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In-Hospital and 1-Year Mortality Trends in a National Cohort of US Veterans with Acute Kidney Injury

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Abstract

Background and objectives AKI, a frequent complication among hospitalized patients, confers excess short- and long-term mortality. We sought to determine trends in in-hospital and 1-year mortality associated with AKI as defined by Kidney Disease Improving Global Outcomes consensus criteria.

Design, setting, participants, & measurements This retrospective cohort study used data from the national Veterans Health Administration on all patients hospitalized from October 1, 2008 to September 31, 2017. AKI was defined by Kidney Disease Improving Global Outcomes serum creatinine criteria. In-hospital and 1-year mortality trends were analyzed in patients with and without AKI using Cox regression with year as a continuous variable.

Results We identified 1,688,457 patients and 2,689,093 hospitalizations across the study period. Among patients with AKI, 6% died in hospital, and 28% died within 1 year. In contrast, in-hospital and 1-year mortality rates were 0.8% and 14%, respectively, among non-AKI hospitalizations. During the study period, there was a slight decline in crude in-hospital AKI-associated mortality (hazard ratio, 0.98 per year; 95% confidence interval, 0.98 to 0.99) that was attenuated after accounting for patient demographics, comorbid conditions, and acute hospitalization characteristics (adjusted hazard ratio, 0.99 per year; 95% confidence interval, 0.99 to 1.00). This stable temporal trend in mortality persisted at 1 year (adjusted hazard ratio, 1.00 per year; 95% confidence interval, 0.99 to 1.00).

Conclusions AKI associated mortality remains high, as greater than one in four patients with AKI died within 1 year of hospitalization. Over the past decade, there seems to have been no significant progress toward improving in-hospital or long-term AKI survivorship.

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Introduction

AKI, an abrupt decline in kidney function, is a serious and deadly complication affecting one in five hospitalized patients (1,2). Previous studies have implicated AKI as an independent risk factor for death, with a more than four-fold higher likelihood of in-hospital mortality (3). Moreover, an episode of AKI is associated with not only in-hospital mortality but also reduced survivorship at 1 year across all AKI stages (4).

Previous studies have indicated that in-hospital mortality among patients with dialysis-requiring AKI has declined from 2000 to 2015 (5–7). Although the trend toward lower in-hospital mortality among patients with dialysis-requiring AKI is encouraging, this comprises only a small fraction of all patients with AKI (8), and mortality trends in patients with dialysis-requiring AKI may not be generalizable to mortality rates across all stages of AKI. To date, few studies have examined mortality trends among less severe stages of AKI. There has been some suggestion that in-hospital mortality among patients with a diagnosis code for AKI has decreased across time (9,10). However, the incidence of AKI using administrative coding has increased across the past two decades (8,11,12). This rise has been most pronounced among hospitalizations with stage 1 AKI (13), as defined by the Kidney Disease Improving Global Outcomes (KDIGO) consensus serum creatinine criteria (14). Therefore, temporal mortality reduction among hospitalized patients with AKI may represent increased coding of mild AKI rather than true reduction in mortality. Alternatively, increased AKI recognition as well as advances in the management of hospitalized patients may have translated into true improvement in AKI outcomes. Whether any potential mortality reduction persists beyond the initial hospitalization period is unknown.

The goal of this study was to examine recent short- and long-term mortality trends in hospitalized patients with AKI as defined by the consensus criteria.

Quantifying long-term outcomes and trends of AKI is critical to understanding the population-level effect of AKI and may influence resource allocation post-AKI. We hypothesized that improved AKI recognition and care have led to decreasing mortality across all KDIGO AKI stages and that this mortality reduction is sustained at 1 year.

Materials and Methods

Data Source/Population

We conducted a retrospective cohort analysis of adult patients (22 years or older) admitted to an acute care facility in the Veterans Health Administration (VHA) from October 1, 2008 to September 30, 2017, corresponding to VHA fiscal years 2009–2017. For simplicity, we will subsequently refer to this time period as 2009–2017. VHA is the largest integrated health care system in the United States. VHA data from the Corporate Data Warehouse include detailed individual patient demographic, clinical, laboratory, and vital status data.

Hospitalizations were included if they had at least one inpatient serum creatinine result; there was no preadmission kidney failure (International Classification of Diseases, ninth revision, Clinical Modification [ICD-9-CM] 585.6 and International Classification of Diseases, tenth revision, Clinical Modification [ICD-10-CM] N18.6), including dialysis (Current Procedure Terminology [CPT] codes 90918, 90919, 90935, 90937, 90940, 90945, 90947, 90951–90970, 90989, 90993, 90997, and 90999) prior to admission; and the patients were not admitted to a long-term care facility. We included patients more than once only if their next hospitalization occurred >365 days from the previous included hospital admission. We excluded hospitalizations with a hospital length of stay >365 days.

This project was conducted at the University of Michigan and funded by the Centers for Disease Control and Prevention. Research using VHA data for this project was approved by the institutional review boards of the University of Michigan and the Ann Arbor VHA.

Data Collection

We extracted Corporate Data Warehouse data for all patients with hospital admissions from October 1, 2008 to September 30, 2017. Data were collected through September 30, 2018 to ensure a full year of follow-up for all patients. Data extracted from the VHA national Corporate Data Warehouse included demographic information (age, sex, and race), inpatient and outpatient procedures and diagnoses (using CPT codes and ICD-9-CM and ICD-10-CM diagnoses), physician order entry, inpatient and outpatient serum creatinine values, and vital status. Baseline data were obtained for 365 days prior to each hospital admission, including ICD-9-CM or ICD-10-CM diagnoses and CPT codes for comorbid conditions.

AKI Definition. The primary exposure of interest was hospitalization with AKI. The 2012 KDIGO AKI consensus guideline (13) recommends a serum creatinine definition for AKI that relies upon change in creatinine from a baseline. We defined the baseline creatinine by a hierarchical approach on the basis of the availability of (*1*) the mean outpatient creatinine between 365 and 7 days prior to admission, (*2*) the earliest outpatient value within the 7 days prior to admission (if no creatinine 7 days prior to admission was available), or (*3*) the lowest inpatient creatinine (if no outpatient creatinine in the year prior to admission was available). A 7-day cutoff was used to avoid selecting an elevated creatinine that may have been associated with the cause for hospitalization. We calculated the corresponding baseline eGFR according to the Chronic Kidney Disease Epidemiology Collaboration equation using race-based values where race was recorded and "non-Black" if race was missing (6% of the cohort).

