ORIGINAL ARTICLE

Risk factors for major adverse kidney events in the first year after acute kidney injury

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ABSTRACT

Background. Acute kidney injury (AKI) survivors are at increased risk of major adverse kidney events (MAKEs), including chronic kidney disease (CKD), end-stage kidney disease (ESKD) and death. High-risk AKI patients may benefit from specialist follow-up, but factors associated with increased risk have not been reported.

Methods. We conducted a retrospective study of AKI patients admitted to a single centre between 2012 and 2016 who had a baseline estimated glomerular filtration rate (eGFR) >30 mL/min/1.73 m^2 and were alive and independent of renal replacement therapy (RRT) at 30 days following discharge. AKI was identified using International Classification of Diseases, Tenth Revision codes and staged according to the Kidney Disease: Improving Global Outcomes criteria. Patients were excluded if they were kidney transplant recipients or if AKI was attributed to intrinsic kidney disease. We performed Cox regression models to examine MAKEs in the first year, defined as the composite of CKD (sustained 25% drop in eGFR), ESKD (requirement for chronic RRT or sustained eGFR <15 mL/min/1.73 m^2) or death. We examined secondary outcomes (CKD, ESKD and death) using Cox and competing risk regression analyses.

Results. We studied 2101 patients (mean ± SD age 69 ± 15 years, baseline eGFR 72 ± 23 mL/min/1.73 m^2). Of these, 767 patients (37%) developed at least one MAKE (429 patients developed CKD, 21 patients developed ESKD, 375 patients died).

MAKEs occurred more frequently with older age [hazard ratio (HR) 1.16 per decade, 95% confidence interval (CI) 1.10–1.24], greater severity of AKI (Stage 2 HR 1.38, 95% CI 1.16–1.64; Stage 3 HR 1.62, 95% CI 1.31–2.01), higher serum creatinine at discharge (HR 1.04 per 10 μmol/L, 95% CI 1.03–1.06), chronic heart failure (HR 1.41, 95% CI 1.19–1.67), liver disease (HR 1.68, 95% CI 1.39–2.03) and malignancy (non-metastatic HR 1.44, 95% CI 1.14–1.82; metastatic HR 2.26, 95% CI 1.80–2.83). Traditional risk factors (e.g. diabetes and cardiovascular disease) had limited predictive value.

Conclusions. More than a third of AKI patients develop MAKEs within the first year. Clinical variables available at the time of discharge can help identify patients at increased risk of such events.

Keywords: acute kidney injury, chronic kidney disease, death, end-stage kidney disease, major adverse kidney events, risk factors

INTRODUCTION

Acute kidney injury (AKI) is a common complication of hospital admission, affecting >130 000 individuals in Australia each year [1]. In addition to its consistent association with in-hospital morbidity [1], mortality [2] and health care cost [3], AKI increases the future risk of major adverse kidney events (MAKEs), including chronic kidney disease (CKD), end-stage kidney disease (ESKD) and death [4]. Although the incidence varies by clinical setting, ~17.76 and 0.47 individuals with AKI will develop CKD and ESKD per 100 person-years of follow up, respectively, while an estimated 13.19 deaths per 100 person-years will also occur [4].

Previous studies have suggested that the risk of developing CKD, ESKD or death after AKI is influenced by patient demographics (older age, female sex) [5–7], comorbidities (diabetes, hypertension, pre-existing kidney, heart or liver disease) [4, 5, 8–10] and the degree of renal injury and recovery (AKI stage, serum creatinine at discharge or follow up) [4, 5, 7, 9, 11]. However, the generalizability and validity of these findings must be interpreted within the limitations of the studies, which have predominantly focused on the critical care setting [5, 9], used non-consensus definitions of AKI [5, 9, 12] or included a large number of patients without AKI in their models [6]. Furthermore, since CKD, ESKD and death are competing outcomes, studies examining the MAKE composite are needed to collectively identify patients at risk of any negative AKI outcome, who may benefit from specialist intervention [13]. Understanding the epidemiology of MAKEs could also assist with power calculation and clinical enrichment for AKI trials, given this is the preferred study endpoint [14, 15].

Therefore, we aimed to describe the incidence of and risk factors for MAKEs in the first year after AKI. We hypothesized that they would be common and that clinical variables available at the time of hospital discharge (e.g. demographics, comorbidities and AKI severity and recovery) would help identify individuals at increased risk.

