The Frequency of Hyperkalemia and Its Significance in Chronic Kidney Disease

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Background: Hyperkalemia is a potential threat to patient safety in chronic kidney disease (CKD). This study determined the incidence of hyperkalemia in CKD and whether it is associated with excess mortality.

Methods: This retrospective analysis of a national cohort comprised 2,103,422 records from 245,808 veterans with at least 1 hospitalization and at least 1 inpatient or outpatient serum potassium record during the fiscal year 2005. Chronic kidney disease and treatment with angiotensin-converting enzyme inhibitors and/or angiotensin II receptor blockers (blockers of the renin-angiotensin-aldosterone system [RAAS]) were the key predictors of hyperkalemia. Death within 1 day of a hyperkalemic event was the principal outcome.

Results: Of the 66,259 hyperkalemic events (3.2% of records), more occurred as inpatient events (n=34,937 [52.7%]) than as outpatient events (n=31,322 [47.3%]). The adjusted rate of hyperkalemia was higher in patients with CKD than in those without CKD among individuals treated with RAAS blockers (7.67 vs 2.30 per 100 patient-months; P < .001) and those without RAAS blocker treatment (8.22 vs 1.77 per 100 patient-months; P < .001). The adjusted odds ratio (OR) of death with a moderate (potassium, ≥5.5 and <6.0 mEq/L [to convert to mmol/L, multiply by 1.0]) and severe (potassium, ≥6.0 mEq/L) hyperkalemic event was highest with no CKD (OR, 10.32 and 31.64, respectively) vs stage 3 (OR, 5.35 and 19.52, respectively), stage 4 (OR, 5.73 and 11.56, respectively), or stage 5 (OR, 2.31 and 8.02, respectively) CKD, with all P < .001 vs normokalemia and no CKD.

Conclusions: The risk of hyperkalemia is increased with CKD, and its occurrence increases the odds of mortality within 1 day of the event. These findings underscore the importance of this metabolic disturbance as a threat to patient safety in CKD.

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Chronic kidney disease (CKD) is a common disease, affecting a growing number of Americans, and it may be associated with a variety of electrolyte disturbances. One such disturbance, hyperkalemia, is of great concern to providers who are treating patients with CKD because of its possible implications for patient safety related to the potential for associated adverse cardiac outcomes. Patients with CKD may be predisposed to hyperkalemia for a variety of reasons. Principal causes include an impaired glomerular filtration rate (GFR) combined with a frequently high dietary potassium intake relative to residual renal function, a commonly observed extracellular shift of potassium caused by the metabolic acidosis of renal failure, and, most importantly, recommended treatment with renin-angiotensin-aldosterone system (RAAS) blockers that inhibit renal potassium excretion.

Few studies have determined the frequency of hyperkalemia in a large CKD population and the extent that this metabolic disturbance is associated with adverse outcomes. Such information is needed to determine the significance of hyperkalemia as a disease-specific patient safety measure. In this study, we examined a national cohort of patients cared for over a single year in the Veterans Health Administration (VHA) to determine the incidence of hyperkalemia in patients with and without CKD and in the presence or absence of treatment with an RAAS blocker. We determined the significance of hyperkalemia by examining its association with subsequent short-term mortality in this population.

Methods

Design, Setting, and Data Sources

This was a retrospective observational study of a national cohort of veterans cared for in the VHA. The setting and data sources used for this study have been previously reported and de-
PARTICIPANTS

The study population consisted of veterans with at least 1 hospitalization from October 1, 2004, through September 30, 2005, an outpatient measure of serum creatinine levels before hospitalization (index CKD date), and complete demographic data (race, sex, and age) to determine the estimated glomerular filtration rate (GFR) and the CKD classification. The index GFR was calculated from the serum creatinine levels obtained between 1 week and 1 year and most proximate to the admission date of the index hospitalization. For inclusion in the study, patients also needed at least 1 potassium value measured during the study year, and this potassium value could be recorded during either an inpatient or an outpatient period. If there was more than 1 record per subject per day, we selected only the record with the highest potassium value of that day for inclusion in the data set.

VARIABLES

The primary exposure was the presence of CKD, defined by an estimated GFR of less than 60 mL/min/1.73m² using the abbreviated Modification of Diet in Renal Disease equation. We elected to use 1 measurement of renal function to classify subjects with or without CKD because of the unavailability of repeated measurements among a substantial portion of the study cohort. The use of a single measurement of renal function to identify patients with CKD is consistent with other large cohort studies. If patients met the requirements for CKD, they were further classified by stage of CKD based on their estimated GFR.

