medicine hospitals

| Variables | | TCMHs | WMHs | P value |
|---|---|---|---|---|
| N (%) | | 1573(8.0) | 18006(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 | 24(1.5) | 924(5.1) | < 0.001 |
| | 40–59 | 133(8.4) | 2526(14) | |
| | 60–79 | 590(37.5) | 6703(37.2) | |
| | ≥ 80 | 826(52.5) | 7853(43.6) | |
| Gender | Female | 653(41.5) | 6642(36.9) | < 0.001 |
| | Male | 920(58.5) | 11364(63.1) | |
| Classification of insurance | BMI | 1166(74.2) | 9659(53.6) | < 0.001 |
| | RCMTI | 109(6.9) | 1376(7.6) | |
| | GMP | 133(8.4) | 3173(17.6) | |
| | OPP | 113(7.2) | 1148(6.4) | |
| | Others | 52(3.3) | 2650(14.7) | |
| Hospital level | Tertiary hospitals | 1481(94.2) | 16038(89.1) | < 0.001 |
| | Second-class hospital | 92(5.8) | 1968(10.9) | |
| Time interval(year) | 2005–2011 | 117(7.4) | 1351(7.5) | |
| | 2012–2017 | 1456(92.6) | 16655(92.5) | |
| Comorbidities(n) | Diabetes | 521(33.1) | 6503(36.1) | 0.02 |

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, MODS = multiple organ dysfunction syndrome, TCMHs = traditional Chinese medicine hospitals, WMHs = western medicine hospitals. Values are expressed as the median (interquartile range and N (%)).

| Variables | | TCMHs | WMHs | P value |
|---|---|---|---|---|
| | Hypertension | 828(52.6) | 9399(52.1) | 0.73 |
| | CKD stage 2 and 3 | 299(19) | 2645(14.7) | < 0.001 |
| | Malignancy | 240(15.2) | 3510(19.5) | < 0.001 |
| | Cirrhosis | 22(1.4) | 778(4.3) | < 0.001 |
| ICU | | 159(10.1) | 6566(36.4) | < 0.001 |
| Types of shock | No shock | 1294(82.2) | 13323(73.9) | < 0.001 |
| | Septic shock | 182(11.6) | 3240(18) | < 0.001 |
| | Hypovolemic shock | 58(3.7) | 930(5.2) | 0.01 |
| | Cardiac shock | 60(3.8) | 879(4.9) | 0.06 |
| | Two or more kinds of shock | 18(1.1) | 327(1.8) | 0.05 |
| Types of infection | Pneumonia | 1260(80) | 13916(77.2) | 0.01 |
| | Urinary infection | 106(6.7) | 1386(7.7) | 0.17 |
| | Intra-abdominal infection | 86(5.5) | 1696(9.4) | < 0.001 |
| | CRBSI | 55(3.5) | 602(3.3) | 0.74 |
| | CNS infection | 3(0.2) | 44(0.2) | 0.68 |
| | Others | 256(16.3) | 2973(16.5) | 0.81 |
| Types of organ function damage | Respiratory insufficiency | 850(54) | 10947(60.7) | < 0.001 |
| | Acute liver injury | 359(22.8) | 3641(20.2) | 0.01 |
| | DIC | 54(3.4) | 626(3.5) | 0.93 |
| | MODS | 305(19.4) | 3081(17.1) | 0.02 |

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, MODS = multiple organ dysfunction syndrome, TCMHs = traditional Chinese medicine hospitals, WMHs = western medicine hospitals. Values are expressed as the median (interquartile range and N (%)).

| Variables | | TCMHs | WMHs | P value |
|---|---|---|---|---|
| | Metabolic encephalopathy | 34(2.2) | 204(1.1) | < 0.001 |
| Expenses | Total expense (Yuan) | 46013.3(20515.42-94055.27) | 61667.38(29297.85-125052.5) | < 0.001 |
| | Average daily expense (Yuan) | 4166.6(2721.57-6398.43) | 5413.71(3248.88-8781.84) | < 0.001 |
| | Western medicine expense (Yuan) | 9744.02(3425.73-21786.67) | 14285.38(5896.72-31166.39) | < 0.001 |
| | Chinese medicine expense (Yuan) | 995.2(182.92-3489.11) | 73.09(0-686.88) | < 0.001 |
| Length of hospital stay (day) | | 13(5–22) | 13(6–23) | 0.03 |

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, MODS = multiple organ dysfunction syndrome, TCMHs = traditional Chinese medicine hospitals, WMHs = western medicine hospitals. Values are expressed as the median (interquartile range and N (%)).