MATERIALS AND METHODS

Study design

We performed a single-centre retrospective observational study of patients admitted to a large academic centre in Melbourne, Australia, between 1 January 2012 and 31 December 2016. Ethics approval was obtained prior to commencement (LNR/18/Austin/286) and the need for informed consent was waived. All reporting was performed in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines [16].

Study population

All adult patients (≥18 years) who were hospitalized during the study enrolment period and were allocated an International Classification of Diseases, Tenth Revision (ICD-10) code for AKI were included [17]. Eligible patients were required to have an estimated glomerular filtration rate (eGFR) >30 mL/min/1.73 m^2 at baseline (as defined below), to be alive and free of kidney replacement therapy at 30 days following hospital discharge and to have had at least one eGFR measurement in the first year. The diagnosis of AKI was confirmed using serum creatinine measurements, and its severity was graded according to the Kidney Disease: Improving Global Outcomes (KDIGO) AKI criteria [18]. The KDIGO criteria define AKI as a rise in serum creatinine of at least 26.5 μmol/L in 48 h or as a >50% increase in serum creatinine from baseline within 7 days. Urine output criteria were not assessed. Patients who did not meet KDIGO criteria for AKI were excluded, as were those who received chronic kidney replacement therapy prior to the index hospitalization and those in whom AKI was attributed to intrinsic kidney disease (i.e. glomerulonephritis, vasculitis, lupus nephritis, thrombotic microangiopathy or pregnancy-related kidney disease).

Data collection

Data pertaining to baseline characteristics were obtained from hospital administrative and pathology databases. Comorbidities were identified using validated ICD-10 and Australian Classification of Health Interventions (ACHI) coding algorithms [19] and included cigarette smoking, diabetes, hypertension, dyslipidaemia, cerebrovascular disease, cardiovascular disease, peripheral vascular disease, chronic heart failure, arrhythmia, valvular heart disease, lung disease, liver disease, haematological disease (leukaemia or lymphoma) and malignancy (non-metastatic and metastatic; Supplementary data, Table S1). Any comorbidity was considered to be absent if no representative codes were identified for that individual. Relevant admission characteristics included admission type (emergency, elective, other), admission unit [nephrology, medicine (excluding nephrology), surgery], length of stay (hospital, intensive care, coronary care), care type (intensive care, coronary care) and discharge destination (home, nursing home, other). The date of death (if applicable) was extracted from the hospital medical record; data on cause of death were not available because this information is not recorded at this centre. All serum creatinine, haemoglobin A1c (HbA1c) glucose and lipid measurements performed in the 12 months prior to, and after, index admission were extracted from the pathology database. Albuminuria status was characterized by urine albumin creatinine ratio measurements performed either during the index admission or in

the 12 months prior. Data on the presence of albuminuria as detected by urine dipstick were not available. To confirm CKD and ESKD status, serum creatinine measurements were extracted for an additional 3 months (i.e. between Months 12 and 15 following hospitalization), to ensure that changes were sustained for a sufficient period of time [20].

Derived indices included Accessibility/Remoteness Index of Australia (ARIA) score and baseline kidney function. ARIA scores were calculated using patient postcode at hospital admission and were categorized as 0 to <1 (major city), 1 to <3 (regional) and 3–4 (remote) [21]. Baseline serum creatinine values were estimated as the median measurement within the 12 months prior to admission. For patients who did not have a serum creatinine measurement performed in this period, the trough inpatient serum creatinine value was used to approximate baseline function, as long as the patient did not receive acute kidney replacement therapy [22]. Baseline eGFR was computed based on age, sex and serum creatinine level using the Chronic Kidney Disease Epidemiology Collaboration Equation (CKD-EPI) equation [23]. To reduce outlier effects, eGFR values >120 mL/min/1.73 m^2 were recorded as 120 mL/min/1.73 m^2.

