Prevalence of acute kidney injury and use of renal replacement therapy in intensive care unit patients in Indonesia

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Abstract

Background : Currently, there is limited epidemiology data on acute kidney injury (AKI) from Southeast Asia, especially from Indonesia which is one of the biggest countries in Southeast Asia. Therefore, we assessed the prevalence of AKI and the utilization of renal replacement therapy (RRT) in Indonesia.

Methods : Demographic and clinical data were collected from 952 ICU participants. The participants were categorized into AKI and non-AKI groups. The participants were further classified according to the 3 different stages of AKI as per the Kidney Disease Improving Global Outcome (KDIGO) criteria. We then assessed the Acute Physiology and Chronic Health Evaluation (APACHE) II score of AKI and non-AKI participants. RRT modalities were listed according to the number of times the procedures were carried out.

Results : Overall incidence of AKI was 43%. The participants were divided into three groups based on the AKI stages: 18.5 % had stage 1, 33% had stage 2, and 48.5 % had stage 3. The use of mechanical ventilation was higher among the participants with AKI compared to the non-AKI participants. Also, AKI participants had higher average APACHE score compared to the non-AKI participants (16.5 vs 9.9). Among the AKI participants, 24.6% required RRT. The most common RRT modalities were intermittent hemodialysis (69.4%), followed by slow low-efficiency dialysis (22.1%), continuous renal replacement therapy (4.2%), and peritoneal dialysis (1.1%).

Conclusions : This study showed that AKI is a common problem in the Indonesian ICU and had a high mortality rate. We strongly believe that identification of the risk factors associated with AKI will help us to develop a predictability score for AKI so we can prevent and improve AKI outcome in the future.

Background

Acute kidney injury (AKI) is a common problem and often associated with high morbidity and mortality rates worldwide. The International Society of Nephrology (ISN) has launched the 0 by 25 campaign. The purpose of this campaign is to have zero deaths from preventable or untreated AKI in resource limited setting (i.e., Africa, Latin America and Asia [1]) by 2025 [please add this reference Mehta et al.: Lancet 2015;385:2616–43]. Patients can develop AKI while in intensive care unit (ICU) and encounter complications that further worsen their clinical condition. Recently, the incidence of AKI in ICU varies between 6% to 70%, and 57% of ICU patients tend to develop AKI [2].

On average, 5% of ICU patients with severe AKI require renal replacement therapy (AKI-RRT) [3]. AKI in ICU patients presents with diverse forms of clinical outcomes such as prolonged ICU stay by 3.5 days, reduced health-related quality of life, require mechanical ventilation, and have detrimental clinical consequences such as acid-base disorders, hypervolemia, hyperkalemia, uremia, immune system and depression. These variables are highly associated with the current mortality rates of AKI patients ranging from 40-60% [4, 5]. These findings suggested that ICU patients are highly susceptible to AKI and most of the time portend a poor prognosis.

There is limited AKI data in Indonesia. As a result of this, we conducted this study to fill in the gap of AKI epidemiology data in Indonesia. In addition, we assessed the risk factors associated with AKI and the incidence of acute RRT-treated in ICU.

Methods

Participants and data collection

This study was a prospective observational study conducted in an ICU of the Gatot Soebroto Indonesia Central Army Hospital. All patients > 15 years old that were admitted to the ICU with risk factors for developing AKI were identified and enrolled into the study. These participants were then followed prospectively until onset of AKI. We extracted medical data from the ICU database for these participants from January 2017 until December 2018. We classified the participants according to the 3 different stages of AKI. Patients with end-stage renal disease (ESRD) on chronic dialysis were excluded (Figure 1). For participants with multiple admissions, we only collected data from the first admission. The study protocol was reviewed and approved by the institutional review boards (IRB No. B/2212/VIII/2016). Informed consent was waived. This study is part of the Southeast Asia-Acute Kidney Injury (SEA-AKI) study that has been previously described by Srisawat et al [6].

Demographic and clinical data from all of the participants were collected such as admission date, sex, age, body mass index (BMI), primary diagnosis at ICU admission, history of comorbid conditions, AKI stages, RRT modes and the use of mechanical ventilation during ICU stay. For critically ill participants, the severity of AKI and prediction of mortality were determined by the Acute Physiology and Chronic Health Evaluation II (APACHE II) and Sequential Organ Failure Assessment (SOFA) scoring system. Four RRT modes were used in this study: acute peritoneal dialysis (PD), intermittent hemodialysis (IHD), sustained low-efficiency dialysis (SLED), and continuous renal replacement therapy (CRRT). For each participant, we recorded how many times each RRT mode was used or as an initiation mode throughout January 2017-December 2018. The data were sequentially collected every day for the first 7 days of ICU admission and then collected weekly on days 14, 21 and 28.

