MAYO CLINIC

Association of Slopes of Estimated Glomerular Filtration Rate With Post–End-Stage Renal Disease Mortality in Patients With Advanced Chronic Kidney Disease Transitioning to Dialysis

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Abstract

Objective: To investigate the association of estimated glomerular filtration rate (eGFR) slopes before dialysis initiation with cause-specific mortality after dialysis initiation.

Patients and Methods: In this retrospective cohort study of 18,874 US veterans who had transitioned to dialysis from October 1, 2007, through September 30, 2011, we examined the association of pre–end-stage renal disease (ESRD) eGFR slopes with all-cause, cardiovascular, and infection-related mortality during the post-ESRD period over a median follow-up of 2.0 years (interquartile range, 1.1-3.2 years). Associations were examined using Cox models with adjustment for potential confounders.

Results: Before the 18,874 patients transitioned to dialysis, 4485 (23.8%), 5633 (29.8%), and 7942 (42.1%) experienced fast, moderate, and slow eGFR decline, respectively, and 814 (4.3%) had increasing eGFR (defined as eGFR slopes of less than −10, −10 to less than −5, −5 to <0, and ≥0 mL/min per 1.73 m^2 per year). During the study period, a total of 9744 all-cause, 2702 cardiovascular, and 604 infection-related deaths were observed. Compared with patients with slow eGFR decline, those with moderate and fast eGFR decline had a higher risk of all-cause mortality (adjusted hazard ratio [HR], 1.06; 95% CI, 1.00-1.11; and HR, 1.11; 95% CI, 1.04-1.18, respectively) and cardiovascular mortality (HR, 1.11; 95% CI, 1.01-1.23 and HR, 1.13; 95% CI, 1.00-1.27, respectively). In contrast, increasing eGFR was only associated with higher infection-related mortality (HR, 1.49; 95% CI, 1.03-2.17).

Conclusion: Rapid eGFR decline is associated with higher all-cause and cardiovascular mortality, and increasing eGFR is associated with higher infection-related mortality among incident dialysis cases.

 ■ Mayo Clin Proc. 2016;91(2):196-207

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Despite numerous advances in our understanding of chronic kidney disease (CKD) progression, the incidence of end-stage renal disease (ESRD) remains exceedingly high. Each year, as many as 115,000 patients transition from advanced non–dialysis dependent CKD (NDD-CKD) to maintenance dialysis in the United States.[1] Furthermore, patients who newly initiate dialysis treatment experience the highest mortality within the first few months after the transition to dialysis.[1-3] In order to improve outcomes in this vulnerable population, intense study and dedicated efforts are needed to identify modifiable risk factors and interventions that may ameliorate the exceptionally high mortality risk of this transition period.[4] At this time, the optimal approach to transitioning patients from NDD-CKD to maintenance dialysis remains unclear.

In recent years, there has been growing interest in the association between change in kidney function and risk of adverse outcomes. Several studies have found strong associations between change in estimated glomerular filtration rate (eGFR) over 1 year and risk of ESRD,[5,6] cardiovascular disease,[7,8] and mortality[5,7-10] among patients with NDD-CKD.

Mayo Clin Proc. ■ February 2016;91(2):196-207 ■ http://dx.doi.org/10.1016/j.mayocp.2015.10.026
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However, these studies have focused primarily on patients with relatively preserved kidney function, and only a few studies have examined the association between increasing eGFR trajectory and risk of adverse outcomes.[6,11-14] Other than one study in patients with advanced CKD,[15] no previous studies have examined the association of change in eGFR including increasing eGFR in late-stage NDD-CKD with cause-specific mortality after dialysis initiation.

In this study, we investigated the association of eGFR slopes before dialysis initiation with all-cause, cardiovascular, and infection-related mortality after dialysis initiation in a national cohort of US veterans with advanced CKD transitioning to dialysis.

PATIENTS AND METHODS

Study Population

We analyzed data from the Transition of Care in Chronic Kidney Disease study, a retrospective cohort study examining US veterans transitioning to dialysis from October 1, 2007, through September 30, 2011. A total of 52,172 US veterans were identified from the US Renal Data System (USRDS)[1] as an initial cohort. In this study, we used only outpatient serum creatinine measurements available from Veterans Affairs (VA) medical centers because of the potential fluctuation of serum creatinine levels among sick inpatients. Therefore, patients whose serum creatinine levels were measured outside the VA medical centers (which were not available for our analyses) or those with only inpatient serum creatinine measurements were excluded (n=24,769). Patients were also excluded if they had less than 2 outpatient serum creatinine measurements before dialysis initiation or if they did not have any serum creatinine measurement at a VA medical center within 6 months of dialysis initiation (n=7823). We also excluded patients who had no serum creatinine measurements for periods of at least 90 days (n=650) and those with insufficient follow-up data (n=56). The final cohort consisted of 18,874 patients (Figure 1).

Covariates

Data from the USRDS patient and medical evidence files were used to determine patients' demographic data including age, sex, race/ethnicity, and marital status at the time of dialysis initiation. We used the national VA Corporate Data Warehouse LabChem data files to extract data about serum creatinine.[16] Laboratory variables except serum creatinine were collected using the Decision Support System National Data Extracts Laboratory Results file,[17] and baseline values were defined as the last quarterly average of each variable before dialysis initiation or the second to last quarterly average if the last one was not available. Data related to medication exposure were obtained from both Centers for Medicare and Medicaid Services (CMS) data and VA pharmacy dispensation records.[18] Patients who received at least one dispensation of medications within 6 months of dialysis initiation were recorded as having been treated with these medications. Information about comorbidities (including the Charlson comorbidity index score) at the time of dialysis initiation was extracted from the VA Inpatient and Outpatient Medical SAS Datasets,[19] using the *International Classification of Diseases, Ninth Revision, Clinical Modification* diagnostic and procedure codes and Current Procedural Terminology codes, as well as from VA/CMS data. Cardiovascular disease was defined as the presence of diagnostic codes for coronary artery disease, angina, myocardial infarction, or cerebrovascular disease. We calculated the Charlson comorbidity index score using the Deyo modification for administrative data sets, without including kidney disease.[20]

Exposure Variable

Estimated glomerular filtration rate was calculated using the Chronic Kidney Disease Epidemiology Collaboration equation.[21] Although 2 indices of decline in eGFR, percentage change and slope (annual change in eGFR), have been used to define CKD progression, we used eGFR slope as the main predictor for the survival models because it has been suggested to be a better predictor for mortality risk than percentage change.[6] The eGFR slope was calculated from an ordinary least squares regression model using all available outpatient eGFR measurements starting not more than 7 years before dialysis initiation. Considering the Kidney Disease: Improving Global Outcomes 2012 Clinical Practice Guideline that defined rapid CKD progression as a decline in eGFR of more than 5 mL/min per 1.73 m^2 per year,[22]