Association of Hepatitis C Seropositivity With Increased Risk for Developing End-stage Renal Disease

Judith I. Tsui, MD, MPH; Eric Vittinghoff, PhD; Michael G. Shlipak, MD, MPH; Daniel Bertenthal, MS; John Inadomi, MD; Rudolph A. Rodriguez, MD; Ann M. O’Hare, MD, MA

Background: Infection with chronic hepatitis C virus (HCV) has been linked to glomerulonephritis. We undertook this study to determine whether having a positive HCV test result was associated with an increased risk for developing treated end-stage renal disease (ESRD).

Methods: Using data from Medicare, the Department of Veterans Affairs, and the United States Renal Data System, we performed a retrospective cohort study of 474,369 adult veterans who had serum creatinine levels measured between October 1, 2000, and September 30, 2001, and HCV antibody testing within 1 year of creatinine testing. Patients were followed up until October 1, 2004, for the outcome of treated ESRD, defined as the onset of chronic dialysis or renal transplantation. Cox proportional hazards models were used to determine the relative hazard for ESRD associated with HCV, adjusted for other covariates (age, sex, race/ethnicity, and comorbidities).

Results: Of 474,369 patients in the cohort, 52,874 (11.1%) had a positive HCV antibody test result. Patients with HCV were more likely to develop ESRD: the rate per 1000 person-years was 4.26 (95% confidence interval, 3.97-4.57) for HCV-seropositive patients vs 3.05 (95% confidence interval, 2.96-3.14) for HCV-seronegative patients. For patients aged 18 to 70 years with an estimated glomerular filtration rate of at least 30 mL/min per 1.73 m², HCV seropositivity was associated with a greater than 2-fold risk for developing ESRD (adjusted hazard rate, 2.80; 95% confidence interval, 2.43-3.23).

Conclusion: In this large national cohort of adult veterans, patients younger than 70 years with HCV seropositivity were at increased risk for developing ESRD treated with dialysis or transplantation.

Arch Intern Med. 2007;167:1271-1276

AN ESTIMATED 3 MILLION Americans have been exposed to the hepatitis C virus (HCV), representing approximately 1.6% of the US population. Although the primary burden of disease associated with HCV is liver related, other organ systems may be involved. Chronic HCV has been linked to several different forms of glomerulonephritis and to albuminuria. However, to date no large-scale longitudinal studies (to our knowledge) have quantified the risk for clinically significant renal outcomes among individuals with HCV compared with uninfected control subjects. We used data from Medicare, the Department of Veterans Affairs (VA), and the United States Renal Data System (USRDS) to determine whether seropositivity for HCV was associated with an increased risk for developing treated end-stage renal disease (ESRD).

METHODS

OVERVIEW

Using the following data sources, we assembled a cohort of patients who had undergone measurement of serum creatinine and HCV antibody levels. We then followed these patients forward to determine rates of treated ESRD.

DATA SOURCES

We used the VA Decision Support System laboratory results file to ascertain outpatient serum creatinine and HCV antibody test results. We used the VA National Patient Care Database and Medicare denominator file to ascertain demographic and comorbidity information. Mortality follow-up was ascertained using the VA Beneficiary Identification Records Locator Subsystem database. These data were then linked to the USRDS, a comprehensive national registry of treated ESRD. A more complete description of data linkage methods has been published previously.

Author Affiliations:
Departments of Medicine (Drs Tsui, Vittinghoff, Shlipak, Inadomi, Rodriguez, and O’Hare) and Epidemiology and Biostatistics (Drs Vittinghoff and Shlipak), University of California, San Francisco, Department of Medicine (Drs Tsui, Shlipak, and O’Hare) and Health Services Research and Development Research Enhancement Award Program (Mr Bertenthal), Veterans Affairs Medical Center, and Department of Medicine, San Francisco General Hospital (Drs Inadomi and O’Hare), San Francisco.
PATIENTS

The study cohort was selected from the larger population of patients who underwent at least 1 serum creatinine measurement within the VA between October 1, 2000, and September 30, 2001 (n = 2,352,384). The date of the first serum creatinine measurement during this period served as the point of cohort entry. We excluded patients who were already undergoing dialysis or who had undergone kidney transplantation (n = 11,125). Among the remaining patients, 474,369 were tested for HCV within 1 year before or 1 year after cohort entry and comprised the analytic cohort for this study.

