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Acute Kidney Injury and Subsequent Frailty Status in Survivors of Critical Illness: a Secondary Analysis

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Reprints will not be ordered/requested

Conflicts of Interest

The authors have no conflicts to declare.

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Abstract

Objective—Acute kidney injury (AKI) frequently complicates critical illness and is associated with high morbidity and mortality. Frailty is common in critical illness survivors, but little is known about the impact of AKI. We examined the association of AKI and frailty within a year of hospital discharge in survivors of critical illness.

Design—Secondary analysis of a prospective cohort study

Setting—Medical/surgical ICU of a US tertiary care medical center

Patients—317 participants with respiratory failure and/or shock

Interventions—None

Measurements and Main Results—AKI was determined using Kidney Disease Improving Global Outcomes stages. Clinical frailty status was determined using the Clinical Frailty Scale (CFS) at 3 and 12 months following discharge. Covariates included mean ICU sequential organ failure assessment (SOFA) score and acute physiology and chronic health evaluation II (APACHE II) score as well as baseline comorbidity (i.e., Charlson Comorbidity Index), kidney function, and CFS score. Of 317 patients, 243 (77%) had AKI and 1 in 4 patients with AKI were frail at baseline. In adjusted models, AKI stages 1, 2, and 3 were associated with higher frailty scores at 3 months (OR 1.92, 95% CI 1.14, 3.24; OR 2.40, 95% CI 1.31, 4.42; OR 4.41, 95% CI 2.20, 8.82; respectively). At 12 months, a similar association of AKI stages 1, 2, and 3 and higher CFS score was noted (OR 1.87, 95% CI 1.11, 3.14; OR 1.81, 95% CI 0.94, 3.48; OR 2.76, 95% CI 1.34, 5.66; respectively). In supplemental and sensitivity analyses, analogous patterns of association were observed.

Conclusions—AKI in survivors of critical illness predicted worse frailty status 3 and 12 months post-discharge. These findings have important implications on clinical decision making among AKI survivors and underscore the need to understand the drivers of frailty to improve patient-centered outcomes.

Keywords

frailty; critical illness; acute kidney injury; prospective cohort; clinical frailty scale; chronic kidney disease; mortality

Introduction

Acute kidney injury (AKI) affects up to half of patients admitted to the ICU (1–4). The incidence of AKI is increasing rapidly, and along with it, the population of survivors for whom optimal care has not been defined (1–4). Most post-AKI research focuses on its long-term impact on organ function. However, less attention is paid to outcomes such as quality of life and functional status (5).

Frailty is a multidimensional condition denoted by a “loss of physiologic reserve and the ability to resist stressors” (6, 7). While associated with aging, frailty is observed in younger patients with acute and chronic diseases and predicts subsequent hospitalizations, functional decline, and death (6–17). This is particularly salient to AKI survivors who experience these outcomes at markedly elevated rates; however, the mechanisms driving this relationship remain unclear.

Although AKI often occurs in patients with multiple comorbidities that may contribute to frailty, AKI may directly promote frailty even after recovery from the acute illness. We hypothesized that among critically ill patients who survived to hospital discharge, AKI would be associated with higher frailty scores at 3 and 12 months. To test this hypothesis, we used data from the prospective BRAIN-ICU cohort of critically ill patients who were assessed at baseline, 3 months, and 12 months using the Clinical Frailty Scale (CFS) (9, 18, 19).

Materials and Methods

Study setting and design

The BRAIN-ICU Study is a prospective cohort of critically ill adults (age ≥ 18 years) with acute respiratory failure and/or shock (septic or cardiogenic) enrolled between 2007 and 2010 at 5 medical centers (9, 18, 20). Follow-up occurred at 3- and 12-months post-discharge. We have previously described BRAIN-ICU enrollment in detail (9, 18, 20). Briefly, patients with recent ICU exposure (i.e., mechanical ventilation within 2 months, 5 ICU days within the prior month), an expected survival of less than 24 hours, inability to be reliably assessed for delirium (i.e., blindness, deafness, or non-English speaking), and a high likelihood of pre-existing cognitive deficits (e.g., neurodegenerative disease, anoxic brain injury, severe dementia) were excluded from the parent study. For this secondary analysis, we restricted the cohort to participants who were enrolled at Vanderbilt University Medical Center since daily serum creatinines were available for this group. Additional exclusion criteria unique to these analyses were (see Figure 1) end-stage renal disease (ESRD, i.e., baseline eGFR < 15 ml/min/1.73m², history of kidney transplant, or receiving maintenance dialysis; n=36), missing sequential organ failure assessment (SOFA) scores (n=2), death prior to hospital discharge (n=83), or alive but absent from both the 3-month and 12-month follow-up visits (n=27). Written informed consent was obtained from all participants and/or their surrogates. The study was approved by the Vanderbilt University Medical Center IRB.

