AJKD
Original Investigation

Receipt of Nephrology Care and Clinical Outcomes Among Veterans With Advanced CKD

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Background: Clinical practice guidelines recommend referral to nephrology when estimated glomerular filtration rate (eGFR) decreases to <30 mL/min/1.73 m^2; however, evidence for benefits of nephrology care are mixed.

Study Design: Observational cohort using landmark analysis.

Settings & Participants: A national cohort of veterans with advanced chronic kidney disease, defined as an outpatient eGFR ≤ 30 mL/min/1.73 m^2 for January 1, 2010, through December 31, 2010, and a prior eGFR < 60 mL/min/1.73 m^2, using administrative and laboratory data from the Department of Veterans Affairs and the US Renal Data System.

Predictor: Receipt and frequency of outpatient nephrology care over 12 months.

Outcomes: Survival and progression to end-stage renal disease (ESRD; receipt of dialysis or kidney transplantation) were the primary outcomes. In addition, control of associated clinical parameters over 12 months were intermediate outcomes.

Results: Of 39,669 patients included in the cohort, 14,983 (37.8%) received nephrology care. Older age, heart failure, dementia, depression, and rapidly declining kidney function were independently associated with the absence of nephrology care. During a mean follow-up of 2.9 years, 14,719 (37.1%) patients died and 4,310 (10.9%) progressed to ESRD. In models adjusting for demographics, comorbid conditions, and trajectory of kidney function, nephrology care was associated with lower risk for death (HR, 0.88; 95% CI, 0.85-0.91), but higher risk for ESRD (HR, 1.48; 95% CI, 1.38-1.58). Among patients with clinical parameters outside guideline recommendations at cohort entry, a significantly higher adjusted proportion of patients who received nephrology care had improvement in control of hemoglobin, potassium, albumin, calcium, and phosphorus concentrations compared with those who did not receive nephrology care.

Limitations: May not be generalizable to nonveterans.

Conclusions: Among patients with advanced chronic kidney disease, nephrology care was associated with lower mortality, but was not associated with lower risk for progression to ESRD.

Am J Kidney Dis. 70(5):705-714.

INDEX WORDS: Chronic kidney disease (CKD); end-stage renal disease (ESRD); nephrology; delivery of health care; nephrology care; disease trajectory; guideline-concordant care; CKD progression; intensity of care; nephrology referral; landmark analysis; immortal time bias.

Chronic kidney disease (CKD) is a common condition among US adults and confers a high risk for mortality and progression to end-stage renal disease (ESRD).[1] Clinical practice guidelines recommend referral to nephrology when estimated glomerular filtration rate (eGFR) decreases to <30 mL/min/1.73 m^2 in order to provide treatments that slow the progression of CKD, prevent or ameliorate metabolic complications, and prepare for dialysis and transplantation.[2,3] Facilitated by the implementation of automated eGFR reporting by many laboratories, the proportion of older patients who have seen a nephrologist at least 1 year before renal replacement therapy increased from 30.0% to 48.5% from 1996 to 2006.[4,5] However, there is conflicting evidence regarding benefits of such care, in part because the risk for progression to ESRD varies widely among patients with low eGFRs.[6,7] Whereas some studies suggest that earlier referral to nephrology (patients having seen a nephrologist 6-12 months before initiation of dialysis therapy) is associated with lower mortality after initiation of dialysis,[8-11] other studies have not.[5,12]

Most previous studies were retrospective analyses of patients who initiated dialysis therapy.[5,13,14] As such, the effect of nephrology care on outcomes such

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Received December 2, 2016. Accepted in revised form June 28, 2017. Originally published online August 12, 2017.

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0272-6386
http://dx.doi.org/10.1053/j.ajkd.2017.06.025

as progression to ESRD and mortality before ESRD could not be assessed. Among the few studies that have examined the association between nephrology care and outcomes in patients with earlier stages of CKD, several, but not all, suggest that nephrology care is associated with better progression-free survival.[15-17] However, studies suggesting favorable effects were restricted to patients with diabetes mellitus or limited to a single center and did not account for the trajectory of kidney function.

Importantly, prior studies were susceptible to survivor treatment bias or immortal time bias because patients who receive nephrology care have a minimum survival time imposed, whereas no such requirement is imposed on patients who do not receive nephrology care.[18] The landmark method is a well-established method used in time-to-event analysis to address survivor treatment bias by defining a fixed period for identifying the exposure of interest, in this case, nephrology care.[19-21]

We sought to determine the relations among frequency of nephrology care, survival, and progression to ESRD in a national cohort of veterans with advanced CKD using landmark analysis. We hypothesized that nephrology care would be associated with lower risks for death and progression to ESRD.