AKI was ascertained and staged according to severity on the basis of the KDIGO serum creatinine definition. Stage 1 AKI was defined as a creatinine level increase ≥0.3 mg/dl (within 48 hours) or an increase of 1.5–1.9 times baseline (within 7 days). Stage 2 AKI is an increase of 2.0–2.9 times baseline. Stage 3 AKI is a serum creatinine level increase >3.0 times baseline, a serum creatinine ≥4.0 mg/dl and ≥0.5 mg/dl above baseline, or AKI requiring the initiation of dialysis. Dialysis-requiring AKI included those meeting creatinine criteria for AKI and additionally having a CPT code for dialysis (ICD-9-CM: 3995 and 5498; ICD-10-CM: 5A1D00Z, 5A1D60Z, and 3E1M39Z). In addition to KDIGO criteria, we also identified AKI separately using ICD-9-CM (584.9) or ICD-10-CM (N17.9) codes.

Mortality Outcomes. We used two separate primary outcomes: all-cause in-hospital mortality and all-cause mortality 1 year from hospitalization (inclusive of in-hospital mortality). We determined the date of death using the Veterans' Vital Status Files. The Vital Status Files combine multiple information sources to ascertain mortality with >97% sensitivity (15).

Covariates. Patient demographics (preadmission age, sex, and race), comorbid conditions, and acute hospitalization characteristics were obtained from the Corporate Data Warehouse. We defined CKD as a baseline eGFR <60 ml/min per 1.73 m^2, prehospital urine albumin-creatinine ratio >30 mg/g, or the presence of an ICD-9-CM or ICD-10-CM code for CKD in the 365 days prior to admission. All other baseline (prehospitalization) patient comorbid conditions were compiled using ICD-9-CM or ICD-10-CM codes for the 365 days prior to admission. Baseline comorbid conditions included CKD, hypertension, diabetes, congestive heart failure, myocardial infarction, peripheral vascular disease, malignancy, liver disease, chronic obstructive pulmonary disease, cerebrovascular accident, and transient ischemic attack. We additionally compiled hospitalization characteristics, including surgical procedures, hospital length of stay, intensive care unit (ICU) utilization, mechanical ventilation, sepsis, and vasopressor use. We used surgery Diagnosis Related Group codes to identify hospitalizations involving inpatient surgical procedures. A surgical Diagnosis Related Group indicates that a hospitalization involved a procedure commonly performed in the operating room. We identified hospitalizations involving an ICU stay by the specialty or bed section codes corresponding to the service location within the hospital. We used ICD-9 CM or ICD-10 codes for sepsis and septic shock to identify sepsis and mechanical ventilation.

Statistical Analyses

To assess mortality trends in the AKI and non-AKI cohorts separately, we performed time-to-event analysis using Cox proportional hazards models with hospital admission date as day 0. We censored patients at hospital discharge when estimating time to in-hospital mortality and at 365 days from hospital admission date for time to 1-year mortality. Our primary interest was to estimate trends in mortality over time. To accomplish this, we included year as a continuous linear variable in the model. We chose to model year as a continuous variable on the basis of visualization of the crude data demonstrating linear trends in in-hospital and 1-year mortality.

We constructed three models to understand potential reasons for the trend. Model 1 included demographic data, including race, sex, and preadmission age. Model 2 included preadmission comorbid diseases in addition to the covariates included in model 1. Comorbid diseases included CKD, hypertension, diabetes, congestive heart failure, myocardial infarction, peripheral vascular disease, malignancy, liver disease, chronic obstructive pulmonary disease, cerebrovascular accident, and transient ischemic attack. Model 3 incorporated hospitalization characteristics in addition to the covariates in model 3. This final model was built with the intent to incorporate markers of acute illness severity. Hospitalization characteristics included hospital admitting service, hospital length of stay, ICU utilization, mechanical ventilation, sepsis, and vasopressor use.

To account for the correlation between repeated hospitalizations for the same person, we estimated the variance using robust variance techniques (16,17). We examined patients with AKI and non-AKI in separate models. For each mortality outcome, we also tested for differences in the mortality trend between patients with and without AKI by fitting a model combining both sets of patients and including an interaction term between AKI and year. We consider a P value ≤ 0.05 to be statistically significant. Because we did observe a significant interaction, all subsequent modeling was performed stratified by whether patients had AKI. Analyses were conducted using SAS 9.4 (SAS Institute, Cary, NC).

Subgroup/Sensitivity Analyses

To address the issue that improvement in mortality reported in previous studies may be related to increased coding of mild AKI rather than true reduction in mortality, we examined crude in-hospital and 1-year mortality trends for hospitalized patients with an ICD-9-CM or ICD-10-CM code for AKI (as opposed to serum creatinine values in our primary analyses).

Additionally, we examined AKI-associated mortality trends among patients with baseline eGFR ≥ 60 ml/min per 1.73 m^2, as the insult required to generate an AKI may be greater for those without than with CKD. Improvements in clinical treatment of AKI over time may appear more evident among this cohort.

Finally, to verify the assumption that time to event mortality conforms to a linear trend across time, we constructed separate Cox proportional hazards models with year as a categorical variable.

Results

Patient Population and Hospitalization Characteristics

After applying exclusion criteria, the study included 2,689,093 qualifying hospitalizations and 1,688,457 unique patients in VHA from 2009 to 2017 (Figure 1). The cohort included 548,782 hospitalizations with AKI and 2,140,311 hospitalizations without AKI. Patient demographic and hospitalization characteristics stratified by AKI status and time period appear in Table 1. The mean ages were 70 (SD 13) and 73 (SD 11) for patients without AKI and patients with AKI, respectively, and did not change substantially during the study period. Several comorbid diseases, including hypertension, CKD, and diabetes, were more prevalent among patients hospitalized with AKI as compared with non-AKI hospitalizations.

