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Factors Associated with Dialysis Discontinuation Outside of the Acute Care Setting

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Introduction

Elective discontinuation of dialysis is an increasingly common occurrence among patients with end-stage kidney disease (ESKD).[1,2] Numerous studies have assessed predictors of the decision to stop dialysis in the inpatient setting and have consistently highlighted factors associated with a higher likelihood of this decision, including white race, female sex, and older age.[3,4] In these settings, the decision to stop dialysis is often made in the context of acute medical complications or hospitalizations. Although these findings are important, there has been less focus on understanding the decision to discontinue dialysis outside of the acute hospitalized setting. In such cases, patients and their loved ones would benefit from shared decision-making, which is recommended to help patients understand their prognosis and make complex treatment decisions.[5]

Reasons for discontinuing dialysis following acute medical illness in the inpatient setting likely differ from those outside of such scenarios; understanding the factors associated with this decision in the outpatient setting could help guide the counseling of these patients, particularly as recommendations for the use of time-limited trials of dialysis in patients with multiple comorbidities increase.[6,7]

The objective of this study was to determine factors associated with dialysis discontinuation in the absence of known acute medical complications, with particular focus on differences in discontinuation according to treatment modality (e.g. peritoneal dialysis (PD) versus hemodialysis (HD)). Additionally, we assessed whether factors that were associated with the decision to stop dialysis differed between patients who chose to discontinue dialysis earlier (within two years of dialysis initiation) versus later in the course of chronic maintenance dialysis.

Materials and Methods

We performed a retrospective observational study using data from the United States Renal Data System (USRDS) and included adults (age ≥ 18 years) who started dialysis between January 1, 2005 and December 31, 2015. We excluded patients if they were missing key data such as age, sex, race/ethnicity, region, and initial treatment modality.

We identified patient demographic factors including age (categorized as 18-29 years, 30-65 years, and > 65 years), sex, race/ethnicity, US census region (West, South, Northeast, Midwest), median neighborhood income by patient's home zip code, and calendar year of dialysis initiation. Covariates of interest included cause of ESKD, history of comorbidities (stroke, heart failure, smoking status, hypertension, drug dependence, peripheral arterial disease, coronary artery disease, malignancy, or diabetes), and treatment modality (peritoneal or hemodialysis, which was time-updated). These key demographic factors and covariates were then used as the primary predictors in our models.

In this study, the primary outcome of interest was death due to discontinuation of dialysis, defined using the CDEATH variable in the Patients file if "withdrawal" was listed as the primary cause of death. Events were subsequently defined using the RXSTOP variable in RXHIST files. The RXHIST file amalgamates data from Medicare Claims, CROWNWeb, the Center for Medicare and Medicaid (CMS)-2728 form, the CMS Death notification form, and the Organ Procurement Transplant Network Treatment files to update ESKD treatment status over time. The RXSTOP variable indicates the reason for why kidney replacement therapy was stopped prior to death and is also derived from the Patients file. Discontinuation events were censored if they occurred after an acute medical complication, but were considered to be discontinuation from dialysis in a non-acute setting if the decision to stop dialysis was noted to

follow access failure, transplant failure, chronic failure to thrive, or other causes according to the RXSTOP variable.

To examine the association between candidate predictors (mentioned above) and the risk of dialysis discontinuation, we used Cox proportional hazards models with time of analysis beginning at the date of dialysis initiation and administrative censoring on December 31, 2017. Patients were censored upon receipt of a transplant or death from other causes besides discontinuation.

Our secondary outcome of interest was early discontinuation, defined as death attributed to stopping dialysis within 1.9 years of dialysis initiation (the median time from dialysis initiation to death among patients discontinuing dialysis during the study period). To examine factors associated with early versus late discontinuation, we used the same Cox model as in the primary analysis, but limited follow-up time to 1.9 years after initiation of dialysis. The model for early discontinuation was adjusted for the same covariates as in our primary analysis.

Results

We identified 1,175,252 outpatients who met our inclusion criteria with median follow-up time of 2.8 years [IQR 1.1, 4.9]. The cohort was predominantly non-Hispanic white (53.6%) and treated exclusively with hemodialysis (86.2%) [Table 1].

