Outpatient Nephrology Referral Rates after Acute Kidney Injury

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ABSTRACT
AKI associates with an increased risk for the development and progression of CKD and mortality. Processes of care after an episode of AKI are not well described. Here, we examined the likelihood of nephrology referral among survivors of AKI at risk for subsequent decline in kidney function in a US Department of Veterans Affairs database. We identified 3929 survivors of AKI hospitalized between January 2003 and December 2008 who had an estimated GFR (eGFR) < 60 ml/min per 1.73 m² 30 days after peak injury. We analyzed time to referral considering improvement in kidney function (eGFR ≥ 60 ml/min per 1.73 m²), dialysis initiation, and death as competing risks over a 12-month surveillance period. Median age was 73 years (interquartile range, 62–79 years) and the prevalence of preadmission kidney dysfunction (baseline eGFR < 60 ml/min per 1.73 m²) was 60%. Overall mortality during the surveillance period was 22%. The cumulative incidence of nephrology referral before dying, initiating dialysis, or experiencing an improvement in kidney function was 8.5% (95% confidence interval, 7.6–9.4). Severity of AKI did not affect referral rates. These data demonstrate that a minority of at-risk survivors are referred for nephrology care after an episode of AKI. Determining how to best identify survivors of AKI who are at highest risk for complications and progression of CKD could facilitate early nephrology-based interventions.


Despite improving sophistication in the provision of hospital care, AKI is increasingly common and remains closely associated with increases in short-term mortality and health care utilization.1–3 Recent observational studies link the progression of CKD, including the development of ESRD, to previous AKI among those who survive to hospital discharge.4–6 As the interaction between AKI and CKD becomes better characterized,7–12 improving care among its survivors will depend on identifying high-risk individuals and facilitating interventions to prevent progression of disease and its complications. One quality of care indicator for patients with persistent CKD after an episode of AKI is the rate of nephrology referral.

Data from the CKD literature suggest that early nephrology referral can reduce morbidity and mortality in patients with advanced kidney disease.13–15 Little is known about the care patterns of patients surviving an episode of AKI. We hypothesized that nephrology referral rates among survivors of AKI would be low even in a high-risk subgroup in which kidney dysfunction persists. To test this hypothesis, we examined nephrology referral rates among a multicenter cohort of patients within the Veterans Administration (VA) Integrated Service Network Health Care system who survived an episode of AKI between January 2003 and December
2008 with impaired kidney function up to 30 days after peak injury.

RESULTS

Patient Characteristics
The study cohort was identified initially from 14,474 first patient hospitalizations complicated by AKI (Figure 1). AKI was defined as a 0.3 mg/dl or 50% increase in serum creatinine from a predmission outpatient serum creatinine to the peak inpatient serum creatinine and was staged according to the Acute Kidney Injury Network (AKIN) classification system. After excluding patients with a history of ESRD or chronic dialysis (n=505), renal transplant (n=98), and those already receiving preadmission nephrology care (n=1825), we further excluded 772 patients with a hospitalization lasting >30 days and 324 patients with no VA encounter during our posthospitalization surveillance period.

To allow for initial recovery and to enrich the cohort with patients at high risk for subsequent decline in kidney function, we selected survivors from the remaining 11,606 patients with persistent kidney impairment (eGFR < 60 ml/min per 1.73 m²) up to 30 days after peak injury (i.e., peak serum creatinine during hospitalization). During this initial 30-day interval, we excluded patients who died or had been referred for hospice (n=1516), recovered kidney function to eGFR ≥ 60 ml/min per 1.73 m² (n=6041), or were receiving ongoing dialysis near the end of the 30-day interval (n=30). Finally, 506 (11.4%) of 4435 remaining survivors were referred for outpatient nephrology care during this early interval.

