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Etiology and outcomes of anuria in acute kidney injury: a single center study

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Abstract

Background: It was previously known that anuric acute kidney injury (AKI) is uncommon and its occurrence suggests complete ureteral obstruction, shock, or a major vascular event. As the epidemiology of AKI has significantly changed over the past decade, it is possible that the incidence, etiology, or clinical characteristics of anuric AKI have also changed.

Methods: A prospective cohort study was conducted that included all patients undergoing renal replacement therapy (RRT) for AKI during a 2-year period in a tertiary hospital. Patients were classified as having anuric, oliguric, or nonoliguric AKI based on their volume of urine when RRT started using the modified Acute Kidney Injury Network criteria.

Results: Of the 203 patients included in the study, 21.2% met the criteria for anuric AKI. Septic and postoperative AKI were the main causes of anuric AKI, with 60.5% of incidences occurring in hospital. Anuric AKI was associated with a younger age, a lower prevalence of pre-morbid chronic kidney disease and diabetes, more frequent continuous RRT requirement, and multi-organ dysfunction. In addition, patients with anuric AKI had a higher rate of in-hospital mortality and long-term dependence on RRT than patients with nonanuric AKI.

Conclusion: Anuric AKI is common, with sepsis as the main etiological insult, and is associated with adverse outcomes among patients with AKI who require RRT.

Introduction

Acute kidney injury (AKI) may be described clinically as oliguric, nonoliguric, or anuric [1,2]. These categories may help to identify the cause and predict the prognosis of each episode of AKI, which may aid in guiding the appropriate diagnostic and therapeutic strategies. Classically, anuric AKI has been reported to be uncommon and is associated with complete ureteral obstruction, shock, or a major vascular event such as bilateral renal artery occlusion and cortical necrosis [1].

The incidence of AKI has been increasing recently and significant changes have occurred in the epidemiology of AKI during the past decade [3]. Several factors, such as older patients and a higher burden of illness, including significant comorbidities, might contribute to the increased incidence of AKI. In addition, patients are now more likely to undergo invasive diagnostic testing and complex surgery or interventions. There is a possibility that the

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incidence and etiology of anuric AKI have also changed; anuric AKI has recently been more commonly encountered in clinical practice even in patients without shock. Nevertheless, information is limited regarding the epidemiology of anuric AKI, although a number of anecdotal case reports have been published.

The aim of this study was to examine the causes, characteristics, and outcomes of patients with anuric AKI and to compare these findings with those for patients with nonanuric AKI. As virtually all patients who are anuric for ≥ 24 hours receive emergency renal replacement therapy (RRT), we selected those patients with the most severe form of AKI – that is, those who required RRT stage 3 based on the Acute Kidney Injury Network (AKIN) criteria [4]—to obtain similar clinical levels of AKI severity in the patients with anuric and nonanuric AKI. We determined the epidemiology of patients with AKI who required dialysis, considering, in particular, the volume of urine at the time of initiation of RRT and the association between urine volume and outcomes, including mortality and long-term dependence on RRT.

Methods

Study population and design

Between March 2010 and February 2012, all adult patients who received RRT for AKI were entered into a prospective registry at the Korea University Anam Hospital, Seoul, Korea. We included patients from both the intensive care unit (ICU; medical, surgical, and cardiac units) and general wards. Emergency RRT encompassed intermittent hemodialysis (IHD) and continuous RRT (CRRT), with the ICU offering both IHD and CRRT. The decision to start RRT was made by the nephrologists at the hospital based on the patients' clinical condition. The study was approved by the Institutional Review Board of the university and written informed consent was obtained from all patients.

We excluded patients with pre-existing advanced chronic kidney disease (CKD)—that is, any evidence of CKD stage 4 or clinically evident end-stage renal disease—for the following reasons: (1) when patients with advanced CKD receive unplanned dialysis, it is often unclear whether this is a result of AKI in addition to CKD, or a rapid progression of their CKD; and (2) the wide range of patients with CKD could have confounding effects on the results. Patients with terminal cancer or those who died within 48 hours of the start of RRT were also excluded because they are commonly in the final stages of multiple organ dysfunction syndrome (MODS), which is fatal.