Definition and classification of acute kidney injury

The diagnosis of AKI was based on the KDIGO criteria [7]. For the baseline serum creatinine, we used the most recent available serum creatinine or serum creatinine within 1 year before hospital admission. If the participants had no available data for baseline serum creatinine, then we estimated the baseline serum creatinine using the lowest value between the serum creatinine at the time of hospital admission (admission serum creatinine) and the back calculation of serum creatinine from the Modification of Diet in Renal Disease (MDRD) equation using a glomerular filtration rate (GFR) of 75 mL/min/1.73m² (MDRD serum creatinine) as recommended in the KDIGO guideline [8]. We also defined AKI stage 3 as severe AKI. We used International Classification of Diseases, 10th Revision coding to classify the primary diagnosis of ICU admission.

We defined renal recovery based on the Acute Dialysis Quality Initiative (ADQI) definition, that is, the participant is alive, had dialysis independent at the time of hospital discharge and the participant's creatinine on the last day of observation was < 1.5 times compared to the baseline serum creatinine levels [9].

Statistical analysis

Categorical data were presented as counts and percentages. Continuous data were presented as mean and standard deviation (SD) if normally distributed, or median with an interquartile range if non-normally distributed. Kaplan-Meier survival curves were also generated for each AKI class. The Chi-square test of independence was used to compare the proportions of different types of participants based on their AKI status. ANOVA was used to compare continuous data of the participants' characteristics based on their AKI status. The univariate and multivariate logistic regression models were performed to examine the association between the factors and the outcomes. Factors which had p-value < 0.20 from the univariate model and had no multicollinearity as measured by Variance Inflation Factor (VIF) statistic were entered into the multivariate model. P-value < 0.05 was considered statistically significant. The statistical software used for all analyses was Stata version 14.0.

Results

Flow chart of the study is shown in Figure 1. Among all study participants (N = 952), 87 were excluded because 1 participant did not have any creatinine data and 86 participants had ESRD. From 865 participants, almost half of them (43%) suffered from AKI. As for the severity of AKI, 48.5% of the participants had stage 3 AKI, 33% had stage 2 AKI and 18.5% had stage 1 AKI.

Among all ICU participants diagnosed with AKI, the average age was 58 ($\pm$ 15) years and 64.6% were male. The primary diagnosis upon ICU admission were most likely due to surgical-related disease (23.5%; N = 87), cardiovascular disease (19.2%; N = 71), and neurologic disease (15.9%; N = 59). The most common metabolic comorbidities among the AKI participants were hypertension (39.4%; N = 147) and diabetes mellitus (38.9%; N = 145). There is a significant difference among AKI and non AKI participants when it comes to using mechanical ventilation as shown in Table 1. One hundred and eighty five (49.6%) AKI participants used mechanical ventilation whereas only 85 (17.3%) non-AKI participants used mechanical ventilation. The severity scoring (APACHE II) was significantly higher in AKI participants (17.1) compared to non-AKI participants (11.2). Non-renal SOFA score was also found to be significantly higher in AKI participants compared to non-AKI participants (5.0 vs 3.0, $p < 0.001$) (Figure 2).

Risk factors associated with the development of AKI are shown in Table 2. Participants that were admitted to the ICU with renal disease as their primary diagnosis were 4.53 times (95% CI: 1.67-12.33, $p = 0.003$) more likely to develop AKI during ICU compared to those who did not have renal disease as their primary diagnosis. Participants who had higher APACHE II scores were 1.14 times (OR per point increase, 95% CI: 1.09-1.20, $p < 0.001$) more likely to develop AKI during ICU compared to those who had less than 1 unit.

Table 3 showed the participants' characteristics and risk factors for developing severe AKI. Out of 373 AKI participants, 48.5% had severe AKI. Based on the multivariate analysis using logistic regression, participants who developed severe AKI were 2.47 times more likely to be male, 9.47 times more likely to have CKD and 3.43 times more likely to have malignancy. They also were more likely to have higher APACHE II score (OR: 1.07; per 1-point increase, 95% CI: 1.01-1.13), compared to less severe AKI participants. Participants with severe AKI were also 5.41 times more likely to use vasopressors during their stay at the ICU. The goodness of fits by Hosmer-Lemeshow (H-L) test for model of AKI risk factors and model of AKI severity were H-L Chi2 = 3.64 (p=0.89), and H-L Chi2 = 3.08 (p=0.93), respectively.

