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Sepsis-associated acute kidney injury in patients with chronic kidney disease: Patient characteristics, prevalence, timing, trajectory, treatment and associated outcomes

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Abstract

Aim: The features and outcomes of sepsis-associated acute kidney injury (SA-AKI) may be affected by chronic kidney disease (CKD). Accordingly, we aimed to compare SA-AKI in patients with or without CKD.

Methods: Retrospective cohort study in 12 intensive care units (ICU). We studied the prevalence, patient characteristics, timing, trajectory, treatment and outcomes of SA-AKI with and without CKD.

Results: Of 84 240 admissions, 7255 (8.6%) involved patients with CKD. SA-AKI was more common in patients with CKD (21% vs 14%; $p < .001$). CKD patients were older (70 vs. 60 years; $p < .001$), had a higher median Charlson co-morbidity index (5 vs. 3; $p < .001$) and acute physiology and chronic health evaluation (APACHE) III score (78 vs. 60; $p < .001$) and were more likely to receive renal replacement therapy (RRT) (25% vs. 17%; $p < .001$). They had less complete return to baseline function at ICU discharge (48% vs. 60%; $p < .001$), higher major adverse kidney events at day 30 (MAKE-30) (38% vs. 27%; $p < .001$), and higher hospital and 90-day mortality (21% vs. 13%; $p < .001$, and 27% vs. 16%; $p < .001$, respectively). After adjustment for patient characteristics and severity of illness, however, CKD was not an independent risk factor for increased 90-day mortality (OR 0.88; 95% CI 0.76–1.02; $p = .08$) or MAKE-30 (OR 0.98; 95% CI 0.80–1.09; $p = .4$).

Conclusion: SA-AKI is more common in patients with CKD. Such patients are older, more co-morbid, have higher disease severity, receive different ICU therapies and have different trajectories of renal recovery and greater unadjusted mortality. However, after adjustment day-90 mortality and MAKE-30 risk were not increased by CKD.

KEYWORDS
acute kidney injury, chronic kidney disease, critical care, sepsis, sepsis-associated acute kidney injury

Summary at a Glance

It was previously unknown how sepsis-associated acute kidney injury affects patients with chronic kidney disease. In a study involving a large group of critically ill patients, it was found that those with CKD were more likely to develop the condition, were older and had more health problems, received different treatments, and had a higher unadjusted mortality rate. However, after adjusting for other factors, there was no significant increase in mortality.

1 | INTRODUCTION

The epidemiology of sepsis-associated acute kidney injury (SA-AKI) in the intensive care unit (ICU) according to the Acute Disease Quality Initiative (ADQI) definition[1] has been recently described.[2,3] Such study demonstrated that SA-AKI is increasing, occurs in one in every six patients and is associated with significant morbidity and mortality risk.[3]

Debate surrounding the assessment of SA-AKI, however, has emphasized the need to understand its interaction with chronic kidney disease (CKD).[2,4,5] This is because current SA-AKI research has not included data on CKD status and because CKD is likely to be a major modifier of the incidence, trajectory, treatment and outcomes of SA-AKI.

In this regard, in the general ICU population, the prevalence of CKD has been increasing[6] and CKD is associated with a higher risk of acute kidney injury (AKI).[7] Moreover, AKI in the presence of CKD, has been associated with higher rates of death in the ICU, as well as an increased risk of long-term dependence on renal replacement therapy

(RRT).[7–9] Furthermore, a recent post hoc analysis of the STARRT-AKI trial demonstrated that allocation to accelerated RRT initiation resulted in a three-fold increase in the risk of long-term RRT dependence at 90 days in patients with CKD.[10]

Given the above consideration, we obtained CKD status for a cohort of critically ill patients. We hypothesized that patients with CKD would have a higher incidence of SA-AKI and that their trajectory, treatments and outcomes would differ from those of SA-AKI patients without CKD.

2 | METHODS

2.1 | Study design

We conducted a multicentre, retrospective cohort study of granular, routinely collected, electronic medical record (EMR)-based clinical data.

2.2 | Study sites

The study was conducted in 12 closed-model, mixed (medical and surgical) ICUs in Queensland, Australia, which included five tertiary, three outer metropolitan, and four regional ICUs. The study evaluated all adult patients admitted between January 1, 2015, and December 31, 2021, except for patients with advanced CKD requiring chronic dialysis, patients admitted with palliative intent, and patients transferred from another participating ICU.