The etiology was determined by the nephrologists based on the clinical diagnosis. When more than one etiology contributed to the AKI, the main factor was considered for the analysis.

Data collection and definitions

Oliguric AKI was defined as a urine output of < 7.2 mL/kg in 24 hours or anuria for 12 hours using the modified AKIN criteria at the time of initiation of RRT (within 1 day prior to or after the day of acute dialysis). However, oliguric patients with AKI with a urine volume of < 50 mL/d were classified as having anuric AKI. Anuria that started several days after the initiation of RRT was not defined as anuric AKI.

The CKD status was determined by evaluating the available data and history for each patient. CKD was defined according to the National Kidney Foundation classification, including known glomerulopathy or structural abnormality with normal estimated glomerular filtration rate (eGFR) [5], where CKD(3) included only patients with CKD stage 3. Patients without previous data, but who had an eGFR ≥ 60 mL/min/1.73 m^2 during the follow-up period were considered to have no prior CKD.

Hepatorenal syndrome was defined according to the 2007 revised hepatorenal syndrome criteria, which include infection as the cause [6]. Cardiorenal syndrome (CRS) was indicated as the main factor in patients with type 1 CRS as defined by the Acute Dialysis Quality Initiative consensus [7]. Hypovolemia was determined as the cause of AKI in patients with massive bleeding (e.g., from obstetric or gastrointestinal causes) or evident dehydration. Hospital-acquired AKI (HA-AKI) was defined as AKI occurring during admission to hospital, whereas community-acquired AKI (CA-AKI) was defined as AKI developing outside the hospital setting. MODS was defined as a patient with at least two of the following criteria: hepatic failure, heart failure, respiratory failure, or coagulopathy (disseminated intravascular coagulation).

The outcomes assessed included in-hospital mortality, 90-day survival, and long-term dialysis dependence (RRT for > 3 months, class E based on the Risk Injury Failure Loss End-Stage outcome criteria).

Statistical analysis

SPSS software, version 14.0 (SPSS Inc., Chicago, IL, USA) was used for the statistical analysis. Data are presented as mean $\pm$ standard deviation values or as absolute numbers with percentages. Comparisons between groups were performed using the Student t test, one-way analysis of variance, the χ^2 test, or Fisher's exact test, as appropriate.

We identified the prognostic factors for the 90-day survival in a Cox proportional hazards model by calculating the crude and adjusted hazard ratios. Variables with $P < 0.05$ in the univariate analyses were assessed as independent predictors using the multivariate model by the forward conditional method. We used Kaplan–Meier curves to demonstrate the relationship between the urine volume and survival. A log-rank test was used to compare the differences in survival.

Results

Study cohort

RRT was performed in 304 patients during the study period and 203 patients were included in the study (Fig. 1). Of the 101 patients excluded from the final study, 64 patients died within 48 hours of the initiation of RRT and 11 patients had pre-existing advanced CKD.

Of the 203 patients included in the study, 43 (21.2%) had anuria at the initiation of RRT despite supportive care, including hydration and diuretic drugs. Fifty-seven patients (28.1%) and 103 patients (50.7%) met the criteria for oliguric and nonoliguric AKI, respectively. A diuretic challenge with furosemide was administered in all patients with anuria and oliguria. We monitored and recorded the patients' urine output throughout the course of the treatment.

