

Survival Benefit of Nephrologic Care in Patients With Diabetes Mellitus and Chronic Kidney Disease

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Background: The association of nephrologic care and survival in patients with diabetes mellitus and chronic kidney disease is unknown.

Methods: Using data from 1997 to 2000, we conducted a retrospective cohort study of Veterans Health Administration clinic users having diabetes mellitus and stage 3 or 4 chronic kidney disease. The baseline period was 12 months and median follow-up was 19.3 months. Degree of consistency of visits to a nephrologist, defined as the number of calendar quarters in which there was 1 visit or more (range, 0-4 quarters), and covariates were calculated from the baseline period. The outcome measure was dialysis-free death.

Results: Of 39 031 patients, 70.0%, 22.4%, and 7.6% had early stage 3, late stage 3, and stage 4 chronic kidney disease, respectively, and 3.1%, 9.5%, and 28.2%, respectively, visited a nephrologist. Dialysis-free mortality rates were 9.6, 14.1, and 19.4, respectively, per 100 person-

years. More calendar quarters with visits to a nephrologist were associated with lower mortality: adjusted hazard ratios were 0.80 (95% confidence interval, 0.67-0.97), 0.68 (95% confidence interval, 0.55-0.86), and 0.45 (95% confidence interval, 0.32-0.63), respectively, when the groups having 2, 3, and 4 visits were compared with those who had no visits. One visit only was not associated with a difference in mortality when compared with no visits (adjusted hazard ratio, 1.02; 95% confidence interval, 0.89-1.16).

Conclusions: The consistency of outpatient nephrologic care was independently associated in a graded fashion with lower risk of deaths in patients with diabetes and moderately severe to severe chronic kidney disease. However, only a minority of patients had any visits to a nephrologist.

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CHRONIC KIDNEY DISEASE (CKD) affects 13% of the general adult US population having type 2 diabetes mellitus¹ and 31% of the Veterans Health Administration (VHA) patient population with diabetes mellitus.² Most patients with CKD die before initiation of renal replacement therapy, and the severity of CKD is independently associated with risk of death.^{3,4}

Although postdialysis survival may be improved by earlier subspecialty nephrologic care,⁵ it is not known whether nephrologic care in patients with moderate (early stage 3), moderately severe (late stage 3), or severe (stage 4) CKD is associated with lower mortality before the need for dialysis occurs. Consequently, the optimal timing for referral to a nephrologist during the course of CKD with diabetes is uncertain. Practice guidelines developed in 2002 by the National Kidney

Foundation Disease Outcomes Quality Initiative (K/DOQI) recommend that patients should be referred to a nephrologist when glomerular filtration rate (GFR) is less than 30 mL/min/1.73m² (onset of stage 4 CKD).⁶ Referral is recommended to coordinate care for eventual renal replacement therapy and to manage comorbid conditions from progressive loss of renal function such as bone disease, hypertension, anemia, neuropathy, and malnutrition. Because these conditions may develop earlier, K/DOQI guidelines further advise that patients should consult with or be comanaged by a nephrologist before there is progression to stage 4 CKD.⁶

The purpose of this study was to test the hypothesis that nephrologic care of patients with diabetes and moderate to severe CKD is associated with dialysis-free survival. Using a national cohort of VHA patients with diabetes and stage 3 or 4

