TITLE

Comparison of Survival among Older Adults with Kidney Failure Treated versus Not Treated with Chronic Dialysis: A Cohort Study

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Abstract

Prior comparisons of survival between dialysis and non-dialysis care for older adults with kidney failure are limited to those managed by nephrologists, and are vulnerable to lead and immortal time biases. We compared time to all-cause mortality among older adults with kidney failure treated vs not treated with chronic dialysis. We did a retrospective cohort study using linked administrative and laboratory data to identify adults aged ≥65 years in Alberta, Canada, with kidney failure (2002-2012). Kidney failure was defined by ≥2 consecutive outpatient eGFR values of <10 mL/min/1.73m^2, spanning ≥90 days. We used marginal structural Cox regression to account for baseline and time-varying differences between dialysis and non-dialysis groups. 838 patients met cohort inclusion criteria with 815 (97.3%) included in the inverse probability of treatment weighted cohort (mean age 79.3; 48.8% male; mean eGFR 7.8 mL/min/1.73m^2). Compared to people not treated with chronic dialysis, dialysis was associated with a lower risk of death in the first 3 years of follow-up (HR 0.47; 95% CI 0.37-0.60, p<0.001), but not after 3 years of follow-up. Results were robust in a number of sensitivity analyses (HR 1.35; 95% CI 0.78-2.34, p=0.28). Among older adults with kidney failure, treatment with dialysis was associated with improved survival up to 3 years after reaching kidney failure. These findings provide information to support shared treatment decision-making.

Introduction

Compared to their younger counterparts, older adults with advanced chronic kidney disease (CKD) 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] The majority of older adults with advanced CKD nevertheless receives or prepares to receive renal replacement therapy,[7] as nearly 30% of patients initiating dialysis in North America are aged ≥75 years.[8,9,10] 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 non-dialysis 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 non-chronic 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/1.73m^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).

Patient characteristics after applying time-dependent weights

After exclusion of 23 patients with weights outside the 1-99 percentile of the distribution (indicating low comparability), we included 481 (96%) adults who received chronic dialysis and 334 (99%) adults who did not receive dialysis. The median duration between the index date and dialysis initiation was 99 (IQR 38, 254) days. Compared to patients not treated with dialysis, patients who eventually received chronic dialysis were more likely to be male (55.3% versus 39.5%), younger (mean age 76.5 versus 83.3 years), treated with ACEi/ARBs (72.6% versus 53.3%), and treated with statins (60.3% versus 38.9%, table 1). Patients treated with dialysis also had a lower comorbidity index (13.1% versus 24.3% with Charlson Comorbidity Index ≥7). Among those who were never treated with dialysis, 16.2% of patients had never been referred to a nephrologist.

Hazard ratio of all-cause mortality

Overall 296 (88.6%) patients in the non-dialysis group (median follow-up 0.78 years, IQR 0.3, 1.7 years) and 344 (71.5%) in the dialysis group (median follow-up 3.0 years, IQR 1.6, 4.5 years) died. Compared to older adults with similar characteristics and not treated with dialysis, treatment with dialysis was associated with a lower risk of all-cause mortality in the first 3 years of follow-up (hazard ratio [HR] 0.47; 95% CI 0.37 to 0.60, p <0.001, table 2). Results by each year of follow-up are shown in figure 2.

After the first 3 years of follow-up we found that dialysis was no longer associated with a reduction in risk of all-cause mortality (HR 1.35; 95% CI 0.78 to 2.34, p=0.283], table 2), although the number of observations was small in this second period of time: 31 patients in the non-dialysis group and 242 in the dialysis group were at risk at 3 years. Non-dialysis patients surviving past 3 years had a median decline in eGFR that was minimal at -0.36 (IQR -0.84, 0.20) mL/min/1.73m^2 compared to -2.3 (IQR -6.3, 0.0) mL/min/1.73m^2 in the dialysis group prior to dialysis initiation. For both time periods, there was no 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 sub-group analysis including patients with a non-rapid decline of eGFR $\leq$5 mL/min/1.73m^2 per year in 3 years prior to index (table 2). We also obtained similar results when we used the full cohort (N=838), i.e. including patients who we excluded from main analysis due to weights outside the 1-99 percentiles of the distribution. When we used eGFR <15 mL/min/1.73m^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 three years of follow-up was also consistent (tables S1-S3).