Etiology of anuric AKI

Table 1 gives the causes of AKI among patients with anuric, oliguric, and nonoliguric AKI. Sepsis was the most common

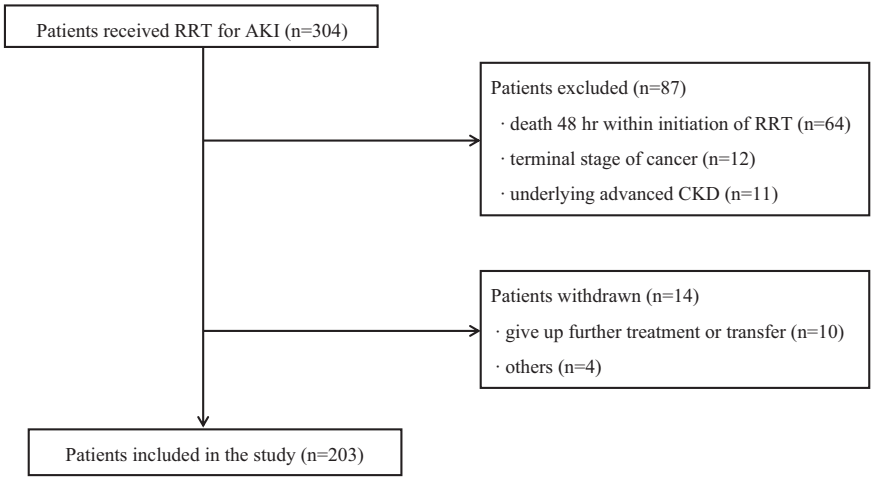

Figure 1. Study cohort.
AKI, Acute kidney injury; CKD, chronic kidney disease; RRT, renal replacement therapy.

Table 1. Causes of acute kidney injury requiring renal replacement therapy

	Anuric AKI ($n=43$)	Nonanuric AKI ($n=160$)	
		Oliguric ($n=57$)	Nonoliguric ($n=103$)
Hospital-acquired AKI	26 (60.5)	29 (50.9)	33 (32.0)
Cause of AKI			
Sepsis	18 (41.8)	29 (50.9)	49 (47.6)
Postoperative AKI	13 (30.2)	7 (12.3)	2 (1.9)
Cardiorenal syndrome	5 (11.6)	5 (8.8)	9 (8.7)
Hepatorenal syndrome	2 (4.7)	2 (3.5)	1 (1.0)
Nephrotoxic drugs	1 (2.3)	2 (3.5)	10 (9.7)
Postrenal*	–	–	11 (10.7)
Hypovolemia	–	3 (5.3)	10 (9.7)
Vasculitis, glomerulopathy	1 (2.3)	1 (1.8)	4 (3.9)
Rhabdomyolysis	1 (2.3)	4 (7.0)	–
Other	2 (4.7)	4 (7.0)	7 (6.8)

* Urinary tract obstruction from stone, malignancy etc.
Data are presented as *n* (%).
AKI, acute kidney injury.

cause of AKI in all groups (41.8%, 50.9%, and 47.6%, respectively). In patients with anuric AKI, postoperative AKI and CRS were the other main causes of AKI (30.2% and 11.6%, respectively). Classically well-known etiologies of anuric AKI, such as complete ureteral obstruction or a major vascular event, were rarely observed. Of note, postoperative AKI accounted for nearly one-third of patients with anuric AKI. Of the 13 patients with postoperative anuric AKI, seven had undergone gastrointestinal surgery and two had undergone transplantation (1 heart transplantation and 1 liver transplantation). Postoperative AKI developed a median (range) of 2 (1–5) days after surgery. The other causes of anuric AKI included hepatitis A and biopsy-proven acute tubulo-interstitial nephritis of unknown cause. The leading causes of nonoliguric AKI, other than sepsis, were postrenal (obstructive nephropathy from stones, malignancy etc), nephrotoxic drugs (or toxins), and hypovolemia (10.7%, 9.7%, and 9.7%, respectively).

In 48 patients (23.6%), multiple etiologies were thought to have contributed to the development of AKI, such as sepsis combined with drug administration. Overall, 43.3% of the cases of AKI requiring RRT occurred in hospital. HA-AKI was significantly more common in patients with anuric AKI than in patients with nonanuric AKI (60.5% vs. 38.8%, $P=0.015$). Sepsis was the major etiology of CA-anuric AKI (58.8%), whereas postoperative AKI was the major component of HA-anuric AKI (50.0%).