Compared with S-AKI patients seen in the TCMS, the vast majority (92%) of S-AKI patients were treated in WMHs. The survival rate of patients treated in the WMHs was significantly higher patients treated in TCMHs (45.5% versus 32.5%, $P < 0.001$, Fig. 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 ($P = 0.03$).

# 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. Certain risk factors 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. Pneumonia was the most likely source of sepsis in this cohort. The reported incidence of S-AKI was higher after KDIGO guideline was 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]. According to the nationwide survey regarding AKI across Mainland China, 28% of AKI episodes occurred in ICU, while 72% occurred in the non-ICU setting. The incidence of S-AKI in LI's paper was only 6.4% [16]. The current literature reported incidence of S-AKI is from 39.4–60.7% in ICU [21,22], which is consistent with our finding (48%).

Our study showed that certain demographic characteristics, including advanced age, male and the presence of comorbidities such as hypertension, CKD and liver cirrhosis, requirements for ICU admission and shock status were significantly associated with the incidence of AKI. These results were consistent with previous studies [13,23]. 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 [4,24]. The healthcare system in China is different from some developed countries where patients can have free access to certain procedures such as dialysis therapy [21], which may be a potential factor contributing to higher mortality rates.

### 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 Acute Kidney Injury (AKI) to enable consistent diagnosis and treatment across different health-care 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 [25]. Despite slight variations in the definitions, systematic review has found that these definitions do not significantly differ in their predictive outcomes [26].

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 finding is similar to previous studies [27,28], 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 population aging 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 [29–31]; significant advancements 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 and so on [31,32]; majority of patients seeking treatment in tertiary hospital, where the highest level of medical staff and equipment exist [33].

### Outcomes between level II and tertiary hospitals

To the best of our knowledge, present studies in literature are limited and do not directly provide 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 more interventional management strategies in the level-II hospital. 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 (e.g. 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) vs Western Medical Hospitals (WMHs)

In China, the health care system is uniquely divided into both a western and traditional Chinese medical system [34]. 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 [35].

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 kinds 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 physicians and patients [36]. The incidence of kidney injury induced by Chinese herbal medicines is difficult to assess. One cross-sectional survey of AKI in China [15] 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%). This high proportion of nephrotoxic drug exposure is probably consistent with the increasing incidence of drug-induced disease in China [37]. Therefore, the use of Chinese herbal medicine may be a double-edged sword in the treatment of AKI patients.

### Strengths and Limitations

To our knowledge, this large retrospective cohort study assessed epidemiological features of S-AKI at the municipal level, in China, consisting 40720 patients and 158 hospitals. 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 RRT and the long-term prognosis of renal function. Therefore, the epidemiology of S-AKI patients is mainly limited to incidence 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 standardised and comprehensive AKI classification system. Finally, there were large differences in the patients' numbers in different time periods and different levels and types 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 |

