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Characteristics and Outcomes of Survivors of Critical Illness and Acute Kidney Injury Followed in a Pilot Acute Kidney Injury Clinic

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Surviving critical illness and acute kidney injury (AKI) carries a burden of morbidity and mortality that may be affected by post-discharge care. However, only 5% to 10% of AKI survivors receive nephrology post-discharge care, despite observational studies suggesting an association between early nephrology follow-up and improved outcomes.[1–3]

Currently, there are no evidence-based care practices for the evaluation and management of survivors of AKI in outpatient settings. Despite the fact that experts recommend that AKI survivors have their kidney function evaluated within 3 months of discharge to determine kidney recovery, up to one-third of AKI survivors have no measurements of kidney function within this time period, and only 6% have proteinuria assessment.[4] Therefore, the development and implementation of comprehensive models of post-AKI care represent an opportunity to have a favorable impact on the evaluation and, possibly, outcomes of AKI survivors. In this context, the main objective of this study was to examine characteristics and outcomes of survivors of critical illness and AKI followed in a pilot model of an AKI clinic in reference to survivors followed under usual care.

RESULTS

Clinical characteristics of 72 survivors of critical illness and AKI followed in the AKI Clinic and 573 survivors followed under usual care after discharge are presented in Table 1. The AKI survivors followed in the AKI Clinic had higher peak serum creatinine (SCr) (median 5.6 [4.8−7.5] vs. 2.6 [1.9−3.8] mg/dl, $P < 0.001$), had higher discharge SCr (median 1.8 [1.3−2.9] vs. 1.1 [0.8−1.6] mg/dl, $P < 0.001$), and more frequently required renal replacement therapy (RRT) (61.1% vs. 8.4%, $P < 0.001$) when compared with AKI survivors followed under usual care. The median time from hospital discharge to first SCr evaluation was similar in survivors of AKI followed in the AKI Clinic and in those followed under usual care (24.3 [12.4−50] days vs. 17 [5.1−49.9] days, respectively, $P = 0.40$).

Clinical outcomes in both survivor groups are reported in Table 2. Rehospitalization at 6 months post-discharge was a frequent outcome in these patients, occurring in 170 of 645 (26.4%) of all AKI survivors. Only 17 patients (2.6%) died during follow-up, 5 patients (0.8%) without rehospitalization. Rehospitalization/death at 6 months post-discharge trended to occur less frequently, albeit not statistically significantly, in patients followed in the AKI Clinic (14/72 patients [19.4%]) versus those followed under usual care (156/573 [27.2%]) ($P = 0.20$) (Table 2). Overall, more rehospitalization events occurred in the first 1 to 3 months (105 events) than in the subsequent 3 to 6 months (65 events) (Supplementary Table S1). The time to first

Table 1. Characteristics of survivors of critical illness and AKI followed in the AKI Clinic versus those followed under usual care

Characteristic	AKI clinic n = 72	Usual care n = 573	*P* value
Age, yr	52.7 ± 14.5	56.3 ± 14.1	0.08
Male, n (%)	39 (54.2)	315 (55.0)	0.90
Race, n (%)			0.15
White	66 (91.7)	509 (88.8)	
Black	4 (5.6)	51 (8.9)	
Other	2 (2.8)	13 (2.3)	
Charlson Comorbidity Index score	2.0 [1.0–4.0]	3.0 [1.0–5.0]	0.17
Diabetes, n (%)	29 (40.3)	222 (38.7)	0.80
Hypertension, n (%)	39 (54.2)	405 (70.7)	0.01
Mechanical ventilation, n (%)	46 (63.9)	264 (46.1)	0.01
Baseline SCr, mg/dl	0.96 [0.8–1.2]	0.87 [0.7–1.1]	0.005
Baseline eGFR, ml/min per 1.73 m^2	77.8 [62.3–98.0]	90.5 [64.1–104.8]	0.04
Peak SCr, mg/dl	5.6 [4.8–7.5]	2.6 [1.9–3.8]	<0.001
AKI KDIGO stage, n (%)			<0.001
Stage 2	1 (1.4)	298 (52.0)	
Stage 3	71 (98.6)	275 (48.0)	
Total days of AKI	16.0 [8.8–28.0]	4.0 [2.0–9.0]	<0.001
Recipient of RRT, n (%)	44 (61.1)	48 (8.4)	<0.001
Total days of RRT	9.0 [3.0–17.5]	10.0 [5.0–19.0]	0.08
Last SCr in the hospital, mg/dl	1.8 [1.3–2.9]	1.1 [0.8–1.6]	<0.001
Days from hospital discharge to first AKI Clinic visit	37.0 [20.8–54.0]	—	—
Days from hospital discharge to first post-discharge SCr	24.3 [12.4–50.0]	17.0 [5.1–49.9]	0.40
Number of outpatient SCr in the first 6 months post-discharge	1.5 [1.0–2.0]	3.0 [1.0–6.0]	<0.001