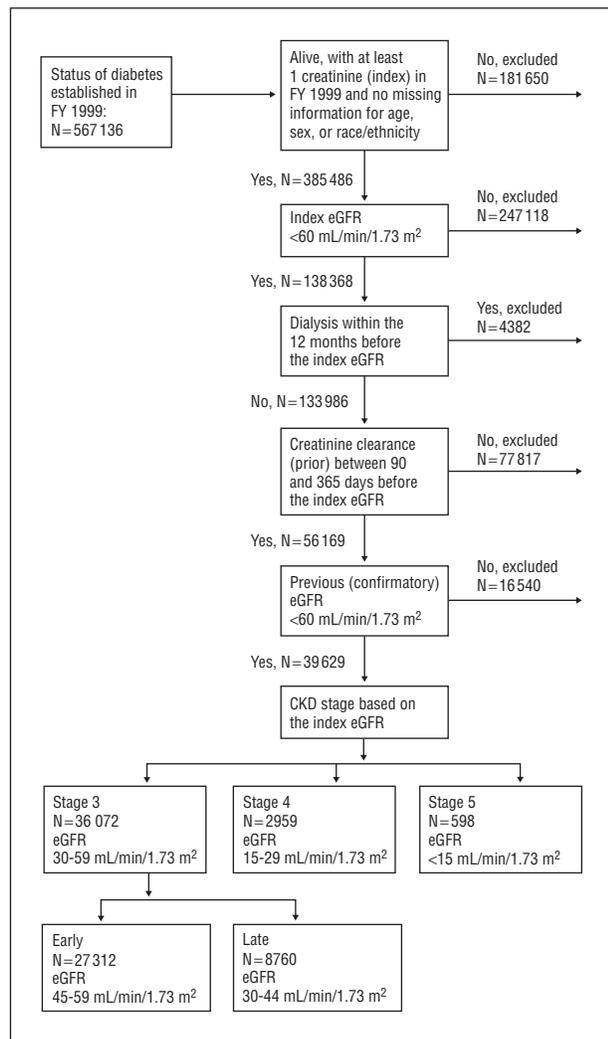


Figure 1. Inclusion and exclusion criteria for creation of the study population. FY indicates fiscal year; eGFR, estimated glomerular filtration rate; CKD, chronic kidney disease.

CKD, we determined (dialysis-free) mortality associated with baseline care by nephrologists, adjusting for selected independent variables and care by cardiologists and endocrinologists.

METHODS

STUDY DESIGN, DATA SOURCES, AND STUDY POPULATION

This longitudinal, retrospective, cohort study included fiscal years (FYs) 1998 through 2000 (October 1, 1997, through September 30, 2000). The baseline period was defined as the 12 months before the index date, defined as the date of the first estimated GFR (eGFR) value in VHA records occurring in FY 1999. All covariates were from the baseline period. Individuals were followed up from the index eGFR date until the end of FY 2000. The study was approved by the Veterans Affairs New Jersey Health Care System Institutional Review Board.

We used a national database of VHA patients with diabetes, the Diabetes Epidemiology Cohorts,⁷ as our population base. Of the 567 136 VHA clinic users in the 1999 Diabetes Epidemiology Cohort, we excluded individuals according to vari-

ous criteria as shown in **Figure 1**. To exclude individuals very close to having end-stage renal disease (ESRD), we excluded those receiving dialysis or having dialysis access codes in the baseline period. Dialysis or dialysis access codes were ascertained from revenue codes (Medicare Part A), *International Classification of Diseases, Ninth Revision, Clinical Modification* diagnosis and procedure codes, *Current Procedural Terminology* codes, and VHA clinic stop codes. We used 2 eGFR values to ensure that individuals classified as having CKD had chronically low eGFRs. The final sample of the study included 39 031 individuals, 36 072 with stage 3 CKD (eGFR 30-59 mL/min/1.73 m²) and 2959 with stage 4 CKD (eGFR 15-29 mL/min/1.73 m²), based on K/DOQI criteria.⁶ Patients with stage 3 CKD were classified into 2 groups, as follows: 27 312 with early-stage 3 disease (eGFR 45-59 mL/min/1.73 m²) and 8760 with late-stage 3 disease (eGFR 30-44 mL/min/1.73 m²).³ We did not include less severe CKD stages (because the accuracy of eGFR diminishes with higher GFR) or stage 5 CKD (because there is certainly regarding the benefits of nephrologic care when the GFR has decreased to less than 15 mL/min/1.73 m²).

OUTCOME MEASURES

The primary end point was dialysis-free death. The outcome was censored if the individual underwent dialysis or was alive at the end of FY 2000. As sensitivity analyses, we also evaluated all deaths (including deaths preceded by dialysis) and incident dialysis; the outcome was censored if the individual was alive at the end of FY 2000 or was alive without dialysis. Deaths were ascertained from the VHA Beneficiary Identification and Records Locator Subsystem and the Medicare Denominator File.⁸

INDEPENDENT VARIABLES

Independent variables included age, sex, race/ethnicity, VHA priority status, index eGFR, health status, subspecialist care, and face-to-face visits. Race/ethnicity was categorized as white, African American, or other (eg, Latino, Native American, Asian, and other racial/ethnic minority groups).

The VHA classifies veteran enrollees into 1 of 8 mutually exclusive priority groups⁹ according to poverty level and service-connected disability. Groups were combined into 1 of 4 categories, as follows: severely disabled (groups 1 and 4), moderately disabled (groups 2, 3, and 6), poor (group 5), and other (groups 7 and 8). Veterans in the last category do not have VHA eligibility for VHA health care services.

We used *International Classification of Diseases, Ninth Revision, Clinical Modification*, codes to determine health status covariates including life-threatening diseases such as cancers (lung, prostate, head and neck, pancreatic, lymphomatous, and hematologic), serious neurologic conditions, and dementia, and the Physical and Mental Comorbidity Indexes of Selim et al⁹ to determine comorbid conditions such as mental disorders and cardiovascular and noncardiovascular physical disorders. The 6 mental conditions from the Mental Comorbidity Index included depression, anxiety, schizophrenia, bipolar disorder, alcohol abuse, and posttraumatic stress disorder.

