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Original Article

Duration of acute kidney injury predicts 90-day mortality and chronic kidney disease progression in elderly patients

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ABSTRACT

Background: This study evaluated the prognostic impact of acute kidney injury (AKI) duration on 90-d mortality and new-onset chronic kidney disease (CKD) progression in elderly patients.

Methods: We retrospectively enrolled elderly patients (≥75 years; $n = 693$) from the Chinese PLA General Hospital between January 1, 2007 and December 31, 2018. The 2012 Kidney Disease Improving Global Outcomes (KDIGO) defined serum creatinine (Scr) criteria were used to identify and classify AKI. Patients were divided into transient AKI (T-AKI) and persistent AKI (P-AKI) groups based on whether Scr levels returned to baseline within 48 h post-AKI. We further classified P-AKI based on AKI duration: (1) short duration: resolving AKI lasting 3–4 days; (2) medium duration: resolving AKI lasting 5–7 days; and (3) long duration: AKI lasting >7 days.

Results: Among patients, 62 (9.0%) had T-AKI (1–2 days), 104 (15.0%) had short-duration, 140 (20.2%) had medium-duration, and 387 (55.8%) had long-duration. In total, 209 (30.2%) died within 90 days; 122 (25.2%) developed CKD. After adjusting for multiple covariates, duration of AKI (3–4 days: hazard ratio [HR] = 2.512; P =0.045; 5–7 days: HR=3.154; P =0.015; >7 days: HR=6.212; P<0.001) was significantly associated with a higher 90-day mortality. Longer AKI duration (3–4 days: odds ratio [OR] = 0.982; P =0.980; 5–7 days: OR=1.322; P =0.661; >7 days: OR=7.007; P<0.001) was significantly associated with new-onset CKD of survivors.

Conclusion: AKI duration is useful for predicting poorer clinical outcomes in elderly patients, emphasizing the importance of identifying an appropriate treatment window for early intervention.

Introduction

Acute kidney injury (AKI) consists of a group of clinical syndromes associated with compromised patient survival, development of chronic kidney disease (CKD), or poor renal function recovery.[1–3] The recent recommendation from the international Kidney Disease Improving Global Outcomes (KDIGO) guidelines defined AKI and classified the stages of AKI severity into three grades, based on the increase and/or decrease in serum creatinine (Scr) and urine output; moreover, an advanced AKI stage has been associated with adverse outcomes.[2,4] In fact, AKI duration has recently been viewed as another independent risk factor for a poor outcome: longer duration of AKI (also called persistent AKI [P-AKI]), typically defined as >48–72 h after onset, has been associated with a higher risk for CKD and death compared to short-duration AKI (also called transient AKI [T-AKI]).[5–9] However, a recent intensive care unit patient-based retrospective study showed that although P-AKI is associated with poorer hospital survival, this association was attenuated after accounting for AKI severity.[10]

AKI is more frequent in the elderly, and a relationship between AKI incidence and age is evident.[2] However, limited information is available on the association between the duration of the increase in Scr and clinical outcomes in elderly patients.[11] We have previously shown that patients with P-AKI (elevated Scr level >3 days) are more likely to experience more severe AKI and have a higher 90-day mortality than patients with T-AKI (in whom Scr returned to baseline levels within 3 days);[8] however, the diagnoses of T-AKI and P-AKI were not made based on the 2017 Acute Disease Quality Initiative (ADQI)

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criteria, and renal function recovery was not assessed 90 days post-AKI.[12]

The current study aimed to evaluate the prognostic impact of AKI duration on 90-day mortality and progression of new-onset CKD in elderly patients after AKI development.

Materials and Methods

Patients and data collection

This was a retrospective observational study conducted at the National Clinical Research Center for Geriatric Diseases. The patients in this center were mostly retired people, and nearly all the patients were retired elderly males. All patients aged ≥75 years with normal renal function who were admitted between January 1, 2007 and December 31, 2018 were enrolled. All procedures involving human participants were performed in accordance with the basic principles of the Declaration of Helsinki. The study design was approved by the Clinical Ethics Committee of the Hospital (ethics approval No. S2017–054–01). The requirement to obtain written informed consent from each patient was waived because this was an observational retrospective study. All patient data were anonymized, and confidentiality was maintained.

The exclusion criteria were as follows: patients who had been previously diagnosed with CKD, hospital stay <48 h, patients with no Scr or only one Scr examination, patients with insufficient medical records, and patients who died within 48 h of admission.

