Adverse Outcomes Associated with Preventable Complications in Hospitalized Patients with CKD

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Abstract

Background and objectives Patients with CKD are at risk of hospital-acquired complications (HACs). We sought to determine the association of preventable HACs with mortality, length of stay (LOS), and readmission.

Design, setting, participants, & measurements All adults hospitalized from April of 2003 to March of 2008 in Alberta were characterized by kidney function and occurrence of preventable HACs. CKD was defined by eGFR<60 ml/min per 1.73 m^2 and/or albumin-to-creatinine ratio >3–30 mg/mmol for >3 months in the time frame from 365 to 90 days before admission. Regression models examined the association of HACs with outcomes.

Results Of 536,549 hospitalizations, 8.5% (n=45,733) had CKD and 9.8% of patients with CKD had one or more potentially preventable HAC. In patients with potentially preventable HACs, proportions of death within index hospitalization and from discharge to 90 days were 17.7% and 6.8%, respectively. In patients with CKD, comparing with those hospitalizations without potentially preventable HACs, the adjusted odds ratio (OR) of mortality during index hospitalization and from hospital discharge to 90 days in patients with one or more preventable HAC was 4.67 (95% confidence interval [95% CI], 4.17 to 5.22) and 1.08 (95% CI, 0.94 to 1.25), respectively. Median incremental LOS in patients with one or more preventable HAC was 9.86 days (95% CI, 9.25 to 10.48). The OR for readmission with preventable HAC was 1.24 (95% CI, 1.15 to 1.34). In a cohort with and without CKD, the adjusted ORs of mortality during index hospitalization in patients with CKD and no preventable HACs, patients without CKD and with preventable HACs, and patients with CKD and preventable HACs were 2.22 (95% CI, 1.69 to 2.94), 5.26 (95% CI, 4.98 to 5.55), and 9.56 (95% CI, 7.23 to 12.56), respectively (referenced to patients without CKD or preventable HACs).

Conclusions Preventable HACs are associated with higher mortality, incremental LOS, and greater risk of readmission, especially in people with CKD. Targeted strategies to reduce complications should be a high priority.

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Introduction

Hospital-acquired complications (HACs) are undesirable and unintended clinical conditions, distinct from the admitting diagnosis and other conditions present at admission, that may occur during hospitalization. HACs are common and occur in 2.9%–23% of all hospitalizations (1–3), and in a general population are associated with poor outcomes, including higher mortality, greater readmission, and longer length of stay (LOS) in hospital, compared with those without complications (4–7). Hospitalization is common among patients with CKD, and may confer susceptibility to HACs because of increased risk of bleeding, electrolyte abnormalities, and adverse drug effects, among others. Studies conducted in the United States and Canada have demonstrated that the presence of CKD is associated with a greater risk of potentially preventable HAC than patients with normal kidney function (8,9). Targeting prevention efforts on patients at high risk of HAC, such as those with CKD, readily identified through commonly conducted laboratory tests, may be warranted.

In hospitalized patients with CKD, the association of mortality, LOS, and readmission with preventable HACs has not been determined to our knowledge. The clinical outcomes associated with preventable HACs are important to understand to frame the potential benefit of strategies aimed at reducing complications. Understanding the consequences of these complications on outcomes will inform prioritization and the scope of investment in prevention efforts.

Using a population-based cohort from Alberta, Canada, we sought to determine the association of preventable HACs on clinical outcomes of mortality, LOS, and readmission, in hospitalized patients including those with CKD.

Materials and Methods

Study Population

The study cohort comprised all adults (aged ≥18 years) in Alberta hospitalized from April 1, 2003 to March 31, 2008 (Figure 1) from the population-based Alberta Kidney Disease Network cohort (10). The first (index) hospitalization was considered for each patient. All medical and surgical admissions with the

