Clinical Kidney Journal, 2025, vol. 18, no. 1, sfae382

https://doi.org/10.1093/ckj/sfae382
Advance Access Publication Date: 29 November 2024
Original Article

ORIGINAL ARTICLE

Outcomes of patients with infective endocarditis–associated acute kidney injury: a retrospective cohort study

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ABSTRACT

Background. The outcomes of patients with infective endocarditis (IE)-associated acute kidney injury (AKI) are poorly understood.

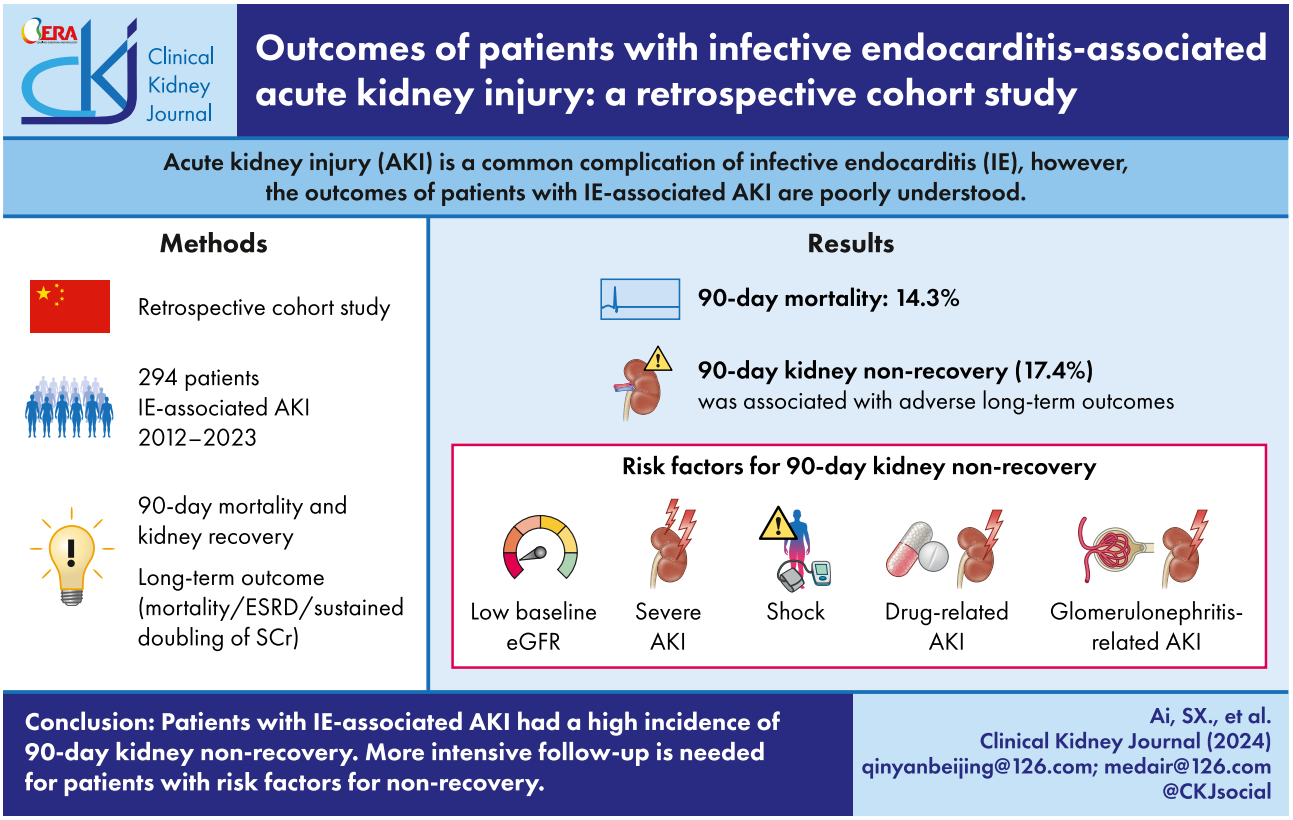
Methods. This retrospective cohort study was conducted in a tertiary hospital in China to analyze the short- and long-term outcomes among patients with IE-associated AKI. The risk factors for 90-day mortality, long-term outcomes and kidney non-recovery were analyzed via multivariable logistic regression, the Cox regression, and the Fine–Gray competing risk model, respectively.

Results. Among 294 patients with IE-associated AKI, 14.3% died within 90 days, and the risk factors for 90-day mortality were similar to those identified in the general IE population. Among the 230 AKI survivors in whom 90-day kidney recovery could be assessed, 17.4% did not recover kidney function at 90 days. Kidney non-recovery at 90 days was associated with an increased risk of the long-term composite outcome of mortality, end-stage renal disease or sustained doubling of serum creatinine [hazard ratio (HR) 3.00, 95% confidence interval (CI) 1.19–7.59]. Five variables were related to kidney non-recovery: low baseline estimated glomerular filtration rate (eGFR) (HR 2.52, 95% CI 1.73–3.65), stage of AKI (HR 3.03, 95% CI 2.07–4.42 for stage 3), shock (HR 5.56, 95% CI 3.02–10.22), glomerulonephritis-related AKI (HR 3.04, 95% CI 1.93–4.77) and drug-related AKI (HR 2.77, 95% CI 1.86–4.13).