Among all hospitalizations with AKI, 82% were KDIGO stage 1, 3% were KDIGO stage 2, and 14% were KDIGO stage 3 (including dialysis-requiring AKI). The relative makeup of AKI severity did not change across time. ICU utilization, mechanical ventilation, sepsis, and vasopressor use were more prevalent among hospitalizations with AKI.

Crude In-Hospital and 1-Year Mortality

The number of hospitalizations at risk and crude mortality rate each year appear in Tables 2 and 3. Across 2009–2017, in-hospital mortality was 6% among hospitalizations with AKI compared with 1% among non-AKI hospitalizations. Sixty-seven percent of all hospital deaths occurred among those with AKI. Notably, in-hospital mortality was relatively similar by method of AKI ascertainment (6% with AKI diagnosis code and 6% with serum creatinine). One-year mortality rates among patients with and without AKI were 28% and 14%, respectively. The crude in-hospital and 1-year mortality trends stratified by AKI status appear in Figure 2.

AKI Severity. We observed higher in-hospital and 1-year mortality with increasing AKI severity by KDIGO stage. Among patients with dialysis-requiring AKI, 16% died during hospitalization, while 41% died within 1 year. Twenty-five percent of patients with KDIGO stage 1 AKI died within 1 year. AKI-associated mortality trends stratified by KDIGO stage appear in Figure 3.

Baseline Estimated Glomerular Filtration Rate. In-hospital AKI-associated mortality rates were similar in those with a baseline eGFR <60 or ≥ 60 ml/min per 1.73 m^2 (6% and 7%, respectively), whereas 1-year mortality was slightly higher in those with a baseline eGFR <60 ml/min per 1.73 m^2 (30% versus 24%).

Mortality Trends

AKI-Associated Mortality Trends. The crude and adjusted Cox proportional hazard models for in-hospital and 1-year mortality among hospitalizations with and without AKI appear in Table 4. From 2009 to 2017, there was a decline in the crude AKI-associated in-hospital mortality (hazard ratio [HR], 0.98 per year; 95% confidence interval [95% CI], 0.98 to 0.99). This trend was slightly attenuated after accounting for patient demographics, comorbid conditions, and acute hospitalization characteristics (model 3 adjusted hazard ratio [aHR], 0.99 per year; 95% CI, 0.99 to 1.00). Across the same time period, crude

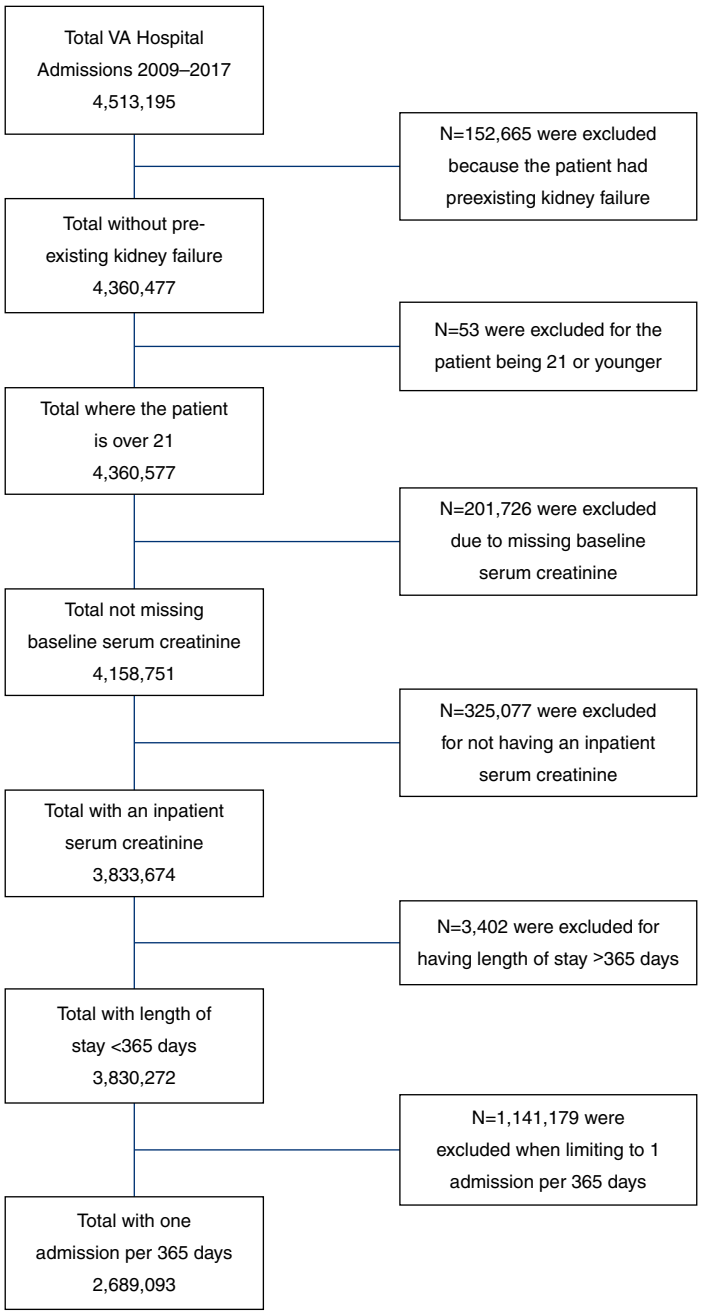

Figure 1. | **Cohort derivation.** VA, Veterans Affairs.

AKI-associated time to 1-year mortality went unchanged (HR, 1.00 per year; 95% CI, 1.00 to 1.00). However, when adjusting for demographics, comorbid conditions, and acute hospitalization characteristics, there was a statistically significant temporal reduction in time to AKI-associated mortality within 1 year (model 3 aHR, 1.00 per year; 95% CI, 0.99 to 1.00). Characteristics most strongly associated with in-hospital and 1-year AKI mortality include malignancy, liver disease, sepsis, mechanical ventilation, and AKI stage (Supplemental Table 1).

In models with year as a categorical variable, we similarly observed modest changes in adjusted hazard for mortality for each subsequent year compared with the baseline (reference) year of 2009 (Supplemental Table 2).