Characteristics of patients with anuric AKI

Table 2 gives the baseline demographics of the patients. There was a trend for patients with anuric AKI to be younger than those with nonanuric AKI (59.4 ± 19.9 vs. 65.4 ± 14.6, $P=0.058$). Interestingly, the prevalence of underlying CKD was lower in the anuric AKI group than in the nonanuric group [26.3% vs. 41.9%, $P=0.046$ for CKD; 21.1% vs. 36.9%, $P=0.056$, for CKD(3)]. The prevalence of diabetes was also significantly lower in the anuric AKI group than in the nonanuric AKI group (22.0% vs. 40.5%, $P=0.030$).

Table 3 presents a comparison of the clinical characteristics among patients with anuric, oliguric, and nonoliguric AKI. Serum creatinine (Cr) levels at the time of initiation of RRT were slightly lower in patients with anuric AKI and oliguric AKI than in patients with nonoliguric AKI, suggesting a delayed initiation of RRT when the urine output was maintained (4.04 ± 2.57 vs. 4.90 ± 2.91, $P=0.05$). However, peak serum Cr levels were not different among the three groups. Overall, 46.8% and 43.8% of the entire cohort received vasoactive drugs and mechanical ventilation at the time of initiation of RRT, respectively, with no significant difference among the groups. However, patients with anuric AKI were more likely to have MODS (39.5% vs. 19.4%, $P=0.008$) and were more likely to start RRT using CRRT rather than IHD (72.1% vs. 53.1%, $P=0.036$), although the RRT modality was changed during the disease course in several patients.

Outcomes of patients with anuric AKI

The in-hospital mortality rate was 44.8%, with 18.7% of discharged patients being dependent on dialysis. Patients with anuric AKI had a higher rate of in-hospital death (60.5% vs.

Table 2. Baseline characteristics of patients with acute kidney injury who required renal replacement therapy

	Anuric AKI ($n=43$)	Oliguric AKI ($n=57$)	Nonoliguric AKI ($n=103$)	P^*	$P_1^\dagger$	$P_2^\ddagger$
Age (y)	59.4 ± 19.9	64.0 ± 14.6	66.1 ± 14.6	0.072	0.071	0.058
Male sex	62.8	49.1	63.1	0.195	0.256	0.605
Baseline Cr (mg/dL)	1.01 ± 0.24	1.03 ± 0.34	1.12 ± 0.36	0.163	0.057	0.269
Baseline eGFR (mL/min/1.73 m^2)	75.1 ± 21.0	73.9 ± 23.6	70.4 ± 24.6	0.514	0.256	0.433
Comorbidities						
CKD	26.3	31.4	48.0	0.028	0.011	0.046
CKD(3)	21.1	26.9	42.9	0.024	0.009	0.056
Diabetes	22.0	36.8	42.6	0.069	0.105	0.030
Liver cirrhosis	5.0	17.0	6.0	0.047	0.205	0.532
Malignancy	26.2	21.4	18.8	0.614	0.488	0.396

* P, obtained by one-way ANOVA or χ^2 test among three groups.
† P_1, obtained by Student t test or Fisher's exact test between two groups (anuric+oliguric vs. nonoliguric).
‡ P_2, between two groups (anuric vs. oliguric+nonoliguric).
Data are presented as mean ± SD values or %.
ANOVA, analysis of variance; AKI, acute kidney injury; CKD, chronic kidney disease; Cr, creatinine; eGFR, estimated glomerular filtration rate; RRT, renal replacement therapy; SD, standard deviation.