2.3 | Data sources

Data was collected from all centres using eCritical MetaVision™ (iMDsoft, Boston, MA, USA) clinical information systems[11–14] and the ANZICS CORE Adult Patient Database (APD).[15–18] The data included daily laboratory reports, medications, microbiology, haemodynamics, fluid balance, patient demographics, diagnoses, severity of illness and outcomes. Primary and secondary diagnoses, from the International Classification of Diseases 10 Australia Modification (ICD-10-AM) codes, as well as mortality data, were collected from the Queensland Hospital Admitted Patient Data Collection (QHAPDC)[19–21] and Queensland births, deaths and marriage registry,[22,23] respectively. As previously published, the amount of missing data for key variables in the dataset was very low.[3] Admission diagnoses were categorized to optimize data accuracy and interpretability (Table S1). The Charlson-defined co-morbidities and index were calculated from the ICD-10 codes (Table S2).[24,25] The conversion of vasopressor dosage to norepinephrine equivalent and calculation of vasoactive inotrope score was carried out as per protocol (Tables S3 and S4).[26]

2.4 | Identification of CKD

Utilising previously published methods, patients with CKD were identified from their ICD-10-AM codes.[6,8,27] The ICD-10-AM codes used to identify patients with CKD are provided in Table S2.

2.5 | Identification of sepsis-associated kidney injury and pre-admission creatinine

Patients with SA-AKI were identified according to the ADQI definition[1] as previously published.[3] AKI was defined according to the Kidney Disease Improving Global Outcomes (KDIGO) criteria using daily serum creatinine and hourly urine output data.[28] Imputation of hourly urine output was performed to manage absent urine output measurements.

As pre-admission serum creatinine was not available in the data set, we estimated baseline serum creatinine using a method previously validated in hospitalized Australian patients with and without CKD where pre-admission creatinine was available for such validation.[29,30] This method utilised the Chronic Kidney Disease–Epidemiology Collaboration (CKD-EPI) equation and assumed a baseline estimated glomerular filtration rate (eGFR) of 40 mL/min/1.73m^2 and 75 mL/min/1.73m^2 for patients with and without CKD, respectively.[29] To ensure robustness, we further performed sensitivity analysis and compared incidence and outcomes in patients with CKD according to different methods used to estimate baseline serum creatinine (Table S5). Using ADQI criteria, SA-AKI was diagnosed if AKI occurred between day 1 and 7 after sepsis diagnosis.[1]

2.6 | Outcomes

The primary outcome was SA-AKI incidence in patients with and without CKD. The secondary outcome was the timing of SA-AKI to ICU admission. The additional secondary outcomes include renal outcomes such as AKI severity, renal recovery status at ICU discharge, and major adverse kidney events at 30 days (MAKE-30) and non-renal outcomes such ICU and hospital length of stay, and ICU, hospital and 90-day mortality. Renal outcome definitions used in this study are provided in Table S6.

2.7 | Statistical analysis

Descriptive statistics were expressed as frequencies and proportions for categorical variables and medians with interquartile ranges (IQR) for continuous variables. Fisher's exact test was used to compare categorical variables. The Wilcoxon rank sum test was used to compare continuous variables. A mixed-effect logistic regression model was developed, including hospitals as a random effect, to examine factors associated with 90-day mortality and MAKE-30. The variables

TABLE 1 Baseline characteristics of SA-AKI patients according to CKD status.