We used provider specialty codes from Medicare and VHA clinic stop codes to identify any visits to a nephrologist (Medicare, 39; VHA, 313), endocrinologist (Medicare, 46; VHA, 305), or cardiologist (Medicare, 06; VHA, 303) as measures of subspecialist care. For each of the 3 types of specialists, we first recorded the presence (coded as 1) or absence (coded as 0) of outpatient visits for each calendar quarter of the 3 calendar quarters in the 12-month baseline period and obtained the sum of these quarterly visit variables (range, 0-4) to measure consistency of subspecialist care.

To capture general health care patterns or access to the health care system, we measured the frequency of face-to-face outpatient visits based on *Current Procedural Terminology* codes. Visits linked to codes used for the subspecialist care variable were not counted. We determined groups (0, 1-6, 7-12, 13-20, and ≥ 21) on the basis of quartiles of the visit distribution; no visit was considered a separate group.

STATISTICAL ANALYSIS

We used Cox proportional hazard models to evaluate the association between visits to a nephrologist and dialysis-free death. A priori, we evaluated the hypotheses of interactions between life-threatening diseases and visits to a nephrologist, and the interactions between CKD stage (and eGFR) and visits to a nephrologist. We entered visits to a nephrologist into the model as a categorical variable in the primary analysis but tested its linear association using its continuous scale (0-4). As sensitivity analyses, we ran 2 additional Cox regression models to understand the issue of informative censoring possibly caused by the close link between visits to a nephrologist and higher likelihood of dialysis (time to dialysis as the outcome) and to re-evaluate the association of visits to a nephrologist by considering all deaths and not censoring patients at dialysis (time to all deaths as the outcome).

RESULTS

POPULATION CHARACTERISTICS

There were 39 031 VHA clinic users with diabetes who had an index eGFR between 15 and 59 mL/min/1.73 m², inclusive (**Table 1**). Of these, 70.0%, 22.4%, and 7.6% had early stage 3, late stage 3, and stage 4 CKD, respectively. Typical of the VHA patient population, only 2.1% were women, and the mean (SD) age was 70 (9) years. Within the group, 81.8% were white, 14.1% were African American, and 4.2% were of other race/ethnicity.

Life-threatening diseases were present in 14.4% of individuals. Most (67.1%) had cardiovascular disease. Almost all study participants (95.3%) had some physical comorbidities other than cardiovascular conditions. Approximately 19.6% had mental comorbidities. More than half (53.4%) were considered poor according to the VHA priority status, 21.3% were severely disabled and 17.9% were moderately disabled, and 7.4% were copayers. During the baseline period, 6.4% of individuals visited a nephrologist, 32.5% visited a cardiologist, and 5.9% visited an endocrinologist.

Individuals having more severe CKD (stage 4) were more likely to be nonwhite, severely disabled, and have cardiovascular conditions (all *P* values $< .001$) compared with individuals with stage 3 disease. Severity of CKD was also strongly associated with visits to a nephrologist or a cardiologist (both *P* values $< .001$) and marginally associated with visits to an endocrinologist (*P* = .06).

MORTALITY RATES

The median follow-up for the 39 031 individuals was 19.3 months (range, < 0.01 -24.0). Of the study group, 6454 individuals (16.5%) had dialysis-free death and 841 (2.2%) were censored because of dialysis (Table 1). The dialysis-free mortality rates were higher in the groups with more

severe disease: 14.1% for individuals with early stage 3 CKD, 20.7% for those with late stage 3 CKD, and 26.7% for those with stage 4 CKD.

ASSOCIATION OF NEPHROLOGIC CARE WITH SURVIVAL

The association between nephrologic care and survival was not modified by the presence or absence of life-threatening disease (*P* = .28), by CKD stage (*P* = .61), or eGFR value (*P* = .17). Therefore, subsequent analyses were based on the overall study population, with life-threatening disease and eGFR considered as covariates.

Overall, higher consistency of patient exposure to outpatient visits to a nephrologist within the baseline period was associated with greater reduction in mortality. The adjusted hazard ratios (AHRs) were 0.80 (95% confidence interval [CI], 0.67-0.97), 0.68 (95% CI, 0.55-0.86), and 0.45 (95% CI, 0.32-0.63), respectively, when the groups having 2, 3, and 5 visits were compared with those with no visits. One visit did not differ significantly from no visits (AHR, 1.02; 95% CI, 0.89-1.16). The risk of death without dialysis was lower by 55% for those with visits in all 4 quarters, but only by 20% for those with visits in only 2 quarters when both groups were compared with those with no visits. We tested the statistical significance of the graded associations by including the quarterly visit variable as an ordinal variable while adjusting for the same set of covariates. The results ("Nephrologist visits, quarters, linear trend" row in **Table 2**) show that a greater number of quarterly visits were associated with lower risk of dialysis-free death (AHR, 0.87; 95% CI, 0.83-0.91).