Table 3. Clinical characteristics and outcomes of patients with acute kidney injury who required renal replacement therapy

	Anuric AKI ($n=43$)	Oliguric AKI ($n=57$)	Nonoliguric AKI ($n=103$)	P^*	$P_1^\dagger$	$P_2^\ddagger$
At start of dialysis						
Serum Cr (mg/dL)	3.8 ± 2.2	4.2 ± 2.8	4.9 ± 2.9	0.071	0.050	0.091
ICU treatment	81.4	86.0	70.9	0.071	0.030	0.543
Vasoactive drugs	53.5	49.1	42.7	0.453	0.262	0.390
Mechanical ventilator	46.5	50.9	38.9	0.215	0.095	0.492
RRT mode (CRRT)	72.1	64.9	46.6	0.007	0.003	0.036
MODS	39.5	29.8	13.6	0.002	0.001	0.008
Peak serum Cr (mg/dL)	5.3 ± 2.7	5.0 ± 2.8	5.4 ± 2.9	0.701	0.465	0.980
In-hospital deaths	60.5	52.6	34.0	0.005	0.002	0.025
Survivors ($n=112$)						
RRT dependence for at least 3 mo	41.2	22.2	10.3	0.010	0.012	0.013

* P obtained by one-way ANOVA or χ^2 test among three groups.
† P_1 obtained by Student t test or Fisher's exact test between two groups (anuric+oliguric vs. nonoliguric).
‡ P_2 between two groups (anuric vs. oliguric+nonoliguric).
Data are presented as mean ± SD values or %.
ANOVA, analysis of variance; AKI, acute kidney injury; CRRT, continuous renal replacement therapy; Cr, creatinine; ICU, intensive care unit; MODS, multiple organ dysfunction syndrome; RRT, renal replacement therapy; SD, standard deviation.

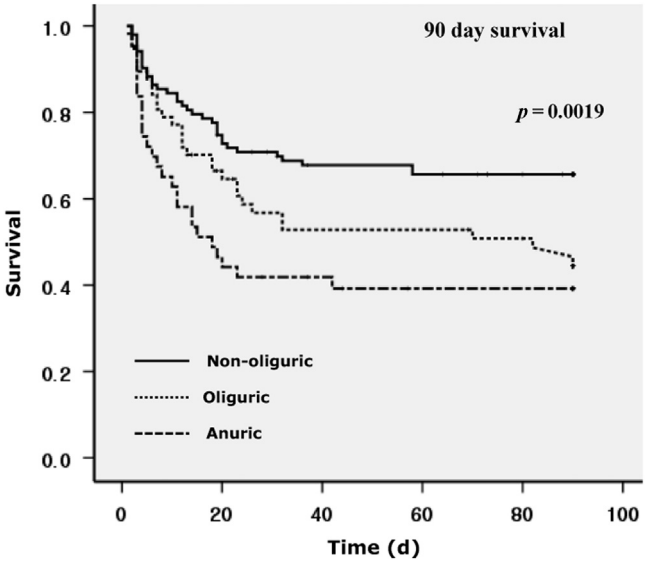

Figure 2. Overall survival curves according to the volume of urine at the time of initiation of renal replacement therapy.

40.6%, $P=0.025$) and a higher rate of long-term dependence on RRT among the survivors (41.2% vs. 13.7%, $P=0.013$) than patients with nonanuric AKI (Table 3).

We plotted Kaplan–Meier survival curves stratified by urine volumes at the time of initiation of renal replacement therapy. Fig. 2 shows that a decreased volume of urine was associated with lower survival ($P=0.0019$ by the log-rank test).

Table 4 shows the factors that significantly correlated with survival based on the univariate and multivariate comparisons in the Cox proportional hazards model. An univariate analysis demonstrated that septic AKI, HA-AKI, the presence of liver cirrhosis, the use of vasopressors and mechanical ventilation, a requirement for CRRT, lower serum Cr at initiation of RRT, and the presence of anuria were associated with lower survival, whereas the presence of pre-existing CKD was associated with greater survival.