Table 1 shows the demographic and baseline characteristics of the remaining 3929 AKI patients included in the primary study cohort. The median age of patients in the study was 73 years (interquartile range, 62–79) with the following comorbidity rates: diabetes mellitus at 58%, hypertension at 90%, and coronary artery disease at 62%. In addition, approximately 60% of patients had evidence of predmission kidney dysfunction as indicated by an outpatient baseline eGFR < 60 ml/min per 1.73 m². As shown in Figure 1, 3402 (87%) patients experienced AKIN stage I, 366 (9%) experienced AKIN stage II, and 161 (4%) experienced AKIN stage III injury.

Competing Risk Analysis for Renal Referral, Dialysis Initiation, Death, and Improvement in Kidney Function
The 3929 patients comprising the primary study cohort were followed for 12 months to assess improvement in kidney function (eGFR ≥ 60 ml/min per 1.73 m²), referral for nephrology care, dialysis initiation, and mortality (30–395 days after peak injury). The overall rate of mortality during the surveillance period was 22%. Figure 2 and Table 2 show the cumulative incidences for the prespecified outcomes of nephrology referral, dialysis initiation, death, and improvement of kidney function to an eGFR of ≥60 ml/min per 1.73 m² as competing risks. We chose a competing risk analysis to account for improvements in kidney function or patients who experience imminent death who may not benefit from outpatient referral. The choice of 60 ml/min per 1.73 m² as a defined threshold was based on National Kidney Foundation Disease Outcomes Quality Initiative (K/DOQI) practice guidelines, which advise co-management or consultation by a nephrologist in patients with stage III CKD and referral to a nephrologist at the onset of stage IV CKD. The cumulative incidence of first receiving nephrology referral before dying, initiating dialysis, or experiencing an improvement in kidney function within the entire cohort was 5.9% (95% CI, 5.2–6.6) at 6 months and 8.5% (95% CI, 7.6–9.4) by the end of the 12-month surveillance period. Finally, referral rates using a competing risk approach continued to be low as the severity of AKI increased: 8.6% (95% CI, 7.7–9.6) for patients with stage I injury (n=3402), 6.3% (95% CI, 4.1–9.1) for stage II injury (n=366), and 10.6% (95% CI, 6.4–15.9) for stage III injury (n=161).

We also repeated our competing risk analysis in a higher-risk subgroup of 1606 patients whose eGFR was <45 ml/min per 1.73 m² up to 30 days after peak injury. Using ≥45 ml/min per 1.73 m² as a
Table 1. Baseline demographic and admission characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>73 (62–79)</td>
</tr>
<tr>
<td>Men</td>
<td>3827 (97)</td>
</tr>
<tr>
<td>White</td>
<td>3510 (89)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>2269 (58)</td>
</tr>
<tr>
<td>CKD</td>
<td>2371 (60)</td>
</tr>
<tr>
<td>Hyper tension</td>
<td>3543 (90)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>2432 (62)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>1387 (35)</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>870 (22)</td>
</tr>
<tr>
<td>Median creatinine (mg/dl)</td>
<td>1.3 (1.2–1.6)</td>
</tr>
<tr>
<td>Median baseline estimated GFR (ml/min per 1.73 m²)</td>
<td>56 (46–68)</td>
</tr>
</tbody>
</table>

Continuous variables presented as median (interquartile range). Other data presented as n (%).

Figure 2. Cumulative incidences of nephrology referral, dialysis initiation, improvement in kidney function, and death analyzed as competing risks. This figure summarizes the cumulative incidences of the prespecified outcomes as competing risks during the 12-month surveillance period (30–395 days following peak injury). Beginning at 30 days after peak injury, the cumulative incidences of first improving kidney function to an eGFR >60 ml/min per 1.73 m², dying, being referred to nephrology, or receiving dialysis were 44.0% (95% CI, 42.4–45.5), 11.5% (95% CI, 10.5–12.5), 8.5% (95% CI, 7.6–9.4), and 0.2% (95% CI, 0.1–0.4), respectively.

The cumulative incidences of the competing risks in this higher-risk subgroup were similar to the parent analysis including 51.8% (95% CI, 49.3–54.2) for improvement in kidney function, 11.7% (95% CI, 10.2–13.3) for death, and 0.4% (95% CI, 0.2–0.9) for dialysis.