Hazard ratio of all-cause hospitalization

Overall, we found the crude rate of all-cause hospitalization was higher in the dialysis than non-dialysis group (2.74 [95% CI 2.60 to 2.89] versus 2.37 [95% CI 2.19 to 2.58] hospitalizations per 1000 patients-days survived, respectively). The adjusted incidence rate ratio of all-cause hospitalization was 1.41 (95% CI 1.17 to 1.70, 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] While some studies have shown a survival advantage associated with dialysis care,[17,18] others report an attenuated or null association among patients with greater comorbidity, older age, or after adjustment in multivariate analysis.[15,16,19–23] These studies, however, are limited to settings managed by nephrologists.[24,25] Prior studies are also limited in their ability to control for important biases including lead-time and immortal time biases.[13] Lead-time gives an illusion of survival benefit when diagnosis is identified prior to its usual clinical presentation.[26] Lead-time bias is

noteworthy among patients in the non-dialysis group, as bias may arise from their identification prior to the date at which they would hypothetically initiate dialysis. We attempted to address this issue by setting a 90-day criterion to define the index date. Immortal time, on the other hand, may bias the measurement of survival times in patients who go on to receive dialysis compared to those who never receive dialysis.[27] A time-varying treatment/exposure analysis was used to minimize the risk of this bias.[27]

Our results have implications for decision-making about dialysis initiation specifically for older adults with kidney failure where the survival advantage of dialysis versus non-dialysis care is unclear given their demographic and clinical characteristics. Support of treatment decision-making for older adults with kidney failure requires close monitoring of clinical information (e.g. indications for dialysis) as well as their individualized goals, expected prognosis, and benefits and harms of dialysis other than survival.[28,29] Although dialysis may reduce risk of death, dialysis may also negatively impact quality of life and the burdens related to dialysis including potential for infections and vascular access issues need to be considered.[30] Compared to non-dialysis care, dialysis patients may spend more time in hospital[31] and have a higher likelihood of death in-hospital (versus at home or in-hospice).[15,31] They may also have a lower likelihood of having advance care planning and palliative care compared to their non-dialysis counterparts.[15] Hence, the survival information generated from this study can be used to educate patients and providers to support treatment decision-making when communicated in the context of the potential negative impacts of dialysis on quality of life.

Previous work sheds light as to why some patients initiate dialysis while others do not. Factors such as older age, remote residence location, and cancer or metastatic cancer have been reported

to be associated with a decreased likelihood of initiating dialysis.[4] In contrast the presence of diabetes and severe proteinuria are associated with an increased likelihood of initiating dialysis.[4] Further, a systematic review of qualitative studies[32] reported four major themes central to treatment decision making: the thoughts, feelings, and attitudes of patients and their families confronting CKD as a life-threatening illness; the perceived lack of choice in treatment decision-making; the ways in which patients and their carers learnt about treatment options; and the influences from patients' desire to maintain their pre-existing lifestyle and opinions of family and friends.

Our study has a number of strengths including its population-based design in a setting with universal access to health care. Also, our study was strengthened by its methodological rigor in addressing treatment-selection, lead-time, and immortal time biases in the examination of survival between dialysis and non-dialysis care groups.