In 1988, the VA launched a major initiative to test all veterans at risk for HCV; the VA has the largest program for screening HCV in the United States.22,23 Screening is recommended among the following: Vietnam-era veterans, recipients of blood transfusions prior to 1992, individuals with a history of intravenous drug use, unexplained liver disease, multiple sexual partners (>10 lifetime), hemodialysis, tattoo or repeated body piercings, intranasal cocaine use, unexplained liver disease, abnormal alanine aminotransferase levels, or heavy alcohol use, and individuals who express a desire to be screened.24 We conducted a descriptive analysis of the patients in the larger data set who had a creatinine measurement but were not screened for HCV. We found that this unscreened population differed from the population who were screened. They were older (mean age, 64 vs 58 years), were more often of white race (74% vs 67%), and had a slightly higher mean serum creatinine level at baseline (1.13 vs 1.10 mg/dL [100 vs 97 µmol/L]). The percentage of women did not differ between the 2 groups.

OUTCOMES

The primary outcome of interest was time to treated ESRD, defined as renal therapy with hemodialysis or renal transplantation. Patients were followed up from the time of cohort entry through October 1, 2004, for this outcome. We also examined the cross-sectional association of HCV with chronic kidney disease (CKD), defined as having an estimated glomerular filtration rate (eGFR) of less than 60 mL/min per 1.73 m² at cohort entry (calculated using the abbreviated Modification of Diet in Renal Disease equation, which is based on age, sex, race/ethnicity, and serum creatinine level).25 We also compared the rate of change in eGFR (in milliliters per minute per 1.73 m² per year) for patients with and without HCV using within-person linear regression analysis on all of his or her outpatient creatinine-based GFR estimates that were spaced at least 1 day apart from the time of cohort entry to 90 days before death, treatment for ESRD, or the end of follow-up. Patients with a maximum eGFR of 15 mL/min per 1.73 m² at cohort entry were excluded (n = 2095) because these patients had already lost most of their GFR. We categorized annual decline in eGFR into the following 4 groups: 0 (ie, no change or increase), greater than 0 to 5 mL/min per 1.73 m², greater than 5 to 10 mL/min per 1.73 m², and greater than 10 mL/min per 1.73 m².

COVARIATES

The main predictor of interest was HCV serostatus. Patients were defined as having HCV seropositivity if their HCV antibody test result was recorded as positive in the VA Decision Support System laboratory results file. The VA follows the recommendations of the Centers for Disease Control and Prevention25 for laboratory testing, using an enzyme immunoassay as its initial screening test for antibodies to HCV. Patients were categorized into 3 groups according to whether their eGFR was at least 60 mL/min per 1.73 m², 30 to 59 mL/min per 1.73 m², or less than 30 mL/min per 1.73 m², corresponding with normal or mildly reduced eGFR, moderately reduced eGFR, or severely reduced eGFR or renal failure.26 Age was divided into 4 quartiles (<50, 50-59, 60-69, and ≥70 years). Additional covariates included sex, race/ethnicity (white, black, other, or unknown), and the following comorbidities: cirrhosis, substance abuse, hypertension, cerebrovascular disease, coronary artery disease, congestive heart failure, peripheral vascular disease, diabetes mellitus (DM), human immunodeficiency virus (HIV) infection, and chronic obstructive pulmonary disease. Comorbidities were assigned based on relevant International Classification of Diseases, Ninth Revision diagnostic and procedure codes and Current Procedural Technology procedure codes in the VA National Patient Care Database and Fee Basis files from October 1, 1997, to the time of cohort entry and in the inpatient and outpatient Medicare claims from January 1, 1999, through the time of cohort entry. For substance abuse, we chose to analyze abuse or dependence on opiates, cocaine, and amphetamines only, as these are illicit drugs that can be injected intravenously and our primary goal was to adjust for potential injection drug use.