	Chronic kidney disease		
Variable	Yes, N = 1492[1]	No, N = 10027[1]	p value[2]
Age (years)	70 (60, 77)	60 (46, 71)	<.001
Female	564 (38%)	4421 (44%)	<.001
Body mass index	29.3 (26.1, 35.5)	27.8 (24.9, 33.8)	<.001
Charlson co-morbidity index*	5 (3, 6)	3 (1, 5)	<.001
Co-morbidities			
Ischaemic heart disease	190 (13%)	750 (7.5%)	<.001
Congestive heart failure	484 (32%)	1445 (14%)	<.001
Peripheral vascular disease	83 (5.6%)	428 (4.3%)	.026
Cerebrovascular Disease	84 (5.6%)	828 (8.3%)	<.001
Chronic pulmonary disease	246 (16%)	1508 (15%)	.15
Mild liver disease	68 (4.6%)	483 (4.8%)	.7
Moderate–severe liver disease	87 (5.8%)	421 (4.2%)	.006
Diabetes	300 (20%)	959 (9.6%)	<.001
Diabetes with complications	798 (53%)	1498 (15%)	<.001
Localised Cancer	132 (8.8%)	1008 (10%)	.15
Metastatic cancer	44 (2.9%)	357 (3.6%)	.26
APACHE diagnosis group			
Cardiovascular	239 (16%)	1212 (12%)	
Gastrointestinal	201 (13%)	1592 (16%)	
Genitourinary	145 (9.7%)	385 (3.8%)	
Haematological	8 (0.5%)	70 (0.7%)	
Metabolic	78 (5.2%)	1314 (13%)	
Neurological	51 (3.4%)	1214 (12%)	
Other	52 (3.5%)	307 (3.1%)	
Respiratory	197 (13%)	1871 (19%)	
Sepsis	520 (35%)	2036 (20%)	
Trauma	1 (<0.1%)	26 (0.3%)	
Admission circumstances			
Post elective surgery	4 (0.3%)	53 (0.5%)	.24
Post rapid response	371 (25%)	1792 (18%)	<.001
Post cardiac arrest	1 (<0.1%)	15 (0.1%)	.71
Readmission	136 (9.1%)	698 (7.0%)	.004
LOS in hospital before ICU (hours)	11.8 (4.9, 66.0)	7.8 (2.9, 35.3)	<.001
Severity of illness			
APACHE 2 score	24 (19, 29)	18 (13, 24)	<.001
APACHE 3 score	78 (65, 93)	60 (44, 79)	<.001
APACHE 3 risk of death	0.29 (0.16, 0.52)	0.12 (0.04, 0.31)	<.001
Day of admission			
Any ventilation	818 (55%)	5822 (58%)	.02
Invasive ventilation	770 (52%)	5547 (55%)	.007
Non-invasive ventilation	48 (3.2%)	275 (2.7%)	.31
Maximum creatinine (μmol/L)	195 (106, 302)	123 (75.8, 201)	<.001
AKI stage			.046
0	667 (45%)	4815 (48%)	
1	364 (24%)	2443 (24%)	

(Continues)

TABLE 1 (Continued)

| Variable | Chronic kidney disease | | p value[2] |
	Yes, N = 1492[1]	No, N = 10027[1]	
2	224 (15%)	1344 (13%)	
3	237 (16%)	1425 (14%)	
RRT	182 (12%)	787 (7.8%)	<.001
Vasopressors	952 (64%)	6053 (61%)	.018
NEE score (μg/kg/min)	0.07 (0.02, 0.16)	0.06 (0.02, 0.14)	.098
Mean MAP (mmHg)	74.7 (69.8, 82.6)	75.8 (70.5, 83.9)	.001
Maximum SOFA score	7 (5, 9)	6 (4, 9)	<.001
Maximum lactate (mmol/L)	2.4 (1.5, 4.6)	2.3 (1.4, 4.2)	.11
ICU level			<.001
Tertiary	880 (59%)	5133 (52%)	
Outer metropolitan	316 (21%)	2072 (21%)	
Regional	291 (20%)	2760 (28%)	
Source of hospital admission			.013
Home	1124 (75%)	7291 (73%)	
Other hospital	350 (23%)	2661 (27%)	
Low acuity facility	3 (0.2%)	21 (0.2%)	
High care facility	15 (1.0%)	54 (0.5%)	
Source of ICU admission			<.001
Emergency department	599 (40%)	4323 (43%)	
Operating theatre	315 (21%)	2489 (25%)	
Ward	508 (34%)	2396 (24%)	
Other hospital	70 (4.7%)	819 (8.2%)	
Treatment goals on admission			<.001
Full active treatment	1216 (82%)	9138 (91%)	
Missing	0 (0%)	1 (<0.1%)	
Treatment limitation order	276 (18%)	888 (8.9%)	

Abbreviations: AKI, acute kidney injury; APACHE, acute physiology and chronic health evaluation; ICU, intensive care unit; LOS, length of stay; NEE, norepinephrine equivalent; RRT, renal replacement therapy; SA-AKI, sepsis-associated acute kidney injury; SOFA, sequential organ failure assessment.
[1]Median (IQR) or frequency (%).
[2]Wilcoxon rank sum test; Pearson's chi-squared test; Fisher's exact test.
*Charlson co-morbidity index calculation excluded chronic kidney disease component.

used for analysis were determined a priori and reflected the clinical utility of available data. The results of the multivariable analysis were reported as odds ratios (OR) with 95% confidence intervals (95% CI). Given the large data set and multiple comparisons, a two-sided p-value of <0.01 was chosen to indicate statistical significance.[31] Statistical analyses were performed using R v.4.0.3.

2.8 | Ethical considerations

This study was approved by the Metro South Hospital and Health Service Human Research Ethics Committee (HREC/2022/QMS/82024) with an individual waiver of consent granted.