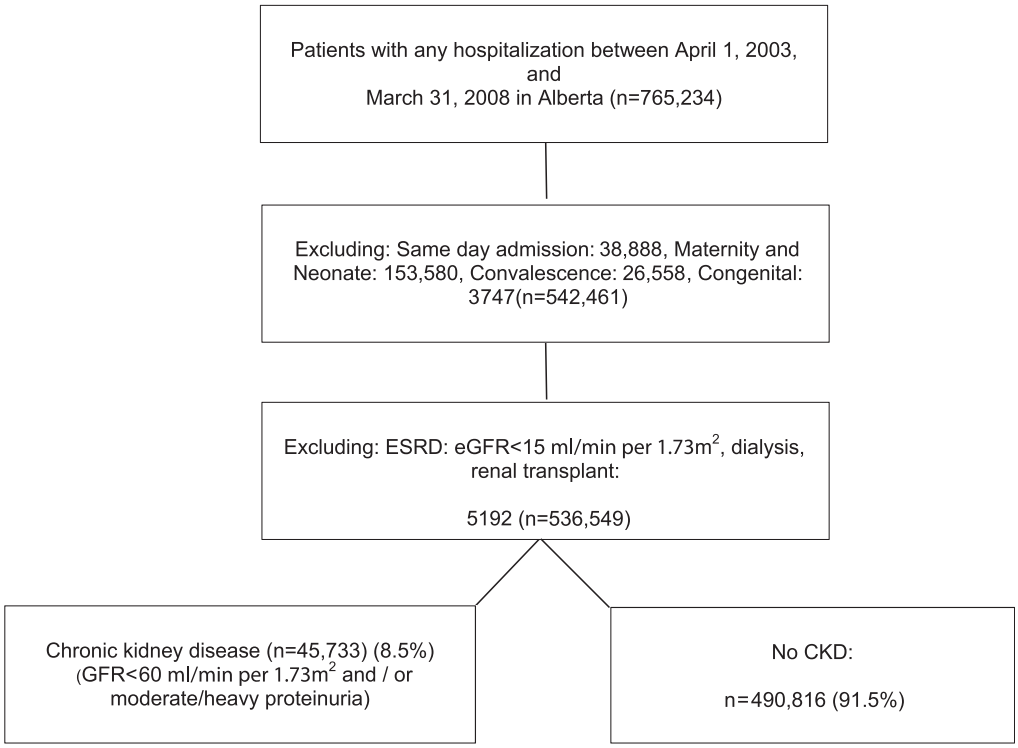

Figure 1. | **Study flowchart to construct cohort of patients with and without CKD.**

exception of maternity/neonatal, congenital malformation, convalescence, and same day admission, were included. We used inpatient administrative data to stratify admissions into medical or surgical, where possible (11).

Assessment of Patient Characteristics

CKD was defined by eGFR<60 ml/min per 1.73 m^2 (estimated using the Modification of Diet in Renal Disease equation) and/or moderate to high albuminuria defined as an albumin-to-creatinine ratio >3–30 mg/mmol. The average of all outpatient eGFR measurements from 365 to 90 days before admission were used; we excluded eGFR measurements within 3 months of admission to ensure that AKI did not affect CKD determination. Patients with ESRD (defined as dialysis, renal transplant, or eGFR<15 ml/min per 1.73 m^2) were excluded. Further categorization using the Kidney Disease Improving Global Outcomes (KDIGO) 2012 Clinical Practice Guidelines (12) was used to categorize CKD as moderate, high, or very high risk; the remaining patients were classified as non-CKD.

Comorbid conditions, including cancer, cerebrovascular disease, congestive heart failure, chronic obstructive pulmonary disease, dementia, diabetes with complications and without complications, HIV/AIDS, metastatic solid tumor, myocardial infarction, mild liver disease, moderate/severe liver disease, para/hemiplegia, peptic ulcer disease, peripheral vascular diseases, and rheumatologic disease were identified using validated algorithms applied to hospitalization discharge abstracts and physician claims data (9,13). The reason for hospitalization was categorized into 16 homogeneous groups using the International Classification of Disease version 10 Canadian Modifications (ICD 10 CA) (Supplemental Appendix A).

Hospital administrative data includes "diagnoses type 2," which captures all HACs. These >4000 ICD 10 CA diagnostic codes were mapped into 16 groups and 76 subgroups according to clinical similarity (Supplemental Appendix B). In the United States, 3M Health Information Systems released a list of hospital complications deemed to be potentially preventable. Briefly, panels of clinicians (two general internists and one pediatrician supplemented by a surgical or obstetric specialist as needed) reviewed each of approximately 14,400 diagnosis values in the International Classification of Disease Ninth Revision Clinical Modification (ICD 9 CM) coding scheme and classified 1562 as potentially preventable in-hospital complications (14,15). Pulmonary embolism, deep vein thrombosis, major gastrointestinal complications with significant bleeding, and decubitus ulcer are examples of potentially preventable complications. That information was used to identify 63 potentially preventable complications by manually remapping ICD-9-CM diagnostic codes to ICD 10 CA. (Supplemental Appendix C).

Hospitalization and vital statistics data were used to determine study outcomes, including LOS of the index hospitalization, mortality during hospitalization and up to 90 days after discharge, and all cause readmission 90 days after discharge. Patients who migrated out of province (n=22) within 90 days after discharge were excluded from analyses of postdischarge events.

Statistical Analyses

In patients with CKD we compared outcomes in patients with and without preventable HACs, and a second analysis included all patients with and without CKD. Mean, SD, 25th