Figure 2 shows survival curves adjusted by covariates (at population average) based on the Cox regression model given in Table 2 by number of visits to a nephrologist. Greater consistency of visits to a nephrologist was associated with progressively lower risk of death without dialysis, but there was no difference between 1 and no visits.

ASSOCIATION OF OTHER INDEPENDENT VARIABLES WITH SURVIVAL

The number of patient visits to a cardiologist or endocrinologist was significantly associated with a lower risk of death without dialysis (Table 2). However, in contrast to visits to a nephrologist, even a minimum number of patient visits to a cardiologist or endocrinologist were significantly associated with a lower risk of death without dialysis. In addition, we observed an exposure-dependent pattern for visits to an endocrinologist (3 and 4 visits being associated with greater reduction in death without dialysis compared with less frequent visits) but not for visits to a cardiologist.

The presence of life-threatening diseases, cardiovascular conditions, mental comorbidities, severe disability, old age, and being African American were significantly associated with greater risk of death without dialysis (Table 2). Being female, having a copay requirement, and having a modest number of face-to-face visits were all associated with lower risk of death without dialysis.

Table 1. Death and Dialysis Outcomes and Baseline Population Characteristics of VHA Clinic Users With Diabetes Mellitus According to CKD Stage^a

| Variable | Total Population, No. (%) (N=39 031) | CKD Stage, No. (%) of Patients | | |
|---|--|--|---------------------------------------|----------------------------------|
| | | Early Stage 3 (n=27 312) ^b | Late Stage 3 (n=8760) ^c | Stage 4 (n=2959) ^d |
| Outcome | | | | |
| Dialysis | 841 (2.2) | 203 (0.7) | 251 (2.9) | 387 (13.1) |
| Dialysis-free death | 6454 (16.5) | 3854 (14.1) | 1810 (20.7) | 790 (26.7) |
| Death | 6934 (17.8) | 3984 (14.6) | 1963 (22.4) | 987 (33.4) |
| Characteristic | | | | |
| Index eGFR, mean (SD) | 48 (10) | 54 (4) | 38 (5) | 23 (4) |
| Age, mean (SD), y | 70 (9) | 70 (9) | 72 (9) | 70 (10) |
| Female sex | 818 (2.1) | 567 (2.1) | 192 (2.2) | 59 (2.0) |
| Race/ethnicity | | | | |
| White | 31 906 (81.8) | 22 582 (82.7) | 7107 (81.1) | 2217 (74.9) |
| African American | 5504 (14.1) | 3643 (13.3) | 1290 (14.7) | 571 (19.3) |
| Other | 1621 (4.2) | 1087 (4.0) | 363 (4.1) | 171 (5.8) |
| Life-threatening diseases | | | | |
| Physical comorbidities, PCI | | | | |
| Cardiovascular conditions | 26 172 (67.1) | 17 721 (64.9) | 6261 (71.5) | 2190 (74.0) |
| Other conditions | 37 207 (95.3) | 25 962 (95.1) | 8405 (96.0) | 2840 (96.0) |
| Mental comorbidities, MCI | | | | |
| Poverty/disability, VA priority status | | | | |
| Poor | 20 853 (53.4) | 14 771 (54.1) | 4598 (52.5) | 1484 (50.2) |
| Severely disabled | 8306 (21.3) | 5614 (20.6) | 1914 (21.8) | 778 (26.3) |
| Moderately disabled | 7001 (17.9) | 4848 (17.8) | 1630 (18.6) | 523 (17.7) |
| Other | 2871 (7.4) | 2079 (7.6) | 618 (7.1) | 174 (5.9) |
| Nephrologist visits, quarters | | | | |
| 0 | 36 518 (93.6) | 26 470 (96.9) | 7923 (90.4) | 2125 (71.8) |
| 1 | 1052 (2.7) | 416 (1.5) | 365 (4.2) | 271 (9.2) |
| 2 | 634 (1.6) | 194 (0.7) | 213 (2.4) | 227 (7.7) |
| 3 | 500 (1.3) | 142 (0.5) | 162 (1.8) | 196 (6.6) |
| 4 | 327 (0.8) | 90 (0.3) | 97 (1.1) | 140 (4.7) |
| Cardiologist visits, quarters | | | | |
| 0 | 26 352 (67.5) | 18 769 (68.7) | 5677 (64.8) | 1906 (64.4) |
| 1 | 5877 (15.1) | 4056 (14.9) | 1314 (15.0) | 507 (17.1) |
| 2 | 3273 (8.4) | 2213 (8.1) | 812 (9.3) | 248 (8.4) |
| 3 | 2122 (5.4) | 1370 (5.0) | 569 (6.5) | 183 (6.2) |
| 4 | 1407 (3.6) | 904 (3.3) | 388 (4.4) | 115 (3.9) |
| Endocrinologist visits, quarters | | | | |
| 0 | 36 725 (94.1) | 25 751 (94.3) | 8206 (93.7) | 2768 (93.6) |
| 1 | 980 (2.5) | 638 (2.3) | 256 (2.9) | 86 (2.9) |
| 2 | 568 (1.5) | 408 (1.5) | 118 (1.4) | 42 (1.4) |
| 3 | 503 (1.3) | 342 (1.3) | 116 (1.3) | 45 (1.5) |
| 4 | 255 (0.7) | 173 (0.6) | 64 (0.7) | 18 (0.6) |
| Face-to-face visits | | | | |
| 0 | 1108 (2.8) | 712 (2.6) | 269 (3.1) | 127 (4.3) |
| 1-6 | 9190 (23.5) | 6410 (23.5) | 2135 (24.4) | 645 (21.8) |
| 7-12 | 10 416 (26.7) | 7523 (27.5) | 2240 (25.6) | 653 (22.1) |
| 13-20 | 9182 (23.5) | 6461 (23.7) | 2031 (23.2) | 690 (23.3) |
| ≥21 | 9135 (23.4) | 6206 (22.7) | 2085 (23.8) | 844 (28.5) |