Conclusion. Patients with IE-associated AKI had a high 90-day mortality, and a substantial proportion of survivors did not recover kidney function at 90 days. Kidney non-recovery at 90 days was associated with adverse long-term outcomes. Low baseline eGFR, severe AKI, shock, drug-related AKI and glomerulonephritis-related AKI were risk factors for kidney non-recovery.

Received: 26.5.2024; Editorial decision: 23.10.2024

GRAPHICAL ABSTRACT



Keywords: acute kidney injury, infective endocarditis, kidney recovery, long-term outcomes

KEY LEARNING POINTS

What was known:

- Acute kidney injury (AKI) is a common complication of infective endocarditis (IE).
- Previous studies reported in-hospital mortality among patients with IE-associated AKI, but data on kidney recovery and long-term outcomes are scarce.

This study adds:

- In the largest cohort of IE-associated AKI (294 cases) published to date, 14.3% of patients died within 90 days, and 17.4% of survivors did not recover kidney function at 90 days.
- Kidney non-recovery at 90 days was associated with adverse long-term outcomes.
- Low baseline estimated glomerular filtration rate, AKI severity, shock, drug-related AKI and glomerulonephritis-related AKI were risk factors for kidney non-recovery.

Potential impact:

- The study revealed a high incidence of 90-day kidney non-recovery and its impacts on long-term outcomes among patients with IE-associated AKI.
- Several risk factors for kidney non-recovery were identified, highlighting more intensive follow-up for patients with these risk factors.

INTRODUCTION

Infective endocarditis (IE) is a potentially lethal disease associated with severe complications and substantial mortality. Acute kidney injury (AKI) is a common complication among patients with IE, with an incidence of 30%–60% reported in previous studies [1–4], and is associated with an increased risk of mortality and adverse kidney events [1–5].

Although previous studies have reported a high in-hospital mortality in patients with IE-associated AKI [1–5], few of them evaluated the prognostic factors of mortality. In addition, AKI recovery at 3 months is associated with long-term mortality and

kidney outcomes in other AKI populations [6–8]. However, data on kidney recovery and long-term outcomes among patients with IE-associated AKI are scarce.

Therefore, we conducted this retrospective cohort study aiming to evaluate the prognostic factors of 90-day mortality and kidney recovery as well as the association between 90-day kidney recovery and long-term outcomes among patients with IE-associated AKI.

MATERIALS AND METHODS

Study design and patients

This was a retrospective cohort study, and findings were reported according to the STROBE (STrengthening the Reporting of OBservational studies in Epidemiology) checklist. Data for this study were obtained from Peking Union Medical College Hospital (Beijing, China), a tertiary hospital with comprehensive experience in the treatment of IE. All adult patients hospitalized between August 2012 and May 2023 for an acute episode of possible or definite IE (according to the modified Duke criteria [9]) were retrieved. Then, patients who developed AKI during the index hospitalization for IE were identified by reviewing medical charts. Participants with end-stage renal disease (ESRD) [estimated glomerular filtration rate (eGFR) <15 mL/min/1.73 m^2 or chronic dialysis] at baseline or incomplete files were excluded. The study was approved by the institutional review board of Peking Union Medical College Hospital (K4420-K23C2137).

Definitions

IE-associated AKI was defined as development of AKI during the hospitalization for IE. We applied the Kidney Disease: Improving Global Outcomes (KDIGO) criteria to define and stage AKI. AKI was defined as an increase in serum creatinine (SCr) by ≥0.3 mg/dL within 48 h or to 1.5 times baseline within 7 days [10]. Baseline SCr was sought in each patient's medical records before the IE admission. When unavailable, the lowest SCr during hospitalization and follow-up was used if the eGFR was ≥75 mL/min/1.73 m^2. In the remaining cases, the baseline SCr was imputed based on a Modification of Diet in Renal Disease (MDRD) eGFR of 75 mL/min/1.73 m^2 as per the KDIGO AKI guidelines [11]. Kidney recovery after AKI was defined as SCr within 25% of the baseline [6]. IE-associated glomerulonephritis was defined as the presence of hematuria with primarily dysmorphic red blood cells and/or proteinuria associated with IE.

Outcomes

The short-term outcomes included mortality and kidney recovery within 90 days after AKI. The long-term outcome was a composite outcome of all-cause mortality, ESRD or sustained doubling of SCr, which were assessed from 90 days after the AKI event to 20 August 2023, or the last follow-up before that date. The long-term outcomes were identified using medical records and/or telephone interviews. ESRD or sustained doubling of SCr was determined using the most recent SCr measurements within 6 months of the last follow-up. For patients who reached the endpoint of ESRD or sustained doubling of SCr, the frequencies of SCr measurements were recorded and compared between patients with kidney recovery and those without to minimize ascertainment bias differences between the two groups.