Non–AKI-Associated Mortality Trends. There was no change in crude in-hospital mortality among non-AKI hospitalizations (HR, 1.00 per year; 95% CI, 0.99 to 1.00), and there was a slightly higher in-hospital mortality in the fully adjusted model (aHR, 1.01 per year; 95% CI, 1.01 to 1.02). A similar trend was demonstrated at 1 year after non-AKI hospitalization (aHR, 1.02 per year; 95% CI, 1.01 to 1.02) (Table 4). Finally, in the additional models combining AKI and non-AKI hospitalizations, the AKI × year interaction term was significant for both in-hospital and 1-year mortality, confirming a difference in trend by AKI status.

Table 1. Hospitalization and patient characteristics by AKI status in US veterans, 2009–2017

Variable	Total		2009–2011		2012–2014		2015–2017	
	No AKI	AKI	No AKI	AKI	No AKI	AKI	No AKI	AKI
Hospitalizations, *n*	2,140,311	548,782	710,859	179,127	714,610	183,195	714,842	186,460
Women, *n* (%)	122,004 (6)	17,174 (3)	37,209 (5)	5254 (3)	40,972 (6)	5613 (3)	43,823 (6)	6307 (3)
Age, *n* (%)								
22–29	4232 (0.2)	282 (0.1)	552 (0.1)	59 (0.0)	1294 (0.2)	93 (0.1)	2386 (0.3)	130 (0.1)
30–39	51,803 (2)	3905 (0.7)	11,785 (2)	803 (0.4)	17,064 (2)	1275 (0.7)	22,954 (3)	1827 (1)
40–49	74,275 (4)	9341 (2)	21,654 (3)	2713 (2)	24,334 (3)	2935 (2)	28,287 (4)	3693 (2)
50–59	221,534 (10)	44,647 (8)	75,113 (11)	15,616 (9)	72,879 (10)	14,807 (8)	73,542 (10)	14,224 (8)
60–69	606,161 (28)	157,212 (29)	203,484 (29)	50,825 (28)	205,469 (29)	54,236 (30)	197,208 (28)	52,151 (28)
70+	1,182,306 (55)	333,395 (61)	398,271 (56)	109,111 (61)	393,570 (55)	109,849 (60)	390,465 (55)	114,435 (61)
Mean age (SD), yr	70 (13)	73 (11)	71 (12)	73 (11)	70 (13)	73 (11)	70 (13)	72 (11)
Race, *n* (%)								
Non-Hispanic White	1,500,678 (70)	357,856 (65)	503,086 (71)	117,846 (66)	503,747 (71)	120,496 (66)	493,845 (69)	119,514 (64)
Non-Hispanic Black	385,185 (18)	123,093 (22)	123,407 (17)	38,495 (22)	127,877 (18)	40,908 (22)	133,901 (19)	43,690 (23)
Hispanic	100,029 (5)	26,075 (5)	28,022 (4)	7094 (4)	31,520 (4)	7918 (4)	40,487 (6)	11,063 (6)
American Indian/ Alaska Native	13,045 (0.6)	2992 (0.5)	3922 (0.6)	818 (0.5)	4451 (0.6)	1034 (0.6)	4672 (0.7)	1140 (0.6)
Asian	19,019 (0.9)	5020 (0.9)	5712 (0.8)	1524 (0.9)	6371 (0.9)	1658 (0.9)	6936 (1)	1838 (1)
Other/unknown	122,355 (6)	33,746 (6)	46,710 (7)	13,350 (8)	40,644 (6)	11,181 (6)	35,001 (5)	9215 (5)
Baseline eGFR								
Baseline eGFR, mean (SD), ml/kg per 1.73 m^2	74 (22)	63 (26)	73 (22)	62 (26)	75 (22)	63 (26)	75 (22)	62 (26)
Baseline eGFR<60, *n* (%)	551,439 (26)	257,478 (47)	192,473 (27)	85,017 (48)	179,168 (25)	84,129 (46)	179,798 (25)	88,332 (47)
Comorbidity, *n* (%)[a]								
HTN	952,322 (45)	284,633 (52)	302,976 (43)	92,423 (52)	321,636 (45)	94,572 (52)	327,710 (46)	97,638 (52)
CKD, no DM	147,179 (7)	88,736 (16)	44,240 (6)	28,041 (16)	48,276 (7)	29,337 (16)	54,663 (8)	31,358 (17)
DM and CKD	114,648 (5)	84,929 (16)	30,221 (4)	23,494 (13)	382,59 (5)	28,021 (15)	46,168 (7)	33,414 (18)
DM, no CKD	411,307 (19)	110,957 (20)	130,039 (18)	36,573 (20)	138,104 (19)	36,669 (20)	143,164 (20)	37,715 (20)
No DM or CKD	1,467,177 (69)	264,160 (48)	506,359 (71)	91,019 (51)	48,9971 (69)	89,168 (49)	470,847 (66)	83,973 (45)
MI	61,970 (3)	19,268 (4)	19,007 (3)	6002 (3)	20,882 (3)	6220 (3)	22,081 (3)	7046 (4)
PVD	157,595 (7)	49,402 (9)	49,936 (7)	16,026 (9)	52,878 (7)	16,643 (9)	54,781 (8)	16,733 (9)
Cancer	40,579 (2)	11,838 (2)	10,738 (2)	3213 (2)	14,533 (2)	4227 (2)	15,308 (2)	4398 (2)
Liver	64,460 (3)	22,606 (4)	12,704 (2)	4767 (3)	15,686 (2)	6136 (3)	36,070 (5)	11,703 (6)
COPD	393,858 (18)	101,899 (19)	123,677 (17)	32,567 (18)	133,521 (19)	34,391 (19)	136,660 (19)	34,941 (19)
CVA/TIA	161,232 (8)	46,445 (9)	52,794 (7)	15,634 (9)	56,623 (8)	16,045 (9)	51,815 (7)	14,766 (8)
Illness severity, *n* (%)								
Surgical DRG	898,982 (42)	207,396 (38)	303,204 (43)	66,853 (37)	302,539 (42)	68,851 (38)	293,239 (41)	71,692 (38)
AKI stage								
Stage 1	—	451,427 (82)	—	146,898 (82)	—	150,626 (82)	—	153,903 (83)
Stage 2	—	18,375 (3)	—	5968 (3)	—	6422 (4)	—	5985 (3)
Stage 3	—	55,450 (10)	—	18,306 (10)	—	18,492 (10)	—	18,652 (10)
AKI with dialysis	—	23,530 (4)	—	7955 (4)	—	7655 (4)	—	7920 (4.2)
ICU	325,520 (15)	122,307 (22)	107,407 (15)	40,493 (23)	106,979 (15)	40,247 (22)	111,134 (16)	41,567 (22)
Mechanical ventilation	31,700 (2)	42,095 (8)	11,901 (2)	15,707 (9)	11,649 (2)	14,973 (8)	8150 (1)	11,415 (6)
Sepsis	46,136 (2)	50,858 (9)	7102 (1)	11,466 (6)	15,582 (2)	17,453 (10)	23,452 (3)	21,939 (12)
Vasopressors use	156,952 (7)	54,685 (10)	49,038 (7)	17,211 (10)	53,150 (7)	18,196 (10)	54,764 (8)	19,278 (10)
LOS, mean (SD)	6.1 (17.9)	11.2 (24.9)	6.6 (19.1)	12.3 (27.3)	5.9 (17.4)	10.9 (23.8)	5.8 (17.1)	10.3 (23.4)