# Declarations

### Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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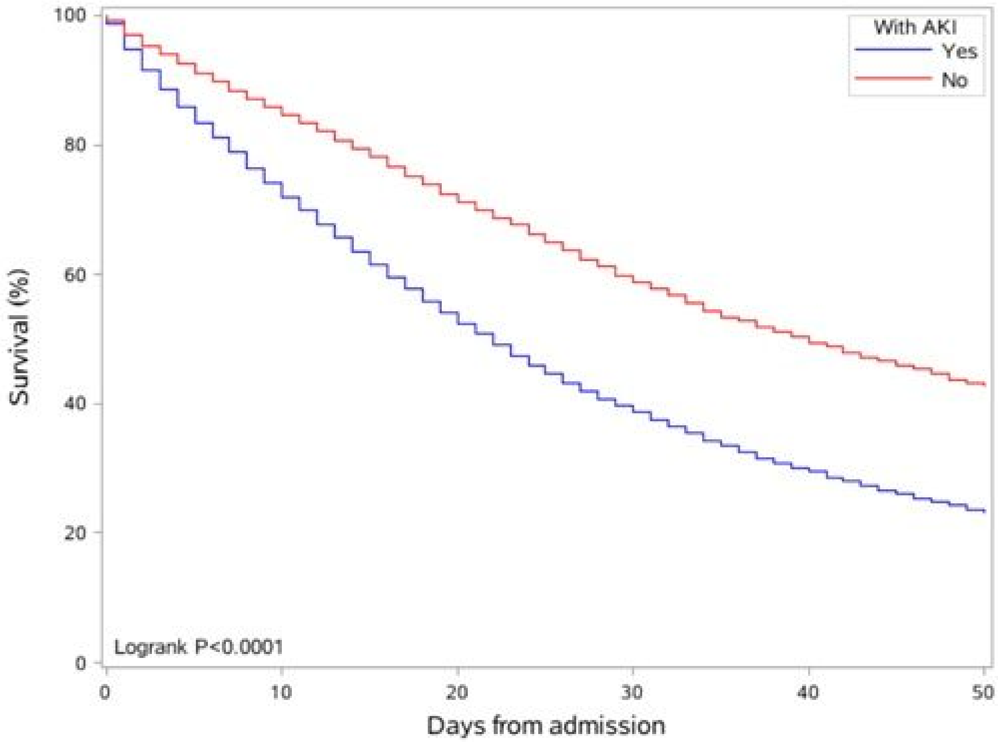
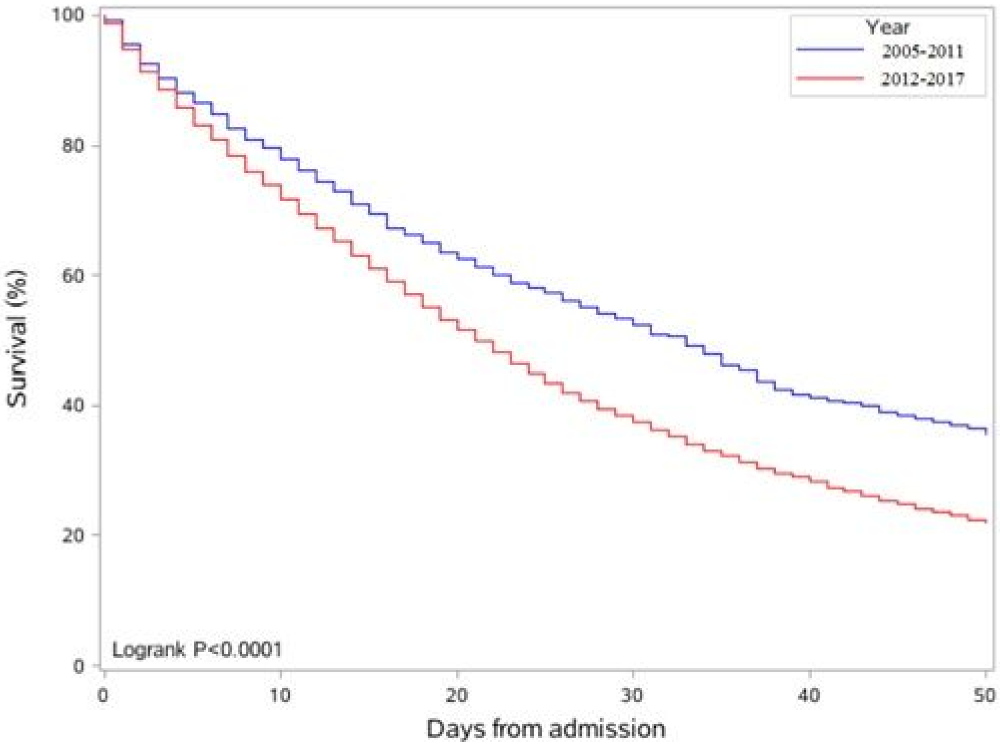
# Figures