The results from our study nevertheless need to be considered in the context of its limitations. We cannot exclude the possibility of residual confounding given our observational design, and were unable to account for potential confounders at baseline including indication for dialysis initiation comprising symptoms or signs attributable to kidney failure (such as pruritus); nutritional status; or frailty.[33] We did not have information on patient values or preferences,[34] or on disease severity for most comorbidities as these data are not available in our administrative data sources. However, we were able to include severity of liver disease (mild or moderate/severe) and severity of kidney disease by taking into account eGFR (progression of eGFR per year) and proteinuria (normal/mild, moderate, or severe). We were also able to identify clinically important demographic characteristics and a wide range of comorbidities,

given that an increased number of comorbidities suggests increased risk of poor health outcomes and complexity of clinical management.[35] The generalizability of the findings is hence limited to patients with baseline characteristics included in the study, notably individuals with lower rates of eGFR progression and lower levels of comorbidity. While the feasibility of a randomized control trial remains to be determined, carefully designed observational studies addressing key methodological issues such as selection and measurement biases[36] may remain the only means to address this study question. We attempted to enhance comparability by creating a synthetic sample of weighted observations in which dialysis treatment was independent of covariates measured at baseline and over time. This method is recommended when time-varying analysis methods are used.[37] We cannot with complete certainty remove lead-time bias as information on clinical symptoms and signs for dialysis initiation was not available. However, we aimed to minimize lead time bias by adopting a conservative and recommended definition of kidney failure.[33] Finally, we reported the rate of hospitalizations but future work is required to examine causes of hospitalizations and lengths of stay as in other studies.[31]

In conclusion, we found that dialysis was associated with a reduced risk of death compared to non-dialysis only within the first 3 years following onset of kidney failure among older adults. The association between dialysis initiation and quality of life or health benefit overall for older adults remains to be determined. These findings can be used to support shared clinical decision-making within nephrology and primary care settings when managing older adults with kidney failure. Future prospective cohort studies are required to identify older patients that benefit from dialysis initiation in terms of not only survival, but also quality of life.

Methods

Study population and cohort definition

We did a retrospective cohort study using population-based laboratory and administrative data from Alberta, Canada.[38] Provincial administrative and laboratory data were linked using unique Alberta Personal Health Numbers to assemble a study cohort of Alberta residents that were ≥65 years of age and identified as having kidney failure between May 15, 2002 and December 31, 2012. The study end date was December 31, 2013 to allow for at least 1 year of follow-up.

We defined kidney failure by a series of ≥2 consecutive outpatient eGFR measurements of <10 mL/min/1.73m^2, calculated using the CKD-EPI equation,[39] spanning at least 90 days. The first eGFR after the 90-day period was used to define the index date for patients (regardless of treatment status) to minimise lead-time bias (figure 3). We chose eGFR <10 mL/min/1.73m^2 to define kidney failure as it reflects a level of kidney function at which patients and providers would have made a decision whether to pursue chronic dialysis or not. Others have previously used similar definitions of kidney failure.[4,16,21,31,40] We found previously that the proportion of patients in Alberta starting dialysis with eGFR <10.5 mL/min/1.73m^2 has increased from 74% to 85% between 2004 and 2013.[41]

We excluded patients who died on their index date as well as those treated with chronic dialysis prior to or on the index date. Patients receiving a kidney transplant at any time during the study period were excluded as they likely represent a healthier population[36] and would not be considered for non-dialysis care.[42]

Definition of exposure

The exposure of interest was chronic dialysis treatment. We identified incident chronic dialysis cases (hemodialysis or peritoneal dialysis) from provincial dialysis registries, which include information on all patients treated with chronic dialysis in Alberta.[43] These chronic dialysis registries establish chronicity of dialysis treatment for kidney failure by duration >90 days as per international clinical practice guidelines, with patients who died within 90 days included if the dialysis was intended to be chronic.[33,44,45] We supplemented classification of chronic dialysis with physicians' claims using similar criteria. *A priori,* we used a time-varying exposure variable to characterize treatment status during follow-up to avoid immortal time bias whilst maximizing our sample size.[27] We assumed that, once a patient started chronic dialysis, he or she was considered on it for the rest of the follow-up.

Outcome

The outcome of interest was all-cause mortality determined from the Alberta Health Registry and Alberta Vital Statistics data. We also examined all-cause hospitalization determined from the Hospital Discharge Abstracts database. We followed patients from their index date to their date of death, out-migration from the province, or study end date (December 31, 2013).