Definitions

The 2012 KDIGO defined Scr criteria were used to identify and classify AKI. The CKD Epidemiology Collaboration was used to calculate baseline estimated glomerular filtration rate (eGFR).[13] The baseline Scr level was the most recent measure taken in the 1–3 months before admission for AKI.[14] Peak Scr was the highest Scr level reached during the episode. "T-AKI" was defined as Scr that returned to baseline within 48 h post-AKI (AKI duration 1–2 days); "P-AKI" was defined as renal dysfunction without recovery within 48 h.[12] We further classified P-AKI into three categories based on AKI duration: (1) AKI lasting 3–4 days; (2) AKI lasting 5–7 days; and (3) AKI lasting >7 days. The outcome of renal function 90 days post-AKI as indicated by eGFR was characterized as non-CKD (eGFR ≥60 mL • min^{-1} • 1.73 m^2) or new-onset CKD (eGFR <60 mL • min^{-1} • 1.73 m^2).[15] Sepsis was defined according to the Surviving Sepsis Campaign Bundle: 2018 update.[16]

Statistical analysis

Continuous variables of parametric data are presented as mean ± standard deviation, or as median with interquartile range (with 25th and 75th percentiles) for nonparametric variables. Categorical variables are presented as numbers (*n*) or percentages (%). Group comparisons were conducted using analysis of variance (ANOVA) or the Kruskal–Wallis H-test for continuous variables and Pearson's chi-squared or Fisher's exact test for categorical variables. Multivariate logistic regression analyses were performed to identify covariates associated with new-onset CKD from AKI. Prognostic survival factors were identified using the Cox proportional hazards regression model. Survival probability was estimated using the Kaplan–Meier method, and curves were compared among groups using the log-rank test. A *P*-value < 0.05 was considered significant. Statistical analyses were performed using SPSS v.21.0 for Windows software (SPSS Inc., Chicago, IL, USA).

Results

Study population

A total of 3861 elderly patients (aged ≥75 years) were hospitalized between January 1, 2007 and December 31, 2018 at the National Clinical Research Center for Geriatric Diseases, and 760 developed AKI during hospitalization. Among these patients, 10 were excluded for hospital stays <48 h, and 3 were excluded owing to missing data. Therefore, 747 AKI patients were suitable for the subsequent analysis, including 685 (91.7%) patients with P-AKI and 62 (8.3%) patients with T-AKI. Of the 747 patients, we further excluded 54 patients owing to death within 48 h post-AKI because the duration of AKI could not be determined. Consequently, 693 AKI patients were included in the final evaluation.The study flowchart is presented in Figure 1.

AKI

As shown in Table 1, the median age of the 693 participants was 88 years, and the majority (656, 94.7%) were male. Of these, T-AKI was documented in 62 (9.0%) and P-AKI in 631 (91.0%) according to our definitions, including 104 (15.0%) with an AKI duration of 3–4 days, 140 (20.2%) with an AKI duration of 5–7 days, and 387 (55.8%) with P-AKI >7 days. Among the 693 patients, 319 (46.0%) had KDIGO stage 1 AKI, 172 (24.8%) had stage 2 AKI, 202 (29.1%) had stage 3 AKI, and 4 (0.6%) needed dialysis. Among all patients, 209 (30.2%) died within 90 days, including 5 (8.1%) with T-AKI and 204 (32.3%) with P-AKI. Of the 484 survivors with AKI in whom eGFR recovery could be assessed, 362 (74.8%) recovered to the baseline level and 122 (25.2%) developed CKD.

Duration of AKI

Table 1 presents baseline and AKI characteristics stratified by AKI duration. Comparison of the four groups indicated no significant differences in sex, body mass index, preexisting comorbidities (hypertension, chronic obstructive pulmonary disease [COPD], and diabetes mellitus), or AKI etiology (hypovolemia, nephrotoxicity, surgery, and others). Similarly, no significant differences were observed in clinical conditions (mean arterial pressure and oliguria), or laboratory results (blood glucose, calcium, phosphate, C–reactive protein, albumin, and serum prealbumin), as well as the need for renal replacement therapy (RRT) on the day of AKI development. The P-AKI group more frequently required mechanical ventilation support. Scr levels, peak Scr levels, peak blood urea nitrogen (BUN) levels, uric acid levels, and sodium levels increased; but hemoglobin decreased as AKI duration prolonged. More patients with P-AKI were evaluated by nephrologists than those with T-AKI.

Table 1
Characteristics of patients with transient and P-AKI.