STATISTICAL ANALYSIS

We compared the demographic and comorbidity profiles of patients with and without a positive HCV test result using χ² and t tests. We also compared the prevalence of each category of baseline eGFR and the rate of annual decline in eGFR by category using χ² test. We used logistic regression analysis to calculate the relative odds for having a low eGFR (<60 mL/min per 1.73 m²) for patients who were seropositive for HCV compared with those who were seronegative.

We calculated the incidence of treated ESRD among patients with and without a positive HCV test result using person-time methods, calculating 95% confidence intervals (CIs) assuming a Poisson distribution. Cox proportional hazards models were used to measure the association of HCV with risk for treated ESRD, adjusted for age, sex, race/ethnicity, DM, HIV, hypertension, coronary artery disease, congestive heart failure, peripheral vascular disease, chronic obstructive pulmonary disease, cerebrovascular disease, and substance abuse (opiates, cocaine, and amphetamines). We used a P < .01 significance level for all hypothesis testing. All models were checked for violation of the proportional hazards assumption by assessing log minus log survival plots for patterns of nonproportionality (convergence, divergence, and crossing of curves), in addition to performing the Schoenfeld test for violation of proportional hazards.27 The log minus log plots and the Schoenfeld test results (P = .43) did not suggest violations of the proportionality assumption. We tested for interactions between HCV and age, sex, race/ethnicity, DM, HIV, and baseline eGFR and reported interactions if they were substantial in magnitude, strongly supported by the data, and biologically plausible.

In secondary analysis, we stratified our fully adjusted Cox proportional hazards model by the presence of cirrhosis to determine if the HCV effect on risk for ESRD was restricted to patients with cirrhosis. In addition, among patients who were treated for ESRD during the follow-up period, we performed a descriptive comparison of primary disease listed as the cause of ESRD in the USRDS among patients with and without a positive HCV test result. STATA statistical software version 8 (StataCorp, College Station, Tex) was used for all analyses. The study was approved by the institutional review board at the University of California, San Francisco, and by the research committee at the Veterans Affairs Medical Center.
Of 474,369 patients in the cohort, 52,874 had a positive HCV antibody test result, a prevalence of 11.1% (95% CI, 11.1%-11.2%). Patients who were HCV seropositive were on average younger and were more likely to be male, of nonwhite race/ethnicity, and to have HIV, cirrhosis, and substance abuse problems but were less likely to have other comorbidities (Table 1). The prevalence of CKD at baseline was lower in patients with a positive HCV antibody test result (9.4% vs 16.6%; P < .01, χ² test). Even after adjustment for age, sex, race/ethnicity, and comorbidities, patients who were seropositive for HCV were slightly less likely to have CKD (adjusted odds ratio, 0.91; 95% CI, 0.88-0.95), and this association did not differ across age groups.

The analysis of annual change in eGFR was based on 3,320,888 outpatient creatinine measurements, including those obtained at baseline. The median number of measurements available per patient was similar for both groups, with 5 (25th to 75th percentile range, 2-8) for HCV-negative patients and 5 (25th to 75th percentile range, 2-9) for HCV-positive patients. When we examined the annual rate of decline in eGFR we found that, although HCV-seropositive patients were slightly less likely to experience a decline in eGFR compared with seronegative patients (56% vs 57%, P < .01), this tended to occur more rapidly when they did progress (Figure). A substantially higher proportion of HCV-seropositive individuals were in the highest category for annual decline in eGFR (>10 mL/min per 1.73 m² per year) compared with patients who were seronegative (14% vs 9%, P < .01). This finding was consistent across all categories of baseline eGFR.