Covariates

Covariates were chosen based on literature review, including demographics, body mass index, comorbidities, baseline kidney function, characteristics and complications of IE, intensive care unit (ICU) admission, cardiac surgery, stage of AKI and adjudicated etiology of AKI.

The study investigators performed manual chart review to determine potential etiologies of AKI for each patient based on clinical presentation, laboratory testing and biospy results, if available. The adjudicated etiologies were primarily categorized into hemodynamic factors, drugs and IE-associated glomerulonephritis. Surgery, hypovolemia, heart failure and shock were classified as hemodynamic factors.

During the analysis of the prognostic factors for long-term outcomes, kidney recovery at 90 days after AKI (90-day kidney recovery) was a candidate variable, which was assessed using the SCr drawn closest to 90 days after AKI (range 30–180 days) [6]. Patients who had no SCr measurements during the specified recovery period (30–180 days) were classified as 90-day recovery unknown.

Statistical analysis

Continuous variables were expressed as mean ± standard deviation or median [interquartile range (IQR)] and analyzed via Student's *t*-test or Mann–Whitney U based on the normality of data. Categorical variables were reported as *n* (%) and compared by χ^2 or Fisher's exact test as appropriate.

Multivariable logistic regression identified pertinent factors for mortality within 90 days by incorporating significant ($P < .10$) univariate indicators into the models iteratively through forward stepwise selection methodology.

Survival curve and log-rank test analysis evaluated the relationship between 90-day kidney recovery status and the long-term outcome via the Kaplan–Meier method. Patients with unknown 90-day recovery status or those lost to follow-up after 90 days were not included in the analysis. The Cox proportional hazards model determined predictors of the long-term outcome, with univariate indicative covariates ($P < .10$) incorporated in the multivariable model through forward stepwise selection.

During the examination of potential hazard indicators linked with kidney non-recovery within 90 days after AKI, mortality constituted a competing event of kidney recovery. The Fine–Gray competing risk model was utilized to evaluate the influence of perilous variables towards kidney non-recovery. Variables demonstrating a *P*-value <0.10 in univariable analysis were incorporated into multivariable competing risk model. To minimize measurement errors of the time to kidney recovery introduced by unspecified frequencies of SCr measurements after AKI, we required evidence of kidney non-recovery within 7 days before kidney recovery.

SPSS version 26 and R 4.3 with the cmprsk package executed all computations. The significance level was set at $P < .05$.

RESULTS

Patient characteristics

Between August 2012 and May 2023, 667 adult patients hospitalized for an acute episode of IE were identified after excluding patients with ESRD or incomplete files. Of these patients, 294 (44%) experienced AKI during hospitalization (Fig. 1), including 133 with AKI stage 1, 65 with stage 2 and 96 with stage 3 (60 required dialysis). Baseline SCr before the admission for IE was