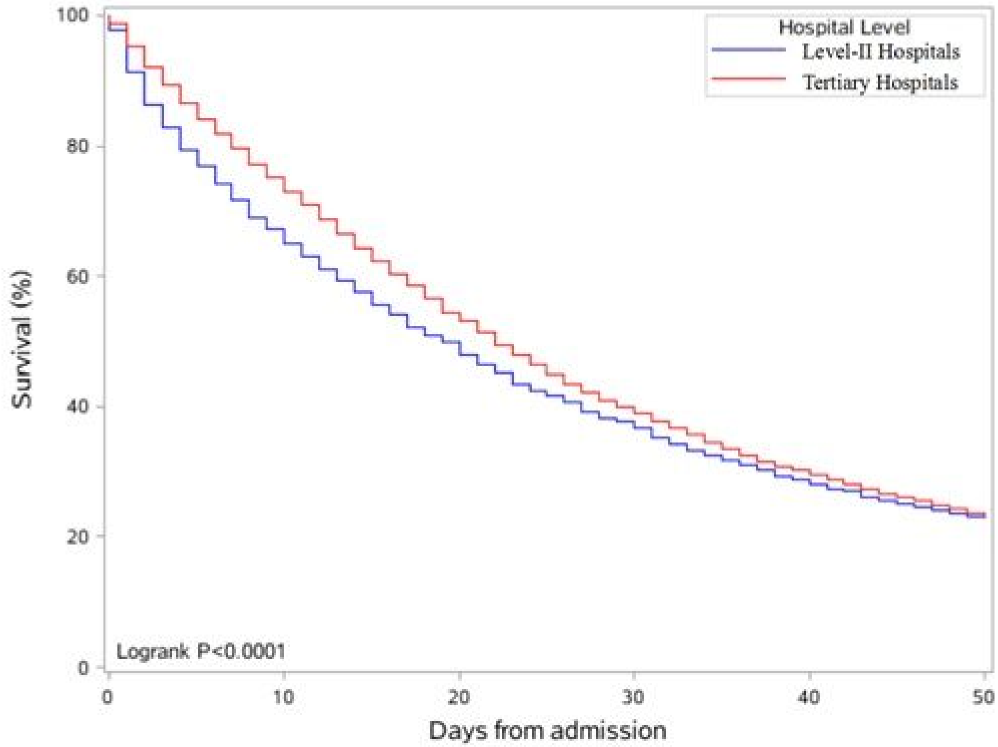

## Figure 1

The hospital survival probability curves of all patients with sepsis. Survival curves of patients classified according to the presence (highlighted in blue) or absence (highlighted in red) of AKI during hospital stay. Patients with AKI had significantly lower hospital survival rate than patients without (45.0% versus 70.7% respectively; p<0.001).



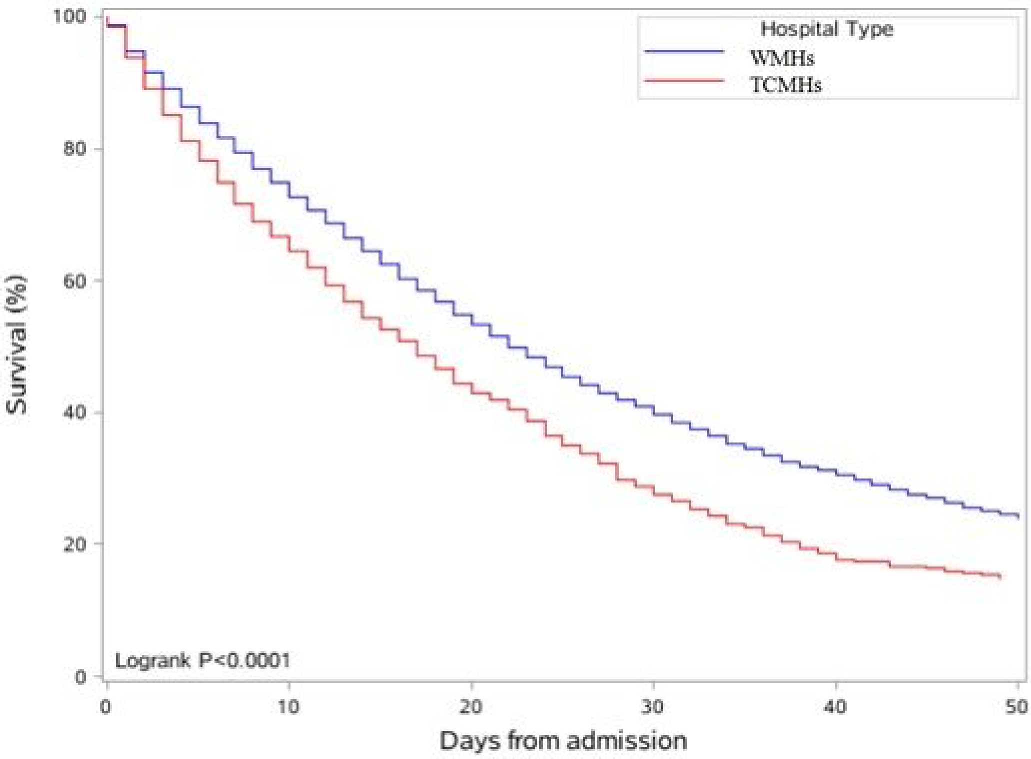

## Figure 2

The hospital survival probability curves of patients with S-AKI classified according to admission date: before (2005-2011, highlighted in blue) or after (2012-2017, highlighted in red) the KDIGO guideline era. Patients admitted after the KDIGO guideline era had higher hospital survival rate than patients admitted before (45.6% versus 36.1% respectively; p<0.001).




## Figure 3

The hospital survival probability curves of patients with S-AKI classified according to hospital levels: level II hospitals (highlighted in blue) and tertiary hospitals (highlighted in red) . The survival rate of S-AKI were significantly lower in level II hospitals than those in tertiary hospitals (37.9% versus 45.9% respectively; p<0.001).




## Figure 4

The hospital survival probability curves of patients with S-AKI classified according to hospital types: Traditional Chinese Medicine hospitals (TCMHs, highlighted in red) and Western Medicine hospitals (WMHs, highlighted in blue). The survival rate of patients treated in the WMHs was significantly higher patients treated in TCMHs (45.5% versus 32.5% respectively; p<0.001).