We also explored the etiology of AKI (Table 4). Sepsis was the leading cause of AKI (206, 55.2%). While, AKI secondary to obstetric complication occurred in only 3 cases (0.8%) (Table 4).

Among those participants who received RRT support, IHD is the most common procedure used as the initial mode of RRT in ICU (66 procedures, 71.7 %), followed by SLED (21 procedures, 22.8%), then CRRT (4 procedures, 4.34%) and acute PD (1 procedure, 1.08%). (Table 5)

Survival analysis was acquired by using the Kaplan-Meier analysis. It was tabulated for 60 days in the hospital and 28 days in the ICU. In Figure 2, the curve estimated the overall survival based on the different stages of AKI while in the hospital. AKI stage 3 was associated with a significant decrease in cumulative survival probability. The median survival time for non-AKI, AKI stage 1, 2, and 3 were 31, 16, 13, and 9 days, respectively (p <0.001).

The renal recovery rate at hospital discharge was only 19% (69 of 368 patients; 5 cases were excluded because the clinical outcome was unknown). For the non-recovery group (299 patients), the hospital mortality rate for AKI was 58% (215 of 368). There were 0.5% (2 of 368 patients) who were alive and dependent on dialysis. Eighty two out of 368 participants (22%) had persistent AKI.

Discussion

Multiple studies have shown the detrimental impact of AKI on ICU patients. Unfortunately, the etiology and mechanism of AKI remain unclear. Various reasons such as infection, trauma and other problems that prompt the patient to be admitted into ICU could induce AKI or worsen any pre-existing condition of AKI.⁽¹⁾ Therefore, it is important to have AKI epidemiology data, including the risk factors that may cause AKI, so the country can appropriately manage the health care for these kinds of patients, especially for Indonesia which has limited resources. AKI has been reported to occur in 20-50% of the patients in ICUs around the world [10]. In Indonesia, at the Central Army Hospital of Gatot Soebroto, almost half of the ICU patients (43%) had AKI. This indicated that AKI was a common problem in Indonesian's ICU (Figure 1). This high incidence of AKI showed that there were problems within the public health system and socioeconomic factors may also affect the epidemiology of AKI in low resource setting [11].

In this study, 373 participants in ICU had AKI of which 181 participants (48.5%) had AKI stage 3 as per the KDIGO criteria. Early diagnosis of AKI in ICU patients is challenging and may explain why our center

had many AKI stage 3 participants (Figure 1). Likewise, our findings are similar to those reported from less developed countries. A recent study conducted by Srisawat, et al., reported that the incidence of AKI stage 3 among patients in ICU was 28.9%; 16.4% of the patients at ICU had AKI stage 2 and 7.5% had AKI stage 1.⁽¹¹⁾ Aside from that, they also showed that when the patients were admitted to ICU, most of the AKI patients progressed to AKI stage 3. This can be explained that AKI was not recognized in time so was not treated appropriately by the time the patients were admitted to the ICU. Hence, the prevalence of AKI patients in developing countries are higher than those in developed country. For example, a recent study conducted in Australia reported that 37.1% of their patients in ICU developed AKI; 18.1% had AKI stage 1, 10.1% had AKI stage 2 and 8.9% had AKI stage 3.⁽¹⁰⁾ The prevalence of AKI in Australia was lower than our study because the doctors there were more vigilant in managing patients with AKI so that their patients did not progress to AKI stage 3. Aside from early diagnosis and treatment, the doctors in Australia have access to many resources and data so have an advantage compared to the developing countries.