Kidney Function During the Surveillance Period

Table 3 summarizes the pattern of eGFR progression for the study cohort stratified by baseline eGFR status during the 12-month surveillance period. Of the 1254 survivors with an initial baseline eGFR ≥60 ml/min per 1.73 m², 50.2% (n=629) recovered to an eGFR ≥60 ml/min per 1.73 m² by the end of the 12-month surveillance period. The remainder demonstrated persistent kidney dysfunction, with a final eGFR measured at between 30 and 59 ml/min per 1.73 m² for 48.1% (n=603) and 15 and 29 ml/min per 1.73 m² for 1.4% (n=18), and ESRD or dialysis in <1% (n=4). Among 1824 survivors with an initial baseline eGFR <60 ml/min per 1.73 m², 50.3% (n=917) had a last eGFR ≥45 ml/min per 1.73 m², 40.2% (n=734) had an eGFR between 30 and 44 ml/min per 1.73 m², 8.7% (n=158) had an eGFR between 15 and 29 ml/min per 1.73 m², and <1% (n=15) had ESRD or were on dialysis at the end of the 12-month surveillance period.

Sensitivity Analyses

In addition to using fee-basis data to capture referrals made to physicians outside the VA system, we performed two additional sensitivity analyses. The first involved extensive manual chart review of 100 Medicare patients selected randomly from our study cohort who survived the surveillance period without receiving dialysis or improving kidney function to an eGFR to ≥60 ml/min per 1.73 m². The rationale was to conduct an intensive investigation among patients with resources to potentially pursue nephrology care outside of the VA system. The medical chart including consultation orders, text of clinic notes, relevant consultations (e.g., urology), discharge summaries, and relevant scanned documents from outside institutions was reviewed. Of note, the majority of these patients (93%) had either a primary care physician or a specialist serving a primary care role (e.g., hematologist, heart transplant), indicating regular usage of the VA system. Among these 100 patients, we found only one patient who was identified as being referred for outpatient nephrology referral before achieving peak injury. Discussion of outpatient VA nephrology referral was noted during the index hospitalization in three other patients, yet no evidence for a consultation order, appointment scheduling, or actual nephrology visit were found. We also performed an analysis in the subcohort of 277 non-Medicare eligible patients (i.e., aged <65 years) known to be 100% VA service-connected at the time of hospitalization. The goal of this analysis was to examine referral rates in patients with a higher likelihood of obtaining their medical care exclusively within the VA healthcare system. At the end of the 12-month surveillance period, the cumulative incidence of nephrology referral in patients not already
Table 2. Cumulative incidences for improvement in kidney function (eGFR > 60 ml/min per 1.73 m²), death, dialysis initiation, and nephrology referral within the entire cohort

<table>
<thead>
<tr>
<th>Event</th>
<th>1 mo</th>
<th>3 mo</th>
<th>6 mo</th>
<th>12 mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>eGFR &gt; 60 ml/min per 1.73 m²</td>
<td>14.8 (13.7–15.9)</td>
<td>27.2 (25.8–28.6)</td>
<td>36.1 (34.6–37.6)</td>
<td>44.0 (42.4–45.5)</td>
</tr>
<tr>
<td>Dialysis (acute or chronic)</td>
<td>0.08 (0.0–0.2)</td>
<td>0.1 (0.04–0.3)</td>
<td>0.13 (0.1–0.3)</td>
<td>0.20 (0.1–0.4)</td>
</tr>
<tr>
<td>Death</td>
<td>4.2 (3.6–4.8)</td>
<td>6.6 (5.9–7.4)</td>
<td>9.0 (8.1–9.9)</td>
<td>11.5 (10.5–12.5)</td>
</tr>
<tr>
<td>Nephrology referral</td>
<td>1.9 (1.5–2.3)</td>
<td>3.8 (3.3–4.5)</td>
<td>5.9 (5.2–6.6)</td>
<td>8.5 (7.6–9.4)</td>
</tr>
</tbody>
</table>

Data indicate the cumulative incidence probabilities in percentages and 95% confidence limits for each event and time interval during the surveillance period. For example, at 6 months, the cumulative incidence of nephrology referral before improvement in kidney function, dialysis, or death among the entire cohort was 5.9% (95% CI, 5.2–6.6).