A total of 5153 patients developed ESRD during the follow-up period (760 were HCV seropositive and 4393 were HCV seronegative). The mean follow-up time for patients was 3.4 years; the median was 3.6 years. Patients who were seropositive for HCV had a significantly higher rate of treated ESRD over time compared with patients who were seronegative (Table 2). Because we found significant interactions (P < .01 for interaction and a large difference in magnitude of effect among strata) for HCV seropositivity with age and eGFR, we present results stratified by those variables. We did not find substantial interactions for HCV seropositivity with DM and HIV (P = .81 and P = .72 for interaction with DM and HIV, respectively). There was some evidence for a stronger effect in black patients (P < .01 for interaction); however, given that race/ethnicity was unknown in 16% of patients and that the magnitude of difference between black subjects (adjusted hazard ratio [HR] for HCV, 1.89; 95% CI, 1.68-2.12) and white subjects (adjusted HR for HCV, 1.42; 95% CI, 1.24-1.63) was small, we chose not to stratify results by this variable.

Hepatitis C virus seropositivity was associated with higher risk for ESRD within the 3 younger age strata but not in the oldest age category (≥70 years). Among patients younger than 70 years, a positive HCV test result remained significantly associated with higher risk for developing ESRD after adjustment for patient characteris-

Table 1. Sample Characteristics by Hepatitis C Virus (HCV) Antibody Status

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>HCV Antibody Positive (n = 52,874)</th>
<th>HCV Antibody Negative (n = 421,495)</th>
<th>Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female sex</td>
<td>6</td>
<td>3</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Age, y</td>
<td>59 ± 13</td>
<td>52 ± 9</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Race/ethnicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>69</td>
<td>53</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>14</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>16</td>
<td>16</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Comorbidities</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Human immunodeficiency virus infection</td>
<td>1</td>
<td>4</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>26</td>
<td>21</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Hypertension</td>
<td>59</td>
<td>47</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>11</td>
<td>6</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>29</td>
<td>16</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>11</td>
<td>6</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>11</td>
<td>6</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>7</td>
<td>3</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>25</td>
<td>22</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>1</td>
<td>6</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Substance abuse‡</td>
<td>10</td>
<td>46</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Baseline eGFR, mL/min per 1.73 m²</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥60</td>
<td>83</td>
<td>91</td>
<td></td>
</tr>
<tr>
<td>30-59</td>
<td>15</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>&lt;30</td>
<td>2</td>
<td>2</td>
<td>&lt;.01</td>
</tr>
</tbody>
</table>

Abbreviation: eGFR, estimated glomerular filtration rate.
†Data are given as percentages or as mean ± SD.
‡Use of opiates, cocaine, or amphetamines.

Figure. Frequencies of categories of estimated glomerular filtration rate (eGFR) decline by hepatitis C virus (HCV) serostatus. Ab indicates antibody.
Finally, when we tabulated the various reported causes of ESRD recorded in the USRDS according to HCV serostatus, we found that DM- and hypertension-associated renal disease accounted for approximately 70% of all diagnoses in both groups (Table 3). However, among the causes that contributed 5% or less to the total, there seemed to be some differences in the frequency of certain diagnoses between the 2 groups. Glomerulonephritis and secondary glomerulonephritis combined accounted for 6.2% of ESRD diagnoses in the HCV-seropositive group, compared with 2.8% in the HCV-seronegative group. In addition, AIDS nephropathy and hepatorenal syndrome were respectively the sixth and ninth most common diagnoses among the HCV-seropositive group but ranked much lower than this among the HCV-seronegative group. However, even among HCV seropositive patients, these diagnoses were still relatively infrequent (2.9% and 1.0%, respectively).

In this large national cohort of veterans who were tested for HCV, seropositive patients were less likely than seronegative patients to have CKD at baseline but were at greater risk for developing treated ESRD during the follow-up period. Although most patients with HCV had stable renal function over time, renal decline was more likely to occur rapidly when they did progress (>10 mL/min per 1.73 m² per year). The risk for ESRD associated with HCV varied by age and by baseline eGFR: the effect was only present in patients younger than 70 years and was stronger for patients with normal or somewhat preserved renal function. Among HCV-seropositive individuals who were younger than 70 years with an eGFR