After multivariate adjustment, septic AKI, the use of mechanical ventilation, low serum Cr levels at the initiation of RRT, and the presence of anuria remained independently associated with the 90-day mortality in the heterogeneous population in whom RRT was started for AKI. Patients with anuric AKI had a 1.86-fold increased risk of death within 90 days compared with the patients with nonanuric AKI.

Stratified analysis and subgroup analysis

As pre-existing CKD was, unexpectedly, significantly more common in patients with nonanuric AKI and was associated with lower mortality in the univariate analysis, we stratified patients

Table 4. Univariate and multivariate analyses for predicting 90-day mortality rates

	Univariate analysis		Multivariate analysis *	
	Crude HR (95% CI)	*P*	Adjusted HR (95% CI)	*P*
Age (y)	1.00 (0.99–1.02)	0.513		
Male sex	1.31 (0.86–2.01)	0.214		
Cause of AKI (septic)	2.64 (1.71–4.07)	<0.001	1.69 (1.04–2.76)	0.036
Cause of AKI (postoperative)	0.41 (0.16–1.01)	0.052		
Hospital-acquired AKI	1.77 (1.17–2.67)	0.007		
Baseline Cr (mg/dL)	0.56 (0.27–1.16)	0.119		
Baseline eGFR (mL/min/1.73 m^2)	1.01 (1.00–1.02)	0.128		
Comorbidities				
CKD	0.52 (0.28–0.96)	0.048		
Diabetes	0.77 (0.49–1.21)	0.263		
Liver cirrhosis	1.99 (1.05–3.77)	0.033		
Malignancy	1.09 (0.66–1.79)	0.745		
At the time of dialysis				
Vasoactive drug	4.93 (3.10–7.86)	<0.001		
Mechanical ventilation	7.36 (4.48–12.08)	<0.001	5.15 (2.89–9.18)	<0.001
RRT Mode (CRRT)	4.10 (2.46–6.81)	<0.001		
Serum Cr (mg/dL)	0.67 (0.59–0.77)	<0.001	0.77 (0.67–0.90)	0.002
Anuric AKI	1.90 (1.21–3.00)	0.006	1.86 (1.11–3.11)	0.019

* Variables with $P < 0.05$ in the univariate analyses were assessed as independent predictors using the multivariate model by the forward conditional method.

AKI, acute kidney injury; CI, confidence interval of the estimated HR; CKD, chronic kidney disease; CRRT, continuous renal replacement therapy; Cr, creatinine; eGFR, estimated glomerular filtration rate; HR, hazard ratio estimated from the Cox proportional hazard model; RRT, renal replacement therapy.

Table 5. Clinical characteristics according to the presence of chronic kidney disease

Variable	Without prior CKD	With prior CKD	*P*
Age (y)	61.1 ± 17.1	69.7 ± 12.1	< 0.001
Male sex	64.4	49.3	0.051
Baseline Cr (mg/dL)	0.90 ± 0.17	1.45 ± 0.34	< 0.001
Baseline eGFR (mL/min/1.73 m^2)	84.6 ± 17.6	47.8 ± 14.7	< 0.001
At the time of RRT initiation			
Vasoactive drugs	51.5	38.0	0.077
Mechanical ventilation	47.7	36.6	0.140
Modality of RRT (CRRT)	64.4	43.7	0.005
MODS	28.8	14.1	0.024
Serum Cr (mg/dL)	5.57 ± 3.0	3.14 ± 1.57	0.003
Anuric AKI	24.6	13.9	0.056
Anuria+Oliguric AKI	55.3	34.7	0.007
Peak serum Cr (mg/dL)	4.97 ± 2.66	5.74 ± 2.88	0.070
Outcome			
In-hospital mortality	50.8	33.8	0.026
RRT dependence for at least 3 mo	16.9	19.1	0.806

Data are presented as mean ± SD values or %.