Baseline kidney function and acute kidney injury

We estimated baseline kidney function by using the mean of all outpatient serum creatinine values from 7 to 365 days prior to the index admission (21). If the mean outpatient serum creatinine was not available, we used the lowest serum creatinine during the hospitalization as the baseline creatinine (22). To improve accuracy, we performed clinical adjudication of baseline serum creatinine in 2 settings. First, if the lowest serum creatinine during the hospitalization was ≥ 0.5mg/dl below the mean of all outpatient serum creatinines from 7 to 365 days prior to index admission. Second, for patients with a baseline serum creatinine that resulted in an eGFR < 60 ml/min/1.73m². In these settings, 2 nephrologists (KA, ES)

blinded to outcomes reviewed the electronic health record (EHR), including scanned documents, to adjudicate baseline serum creatinine by consensus. Differences in baseline creatinine values between the nephrologists were nearly always on the order of 0.1mg/dl. Notably, 21 patients' baseline creatinine values were adjusted by clinical adjudication. We used baseline creatinine values to calculate the baseline eGFR from the CKD-EPI equation (23).

We determined AKI status (i.e., exposure of interest) using serum creatinine values collected during routine clinical care. In the vast majority of cases, patients' serum creatinine values were available daily. We staged AKI according to Kidney Disease Improving Global Outcomes (KDIGO) creatinine criteria using the difference between baseline and peak serum creatinine (i.e., peak injury) (24). Specifically, stage 1 injury required a 50% increase from baseline creatinine or an absolute increase in baseline creatinine of 0.3mg/dl, stage 2 injury required a 100% increase from baseline serum creatinine, and stage 3 injury required a 200% increase from baseline serum creatinine or initiation of dialysis.

In addition, to examine the relationship between unresolved AKI at hospital discharge and frailty, we *a priori* decided to calculate KDIGO stages at hospital discharge using the serum creatinine in closest proximity to discharge (i.e., injury at discharge). To examine the potential effect of dialysis on the association between AKI and frailty, we also included receipt of dialysis at time of discharge as a separate covariate in a supplemental analysis. Further, to examine the impact of timing of AKI onset, we adjusted for peak injury occurring within 48 hours (i.e., peak creatinine within 48 hours of admission) versus beyond 48 hours in a supplemental analysis.

Covariates

In addition to baseline kidney function, we also chose to adjust for the following potential confounders, selected *a priori* based on biologic plausibility and prior research (9, 17, 22, 25, 26): age, gender, race, modified Charlson comorbidity index (CCI) (27), mean modified sequential organ failure assessment (SOFA) score (28), acute physiology and chronic health evaluation II (APACHE II) score (29), and baseline CFS score (described below). We modified the CCI and SOFA to remove the renal components of these indices since they were included separately in our analyses. In a supplemental analysis, we also controlled for length of study time mechanically ventilated to further adjust for potential differences in severity of illness. In the 11% of patients who were not mechanically ventilated (evenly distributed between exposure arms), the time mechanically ventilated was set to 0. We did not include length of hospital stay as a covariate because AKI has been consistently associated with longer hospital admissions, often related to monitoring of kidney function (22). All covariates were assessed at enrollment or during the enrollment hospitalization (e.g., SOFA scores) only and were not updated following discharge.

Clinical frailty assessment

Upon enrollment (i.e., within 72 hours of ICU admission), study team members trained by a geriatrician with frailty expertise, interviewed the patient and/or surrogate and reviewed the EHR to determine a pre-hospitalization CFS score (i.e., baseline CFS score). The CFS is a

validated measure of clinical frailty with scores that range from 1 (very fit) to 7 (severely frail/terminally ill) (19, 30). Scores ≥ 5 indicate the presence of clinical frailty. Because every point increase in CFS score has been associated with poorer outcomes (19, 30), we analyzed the CFS as an ordinal measure (31–34).