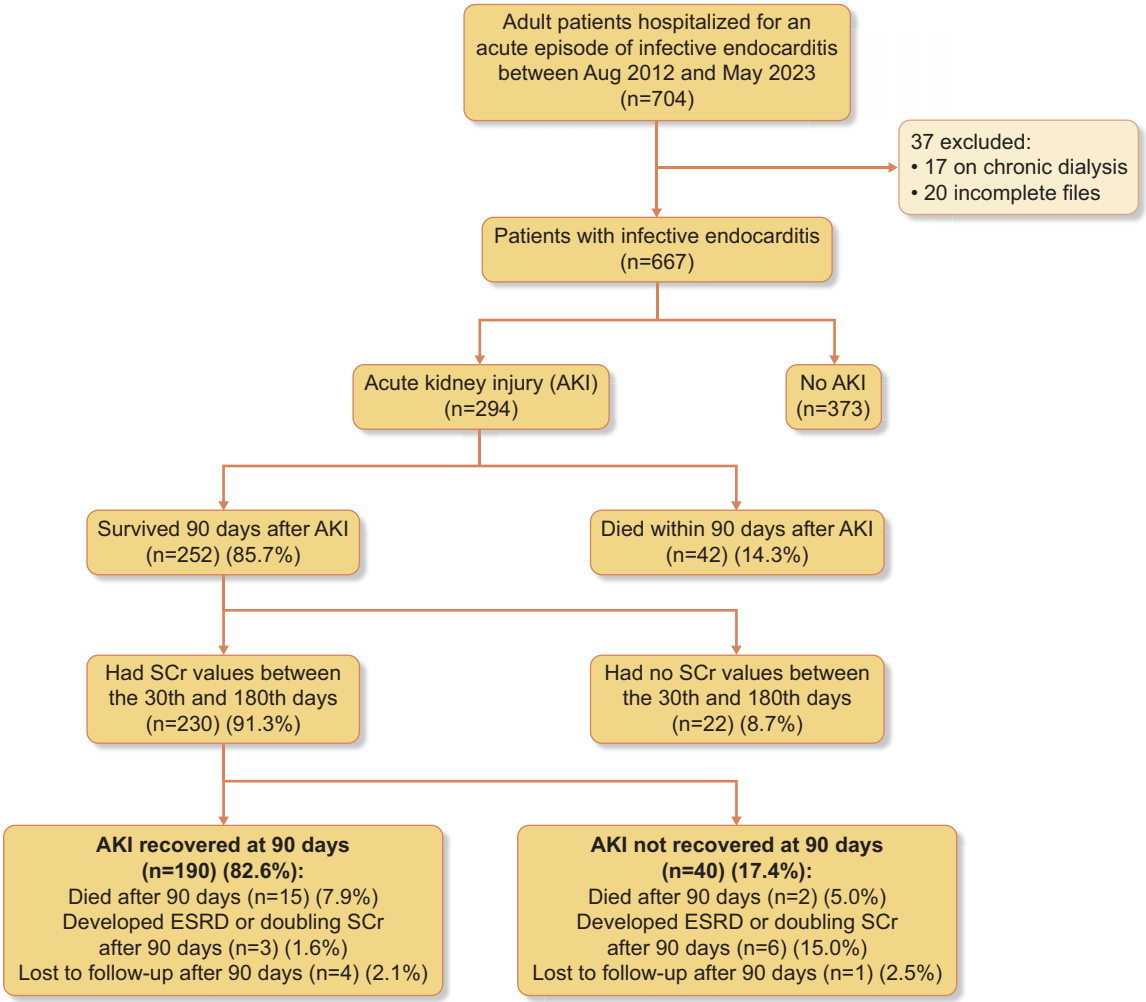


Figure 1: Study flowchart.

available for 99 patients. The lowest SCr during hospitalization and follow-up (eGFR ≥75 mL/min/1.73 m^2) was used as baseline SCr in 176 patients. In the remaining 19 cases with no past history of kidney diseases, the baseline SCr was imputed based on a MDRD eGFR of 75 mL/min/1.73 m^2.

Table 1 shows the clinical characteristics of patients with IE-associated AKI. The median age of patients was 52 years, with a predominance of males (69.4%). Prosthetic valves were involved in 11.6% of patients. *Streptococcus viridans* were the most common microorganisms (33.4%), followed by *Staphylococcus aureus* (18.1%). Complications were common, including decompensated heart failure (New York Heart Association classification III–IV) (53.1%), shock (21.1%, primarily cardiac and septic shock) and embolism (57.5%). All patients received antibiotics, and 85.4% underwent cardiac surgery during hospitalization. A total of 239 patients had ICU stays, including 64 patients who were admitted to the ICU before cardiac surgery.

The most frequently adjudicated etiologies of AKI were hemodynamic factors (91.5%), including surgery (67.3%), heart failure (29.6%), shock (17.7%) and hypovolemia (15.0%). Drugs and IE-associated glomerulonephritis were identified as etiologies of AKI in 27.9% and 14.3% of cases, respectively. The causal drugs of AKI were predominantly antibiotics, with vancomycin as the most frequent culprit. IE-associated glomerulonephritis was identified as the etiology of AKI in 42 patients, among whom 23 were diagnosed with rapidly progressive glomerulonephritis, and 6 underwent kidney biopsy.

Risk factors for mortality within 90 days

The mortality within 90 days after AKI was 14.3% (42/294). A comparison of characteristics of patients who died or survived is presented in Table 1. In multivariable analysis, five variables were independently associated with 90-day mortality: age >65 years [odds ratio (OR) 3.81, 95% CI 1.26–11.54], heart failure (OR 6.65, 95% CI 1.89–23.37), shock (OR 31.97, 95% CI 10.45–97.79), cerebral embolism (OR 3.95, 95% CI 1.40–11.10) and surgery (OR 0.07, 95% CI 0.02–0.21) (Table 2). A trend towards increasing mortality with the AKI stage was noted, but statistical significance was not reached.

Ninety-day kidney recovery and its impact on long-term outcomes

Among the 252 patients who survived 90 days after AKI, 90-day kidney recovery could be assessed in 230 patients who had SCr measurements during the specified period (30–180 days). The remaining 22 patients were classified as 90-day recovery

Table 1: Patient characteristics.