Data are for hospitalizations. Characteristics of patients with multiple hospitalizations during the study period are represented more than once. HTN, hypertension; DM, diabetes mellitus; MI, myocardial infarction; PVD, peripheral vascular disease; COPD, chronic obstructive pulmonary disease; CVA/TIA, cerebrovascular accident/transient ischemic attack; DRG, Diagnosis Related Group; —, not applicable; ICU, intensive care unit; LOS, length of stay.

[a]CKD includes eGFR<60 ml/min per 1.73 m^2, urinary albumin-creatinine ratio >30 mg/g, or International Classification of Diseases, ninth revision, Clinical Modification (ICD-9-CM) or International Classification of Diseases, tenth revision, Clinical Modification (ICD-10-CM) code for CKD in the 365 days prior to admission. All other comorbid conditions are defined according to corresponding ICD-9-CM or ICD-10-CM codes.

Table 2. Crude trends in in-hospital and 1-year mortality among US veterans with and without AKI, 2009–2012

Patient Group	Total		2009		2010		2011		2012	
	N at Risk	Rate	*N* at Risk	Rate	*N* at Risk	Rate	*N* at Risk	Rate	*N* at Risk	Rate
In-hospital mortality										
All hospitalized patients	2,689,093	1.9	298,720	2.1	294,371	1.9	296,895	1.9	297,198	1.8
AKI serum creatinine	548,782	6.1	61,181	7.0	56,132	6.6	61,814	6.1	60004	6.1
AKI diagnosis code	329,573	5.9	23,614	8.4	26,859	7.2	31,606	6.5	34,282	5.8
Non-AKI	2,140,311	0.8	237,539	0.8	238,239	0.8	235,081	0.8	237,194	0.7
AKI KDIGO stage										
Stage 1	451,427	4.5	50,139	5.0	46,085	4.7	50,674	4.5	49,009	4.5
Stage 2	18,375	13.8	2081	16.5	1844	16.7	2043	13.8	2102	13.1
Stage 3	55,450	12.7	6188	14.7	5615	13.9	6503	12.0	6196	12.4
AKI-D	23,530	16.4	2773	18.0	2588	17.6	2594	15.9	2587	17.0
AKI and eGFR≥60 ml/min per 1.73 m^2	291,304	6.5	31,510	7.4	29,880	6.8	32,720	6.4	32,232	6.5
AKI and eGFR <60 ml/min per 1.73 m^2	257,478	5.8	29,671	6.6	26,252	6.4	29,094	5.7	27,772	5.7
1-yr mortality										
All hospitalized patients	2,689,093	16.4	298,720	16.4	294,371	16.4	296,895	16.4	297,198	16.6
AKI	548,782	27.7	61,181	27.2	56,132	26.7	61,814	26.6	60,004	26.7
AKI diagnosis code	329,573	30.7	23,614	29.6	26,859	28.6	31,606	27.7	34,282	28.1
Non-AKI	2,140,311	13.5	237,539	13.8	238,239	13.7	235,081	13.8	237,194	14.0
AKI KDIGO stage										
Stage 1	451,427	25.3	50,139	24.9	46,085	24.7	50,674	24.6	49,009	24.9
Stage 2	18,375	36.1	2081	36.9	1844	32.8	2043	32.0	2102	31.5
Stage 3	55,450	37.9	6188	37.0	5615	34.8	6503	35.0	6196	34.3
AKI-D	23,530	40.8	2773	41.3	2588	40.3	2594	41.4	2587	39.7
AKI and eGFR≥60 ml/min per 1.73 m^2	291,304	24.2	31,510	25.9	29,880	25.0	32,720	24.5	32,232	24.2
AKI and eGFR<60 ml/min per 1.73 m^2	257,478	29.7	29,671	29.6	26,252	29.8	29,094	29.2	27,772	29.5

eGFR refers to baseline preadmission eGFR. KDIGO, Kidney Disease Improving Global Outcomes; AKI-D, dialysis-requiring AKI.

Table 3. Crude trends in in-hospital and 2-year mortality among US veterans with and without AKI, 2013–2017