At 3- and 12-month follow-up, trained study team members, who were blinded to the events of the ICU course, conducted in-person CFS assessments. Because CFS scores at ICU admission were associated with mortality (9), we *a priori* chose to categorize death as a CFS score of 8 to reduce the effect of survivor bias in our primary analyses. In sensitivity analyses (described below), we used the 1 to 7 CFS scoring system and excluded patients who died before the respective follow-up time point.

Statistical analysis

Since CFS is an ordinal response variable (31–34), we used ordinal logistic regression to model the dependency of CFS on AKI status while adjusting for potential clinical and demographic confounders. We fit separate models for different markers of AKI, e.g., peak AKI stage and discharge AKI stage. Sociodemographic covariates of interest were age, gender, and race. Clinical covariates were baseline (i.e., pre-illness) CFS score, modified CCI score, modified mean daily SOFA score, APACHE II score, baseline creatinine, and days mechanically ventilated. We included age as a non-linear term in the models using restricted cubic splines with 3 knots. We modeled baseline creatinine both as a linear term as well as a non-linear term with restricted cubic splines. The non-linear baseline creatinine term did not change or improve representation of the data, so all of our final models relied on a linear baseline creatinine term. We also tested for an interaction between AKI status and baseline creatinine using both linear and non-linear terms for baseline creatinine. The interaction terms were uniformly non-significant and were dropped from the model for parsimony. We report the odds ratios (OR) and 95% confidence intervals (95% CI) obtained using robust standard errors from the models.

In sensitivity analyses, we repeated our main analyses while: 1) restricting the cohort to patients with a known outpatient baseline creatinine (n=177) 2) restricting the cohort to patients with a baseline CFS score ≤ 5 (i.e., mildly frail or better), and 3) restricting the cohort to survivors at 3 or 12 months, respectively (in order to understand better whether the association between AKI and frailty was driven primarily by death). Due to the smaller sample size in the analysis restricted to survivors, we combined AKI stages 2 and 3. All analyses use 95% confidence intervals. Analyses were performed using R version 3.3.0 (35).

Results

For our primary analyses, 371 patients met inclusion criteria (Parent Cohort, Figure 1). Of these, 317 and 318 were in our analytic cohorts at 3 and 12 months, respectively (Figure 1). In the analytic cohort, at baseline, participants had a median age of 57 years, 90% were white, median non-renal SOFA score at enrollment was 8, and median APACHEII score was 25. Participants had a median non-renal Charlson score of 2 and median baseline creatinine of 0.9 (Table 1). At baseline, 75 of 317 (24%) participants were clinically frail (Table 1). AKI occurred in 243 (77%) patients and was still present at discharge in 87 (27%) patients

(Table 1). Approximately, 27% (65 of 243) versus 13% (10 of 74) of AKI and non-AKI patients were considered frail at baseline (i.e., CFS = 5), respectively (Table 1 and Figure 2A). At 3- and 12-month follow-up, unadjusted CFS scores increased in all groups compared with baseline, and about 50% to 62% of AKI patients were considered clinically frail (Figure 2B and 2C, Supplemental Figure 1).

Association between Peak AKI and Frailty

In fully adjusted models, relative to no AKI, peak AKI stage 1, 2, and 3 were associated with higher CFS scores at 3 months (OR 1.92, 95% CI 1.14, 3.24; OR 2.40, 95% CI 1.31, 4.42; OR 4.41, 95% CI 2.20, 8.82) respectively; Table 2). Similarly, peak AKI was generally associated with higher CFS scores at 12 months (AKI stage 1: OR 1.87, 95% CI 1.11, 3.14; AKI stage 2: OR 1.81, 95% CI 0.94, 3.48; AKI stage 3: OR 2.76, 95% CI 1.34, 5.66; Table 2). The fully adjusted probabilities of having a CFS score that increased from 4 (apparently vulnerable) or less to 5 or greater (frail) based on peak AKI stage are shown in Figure 3. There was no significant interaction between AKI stage and baseline creatinine in any of the peak AKI and frailty analyses.

Supplemental Analyses

In fully adjusted models, AKI stage 2 and 3 at discharge were associated with higher CFS scores at 3 months (Supplemental Table 1). At 12 months, AKI stage 3 at discharge remained associated with higher CFS scores, while AKI stage 1 and 2 at discharge trended towards an association (Supplemental Table 1).