---

**Table 3. Leading Diagnoses for End-stage Renal Disease Listed in the United States Renal Data System by Hepatitis C Virus (HCV) Serostatus**

<table>
<thead>
<tr>
<th>HCV Negative* (n = 3482)</th>
<th>HCV Positive† (n = 593)</th>
<th>No. (%)</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DM associated, type 2</td>
<td>1630 (46.8)</td>
<td>241 (40.6)</td>
<td></td>
</tr>
<tr>
<td>Hypertension associated</td>
<td>807 (23.2)</td>
<td>156 (26.3)</td>
<td></td>
</tr>
<tr>
<td>Etiology uncertain</td>
<td>150 (4.3)</td>
<td>31 (5.2)</td>
<td></td>
</tr>
<tr>
<td>Glomerulonephritis</td>
<td>97 (2.8)</td>
<td>28 (4.7)</td>
<td></td>
</tr>
<tr>
<td>Focal glomerulosclerosis</td>
<td>76 (2.2)</td>
<td>22 (3.7)</td>
<td></td>
</tr>
<tr>
<td>DM associated, type 1</td>
<td>73 (2.1)</td>
<td>17 (2.9)</td>
<td></td>
</tr>
<tr>
<td>Renal artery stenosis</td>
<td>67 (1.9)</td>
<td>15 (2.5)</td>
<td></td>
</tr>
<tr>
<td>Polycystic kidney disease</td>
<td>60 (1.7)</td>
<td>10 (1.7)</td>
<td></td>
</tr>
<tr>
<td>Tubular necrosis</td>
<td>59 (1.7)</td>
<td>6 (1.0)</td>
<td></td>
</tr>
<tr>
<td>Acquired obstructive uropathy</td>
<td>46 (1.3)</td>
<td>6 (1.0)</td>
<td></td>
</tr>
</tbody>
</table>

**Abbreviation:** DM, diabetes mellitus.

*Of 60 total diagnoses listed for HCV negative.
†Of 36 total diagnoses listed for HCV positive.

HCV test result was associated with a more than 2-fold risk for developing ESRD (adjusted HR, 2.80; 95% CI, 2.43-3.23). This magnitude of effect was stronger than the effect of HIV (adjusted HR, 1.80; 95% CI, 1.34-2.43) but less than that of DM (adjusted HR, 4.97; 95% CI, 4.36-5.66).

In secondary analysis, we separated patients by whether or not they had been diagnosed as having cirrhosis. The association of HCV with ESRD risk was similar among patients with cirrhosis (adjusted HR, 1.65; 95% CI, 1.17-2.31) and without cirrhosis (adjusted HR, 1.85; 95% CI, 1.69-2.02) (P=.74 for interaction).
of at least 30 mL/min per 1.73 m², there was more than a 2-fold increase in risk for developing treated ESRD compared with HCV-seronegative patients.

This is the first study, to our knowledge, that demonstrates an association between HCV and ESRD in a national cohort of health care users. Two prior studies on a similar cohort of patients tested for HCV was as high as 7%. The use of the serum creatinine level is a poor measure of GFR among patients with cirrhosis. Therefore, we cannot rule out the possibility that our findings may in part reflect differential misclassification of level of renal function in patients with and without HCV. We also did not have information on proteinuria or albuminuria in our cohort, as it was infrequently ordered by physicians; therefore, we could not determine whether proteinuria was a risk factor for ESRD risk among patients with HCV because of muscle wasting or abnormalities in protein metabolism. Prior research has shown that the use of the International Classification of Diseases, Ninth Revision codes for comorbidity diagnoses, which are often insensitive and do not provide information on severity or control of the disease condition. There may have been other important confounders that were not adjusted for in the analysis. Finally, our follow-up time was short given the natural history of most types of kidney disease; it is possible that the strength and magnitude of the associations described herein might differ during a longer follow-up period.