	All AKI ($n = 294$)	Died ($n = 42$)	Survived ($n = 252$)	P of died versus survived	Not recovered at 90 days ($n = 40$)	Recovered at 90 days ($n = 190$)	P of recovered versus not recovered
Age (years), median (IQR)	52 (39–60)	57 (43–67)	50 (38–59)	.012	54 (43–64)	50 (37–58)	.065
>65 years, *n* (%)	46 (15.6)	14 (33.3)	32 (12.7)	.001	9 (22.5)	20 (10.5)	.038
Male sex, *n* (%)	204 (69.4)	26 (61.9)	178 (70.6)	.256	23 (57.5)	142 (74.7)	.028
BMI[a]	22.51 ± 3.72	22.50 ± 3.95	22.51 ± 3.69	.989	21.82 ± 2.99	22.73 ± 3.76	.168
Comorbidities, *n* (%)							
Hypertension	89 (30.3)	15 (35.7)	74 (29.4)	.407	15 (37.5)	51 (26.8)	.176
Diabetes	36 (12.2)	5 (11.9)	31 (12.3)	.942	3 (7.5)	26 (13.7)	.284
Coronary heart disease	38 (12.9)	5 (11.9)	33 (13.1)	.831	7 (17.5)	24 (12.6)	.412
Cerebrovascular disease	26 (8.8)	5 (11.9)	21 (8.3)	.393	7 (17.5)	13 (6.8)	.056
Malignancy	18 (6.1)	7 (16.7)	11 (4.4)	.007	2 (5.0)	8 (4.2)	.687
Characteristics of IE, *n* (%)							
Right-sided IE	53 (18.0)	3 (7.1)	50 (19.8)	.047	5 (12.5)	38 (20.0)	.269
Prosthetic valve	34 (11.6)	8 (19.0)	26 (10.3)	.117	7 (17.5)	19 (10.0)	.176
Microorganisms[b], *n* (%)				.153			.159
Streptococcus viridans	98 (33.4)	9 (21.4)	89 (35.5)		10 (25.6)	72 (37.9)	
Staphylococcus aureus	53 (18.1)	12 (28.6)	41 (16.3)		4 (10.3)	33 (17.4)	
Other	69 (23.5)	11 (26.2)	58 (23.1)		11 (28.2)	42 (22.1)	
Culture negative	73 (24.9)	10 (23.8)	63 (25.1)		14 (35.9)	43 (22.6)	
Heart failure (NYHA III–IV)	156 (53.1)	36 (85.7)	120 (47.6)	<.001	23 (57.5)	86 (45.3)	.159
Shock	62 (21.1)	32 (76.2)	30 (11.9)	<.001	8 (20.0)	20 (10.5)	.111
Embolism	169 (57.5)	26 (61.9)	143 (56.7)	.531	19 (47.5)	108 (56.8)	.280
Cerebral embolism	91 (31.0)	20 (47.6)	71 (28.2)	.012	11 (27.5)	54 (28.4)	.906
Pulmonary embolism	40 (13.6)	4 (9.5)	36 (14.3)	.405	5 (12.5)	29 (15.3)	.655
Kidney embolism	8 (2.7)	2 (4.8)	6 (2.4)	.320	0 (0.0)	4 (2.1)	>.999
Hematuria[c]	177 (64.1)	23 (65.7)	154 (63.9)	.834	25 (65.8)	117 (63.9)	.828
Proteinuria[c]	119 (43.1)	18 (51.4)	101 (41.9)	.288	19 (50.0)	74 (40.4)	.277
Surgery	251 (85.4)	19 (45.2)	232 (92.1)	<.001	38 (95.0)	173 (91.1)	.540
ICU stay	239 (81.3)	38 (90.5)	201 (79.8)	.099	37 (92.5)	148 (77.9)	.034
Baseline kidney function							
Serum creatinine (μmol/L), median (IQR)	70 (61–81)	72 (61–94)	70 (60–80)	.136	73 (64–92)	70 (60–80)	.122
eGFR (mL/min/1.73 m^2), median (IQR)	106 (85–130)	91 (75–123)	108 (89–131)	.006	94 (79–121)	112 (91–133)	.001
eGFR categories (mL/min/1.73 m^2), *n* (%)				.002			.008
≥120	103 (35.0)	11 (26.2)	92 (36.5)		10 (25.0)	72 (37.9)	
90–119	105 (35.7)	11 (26.2)	94 (37.3)		12 (30.0)	76 (40.0)	
60–89	72 (24.5)	13 (31.0)	59 (23.4)		14 (35.0)	39 (20.5)	
<60	14 (4.8)	7 (16.7)	7 (2.8)		4 (10.0)	3 (1.6)	
Stage of AKI, *n* (%)				.001			<.001
1	133 (45.2)	9 (21.4)	124 (49.2)		9 (22.5)	100 (52.6)	
2	65 (22.1)	9 (21.4)	56 (22.2)		7 (17.5)	43 (22.6)	
3 (non-dialysis)	36 (12.2)	5 (11.9)	31 (12.3)		8 (20.0)	22 (11.6)	
3 (dialysis)	60 (20.4)	19 (45.2)	41 (16.3)		16 (40.0)	25 (13.2)	
Adjudicated etiology of AKI, *n* (%)							
Hemodynamic factors	269 (91.5)	40 (95.2)	229 (90.9)	.550	35 (87.5)	173 (91.1)	.553
Drugs	82 (27.9)	8 (19.0)	74 (29.4)	.167	20 (50.0)	48 (25.3)	.002
Glomerulonephritis	42 (14.3)	4 (9.5)	38 (15.1)	.341	12 (30.0)	26 (13.7)	.012

AKI recovered defined as serum creatinine within 25% of the baseline.
[a]Missing values for 16 patients.
[b]missing values for one patient.
[c]missing values for 18 patients.
NYHA, New York Heart Association.

unknown, and their clinical features were not significantly different from those of the 230 patients with known 90-day recovery, except for a lower proportion of AKI stage 3 (Supplementary data, Table S1).