The incidence of hyperkalemia was the primary outcome. Using previously defined thresholds for hyperkalemia, we set moderate hyperkalemia to be a serum potassium level greater than or equal to 5.5 mEq/L (to convert to mmol/L, multiply by 1.0) but less than 6.0 mEq/L, with more severe hyperkalemia set at greater than or equal to 6.0 mEq/L. To determine the significance of hyperkalemia after its occurrence, mortality on the day of or the day after (1-day mortality) the hyperkalemic event was chosen as the key adverse outcome. If there were multiple potassium records associated with a 1-day period, the record with the highest potassium value was included in the analysis, regardless of when it occurred in the 1-day period. We chose this short time interval to ensure a feasible link between the hyperkalemic event and mortality and to minimize the effect of potential case-mix confounders to this association.

COVARIATES

Standard demographic characteristics, comorbidities, and use of RAAS blockers were included in the analysis. Demographic data included sex, age at date of hospital admission (18-56, 57-64, 65-75, and ≥76 years), and race, which was characterized as white, African American, or other. Comorbidities used in the analysis included cancer (excluding nonmelanomatous skin cancer), cardiovascular disease (a composite of cerebrovascular disease, myocardial infarction, and/or congestive heart failure), and diabetes. The Charlson Comorbidity Index was computed for each patient for descriptive purposes and excluded cancer, diabetes, and cardiovascular disease. All comorbidities were determined using International Classification of Diseases, Ninth Revision, Clinical Modification, diagnosis codes from inpatient and outpatient VHA records from October 1, 1999, to the index date. A variable indicating whether the patient had a prescription for angiotensin II receptor blockers (ARBs) and/or angiotensin-converting enzyme inhibitors (ACE-Is) within 30 days of a potassium record was included in the analysis.

MEASUREMENTS

To determine the incidence of hyperkalemia, we expressed the cumulative frequency of events per 100 patient-months of the contributed time of veterans to each subgroup during the study period. To determine the association between hyperkalemia and mortality, survival status within 1 day was linked with each record. We also conducted subanalyses of inpatient and outpatient events.

STATISTICAL METHODS

For descriptive analyses, we reported continuous variables with their mean (standard error) values and numbers (percentages) for categorical variables. We used a Poisson regression model, allowing for multivariate adjustments and variable follow-up times, to determine the incidence rates of hyperkalemia in individuals with and without CKD. Results were reported as adjusted rates (events per 100 patient-months) within key strata, including with and without CKD, with or without exposure to an RAAS blocker, and the average for each adjustment variable.

To determine the adjusted risk of mortality associated with a potassium event, we calculated an odds ratio (OR) of 1-day mortality using generalized estimating equations. This method allowed us to use repeated assessments of serum potassium and repeated vital status assessments within each subject and to control for multiple covariates.

RESULTS

PARTICIPANTS

The base study cohort included 247,176 patients; however, 1,368 patients were excluded because of missing index GFRs (n=16) or potassium values (n=1,352). The final study population of 245,808 individuals had 2,764,638 potassium records; this set of records was further restricted by the limitation of multiple values on any given day, leaving the final data set comprising 2,103,422 records.

DESCRIPTIVE DATA

Table 1 lists the baseline characteristics of the study patients classified into groups based on CKD status and on whether or not the patient had experienced any hyperkalemic event (≥5.5 mEq/L). Patients with CKD were older and more likely to be male, white, and taking ACE-Is and/or ARBs and have diabetes, cardiovascular disease, cancer, and other comorbidities represented by the Charl-
son Comorbidity Index. Patients who experienced hyperkalemia were more likely to be male, African American, and older and have diabetes, cardiovascular disease, and CKD across all stages. Table 1 also includes the results of a logistic regression model identifying risk factors for hyperkalemia in the study population. The strongest risk factor for the development of hyperkalemia was the presence and severity (stage) of CKD. As renal function declined, the odds of developing hyperkalemia greatly increased. The use of ACE-Is and/or ARBs was also a significant risk factor for the development of hyperkalemia, as was the presence of diabetes and 2 or more other comorbidities represented by the Charlson Comorbidity Index.