3 | RESULTS

3.1 | Incidence of SA-AKI

Between January 1, 2015, and December 31, 2021, there were 89 184 adult admissions to the participating ICUs for which data linkage was complete. After the exclusion of patients admitted with palliative intent (543; 0.6%), transferred from another ICU (2541; 2.8%), and history of advanced CKD requiring chronic dialysis (1942; 2.2%), 84 240 patients remained. Pre-morbid CKD was identified in 7255 (8.6%) of patients. Among study patients, SA-AKI was more common (p < .001) in patients with CKD (1492; 21.0%) than in patients without CKD (10 546; 13.7%).

3.2 | Patient characteristics

The key characteristics of SA-AKI patients with and without CKD are displayed in Table 1. Patients with CKD were older and had a higher median Charlson co-morbidity index (CCI) than those without CKD. Moreover, they had higher rates of co-morbidities related to cardio-vascular diseases, renal diseases, diabetes and moderate–severe liver disease, but were less likely to have been diagnosed with a gastroin-testinal or respiratory-related illness during admission. Both groups had similar admission circumstances, although the CKD group had slightly higher rates of post-rapid response admissions and readmissions.

Upon admission, patients with CKD exhibited more severe illness as indicated by higher acute physiology and chronic health evaluation (APACHE) scores and SOFA scores. Additionally, there was no differ-ence in the administration of vasopressors or ventilation by CKD status. On the day of admission to the ICU, patients with CKD had significantly higher rates of RRT.

3.3 | Timing and characteristics of SA-AKI diagnosis

As shown in Table S7, the median ICU Day for the diagnosis of sepsis was Day 1 (IQR 1–1) in both CKD and non-CKD patients. For both groups, the diagnosis of sepsis and AKI essentially occurred simulta-neously. At diagnosis of SA-AKI, patients with CKD had more advanced AKI as evidenced by higher stages of AKI and higher rates of RRT. Furthermore, they were more likely to be diagnosed with AKI by both urine output and creatinine.

3.4 | Trajectory of SA-AKI

We examined the trajectory of SA-AKI patients over 14 days from ICU admission. The mean daily serum creatinine for patients with a history of CKD was >250 μmol/L, rapidly declined to <200 μmol/L over 4 days then steadily decreased to <175 μmol/L by day 14 of ICU. In patients without CKD, the mean serum creatinine remained relatively constant between 140 and 160 μmol/L (Figure 1).

The mean UO for patients with and without CKD is demon-strated in Figure 2. Patients with CKD had a steady improvement in mean hourly UO after ICU admission with a high of 1 mL/kg/h 120 hours after ICU admission. Similarly, patients without CKD had an improvement in UO to nearly 1.2 mL/kg/h at 96 hours after ICU admission.