Clinical outcomes

The primary outcome of the study was the development of a MAKE within the first year, measured from the date of hospital discharge. A MAKE was defined as the composite of new or progressive CKD (25% reduction in eGFR from baseline sustained for a minimum of 3 months), ESKD (eGFR ≤15 mL/min/1.73 m^2 sustained for a minimum of 3 months or initiation of chronic kidney replacement therapy in the form of haemodialysis, peritoneal dialysis or kidney transplantation) or death. This definition is in keeping with previously published work [24–26]. The date of developing a MAKE was defined as the date of the first qualifying event (e.g. the first date on which a patient's kidney function declined sufficiently to meet the relevant criteria, without rising above that threshold again). The secondary outcomes examined each individual component of the MAKE composite (CKD, ESKD, death). Patients were followed until death, loss to follow-up (i.e. the date of the last available pathology test) or until 365.25 days after discharge from hospital.

Statistical analysis

Baseline characteristics were expressed as frequencies (*n*, %), means [standard deviation (SD)] or medians [interquartile range (IQR)], as dictated by data type. Between-group comparisons were performed using the chi-squared test, unpaired *t*-test or Wilcoxon rank-sum test, as appropriate. Predictors of the time to a MAKE within the first year were analysed using univariable and multivariable Cox regression models. Candidate predictor variables were identified from a review of the literature. The final multivariable model included all variables associated with the outcome of interest either on univariable analyses (P < 0.2) or based on biological plausibility. Pre-specified first-order interaction terms between covariates were examined (baseline creatinine, discharge creatinine, AKI stage). Competing risk regression analyses were used to examine CKD and ESKD as secondary outcomes. Death was the competing risk. Predictors of time to death were investigated by Cox regression models. Cumulative incidence function curves were generated for each outcome. Proportional hazards and sub-hazards assumptions

were confirmed graphically and by modified Schoenfeld residuals [27]. Linearity assumptions were validated by dividing continuous data into quartiles and fitting as categorical variables. Only individuals with complete comorbidity and outcome data were included; no imputation for missing data was performed for the primary analysis.

Four sensitivity analyses were performed to test the robustness of our findings to various clinical and methodological assumptions. In the first, an alternative definition of new or progressive CKD was used: reduction in eGFR ≤30 mL/min/1.73 m^2 sustained for ≥3 months. Critically ill patients were excluded in the second sensitivity analysis, while in the third, multiple imputation was performed for missing albuminuria data to enable inclusion of this candidate predictor variable in the final model. Two *post hoc* sensitivity analyses were also performed. Because some patients had a single eGFR measurement potentially reflecting new or progressive CKD with no subsequent test, a sensitivity analysis was performed under the assumption that this change was sustained for 3 months. Also, because some patients had incomplete follow-up data, a sensitivity analysis using multiple imputation for outcome was done to ensure results remained consistent. Data were analysed using Stata/SE14.0 (College Station, TX, USA). Two-sided P < 0.05 was considered statistically significant.

RESULTS

Between 1 January 2012 and 31 December 2016, 2909 hospitalized adults with a baseline eGFR ≥30 mL/min/1.73 m^2 were allocated an ICD-10 code for AKI (Figure 1). Of these, 1256 patients (60%) met the diagnostic criteria for KDIGO Stage 1 AKI, while 519 (25%) and 326 (16%) patients were classified as having KDIGO Stages 2 and 3 AKI, respectively. Seventy-one patients with KDIGO Stage 3 AKI required acute kidney replacement therapy. The KDIGO criteria were not met by 808 patients, who were subsequently excluded from the analysis, giving a final sample size of 2101 patients. The median number of available serum creatinine measurements performed in the 12 months prior to admission, during admission and between discharge and the end of follow-up were 6 (IQR 2–15), 10 (IQR 5–21) and 11.5 (IQR 5–26), respectively.

The frequency of missing baseline characteristic data is reported in Table 1. Data were most commonly missing for low-density lipoprotein cholesterol (*n* = 1638, 78%) and albuminuria (*n* = 1518, 72%). In terms of outcome data, a total of 357 patients (17%) had incomplete follow-up, for whom the median time before being lost to follow-up was 134 days (IQR 43–242). Compared with patients with complete follow-up, those for whom follow-up was incomplete were more likely to have better kidney function at baseline and at hospital discharge (Supplementary data, Table S2). A sensitivity analysis using multiple imputation for the outcome variable was not different from the primary analysis (Supplementary data, Table S3).