Characteristic	AKI patients (n =693)	Duration of AKI				t/χ^2	P-value
		1–2 days (n =62, 9.0%)	3–4 days (n =104, 15.0%)	5–7 days (n =140, 20.2%)	>7 days (n =387, 55.8%)		
Age (years)	88 (84–91)	87 (84–91)	86 (83–89)	88 (84–91)	88 (84–91)	15.652	0.001
75–79	82 (11.8)	10 (16.1)	18 (17.3)	15 (10.7)	39 (10.1)	21.811	0.040
80–85	154 (22.2)	10 (16.1)	34 (32.7)	33 (23.6)	77 (19.9)		
86–90	255 (36.8)	25 (40.3)	33 (31.7)	52 (37.1)	145 (37.5)		
91–95	155 (22.4)	12 (19.4)	16 (15.4)	27 (19.3)	100 (25.8)		
≥96	47 (6.8)	5 (8.1)	3 (2.9)	13 (9.3)	26 (6.7)		
Male sex	656 (94.7)	57 (91.9)	99 (95.2)	131 (93.6)	369 (95.3)	1.542	0.973
Body mass index (kg/m^2)	23.0 ± 3.1	22.6 ± 4.1	23.4 ± 3.3	23.1 ± 3.0	23.0 ± 2.9	1.037	0.376
Comorbidity							
Coronary disease	527 (76.0)	51 (82.3)	67 (64.4)	113 (80.7)	296 (76.5)	10.742	0.013
Hypertension	505 (72.9)	52 (83.9)	74 (71.2)	100 (71.4)	279 (72.1)	4.216	0.239
COPD	477 (68.8)	43 (69.4)	63 (60.6)	100 (71.4)	271 (70.0)	4.008	0.261
Diabetes	266 (38.4)	26 (41.9)	42 (40.4)	47 (33.6)	151 (39.0)	1.943	0.584
Baseline Scr (μmol/L)	72.0 (60.0–83.0)	70.0 (60.0–80.0)	71.0 (62.0–80.0)	70.0 (57.0–80.0)	75.0 (62.0–85.0)	15.462	0.001
Baseline eGFR (mL • min^{-1} • 1.73 m^2)	78.4 (71.7–84.9)	80.2 (75.0–85.5)	79.7 (75.4–86.0)	80.0 (75.5–86.6)	77.0 (69.7–83.8)	21.829	<0.001
Baseline eGFR (mL • min^{-1} • 1.73 m^2)						26.656	0.002
60–69	141 (20.3)	9 (14.5)	11 (10.6)	21 (15.0)	100 (25.8)		
70–79	258 (37.2)	20 (32.3)	42 (40.4)	50 (35.7)	146 (37.7)		
80–89	209 (30.2)	28 (45.2)	36 (34.6)	46 (32.9)	99 (25.6)		
>90	85 (12.3)	5 (8.1)	15 (14.4)	23 (16.4)	42 (10.9)		
Etiology of AKI							
Sepsis	285 (41.1)	19 (30.6)	40 (38.5)	71 (50.7)	155 (40.1)	8.618	0.035
Hypovolemia	143 (20.6)	12 (19.4)	17 (16.3)	32 (22.9)	82 (21.2)	1.725	0.631
Cardiovascular events	106 (15.3)	15 (24.2)	24 (23.1)	10 (7.1)	57 (14.7)	15.927	0.001
Nephrotoxicity	88 (12.7)	4 (6.5)	11 (10.6)	16 (11.4)	57 (14.7)	4.247	0.236
Surgery	48 (6.9)	9 (14.5)	7 (6.7)	6 (4.3)	26 (6.7)	6.072	0.108
Others	23 (3.3)	3 (4.8)	5 (4.8)	5 (3.6)	10 (2.6)	1.756	0.624
Clinical conditions							
Mean arterial pressure (mmHg)	79 ± 14	81 ± 14	78 ± 14	78 ± 14	79 ± 13	1.145	0.330