Currently, there is limited epidemiology data on AKI in Indonesia. As a result of this, we conducted this study to fill in the gaps so that other organizations in the country can use our data as the reference. In our center, based on the multivariate analysis using logistic regression, the significant factors that were associated with severe AKI were male, CKD and malignancy, high APACHE II score, and use of a vasopressor (Table 3). Even though age was not significantly associated with severe AKI, however, we noticed that the older the participant was, the more severe the AKI was. For our study, the mean age of our participants with AKI was 58 years ($\pm$ 15 years old). Our findings corroborated the results from a study conducted in Malaysia which showed that the mean age of the AKI patients was 53 years ($\pm$ 16 years old) and that 56% of the patients had AKI stage 3, 25% had AKI stage 2 and 18% had AKI stage 1 [12]. At the moment, we do not know why age was associated with the severity of AKI. It is possible that age among different ethnicities and countries could have an affect on the severity of AKI. It is also possible that our sample size was not large enough to detect age as one of the risk factors associated with AKI. Another explanation could be that as people age, the more comorbidities they will have, and the kidney, similarly also undergoes age-dependent structural and functional alterations over time [13]. One experimental study using rats showed that aged rats exhibited reduced antioxidant potential and increased oxidative stress after ischemia-reperfusion compared to young rats [14]. The authors showed that the total plasma antioxidant potential (AOP) of aged rats was lower than that of the young rats regardless whether they underwent ischemia-reperfusion or not. Besides this, the renal tissue 8-OHdG levels, which contributes to the destruction of the kidney, were increased in aged rats after reperfusion injury. Thus, this may explain why elderly patients have an increased risk for non-recovery of the renal function after acute ischemia and heightened susceptibility to AKI [15].

Aside from age, our study showed that comorbidities were associated with the severity of AKI. The two most common comorbidities of AKI in our study were diabetes mellitus (N=145) and hypertension (N=147). A previous study showed that having diabetes had a 2.8 fold of increased risk for developing AKI [16]. The mechanism by which diabetes increases the severity of AKI has not yet been well

established, but a great deal of research supports the connection between obesity, inflammation, and insulin resistance [17]. Inflammatory cytokines such as tumor necrosis factor- α (TNF- α) and interleukin-6 (IL-6) are produced by adipocytes and have been shown to cause insulin resistance [18].

As for hypertension, it too has been shown to increase the risk of developing AKI (OR, 1.13; 95% CI, 1.02-1.05). Hypertension is commonly found in patients with AKI and vice versa due to several mechanisms with inter-related complications, such as balance disorders of the vascular active substances, renin-angiotensin system activation, changes in the inflammatory factors, and increases in the active oxygen species [19]. Inflammation causes changes in the endothelial function and further increases in the arterial stiffness, oxidative stress and increased circulating angiotensin II levels. Not only that, but it can also reduce the availability of nitric oxide (NO) and worsen the vascular damage. Hence, the combination of hypertension, increased angiotensin II levels and oxidative stress can initiate events that can result in the damage of the renal system [20].

Another comorbidity detected in our study to be associated with AKI was CKD. In this study, our participants were 9.47 times more likely to have CKD as one of their comorbidities. In recent years, studies from different regions reported that CKD is a strong risk factor for the development of AKI, mainly in septic patients. Currently, CKD is found in 30% of the patients who develop AKI in ICU [21]. It is noteworthy that CKD has the highest percentage of association with AKI and is a strong predictor of developing AKI in critically ill patients.

Beside this, almost half of the AKI participants (49.6%) used mechanical ventilation while less than a fifth (17.3%) of non-AKI participants used mechanical ventilation. When we compared the ventilated non-AKI participants to the ventilated AKI participants, the ventilated AKI participants had a higher APACHE score and three days SOFA score. This finding confirmed that AKI in ICU is a prominent risk factor that can worsen the patients' health conditions, more specifically in low-risk AKI-RRT patients [22]. In addition, Vieira, et al., showed that renal dysfunction had a serious consequence during the use of mechanical ventilation and weaning from mechanical ventilation. The median duration of mechanical ventilation use in AKI patients was 3 days longer than non-AKI patients (10 vs 7 days) [23]. The underlying mechanism that may contribute to the use of mechanical ventilation in AKI patients is severe acute respiratory insufficiency. In order to reach the acceptable gas exchange level, therefore mechanical ventilation is needed to increase the intrathoracic pressure to compensate for these negative changes. If mechanical ventilation is not used, then the AKI patients can progress to renal dysfunction such as renal tubular apoptosis [22].

Apart from the need of mechanical ventilators, RRT is another item that is needed for our AKI participants. In our study, 92 (24.6%) AKI participants required RRT (AKI-RRT). Thus, this finding indicated that RRT in ICU settings is important [24]. It is crucial that AKI patients have access to RRT because the mortality rates among AKI patients are high, especially in critically ill patients in ICU setting [25]. Because of this, facilities should try to overcome challenges of not having various modalities of RRT and hire, at least, one nephrologist.