All continuous data are reported as median [25^{th}–75^{th} percentile], except for age which is reported as mean (SD).
AKI, acute kidney injury; eGFR, estimated glomerular filtration rate; KDIGO, Kidney Disease: Improving Global Outcomes; RRT, renal replacement therapy; SCr, serum creatinine.

rehospitalization was not different in both groups of AKI survivors (Supplementary Table S2). In multivariable analysis, follow-up in the AKI Clinic (vs. usual care) was independently associated with a lower risk of rehospitalization/death at 6 months post-discharge (adjusted odds ratio = 0.46, 95% confidence interval = 0.23–0.88, $P = 0.024$) (Supplementary Table S3). The main causes of the first rehospitalization at 6 months post-discharge are reported in Supplementary Table S4. Notably, common causes of rehospitalization in both groups were related to sepsis and cardiovascular disease. Adjusted probabilities of rehospitalization/death were 10% vs. 16% at 1 to 3 months and 8% vs. 10% at 3 to 6 months in AKI survivors followed in the AKI Clinic vs. those followed under usual care, respectively (Supplementary Figure S1).

In Supplementary Figure S2, we describe specific medication-related processes of care in AKI survivors who were followed in the AKI Clinic. We also simulated sample size estimates for clinical trials targeting AKI Clinic–related interventions to decrease rehospitalizations (Supplementary Table S5).

DISCUSSION

The potential impact of nephrologist-guided post-AKI care was demonstrated in an observational study

Table 2. Clinical outcomes of survivors of critical illness and AKI followed in the AKI clinic versus those followed under usual care

Study outcomes	AKI clinic n = 72	Usual care n = 573	*P* value
Primary outcome			
Death or rehospitalization at 6 mo post-discharge	14 (19.4)	156 (27.2)	0.20
Secondary outcomes			
Death or rehospitalization at 3 mo post-discharge	8 (11.1)	97 (16.9)	0.24
Death at 6 mo post-discharge	2 (2.8)	15 (2.6)	0.99
Death or ESKD at 6 mo post-discharge	2 (2.8)	18 (3.1)	0.99
eGFR decline ≥30% from baseline using last outpatient SCr 3–6 months post-discharge[a]	6/72 (8.3)	29/279 (10.4)	0.83
Rehospitalization with AKI episode at 6 months post-discharge	4 (5.6)	68 (11.9)	0.16
AKI stage 1	2	41	
AKI stage 2	1	12	
AKI stage 3	1	15	

Data are n (%).
AKI, acute kidney injury; eGFR, estimated glomerular filtration rate; ESKD, end-stage kidney disease.
[a]The use of this timepoint SCr was determined to avoid misclassification during the period of AKD (up to 90 days post–AKI onset) and was determined only for patients with at least 1 SCr measure at 3 to 6 months post-discharge.

showing lower all-cause mortality (8.4 vs. 10.6 per 100-patient years) when survivors of RRT-requiring AKI were seen by a nephrologist within 90 days of discharge, compared to matched AKI survivors without nephrology follow-up.[2] Among patients with AKI requiring RRT who recovered, only 37% of patients in a Taiwan cohort had nephrology follow-up, which was associated with decreased risk of cardiovascular events, sepsis, and mortality.[3] Studies have also described poor patient knowledge and awareness of AKI among AKI survivors. Surprisingly, 80% of AKI survivors were unaware of their condition by the time of discharge, and 21% were unaware of their AKI diagnosis at the first AKI Clinic visit.[5,6] The AKI survivors were also shown to be at higher risk for rehospitalization than their counterparts without AKI. A population-based study showed that 18% of AKI survivors were readmitted within the first 30 days of discharge.[7]