Measurement of covariates

We identified baseline characteristics at the index date. Demographic characteristics identified from the Alberta Health Registry file included age, sex, and First Nations status based on the Federal Indian Act.[46] We used the Canadian Census (2001, 2006, and 2011 that was nearest to the index date)[47] with the Statistics Canada Postal Code Conversion File[48] to determine rural

location of residence, which was defined by a population size of <1000 or density <400 individuals per square km outside a metropolitan area.[48]

Diabetes[49] and hypertension[50] were identified from hospital discharge records and physician claims using validated algorithms. We identified other comorbidities based on the Deyo classification of Charlson comorbidities (dementia; cerebrovascular disease; myocardial infarction; congestive heart failure; peripheral vascular disease; chronic obstructive pulmonary disease; mild liver disease; moderate and severe liver disease; peptic ulcer disease; rheumatologic disease; paraplegia and hemiplegia; and cancer) using validated International Classification of Diseases (ICD), Ninth Revision and ICD-10 coding algorithms from physician claims and hospitalization data, respectively.[51] At least one diagnostic code identified up to three years prior to cohort entry was used to identify these comorbidities.

Angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers, and statin use were defined as at least one prescription for these medications within the year prior to index date according to the Alberta Health drug file. We used the most recent outpatient albuminuria measurement within two years prior to the index date. Albuminuria was categorized in accordance with international guidelines as normal/mild, moderate, severe, or unmeasured, with the following types of measurement in descending order of preference: albumin to creatinine ratio (<3; 3 to 30; >30 mg/mmol or <30; 30 to 300; >300 mg/g), protein creatinine ratio (<15; 15 to 50; >50 mg/mmol or <150; 150 to 500; >500 mg/g), and urine dipstick (negative or trace; 1+; ≥2+).[33] Rapid progression of eGFR was defined as a >5 mL/min/1.73m^2 decline per year based on eGFR values within three years prior to the index date.[33,52] Time-varying eGFR was defined

using the mean eGFR value over 30-day time intervals, or the most recent eGFR value if there was no creatinine measure in that interval.

Statistical analysis

To enhance comparability across exposure categories (receipt versus no receipt of dialysis therapy), we used a marginal structural Cox model with stabilized inverse-probability of treatment and censoring weights (IPWs) to account for the baseline covariates and for the potential time-varying confounding effect of eGFR.[53] We used logistic regression to obtain treatment weights (inverse probabilities of starting dialysis therapy) and censoring weights (inverse probabilities of being uncensored) in each month interval from index date to end of follow-up. We obtained stabilized IPWs following standard approaches.[54,55] After stabilization, the IPWs ranged from 0.02 to 347576, with 1st and 99th percentiles at 0.30 and 2.27. Following assessment of the distribution of the weights by visual inspection including the mean and range of stabilized weight (mean weight of 1 with small range of values represents well-balanced weights), we excluded individuals with IPWs from below and above the 1st and 99th percentiles (mean weight 0.93 [SD 0.26]). This method created a pseudo-population using IPWs by which the covariate distributions become balanced across dialysis and non-dialysis groups. The exposure-outcome association was then estimated in the weighted sample. The proportional hazards assumption was assessed graphically and using Schoenfeld residuals.[56] We found a time-dependent association between dialysis therapy and mortality violating the proportional hazard requirement.[57] We hence examined the HR for each 1-year increase in follow-up time to identify two discrete time periods where hazards were proportional between treatment groups, namely 0 to 3 years and ≥3 years (figure 3). The estimates for each time period were obtained from one

316 model including the time-dependent measures of association. Finally, we used interaction terms
317 and subgroup analyses to assess for potential effect modification by age (categories 65 to 74; 75
318 to 84; and ≥85 years)[5,58] and level of comorbidity using the Charlson Comorbidity Index
319 (including kidney disease; score <7 versus ≥7).[21,59] We used the same approaches to study the
320 risk of hospitalization, considering repeated hospital admissions within each patient. We used
321 cluster (robust) methods to take into account event-correlation within patients.[60]

