Survival among older adults with kidney failure is better in the first three years with chronic dialysis treatment than not

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Comparisons of survival between dialysis and nondialysis care for older adults with kidney failure have been limited to those managed by nephrologists, and are vulnerable to lead and immortal time biases. So we compared time to all-cause mortality among older adults with kidney failure treated vs. not treated with chronic dialysis. Our retrospective cohort study used linked administrative and laboratory data to identify adults aged 65 or more years of age in Alberta, Canada, with kidney failure (2002-2012), defined by two or more consecutive outpatient estimated glomerular filtration rates less than 10 mL/min/1.73m^2, spanning 90 or more days. We used marginal structural Cox models to assess the association between receipt of dialysis and all-cause mortality by allowing control for both time-varying and baseline confounders. Overall, 838 patients met inclusion criteria (mean age 79.1; 48.6% male; mean estimated glomerular filtration rate 7.8 mL/min/1.73m^2). Dialysis treatment (vs. no dialysis) was associated with a significantly lower risk of death for the first three years of follow-up (hazard ratio 0.59 [95% confidence interval 0.46-0.77]), but not thereafter (1.22 [0.69-2.17]). However, dialysis was associated with a significantly higher risk of hospitalization (1.40 [1.16-1.69]). Thus, among older adults with kidney failure, treatment with dialysis was associated with longer survival up to three years after reaching kidney failure, though with a higher risk of hospital admissions. These findings may assist shared decision-making about treatment of kidney failure.

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Compared with their younger counterparts, older adults with advanced chronic kidney disease experience higher morbidity[1–3] and mortality,[4] and are more likely to die than progress to kidney failure requiring renal replacement therapy.[4–6] Most older adults with advanced chronic kidney disease nevertheless receive or prepare to receive renal replacement therapy,[7] as nearly 30% of patients initiating dialysis in North America are aged ≥75 years.[8–10] Complicating treatment decision-making, the life expectancy of this population is limited and the impact of dialysis on survival is not clear.[11]

Although the decision to initiate dialysis is complex, including quality-of-life considerations and the impact of treatment on patients and their families,[12] the evidence to support the potential for dialysis to prolong survival among older adults is limited. A recent systematic review reported similar 1-year survival among older adults with kidney failure regardless of whether they received dialysis or not.[13] This review, however, was based on heterogeneous studies with small numbers of patients, particularly in nondialysis groups who were managed by nephrology teams. There were also considerable differences in demographic and/or clinical characteristics (e.g., age, diabetes, other comorbidities) between those treated and not treated with dialysis, and the timing of renal replacement therapy initiation, with potential for lead-time and immortal time biases.[13–16]

Given the limited evidence regarding survival comparisons in this patient population, our research objective was to assess all-cause mortality associated with chronic dialysis versus nonchronic dialysis care among older adults with kidney failure, taking into account differences in baseline and time-varying patient data. We addressed the risk of lead-time bias by using a consistent definition of sustained kidney failure for both groups and the risk of immortal time bias using a time-varying exposure.

RESULTS

Patient characteristics

We identified 5238 Alberta residents aged ≥65 years with kidney failure defined by sustained estimated glomerular

filtration rate (eGFR) <10 ml/min per 1.73 m^2. Following exclusion of patients who initiated dialysis on or before the index date, those who died on index date, and those with a kidney transplant, the final cohort included 838 older adults (Figure 1); 500 (59.7%) received chronic dialysis and 338 (40.3%) did not (Table 1).

The median duration between the index date and dialysis initiation was 102 (interquartile range 39, 268) days. Compared with patients not treated with dialysis, patients who received chronic dialysis were more likely to be male (54.6% vs. 39.6%), younger (mean age 76.3 vs. 83.2 years), and treated with angiotensin-converting enzyme inhibitors/angiotensin-receptor blockers (73.0% vs. 53.6%) or statins (60.2% vs. 38.8%, Table 1). Patients treated with dialysis also had a lower comorbidity index (13.0% vs. 24.3% with Charlson Comorbidity Index ≥7). Overall, 16% of patients not treated with dialysis had never been referred to a nephrologist.