The trajectory of renal function in patients with and without CKD over the first 7 days of SA-AKI, as determined by the AKI stage, is shown in Figure 3. In CKD patients, nearly 60% of patients with CKD still had AKI by day seven of ICU. Further, the proportion of patients with Stage 3 AKI increased over time to greater than 30% on day seven. In contrast, the proportion of non-CKD patients without AKI steadily increased to greater than 50% and patients with Stage 3 AKI remained less than 30% on day seven of ICU admission.
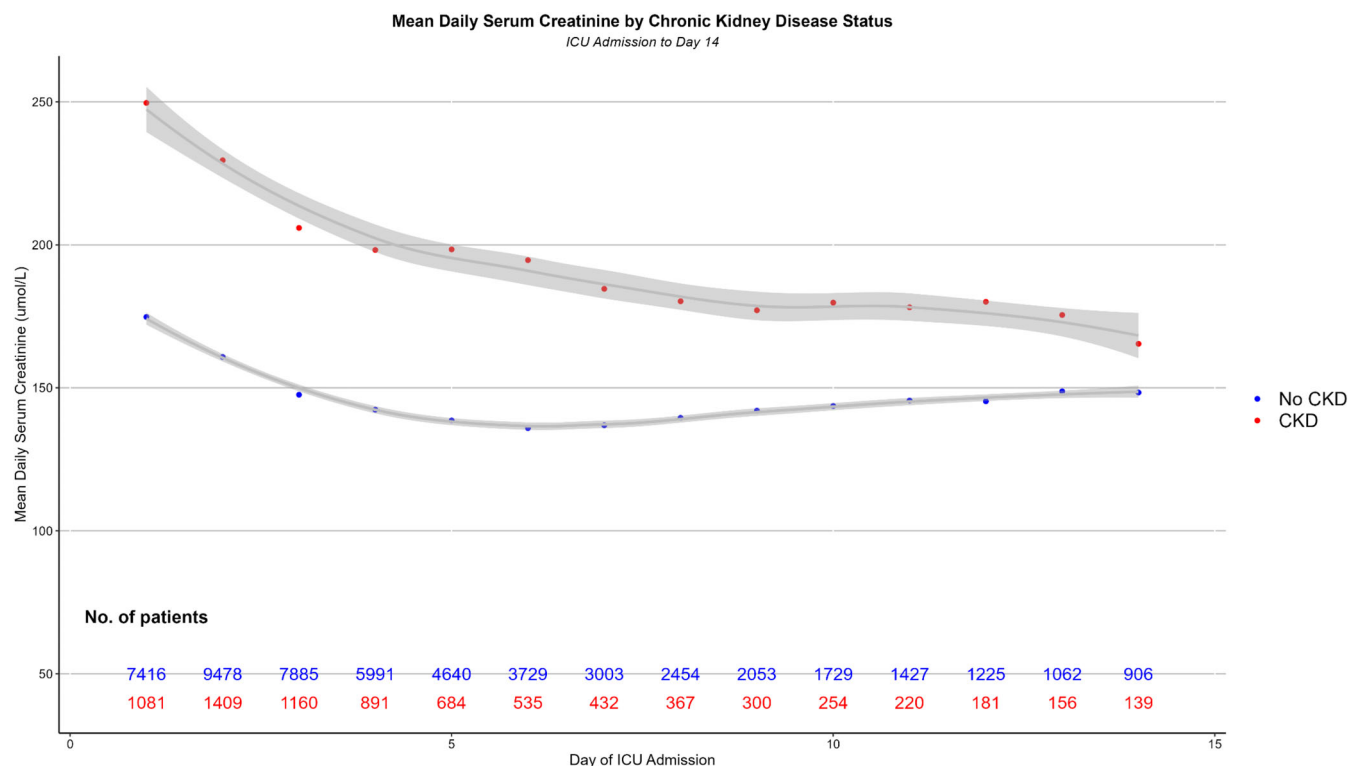

FIGURE 1 Mean daily serum creatinine by chronic kidney disease (CKD) status. ICU, intensive care unit.

3.5 | Treatment during first 7 days of ICU admission

The treatment of patients with SA-AKI by CKD status over the first 7 days of their ICU admission is shown in Table 2. Patients with CKD had similar ventilation and vasopressor treatment but were significantly more likely to require RRT. However, in patients receiving ventilation and vasopressors, the median duration of such support was comparable between groups.

3.6 | Associated outcomes

The outcomes of patients with and without CKD are demonstrated in Table 3. The maximum AKI stage during ICU admission was greater in patients with CKD. The length of stay in ICU was comparable between the groups; however, those with CKD had a significantly longer hospital length of stay. Additionally, patients with CKD were less likely to have renal recovery at ICU discharge as well as at a significantly higher risk of MAKE-30. When looking at mortality, CKD status was associated with an increased risk of ICU, hospital, 90-day and 1-year mortality.

In a multivariable logistic regression model for Day-90 mortality (Table 4), after adjusting for patient characteristics and severity of illness, a history of CKD was not associated with an increased risk of mortality at 90-day (OR 0.88; 95% CI 0.76–1.02; $p = 0.08$). A higher modified Charlson co-morbidity index, admission post-rapid response team review, a treatment limitation order on admission to ICU, and a higher APACHE 3 score were significantly associated with an increased risk of mortality. In addition, a multivariable logistic regression model for MAKE-30 (Table S8), demonstrated no independent association with CKD status (OR 0.93; 95% CI 0.08–1.09; $p = .40$).