The mean age of patients was 69.1 years (SD 15.2) and 58% were male (*n* = 1225). Baseline eGFR was 72.4 mL/min/1.73 m^2 (SD 22.5), while eGFR at the time of discharge was reduced at 61.4 mL/min/1.73 m^2 (SD 25.0). As few as 20 patients (<1%) with AKI were admitted under the nephrology unit, with an additional 10 patients (<1%) being transferred to their care during admission. Albuminuria was infrequently quantified (*n* = 583, 25.3%). Only three patients had missing data on covariates in the primary analysis (<1%). The baseline characteristics of the study population are reported in Table 1.
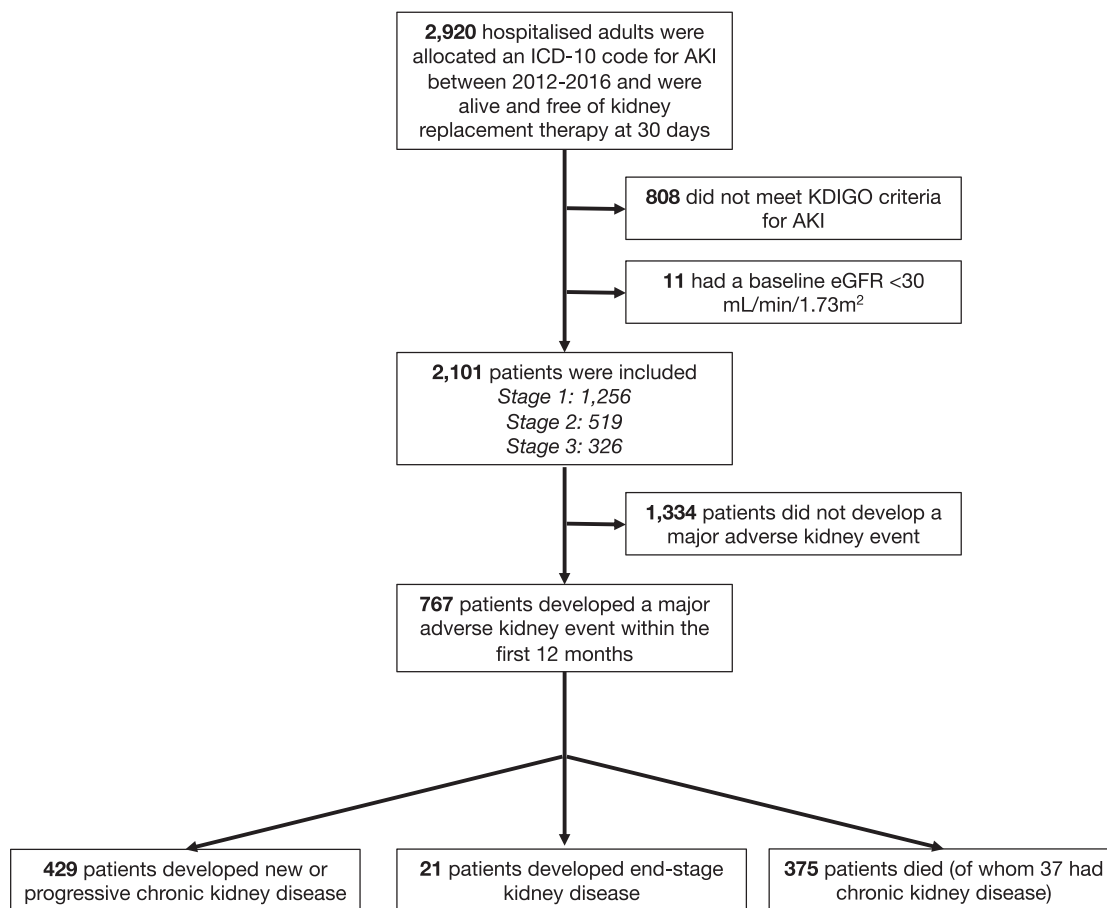
2,920 hospitalised adults were allocated an ICD-10 code for AKI between 2012–2016 and were alive and free of kidney replacement therapy at 30 days

808 did not meet KDIGO criteria for AKI

11 had a baseline eGFR <30 mL/min/1.73m²

2,101 patients were included
Stage 1: 1,256
Stage 2: 519
Stage 3: 326

1,334 patients did not develop a major adverse kidney event

767 patients developed a major adverse kidney event within the first 12 months

429 patients developed new or progressive chronic kidney disease

21 patients developed end-stage kidney disease

375 patients died (of whom 37 had chronic kidney disease)

FIGURE 1: Study flow diagram.