When adjusting for dialysis status at discharge, the findings were similar; AKI was associated with higher CFS scores at 3 and 12 months (Supplemental Table 2). In addition, when adjusting for timing of AKI onset as a covariate (peak creatinine < 48 hours vs. > 48 hours), the findings were similar; AKI was associated with higher CFS scores at 3 and 12 months (Supplemental Table 3). Notably, timing of AKI (>48 hours) was also associated with frailty status; however, controlling for this did not abrogate the association between AKI and frailty, which remained robust (Supplemental Table 3). When adjusting for length of study time mechanically ventilated, the results were similar with AKI stage 1 and 3 associated with higher CFS scores at 3 and 12 months (Supplemental Table 4).

Sensitivity Analyses

In the sensitivity analysis restricted to patients with a known outpatient baseline creatinine (Supplemental Table 5), the findings were modestly attenuated and the confidence intervals widened. AKI stage 1 was no longer significantly associated with frailty scores at 3 or 12 months (OR 1.71, 95% CI 0.86, 3.38; OR 1.65, 95% CI 0.85, 3.22, respectively) although the direction of the association and point estimate of the effect remained similar. AKI stage 2 was not associated with higher CFS scores (3 months: OR 2.02, 95% CI 0.84, 4.88; 12 month: OR 1.16, 95% CI 0.44, 3.10); however, AKI stage 3 was associated with higher CFS scores (3 months: OR 5.77, 95% CI 2.33, 14.30; 12 months: OR 3.54, 95% CI 1.43, 8.75).

In analyses restricted to patients with baseline CFS score = 5 (i.e., mildly frail), the main results were unchanged; AKI stages were associated with higher CFS scores at 3 and 12

months (Supplemental Table 6). In the sensitivity analysis restricted to survivors at 3 or 12 months, respectively, AKI stage 1 was not associated with CFS score at 3 months but bordered on an association with higher CFS scores at 12 months (3 months: OR 1.59, 95% CI 0.88, 2.88; 12 months: OR 1.85, 95% CI 0.97, 3.53; respectively). Conversely, AKI stage 2+ was associated with higher CFS scores at 3 months only (3 month: OR 2.11, 95% CI 1.14, 3.91; 12 month: OR 1.13, 95% CI 0.58, 2.19; Supplemental Table 7).

Discussion

In this study, we demonstrated that more than half of the survivors of critical illness who experienced AKI were frail 3 and 12 months after hospital discharge. Further, AKI was associated with worse clinical frailty scores in survivors after adjusting for illness severity. This relationship was robust for severe AKI (KDIGO stages 3), and appeared stronger if injury persisted to hospital discharge.

Our data suggest that AKI may play a role in the link between kidney disease and frailty. While our analyses cannot establish causality, potential renal-specific contributions to frailty include the well-recognized complications of volume overload (36), which may limit mobility and physical exertion; anemia (37), which can contribute to fatigue and decreased physical activity; and potential cognitive deficits (20, 38) and medication toxicities (39). Moreover, AKI has been consistently associated with longer hospital stays (22), which may worsen muscle deconditioning (40). AKI is also associated with subclinical pathophysiologic changes including inflammation, immune compromise, and metabolic derangements (36, 41, 42). These effects may be especially evident in patients with more severe AKI or in those who do not recover from their AKI. Future studies are needed to clarify whether the intersection of AKI and frailty results from the kidneys acting as a sensitive and easily assessed barometer of clinical status and/or the deleterious effects of AKI on health.

The American Society of Nephrology has identified the transition of care following AKI as an opportunity to improve long-term outcomes of the disease. (43) This has become especially important in light of reports highlighting a rapid growth in the incidence of AKI. (44) To our knowledge, this is the first study to examine the effect of AKI on frailty. For critical care providers, our findings highlight that critical illness survivors with AKI, especially those with severe or persistent injury, are at higher risk for clinical frailty for a prolonged duration. Interventions such as physical rehabilitation (including home-based therapy), nutritional evaluation and supplementation (and home-based meal assistance if necessary), and psychosocial support (including psychiatric evaluation and efforts to increase social engagement) may improve or mitigate the development of frailty. (45) Hence, close attention to these factors is necessary, especially during transitions of care. Further, our findings may inform patient and family discussions regarding the increased likelihood for a prolonged rehabilitation and for experiencing important patient-centered manifestations of clinical frailty, such as fatigue, slowing, and decrements in independence.