Oliguria	35 (5.1)	2 (3.2)	3 (2.9)	8 (5.7)	22 (5.7)	2.123	0.547
Mechanical ventilation	260 (37.5)	8 (12.9)	34 (32.7)	54 (38.6)	164 (42.4)	21.022	<0.001
Laboratory parameters							
Scr (μmol/L)	128.0 (115.0–143.6)	116.1 (107.0–134.9)	123.0 (111.1–137.9)	124.4 (109.0–138.0)	132.0 (120.0–148.0)	35.617	<0.001
Peak Scr (μmol/L)	142.0 (123.2–204.5)	117.9 (109.8–136.2)	124.9 (113.1–146.0)	137.9 (118.6–181.0)	156.0 (134.8–247.8)	103.960	<0.001
BUN (mmol/L)	12.3 (8.8–20.1)	9.3 (7.2–12.8)	11.1 (7.6–17.3)	14.0 (9.5–22.3)	12.9 (9.2–20.7)	29.697	<0.001
Peak BUN (mmol/L)	16.8 (10.4–32.2)	10.8 (8.1–15.6)	13.1 (9.1–23.6)	18.1 (11.5–32.6)	20.7 (11.1–36.0)	48.164	<0.001
Uric acid (μmol/L)	363.0 (285.8–461.0)	338.3 (268.9–419.4)	343.6 (270.8–433.9)	361.0 (297.8–470.2)	371.1 (293.7–471.0)	8.557	0.036
Blood glucose (mmol/L)	7.3 (5.8–10.0)	7.6 (6.2–9.8)	7.4 (6.0–9.8)	7.6 (6.1–10.0)	7.0 (5.4–10.3)	4.772	0.189
K (mmol/L)	4.1 (3.8–4.6)	4.1 (3.8–4.3)	4.0 (3.8–4.5)	4.3 (3.9–4.9)	4.1 (3.8–4.7)	8.201	0.042
Na (mmol/L)	140.0 (136.0–146.0)	138.0 (132.0–142.0)	139.0 (133.0–145.0)	140.0 (136.0–148.0)	141.0 (137.0–147.0)	17.909	<0.001
Ca (mmol/L)	2.2 (2.1–2.4)	2.2 (2.0–2.3)	2.2 (2.1–2.4)	2.2 (2.1–2.4)	2.2 (2.1–2.4)	2.227	0.527
P (mmol/L)	1.2 (0.9–1.4)	1.1 (0.9–1.5)	1.1 (0.9–1.3)	1.1 (0.9–1.4)	1.2 (1.0–1.4)	3.008	0.390
Mg (mmol/L)	0.9 (0.8–1.0)	0.9 (0.7–1.0)	0.9 (0.8–1.0)	0.9 (0.8–1.0)	0.9 (0.8–1.0)	8.793	0.032
C–reactive protein (mmol/L)	3.7 (1.8–9.1)	3.5 (1.6–8.4)	4.2 (1.9–9.9)	4.7 (1.8–10.1)	3.5 (1.8–8.5)	2.392	0.495
Albumin (g/L)	34.5 ± 5.5	36.1 ± 5.3	34.6 ± 6.0	34.5 ± 5.8	34.2 ± 5.2	2.323	0.074
Prealbumin (g/L)	180.0 (139.0–232.0)	187 (143–235)	174 (137–217)	175 (135–230)	180 (140–240)	2.266	0.519
Hemoglobin (g/L)	112 ± 22	119 ± 20	118 ± 21	114 ± 22	109 ± 22	7.399	<0.001
AKI stage						37.892	<0.001
1	319 (46.0)	39 (62.9)	65 (62.5)	58 (41.4)	157 (40.6)		
2	172 (24.8)	18 (29.0)	22 (21.2)	42 (30.0)	90 (23.3)		
3	202 (29.1)	5 (8.1)	17 (16.3)	40 (28.6)	140 (36.2)		
Nephrology consultation	180 (26.0)	7 (11.3)	16 (15.4)	27 (19.3)	130 (33.6)	27.955	<0.001
90-day outcome							
RRT	4 (0.6)	0	0	0	4 (1.0)	4.679	0.197
Mortality	209 (30.2)	5 (8.1)	27 (26.0)	46 (32.9)	131 (33.9)	18.226	<0.001