322 We conducted a number of sensitivity analyses to assess the robustness of the findings. First, we
323 limited analysis to patients seen by a nephrologist (before or after index date) and patients with
324 >90 days between their first nephrology visit and initiation of dialysis.[61] Second, we limited
325 analysis to patients with non-rapid decline of eGFR prior to index. Third, the full weighted
326 cohort was used, modelling exposure as time-varying, to examine the effect of dialysis on
327 mortality after accounting for baseline covariates. Finally, we explored the association at a
328 higher eGFR threshold for defining kidney failure (i.e. <15 mL/min/1.73m^2). Also, we
329 descriptively examined eGFR decline from index date to time of dialysis initiation (and to the
330 last eGFR measurement in the non-dialysis group). Statistical analyses were conducted with
331 Stata 14 software.[62] Ethical approval and waiver of patient consent was granted from the
332 Conjoint Health Research Ethics Review Board at the University of Calgary.

DISCLOSURE

None

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Figure 1 Cohort formation of older adults with kidney failure

Figure 2 Hazard ratio of mortality for each 1-year increase in follow-up time.
Note: HR=hazard ratio; CI=confidence interval

Figure 3 Retrospective cohort study design

Table 1 Baseline characteristics of older adults with kidney failure by dialysis versus non-dialysis care in the unweighted cohort and the weighted cohort

Characteristic	Unweighted cohort (N=838)		Weighted cohort (N=815)	
	Ever treated with dialysis N=500	**Exclusively not treated with dialysis N=338**	**Ever treated with dialysis N=481**	**Exclusively not treated with dialysis N=334**
Male	273 (54.6)	134 (39.6)	266 (55.3)	132 (39.5)
Mean age (SD)	76.3 (6.4)	83.2 (7.2)	76.5 (6.5)	83.3 (7.1)
Age in years				
65 to <75	228 (45.6)	45 (13.3)	213 (44.9)	42 (12.6)
75 to <85	220 (44.0)	143 (42.3)	216 (44.9)	143 (42.8)
≥85	52 (10.4)	150 (44.4)	52 (10.8)	149 (44.6)
Rural location of residence	101 (20.2)	48 (14.2)	96 (20.0)	48 (14.4)
First Nations status	15 (3.0)	7 (2.1)	13 (2.7)	7 (2.1)
Mean eGFR at index (SD)	7.8 (1.4)	7.7 (1.6)	7.8 (1.3)	7.7 (1.6)
Index eGFR (mL/min/1.73m^2) category				
<4	7 (1.4)	9 (2.7)	7 (1.5)	9 (2.7)
4 to <6	37 (7.4)	38 (11.2)	34 (7.1)	38 (11.4)
6 to <8	226 (45.2)	113 (33.4)	220 (45.7)	110 (32.9)
8 to <10	230 (46.0)	178 (52.7)	220 (45.7)	177 (53.0)
Mean (SD) progression of eGFR per year*	-5.8 (5.0)	-5.8 (6.7)	-5.6 (4.6)	-5.8 (6.5)
Rapid decline of eGFR per year in 3 years prior to index (>5 mL/min/1.73m^2 per year)	231 (46.2)	143 (42.3)	215 (44.7)	139 (41.6)
Medications				
ACEi/ARBs	365 (73.0)	181 (53.6)	349 (72.6)	187 (53.3)
Statins	301 (60.2)	131 (38.8)	290 (60.3)	130 (38.9)
Proteinuria category				
Normal or mild	21 (4.2)	36 (10.4)	20 (4.2)	35 (10.5)
Moderate	43 (8.6)	36 (10.7)	41 (8.5)	36 (10.8)
Severe	334 (66.8)	193 (57.1)	322 (66.9)	189 (56.6)