Patient Group	2013		2014		2015		2016		2017	
	N at Risk	Rate	*N* at Risk	Rate	*N* at Risk	Rate	*N* at Risk	Rate	*N* at Risk	Rate
In-hospital mortality										
All hospitalized patients	293,974	1.8	306,633	1.7	304,526	1.7	300,969	1.6	295,807	1.5
AKI serum creatinine	60,651	5.8	62,540	5.5	63,492	5.4	62,358	5.0	60,610	4.9
AKI diagnosis code	36,822	5.8	41,349	5.2	43,222	5.1	45,101	4.6	46,718	4.5
Non-AKI	23,323	0.8	244,093	0.7	241,034	0.7	238,611	0.7	235,197	0.6
AKI KDIGO stage										
Stage 1	49,927	4.4	51,580	4.0	52,466	3.9	51,543	3.7	49,894	3.6
Stage 2	229	10.6	2091	12.3	2049	11.8	2011	11.1	1925	11.2
Stage 3	6080	11.7	6216	11.3	6427	12.0	6236	10.2	6089	10.0
AKI-D	2415	16.2	2653	15.3	2550	14.6	2668	14.9	2702	14.2
AKI and eGFR≥60 ml/min per 1.73 m^2	33,084	6.1	33,750	5.7	33,980	5.7	33,076	5.4	31,072	5.3
AKI and eGFR <60 ml/min per 1.73 m^2	27,567	5.5	28,790	5.1	29,512	5.2	29,282	4.6	29,538	4.6
1-yr mortality										
All hospitalized patients	293,974	16.6	306,633	16.7	304,526	16.4	300,969	16.5	295,807	16.4
AKI	60,651	26.6	62,540	26.9	63,492	26.2	62,358	26.5	60,610	27.7
AKI diagnosis code	36,822	27.6	41,349	27.6	43,222	26.9	45,101	26.6	46,718	30.7
Non-AKI	23,323	14.1	244,093	14.0	241,034	13.8	238,611	13.9	235,197	13.5
AKI KDIGO stage										
Stage 1	49,927	24.7	51,580	24.7	52,466	24.4	51,543	24.7	49,894	25.3
Stage 2	229	30.8	2091	33.1	2049	31.4	2011	30.1	1925	36.1
Stage 3	6080	35.0	6216	36.9	6427	33.8	6236	35.2	6089	37.9
AKI-D	2415	40.2	2653	40.7	2550	39.3	2668	38.7	2702	40.8
AKI and eGFR≥60 ml/min per 1.73 m^2	33,084	24.2	33,750	23.7	33,980	23.7	33,076	23.5	31,072	23.5
AKI and eGFR<60 ml/min per 1.73 m^2	27,567	29.6	28,790	30	29,512	30.5	29,282	29.3	29,538	29.7

eGFR refers to baseline preadmission eGFR. KDIGO, Kidney Disease Improving Global Outcomes; AKI-D, dialysis-requiring AKI.

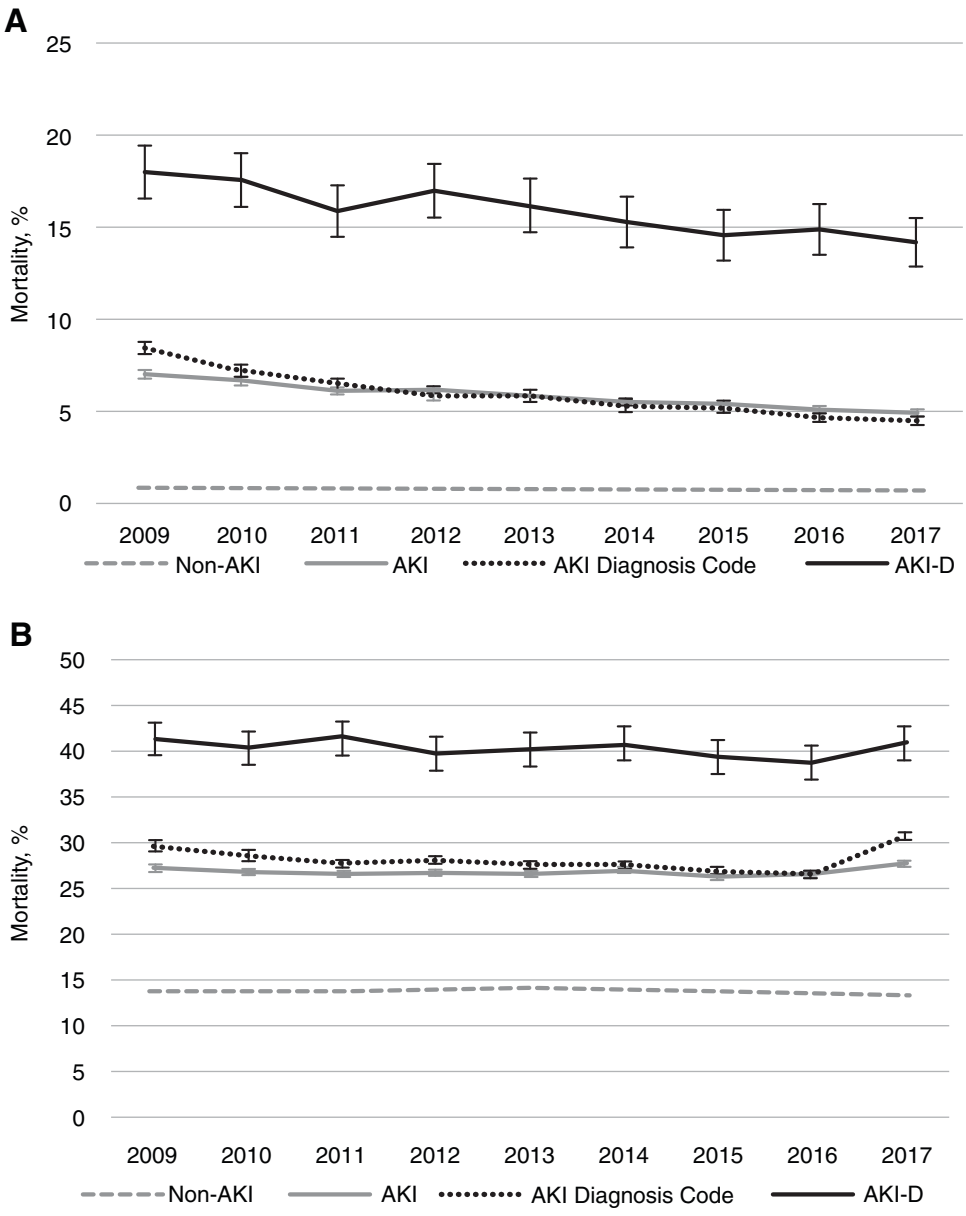

Figure 2. | **Crude mortality trends among US veterans stratified by AKI status, 2009–2017.** (A) In-hospital mortality; (B) 1-year mortality. Vertical bars represent 95% confidence intervals. AKI-D, dialysis-requiring AKI.

Discussion

In this study examining mortality trends in a large national cohort of hospitalized veterans, in-hospital and 1-year mortality in patients with AKI declined modestly from 2009 to 2017. However, this trend was attenuated when accounting for changing patient and hospitalization characteristics, resulting in a relatively flat adjusted hazard for mortality. Further, our findings highlight the poor prognostic implications of having AKI, as more than one in four patients with AKI experienced death within 1 year of hospital admission.