and 75th percentiles, and median were used to describe continuous variables. Categorical variables were described as proportions of the cohort with or without a condition. Multivariable regression, logistic regression, Poisson, and quantile analyses (where appropriate) were used in this study. The independent association of one or more potentially preventable HACs with risk of mortality within index hospitalization, mortality from discharge to 90 days, and readmission within 90 days were analyzed using a logistic regression model; a multivariable regression model was used to analyze incremental LOS associated with one or more potentially preventable HACs. Poisson regression was used to calculate population-attributable risk. Quantile regression was used to determine association of outcomes with one or more potentially preventable HACs within quantiles of LOS. Quantile regression models allow one to assess how any quantile of a conditional distribution changes with patient characteristics, for example, LOS (0%–25%, 25%–50%) (16). All models were accounted for potential confounders. We used purposeful selection model building, and interaction between CKD and potentially preventable HACs was tested. The fully adjusted models included reason for admission, age, sex, admission type (categorical; urgent versus elective defined in hospital administrative data), LOS, severity of CKD (where appropriate), and 16 comorbid conditions. All analyses were also adjusted for complications deemed not to be preventable. The attributable risk percentage was calculated to determine the proportion of mortality and readmission that may be attributable to preventable HACs in patients with CKD, and this formula was used: Population Attributable Risk percent (PAR%) =Pe(RRe-1)/(1+Pe[RRe-1]), where RRe is relative risk and Pe is proportion of outcomes in cohort of patients with and without HACs (17). In additional analyses, we categorized the number of preventable HACs as one, two to three, four to five, and more than five preventable HACs. We stratified patients with CKD to examine moderate risk, high risk, and very high risk CKD as defined by KDIGO, and determined outcomes in these subgroups in a sensitivity analysis. Analyses were conducted among patients with CKD only, as well as the larger cohort with and without CKD. In additional sensitivity analyses, we considered all HACs (preventable and nonpreventable) as the exposure variable. Longer LOS may increase exposure of patients to complications; as such, a quantile regression model was used to determine association of outcomes of interest and potentially preventable HACs by LOS quantile. In other sensitivity analyses, the association of mortality with preventable HACs was determined considering the time frame from hospital admission to 90 days after hospital discharge in patients with CKD. The analysis was undertaken using Stata, version 13. The Health Research Ethics Board of the University of Alberta and University of Calgary approved the study.

Results

Patient Characteristics

During the study period, 765,234 patients were admitted to hospitals in Alberta, Canada, and 536,549 hospitalizations met the inclusion criteria (Figure 1). In the full cohort, 6.7% and 2.6% of patients had an eGFR<60 ml/min per 1.73 m^2 and moderate to heavy proteinuria, respectively, and 45,733 patients (8.5% of cohort) had CKD. In patients with CKD, the proportion of hospitalizations with one or more preventable HAC was 9.8%. (Table 1) Patients with preventable HACs experienced a high proportion of nonpreventable complications (32.8%); only 2.1%–3.6% of patients without preventable HACs had nonpreventable complications. The mean age of patients with CKD with preventable HACs was greater than patients without preventable HAC cases. In patients with CKD and without potentially preventable HACs, the median LOS in hospitalizations without a preventable HAC was 5 days (25th–75th percentile; 2–9 days) compared with 13 days (25th–75th percentile; 7–29 days) in those hospitalizations with preventable HACs. Post-procedural complications (cardiovascular, respiratory, and other complications of surgical and medical care) were the most common preventable HACs, followed by anemia and acid-base balance, fluid electrolyte balance, or metabolic disorders (9) in patients with CKD (Supplemental Appendix D).

Patients without CKD were younger and experienced a shorter LOS. Cardiovascular disease comprised the highest proportion of "most responsible" (principal) diagnosis in non-CKD patients with any potentially preventable HACs, accounting for 23% of admissions. In patients without CKD, the proportion of hospitalizations with one or more preventable HAC was 5.4% (Table 1). In patients without CKD who developed potentially preventable HACs, 27% of hospitalizations experienced non-preventable complications..

Risk of Mortality in Index Hospitalization among Patients with CKD

The unadjusted probability of hospital mortality in patients with and without preventable HACs was 17.6% and 3.7%, respectively, and was similar when stratified by medical or surgical admission. In fully adjusted analyses, the odds ratio (OR) of death during index hospitalization in patients with one or more preventable hospital complications was 4.67 (95% confidence interval [95% CI], 4.17 to 5.22). The OR of mortality was higher among patients with more potentially preventable HACs (Table 2). The population-attributable risk percentage of in-hospital mortality that may be because of a preventable HAC was 27%.

Risk of Mortality from Discharge to 90 Days in Patients with CKD

Among patients surviving the index admission, 6.8% with any preventable HAC died within 90 days postdischarge, compared with 4.8% in patients without preventable HACs. The fully adjusted OR of mortality from discharge to 90 days in patients with one or more preventable HAC was 1.08 (95% CI, 0.94 to 1.25) (Table 2).

Incremental LOS in Index Hospitalization in Patients with CKD

After controlling for all variables, incremental LOS was 9.86 days (95% CI, 9.25 to 10.47) in patients with one or more preventable HAC, and higher LOS was observed with more potentially preventable HACs, with an incremental 17.14 days (95% CI, 14.94 to 19.34) in patients with four to five preventable HACs (Table 2).

Risks of Readmission from Discharge to 90 Days in Patients with CKD

Among surviving patients, 29.5% of those with one or more preventable HACs were readmitted within 90 days of