AKI, acute kidney injury; CKD, chronic kidney disease; Cr, creatinine; CRRT, continuous renal replacement therapy; eGFR, estimated glomerular filtration rate; MODS, multiple organ dysfunction syndrome; RRT, renal replacement therapy; SD, standard deviation.

according to the presence of underlying CKD and compared their characteristics and outcomes (Table 5). The mean baseline eGFR was 84.6 ± 17.6 mL/min/1.73 m^2 and 47.8 ± 14.7 mL/min/1.73 m^2 in the non-CKD and CKD groups, respectively. Patients without pre-morbid CKD were younger, predominantly male, and were associated with a higher acuity of illness, as evidenced by the need for more frequent CRRT and MODS at the initiation of dialysis, suggesting that the insult causing AKI may have been greater.

In addition, we performed a subgroup analysis among patients who did not have MODS ($n = 155$). Anuria was not significantly associated with a lower survival in the multivariate Cox proportional hazards model. However, the presence of anuria was the only significant predictor of long-term dependence on RRT among discharged patients in the multivariate Cox regression analysis (hazard ratio 3.124; confidence interval 1.25–7.83; $P = 0.015$; data not shown).

Discussion

We found that anuric AKI was present in a substantial proportion of patients with AKI who required dialysis. Sepsis was the most common cause contributing to the development of AKI in both the anuric and nonanuric AKI groups. Postoperative AKI and CRS were the other main causes of anuric AKI and 60.5% of the cases of anuric AKI occurred in hospital. Patients with anuric AKI were younger, had a lower prevalence of pre-morbid CKD and diabetes, and were more likely to have MODS than patients with nonanuric AKI. Patients with anuric AKI had a

higher rate of long-term dependence on RRT and a lower survival rate. After controlling for potential confounders in the multivariate Cox analysis, the presence of anuria remained independently associated with a higher risk of death.

Although this study was conducted at a single center, it has several important strengths. First, our cohort included patients who received acute RRT for AKI, by both hemodialysis and CRRT, in the ICU and on other wards. Although there have been many advances in the definitions and epidemiology of AKI during the past decade, our current understanding is based almost exclusively on studies of critically ill patients in the ICU. The incidence of patients receiving their first RRT for AKI in the wards is reported to be up to 40–50% [8]. In this study, 21.2% of the total cohort received their first RRT in the ward; even for patients with anuric AKI, 18.6% of acute dialysis was performed in the wards (postoperative, rhabdomyolysis, and acute tubulo-interstitial nephritis). Notably, 41.8% of the patients with anuric AKI did not have shock, did not require vasoactive drugs nor mechanical ventilation, and had no evidence of MODS. Second, we captured extensive data on comorbidities, which allowed us to adjust for these factors when considering the outcomes. In particular, we recorded the baseline serum Cr level of each patient, whereas many previous studies on CKD have only determined the presence of CKD, used admission databases for the baseline Cr, or assigned a GFR of 75 mL/min/1.73 m^2 to patients without a known history of CKD. Third, we assessed the influence of the volume of urine in the most severe form of AKI using the AKIN urine output criteria.

Overall, sepsis was the primary contributing factor in 47.2% of patients, which is in accordance with the findings of several studies, with rates ranging from 32% to 48% in a cohort of ICU patients [9–11]. Moreover, sepsis was the most common cause of anuric AKI (41.8%) and was an independent risk factor for mortality.

The overall in-hospital mortality rate in the cohort was 44.8%, which is similar to the mortality rates in previous studies: 38–65.9% (in-hospital) and 48.3% (90-day) in patients with AKI requiring dialysis [8,12,13]. However, the clinical outcomes were significantly worse in patients with anuric and oliguric AKI, despite all the patients with severe AKI requiring dialysis and the peak serum Cr concentrations being comparable among groups. Patients with anuric AKI had higher in-hospital mortality rates and were more likely to become dependent on dialysis than patients with nonanuric AKI.