One of the most common RRT modality used in this study was IHD. Like most hospitals in developing countries, IHD is also the most commonly used method (66 procedures, 71.7%). On the other hand, an online questionnaire study that targeted members from the European Society of Intensive Care Medicine from 50 countries showed that half of the intensivists preferred to use CRRT compared to IHD. The reason why they preferred to use CRRT was because they perceived that this modality had a better hemodynamic stability, had a better therapeutic effect since it can remove the cytokines and can easily control the balance of the fluid [26].

In regards to mortality among patients with AKI, it was shown that the hospital mortality and ICU mortality rates were both worse in patients with AKI at any given stage compared to the in-hospital mortality rate of non-AKI patients. This data was obtained from a cohort study conducted by Mandelbaum, et al., which assessed the hospital mortality and ICU mortality rates in critically ill patients with AKI. The mortality rate in non-AKI patients was 6.25%, in AKI stage 1 patients it was 13.87%, in AKI stage 2 patients it was 16.42%, and in AKI stage 3 patients it was 33.76%. The ICU mortality rate was also higher in AKI patients as follows: 4.54% for non-AKI patients, 10.06% for AKI stage 1 patients, 13.15% for AKI stage 2 patients, and 30.48% for AKI stage 3 patients [27].

Next, we looked at the Kaplan-Meier survival curves according to the presence of AKI and we saw that there was a significant survival difference between AKI participants and non-AKI participants. The survival curve for AKI participants were steeper than the non-AKI participants. This finding showed that the survival rate in AKI participants was worse compared to non-AKI participants. Previous studies clearly showed that AKI patients had worse outcomes compared to non-AKI patients. Hence, it is important to prevent AKI from happening or manage AKI at an earlier stage. This will be beneficial to both the country and the patients. This will help decrease the healthcare burden and increase the patients' overall survival rates [28].

This study has several strengths. First, we were able to identify the risk factors for developing AKI which can be used to develop a predictability score to prevent AKI and ultimately improve AKI outcome. Also, these risk factors can be utilized in the hospitals so that we can prevent the occurrence of AKI and help the AKI patients have a better prognosis. Another key strength of this study was the availability of the data for mild (AKI stage 1/2) and severe AKI (AKI stage 3). These data made it possible for us to identify the risk factors associated with the development of AKI in ICU participants. The other strength was that our AKI criteria was based on the KDIGO criteria which employed both the creatinine level and urine output data. Because of this, the finding from this study can be used as a reference for other AKI studies conducted in ICU in other hospitals, especially in Indonesia. Last, our findings were able to fill in the gap by providing the country its AKI epidemiological data.

Our study did have some limitations. We collected data from only one site, at the Gatot Soebroto Hospital. Therefore, our data may not truly represent the incidence of AKI in all hospitalized ICU patients across Indonesia. Second, we only collected the data from ICU. Hence, it is possible that our participants could have developed AKI before ICU admission. Third, we only had baseline creatinine level from 9.9% of

the participants. However, we were able to determine the baseline creatinine by choosing the reference creatinine from the lower value between the first serum creatinine on the day of admission and the creatinine from the MDRD formula which assumed that the GFR was at least 75mL/min/1.73m². We demonstrated that it was feasible to exclusively use the MDRD-derived values to generate the baseline serum creatinine levels for our participants [29-31]. We also know that the limitation of MDRD back calculation is based on the assumption that the participant did not have CKD. This was not a problem for our study. For us, our database has the CKD status of the participant before ICU admission. If the participant had a history of CKD, then we used the first available serum creatinine as the baseline serum creatinine level, not the MDRD back calculation. Last, we did not collect data on the drugs used by the participants which could affect the level of the serum creatinine.

Conclusion

In Indonesia, like other developing countries, many ICU patients are at risk of developing AKI. The incidence of AKI in our center was 43% and 48.5% had AKI stage

Abbreviations

AKI: Acute Kidney Injury; RRT: Renal Replacement Therapy; KDIGO: Kidney Disease Improving Global Outcome; APACHE: Acute Physiology and Chronic Health Evaluation; ICU: Intensive Care Unit; ESRD: End Stage Renal Disease; SOFA: Sequential Organ Failure Assessment; PD: Peritoneal Dialysis; IHD: Intermittent Hemodialysis; SLED: sustained low-efficiency dialysis; CRRT: Continuous Renal Replacement Therapy; GFR: Glomerular Filtration Rate; MDRD: Modification of Diet in Renal Disease; ADQI: Acute dialysis Quality Initiative; SD: Standard Deviation; VIF: Variance Inflation Factor; CKD: Chronic Kidney Disease.

Declarations

Ethics approval and consent to participate

The study protocol was reviewed by the institutional review boards (IRB No. B/2212/VIII/2016). The study was approved on 16 August 2016. Informed consent was waived.