Among the 230 survivors with known 90-day kidney recovery status, 82.6% (190) recovered kidney function at 90 days, and 17.4% (40) did not recover (22 had SCr 25%–49% of baseline, and 18 had SCr ≥50% of baseline). The SCr measurements used to determine 90-day kidney recovery were drawn at a median of 90 (IQR 54–95) days after AKI. A comparison of features between survivors with 90-day kidney recovery and those without is presented in Table 1.

Table 2: Risk factors associated with 90-day mortality.

	Univariable logistic regression			Multivariable logistic regression		
Variables	Odds ratio	95% CI	*P*-value	Odds ratio	95% CI	*P*-value
Age >65 years	3.44	1.64–7.21	.001	3.81	1.26–11.54	.018
Malignancy	4.38	1.59–12.05	.004			
Right-sided IE	0.31	0.09–1.05	.059			
Heart failure (NYHA III–IV)	6.60	2.69–16.22	<.001	6.65	1.89–23.37	.003
Shock	23.68	10.58–53.02	<.001	31.97	10.45–97.79	<.001
Cerebral embolism	2.32	1.19–4.51	.013	3.95	1.40–11.10	.009
Surgery	0.07	0.03–0.15	<.001	0.07	0.02–0.21	<.001
Baseline eGFR (mL/min/1.73 m^2)			.003			
≥120	Ref					
90–119	0.98	0.40–2.37	.962			
60–89	1.84	0.77–4.39	.167			
<60	8.36	2.47–28.33	.001			
Stage of AKI			.001			
1	Ref					
2	2.21	0.83–5.88	.111			
3 (non-dialysis)	2.22	0.70–7.10	.178			
3 (dialysis)	6.39	2.68–15.21	<.001			

NYHA, New York Heart Association.

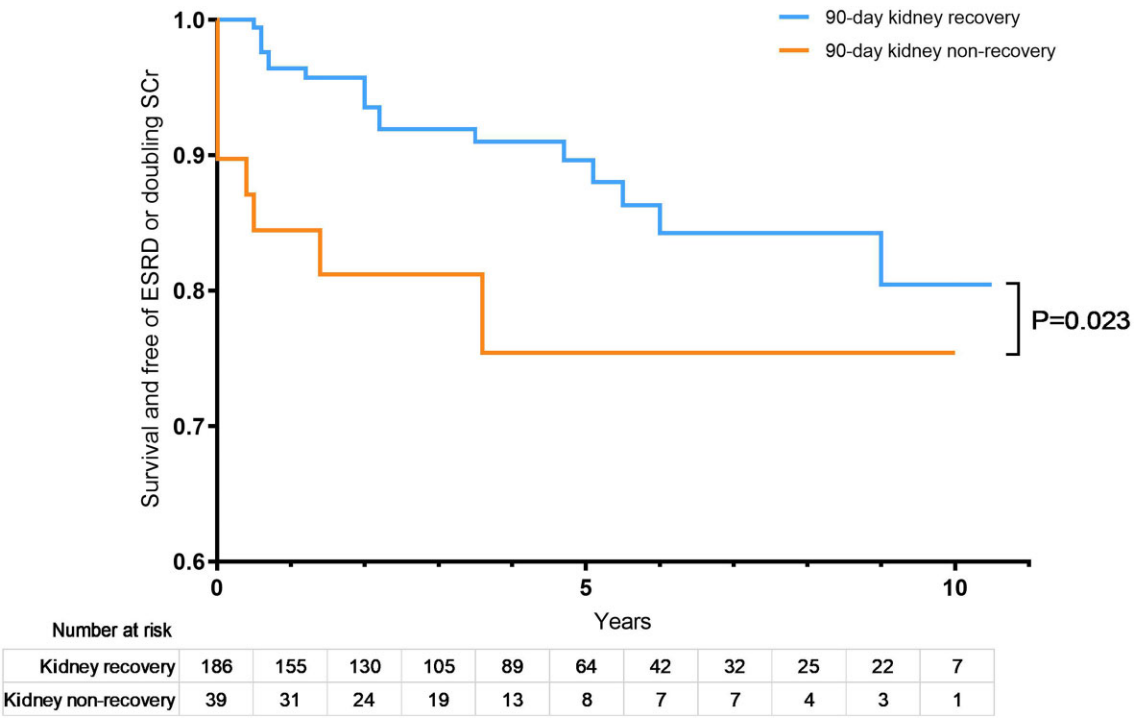


Figure 2: Kaplan–Meier survival curves for the long-term composite outcome of death or ESRD or sustained doubling of SCr by 90-day kidney recovery status.

Among the 230 survivors, 5 were lost to follow-up after 90 days. The remaining 225 survivors were followed up for a median of 3.5 (IQR 1.2–5.5) years from 90 days after the AKI event. Over the follow-up period, 9.7% (18) of patients with 90-day kidney recovery reached the composite outcome of mortality or ESRD or sustained doubling of SCr, compared with 20.5% (8) of patients without recovery. The Kaplan–Meier survival curves for 90-day kidney recovery status and the long-term composite outcome are presented in Fig. 2. In the Cox proportional hazard model, 90-day kidney non-recovery was associated with an increased risk of the long-term composite outcome (adjusted HR 3.00, 95% CI 1.19–7.59) after adjusting for age, diabetes, heart failure and surgery (Table 3).