Existing literature suggests that in-hospital mortality in those with AKI has rapidly declined. In an early analysis using the National Inpatient Sample (NIS), Waikar *et al.* (9) noted a nearly 50% reduction in in-hospital mortality from 1988 to 2002 among patients with AKI, falling from 40% to 20% ($P<0.001$). More recently, using NIS data from 2000 to 2011, Brown *et al.* (10) reported that although the number of in-hospital deaths associated with AKI nearly doubled, in-hospital AKI-associated mortality declined by 58% (22% to 99%). However, assessing AKI-associated mortality on the basis of claims data can present significant challenges and may not be an accurate representation of true trends. Claims data may inflate the apparent mortality reduction through increased recognition of mild AKI over time (11). Importantly, our study corroborated this issue, as it found a crude relative mortality reduction of 46% across 9 years when ascertaining AKI using diagnosis codes compared with 30% when ascertaining AKI by consensus creatinine criteria.

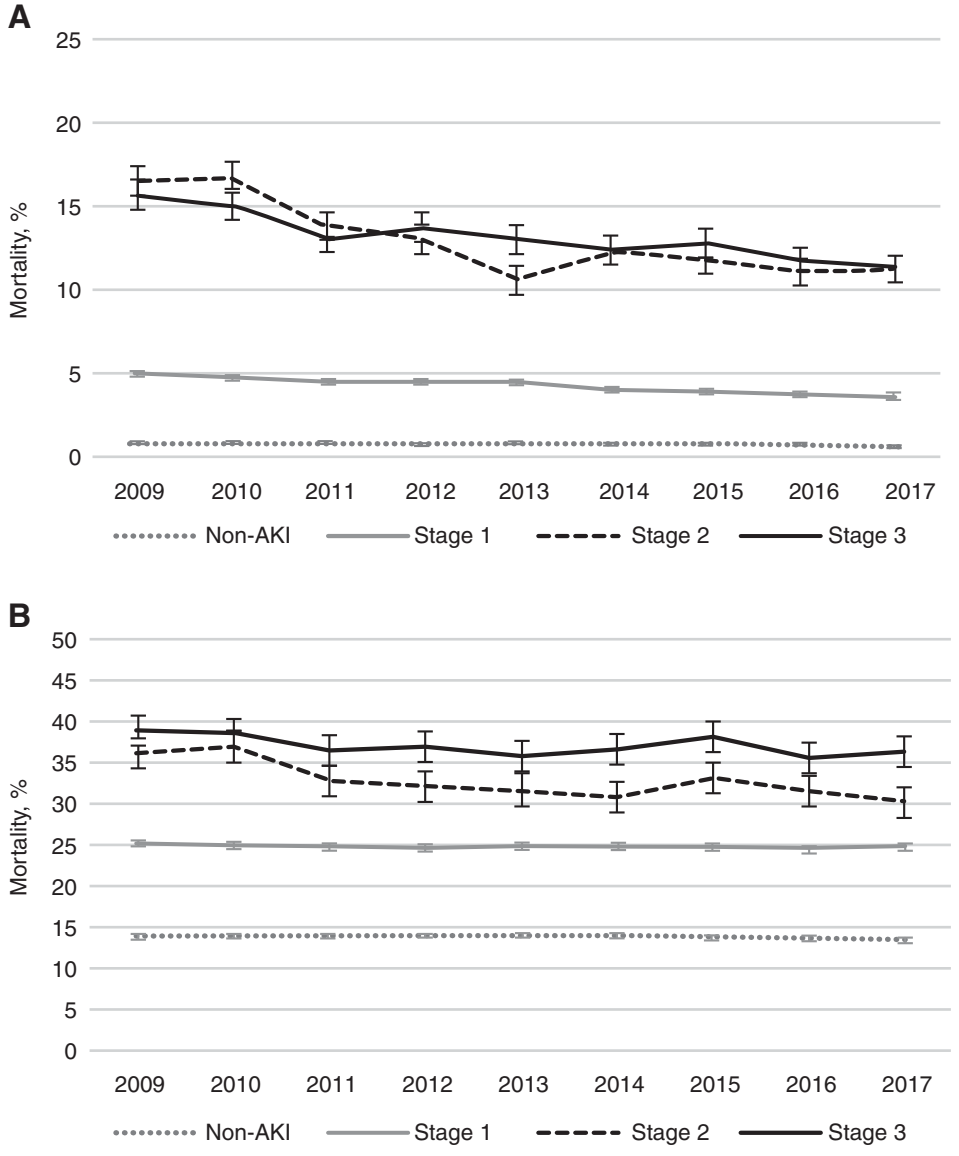

Figure 3. | **Crude mortality trends among US veterans stratified by Kidney Disease Improving Global Outcomes AKI stage, 2009–2017.** (A) In-hospital mortality; (B) 1-year mortality. Stage 3 AKI includes AKI-D. Vertical bars represent 95% confidence intervals.

Other studies have examined mortality trends in dialysis-requiring AKI, as dialysis-requiring AKI is less susceptible to ascertainment bias. Hsu *et al.* (5) reported decreasing mortality during hospitalization with dialysis-requiring AKI from 2001 to 2009 (29% to 24%). However, even in-hospital mortality trends in dialysis-requiring AKI could overestimate mortality reduction, as changes in practices related to initiation of acute dialysis may affect trends over time. Our study among a national cohort of hospitalized patients with serum creatinine–defined AKI found a very small yearly reduction in AKI-associated mortality hazard from 2009 to 2017. Over a period of 10 years, this amounts to a modest reduction in mortality hazard (2017 aHR, 0.89 [reference 2009]; 95% CI, 0.83 to 0.85 [Supplemental Table 2]). Unfortunately, mortality among patients hospitalized with AKI remains high.