Of the 33,637 individuals who experienced hyperkalemia, 17,822 (53.0%) had only 1 hyperkalemic event greater than or equal to 5.5 mEq/L during the study period, and the remainder had more than 1 event. There were 70 individuals (0.21%) who had more than 20 events, and a greater proportion of these patients had CKD, ACE-I and/or ARB use, and diabetes than the general population with hyperkalemia.

### Table 1. Patient Characteristics by Chronic Kidney Disease (CKD) and Hyperkalemia Status

<table>
<thead>
<tr>
<th>Variable</th>
<th>No CKD</th>
<th>CKD</th>
<th>Potassium ≥5.5 mEq/L</th>
<th>Potassium ≥5.5 mEq/L</th>
<th>Odds of Potassium ≥5.5 mEq/L, OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>174,935 (71.2)</td>
<td>70,873 (28.8)</td>
<td>212,171 (86.3)</td>
<td>33,637 (13.7)</td>
<td>1 [Reference]</td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td>167,202 (95.6)</td>
<td>68,572 (96.8)</td>
<td>202,867 (95.6)</td>
<td>32,907 (97.8)</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>7,733 (4.4)</td>
<td>2,301 (3.2)</td>
<td>9,304 (4.4)</td>
<td>730 (2.2)</td>
</tr>
<tr>
<td>Race</td>
<td>White</td>
<td>139,213 (79.6)</td>
<td>58,745 (82.9)</td>
<td>172,054 (81.1)</td>
<td>25,904 (77.0)</td>
</tr>
<tr>
<td></td>
<td>African American</td>
<td>34,000 (19.4)</td>
<td>11,332 (16.0)</td>
<td>37,958 (17.9)</td>
<td>7,374 (21.9)</td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>1,722 (1.0)</td>
<td>796 (1.1)</td>
<td>2,159 (1.0)</td>
<td>359 (1.1)</td>
</tr>
<tr>
<td>Age, mean (SE), y</td>
<td>61.0 (0.1)</td>
<td>73.0 (0.1)</td>
<td>64.0 (0.1)</td>
<td>68.0 (0.1)</td>
<td>1.01 (1.00-1.01)</td>
</tr>
<tr>
<td>ACE-I/ARB</td>
<td>None</td>
<td>89,928 (51.4)</td>
<td>24,410 (34.4)</td>
<td>102,953 (48.5)</td>
<td>11,385 (33.8)</td>
</tr>
<tr>
<td></td>
<td>Either</td>
<td>82,528 (47.2)</td>
<td>44,047 (62.1)</td>
<td>105,492 (49.7)</td>
<td>21,083 (62.7)</td>
</tr>
<tr>
<td></td>
<td>Both</td>
<td>2,479 (1.4)</td>
<td>2,416 (3.4)</td>
<td>3,726 (1.8)</td>
<td>1,169 (3.5)</td>
</tr>
<tr>
<td>CCI</td>
<td>0</td>
<td>86,402 (49.4)</td>
<td>27,977 (39.5)</td>
<td>101,850 (48.0)</td>
<td>12,529 (37.2)</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>59,589 (34.1)</td>
<td>26,786 (37.8)</td>
<td>73,745 (34.8)</td>
<td>12,630 (37.5)</td>
</tr>
<tr>
<td></td>
<td>≥2</td>
<td>29,944 (16.5)</td>
<td>16,110 (22.7)</td>
<td>36,576 (17.2)</td>
<td>8478 (25.2)</td>
</tr>
<tr>
<td>Cancer</td>
<td>No</td>
<td>135,842 (77.7)</td>
<td>51,359 (72.5)</td>
<td>162,591 (76.6)</td>
<td>24,610 (73.2)</td>
</tr>
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<td></td>
<td>Yes</td>
<td>39,093 (22.3)</td>
<td>19,514 (27.5)</td>
<td>49,580 (23.4)</td>
<td>9027 (26.8)</td>
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<td>Diabetes</td>
<td>No</td>
<td>117,799 (67.3)</td>
<td>35,129 (49.6)</td>
<td>137,417 (64.8)</td>
<td>15,511 (46.1)</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>57,130 (32.7)</td>
<td>35,744 (50.4)</td>
<td>74,754 (35.2)</td>
<td>18,126 (53.9)</td>
</tr>
<tr>
<td>CVD</td>
<td>No</td>
<td>124,946 (71.4)</td>
<td>33,156 (46.8)</td>
<td>140,886 (66.4)</td>
<td>17,216 (51.2)</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>49,899 (28.6)</td>
<td>37,717 (53.2)</td>
<td>71,285 (33.6)</td>
<td>16,421 (48.8)</td>
</tr>
<tr>
<td>CKD Status b</td>
<td>No CKD</td>
<td>174,935 (100)</td>
<td>0</td>
<td>159,450 (75.2)</td>
<td>15,485 (46.0)</td>
</tr>
<tr>
<td></td>
<td>Stage 3</td>
<td>0</td>
<td>57,979 (81.6)</td>
<td>45,840 (21.6)</td>
<td>11,958 (35.6)</td>
</tr>
<tr>
<td></td>
<td>Stage 4</td>
<td>0</td>
<td>8351 (11.8)</td>
<td>4835 (2.3)</td>
<td>3516 (10.5)</td>
</tr>
<tr>
<td></td>
<td>Stage 5</td>
<td>0</td>
<td>4724 (6.7)</td>
<td>2046 (1.0)</td>
<td>2678 (8.0)</td>
</tr>
</tbody>
</table>