Abbreviations: CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; MCI, Mental Comorbidity Index (of Selim et al⁹); PCI, Physical Comorbidity Index (of Selim et al⁹); VA, Veterans Administration; VHA, Veterans Health Administration.

^aBecause of rounding, percentages may not equal 100.

^beGFR 45-59 mL/min/1.73 m².

^ceGFR 30-44 mL/min/1.73 m².

^deGFR 15-29 mL/min/1.73 m².

SENSITIVITY ANALYSIS

The last 2 columns in Table 2 give the results for models using time to all deaths and time to dialysis, respectively, as the outcome. The model of time to dialysis confirmed that visits to a nephrologist in the baseline period were associated with dialysis. Our additional analyses (not shown)

revealed that 28.0% of individuals receiving dialysis and 7.1% of individuals not receiving dialysis visited a nephrologist during the baseline period. Moreover, of the 841 individuals in whom dialysis was initiated, 480 (57%) died during follow-up. However, the model of time to all deaths shows that visits to a nephrologist in the baseline period remained associated with lower risk of death.

Table 2. Adjusted Hazard Ratios for Dialysis-Free Death, All Deaths, and Dialysis in VHA Clinic Users With Diabetes^a

| Variable | Dialysis-Free Death | All Deaths | Dialysis |
|--|---------------------|------------------|------------------|
| Nephrologist visits, quarters, linear trend ^b | 0.87 (0.83-0.91) | 0.91 (0.87-0.95) | 1.10 (1.03-1.17) |
| Nephrologist visits, quarters | <i>P</i> < .001 | <i>P</i> < .001 | <i>P</i> = .01 |
| 0 | 1 [Reference] | 1 [Reference] | 1 [Reference] |
| 1 | 1.02 (0.89-1.16) | 1.04 (0.92-1.18) | 1.32 (1.03-1.69) |
| 2 | 0.80 (0.67-0.97) | 0.85 (0.72-1.01) | 1.23 (0.92-1.63) |
| 3 | 0.68 (0.55-0.86) | 0.74 (0.61-0.90) | 1.12 (0.82-1.53) |
| 4 | 0.45 (0.32-0.63) | 0.61 (0.47-0.80) | 1.64 (1.21-2.21) |
| Cardiologist visits, quarters | <i>P</i> < .001 | <i>P</i> < .001 | <i>P</i> = .89 |
| 0 | 1 [Reference] | 1 [Reference] | 1 [Reference] |
| 1 | 0.94 (0.88-1.01) | 0.95 (0.89-1.02) | 0.98 (0.81-1.19) |
| 2 | 0.83 (0.76-0.91) | 0.84 (0.77-0.92) | 1.06 (0.83-1.35) |
| 3 | 0.80 (0.71-0.89) | 0.81 (0.73-0.90) | 1.01 (0.77-1.34) |
| 4 | 0.83 (0.73-0.94) | 0.85 (0.75-0.96) | 1.15 (0.84-1.59) |
| Endocrinologist visits, quarters | <i>P</i> = .001 | <i>P</i> < .001 | <i>P</i> = .77 |
| 0 | 1 [Reference] | 1 [Reference] | 1 [Reference] |
| 1 | 1.04 (0.89-1.21) | 1.04 (0.90-1.20) | 1.13 (0.79-1.62) |
| 2 | 0.78 (0.63-0.98) | 0.82 (0.66-1.02) | 1.20 (0.72-2.01) |
| 3 | 0.75 (0.58-0.96) | 0.78 (0.62-0.99) | 0.89 (0.50-1.57) |
| 4 | 0.58 (0.40-0.85) | 0.58 (0.40-0.83) | 0.69 (0.29-1.67) |
| Index eGFR, mL/min/1.73 m ² | 0.98 (0.98-0.98) | 0.98 (0.97-0.98) | 0.91 (0.91-0.92) |
| Age, y | 1.03 (1.02-1.03) | 1.02 (1.02-1.03) | 0.98 (0.98-0.99) |
| Female sex | 0.79 (0.65-0.96) | 0.74 (0.61-0.90) | 0.29 (0.12-0.70) |
| Race/ethnicity | <i>P</i> < .001 | <i>P</i> < .001 | <i>P</i> = .03 |