Consent for publication

Not applicable

Availability of data and materials

The datasets used for the current study are available from the corresponding author if the requests are reasonable.

Authors' contributions

Conceived and designed the study: J, NS. Enrolled the participants and conducted the study: J, MH, VA, AJ, LH, VK, NS. Analyzed the data: J, NS. Wrote the paper: J, NS. All authors have read and approved the final manuscript.

Competing interests

All authors declare that they have no competing interests.

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Tables

Table 1. Patients' characteristics stratified by AKI status (N = 865)

Characteristics	Non-AKI (N=492)	AKI (n=373)	All (N=865)	P-value
Age, years, mean (sd)	55 (15)	58 (15)	57 (15)	0.008
Male sex, n (%)	297 (60.4)	219 (58.7)	516 (59.7)	0.62
Reimbursement	(N=486)	(N=362)	(N=848)	0.45 ¹
- Government officer	261 (53.7)	190 (52.5)	451 (53.2)	
- Private health insurance	0 (0.0)	2 (0.6)	2 (0.2)	
- Social security system	211 (43.4)	159 (43.9)	370 (43.6)	
- Cash/self-pay	14 (2.9)	10 (2.8)	24 (2.8)	
- Unknown	0 (0.0)	1 (0.3)	1 (0.1)	
BMI, n (%)				<0.001
- Underweight	14 (2.8)	16 (4.3)	30 (3.5)	
- Normal	421 (85.6)	287 (76.9)	708 (81.8)	
- Overweight	54 (11.0)	56 (15.0)	110 (12.7)	
- Obese	3 (0.6)	14 (3.8)	17 (2.0)	
Primary diagnosis, n (%)	(N=491)	(N=370)	(N=861)	<0.001
- Cardiovascular diseases	106 (21.6)	71 (19.2)	177 (20.6)	
- Endocrine Diseases	11 (2.2)	18 (4.9)	29 (3.4)	
- Gastrointestinal Diseases	13 (2.6)	18 (4.9)	31 (3.6)	
- Hematologic Diseases	1 (0.2)	1 (0.3)	2 (0.2)	
- Infectious Diseases	14 (2.9)	36 (9.7)	50 (5.8)	
- Neurologic Diseases	42 (8.6)	59 (15.9)	101 (11.7)	
- Oncologic Diseases	13 (2.6)	12 (3.2)	25 (2.9)	
- Renal Diseases	9 (1.8)	29 (7.8)	38 (4.4)	
- Respiratory Diseases	17 (3.5)	36 (9.7)	53 (6.2)	
- Rheumatologic Diseases	0 (0.0)	3 (0.8)	3 (0.3)	
- Surgical related diseases	265(54.0)	87(23.5)	352(40.9)	
Comorbidity, n (%)				
HT	210 (42.7)	147 (39.4)	357 (41.3)	0.33
DM	114 (23.2)	145 (38.9)	259 (29.9)	<0.001
CKD	3 (0.6)	43 (11.5)	46 (5.3)	<0.001 ¹
Cerebrovascular	4 (0.8)	11 (2.9)	15 (1.7)	0.017
Malignancy	24 (4.9)	18 (4.8)	42 (4.9)	0.97
CAD	52 (10.6)	19 (5.1)	71 (8.2)	0.004
APACHE-II score, mean (sd)	9.9 (4.4)	16.5 (7.3)	12.7 (6.7)	<0.001
Non-renal SOFA score, mean (sd)	3.0 (1.6)	5.0 (2.5)	3.9 (2.3)	<0.001
Vasopressors, n (%)	4 (0.8)	41 (11.0)	45 (5.2)	<0.001
Mechanical ventilation, n (%)	85 (17.3)	185 (49.6)	270 (31.2)	<0.001

BMI: body mass index, DM: diabetes mellitus, CAD: coronary artery disease, CVD: cerebrovascular disease, APACHE II: acute physiologic and chronic health evaluation II, SOFA: sequential organ failure assessment.

†All of these parameters came from the first day of ICU admission.