In patients with CKD, frailty correlates with quality of life and is an important prognostic marker (10, 11, 46–49). In addition, frail incident ESRD patients are more than three times

as likely to die within 1 year of initiating dialysis. Hence, frailty is an important consideration that informs dialysis-decision-making in this population.(46, 48–50) Because patients who survive severe AKI are at the highest risk for developing advanced stages of CKD and ESRD, the high prevalence of frailty in this population suggests that routine assessments be considered.(51) Future studies will need to determine the impact of frailty on recovery from AKI and downstream outcomes and whether interventions that can decrease frailty can improve clinical and patient-centered outcomes. Because survivors of severe AKI often suffer marked declines in quality of life,(25) additional information to guide patient and clinician decision making is essential.(51)

Although we observed an association between frailty and AKI in survivors of critical illness, this relationship was attenuated in our 12-month analysis that excluded death. Patients with the most severe AKI die at markedly elevated rates, which may limit longitudinal assessments in some patients leaving relatively healthier survivors (Supplemental Table 8). We attempted to address these issues by including death as the most severe frailty score, under the assumption that decedents had worsened frailty status shortly prior to death. However, some decedents may have died from sudden events that were not preceded by frailty. Reassuringly, 85% of patients with AKI 2+ who died between 3 and 12 months, were clinically frail at their 3 month assessment (data not shown). Moreover, our sensitivity analyses continued to support an association between AKI 2+ and frailty at 3-month follow-up after excluding patients who died.

Our study has several notable strengths: we systematically measured CFS at baseline and longitudinally in a critically ill cohort, follow-up rates were high given the cohort disease burden, and creatinine data were available to provide granular phenotyping of AKI. Our study also has several important limitations. First, this was a single-center study that requires confirmation, and our findings may not be generalizable to the extremely healthy or the severely chronically ill, as few patients had baseline CFS scores in this range. Second, the observational design of this study is unable to determine whether the association between AKI and frailty was causative; we did not have data to explore postulated mediators of the AKI—frailty association further and residual confounding may be present. Third, while the CFS is pragmatic, validated, and well-suited for use in critically ill patients, it is subjective and may not optimally differentiate patients across the spectrum of frailty. However, referent frailty instruments often include performance based measures that are quite difficult to obtain in patients with acute critical illness and provider-based clinical frailty assessments appear to perform comparably to more objective measures.(52, 53) Fourth, we did not have an outpatient assessment of baseline kidney function in all patients. However, our sensitivity analyses continued to demonstrate an association between severe AKI and frailty score. Fifth, the relatively few patients in the non-AKI exposure arm, which is expected in an ICU study requiring acute respiratory failure or shock, is a potential challenge for generalizing the results of non-AKI subjects. Sixth, we did not adjudicate patients' AKI etiology. However, because the cohort consisted of ICU patients with a high severity of illness and shock, we anticipate that the predominant etiology would be ischemic acute tubular necrosis, consistent with prior ICU studies.(54) Finally, we did not have systematic, longitudinal follow-up of renal function to allow us to examine how long-term kidney function trajectories (e.g., ESRD) relate to frailty.

Conclusions

In conclusion, the majority of survivors of critical illness complicated by AKI are clinically frail 3 and 12 months after discharge, and AKI is independently associated with frailty. Further research is needed to understand potential mechanistic links and the effect of frailty on outcomes in patients who develop AKI during critical illness. Because frailty is associated with functional decline in the critically ill, interventions to maintain independent function among patients who survive AKI are needed. As the US population ages and the incidence of AKI and AKI risk factors increase, such information will be integral to engaging patients and families in informed discussions of treatment options and anticipated outcomes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.
Study Enrollment and Exclusion. Analysis set: those with follow-up (frailty) data

Figure 2.

Clinical Frailty Scale scores by acute kidney injury status using stage based on peak injury. In this BRAIN-ICU cohort, only 1 in 6 patients without AKI and 1 in 4 with AKI were frail at baseline. At both 3- and 12-month evaluations, over 1 in 2 AKI patients were frail. For each KDIGO stage, the percentage of Clinical Frailty Scale scores ≥ 5 (i.e., frail) is given below the boxplots.

Figure 3.

Estimated probability of an increase in Clinical Frailty Scale score from 4 (apparently vulnerable) or less to 5 or greater (frail) at 3 and 12 months by acute kidney injury status based on peak creatinine.