**Abbreviations:** ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; CCI, Charlson Comorbidity Index; CI, confidence interval; CVD, cardiovascular disease; OR, odds ratio.

SI conversion factor: To convert potassium to millimoles per liter, multiply by 1.0.

a Inclusive of all hyperkalemic events.

b Stage 3, a glomerular filtration rate (GFR) less than 60 mL/min/1.73 m² and greater than or equal to 30 mL/min/1.73 m²; stage 4, a GFR less than 30 mL/min/1.73 m² and greater than or equal to 15 mL/min/1.73 m²; and stage 5, a GFR less than 15 mL/min/1.73 m².

### INCIDENCE OF HYPERKALEMIA

Table 2 categorizes the subjects into 4 groups based on CKD and treatment status with ACE-Is and/or ARBs. For each of these groups, the cumulative number of hyperkalemic events, based on severity, was summed within the cumulative 100 patient-months of that group. A total of 66,259 hyperkalemic events (3.2% of total laboratory values) were recorded, with a decreasing incidence of more severe events. The adjusted rates show that, regardless of treatment status, individuals with CKD were more likely to have a hyperkalemic event than those without CKD. However, the highest number of hyperkalemic events per 100 patient-months occurred in patients who had CKD and no treatment with an ACE-I and/or an ARB within the prior 30 days.

### RISK OF MORTALITY WITH HYPERKALEMIA

There were 5945 patients (2.4%) who died within 1 day of a blood draw when potassium levels were recorded.
The Figure shows the adjusted 1-day odds of death associated with each hyperkalemic event based on severity of hyperkalemia and stage of CKD. The reference group included those normokalemic records from individuals without CKD or hyperkalemia. Of note, among normokalemic events, there was a tendency toward a higher risk of 1-day mortality when the events occurred in individuals with CKD, and the risk reached significance among patients with stage 5 CKD relative to their counterparts without CKD. For those events recorded within each stage of CKD, as the level of hyperkalemia increased, the odds of death also increased. In contradistinction to the trend seen with normokalemia, within each discrete level of hyperkalemia there was an inverse relationship between stages of CKD and odds of death; as the stage of CKD became more severe, the odds of death decreased.

Table 3 illustrates the odds of 1-day mortality associated with inpatient and outpatient records from patients with and without CKD. The reference group in both the inpatient and the outpatient analyses consisted of normokalemic records from patients without CKD. Of the 66,259 hyperkalemic events, 34,937 (52.7%) occurred as inpatient events and 31,322 (47.3%) occurred as outpatient events. In both the inpatient and the outpatient analyses, the trends were the same. The odds of death increased with severity of hyperkalemia; however, the risk of death was greater in the absence of CKD than in the presence of CKD. The risk estimates in all categories tended to be higher in inpatient records than in outpatient records.

The Figure shows the adjusted 1-day odds of death associated with each hyperkalemic event based on severity of hyperkalemia and stage of CKD. The reference group included those normokalemic records from individuals without CKD or hyperkalemia. Of note, among normokalemic events, there was a tendency toward a higher risk of 1-day mortality when the events occurred in individuals with CKD, and the risk reached significance among patients with stage 5 CKD relative to their counterparts without CKD. For those events recorded within each stage of CKD, as the level of hyperkalemia increased, the odds of death also increased. In contradistinction to the trend seen with normokalemia, within each discrete level of hyperkalemia there was an inverse relationship between stages of CKD and odds of death; as the stage of CKD became more severe, the odds of death decreased.