Data are presented as n (%), mean ± standard deviation, or median (interquartile range).

AKI: Acute kidney injury; BUN: Blood urea nitrogen; COPD: Chronic obstructive pulmonary disease; eGFR: Estimated glomerular filtration rate; P-AKI: Persistent AKI; RRT: Renal replacement therapy; Scr: Serum creatinine.

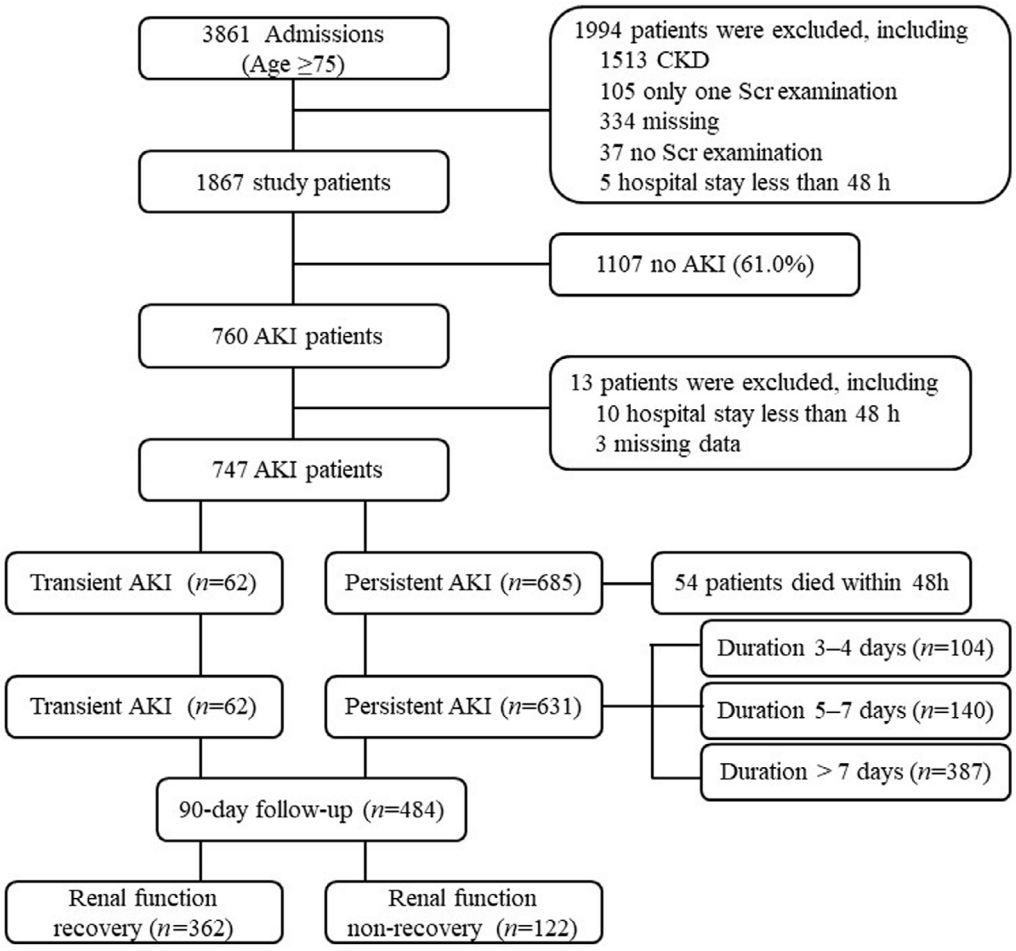

Figure 1. Flow chart for patient inclusion and exclusion. AKI: Acute kidney injury; CKD: Chronic kidney disease; Scr: Serum creatinine.

Table 2
Prevalence of AKI duration and KDIGO stage relative to mortality and renal function outcomes.

Characteristic	Non-survivors (*n* =209, 30.2%)	Survivors (*n* =484, 69.8%)	*P*-value	New-onset CKD (*n* =122, 25.2%)	Non-CKD (*n* =362, 74.8%)	*P*-value
Duration of AKI			<0.001			<0.001
1–2 days	5 (2.4)	57 (11.8)		4 (3.3)	53 (14.6)	
3–4 days	27 (12.9)	77 (15.9)		5 (4.1)	72 (19.9)	
5–7 days	46 (22.0)	94 (19.4)		9 (7.4)	85 (23.5)	
>7 days	131 (62.7)	256 (52.9)		104 (85.2)	152 (42.0)	
AKI stage			<0.001			0.765
1	15 (7.2)	304 (62.8)		78 (63.9)	226 (62.4)	
2	50 (23.9)	122 (25.2)		28 (23.0)	94 (26.0)	
3	144 (68.9)	58 (12.0)		16 (13.1)	42 (11.6)	

Data are presented as *n* (%).
AKI: Acute kidney injury; CKD: Chronic kidney disease; KDIGO: Kidney Disease Improving Global Outcomes.

90-day mortality and new-CKD progression according to AKI duration and KDIGO stage

A total of 209 patients died within 90 days. Among the survivors, 25.2% (122/484) experienced CKD progression and 74.8% (362/484) did not. The 90-day mortality was 8.1% in patients with T-AKI and 32.3% in those with P-AKI, including 26.0% with an AKI duration of 3–4 days, 32.9% with an AKI duration of 5–7 days, and 33.9% with P-AKI >7 days (P<0.001; Table 1). Accordingly, as shown in Table 2, the prevalence of P-AKI was significantly higher in the non-surviving group (97.6% *vs.* 88.2%, P<0.001); AKI of duration 5–7 days and P-AKI >7 days occurred more frequently among non-survivors than survivors (22.0% *vs.* 19.4% and 62.7% *vs.* 52.9%, respectively; P<0.001). The Kaplan–Meier survival plot demonstrated that within the AKI groups, higher mortality was found in patients with a longer duration of AKI than those with a shorter AKI duration (log-rank P = 0.002; not shown).

Table 2 shows that the 90-day mortality rates were 7.2%, 23.9%, and 68.9% for AKI stages 1, 2, and 3, respectively (P<0.001). Figure 2 shows the 90-day mortality curves in the different AKI groups for each AKI stage. The 90-day mortality rates among the AKI groups for each AKI stage were significantly different (all P<0.001, log–rank test), but there was no differ-