Characteristic	Unweighted cohort (N=838)		Weighted cohort (N=815)	
	Ever treated with dialysis N=500	Exclusively not treated with dialysis N=338	Ever treated with dialysis N=481	Exclusively not treated with dialysis N=334
Unmeasured	102 (20.4)	74 (21.9)	98 (20.4)	74 (22.2)
Comorbidities				
Dementia	26 (5.2)	82 (24.3)	26 (5.4)	82 (24.6)
Cerebrovascular disease	48 (9.6)	62 (18.3)	48 (10.0)	61 (18.3)
Myocardial infarction	74 (14.8)	68 (20.1)	72 (15.0)	67 (20.1)
Congestive heart failure	143 (28.6)	141 (41.7)	134 (27.9)	140 (41.9)
Peripheral vascular disease	73 (14.6)	39 (11.5)	72 (15.0)	39 (11.7)
Chronic obstructive pulmonary disease	132 (26.4)	116 (34.3)	123 (25.6)	114 (34.1)
Mild liver disease	12 (2.4)	2 (0.6)	11 (2.3)	2 (0.6)
Moderate/severe liver disease	1 (0.2)	2 (0.6)	1 (0.2)	2 (0.6)
Peptic ulcer disease	32 (6.4)	23 (6.8)	30 (6.2)	23 (6.9)
Diabetes	273 (54.6)	173 (51.2)	260 (54.1)	172 (51.5)
Hypertension	482 (96.4)	309 (91.4)	467 (97.1)	305 (91.3)
Rheumatologic disease	15 (3.0)	7 (2.1)	15 (3.1)	7 (2.1)
Para/hemiplegia	9 (1.6)	1 (0.3)	8 (1.7)	1 (0.3)
Cancer	78 (15.6)	69 (20.4)	75 (15.6)	66 (19.8)
Metastatic solid tumor	4 (0.8)	16 (4.7)	3 (0.6)	15 (4.5)
Days between first and index eGFR, median (IQR)	102 (93,116)	107 (95,123)	102 (93,116)	107 (95,124)

N(%) reported unless indicated otherwise.

SD=standard deviation; IQR=interquartile range; eGFR=estimated glomerular filtration rate in mL/min/1.73m^2; ACEi=angiotensin-converting enzyme inhibitors; ARB=angiotensin-receptor blockers

*Median (IQR) progression of eGFR per year: -4.6 (-7.8,-2.7) mL/min/1.73m^2 for dialysis and -4.0 (-7.6,-2.2) mL/min/1.73m^2 for non-dialysis (entire cohort); -4.5 (-7.5,-2.7) mL/min/1.73m^2 for dialysis and -4.0 (-7.6,-2.2) mL/min/1.73m^2 for non-dialysis (weighted cohort)

Table 2 Hazard ratios of mortality from primary and sensitivity analyses for dialysis versus non-dialysis care using marginal structural models, by years of follow-up from onset of kidney failure defined with sustained eGFR <10 mL/min/1.73m²

Weighted cohort	Dialysis	Non-dialysis	N	0 to 3 years			≥3 years		
				HR	95% CI	p-value	HR	95% CI	p-value
Cohort excluding people with weights outside 1-99 percentile distribution	481	334	815	0.47	0.37-0.60	<0.001	1.35	0.78-2.34	0.283
Exclude late or non-referred to nephrologist	461	280	741	0.51	0.40-0.66	<0.001	1.20	0.70-2.06	0.517
Non-rapid decline of eGFR per year in 3 years prior to index (≤5 mL/min/1.73m² per year)	266	195	461	0.59	0.43-0.81	0.001	1.35	0.81-2.27	0.251
Entire cohort without exclusions	500	338	838	0.67	0.48-0.92	0.017	1.55	0.79-3.04	0.198

N=number of people; HR=Hazard ratio; CI=Confidence Interval; eGFR=estimated glomerular filtration rate

Supplementary Material

Table S1 Hazard ratios of mortality from sensitivity analyses for dialysis versus non-dialysis care, by years of follow-up from onset of kidney failure defined with a higher eGFR threshold of <15 mL/min/1.73m^2

Table S2 In-hospital dialysis start by cohort

Table S3 eGFR progression post-index date by cohort

Supplementary information is available at KI Report's website

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