In summary, we found that HCV seropositivity was associated with an increased risk for developing treated ESRD in a large national cohort of adult veterans aged 18 to 70 years who were tested for HCV and that this effect was most pronounced in patients with an eGFR that was less than 60 mL/min per 1.73 m². At this advanced stage of CKD, patients with or without HCV infection are at extremely high risk for developing renal failure; therefore, rates of treated ESRD may depend more heavily on unmeasured factors that contribute to the decision of whether to initiate treatment. Hepatitis C virus seropositivity was not associated with ESRD among adults 70 years or older.

Our observation that patients with a positive HCV test result were less likely to have prevalent CKD is also consistent with prior research. Using data from a nationally representative sample, it was found that HCV seropositivity was associated with a higher prevalence of proteinuria in older adults and, paradoxically, with a higher mean eGFR, even after adjustment for age and other patient factors. A somewhat analogous phenomenon was observed among African Americans, who experience higher rates of ESRD, despite having a similar or lower prevalence of CKD. However, the risk for ESRD attributable to HCV is underrecognized as the primary cause of end-stage renal disease, particularly among African Americans, who experience higher rates of ESRD than white Americans, despite having a similar or lower prevalence of CKD.

The results of our analysis of annual change in eGFR support the hypothesis that patients with HCV are more likely to experience rapid decline in renal function. Rates of ESRD in this cohort were similar to those reported in another study of health care users in a managed care program. Given that ESRD is a rare occurrence, most patients with HCV will not develop ESRD. However, the risk for ESRD attributable to HCV in this cohort of patients tested for HCV was as high as 7%. The risk for ESRD attributable to HCV was higher for patients with HCV and CKD, and glomerular hyperfiltration in early stages of CKD for patients with HCV. The results of our analysis of annual change in eGFR support the hypothesis that patients with HCV are more likely to experience rapid decline in renal function.

In summary, we found that HCV seropositivity was associated with an increased risk for developing treated ESRD in a large national cohort of adult veterans aged 18 to 70 years who were tested for HCV and that this effect was most pronounced in patients with an eGFR that was less than 60 mL/min per 1.73 m². At this advanced stage of CKD, patients with or without HCV infection are at extremely high risk for developing renal failure; therefore, rates of treated ESRD may depend more heavily on unmeasured factors that contribute to the decision of whether to initiate treatment. Hepatitis C virus seropositivity was not associated with ESRD among adults 70 years or older.

One explanation is that older adults may have a less robust immune response and may be less likely to develop autoimmune responses to HCV that lead to glomerulonephritis. Alternatively, fewer patients 70 years or older who were seropositive for HCV may have had chronic HCV infection if patients who were chronically infected were more likely to die from complications of their liver disease at an earlier age.
normal or only moderately reduced at baseline. Additional research is needed to confirm these results in other populations and to develop methods for preventing kidney disease progression in patients with HCV.

Accepted for Publication: February 25, 2007.
Correspondence: Judith I. Tsui, MD, MPH, Department of Medicine, Veterans Affairs Medical Center, General Internal Medicine Section 111A1, 4150 Clement St, San Francisco, CA 94124 (Judith.Tsui@ucsf.edu).

Author Contributions: Study concept and design: Tsui, Shlipak, Bertenthal, Rodriguez, and O’Hare. Acquisition of data: Tsui, Bertenthal, and O’Hare. Analysis and interpretation of data: Tsui, Vittinghoff, Shlipak, Inadomi, and O’Hare. Drafting of the manuscript: Tsui and Inadomi. Critical revision of the manuscript for important intellectual content: Tsui, Vittinghoff, Shlipak, Bertenthal, Rodriguez, and O’Hare. Statistical analysis: Tsui, Vittinghoff, Bertenthal, and O’Hare. Obtained funding: Tsui and O’Hare. Administrative, technical, and material support: Shlipak. Study supervision: Shlipak, Inadomi, Rodriguez, and O’Hare.

Financial Disclosure: None reported.

Funding/Support: This study was supported in part by grants KL2 RR024130 from the National Center for Research Resources, a component of the National Institutes of Health (NIH) and NIH Road map for Medical Research (Dr Tsui) and K23 AG28980-01 from the National Institute on Aging (Dr O’Hare).

REFERENCES