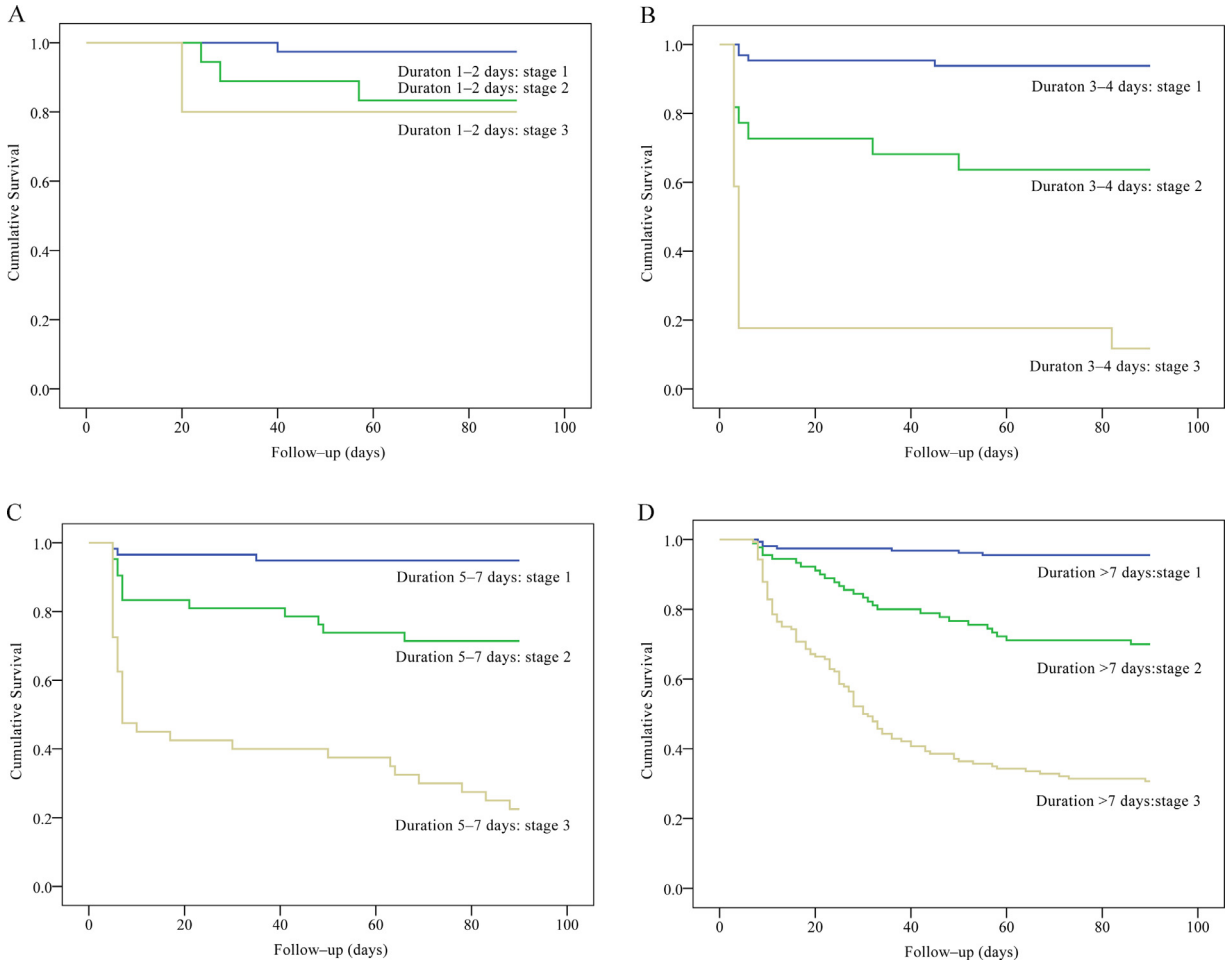

Figure 2. Kaplan-Meier survival curves according to AKI duration and the KDIGO stage. A: AKI duration 1–2 days(log-rank test: *P*=0.104); B: AKI duration 3–4 days (log-rank test: *P*<0.001); C: AKI duration 5–7 days (log-rank test: *P*<0.001); D: AKI duration >7 days (log-rank test: *P*<0.001).
AKI: Acute kidney injury; KDIGO: Kidney Disease Improving Global Outcomes.

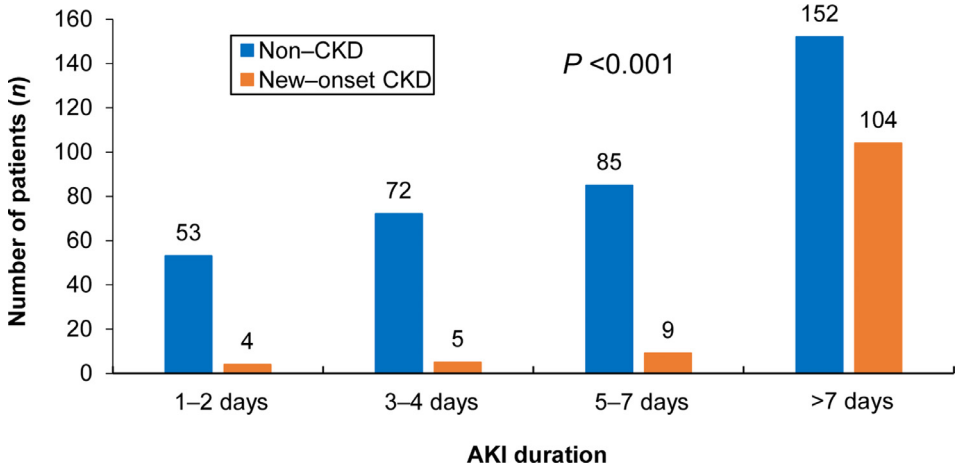

Figure 3. Renal function outcomes of different AKI durations in patients with AKI (log–rank test: *P*<0.001). AKI: Acute kidney injury; CKD: Chronic kidney disease.

ence in T-AKI (duration 1–2 days) among the different AKI stage groups (log-rank test: *P* =0.104; Figure 2A).