* P-value from Fisher's exact test

Table 2. Risk factors for AKI development using logistic regression analysis.† (N =850)

Characteristics‡	Unadjusted OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value
Age, 10-year increment	1.11 (1.02, 1.22)	0.019	0.90 (0.80, 1.02)	0.11
Male sex, n (%)	0.93 (0.70, 1.22)	0.598		
Reimbursement, N=834				
- Government officer	0.98 (0.74, 1.29)	0.869		
- Social security system	Reference			
- Private health insurance /Cash/self-pay	1.18 (0.53, 2.61)	0.690		
BMI				
- Underweight	1.60 (0.76, 3.36)	0.217	1.18 (0.48, 2.91)	0.73
- Normal	Reference		Reference	
- Overweight / obese	1.67 (1.14, 2.47)	0.009	1.55 (0.97, 2.49)	0.07
Primary diagnosis, N=846				
- Cardiovascular diseases	0.90 (0.64, 1.26)	0.528		
- Endocrine Diseases	2.31 (1.08, 4.95)	0.032	0.97 (0.38, 2.49)	0.95
- Gastrointestinal Diseases	1.94 (0.94, 4.02)	0.073	1.20 (0.49, 2.99)	0.69
- Hematologic Diseases	1.37 (0.09, 21.99)	0.824		
- Infectious Diseases	3.81 (2.02, 7.17)	<0.001	1.15 (0.51, 2.57)	0.74
- Neurologic Diseases	2.06 (1.35, 3.15)	0.001	0.97 (0.53, 1.77)	0.92
- Oncologic Diseases	1.27 (0.57, 2.83)	0.552		
- Renal Diseases	3.87 (1.61, 9.31)	0.003	4.53 (1.67, 12.33)	0.003
- Respiratory Diseases	2.92 (1.61, 5.32)	<0.001	1.53 (0.72, 3.25)	0.27
- Surgical related diseases	0.27 (0.20, 0.37)	<0.001	0.60 (0.39, 0.93)	0.021
Comorbidity				
HT	0.88 (0.66, 1.16)	0.348		
DM	2.05 (1.52, 2.77)	<0.001	1.08 (0.73, 1.61)	0.71
Cerebrovascular	3.83 (1.21, 12.13)	0.022	1.55 (0.39, 6.17)	0.53
Malignancy	1.02 (0.55, 1.91)	0.946		
CAD	0.47 (0.27, 0.81)	0.006	0.50 (0.26, 0.98)	0.042
APACHE-II score	1.21 (1.17, 1.25) per 1-point increase	<0.001	1.14(1.09, 1.20) per 1-point increase	<0.001
Non-renal SOFA score	1.62 (1.49, 1.76) per 1-point increase	<0.001	1.14 (1.00,1.31) per 1-point increase	0.050
Vasopressors	13.08 (4.61, 37.17)	<0.001	2.99 (0.93, 9.62)	0.067
Mechanical ventilation	4.76 (3.49, 6.51)	<0.001	1.29 (0.80, 2.08)	0.30

† 15 participants who had AKI as the primary diagnosis for ICU admission were excluded from the analysis
‡ All these parameters came from the first day of ICU admission
BMI: body mass index, DM: diabetes mellitus, CAD: coronary artery disease, CVD: cerebrovascular disease,
APACHE II: acute physiologic and chronic health evaluation I, SOFA: sequential organ failure assessment.

Table 3. Patients’ characteristics and risk factors for severity of AKI using logistic regression analysis (N=226)