Table 1. Cohort characteristics

Cohort Characteristics			With Potentially Preventable HACs[a]	Without Potentially Preventable HACs[a]
Demographics for All Patients				
No. of patients (%)	With CKD	45,733 (100)	4494 (9.8)	41,239 (90.2)
	No CKD	490,816 (100)	26,374 (5.4)	464,442 (94.6)
Age, yr, mean (SD)	With CKD	72 (14)	74 (13)	71 (15)
	No CKD	50 (22)	61 (20)	50 (22)
Men, %	With CKD	43.6	45.9	43.4
	No CKD	50	51	49
Top three most responsible diagnoses (reason for admission) categories in patients with CKD, %				
Diseases of circulatory system	With CKD	21	29	20
	No CKD	12	23	11
Neoplasm	With CKD	11	15	11
	No CKD	9	17	9
Diseases of the digestive system	With CKD	11	10	11
	No CKD	14	13	14
Admission type, % (urgent)	With CKD	70	67	71
	No CKD	71	65	72
Medical admission[b]	With CKD	19,524 (54)	1581 (45)	17,943 (55)
	No CKD	208,926(57)	9640 (46)	199,286 (57)
Surgical admission[b]	With CKD	16,275 (45)	1928 (54)	14,347 (44)
	No CKD	156,361 (42)	10,966 (53)	145,395 (42)
Preventable HACs				
None (%)	With CKD	—	—	41,239 (90.2)
	No CKD	—	—	464,442 (94.6)
1	With CKD	—	2861 (6.3)	—
	No CKD	—	18,083 (3.7)	—
2–3	With CKD	—	1231 (2.7)	—
	No CKD	—	6488 (1.3)	—
4–5	With CKD	—	284 (0.6)	—
	No CKD	—	1244 (0.2)	—
>5	With CKD	—	118 (0.3)	—
	No CKD	—	599 (0.1)	—
Nonpreventable HACs, %	With CKD	2952 (6.5)	1475 (32.8)	1477 (3.6)
	No CKD	16,830 (3.4)	7139 (27.0)	9691 (2.1)
CKD category, %[c] (only CKD cohort)	Moderate risk	26,930 (58.9)	2249 (54.1)	24,501 (59.4)
	High risk	12,364 (27.0)	1287 (28.7)	11,077 (26.8)
	Very high risk	6439 (14.1)	778 (17.3)	5661 (13.7)
LOS mean (SD) [25th–75th percentile]	With CKD	10 (20) [2–11]	23 (30) [7–29]	9 (17) [2–9]
	No CKD	7 (21) [2–6]	20 (35) [6–23]	6 (19) [1–6]
LOS median	With CKD	5	13	5
	No CKD	3	11	3
Mortality in index hospitalization, %	With CKD	2315 (5.1)	790 (17.7)	1525 (3.7)
	No CKD	8858 (1.8)	2884 (11.0)	5974 (1.3)
Mortality from discharge to 90 d, %	With CKD	2228 (5.0)	304 (6.8)	1978 (4.8)
	No CKD	10,034 (2.0)	1085 (4.1)	8049 (1.9)
All-cause readmission within 90 d	With CKD	11,281 (24.7)	1326 (29.5)	9955 (24.1)
	No CKD	85,816 (17.5)	7027 (26.4)	78,710 (17.0)

HAC, hospital-acquired complication; —, not applicable; LOS, length of stay.
[a]*P* value <0.001 in all characteristics between patients with and without potentially preventable HACs.
[b]Some admissions could not be classified as medical/surgical.
[c]Using the Kidney Disease Improving Global Outcomes risk classification.

Table 2. Association of outcomes in patients with CKD with potentially preventable HACs

Potentially Preventable HACs	Mortality: Index Hospitalization[a] (95% CI)	Mortality: Discharge to 90 d[a] (95% CI)	Incremental LOS (d),[b] median (95% CI)	Readmission Discharge to 90 d[a] (95% CI)
≥1	4.67 (4.17 to 5.22)	1.08 (0.94 to 1.25)[c]	9.86 (9.25 to 10.47)	1.24 (1.15 to 1.34)
1	3.56 (3.11 to 4.07)	1.17(0.99 to 1.38)[c]	7.20 (6.54 to 7.96)	1.21(1.11 to 1.32)
2–3	6.52 (5.50 to 7.73)	0.91 (0.71 to 1.18)[c]	12.09 (11.81 to 13.98)	1.28 (1.12 to 1.46)
4–5	10.47 (7.78 to 14.08)	0.88 (0.54 to 1.44)[c]	17.14 (14.94 to 19.34)	1.35 (1.04 to 1.75)
>5	18.89 (12.12 to 29.44)	1.29 (0.67 to 2.47)[c]	39.92 (36.54 to 43.30)	1.48 (1.00 to 219)

HAC, hospital-acquired complication; 95% CI, 95% confidence interval; LOS, length of stay.
[a]Fully adjusted for age, admission type (elective versus urgent), sex, LOS, severity of CKD, nonpreventable complications, and 16 comorbid conditions.
[b]Fully adjusted for age, admission type (elective versus urgent), sex, severity of CKD, nonpreventable complications, and 16 comorbid conditions. Comorbid conditions: cancer, cerebrovascular disease, congestive heart failure, chronic obstructive pulmonary disease, dementia, diabetes with complications, diabetes with no complications, HIV/AIDS, metastatic solid tumor, myocardial infarction, mild liver disease, moderate/severe liver disease, para/hemiplegia, peptic ulcer disease, peripheral vascular diseases, rheumatologic diseases; reference: admissions without HAC.
[c]Nonsignificant.

discharge, compared with 24.1% in those without. In fully adjusted analyses, patients with one or more preventable HACs were more likely to be readmitted to hospital with an OR of 1.24 (95% CI, 1.15 to 1.34). Patients with one preventable HAC were rehospitalized 21% more often than those without HACs (OR, 1.23; 95% CI, 1.17 to 1.35) and the OR was 1.48 (95% CI, 1.08 to 2.34) in patients with CKD and more than five HACs. (Table 2). Population-attributable risk of readmission because of preventable HACs was 2.6%

Population-Attributable Risk Percentage

PAR estimates are useful for providing a measure of the proportion of outcomes that can be attributed to individual or multiple causal factors. Given the proportion of patients with CKD and potentially preventable complications (Figure 1, Table 1), hospital admissions with one or more (mean, 1.7) potentially preventable HACs may lead to an additional 45,000 in-hospital patient deaths, 21,000 readmissions within 90 days, and 4.5 million additional hospital days when extrapolated to the population of North America.