As shown in Table 2, the incidence rates of P-AKI were 96.7% in patients with new-onset CKD *vs.* 85.4% in the non-CKD group. AKI duration >7 days was more likely to be seen in new-onset CKD than in the non-CKD group (85.2% *vs.* 42.0%, *P*<0.001). Figure 3 shows the significant differences in new-onset CKD among the four groups (*P*<0.001). Table 2 shows the relationship between the AKI stage and CKD progression. Surprisingly, AKI severity was not significantly associated with progression of new-onset CKD (63.9% *vs.* 62.4% for stage 1 patients, 23.0% *vs.* 26.0% for stage 2,

Table 3
Multivariate proportional hazard model analysis of risk factors for AKI 90-day outcomes.

Risk factor	90-day mortality, HR (95% CI)	*P*-value	New-onset CKD, OR (95% CI)	*P*-value
Duration of AKI		<0.001		<0.001
1–2 days	Reference		Reference	
3–4 days	2.512 (1.021–6.181)	0.045	0.982 (0.247–3.900)	0.980
5–7 days	3.154 (1.250–7.960)	0.015	1.322 (0.381–4.592)	0.661
>7 days	6.212 (2.383–16.192)	<0.001	7.007 (2.417–20.311)	<0.001
AKI stage		<0.001	–	–
1	Reference		–	–
2	7.365 (4.114–13.183)	<0.001	–	–
3	28.414 (16.360–49.350)	<0.001	–	–
Body mass index	0.910 (0.870–0.953)	<0.001	–	–
Baseline eGFR	–	–	0.928 (0.901–0.956)	<0.001

–: No data. AKI: Acute kidney injury; CKD: Chronic kidney disease; CI: Confidence interval; eGFR: Estimated glomerular filtration rate; HR: Hazard ratio; OR: Odds ratio.

and 13.1% *vs.* 11.6% for stage 3; P = 0.765 for the three stages).

Influence of AKI duration and KDIGO stage on 90-day patient mortality and new-onset CKD progression

When AKI duration was considered a binary variable (transient and P-AKI), P-AKI was associated with 90-day mortality (hazard ratio [HR] = 2.522; 95% confidence interval [CI]: 1.028–6.186; P =0.043) and the progression of new-onset CKD (odds ratio [OR] = 3.907; 95% CI: 1.331–11.463; P =0.013) in a multivariate regression analysis (data not shown).

When AKI duration was considered an ordinal variable (1–2 days, 3–4 days, 5–7 days, and >7 days), the independent risk factors for 90-day mortality were as follows: duration of AKI (3–4 days: HR = 2.512; 95% CI: 1.021–6.181; P=0.045, 5–7 days: HR=3.154; 95% CI: 1.250–7.960; P=0.015; >7 days: HR=6.212; 95% CI: 2.383–16.192; P<0.001), more advanced AKI stage (stage 2: HR=7.365; 95% CI: 4.114–13.183; P<0.001; stage 3: HR=28.414; 95% CI: 16.360–49.350; P<0.001), and low body mass index (HR=0.910; 95% CI: 0.870–0.953; P<0.001; Table 3). The independent risk factors for the progression of new-onset CKD were duration of AKI (3–4 days: OR=0.982; 95% CI: 0.247–3.900; P=0.980; 5–7 days: OR=1.322; 95% CI: 0.381–4.592; P=0.661; >7 days: OR=7.007; 95% CI: 2.417–20.311; P<0.001) and baseline eGFR (OR=0.928; 95% CI: 0.901–0.956; P<0.001; Table 3).

Discussion

In the present study, approximately 91% of geriatric patients had AKI lasting >48 h during hospitalization, demonstrating a high incidence of P-AKI in this patient population. Furthermore, P-AKI in geriatric patients was independently associated with a higher 90-day mortality. Among patients who survived >90 days, an AKI duration of >7 days was associated with a progression to CKD at 90 days after the occurrence of AKI.

With wider recognition of the pathogenesis of AKI along with the greater economic and social burden it brings, the International Society of Nephrology (ISN) launched a global target of "0 by 25," i.e., by 2025, there should be no deaths in low-resource regions as a result of untreated AKI, and this is to be ensured by improving the diagnosis and treatment of AKI.[17] Early identification of P-AKI is vital to initiate an extended evaluation and management protocol to avoid further kidney damage and reduce mortality. However, only 21–44% of patients receive a timely diagnosis of AKI in China, the largest developing country in the world with approximately 20% of the global population. Furthermore, the rate of missed diagnosis is 53–74%.[18–20] One possible reason for these results may be the obscure definition in the KDIGO AKI criteria (48-h and 7-day time windows), which is neither widely recognized nor accepted by physicians.[21] Other potential reasons include insufficient recognition of AKI severity, insufficient renal function surveillance during hospital stay, untimely Scr measurements among patients at higher risk, as well as the often ignored importance of a slight increase in Scr and subsequent reexaminations.[18–20,22–24] Therefore, vital treatment windows are often missed. In addition, some patients with T-AKI may progress to P-AKI, leading to a delayed or no nephrology referral.[21]