MAKEs

By the end of the first year, as many as 767 patients (37%) had developed a MAKE (46 events per 100 person-years; Table 2, Figures 2 and 3). Of these, 429 patients developed CKD, 21 developed ESKD (in addition to CKD) and 375 died (37 patients who died had previously developed CKD). Patients with a MAKE were more likely to be older [adjusted hazard ratio (HR) 1.16 per decade, 95% confidence interval (CI) 1.10–1.24, P < 0.001) and had more comorbidities, with a history of chronic heart failure (HR 1.41, 95% CI 1.19–1.67; P < 0.001), liver disease (HR 1.68, 95% CI 1.39–2.03; P < 0.001) or malignancy (non-metastatic HR 1.44, 95% CI 1.14–1.82; metastatic HR 2.26, 95% CI 1.80–2.83; overall P < 0.001). They were also more likely to have experienced more severe AKI (Stage 2 HR 1.38, 95% CI 1.16–1.64; Stage 3 HR 1.62, 95% CI 1.31–2.01; overall P < 0.001) or to have had a higher serum creatinine at discharge (HR 1.04 per 10 µmol/L increase, 95% CI 1.03–1.06; P < 0.001).

CKD

Of all patients who experienced a MAKE, 429 patients (20%) developed new or progressive CKD (26 events per 100 person-years), including 171 patients who reached this end point on hospital discharge (i.e. non-recovery of AKI). Development of CKD was more common in female patients [adjusted sub-hazard ratio (SHR) 1.55, 95% CI 1.27–1.89; P < 0.001] or in those with a history of hypertension (SHR 1.28, 95% CI 1.04–1.58; P = 0.02), chronic heart failure (SHR 1.25, 95% CI 1.01–1.56;

P = 0.04) or liver disease (SHR 1.63, 95% CI 1.28–2.09; P < 0.001). Greater severity of AKI (Stage 2 SHR 1.61, 95% CI 1.29–2.02; Stage 3 SHR 1.94, 95% CI 1.50–2.52; overall P < 0.001) or higher serum creatinine at discharge (SHR 1.06 per 10 µmol/L increase, 95% CI 1.04–1.07; P < 0.001) were also associated with a heightened risk. There was no association between older age (SHR 0.98 per decade, 95% CI 0.91–1.06; P = 0.63) or diabetes (SHR 1.10, 95% CI 0.90–1.34; P = 0.36) and the risk of developing CKD in the first year after AKI.

ESKD

A total of 21 patients (1%) developed ESKD by 1 year (1 event per 100 person-years). Due to the small number of patients reaching this outcome, two variables were selected for inclusion in the multivariable model on the basis of the magnitude and significance of their effect and their biological plausibility. The risk of ESKD was greater in female patients (SHR 4.86, 95% CI 1.79–13.22; P = 0.002) and in those with a higher serum creatinine at discharge (SHR 1.14 per 10 µmol/L increase, 95% CI 1.10–1.19; P < 0.001).

Death

Within the first year, 375 patients (18%) died (22 events per 100 person-years). Death occurred more commonly in patients who were older (HR 1.33 per decade, 95% CI 1.22–1.46; P < 0.001) or in those with a history of chronic heart failure (HR 1.47, 95% CI 1.16–1.86; P = 0.001) or non-metastatic (HR 2.02, 95% CI 1.45–2.82;

Table 1. Baseline characteristics of 2101 hospitalized adults with AKI at a single centre between 2012 and 2016