Despite recent emphasis on improving post-AKI care (18–20), we did not observe clinically significant improvement in the long-term mortality outcomes post-AKI. The long-term poor adverse health consequences associated with even mild AKI are highly significant, as one in four patients with stage 1 AKI died within a year of AKI hospitalization. Mortality was higher with worse AKI stage, and only 60% of patients with dialysis-requiring AKI survived to 1 year of hospitalization. Factors most strongly associated with death included men, malignancy, liver disease, sepsis, and mechanical ventilation. Such nonmodifiable factors reflect the role of significant comorbidity in contributing to long-term mortality. However, the significant excess mortality seen between hospital discharge and 1 year also presents an important opportunity to optimize postacute care. The lack of improvement in AKI-associated mortality in recent years is in stark contrast to the tremendous gains

Table 4. Crude and adjusted Cox proportional hazards models for trend in time to mortality among US veterans with AKI and non-AKI hospitalizations, 2009–2017

Patient Group	Hazards Ratio (95% Confidence Interval)			
	Unadjusted	Model 1[a]	Model 2[b]	Model 3[c]
In hospital				
AKI	0.98 (0.98 to 0.99)	0.99 (0.98 to 0.99)	1.00 (0.99 to 1.00)	0.99 (0.99 to 1.00)
Non-AKI	1.00 (0.99 to 1.00)	1.03 (1.03 to 1.03)	1.02 (1.02 to 1.02)	1.01 (1.01 to 1.02)
1 yr				
AKI	1.00 (1.00 to 1.00)	1.00 (1.00 to 1.01)	1.00 (0.99 to 1.00)	1.00 (0.99 to 1.00)
Non-AKI	1.02 (1.02 to 1.03)	1.03 (1.03 to 1.03)	1.02 (1.02 to 1.02)	1.02 (1.01 to 1.02)

Hazards ratios are presented for year as a continuous variable.
[a]Model 1 includes patients demographics, including preadmission age, sex, and race (Black or other).
[b]Model 2 contains model 1 plus prehospital comorbid diseases, including hypertension, diabetes mellitus, CKD, congestive heart failure, myocardial infarction, peripheral vascular disease, malignancy, liver disease, chronic obstructive pulmonary disease, and cerebrovascular disease.
[c]Model 3 contains model 2 plus acute hospitalization characteristics, including AKI stage, mechanical ventilation, intensive care unit utilization, sepsis, vasopressor use, hospital length of stay, and primary admitting service (surgical versus other).

in mortality reduction among patients with kidney failure, another population with high comorbidity (21). Our findings point to an urgent need to continue identifying opportunities both to prevent AKI and to improve post-AKI outcomes.

This study has several limitations. VHA is composed of a population of predominantly men; however, our study included >28,000 AKI hospitalizations among women. AKI-associated mortality among those requiring ICU admission in our sample appeared lower than reported in other literature (22,23). However, VHA facilities represent community hospital settings where most patients seek care as opposed to large tertiary academic institutions. Although we adjusted for patient demographics and a robust set of comorbid diseases and markers of acute illness severity, we are unable to account for all confounders that may explain trends in mortality. Future work may elucidate whether post-AKI follow-up care, such as primary care and nephrology office visit, associates with long-term outcomes following AKI. It is also possible that in-hospital mortality may be underestimated, as some patients are transferred to tertiary hospitals for higher levels of care. However, a major strength of this study is the excellent ascertainment of mortality at 1 year by utilizing the VHA Vital Status Files.

Our study evaluating in-hospital and 1-year mortality among hospitalized patients experiencing a consensus creatinine-defined AKI provides valuable insight into the recent trends in AKI-associated mortality. In contrast to prior earlier studies, we found a relatively stable recent trend in in-hospital and 1-year mortality in those with AKI after accounting for changing patient and hospitalization characteristics. The poor prognostic implications of an episode of AKI persist, with overall 1-year mortality exceeding 25%. Our findings highlight the persistent urgent need for interventions to improve both short- and long-term outcomes in this vulnerable population.

Disclosures

N.R. Burrows reports employment with the Centers for Disease Control and Prevention. M. Heung reports consultancy agreements with Reata Pharmaceuticals and Wolters Kluwer (Lexicomp), receiving research funding from Spectral Medical Inc., receiving honoraria from the National Kidney Foundation, and serving as an associate editor of *Advances in Chronic Kidney Disease*. C.-y. Hsu has consulted for legal cases involving acute kidney disease or CKD; consults on an *ad hoc* basis for companies regarding kidney disease; and reports receiving honoraria from Satellite Healthcare, research funding from Satellite Healthcare, and royalties from UpToDate. M.E. Pavkov reports employment with the Centers for Disease Control and Prevention and serving on the Kidney Health Initiative Board of Directors. N. Powe reports receiving honoraria from the Patient Centered Outcomes Research Institute and the Robert Wood Johnson Foundation and serving as a scientific advisor or member of the Patient Centered Outcomes Research Institute, the Robert Wood Johnson Foundation, the University of Washington, Vanderbilt University, and Yale University. R. Saran reports consultancy agreements with KHK, Japan; receiving honoraria from Baylor Scott and White Health System, Fresenius Medical Care, the Japanese Society of Dialysis and Transplantation, Nutek Food Sciences, Reata, and the Renal Research Institute; serving as a scientific advisor or member of the National Kidney Foundation of Michigan Scientific Advisory Board and Reata Pharmaceuticals; and serving as an American Nephrologists of Indian Origin Steering Committee member and a World Federation of Noncommunicable Diseases International Advisory Council member. K. Zivin reports employment with the Department of Veterans Affairs and Mathematica. All remaining authors have nothing to disclose.

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M. Heung, R. Saran, V. Shahinian, and R. Sohaney were responsible for study concept and design; R. Saran, D. Steffick, and H. Yin were responsible for data acquisition; all authors were responsible for data analysis and/or interpretation; M. Heung, V. Shahinian, R. Sohaney, D. Steffick, and H. Yin drafted the manuscript; and all authors were responsible for critical revision of the manuscript for important intellectual content.

Supplemental Material

This article contains the following supplemental material online at http://cjasn.asnjournals.org/lookup/suppl/doi:10.2215/CJN.01730221/-/DCSupplemental.

Supplemental Table 1. Adjusted Cox proportional mortality hazards models among United States veterans with an AKI hospitalization from 2009 to 2017.

Supplemental Table 2. Unadjusted and adjusted Cox proportional mortality hazard models among patients with and without AKI hospitalization from 2009 to 2017.

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