Several studies have examined the prognostic impact of AKI duration using various diagnostic criteria as follows: transient azotemia (≤3 days) and acute tubular necrosis (≥4 days or needs RRT);[25] short (≤2 days), medium (3–6 days), and long (≥7 days or needs RRT) using the Acute Kidney Injury Network (AKIN) criteria;[6,26] T-AKI (≤7 days) and P-AKI (>7 days) using the KDIGO criteria;[15,27] T-AKI (Scr ≤115 μmol/L at discharge) and P-AKI (Scr >115 μmol/L at discharge) using the KDIGO criteria;[28] T-AKI (≤3 days) and P-AKI (>3 days) using the AKIN criteria;[10] and short (≤2 days), medium (3–7 days), and long (>7 days) using the KDIGO criteria.[7] In the present study, no independent associations were observed between T-AKI and poor outcomes. The discrepancies between these studies might reflect the substantial variety in the duration of recovery from AKI according to the various definitions of AKI, T-AKI, or P-AKI according to different study populations, patient ages, and etiologies of AKI.

Clinical studies have indicated that the duration of AKI is associated with a higher risk of adverse outcomes, but they ignore a potentially important factor after AKI develops: early and prolonged nephrology follow-up. Delayed or absent nephrology referrals are associated with higher mortality and a requirement for dialysis.[19] Interestingly, we found in this study that only 26% of AKI patients were evaluated by nephrologists. Thus, increasing the likelihood of a timely AKI diagnosis and identifying patients who are indicated for a nephrologist consultation remains a challenge. Clearly, the high likelihood of a missed diagnosis is mainly attributed to the uniformly known KDIGO AKI criteria in which routine daily Scr measurements are not warranted.[18,21] The ISN 0by25 initiative recommends more fre-

quent Scr monitoring in high-risk populations, electronic alerting systems for AKI, and timely nephrology referral and follow-up to document renal function recovery.[17,29] Although the exact pathophysiology has not been clearly elucidated, experimental models have shown that even with apparent renal function recovery from AKI, histological and physiological changes may persist after AKI and can predispose patients to long-term CKD risk. However, our findings indicate that only patients with P-AKI for >7 days had greater CKD progression, whereas those with ≤7 days of P-AKI did not. One possible explanation for this association with CKD progression is that many patients with P-AKI have structural kidney injury, the duration of AKI increases, and CKD increases.

Another important issue is the timing of recovery assessment; i.e., some studies determined "recovery" after 3–7 days to make the distinction between T-AKI and P-AKI, while most studies report recovery at hospital discharge, or after 1 year.[30–32] In the present study, renal function outcome was evaluated 90 days after an AKI episode based on the KDIGO AKI guidelines; however, 74% of patients who survived an AKI episode did not see a nephrologist at all. Findings of studies from the USA and the UK show that within 1 year, only 60% of patients are seen by any physician and only 10–15% are seen by a nephrologist, even though intervention by a nephrologist improves recovery rates.[33,34] This practice may represent a missed treatment window to improve outcomes after an episode of severe AKI. Of course, there are not nearly enough nephrologists to see all very elderly patients with P-AKI.[35]

Effective treatment for AKI is strongly dependent on timely recognition and early nephrological care. Based on the results of this study and experience from developed countries, an electronic alerting system for AKI and timeous nephrology consultation may be suitable and needed.[18] Nephrologists need to take responsibility for organizing the battle against AKI, including education and training. Non-nephrologists should also fully understand the pathophysiological features of aging kidneys; raise the level of understanding and awareness of AKI; be familiar with the definition and diagnostic criteria of AKI; and invite a nephrologist to intervene in a timely manner, which is important for improving the prognosis of elderly AKI patients.[36]

The strengths of this study include the advanced age of the sample, the use of a consensus definition for the AKI/CKD diagnosis, the KDIGO/ADQI guidelines and stages, and the availability of baseline Scr for the entire sample of patients. However, there were several limitations in this study. (1) This was a single-center retrospective study, with a 90-day follow-up; however, data were insufficient to analyze a long-term follow-up. (2) We did not have data on urine output, which is a component of the KDIGO definition; therefore, the incidence of AKI in our study may have been underestimated. (3) The patients at this center were mainly retired, and nearly all patients were male. Hence, the results cannot be generalized to other hospitals in which diagnostic or practice patterns may vary across older populations. (4) Factors influencing the AKI prognosis are complicated, such as the Acute Physiologic and Chronic Health Evaluation II score and the sequential organ failure assessment score, which can also be used to predict AKI patient outcomes.

In conclusion, AKI duration is an additional parameter for predicting poorer clinical outcomes in elderly patients, emphasizing the importance of identifying a treatment window and those who may benefit from an early intervention.

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Ethical Approval

This study has been approved by the Ethics Committee of the Chinese PLA General Hospital (Number: S2017–054–01). The requirement for written informed consent was waived by the ethics committee of the designated hospital because this was an observational retrospective study.

Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflicts of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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