Post-AKI care requires comprehensive medication management and coordination of care. In a study of AKI survivors attending AKI clinics, it was found that renin−angiotensin−aldosterone system inhibitors (RAASi) are commonly discontinued in the setting of hospitalized AKI, and that acute exposure to RAASi during hospitalization does not appear to increase the risk of persistent kidney dysfunction at 3 months post-discharge.[8] Another study showed that among survivors with and without AKI during hospitalization, exposure to RAASi evaluated at 3 months post-discharge was not associated with a higher risk of recurrent hospitalized AKI, death, kidney disease progression, or heart failure events during a median follow-up of 4.9 years.[9] Reinstitutions of RAASi should be considered in specific settings in which benefits have been demonstrated (e.g., heart failure, recent myocardial infarction, proteinuric chronic kidney disease). In our study, approximately 1 in 3 AKI survivors followed in the AKI Clinic received an intervention related to the management of RAASi or diuretics (Supplementary Figure S2).

Our study has limitations to acknowledge. First, this is an observational study from a single institution that cannot prove the benefit of nephrologist-guided post-AKI care (vs. usual care) in the reduction of rehospitalizations after discharge. Second, the usual care group was derived from a cohort of critical illness survivors who may have been subject to evolving change in post−intensive care unit and/or post-AKI care. However, we restricted this cohort to survivors of critical illness and AKI who were discharged from the hospital before the pilot AKI Clinic was implemented at the same institution. It is still possible that some of these patients were referred to nephrology by their primary care providers at some point after discharge. Third, our observations can be extrapolated to only a subset of AKI survivors, those who had severe AKI (stage $\geq$2) and required intensive care unit care.

Our study has also notable strengths. First, we applied specific inclusion and exclusion criteria to examine survivors of critical illness and AKI who were followed in the AKI Clinic, as well as those who received usual care after hospital discharge but may have been eligible for follow-up in the AKI Clinic in the event that this clinic was already implemented (e.g., we excluded patients discharged to rehabilitation facilities) (Supplementary Figure S3). Second, our study was carefully designed to address immortal time bias by excluding patients in both groups (AKI Clinic and usual care) with primary outcomes occurring in the first month after hospital discharge. This was done because patients were followed in the AKI Clinic according to protocol within the first 4 weeks of hospital discharge.

In conclusion, our study showed that follow-up in a specialized AKI clinic was associated with a lower risk of rehospitalization in the first 6 months post-discharge when compared to usual care in survivors of critical illness and severe AKI. We also showed that the implementation of AKI clinics may represent a feasible intervention that could potentially improve outcomes in survivors of AKI who were admitted to the intensive care unit. Our data support conducting interventional studies to test the efficacy of AKI clinics on the prevention of rehospitalizations following discharge in high-risk groups of AKI survivors.

DISCLOSURE

JAN reports consulting fees from Baxter Healthcare and Biomedical Insights. OMG reports receiving honoraria and grant support from Akebia and Amgen; grant support from GSK; consulting fees from QED; and honoraria from AstraZeneca, Reata, and Ardelyx. SAS has received speaking fees from Baxter Canada. EDS reports consulting fees from Akebia Therapeutics 4/19, receiving royalties from UptoDate, and serving on the editorial board for the *Clinical Journal of the American Society of Nephrology*.

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AUTHOR CONTRIBUTIONS

LJL and JAN designed the study; HL and VOS collected and validated the data; HL, LJL, and YL contributed to different portions of the statistical analysis; HL and JAN drafted the manuscript; all authors reviewed the manuscript and contributed important intellectual portions of the study; all authors approved the final version of the manuscript.

AVAILABILITY OF DATA AND MATERIALS

Data and materials may be made available upon written request to the corresponding author.

SUPPLEMENTARY MATERIAL

Supplementary File (Word)

Supplementary Text

Table S1.

Table S2.

Table S3.

Table S4.

Table S5.

Table S6.

Figure S1.

Figure S2.

Figure S3.

CONSORT Statement

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