Outcomes in Entire Cohort

Further analyses were done to determine the effect of the presence or absence of both potentially preventable HACs as well as CKD. A new cohort that included patients with and without CKD was assembled. The presence of both CKD and potentially preventable HACs were associated with all outcomes of interest (Table 3). A significant interaction between CKD and potentially preventable HACs was found for all outcomes. A graded increase in the risk of mortality in index hospitalization, mortality from discharge to 90 days, LOS stay, and readmission within 90 days were noted with the presence of CKD and preventable complications. For example, the association of index mortality and incremental LOS were 9.56 (95% CI, 7.23 to 12.65) and 11.42 (95% CI, 9.93 to 12.91), respectively, in patients with CKD and potentially preventable HACs compared with patients without CKD and without potentially preventable HACs.

Sensitivity Analyses

The association of higher mortality with preventable HACs persisted when patients with CKD were subdivided into LOS quantiles. The OR of in-hospital mortality in patients who developed preventable HACs was numerically largest in the 0%–25% quantile (all patients LOS ≤7 days) with an OR of 20.6 (95% CI, 16.44 to 25.8), and was lower but was still significant in the subsequent quantiles (Table 4). The absolute risk of mortality was low in patients without potentially preventable HACs, which is a contributor to the large value of the OR in first quantile. When mortality was assessed over a time frame from admission to 90 days after discharge, the OR associated with one or more preventable HACs was 3.06 (95% CI, 2.77 to 3.37).

Discussion

In this large population-based cohort of hospitalized patients, we found that the risk of mortality, LOS in hospital, and 90-day readmission was higher in patients who experienced one or more potentially preventable complication during a hospitalization; this risk was even greater among patients with CKD. The risk of these clinically important outcomes was higher in patients with more potentially preventable complications. The magnitude of this association is large, with a five-fold higher risk of mortality in index hospitalization, and almost 30% higher risk of rehospitalization within 90 days after discharge in patients with CKD and one or more preventable HAC. As an example of the potential implications, we extrapolated our findings to North America. It is estimated that in 2013, approximately 3.25 million patients with CKD (8.5%) were admitted in North America (18,19). Although there are acknowledged limitations and potential biases for using the population-attributable risk percentage, if the association of preventable complications and adverse outcomes is causal, they lead to an additional 45,000 in-hospital patient deaths, 21,000 readmissions within 90 days, and 4.5 million additional hospital days—although this is speculative, particularly in the United States where the health care system differs from Canada. Considerable

Table 3. Association of outcomes in patients with and without CKD with potentially preventable HACs

Cohort	Mortality: Index Hospitalization[a] (95% CI)	Discharge to 90-d Mortality[a] (95% CI)	Incremental LOS (d),[b] Median (95% CI)	Readmission Discharge to 90 d[a] (95% CI)
With CKD and no preventable HACs	2.22 (1.69 to 2.94)	1.49 (1.11 to 2.00)	1.67 (0.29 to 3.06)	1.45 (1.25 to 1.69)
Non-CKD and with preventable HACs	5.26 (4.98 to 5.55)	1.20 (1.12 to 1.29)	9.73 (9.4 to 9.98)	1.41 (1.36 to 1.45)
With CKD and preventable HACs	9.56 (7.23 to 12.65)	1.68 (1.23 to 2.29)	11.42 (9.93 to 12.91)	1.67 (1.42 to 1.96)

HAC, hospital-acquired complication; 95% CI, 95% confidence interval; LOS, length of stay. Reference group: patients without CKD and without potentially preventable HACs.
[a]Fully adjusted for age, admission type (elective versus urgent), sex, LOS, nonpreventable complications, and 16 comorbid conditions.
[b]Fully adjusted for age, admission type (elective versus urgent), sex, nonpreventable complications, and 16 comorbid conditions.

gains in health outcomes would be achieved if even a proportion of these attributable consequences can be reduced.

HACs can be reduced, although the approach can be complex. In a general hospitalized population, various strategies have been implemented, including environmental efforts to control hospital infections and procedures for management of patients with Foley catheters, leading to a relatively high preventable HAC rate (48.73 and 58.17 per 1000 discharge) being reduced to 32.36 and 48.15, respectively (20). Preventive strategies targeted at patients with greater risk of preventable HACs may result in a proportionately greater reduction of poor clinical outcomes.