	All (n = 2101)	No MAKE (n = 1334)	MAKE (n = 767)	P-value
Male	1225 (58)	787 (59)	438 (57)	0.40
Age, years	69.1 (15.2)	68.3 (15.6)	70.5 (14.4)	0.001
ARIA score				0.72
Major city	1829 (87)	1156 (87)	673 (88)	
Regional	263 (13)	172 (13)	91 (12)	
Remote	7 (<1)	5 (<1)	2 (<1)	
Missing	2 (<1)	1 (<1)	1 (<1)	
Smoking	856 (41)	545 (41)	311 (41)	0.89
Diabetes	817 (39)	508 (38)	309 (40)	0.32
Hypertension	629 (30)	392 (29)	237 (31)	0.47
LDL cholesterol, mmol/L				
<2	241 (11)	160 (12)	81 (11)	
2–4	194 (9)	122 (9)	72 (9)	
>4	28 (1)	14 (1)	14 (2)	
Unmeasured	1638 (78)	1038 (78)	600 (78)	
Cerebrovascular disease	139 (7)	94 (7)	45 (6)	0.30
Cardiovascular disease	386 (18)	243 (18)	143 (19)	0.81
Peripheral vascular disease	229 (11)	150 (11)	79 (10)	0.50
Chronic heart failure	450 (21)	249 (19)	201 (26)	<0.001
Arrhythmia	625 (30)	393 (29)	232 (30)	0.70
Valvular disease	126 (6)	71 (5)	55 (7)	0.09
Lung disease	348 (17)	212 (16)	136 (18)	0.27
Liver disease	360 (17)	197 (15)	163 (21)	<0.001
Haematological disease				0.10
Leukaemia	81 (4)	43 (3)	38 (5)	
Lymphoma	9 (<1)	7 (1)	2 (<1)	
Malignancy				<0.001
Non-metastatic	250 (12)	137 (10)	113 (15)	
Metastatic	157 (7)	65 (5)	92 (12)	
Baseline creatinine, μmol/L	88.5 (27.4)	89.1 (27.7)	87.4 (27.0)	0.18
Baseline eGFR, mL/min/1.73 m^2	72.4 (22.5)	72.3 (22.7)	72.5 (22.0)	0.86
Albuminuria, mg/mmol				0.23
None	371 (18)	222 (17)	149 (19)	
3–30	144 (7)	96 (7)	48 (6)	
>30	68 (3)	46 (3)	22 (3)	
Unmeasured	1518 (72)	970 (73)	548 (71)	
AKI stage				<0.001
Stage 1	1256 (60)	842 (63)	414 (54)	
Stage 2	519 (25)	309 (23)	210 (27)	
Stage 3	326 (16)	183 (14)	143 (19)	
Discharge creatinine, μmol/L	109.5 (48.8)	104.6 (43.4)	117.9 (56.0)	<0.001
Discharge eGFR, mL/min/1.73 m^2	61.4 (25.0)	64.0 (24.9)	56.9 (24.5)	<0.001
Admission type				0.01
Emergency	1696 (81)	1064 (80)	632 (82)	
Elective	309 (15)	217 (16)	92 (12)	
Other	96 (5)	53 (4)	43 (6)	
Admission unit				0.01
General medicine	717 (34)	459 (34)	258 (34)	
Specialty medicine	673 (32)	398 (30)	275 (36)	
General surgery	372 (18)	240 (18)	132 (17)	
Specialty surgery	306 (15)	216 (16)	90 (12)	
Renal	20 (1)	12 (1)	8 (1)	
Missing	13 (1)	9 (1)	4 (1)	
Admission ward				
Intensive care unit	621 (30)	410 (31)	211 (28)	0.12
Coronary care unit	219 (10)	144 (11)	75 (10)	0.46
Hospital length of stay, days	9.0 (5.0–18.0)	9.0 (5.0–17.0)	10.0 (6.0–19.0)	<0.001
Intensive care unit, days	3.4 (1.7–6.5)	2.9 (1.6–6.0)	4.0 (1.9–7.8)	0.007
Coronary care unit, days	2.5 (1.3–4.1)	2.4 (1.5–4.1)	2.6 (1.2–3.9)	0.39
Discharge destination				0.59

(continued)

Table 1. Continued

	All (n = 2101)	No MAKE (n = 1334)	MAKE (n = 767)	P-value
Home	1879 (89)	1189 (89)	690 (90)	
Nursing home	127 (6)	80 (6)	47 (6)	
Other	95 (5)	65 (5)	30 (4)	

LDL, low-density lipoprotein.