| White | 1 [Reference] | 1 [Reference] | 1 [Reference] |
| African American | 1.14 (1.07-1.23) | 1.16 (1.08-1.24) | 1.25 (1.05-1.49) |
| Other | 1.09 (0.96-1.23) | 1.08 (0.96-1.22) | 1.21 (0.90-1.64) |
| Poverty/disability, VA priority status | <i>P</i> < .001 | <i>P</i> < .001 | <i>P</i> = .21 |
| Poor | 1 [Reference] | 1 [Reference] | 1 [Reference] |
| Severely disabled | 1.24 (1.16-1.31) | 1.22 (1.15-1.30) | 1.04 (0.89-1.23) |
| Moderately disabled | 1.05 (0.99-1.13) | 1.04 (0.98-1.11) | 0.93 (0.76-1.13) |
| Other | 0.72 (0.64-0.80) | 0.72 (0.64-0.80) | 0.74 (0.54-1.02) |
| Life-threatening diseases | 1.64 (1.54-1.74) | 1.60 (1.51-1.70) | 0.97 (0.79-1.18) |
| Physical comorbidities, PCI | | | |
| Cardiovascular conditions | 1.30 (1.27-1.32) | 1.29 (1.27-1.32) | 1.25 (1.17-1.33) |
| Other conditions | 1.01 (0.99-1.02) | 1.01 (1.00-1.02) | 1.04 (1.00-1.08) |
| Mental comorbidities, MCI | 1.08 (1.04-1.12) | 1.06 (1.02-1.10) | 0.84 (0.75-0.96) |
| Face-to-face visits | <i>P</i> < .001 | <i>P</i> < .001 | <i>P</i> = .24 |
| 0 | 1.56 (1.35-1.80) | 1.52 (1.32-1.75) | 1.20 (0.79-1.83) |
| 1-6 | 0.99 (0.92-1.07) | 0.98 (0.91-1.06) | 0.91 (0.73-1.13) |
| 7-12 | 0.86 (0.80-0.93) | 0.86 (0.80-0.92) | 0.83 (0.68-1.01) |
| 13-20 | 0.91 (0.85-0.97) | 0.91 (0.85-0.97) | 0.90 (0.75-1.09) |
| ≥21 | 1 [Reference] | 1 [Reference] | 1 [Reference] |

Abbreviations: eGFR, estimated glomerular filtration rate; MCI, Mental Comorbidity Index (of Selim et al⁹); PCI, Physical Comorbidity Index (of Selim et al⁹); VA, Veterans Administration; VHA, Veterans Health Administration.

^aValues are given as adjusted hazards ratios (95% confidence interval).

^bWe separately tested the hypothesis that nephrologist visits are linearly related to risk of dialysis-free death using a multivariate Cox regression model with the same set of independent variables; only the result for the linear trend is listed (the first row; in parentheses). The primary analysis uses a categorical version of nephrologist visits and all other independent variables in a multivariate Cox regression model; the results from this model are given after the "Nephrologist visits, quarters, linear trend" row. A *P* value is for the test of the overall effect of the variable while controlling for other independent variables.

COMMENT

ASSOCIATION OF NEPHROLOGIC CARE WITH DIALYSIS-FREE SURVIVAL

In patients with diabetes treated in the VHA system, outpatient nephrologic care is associated with lower dialysis-free death for individuals with moderate and severe CKD (stages 3 and 4), depending on exposure. Patients with greater consistency of quarterly visits to a nephrologist were less likely to die in the follow-up period than were patients with less consistent or no vis-

its. In individuals with visits in 2 quarters in the baseline period, the risk of death was lowered by 20%, and, in those with visits in all 4 quarters, the risk was lowered by 55%.