Patients with CKD are predisposed to complications during hospitalization (21), possibly because of factors such as impaired coagulation, altered renal handling of medications requiring drug dosing changes, predisposition to drug toxicity, and susceptibility to infection, among others. An analysis of data from the Veterans Health Administration for 2004–2005, demonstrated that patients with CKD had a higher risk for several HACs compared with patients with normal kidney function (adjusted incidence rate ratio, 1.19; 95% CI, 1.13 to 1.25) (8). Similarly, our previous work examining a population-based cohort found that patients with CKD had an OR of preventable HACs of 1.20 (95% CI, 1.16 to 1.24) (9). As CKD is readily identifiable using routine and commonly performed laboratory tests, targeting patients with CKD to prevent complications may be feasible. Implementing preventive strategies in the general population including patients with CKD may improve quality of care; however, patients with CKD may benefit more from such interventions.

Other findings from our study merit consideration. First, patients with preventable HACs also had more nonpreventable complications, compared with those with no preventable HACs. It is not clear why complications cluster in certain patients, but we speculate that this may occur in more complex patients, may accrue as patients stay in hospital longer, or be a follow-on effect (for example, management of a complication may predispose to other complications). The effect of any preventative strategy on this clustering of complications is unknown. Second, although in general greater severity of CKD is associated with poorer clinical outcomes in a graded fashion (22), this was not observed in our study. (Supplemental Appendix F) Although CKD is a risk factor for the occurrence of preventable HACs, we speculate that over this very short time frame of observation, preventable HACs appear to have primacy with respect to adverse outcomes, and the severity of CKD may not exert its influence.

To our knowledge no study has investigated the association of clinical outcomes with preventable HACs in patients with CKD. Previous studies on hospital complications and subsequent clinical outcomes in general hospitalized patients have reported significant consequences for patients and health care networks, including 6 days longer LOS, four more deaths in 1000 hospitalizations, and $US 40,000 incremental cost (15). Although the results of our study examining the combined CKD and non-CKD patients are similar to other studies, the magnitude in the

Table 4. ORs of index hospitalization mortality, by LOS quantile, in a CKD cohort with potentially preventable HACs (referenced to the CKD cohort without potentially preventable HACs)

Quantile	0%–25%	25%–50%	50%–70%	75%–100%
LOS	≤7	8 to ≤23	24 to ≤29	>29
OR (95% CI)	20.60 (16.44 to 25.80)	3.6 (3.02 to 4.29)	2.20 (1.45 to 3.34)	2.37 (1.89 to 2.97)
Absolute no. of deaths (%)	224 (25)	277 (33)	62 (41)	227 (50)

Fully adjusted for age, admission type (elective versus urgent), sex, severity of CKD, nonpreventable complications, and 16 comorbid conditions. OR, odds ratio; LOS, length of stay; HAC, hospital-acquired complication; 95% CI, 95% confidence interval.

CKD population who develop preventable HACs appears larger, which is perhaps a reflection of this sicker patient population.

Strengths of this study include the use of a population-based cohort and inclusion of community, teaching, and specialized hospitals, which may improve generalizability. Outpatient laboratory data including eGFR and eGFR and proteinuria level values were used before hospitalization to define patients with CKD. We adjusted our model for LOS, age, sex, admission type (urgent versus elective), severity of CKD, and comorbid conditions, as well as for hospital complications that are not considered to be preventable, the latter of which has not been performed in other studies to the best of our knowledge.

Our findings are subject to a number of limitations. First, we do not have access to certain clinical variables, such as BP control, lifestyle factors (smoking, exercise, and diet), and severity of admitting disease and comorbid conditions. Second, hospital-level factors including volume, location, and hospital type were not available. Third, the nature and behavior of preventable HACs is not precisely defined given the use of administrative data to identify these complications; details including circumstances leading to a complication, the extent to which complications alter the process of disease and care, and how complications and comorbid conditions interact are unknown. This limitation could only be overcome by conducting a chart review or prospective study, which would lack the power of a population-based analysis. Fourth, misclassification of preventable complications may take place, however this should not invalidate results as our sensitivity analyses examining all HACs showed similar results. (Supplemental Appendix E). Fifth, there are limitations and potential biases in using the population-attributable risk percentage, which may alter the results of PAR percentage. Finally, the association of outcomes of interest with preventable HACs may mediate through other pathways, such as greater exposure to develop HACs by longer LOS or burden of illness, although our analyses adjusted for available data on comorbidity as well as days in hospital. In sensitivity analyses, this association was persistent in all quantiles of LOS, which may indicate that preventable HACs independent from LOS lead to higher risk of mortality. Although absolute mortality was smaller in the 0%–25% quantile of LOS (<7 days), the magnitude of association of preventable HACs and mortality was greater. The explanation for this has yet to be fully explored; we speculate that HACs that occur earlier in a hospital admission when patients may be more unwell may have a greater effect.

Preventable HACs are associated with a dramatic increase in risk of in-hospital mortality, as well as longer LOS, mortality at 90 days after discharge, and readmission at 90 days. The magnitude of this association is larger in patients with CKD compared with those without. Our findings may inform prioritization of prevention efforts and reduce the rate of preventable complications with attributable clinical outcomes, eventually improving health care in this patient population. Further investigations are needed to examine evidence-based preventive strategies on the risk of potentially preventable HACs, with the goal of improving quality of care and outcomes for hospitalized patients with CKD.

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Disclosures

None.