Table 2. Multivariable Cox regression analysis of MAKEs within the first year in hospitalized adults with AKI at a single centre between 2012 and 2016

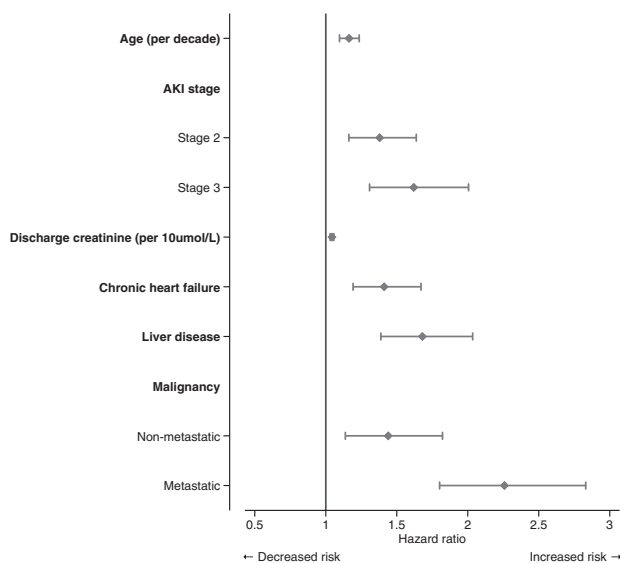|	Hazard ratio	95% CI	P-value
Age, per decade	1.16	1.10–1.24	<0.001
AKI stage			
Stage 1	(Ref)		<0.001
Stage 2	1.38	1.16–1.64	
Stage 3	1.62	1.31–2.01	
Discharge creatinine, per 10 μmol/L	1.04	1.03–1.06	<0.001
Length of stay, per 10 days	1.02	0.99–1.06	0.24
Chronic heart failure	1.41	1.19–1.67	<0.001
Liver disease	1.68	1.39–2.03	<0.001
Haematological disease			
Nil	(Ref)		0.38
Leukaemia	1.29	0.89–1.88	
Lymphoma	0.80	0.20–3.26	
Malignancy			
Nil	(Ref)		<0.001
Non-metastatic	1.44	1.14–1.82	
Metastatic	2.26	1.80–2.83	

FIGURE 2: Multivariable Cox regression analysis of MAKEs within the first year in 2101 hospitalized adults with AKI. Estimates shown include adjusted HR with 95% CI.

P < 0.001) or metastatic (HR 4.46, 95% CI 3.40–5.85; P < 0.001) malignancy. AKI stage, discharge serum creatinine or a history of other comorbidities including diabetes and cardiovascular disease were not associated with the risk of death at 1 year after an episode of AKI.

Sensitivity analyses

When an alternative definition of CKD was used (eGFR <30 mL/min/1.73 m^2 for at least 3 months), the development of a MAKE was no longer associated with AKI stage; however, the number of individuals reaching the outcome was greatly reduced and this analysis may have been underpowered to detect an association (Supplementary data, Table S4). For the second and third sensitivity analyses, there were no qualitative differences in our findings when patients admitted to the intensive care unit were excluded or when albuminuria was included in the multivariable model following multiple imputation of missing data (Supplementary data, Tables S5 and S6). A total of 76 patients had an eGFR measurement of 25% below baseline with no subsequent test. When it was assumed that this group had CKD, our findings were similar (Supplementary data, Table S7).

DISCUSSION
Key findings

More than one in three patients with AKI developed a MAKE within the first year, despite having an eGFR >30 mL/min/

1.73 m^2 at baseline. The development of a MAKE within the first year was associated with older age, chronic heart failure, liver disease, metastatic and non-metastatic malignancy, greater AKI severity and higher serum creatinine level at discharge. Female sex and hypertension were important additional risk factors for the development of CKD and ESKD. Other traditional risk factors for adverse kidney outcomes, including diabetes and cardiovascular disease, were not associated with the early development of MAKEs and therefore may have limited utility in this setting. Very few patients with AKI were under the care of the nephrology unit at the time of admission or hospital discharge and the majority did not undergo albuminuria testing during their hospital stay.