4 | DISCUSSION

4.1 | Key findings

In this retrospective multicentre study of approximately 85 000 critically ill admissions, we found that almost one in 10 patients had a history of CKD. Patients with CKD had a two-fold higher prevalence of SA-AKI than non-CKD patients. They were older, had a higher burden of chronic disease, were more severely ill on admission to the ICU and, accordingly, had a higher rate of treatment limitation orders.
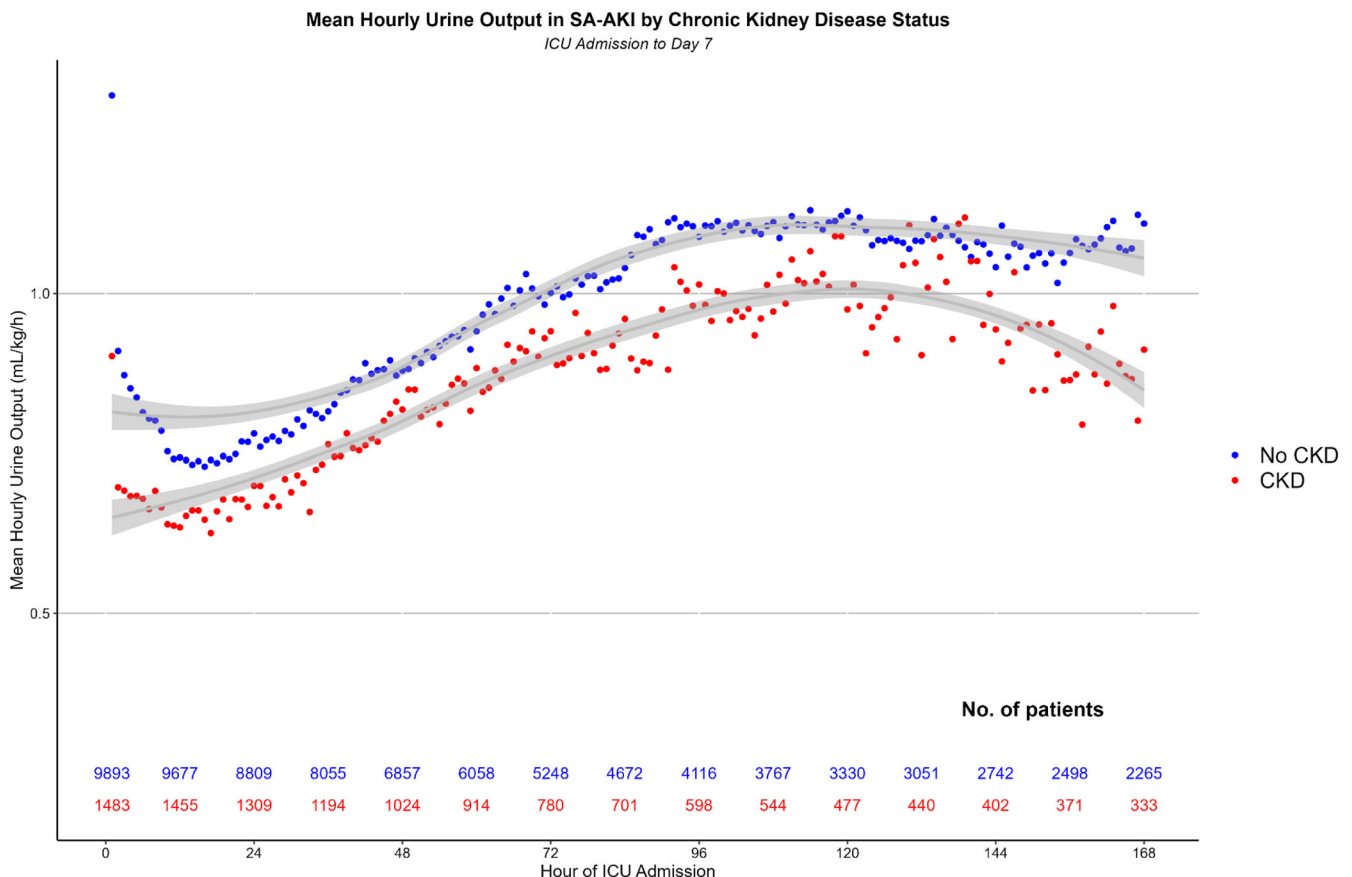
FIGURE 2 Mean hourly urine output by chronic kidney disease (CKD) status. ICU, intensive care unit; SA-AKI, sepsis-associated acute kidney injury.

Proportion of Patients by AKI Stage according to Chronic Kidney Disease Status
ICU Admission to Day 7

FIGURE 3 Proportion of patients by acute kidney injury (AKI) stage according to chronic kidney disease (CKD) status. ICU, intensive care unit.

Ventilation and vasopressor treatment did not differ between the two groups; however, patients with CKD had higher rates of RRT. Patients with CKD also had significantly worse unadjusted outcomes, with less renal recovery, higher MAKE-30 rates, and increased risk of mortality at long-term follow-up. However, after adjusting for patient characteristics and severity of illness, CKD was not independently associated with a different risk of 90-day mortality nor MAKE-30 risk.

4.2 | Relationship to literature

To our knowledge, no other study has examined the epidemiology of SA-AKI in CKD patients admitted to ICU. Recent research examined the epidemiology of SA-AKI in critically ill patients; however, it did not differentiate such epidemiology by CKD status.[3] A post-hoc analysis of the REVIVAL study was conducted to investigate the efficacy of recombinant human alkaline phosphatase in 649 patients with SA-AKI.[32] The study showed that the intervention had a different effect on the 49 patients with CKD compared with the majority of patients who did not have CKD.