Table 3. Outpatient kidney function among survivors during the 12-month surveillance period

<table>
<thead>
<tr>
<th>Baseline eGFR</th>
<th>30 d</th>
<th>6 mo</th>
<th>12 mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline eGFR ≥60 ml/min per 1.73 m² (n=1558)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients alive at the end of each prespecified interval</td>
<td>1476</td>
<td>1346</td>
<td>1254</td>
</tr>
<tr>
<td>eGFR ≥60 ml/min per 1.73 m²</td>
<td>327 (22.2)</td>
<td>633 (47)</td>
<td>629 (50.2)</td>
</tr>
<tr>
<td>eGFR 30–59 ml/min per 1.73 m²</td>
<td>1116 (75.6)</td>
<td>688 (51.1)</td>
<td>603 (48.1)</td>
</tr>
<tr>
<td>eGFR 15–29 ml/min per 1.73 m²</td>
<td>27 (1.8)</td>
<td>20 (1.5)</td>
<td>18 (1.4)</td>
</tr>
<tr>
<td>ESRD or dialysis</td>
<td>6 (0.4)</td>
<td>5 (0.4)</td>
<td>4 (0.3)</td>
</tr>
<tr>
<td>Baseline eGFR &lt;60 ml/min per 1.73 m² (n=2371)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients alive at the end of each prespecified interval</td>
<td>2267</td>
<td>2023</td>
<td>1824</td>
</tr>
<tr>
<td>eGFR ≥ 45 ml/min per 1.73 m²</td>
<td>1117 (49.3)</td>
<td>1049 (51.9)</td>
<td>917 (50.3)</td>
</tr>
<tr>
<td>eGFR 30–44 ml/min per 1.73 m²</td>
<td>917 (40.5)</td>
<td>778 (38.5)</td>
<td>734 (40.2)</td>
</tr>
<tr>
<td>eGFR 15–29 ml/min per 1.73 m²</td>
<td>214 (9.4)</td>
<td>178 (8.8)</td>
<td>158 (8.7)</td>
</tr>
<tr>
<td>ESRD or dialysis</td>
<td>19 (0.8)</td>
<td>18 (0.9)</td>
<td>15 (0.8)</td>
</tr>
</tbody>
</table>

Data are presented as n or n (%). Values are taken from those still alive at the prespecified cutoff points using serum creatinine closest up to each time cutoff. For patients without values but known to be alive at each time cutoff, the last prior value was carried forward.

demonstrating improvement in kidney function or death was similarly low at 9.8% (95% CI, 6.6–13.6).

In addition, because the primary goal of the study was to examine referral rates among patients most likely to benefit from nephrology referral (i.e., alive with persistently low eGFR), our prespecified surveillance period began 30 days after peak injury. However, 506 of 11,606 patients with AKI were referred for outpatient nephrology care before this period began. To examine the effect of these patients on overall referral rates, our competing risk analysis was repeated beginning at peak injury in these 11,606 patients. By the end of the surveillance period, the probability of nephrology referral before any of the same competing risks was similarly low at 8.4% (95% CI, 7.9–8.9).

Comparison of Referred and Nonreferred Patients

To determine if nonreferred patients had a potentially higher AKI severity or comorbidity burden as a potential reason for their lack of referral, we compared the basic demographics, comorbidity rates, and AKI severity of patients who survived the 12-month surveillance period without demonstrating improvement in kidney function to an eGFR > 60 ml/min per 1.73 m² (Table 4). Nonreferred patients tended to be slightly older, were less likely to have a diagnosis of diabetes mellitus or a diagnosis of congestive heart failure, and had a modestly higher eGFR at baseline. There were no statistically significant differences in race, sex, or rates of coronary artery disease, hypertension, peripheral vascular disease, or severity of AKI.