Characteristics†	Severity of AKI, n (%)		Unadjusted OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value
	Non-severe (N=192)	Severe (N=181)				
Age, 10-year increment‡	59 (14)	57 (15)	0.93 (0.81, 1.07)	0.284		
Male sex, n (%)	98 (51.0)	121 (66.9)	1.93 (1.27, 2.94)	0.002	2.47 (1.48, 4.12)	0.001
Reimbursement, N=361						
- Government officer	96 (51.3)	94 (54.0)	1.04 (0.68, 1.59)	0.85		
- Social security system	82 (43.9)	77 (44.3)	Reference			
- Private health insurance/Cash/self-pay	9 (4.8)	3 (1.7)	0.35 (0.09, 1.36)	0.13		
BMI						
- Underweight	6 (3.1)	10 (5.5)	2.32 (0.82, 6.56)	0.11	2.26 (0.7, 7.32)	0.18
- Normal	167 (87.0)	120 (66.3)	Reference		Reference	
- Overweight / obese	19 (9.9)	51 (28.2)	3.74 (2.10, 6.65)	<0.001	2.26 (0.7, 7.32)	0.18
Primary diagnosis, N=370						
- Cardiovascular diseases	40 (21.1)	31 (17.2)	0.78 (0.46, 1.31)	0.35		
- Endocrine Diseases	12 (6.3)	6 (3.3)	0.51 (0.19, 1.39)	0.19	0.41(0.12, 1.44)	0.16
- Gastrointestinal Diseases	11 (5.8)	7 (3.9)	0.65 (0.25, 1.74)	0.40		
- Hematologic Diseases	0 (0.0)	1 (0.6)	NA			
- Infectious Diseases	13 (6.8)	23 (12.8)	2.00 (0.98, 4.07)	0.058	1.24 (0.51, 2.97)	0.64
- Neurologic Diseases	27 (14.2)	32 (17.8)	1.31 (0.75, 2.28)	0.35		
- Oncologic Diseases	6 (3.2)	6 (3.3)	1.06 (0.33, 3.34)	0.92		
- Renal Diseases	8 (4.2)	21 (11.7)	3.00 (1.30, 6.97)	0.010	1.5 (0.5, 4.56)	0.47
- Respiratory Diseases	16 (8.4)	20 (11.1)	1.36 (0.68, 2.71)	0.38		
- Rheumatologic Diseases	1 (0.5)	2 (1.1)	2.12 (0.19, 23.62)	0.54		
- Surgical related diseases	56 (29.5)	31 (17.2)	0.50 (0.30, 0.82)	0.006	0.8 (0.43, 1.49)	0.48
Comorbidity						
HT	70 (36.5)	77 (42.5)	1.29 (0.85, 1.96)	0.23		
DM	63 (32.8)	82 (45.3)	1.70 (1.11, 2.58)	0.014	1.15 (0.65, 2.02)	0.63
CKD	4 (2.1)	39 (21.5)	12.91 (4.51, 36.96)	<0.001	9.47 (3.1, 28.91)	<0.001
Cerebrovascular	8 (4.2)	3 (1.7)	0.39 (0.10, 1.48)	0.17		
Malignancy	6 (3.1)	12 (6.6)	2.20 (0.81, 5.99)	0.12	3.43 (1.11, 10.57)	0.032

CAD	10 (5.2)	9 (5.0)	0.95 (0.38, 2.40)	0.92		
APACHE-II score†	14.8 (6.9)	18.3 (7.3)	1.07 (1.04, 1.10) per 1-point increase	<0.001	1.07 (1.01, 1.13) per 1-point increase	0.018
Non-renal SOFA score†	4.6 (2.4)	5.5 (2.6)	1.14 (1.05, 1.24) per 1-point increase	0.002	0.92 (0.78, 1.08) per 1-point increase	0.29
Vasopressors	5 (2.6)	36 (19.9)	9.29 (3.55, 24.26)	<0.001	5.41 (1.8, 16.29)	0.003
Mechanical ventilation	83 (43.2)	102 (56.4)	1.70 (1.13, 2.55)	0.012	1.31 (0.69, 2.49)	0.41

† All of these parameters came from the first day of ICU admission

‡ Value in cell is mean (sd) instead of n (%)

BMI: body mass index, DM: diabetes mellitus, CAD: coronary artery disease, CVD: cerebrovascular disease, APACHE II: acute physiologic and chronic health evaluation II, SOFA: sequential organ failure assessment
NA: not included in the multivariable model even though the P-value was <0.20 because there were limited data

Table 4. Etiology of AKI

Etiology of AKI	N (%)
Renal hypoperfusion	76 (20.4)
Liver ^a	1 (0.3)
Cardiovascular ^b	71 (19.0)
Obstructive uropathy	16 (4.3)
Pregnancy ^c	3 (0.8)
Sepsis	206 (55.2)

^aRenal hypoperfusion included hypovolemic shock, dehydration, renal artery stenosis

^bLiver included hepatorenal syndrome, liver cirrhosis, acute liver failure, acute hepatitis

^c Cardiovascular included myocardial infarction, heart failure, heart valve disorder, pulmonary embolism, bacterial endocarditis, and cardiorenal syndrome.

^dPregnancy included preeclampsia

Table 5. Modes of RRT (initiation mode if many were used simultaneously)

Mode of RRT	N (%)
IHD	66 (71.7)
CRRT	4 (4.34)
PD	1 (1.08)
SLED	21 (22.8)

IHD: intermittent hemodialysis, CRRT: continuous renal replacement therapy, PD: peritoneal dialysis, SLED; sustained low efficiency dialysis

Figures

Figure 1

Study flow chart ICU, Intensive Care Unit; ESRD, End Stage Renal Disease; AKI, Acute Kidney Injury

Figure 2

Hospital mortality based on the Kaplan-Meier survival curves for each AKI stage