It has been demonstrated previously that earlier referral to a nephrologist is associated with lower mortality and morbidity in patients starting dialysis, particularly those with diabetes.^{5,10} The present study extends previous findings in that outpatient nephrologic care in patients with diabetes and CKD is associated with lower mortality, not only at the onset of ESRD but also in patients with CKD not receiving dialysis.

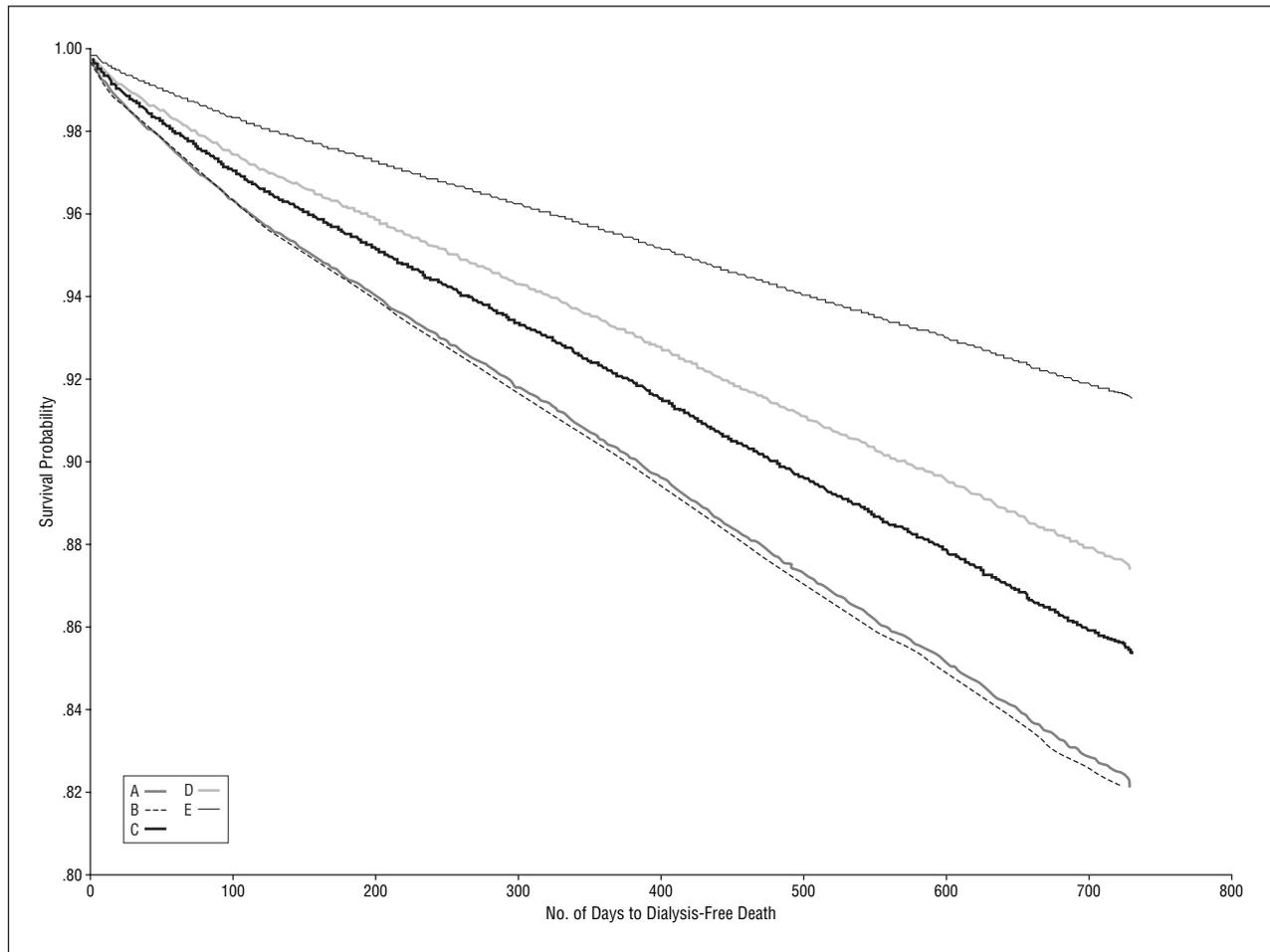


Figure 2. Dialysis-free death survival curves by consistency of nephrologic care. A indicates no visits; B, 1 quarterly visit; C, 2 quarterly visits; D, 3 quarterly visits; and E, 4 quarterly visits.

The period preceding renal replacement therapy is associated with a high risk of death from cardiovascular disease in patients with CKD.^{3,6,11,12} In the present study, almost 7 of 10 individuals had some form of cardiovascular disease. Cardiovascular disease was associated with greater risk of dialysis-free death, but outpatient care by cardiologists was associated with lower risk. However, the survival benefit of nephrologic care was independent of all other considered covariates.