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Supplemental Material

Appendix A. Classification of reason for admission

Chapter Number	ICD-10-CA Chapter Title	Code Range
I	Certain infectious and parasitic diseases	A00–B99
II	Neoplasms	C00–D48
III	Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	D50–D89
IV	Endocrine, nutritional and metabolic diseases	E00–E90
V	Mental and behavioural disorders	F00–F99
VI	Diseases of the nervous system	G00–G99
VII	Diseases of the eye and adnexa	H00–H59
VIII	Diseases of the ear and mastoid process	H60–H95
IX	Diseases of the circulatory system	I00–I99
X	Diseases of the respiratory system	J00–J99
XI	Diseases of the digestive system	K00–K93
XII	Diseases of the skin and subcutaneous tissue	L00–L99
XIII	Diseases of the musculoskeletal system and connective tissue	M00–M99
XIV	Diseases of the genitourinary system	N00–N99
XV	Pregnancy, childbirth and the puerperium	O00–O99
XVI	Certain conditions originating in the perinatal period	P00–P96
XVII	Congenital malformations, deformations, and chromosomal abnormalities	Q00–Q99
XVIII	Symptoms, signs and abnormal clinical and laboratory findings not elsewhere classified	R00–R99
XIX	Injury, poisoning and certain other consequences of external causes	S00–T98
XX	External causes of morbidity and mortality	V01–Y98
XXI	Factors influencing health status and contact with health services	Z01–Z99
XXII	Morphology of Neoplasms	8000/0-9989/1
XXIII	Provisional codes for research and temporary assignment	U00-U99

Appendix B. Example for HAC group and subgroup classification using ICD 10 codes

Group	Subgroups	ICD 10 CA Codes
A: Infections	**A_2: Central nervous system(meningitis, brain abscess, encephalitis .....), intracranial phlebitis**	**G002:** Streptococcal meningitis Includes: Non-pneumococcal, streptococci (Streptococcus, Group A) (Streptococcus, Group B) **G008:** Other bacterial meningitis Includes: Meningitis due to: Escherichia coli, Friedlander bacillus, Klebsiella **G009:** Bacterial meningitis, unspecified Includes: Meningitis: purulent NOS, pyogenic NOS. suppurative NOS **G030:** Non-pyogenic meningitis Includes: Nonbacterial meningitis **G039:** Meningitis, unspecified Includes: Arachnoiditis (spinal) NOS **G048:** Other encephalitis, myelitis and encephalomyelitis Includes: Post-infectious encephalitis and encephalomyelitis NOS **G049:** myelitis and encephalomyelitis, unspecified Includes: Ventriculitis (cerebral) NOS **G060:** Intracranial abscess and granuloma Includes: Abscess (embolic)(of): brain [any part], cerebellar, cerebral, otogenic, Intracranial abscess or granuloma: epidural, extradural, subdural **G061:** Intra-spinal abscess and granuloma Includes: Abscess (embolic) of spinal cord [any part]Intra-spinal abscess or granuloma: epidural, extradural subdural **G062:** Extradural and subdural abscess, unspecified D432: G08 C760 A858 D352 A178 D320 A879 G062 B004 C700 G008 G040 C793 G060 G061 G003 G049 A170 G042

Appendix C

PPC Description

01 Stroke & Intracranial Hemorrhage
02 Extreme CNS Complications
03 Acute Pulmonary Edema and Respiratory Failure without Ventilation
04 Acute Pulmonary Edema and Respiratory Failure with Ventilation
05 Pneumonia & Other Lung Infections
06 Aspiration Pneumonia
07 Pulmonary Embolism
08 Other Pulmonary Complications
09 Shock
10 Congestive Heart Failure
11 Acute Myocardial Infarction
12 Cardiac Arrythmias & Conduction Disturbances
13 Other Cardiac Complications
14 Ventricular Fibrillation/Cardiac Arrest
15 Peripheral Vascular Complications Except Venous Thrombosis
16 Venous Thrombosis
17 Major Gastrointestinal Complications without Transfusion or Significant Bleeding
18 Major Gastrointestinal Complications with Transfusion or Significant Bleeding
19 Major Liver Complications
20 Other Gastrointestinal Complications without Transfusion or Significant Bleeding
21 Clostridium Difficile Colitis
22 Urinary Tract Infection
23 GU Complications Except UTI
24 Renal Failure without Dialysis
25 Renal Failure with Dialysis
26 Diabetic Ketoacidosis & Coma
27 Post-Hemorrhagic & Other Acute Anemia with Transfusion
28 In-Hospital Trauma and Fractures
29 Poisonings Except from Anesthesia
30 Poisonings due to Anesthesia
31 Decubitus Ulcer
32 Transfusion Incompatibility Reaction
33 Cellulitis
34 Moderate Infections
35 Septicemia & Severe Infections
36 Acute Mental Health Changes
37 Post-Operative Infection & Deep Wound Disruption without Procedure
38 Post-Operative Wound Infection & Deep Wound Disruption with Procedure
39 Reopening Surgical Site

40 Post-Operative Hemorrhage & Hematoma without Hemorrhage Control Procedure or I&D Procedure

41 Post-Operative Hemorrhage & Hematoma with Hemorrhage Control Procedure or I&D Procedure
42 Accidental Puncture/Laceration During Invasive Procedure