Hazard ratio of all-cause mortality

Overall 285 (84.3%) patients in the nondialysis group (median follow-up 0.79 years, interquartile range 0.3, 1.8 years) and 305 (61.0%) in the dialysis group (median follow-up 3.0 years, interquartile range 1.6, 4.5 years) died. Using a marginal structural Cox model, treatment with dialysis was associated with a lower risk of all-cause mortality in the first 3 years of follow-up (hazard ratio 0.59; 95% confidence interval [CI] 0.46–0.77; $P < 0.001$; Table 2). Results during each year of follow-up are shown in Supplementary Figure S1. For purposes of comparison, results based on an unadjusted Cox model and adjusted Cox model are also provided in Table 2.

After the first 3 years of follow-up, dialysis was no longer associated with a reduction in risk of all-cause mortality (hazard ratio 1.22; 95% CI 0.69–2.17; $P = 0.496$; Table 2), although the number of observations was small. For both time periods, we found no statistically significant evidence of effect modification by age or level of comorbidity.

Sensitivity analyses

Results were similar when we excluded patients referred late or never referred to a nephrologist, and in a subgroup analysis including only patients with a nonrapid decline of eGFR ≤5 ml/min per 1.73 m^2 per year in 3 years before index (Table 2). When we used eGFR <12 ml/min per 1.73 m^2 as an alternative definition of sustained (at least 90 days) kidney failure, the association between receipt of dialysis versus no dialysis and reduced mortality in the first 3 years of follow-up was also consistent (Supplementary Table S1).

Hazard ratio of all-cause hospitalization

Overall, we found the crude rate of all-cause hospitalization was higher in the dialysis than nondialysis group (2.82 [95% CI 2.67–2.99] vs. 2.40 [95% CI 2.21–2.60] hospitalizations per 1000 patients-days survived, respectively). The adjusted hazard ratio of all-cause hospitalization was 1.40 (95% CI 1.16–1.69; $P = 0.001$).

DISCUSSION

In this population-based cohort study of older adults with kidney failure, we found that dialysis was associated with a lower risk of death during the first 3 years following kidney failure, relative to those not treated with chronic dialysis. This relationship was not modified by age or comorbidity. However, the reduction in risk of death was no longer evident after 3 years of follow-up. These results were robust in a number of sensitivity analyses, including the exclusion of patients who were late or never referred to a nephrologist.

Results from previous observational studies are inconsistent.[14] Although some studies have shown a survival advantage associated with dialysis care,[17,18] others report an attenuated or null association among patients with greater

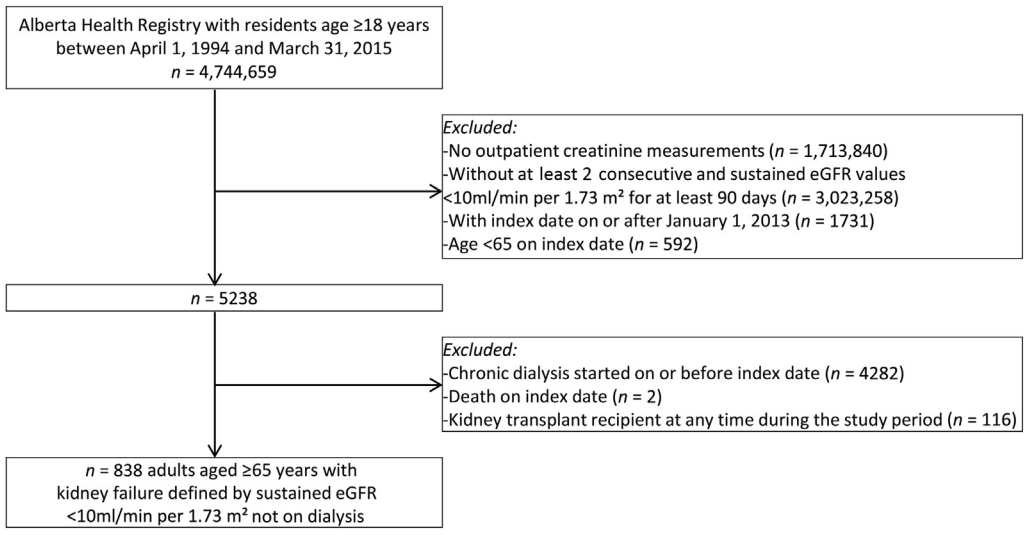

Figure 1 | Cohort formation of older adults with kidney failure. eGFR, estimated glomerular filtration rate.