DISCUSSION

AKI is becoming increasingly recognized as an important determinant of incident CKD,5,12 progression to ESRD,4,11,18,19 and long-term mortality.20,21 Improving care among AKI survivors will depend on increasing recognition of the associated longitudinal risks as well as identifying and intervening upon key modifiable risk factors. In addition to a high mortality rate, our study showed that patients surviving an episode of AKI with persistently diminished kidney function are infrequently referred for nephrology care. Because referral to a nephrologist may slow progression of CKD or better prepare patients for ESRD, this may represent a missed opportunity to improve care in this population. These findings also motivate research to better risk-stratify the subset of surviving AKI patients who are likely to progress to advanced CKD.

The K/DOQI practice guidelines advise co-management or consultation by a nephrologist in patients with stage III CKD and referral to a nephrologist at the onset of stage IV CKD.17 In support of these guidelines are observational data in both the veteran and general populations suggesting that early nephrology referral may improve outcomes in patients with moderate to severe CKD.15,22,23 Tseng et al.15 demonstrated that consistent outpatient nephrology care in patients with diabetes and stage III–IV CKD associates with an adjusted 20%–55% reduction in mortality. Although the care elements driving this observed benefit are not fully understood, better recognition and control of both traditional cardiovascular risk factors and secondary complications of CKD are likely contributors.24
Even among those who eventually initiate dialysis, predialysis care by a nephrologist in the time period immediately before initiation has been associated with improvement in outcomes. One example of benefit conferred during this time may be early access placement. A recent Department of Defense and Veterans Affairs study indicates that patients initiating dialysis are more likely to undergo timely arteriovenous fistula placement than patients with other types of insurance coverage. These results suggest an opportunity to further improve upon the care of patients not already being targeted for transitional care in this population.

Recent data suggest that recognition of CKD and the need to pursue further diagnostic workup is variably low among primary care physicians. The high proportion of patients in this study with pre-existing decrements in kidney function not already receiving nephrology input into their care support this finding. The importance of these observations is highlighted by recent Medicare data indicating that elderly patients with a discharge diagnosis of AKI are almost four times more likely to see their primary care physician than a nephrologist during the surveillance period. However, even if we liberally exclude all patients who experienced improvement in kidney function along with all other competing risks from consideration, fewer than one in five of these patients were referred for nephrology care (absolute referral rate 19%, 31% – 33%). The latter may be partially mediated by enhanced angiotensin II sensitivity, suggesting a contribution of AKI to distal cardiovascular complications and a potential role for renin-angiotensin-aldosterone axis blockade. These observations illustrate the need for well designed prospective studies able to identify factors that can predict CKD progression and other important disease processes after AKI. The latter is especially relevant given the number of patients who demonstrated improvement in kidney function to >60 ml/min per 1.73 m² during the surveillance period. However, even if we liberally exclude all patients who experienced improvement in kidney function along with all other competing risks from consideration, fewer than one in five of these patients were referred for nephrology care (absolute referral rate 19%, 31% in the analysis using eGFR ≥45 ml/min per 1.73 m² as a threshold for improving kidney function). As the burden of this disease is increasing, better understanding of its effect on health care utilization, policy implications, and the optimal patient care models to meet this need is also warranted.