Previous literature has examined the outcomes of critically ill CKD patients with AKI.[6,7] Using the Swedish intensive care registry, investigators compared 998 patients with AKI and a history of CKD to

92 509 patients with no renal disease and no AKI, demonstrating an increased mortality risk at 5 years with CKD. Other investigators examined 524 mechanically ventilated patients with CKD and reported that higher stages of CKD were associated with a greater risk of one-year mortality. Unlike our study, neither study mentioned critically ill patients with SA-AKI based on the presence or absence of CKD or adjusted for detailed baseline characteristics.

4.3 | Implications of the study findings

Our study findings indicate that CKD is prevalent among critically ill patients with sepsis. Furthermore, they suggest that critically ill patients with CKD face an increased risk of developing SA-AKI. Additionally, the findings demonstrate that CKD patients who develop SA-AKI differ significantly from those with CKD who do not develop SA-AKI. Specifically, they have a higher burden of chronic disease, require different ICU therapies, follow different trajectories and experience worse unadjusted outcomes. Moreover, our findings imply that patients with CKD who develop SA-AKI represent a distinct pathophysiological group. Finally, they imply that future interventional trials examining SA-AKI should stratify randomization based on CKD status.

TABLE 2 Treatment during the first 7 days according to chronic kidney disease status.

| Variable | Chronic kidney disease | | p value[2] |
	Yes, N = 1492[1]	No, N = 10027[1]	
Any			
Ventilation	949 (64%)	6635 (66%)	.053
Invasive ventilation	908 (61%)	6373 (64%)	.044
Non-invasive ventilation	88 (5.9%)	498 (5.0%)	.13
Vasopressors	1118 (75%)	7319 (73%)	.2
Diuretics	85 (5.7%)	413 (4.1%)	.002
RRT	373 (25%)	1726 (17%)	<.001
Days of intervention			
Ventilation	2 (0, 5)	2 (0, 5)	.032
Invasive ventilation	2 (0, 4)	2 (0, 5)	.026
Non-invasive ventilation	0 (0, 0)	0 (0, 0)	.14
Vasopressors	2 (0, 5)	2 (0, 5)	.032
RRT	2 (0, 4)	2 (0, 3)	.014
Mean daily			
NEE score (ug/kg/min)	0.05 (0.02, 0.10)	0.05 (0.02, 0.10)	.3

Abbreviations: NEE, norepinephrine equivalent; RRT, renal replacement therapy.
[1]Median (IQR) or frequency (%).
[2]Pearson's chi-squared test; Wilcoxon rank sum test.

4.4 | Strengths and limitations

Our study has several strengths. First, to diagnose SA-AKI, we relied on previously published methods that utilised the ADQI consensus definition. By utilising established techniques, we were able to ensure that our classification was accurate and reliable. Second, our research involved patients who were in critical condition and receiving treatment in 12 distinct intensive care units, thus highly likely to be representative of the broader Australian population and probably of similar populations in resource rich countries. Third, our study made use of routinely collected detailed data, which allowed us to accurately detect cases of AKI based on urine output criteria. Additionally, this data enabled us to conduct a detailed analysis of the trajectory of SA-AKI in patients with CKD, which had not been previously observed.

We acknowledge some limitations. First, the determination of SA-AKI and CKD was done electronically and though these methods have been previously used, misclassification could have occurred. Second, the study cohort's baseline serum creatinine was not available and needed to be estimated. This is a frequent problem as the availability to pre-admission is uncommon in Australia as shown by the RENAL trial[33] and such estimation is often necessary. As estimates of baseline serum creatinine are imperfect, to ensure greater accuracy and reproducibility, we conducted a sensitivity analysis using four different

TABLE 3 Outcomes in all SA-AKI patients according to chronic kidney disease status.

| Variable | Chronic kidney disease | | p value[2] |
	Yes, N = 1492[1]	No, N = 10027[1]	
Maximum AKI stage in ICU			<.001
1	505 (34%)	3971 (40%)	
2	394 (26%)	2703 (27%)	
3	593 (40%)	3353 (33%)	
Any RRT during ICU admission	392 (26%)	1803 (18%)	<.001
ICU LOS (days)	4.0 (3.0, 8.0)	4.0 (3.0, 8.0)	.4
Hospital LOS (days)	15 (8, 26)	10 (5, 19)	<.001
Renal recovery at ICU discharge			<.001
Full	709 (48%)	6007 (60%)	
Partial	90 (6.0%)	518 (5.2%)	
None	693 (46%)	3502 (35%)	
MAKE-30*	568 (38%)	2722 (27%)	<.001
ICU mortality	180 (12%)	913 (9.1%)	<.001
Hospital mortality	311 (21%)	1257 (13%)	<.001
Day 30 mortality	336 (23%)	1352 (13%)	<.001
Day 90 mortality	410 (27%)	1641 (16%)	<.001
1 year mortality	535 (36%)	2152 (21%)	<.001