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Over the past decade, research has increasingly focused on studying patient safety in the general population. Little attention, however, has been given to disease-specific measures of patient safety that are relevant to populations with chronic illnesses such as CKD. In this analysis, we focused on hyperkalemia as 1 measure of disease-specific patient safety relevant to health care providers treating patients with CKD.

Our results demonstrate that patients with CKD were more likely than patients without CKD to have a hyperkalemic event at all stages of renal disease. The results, however, indicate that patients with CKD who are treated with an RAAS blocker are slightly less likely to have both...
Other trials have shown similar increases among patients who were randomized to treatment with an ACE-inhibitor. Elevations in serum potassium levels between 0.3 and 0.6 mEq/L occurred in 3% to 5% of the patients in chronic renal insufficiency, prior studies have documented. As the GFR declines, serum potassium levels may rise until they reach levels sufficient to increase the risk of hyperkalemia. When aldosterone or other kaliuretic factors fail to maintain potassium homeostasis, extracellular potassium levels may rise until they reach levels sufficient to produce a sustained increase in renal potassium excretion. The lower mortality seen with hyperkalemia in patients with chronic renal insufficiency, prior studies have described a compensatory response to chronic hyperkalemia in which the body eventually develops a new steady state potassium level that is often substantially higher than normal. As the GFR declines, serum potassium levels increase as potassium filtration and secretion decrease. When aldosterone or other kaliuretic factors fail to maintain potassium homeostasis, extracellular potassium levels may rise until they reach levels sufficient to produce a sustained increase in renal potassium excretion. Increased extrarenal potassium excretion through the gut is another adaptive mechanism that gradually develops in patients with chronic renal failure as kidney function declines. The observed lower 1-day mortality rate among patients with CKD who are not receiving this treatment. The 1-day odds of death were greater after a hyperkalemic event than after a normokalemic event. However, hyperkalemic events in patients without CKD were associated with higher odds of 1-day mortality than hyperkalemia events in patients with CKD. There tended to be an inverse relationship between the severity (stage) of CKD and odds of 1-day mortality after a hyperkalemic event, and more severe hyperkalemia was associated with higher odds of death.

Prior studies have documented modest hyperkalemia associated with the use of ACE-I s and/or ARBs in patients with CKD in the setting of a clinical trial. In 6 separate clinical trials of more than 1500 individuals with renal insufficiency, elevations in serum potassium levels between 0.3 and 0.6 mEq/L occurred in 3% to 5% of the patients who were randomized to treatment with an ACE-I. Other trials have shown similar increases among patients assigned to treatment with ARBs. The observation in the present study that hyperkalemia is less common among patients with CKD who are treated with an RAAS blocker has several potential explanations. It is possible that the predisposition to the development of hyperkalemia among patients with CKD may cause physicians to screen out those who are prone to this metabolic disturbance before treatment. In those patients whom they elect to treat with an RAAS blocker, physicians may increase their surveillance for hyperkalemia or spend more time determining means by which a patient can avoid this consequence of therapy. However, our ability to elucidate the mechanism underlying this finding is limited and beyond the scope of this study.

The observed lower 1-day mortality rate among patients with CKD than among patients without CKD and hyperkalemia has some plausible explanations. First, as kidney function declines, there is likely to be an adaptive response that leads to a new increased steady state serum potassium level. In patients with more severe kidney disease, there is also an increased level of gut potassium excretion. Potassium adaption is the response of the kidneys to a high dietary potassium intake. In patients with chronic renal insufficiency, prior studies have described a compensatory response to chronic hyperkalemia in which the body eventually develops a new steady state potassium level that is often substantially higher than normal. As the GFR declines, serum potassium levels increase as potassium filtration and secretion decrease. When aldosterone or other kaliuretic factors fail to maintain potassium homeostasis, extracellular potassium levels may rise until they reach levels sufficient to produce a sustained increase in renal potassium excretion. Increased extrarenal potassium excretion through the gut is another adaptive mechanism that gradually develops in patients with chronic renal failure as kidney function declines.