METHODS

Cohort

We constructed a cohort of US veterans with advanced CKD using laboratory and administrative data from the Veterans Health Administration, Department of Veterans Affairs (VA); Medicare claims; and the US Renal Data System (USRDS), a national registry of patients receiving therapy for ESRD (dialysis or kidney transplantation). We used laboratory data from the VA Decision Support System Laboratory Results file to identify veterans with an outpatient serum creatinine measurement during 2010. We calculated eGFR from the CKD-EPI (CKD Epidemiology Collaboration) creatinine equation.[22] Individuals with missing race (1.2%) were assigned black race to estimate GFR. We identified 91,544 veterans with advanced CKD, defined as an outpatient eGFR $\leq$ 30 mL/min/1.73 m^2 for January 1, 2010, through December 31, 2010, and at least 1 additional outpatient eGFR $<$ 60 mL/min/1.73 m^2 within 1 year before the index eGFR.

We used landmark analysis[19] to determine relationships among outpatient nephrology care and clinical outcomes. We used a landmark period of 12 months after the index eGFR date to ascertain the presence or absence of nephrology care. Figure S1 (provided as online supplementary material) illustrates the ascertainment of exposure and outcomes. We excluded: (1) patients who died before the landmark date, (2) patients with fewer than 3 total outpatient VA visits or more than 1 Medicare outpatient visit to ensure that the cohort was composed of regular VA users, and (3) patients who progressed to ESRD before the landmark date. Finally, we excluded patients whose eGFR increased to $>$60 mL/min/1.73 m^2 at the end of the landmark period. Baseline characteristics were ascertained at the landmark date. The final analytic cohort had 39,669 patients (Fig 1). This study was approved by the Institutional Review Board at Stanford University (IRB-30539) and was deemed exempt from informed consent.

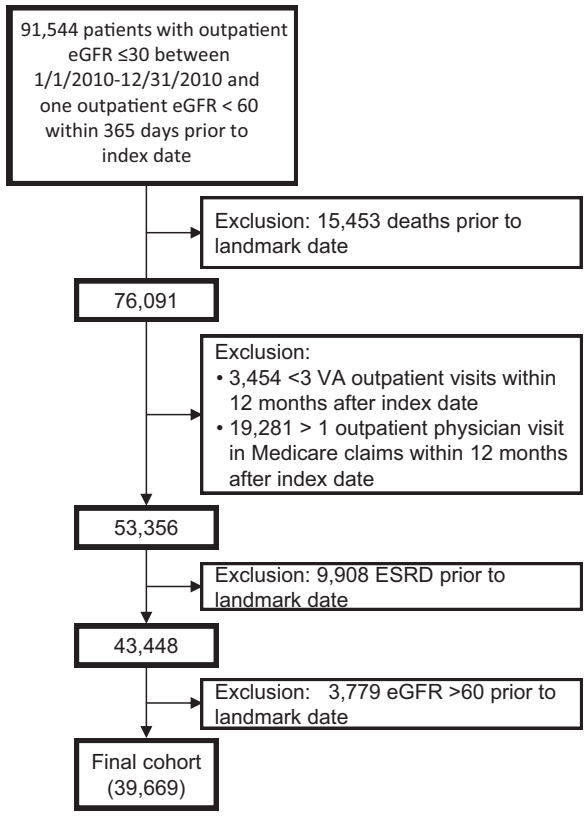

Figure 1. Cohort entry diagram. Abbreviations: eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease; VA, Veterans Affairs.

Nephrology Care

The key exposure of interest was an outpatient visit to a VA nephrology provider within a 12-month period from an index eGFR measurement $\leq$ 30 mL/min/1.73 m^2, which we ascertained based on the provider type and clinic location from the VA Medical SAS data sets, hereafter referred to as "nephrology care." Our primary analysis compared any nephrology visits to none; we conducted secondary analyses comparing zero, 1 to 2, 3 to 4, and 5 or more visits to gauge associations by the frequency of visits.

Outcomes

The primary outcomes were death from any cause, ascertained from the VA Vital Status files; progression to ESRD, defined as the initiation of maintenance dialysis therapy or kidney transplantation, ascertained from the USRDS; and the composite outcome of death or progression to ESRD. To assess whether the ESRD outcome was influenced by the use or timing of renal replacement therapy, we used 2 alternative ESRD definitions in sensitivity analyses. First, we defined ESRD as initiation of maintenance dialysis therapy, kidney transplantation, or progression to a sustained eGFR $<$ 15 mL/min/1.73 m^2 ($>$2 measurements separated by at least 5 days, with at least 1 outpatient measurement). Second, we assessed the eGFR at dialysis therapy initiation reported to the USRDS on the Medical Evidence Form. We ascertained death and ESRD through September 30, 2014. We also assessed management of CKD as an intermediate outcome in the relationship between nephrology care and death or ESRD. To assess management of CKD, we abstracted the first and last serum potassium, albumin, hemoglobin, calcium, phosphorus, and blood