Abbreviations: AKI, acute kidney injury; ICU, intensive care unit; LOS, length of stay; MAKE-30, major adverse kidney events at day 30; RRT, renal replacement therapy.
[1]Median (IQR) or frequency (%).
[2]Pearson's chi-squared test; Wilcoxon rank sum test.
*MAKE-30 defined as mortality at 30 days or serum creatinine is twice the estimated pre-admission value at the time of ICU discharge, or the patient is still on renal replacement therapy at the time of ICU discharge.

methods to estimate baseline serum creatinine, which did not demonstrate a difference in our study's conclusion. Furthermore, the sensitivity analysis is robust as it included the Larsen equations that were validated from known pre-admission serum creatinine values in Australian patients with and without CKD who were admitted to the hospital.[29,30] The results indicated minimal variation in SA-AKI incidence and outcomes, indicating that the approach to baseline creatine estimation would likely not affect the study's conclusions. Third, the censoring of RRT data, and dependent outcomes such as MAKE-30 at ICU discharge, may introduce an ascertainment bias. Fourth, we lacked data on the stage of CKD; thus, the outcomes demonstrated may vary for patients with different stages of CKD. Fifth, we did not have microbiological data, therefore, we could not control for microorganisms in our analysis. As CKD patients have a higher risk of multiresistent and opportunistic infections there may be unaccounted for bias. Finally, CKD was detected by electronic coding, and though previously validated, this approach may have unintentionally misclassified some patients.

TABLE 4 Multivariate regression analysis for Day 90 mortality.

Variable	OR[1]	95% CI[1]	p-value
Chronic kidney disease	0.88	0.76, 1.02	.082
Age	0.97	0.91, 1.05	.5
Body mass index	0.98	0.94, 1.03	.4
Female	0.89	0.80, 1.00	.042
Charlson co-morbidity index*	1.50	1.40, 1.59	<.001
Elective admission	0.95	0.47, 1.91	.9
Admitted post-rapid response	1.39	1.22, 1.58	<.001
Treatment limitation	3.00	2.58, 3.49	<.001
APACHE 3 score	2.76	2.59, 2.94	<.001
Any RRT at SA-AKI diagnosis	0.92	0.78, 1.10	.4
Any vasopressors at SA-AKI diagnosis	0.92	0.82, 1.04	.2
Any ventilation at SA-AKI diagnosis	1.06	0.95, 1.20	.3

Abbreviations: APACHE, acute physiology and chronic health evaluation; RRT, renal replacement therapy; SA-AKI, sepsis-associated acute kidney injury; SOFA, sequential organ failure assessment.
[1]OR = Odds Ratio, CI = Confidence interval.
*Charlson co-morbidity index calculation excluded chronic kidney disease component.

5 | CONCLUSION

Our study shows that patients with a history of CKD have a higher risk of SA-AKI and, when diagnosed with SA-AKI, had worse unadjusted outcomes compared with those without CKD. Additionally, CKD patients with SA-AKI required RRT often and had lower rates renal recovery.

However, our study also found that, once adjustment for baseline features was applied, CKD was not an independent risk factor for mortality or MAKE-30. This suggests that the identification and stratification for CKD status is crucial for future interventional trials in patients with SA-AKI.

AUTHOR CONTRIBUTIONS

The study conception and design (KW, KL, RB); data acquisition (KW, RH, PC); analysis (KW, AS); interpretation of data (all authors); article drafting (KW, KL, RB), article revision for important intellectual content (all authors); final approval of the version submitted for publication (all authors); agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved (KW, KL, RB).

CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to declare.

DATA AVAILABILITY STATEMENT

Data cannot be shared publicly due to institutional ethics, privacy and confidentiality regulations. Data released for research under Sect. 280 of the Public Health Act 2005 requires an application to the Director-General of Queensland Health (pha@health.qld.gov.au).

ETHICS STATEMENT

This study was approved by the Metro South Hospital and Health Service Human Research Ethics Committee (HREC/2022/QMS/82024) with an individual waiver of consent granted.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.