The mechanism by which nephrologic care may reduce deaths in patients with diabetes and CKD is not addressed in this study. Death in patients with CKD has been associated with anemia, diabetes, proteinuria, and cardiovascular disease.^{3,6,12} It is possible that nephrologic care decreases mortality by better controlling traditional risk factors such as anemia, hypertension, proteinuria, an activated renin-angiotensin system, abnormal mineral metabolism, or secondary hyperparathyroidism.^{13,14} We speculate that nephrologists offer superior care of acidemia, malnutrition, and electrolyte imbalances, conditions that increase in severity with worsening renal function and that contribute to death.^{7,15-17}

At multivariate analysis, visits to a cardiologist or endocrinologist were significantly associated with visits to a nephrologist ($P < .001$, data not shown). These findings were consistent with those of a previous study that

showed that subspecialty care was associated with earlier referral to a nephrologist in individuals with diabetes and CKD.¹⁸ In our study, we also adjusted for general health care or access to health care using face-to-face visits to factor out the benefits from more appropriate access to or use of health care systems. Despite adjustment, we still observed the beneficial association of nephrologic care with survival.

About 14.4% of patients in the present study had diagnoses of near-term life-threatening disease including malignant neoplasms and end-stage cirrhosis. Practitioners may consider referral of such patients to a nephrologist futile,^{19,20} although there is evidence that nephrologists are involved in palliation for such patients during end-of-life care.²¹ To avoid potential confounding caused by failure to consult nephrologists in patients with life-threatening disease as a covariate in the final model testing the association of nephrologic care with mortality. As expected, life-threatening disease was significantly associated with death. However, the inclusion of the covariate did not appreciably alter the lower mortality associated with nephrologic care, suggesting that the presence of life-threatening disease does not limit referral to a nephrologist.

MORTALITY IN CKD

In the present study, the additional effect of age on mortality is demonstrated. The mortality rate in the oldest group was more than twice that in the youngest group (19.3 vs 7.4 deaths per 100 patient-years in FY 2000; data not shown) and the rate difference was more than 4-fold in individuals with stage 4 CKD. Given that the VHA patient population with diabetes is predominantly elderly, with the prevalence of CKD estimated at approximately 30%,² the lower mortality rate noted with consistent nephrologic care could potentially reduce the number of dialysis-free deaths in VHA patients in a meaningful way.

SENSITIVITY ANALYSIS

The additional analyses on incident dialysis and all deaths served as sensitivity analyses for the robustness of our findings of the association between visits to a nephrologist and lower risk of death. Patients who are sicker may have greater need to receive dialysis sooner (hence their being censored) and to be seen by a nephrologist. As shown in the "Results" section, individuals receiving dialysis had a high mortality rate and were more likely to receive nephrologic care during the baseline period. If such patients are removed from the risk pool at the time of initiation of dialysis, this alone could explain the survival benefit associated with nephrologic care, inasmuch as our primary outcome was dialysis-free death. However, the consistency of our findings from both mortality models has strengthened our confidence in the conclusion that early nephrologic care is associated with a survival benefit in patients with diabetes and CKD.

LIMITATIONS OF THE STUDY

First, the generalizability of this study to other patient populations may be limited because our population consisted largely of elderly men and because we only included patients for whom we could definitely determine CKD stage. Second, the study used administrative data to ascertain subspecialist visits and may not have captured all visits. Third, we did not consider renal transplantation a censoring event; however, because the incidence of renal transplantation preempting first dialysis is rare in the VHA patient population, lack of ascertainment should have no appreciable effect. Fourth, we may have censored patients with acute renal failure rather than ESRD. However, this limitation is consistent with our goal to examine the effect of nephrologic care on survival before the absolute requirement for nephrologic management, as in acute renal failure requiring dialysis.

NEPHROLOGIC CARE IS LACKING: THERAPEUTIC GAP

The results of our study support the National Kidney Foundation K/DOQI guideline to initiate comanagement with a nephrologist in patients with stage 3 CKD and to refer patients to a nephrologist at the onset of

stage 4 CKD.⁶ However, only 6.4% of all patients visited a nephrologist during the baseline period compared with only a minority (28.2%) of all patients with stage 4 CKD. Current estimates project an 85% growth in prevalence of ESRD from 2000 to 2015.²² The number of practicing nephrologists may be insufficient to meet the growing demand.²³ New care models will need to be developed to enable nephrologists to actively comanage patients with cardiologists, diabetologists, and primary care physicians.^{24,25}

In summary, we found that outpatient care by nephrologists is associated with decreased mortality in patients with diabetes with moderately severe or severe CKD during the dialysis-free phase. Greater consistency of care is associated with greater decreases in mortality, but only a minority of patients received nephrologic care.

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