Severe AKI in which the GFR falls to very low levels is not necessarily associated with a parallel reduction in the output of urine, which can vary from oliguria to relatively normal values [14]. Although oliguric AKI has previously been found to be associated with a poor prognosis compared with nonoliguric AKI, the exact mechanisms remain uncertain [14–17]. Pharmacological conversion from oliguric to nonoliguric status has not resulted in improved AKI survival [18]. There are several possible explanations for the poor prognosis of patients with anuric AKI in this present. First, the severity of parenchymal structural change may be greater in patients with anuric AKI than in patients with nonanuric AKI, despite comparable peak serum Cr levels. It has been previously shown in animal models that tubular damage was more pronounced in oliguric kidneys than in nonoliguric kidneys, although the glomerular injuries were not significantly different [19]. Therefore it is possible that patients with anuric AKI have more tubular injuries and greater tubular back-leakage, although the GFR might be comparable among groups. Second, it is likely that anuria frequently occurs in the context of multi-organ failure and the critical illness that underlies the AKI becomes overwhelming. This explanation is supported by the results showing that anuric AKI was more frequently associated with MODS and requirement for CRRT, despite the comparable hemodynamic instability (e.g., the use of vasoactive drugs or ICU care). Third, maintaining urine output may confer direct outcome benefits. It is easier to control the volume status, hemodynamic stability, and RRT interval in nonoliguric patients. It has also been reported that excessive fluid retention *per se* is an independent risk factor for mortality, although we did not assess the fluid balance in this study [20].

An interesting finding was that pre-existing CKD or diabetes were associated with a maintained urine volume rather than anuria (Table 2). It is well-known that underlying CKD increases the risk of developing AKI (i.e., it predisposes patients to AKI) [21] and recent studies have suggested that AKI accelerates the progression of CKD [22]. However, the influence of pre-existing CKD on AKI is unclear.

In terms of the outcome of AKI, previous studies have not infrequently described that prior CKD is associated with lower in-hospital mortality rates for critically ill patients with AKI [8,23,24]. In this study, the presence of CKD was associated also with better survival in the univariate analysis. One plausible explanation for this paradoxical association is that patients with underlying CKD may require a lower burden of disease to reach the point where dialysis is needed, whereas those without CKD represent an extremely ill cohort; our explanation is supported by the results in Table 5, which show that patients without prior CKD were more frequently associated with a requirement for CRRT and MODS. More importantly, pre-existing CKD was not independently associated with mortality after adjusting for other covariates in the multivariate Cox proportional hazards model.

Apart from the relation between the outcome of AKI and pre-existing CKD, there are limited data about the influence of CKD on the clinical features of AKI. In this study, prior CKD was associated with maintained urine volume rather than oliguria, which may have potential explanations. First, as mentioned earlier, CKD patients have a lower burden of disease and start RRT at an earlier stage. Hence the degree of renal structural injury might be lower in patients with CKD than in patients without CKD. Second, patients with CKD may have an altered susceptibility to the insults that cause AKI by innate mechanisms such as “ischemic preconditioning” [25]. Therefore younger patients and those without prior CKD may fail a kidney “stress test” more easily after exposure to acute insults and the clinical features may show as “anuria”, whereas patients with CKD could maintain their urine output to some degree by unclear mechanisms. The resulting short-term and long-term prognoses of AKI between the two groups might be worthy of further research.

In addition, as only patients in the early stages of CKD were included in this study, our findings should be interpreted with caution; patients with advanced CKD or end-stage renal disease might show different patterns of disease course. In fact, Oppert et al [26] have previously reported that the ICU and hospital mortality rates were markedly higher in patients with pre-existing dialysis-dependent renal failure than in those with CKD not dependent on dialysis or those without AKI.

In conclusion, anuric AKI was not rare, with the most common cause of AKI being sepsis. Anuric AKI was more frequently observed in younger patients without prior CKD and was

associated with higher mortality rates and dependence on RRT. Whether the renal outcomes of patients with anuric, oliguric, and nonoliguric AKI will continue to diverge after hospital discharge remains uncertain, but deserves further investigation.

Conflict of interest

The authors declare that they have no competing interests.

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