43 Accidental Cut or Hemorrhage During Other Medical Care
44 Other Surgical Complication - Moderate
45 Post-procedure Foreign Bodies
46 Post-Operative Substance Reaction & Non-O.R. Procedure for Foreign Body
47 Encephalopathy
48 Other Complications of Medical Care
49 Iatrogenic Pneumothrax
50 Mechanical Complication of Device, Implant & Graft
51 Gastrointestinal Ostomy Complications
52 Inflammation & Other Complications of Devices, Implants or Grafts Except Vascular Infection
53 Infection, Inflammation and Clotting Complications of Peripheral Vascular Catheters and Infusions
54 Infections due to Central Venous Catheters
55 Obstetrical Hemorrhage without Transfusion
56 Obstetrical Hemorrhage with Transfusion
57 Obstetric Lacerations & Other Trauma without Instrumentation
58 Obstetric Lacerations & Other Trauma with Instrumentation
59 Medical & Anesthesia Obstetric Complications
60 Major Puerperal Infection and Other Major Obstetric Complications
61 Other Complications of Obstetrical Surgical & Perineal Wounds
62 Delivery with Placental Complications
63 Post-Operative Respiratory Failure with Tracheostomy
64 Other In-Hospital Adverse Events

Appendix D. Potentially preventable HAC in patients with CKD

Complications	Description	N of cases	%
A. Infections	A_3: Respiratory (pneumonia, mediastinitis, pulmonary abscess ...)	455	4
	A_5: Genitourinary infection (UTI, cystitis, pyelonephritis ...)	481	4
B: Electrolyte imbalance	B_3: Acid-base, fluid, and electrolyte balance, metabolic disorders	493	4
D: Cardiovascular complications	D_4: Acute myocardial infarction	449	4
	D_16: Post procedural complications	542	4
E: Respiratory complications	E_6: Post procedural disorders (Pneumothorax included)	528	4
M: Hematologic complications	M_4: Anemia due to bleeding	494	4
P: Surgical medical complications	P_2: Other complications of surgical and medical care , not elsewhere classified	439	4
Others		3939	50
Potentially preventable complications		7820	63.11
Total recorded complications (HACs)		12126	100

Supplemental material is neither peer-reviewed nor thoroughly edited by CJASN. The authors alone are responsible for the accuracy and presentation of the material.

Appendix E. Association of outcomes in patients with CKD with all HACs

	Index hospitalization Mortality [A] (95% CI)	Discharge to 90-day Mortality [A] (95% CI)	Incremental LOS(days) [B] (median) (95% CI)	90-days re-admission [A] (95% CI)
≥ 1 Potentially preventable HACs	5.28(4.79 – 5.82)	1.37 (1.22 – 1.53)	14.32 (13.81 – 14.83)	1.27 (1.19 – 1.35)
One	3.55 (3.13 – 4.03)	1.40 (1.21 – 1.61)	9.31 (8.67 – 9.96)	1.21 (1.11 – 1.31)
2-3	6.26 (5.42 – 7.24)	1.34 (1.11 – 1.62)	16.12 (15.24 – 17.00)	1.34 (1.21 – 1.49)
4-5	14.86 (11.85 – 18.64)	1.04 (0.71 – 1.53) *	24.05 (22.39 – 25.71)	1.37 (1.12 – 1.67)
>5	17.40 (13.15 – 23.03	1.71 (1.15 – 2.53)	42.91 (40.88 – 44.94)	1.50 (1.18 – 1.90)

A. Fully adjusted for age, admission type (elective vs urgent), gender, LOS, severity of CKD, non-preventable complications, and 16 comorbid conditions.
B. Fully adjusted for age, admission type (elective vs urgent), gender, severity of CKD, non-preventable complications, and 16 comorbid condition.
- Reference; admissions without HAC

*Non-significant

Appendix F. Association of outcomes in patients with CKD with potentially preventable HACs by severity of CKD

CKD Severity	Mortality: Index hospitalization [A] (95% CI)	Mortality: Discharge to 90-days[A] (95% CI)	Length of stay [B] (mean) (95% CI)	Re-Admission Discharge to 90-days[A] (95% CI)
Moderate	4.81 (4.09 – 5.67)	1.06 (0.81 –1.31) *	9.86 (8.91 – 10.32)	1.32 (1.20 – 1.43)
High	4.51 (3.71 – 5.46)	1.32 (1.04 – 1.69)	10.24 (8.87 – 11.61)	1.15 (1.00 – 1.32)
Very high	4.81 (3.76 – 6.13)	0.84 (0.61 – 1.15) *	10.23 (8.54 – 11.91)	1.12 (0.94 – 1.35) *

A. Fully adjusted for age, admission type (elective vs urgent), gender, LOS, severity of CKD, non-preventable complications, and 17 comorbid conditions

B. Fully adjusted for age, admission type (elective vs urgent), gender, severity of CKD, non-preventable complications, and 17 comorbid condition; Comorbid conditions: cancer, cerebrovascular disease, congestive heart failure, COPD, dementia, diabetes with complications, diabetes with NO complications, HIV/AIDS, metastatic solid tumor, myocardial infarction, mild liver disease, moderate/severe liver disease, para/hemiplegia, peptic ulcer disease, peripheral vascular diseases, rheumatologic diseases

- Reference; admissions without HAC

*Non-significant