### Table 3. Odds of Death Within 1 Day of a Hyperkalemic Event, by Potassium Category and Chronic Kidney Disease (CKD)

<table>
<thead>
<tr>
<th>Potassium Category</th>
<th>No. (%) of Death Events</th>
<th>OR (95% CI)</th>
<th>Adjusted for confounders: race, sex, age, Charlson Comorbidity Index, cancer, diabetes, cardiovascular disease, and treatment with renin-angiotensin-alderosterone system blocker within 30 days.</th>
</tr>
</thead>
<tbody>
<tr>
<td>No CKD</td>
<td>200 (0.07)</td>
<td>0.99 (0.62-1.51)</td>
<td>27 (0.4) 54 (1.7) 13.06 (9.85-17.30)</td>
</tr>
<tr>
<td>CKD</td>
<td>2304 (0.3)</td>
<td>1.12 (0.75-1.61)</td>
<td>5.40 (3.72-6.18) 15.82 (13.97-17.93)</td>
</tr>
<tr>
<td>No CKD</td>
<td>554 777 7419 3270</td>
<td>6.17 (4.16-9.16)</td>
<td>27.74 (20.66-37.25)</td>
</tr>
<tr>
<td>CKD</td>
<td>129 029 2660</td>
<td>1.12 (1.05-1.19)</td>
<td>5.17 (3.28-6.18) 15.82 (13.97-17.93)</td>
</tr>
<tr>
<td>No CKD</td>
<td>762 136 9620</td>
<td>1.00 (Reference)</td>
<td>6.17 (4.16-9.16) 27.74 (20.66-37.25)</td>
</tr>
<tr>
<td>CKD</td>
<td>10 605</td>
<td>0.99 (0.62-1.51)</td>
<td>27 (0.4) 54 (1.7) 13.06 (9.85-17.30)</td>
</tr>
</tbody>
</table>
6.0 mEq/L without apparent electrocardiographic or cardiovascular manifestations. Acute hyperkalemia can cause a rapid reduction in resting membrane potential, leading to increased cardiac depolarization, muscle excitability, and possible electrocardiographic changes. These cardiac changes may be altered in the renal population, in which the presence of other electrolyte disturbances could influence the cardiac membrane potential.

The findings reported in this study have important clinical implications. They suggest that patients with CKD and those who are treated with RAAS blockers have an increased risk of hyperkalemia, but that risk may be somewhat lowered with the proper patient selection for RAAS treatment. The increased risk of death associated with hyperkalemia underscores the importance of clinical monitoring and follow-up of patients with CKD or patients who are treated with RAAS blockers to avoid the adverse outcomes that are associated with this metabolic disturbance. Other authors have reported that a substantial percentage of patients who have hyperkalemia detected in a clinical setting do not have timely follow-up of this abnormal laboratory value. Even though this study revealed an attenuation in the morality risk associated with hyperkalemia and CKD that was consistent with the adaptive mechanisms described, the higher frequency of this metabolic disturbance in this disease population suggests that patients with CKD should be closely monitored to minimize adverse outcomes.

Retrospective analyses such as this one have several inherent limitations that should be considered when interpreting the findings. First, the incidence of hyperkalemia is detected only at the time of a clinically ordered blood test and does not account for the occurrence of this metabolic disturbance at unobserved times. Therefore, our estimation of the incidence of hyperkalemia was subject to the frequency of laboratory monitoring, which was nonrandom among the veterans in this cohort. Nevertheless, the demonstrated odds of death associated with hyperkalemia in both inpatient and outpatient laboratories highlights the importance of the detected events in this study. Using 1-day mortality as the outcome, we were able to minimize the influence of confounding by severity of illness in the study. The results of this study only included RAAS blockers, which are known to increase serum potassium levels. However, it is quite possible that other agents may have influenced the incidence of hyperkalemia. The emphasis in this study, however, was on that class of agents that are a key element to disease management in CKD. Finally, patients with stage 5 CKD may have included individuals with end-stage renal disease who are receiving dialysis and as a result may handle potassium differently than those individuals who were dialysis independent. Given the small number of patients with stage 5 CKD in the cohort, the percentage of patients who were receiving dialysis was likely to be small.

The findings of this study support the consideration of hyperkalemia as a patient safety measure in CKD. We have shown that this metabolic disturbance is more common in patients with CKD than in patients without this condition. Moreover, hyperkalemia is linked to increased odds of mortality, although the risk is lower in CKD populations than in non-CKD populations. These findings suggest that the role of disease management in the manifestation of this candidate safety measure is complex. However, given the association of hyperkalemia with CKD and the elevated odds of death associated with hyperkalemia, this metabolic disturbance should be considered a disease-specific patient safety event. More work is needed to see what extent alterations in disease management will reduce the incidence of this patient safety indicator.

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REFERENCES