The relative strengths of this study include use of serum creatinine levels to define baseline and postdischarge kidney function as well as the magnitude of kidney injury. In addition, we selected patients with either diminished function immediately after AKI or those with acute on chronic kidney injury to enrich for those at highest risk for advanced kidney disease and its complications. Limitations of the study include inclusion of an older veterans study population that may limit generalizability to other care settings. In addition, despite incorporating “fee-basis” billing data for outpatient referrals, it is likely that some patients obtaining nephrology care at an outside healthcare facility were not captured. However, multiple sensitivity analyses performed showed consistently low referral rates and match recent data from a Medicare population, suggesting system-wide low referral rates. Our study adds to this early report in that AKI was more rigorously defined, was not restricted to an insured elderly population, and accounted for competing risks that might obviate the need for referral. Although requiring a baseline creatinine helped to more accurately identify patients with AKI, doing so might...
also exclude a younger and healthier group of patients. However, it can be argued that this group is also at lower risk for AKI and its attendant complications and less likely to be the target population of interest. Finally, despite exclusion of patients with known hospice referral or those who died within 30 days of peak injury, other appropriate reasons for nonreferral, including decisions to limit care, were not extensively available. Nonreferred AKI survivors with persistent kidney dysfunction were indeed slightly older, but also had modestly better kidney function and were less likely to have diabetes and congestive heart failure. There were no statistically significant differences between the rates of other major comorbid conditions between referred and nonreferred survivors. Even if decisions to limit care represented a significant proportion of reasons for nonreferral, a significant proportion of patients would likely remain whose care may benefit from nephrology-based input. Furthermore, the need and ability of the nephrologist to contribute meaningfully to the palliative care of patients with advanced kidney disease is also becoming increasingly recognized.37,38

In summary, the increasing incidence of AKI and its downstream complications are becoming an important public health issue. Although patients who experience AKI with residual decrements in kidney function constitute a group at risk for the development and progression of CKD, few are referred for specialized care by a nephrologist. Increasing awareness of these risks may lead to earlier and improved management of CKD-related complications. Further detailed efforts to identify potential gaps in care in this population, determine the effect of nephrology referral on outcomes such as GFR decline and mortality, identify and validate predictors of CKD after AKI, and develop care models to meet this potential need are warranted.

CONCISE METHODS

Study Setting
This study involved data from five VA medical centers located in Tennessee, Kentucky, and West Virginia. The clinical enterprise encompasses acute inpatient hospitals, outpatient primary care and subspecialty clinics, outpatient pharmacies, rehabilitation facilities, and long-term care facilities and domiciliaries. Data extracted from the regional data warehouse included general demographic information (e.g., age, sex, race, admitting service, and location), inpatient and outpatient procedure and diagnosis codes using both Current Procedural Terminology (CPT) and International Classification of Diseases-9 (ICD-9) coding, laboratory data, fee-basis records (non-VA care ordered by a VA provider), and computerized physician order entry records (Supplemental Material). Comorbidities shown in Table 1 were collected from data before hospital admission. All data were transferred for analysis to a secure research server within the VA computer network. The Tennessee Valley Health System Veteran’s Health Administration Institutional Review Board and Research and Development Committees approved this study.

Study Population and Design
A retrospective cohort of adults (aged ≥18 years) was formed among patients with a hospitalization complicated by AKI during a 5-year period between January 2003 and December 2008. AKI was defined as a 0.3 mg/dl or 50% increase in serum creatinine using the difference between peak hospitalization and baseline serum creatinine and staged according to AKIN creatinine criteria.16 The baseline creatinine was defined as the most recent outpatient creatinine between 7 and 365 days before admission.

Inclusion criteria were patients with at least one outpatient creatinine from 7 to 365 days before hospital admission and at least two inpatient serum creatinine values during the study period. We retained only the first (index) hospitalization (n=14,474) for each patient that met these criteria (Figure 1). The former was enforced in order to accurately describe the magnitude of renal injury as well as premorbid kidney function. Because the main focus of this study was to examine referral rates in patients after resolution of the acute phase of illness, our 12-month surveillance period began at 30 days after peak injury.39 The rationale for doing so was that there are common “appropriate” reasons for nonreferral during the acute setting, including anticipated death or improvements in kidney function, the latter often not being observed until after discharge. Including these patients by beginning the surveillance period during this dynamic time would likely include a high proportion of patients in whom nephrology referral may not be beneficial (e.g., high likelihood of recovery, death, or hospice referral).