*Specifically, the presented probabilities are for white males, age 57 years, baseline creatinine = 1, Apache = 24, non-renal Charlson = 2, average non-renal SOFA = 7, and baseline Clinical Frailty Scale score = 4 (apparently vulnerable)

Table 1

Baseline characteristics

Characteristic	Non-AKI (N = 74)	AKI (N=243)
Age (years)	56 (43, 66)	57 (47, 67)
Female	37 (50)	113 (47)
Race		
White	68 (92)	217 (89)
African-American	6 (8)	26 (11)
Education (years)	12.0 (12.0, 14.0)	12.0 (12.0, 14.0)
BMI	27 (24, 32)	30 (25, 36)
Mean SOFA *	6.1 (5.0, 7.3)	7.0 (5.7, 8.5)
APACHE II at ICU admission	22 (17, 26)	26 (19, 31)
ICU LOS (days)	2.0 (1.2, 3.9)	5.9 (2.8, 11.9)
LOS (days)	7 (5, 12)	13 (9, 22)
Mechanically ventilated	65 (88)	219 (90)
Days mechanically ventilated	0.9 (0.2, 2.0)	2.9 (0.9, 7.9)
CCI *	2 (0, 3)	2 (1, 3)
Baseline serum creatinine (mg/dl)	0.90 (0.71, 1.12)	0.95 (0.74, 1.25)
Baseline eGFR (ml/min/1.73m ²)	88 (64, 105)	79 (55, 101)
AKI KDIGO stage (peak)		
0	74 (100)	0 (0)
1	NA	104 (43)
2	NA	70 (29)
3	NA	69 (28)
AKI KDIGO stage (discharge)		
0	74 (100)	156 (64)
1	NA	50 (21)
2	NA	7 (3)
3	NA	30 (12)
Baseline CFS score		
1: Very fit	3 (4)	13 (5)
2: Well	15 (20)	37 (15)
3: Well, with comorbidities	33 (45)	82 (34)
4: Apparently vulnerable	13 (18)	46 (19)
5: Mildly frail	7 (9)	29 (12)
6: Moderately frail	3 (4)	29 (12)
7: Severely frail	0 (0)	7 (3)

Continuous variables are presented as medians (and interquartile ranges). Categorical variables are expressed as frequencies (and percentages).

* SOFA and CCI were modified to remove their renal components

BMI body mass index, SOFA sequential organ failure assessment, APACHE II acute physiology and chronic health evaluation II, ICU intensive care unit, LOS length of stay, CCI Charlson Comorbidity Index, eGFR estimated glomerular filtration rate, AKI acute kidney injury, KDIGO Kidney Disease Improving Global Outcomes, CFS clinical frailty scale

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Table 2

Adjusted Association of Peak Acute Kidney Injury Stage and Clinical Frailty Scale Scores at 3- and 12-months

Variable	3-month CFS Model	12-month CFS model
	OR (95% CI)	OR (95% CI)
AKI stage 1	1.92 (1.14, 3.24)	1.87 (1.11, 3.14)
AKI stage 2	2.40 (1.31, 4.42)	1.81 (0.94, 3.48)
AKI stage 3	4.41 (2.20, 8.82)	2.76 (1.34, 5.66)
Baseline creatinine *	0.83 (0.52, 1.34)	1.07 (0.63, 1.80)
Age *	--	--
Female	0.89 (0.59, 1.32)	1.07 (0.72, 1.61)
Black	1.34 (0.68, 2.65)	0.98 (0.45, 2.12)
Charlson Score †	1.12 (0.99, 1.26)	1.11 (0.98, 1.26)
SOFA Score †	0.90 (0.82, 1.00)	0.89 (0.80, 1.00)
APACHE	0.99 (0.96, 1.02)	1.01 (0.98, 1.03)
Baseline CFS=2	2.95 (0.66, 13.23)	1.55 (0.53, 4.54)
Baseline CFS=3	4.11 (0.90, 18.84)	1.84 (0.62, 5.46)
Baseline CFS=4	6.70 (1.32, 34.10)	3.06 (0.94, 10.00)
Baseline CFS=5	7.56 (1.43, 40.01)	4.75 (1.49, 15.17)
Baseline CFS=6	19.17 (3.67, 100.24)	4.67 (1.41, 15.48)
Baseline CFS=7	22.48 (2.39, 211.11)	8.89 (0.71, 111.17)

* Baseline creatinine was centered. Age was modeled nonlinearly using restricted cubic splines with 3 knots; individual ORs are not generalizable.

† The Charlson Comorbidity Index and SOFA score were modified to remove the chronic kidney disease and acute kidney injury terms, respectively.

CFS Clinical Frailty Scale, AKI acute kidney injury, SOFA Sequential Organ Failure Assessment, APACHE Acute Physiology and Chronic Health Evaluation