A total of nine patients reached the endpoint of ESRD or sustained doubling of SCr, among whom four already reached the endpoint at time zero (90 days after AKI). For the remaining five patients, there were no significant differences in the frequencies of SCr measurements between patients with 90-day kidney recovery and those without (2.1 versus 2.7 times per year, $P = .735$).

Table 3: Risk factors associated with the long-term composite outcome.

	Univariable Cox regressionregression			Multivariable Cox regression		
Variables	Hazard ratio	95% CI	*P*-value	Hazard ratio	95% CI	*P*-value
90-day kidney non-recovery	2.54	1.10–5.87	.029	3.00	1.19–7.59	.020
Age >65 years	9.28	4.24–20.28	<.001	7.82	3.45–17.70	<.001
Hypertension	2.74	1.26–5.95	.011			
Diabetes	3.51	1.52–8.09	.003	3.63	1.45–9.10	.006
Coronary heart disease	2.96	1.29–6.81	.011			
Cerebrovascular	3.94	1.46–10.60	.007			
Malignancy	6.10	2.09–17.79	.001			
Heart failure	2.20	0.98–4.94	.056	2.42	1.06–5.53	.037
Surgery	0.28	0.11–0.70	.007	0.35	0.13–0.95	.040
Baseline eGFR (mL/min/1.73 m^2)			.003			
≥120	Ref					
90–119	3.30	1.06–10.24	.039			
60–89	4.08	1.22–13.64	.022			
<60	25.55	4.47–146.00	<.001			

Table 4: Risk factors associated with kidney non-recovery.

	Univariable analysis			Multivariable analysis		
Variables	Hazard ratio	95% CI	*P*-value	Hazard ratio	95% CI	*P*-value
Male sex	0.63	0.45–0.88	.006			
Age >65 years	1.44	0.91–2.29	.120			
Baseline eGFR (mL/min/1.73 m^2)[a]						
≥120	Ref			Ref		
90–119	1.16	0.84–1.58	.360	1.32	0.94–1.84	.097
<90[a]	2.92	1.97–4.31	<.001	2.49	1.69–3.66	<.001
Glomerulonephritis-related AKI	2.83	1.90–4.22	<.001	3.02	1.92–4.76	<.001
Drug-related AKI	1.87	1.37–2.54	<.001	2.77	1.86–4.13	<.001
Stage of AKI						
1	Ref			Ref		
2	2.17	1.53–3.05	<.001	2.18	1.51–3.16	<.001
3 (non-dialysis)	4.58	2.73–7.66	<.001	2.91	1.83–4.62	<.001
3 (dialysis)	8.77	5.27–14.58	<.001	3.16	1.92–5.21	<.001
Shock	4.59	2.82–7.46	<.001	5.51	2.97–10.24	<.001
Heart failure	2.25	1.70–2.97	<.001			
ICU stay	1.82	1.31–2.53	<.001			
Surgery	0.41	0.25–0.67	<.001			
Prosthetic valve	1.58	0.97–2.58	.066			
Cerebral vascular disease	1.87	1.04–3.38	.037			

[a]Baseline eGFR 60–90 mL/min/1.73 m^2 and eGFR <60 mL/min/1.73 m^2 were combined into eGFR <90 mL/min/1.73 m^2 in the analysis because the number of patients with eGFR <60 mL/min/1.73 m^2 was too small.

Risk factors for kidney non-recovery

We further explored risk factors for kidney non-recovery within 90 days. In the multivariable competing risk model accounting for the competing risk of death, five variables were independently associated with kidney non-recovery: baseline eGFR <90 mL/min/1.73 m^2 (HR 2.52, 95% CI 1.73–3.65), stage of AKI (HR 2.18, 95% CI 1.51–3.16 for stage 2; HR 3.03 for stage 3, 95% CI 2.07–4.42), shock (HR 5.56, 95% CI 3.02–10.22), glomerulonephritis-related AKI (HR 3.04, 95% CI 1.93–4.77) and drug-related AKI (HR 2.77, 95% CI 1.86–4.13) (Table 4).

DISCUSSION

The present study presented the largest cohort of IE-associated AKI published to date. For the first time, we evaluated the prognostic factors of short- and long-term survival and kidney outcomes among patients with IE-associated AKI. We identified several risk factors for kidney non-recovery, and confirmed an association between 90-day kidney recovery and long-term outcomes.

To the authors' knowledge, no previously published study reported the prognostic factors of mortality in patients with IE-associated AKI. Our study showed that old age, heart failure, shock and cerebral embolism were associated with an increased risk of 90-day mortality, whereas surgery was associated with a lower risk. The prognostic factors of mortality identified in our cohort are consistent with those identified in the general IE population [12–15], suggesting similar prognostic factors in IE patients with or without AKI. In addition, we observed an increasing mortality with increasing AKI stage, with a 90-day mortality of 25.0% in AKI stage 3, highlighting the poor prognosis in

patients with severe AKI. This finding was consistent with previous studies [1, 2].