Outcome and Data Definitions
The study outcome was time to nephrology referral with time to improvement in kidney function, dialysis, and mortality as competing risks. Nephrology referral was defined as an order for outpatient nephrology consultation in any clinical setting. Computerized orders for referral were used instead of receipt of care in order to assess clinician intent without including potential resource availability constraints. Nephrology consultation orders were ascertained through the electronic health record computerized physician order entry system. Dialysis was defined as a collection of ICD-9 and CPT procedural codes. Death was ascertained through the use of VA administrative codes, which is updated through the use of the national death index as well as patient family reports, VA personnel direct family contact, and federal third-party notifications. Estimated GFR for all serum creatinine measures was derived using the abbreviated Modification of Diet and Renal Disease (MDRD) equation.40 CKD was defined as a calculated eGFR <60 ml/min per 1.73 m² from the most recent preadmission (baseline) outpatient serum creatinine value. To enrich the study population for those at highest risk for subsequent decline in kidney function, we selected patients exhibiting persistent kidney impairment (eGFR <60 ml/min per 1.73 m²) based on the latest serum creatinine value up to 30 days after peak injury (i.e., peak serum creatinine during hospitalization). Improvement in kidney function was defined as a measured eGFR ≥60 ml/min per 1.73 m² ascertained by serum creatinine measurement. Diabetes mellitus, hypertension, coronary artery disease, congestive heart failure, and peripheral vascular disease were defined by ICD-9 diagnosis codes. A summary of each definition is included.
in Supplemental Material. Extensive ICD-9 validation work has been performed previously in the VA. Validation for congestive heart failure (428.0/1/9), coronary artery disease (410-414), hypertension (401.1/401.9), with sensitivity/specificity values in the VA population of 0.73/1.00, 0.49/1.00, and 0.73/0.98, respectively. Similarly, these codes have found to be highly specific in multiple non-VA data sources (91%–100%). Manual validation for ICD-9 codes 250.xx (diabetes mellitus) have been performed at Vanderbilt University as part of an effort to detect robust genotype-phenotype associations using the Vanderbilt University Medical Center DNA biobank. Additional related ICD-9 codes used were aimed at increasing sensitivity to these validated codes.

Statistical Analyses
Patients’ baseline characteristics, demographics, and injury stage were summarized as medians and interquartile ranges for continuous variables and frequencies (%) for categorical variables. We used cumulative incidence functions (CIF) to estimate cumulative probabilities of renal referral, dialysis, recovery, and death, treating these events as competing risks. Patients who did not experience referral, dialysis, recovery, or death at the end of the surveillance period were censored. Aalen’s variance estimator was used to estimate confidence intervals of cumulative probabilities. All analyses were performed in R, free software for statistical computing (version 2.12.1; http://www.r-project.org/).

CIF function was preferred over Kaplan–Meier function because in the context of the Kaplan–Meier approach, patients who improved kidney function, had dialysis, or died would be censored and likely overestimate referral probability. Furthermore, the CIF allows for the summarization of cumulative probabilities of competing events such as recovery, dialysis, and death. The CIF method provided an adequate summary of all relevant events after AKI and, specifically, the main event of interest, renal referral. Cumulative incidence curves for each event were presented and the cumulative probabilities of (1) referral before recovery, dialysis, or death; (2) recovery before referral, dialysis, or death; (3) dialysis before referral, recovery, or death; and (4) death before recovery, referral, or dialysis were estimated at the time of 3, 6, 9, and 12 months.

ACKNOWLEDGMENTS
This work was funded by Grant R01 LM009965-01 from the National Library of Medicine; Grants K24 DK62849 and U01DK82192 from the National Institute of Diabetes, Digestive and Kidney Diseases; and Clinical Translational Science Award 1UL1-RR024975 from the National Center for Research Resources. E.D.S. is supported by the National Institute of Diabetes, Digestive, and Kidney Diseases; and Clinical Translational Science Award 1UL1-RR024975 from the National Center for Research Resources. E.D.S. is supported by Veterans Administration HSR&D Career Development Award CDA-08-020.

The views presented in this work are solely those of the authors and do not necessarily represent the position or the policy of the US Department of Veterans Affairs or the National Institutes of Health.

DISCLOSURES
None.

REFERENCES

This article contains supplemental material online at http://jasn.asnjournals.org/lookup/suppl/doi:10.1681/ASN.2011030315/-/DCSupplemental.