Relationship to previous studies

Our findings suggest that MAKEs occur commonly in the first year after AKI. This is in keeping with two previous studies that reported the incidence of MAKEs to be 30 and 39% following AKI using the US Veterans database [25, 28]. Although those studies did not investigate risk factors for developing a MAKE, several clinical variables identified by our analysis have been found to be associated with either CKD or death in other studies, supporting their validity. While factors such as female sex [7], hypertension [8] and the degree of renal injury and recovery [4, 5, 7, 9, 11] have been found to be important predictors of developing CKD after AKI, other factors such as older age [5–7], chronic heart failure [4], liver disease [9] and malignancy [5] appear to be important predictors of death. The important contribution of
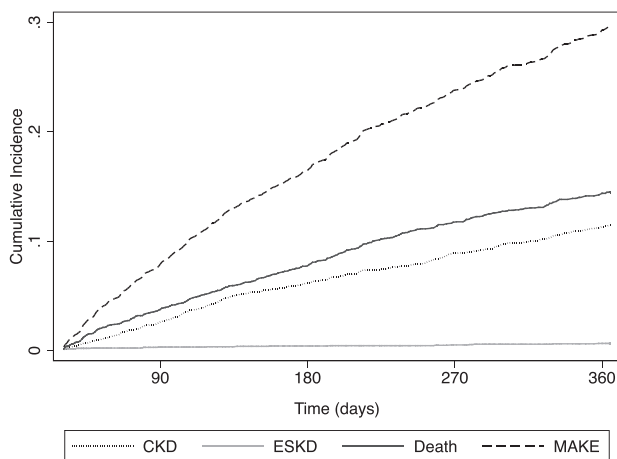
FIGURE 3: Cumulative incidence of MAKEs, CKD, ESKD and death occurring between 30 and 365 days following discharge in 2101 hospitalized adults with AKI.

coexistent malignancy to outcome was also recently reported by Silver *et al.*, who found that cancer-related death after hospitalization with AKI was as common as cardiovascular death [29]. Despite these similarities, other findings from our study conflict with published literature. In contrast to the large study by James *et al.* [7], we did not find albuminuria to be associated with the development of CKD within the first year. This discrepancy may be explained by the frequency with which albuminuria measurements were missing in our dataset or by differences between the two studies in the definition of CKD (25% decline in eGFR versus eGFR <30 mL/min/1.73 m^2). Interestingly, neither study found diabetes or cardiovascular disease to be important risk factors for CKD within the first year after AKI.

Implications of study findings

The ability to identify patients at increased risk of MAKEs after AKI has important implications for patients, health services and health governance bodies. Communicating future risk to survivors of AKI provides the opportunity to encourage engagement in health-seeking behaviours, including compliance with planned outpatient laboratory testing and post-discharge follow-up. In light of our epidemiologic information, health services could plan and ensure that existing systems are capable of identifying high-risk patients during routine clinical care and that hospital infrastructure can accommodate chronic disease surveillance for patients at greatest risk. From a health governance perspective, the increasing incidence of AKI coupled with the high frequency of subsequent MAKEs provides insight into the future burden of CKD and ESKD associated with AKI, which should be used to guide health service planning and delivery.

Strengths and limitations

The strengths of this study lie in its large sample size, representative cohort of hospitalized adults with AKI and its rigorous methodology, as evidenced by the robustness of our findings across sensitivity analyses. The clinical utility of our findings is strengthened by the use of clinical variables that are collected as part of routine care and which are readily available at the time of hospital discharge. However, these strengths must be weighed against the limitations of this study, including its single-centre design and the exclusion of patients lost to follow-up

(i.e. those who did not undergo any post-discharge serum creatinine testing), who may have been at lower risk of developing a MAKE, leading to overestimation of its incidence. The use of ICD-10 codes to identify AKI may have selected for patients with more severe AKI and influenced our reported risk of a future MAKE, although it should be noted that the proportions of patients with each stage of AKI in our study were similar to other published cohorts. Furthermore, a key limitation of this study is the potential for missing data arising from the use of non-hospital-based pathology services or other hospitals; however, the median number of outpatient serum creatinine measurements in the first year was considered to be acceptable. As an observational study, our findings are limited to associations and residual confounding cannot be excluded.

CONCLUSIONS

In summary, this study found that MAKEs are common in the first year after AKI and that readily available clinical variables can be used to identify patients at increased risk. Identifying such patients could assist clinicians to prioritize outpatient care. Although these findings provide important insight, their utility in clinical practice requires further exploration and validation in other centres and across other clinical settings.

SUPPLEMENTARY DATA

Supplementary data are available at ckj online.

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CONFLICT OF INTEREST STATEMENT

None declared. The results presented in this article have not been published previously in whole or part, except in abstract form.

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