Evaluation of kidney recovery at 3 months is recommend in the KDIGO guidelines, and has recently attracted more attention [10, 16, 17]. Kidney recovery at 3 months is reported to be associated with long-term outcomes in other AKI populations [6–8], but has not been evaluated in IE-associated AKI. In addition, there is a paucity of data on long-term outcomes of patients with IE-associated AKI. We are aware of only one previous study reporting the incidence of 1-year mortality and chronic kidney disease in patients with IE-associated AKI. Still, prognostic factors were not analyzed [3]. The present study revealed that 17.4% of AKI survivors did not recover kidney function at 90 days, and 90-day non-recovery was associated with an increased risk of the long-term composite outcome of death, ESRD or sustained doubling of SCr. Our study confirmed an association between AKI non-recovery at 3 months and adverse long-term outcomes in patients with IE-associated AKI, highlighting the importance of kidney recovery evaluation at 3 months for risk stratification and follow-up arrangement.

Risk factors for non-recovery after AKI include patient-related factors, type and severity of acute disease, and severity of AKI [18]. We are aware of only one previous study describing kidney recovery in patients with IE, but participants were restricted to dialysis-requiring AKI, with inadequate analysis of risk factors for kidney recovery [19]. The present study is the first to report risk factors of kidney non-recovery in the whole population of IE-associated AKI. We identified low baseline eGFR and higher stage of AKI as risk factors for non-recovery, consistent with previous findings [18, 20–22]. We also identified shock, drug-induced AKI, and glomerulonephritis-related AKI as independent risk factors for non-recovery. Shock was present in 21.1% of our cohort, primarily cardiac and septic shock. The association between shock and AKI non-recovery can be explained by irreversible kidney injury caused by prominent hemodynamic instability. This finding is supported by previous studies that reported an association between vasopressors and kidney non-recovery [23, 24]. Preventing and promptly correcting shock through effective anti-microbial therapy, timely cardiac surgery and maintaining hemodynamic stability should be helpful to promote kidney recovery after IE-associated AKI.

We determined AKI etiology for each patient, and found that AKI etiology was associated with kidney recovery. Specifically, drug-related AKI and glomerulonephritis-related AKI were risk factors for non-recovery, whereas hemodynamic-related AKI was not. This result is unsurprising because hemodynamic-related AKI typically presents with pre-renal AKI or acute tubular necrosis, usually with a favorable outcome. In contrast, a significant proportion of patients with drug-induced AKI or infection-associated glomerulonephritis do not recover kidney function [25–28]. Our study highlights more attention to drug- and glomerulonephritis-related AKI in patients with IE. Nephrotoxic drugs should be avoided as much as possible, using therapeutic drug monitoring if applicable. Nephrology consultation should be helpful for patients with glomerulonephritis-related AKI.

CONCLUSION

In conclusion, the present study indicated a high 90-day mortality (14.3%) in patients with IE-associated AKI who shared similar prognostic factors of short-term mortality with the general IE population. A substantial proportion (17.4%) of survivors did not recover kidney function at 90 days, and 90-day kidney non-recovery was associated with adverse long-term outcomes. Low baseline eGFR, severe AKI, shock, drug-related AKI and glomerulonephritis-related AKI were independent risk factors of kidney non-recovery. Drug-related AKI is a modifiable risk factor, and should be avoided as much as possible.

Limitations

Our study has several limitations. First, AKI was defined based on SCr without using urine output data due to the unavailability of data at the time of AKI diagnosis for many patients. Second, when pre-admission baseline SCr was unknown, the MDRD imputation and the lowest SCr during follow-up were used as surrogates of baseline SCr, which might introduce error on AKI classification and outcomes. Third, 22 patients with unknown 90-day kidney recovery status and 5 patients lost to follow-up after 90 days were not included in the analysis of long-term outcomes, which was subjected to potential selection bias. In addition, although this study presents the largest cohort of IE-associated AKI published to date, the sample size remains relatively small considering the low event rates during the long-term follow-up. Furthermore, the study was conducted in a tertiary center including a high proportion of patients with severe heart failure, cardiac surgery and ICU stay. This may influence the generalizability of our results to other IE populations with less severe conditions.

SUPPLEMENTARY DATA

Supplementary data are available at *Clinical Kidney Journal* online.

FUNDING

This work was supported by the National High-Level Hospital Clinical Research Funding (2022-PUMCH-B-020 to Y.Q.) and the National Natural Sciences Foundation of China (Grant 81970621 to Y.Q.).

AUTHORS' CONTRIBUTIONS

S.X.A. contributed to the study design, data management and analysis, and wrote the initial manuscript. X.F. contributed to the study design, data management and analysis. K.S. and G.C. contributed to data analysis and manuscript review. X.P.L. and Q.M. contributed to data acquisition. Y.Q., G.C. and X.M.L. contributed to the study design and manuscript review.

DATA AVAILABILITY STATEMENT

The data in the current study are available from the corresponding author on reasonable request.

CONFLICT OF INTEREST STATEMENT

None.

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Received: 26.5.2024; Editorial decision: 23.10.2024