A total of 29,212 (2.5%) patients discontinued dialysis, which accounted for 3.9% of all deaths during the study period. The median time from start of dialysis to its discontinuation was 1.9 years [IQR 0.66, 3.79 years]. Compared to patients treated exclusively with HD, patients treated exclusively with PD had a lower risk of discontinuation (HR = 0.45, 95% CI 0.42-0.49). Additionally, patients who switched from PD to HD had a higher risk of stopping dialysis in

comparison to those treated exclusively with PD (HR = 2.73, 95% CI 2.46-3.03). The risk of discontinuation among patients who switched from HD to PD (HR = 1.02, 95% CI 0.97-1.07) was similar to patients treated exclusively with HD (Table 2).

We also found an association between the calendar year of dialysis initiation and the risk of discontinuation, with patients who initiated dialysis in more recent years at higher risk of stopping dialysis outside of acute medical complication settings. Compared to patients who started dialysis between 2005 and 2008, those who initiated dialysis between 2009 and 2012 were 1.22 (1.18-1.25) times more likely to discontinue therapy. Patients who initiated dialysis between 2013 and 2015 had an even greater risk of discontinuation (HR = 1.61, 95% CI 1.56, 1.66).

Among those who did discontinue dialysis, 14,608 (50%) did so within 1.9 years of starting dialysis. Notably, Hispanic and non-Hispanic black patients were less like to discontinue therapy early compared with non-Hispanic white patients [HR = 0.27 (95% CI 0.25-0.29) and HR = 0.31 (95% CI 0.30-0.33), respectively]. Similar to the overall cohort, patients who initiated dialysis in more recent years were more likely to stop dialysis earlier during treatment as compared to those beginning dialysis in 2005-2008 (all $p < 0.01$, Table 2). Finally, compared to patients treated exclusively with HD, patients who changed from HD to PD (HR = 0.74, 0.67-0.82) or were treated exclusively with PD (HR = 0.37, 0.33-0.41) were less likely to discontinue dialysis early during treatment.

Discussion

Dialysis discontinuation is a common end-of-life decision considered by patients with ESKD. In this study, we aimed to better characterize factors associated with this decision outside

the context of acute medical complications. Similar to previously published studies that focused on inpatients who likely had an acute critical event (e.g. sepsis, myocardial infarction, stroke), we found that non-Hispanic white patients, women, and older patients had a higher risk of stopping dialysis outside of the context of acute medical complications during their usual state of health. We also found that patients who initiated dialysis in recent years were more likely to discontinue dialysis than those who initiated in the early 2000s, and they were more likely to stop dialysis early, which we defined as discontinuation within the first two years of starting kidney replacement therapy. We believe these findings are important given the results of a recent retrospective study which used simulations to demonstrate that much of the observed ESKD-related mortality difference between ethnicities would be attenuated if dialysis discontinuation practices were to be more similar.

Our finding of a trend towards increasing early discontinuation of dialysis (Table 2) is notable, as the factors that are driving these trends are important to understand.[8] While the rate of palliative care utilization remains low, there is increasing education and awareness about the option of stopping dialysis, which may in part explain the increase in early discontinuation rates.[9] It is also possible that patients who are less likely to thrive on dialysis or who have more comorbidities are being offered dialysis more frequently in recent years, and this subset subsequently decides to discontinue dialysis. Unlike in settings where an acute medical illness may precede the decision to stop dialysis, decisions made by patients outside of the acute setting may occur in the context of prolonged failure to thrive. Further research is needed to identify factors related to patients' preferences, values, priorities, and quality-of-life considerations that may have led to the decision to stop dialysis. Additionally, the role for surrogate decision-

makers, spirituality, prognostic awareness, and decisional regret are all important factors that warrant further investigation.

Apart from the temporal trend in dialysis discontinuation, we also found that patients treated with peritoneal dialysis had a lower risk of discontinuation compared to those treated with hemodialysis. In addition, those who converted from peritoneal dialysis to hemodialysis had a higher risk of discontinuation compared with those who were treated exclusively with PD. Interestingly, this finding was absent among patients who converted from HD to PD. Data on differences in rates of dialysis discontinuation by treatment modality have been scarce, as many studies limit analyses to patients treated with either HD or PD exclusively. We believe our findings are unique in that they incorporate data from patients receiving either treatment modality, including patients who changed modalities. It is possible that peritoneal dialysis provides better quality of life, and patients who are subsequently exposed to hemodialysis represent an especially high-risk group for a significant decline in quality of life.[10,11] Whether maximizing the amount of time spent on peritoneal dialysis in patients who have multiple comorbidities may decrease the likelihood of stopping chronic dialysis has not been examined and deserves further exploration.

The strengths of the study include the large size of a national cohort encompassing over one million patients and the ability to track changes in treatment modalities over time. Additionally, this nationally representative sample allows for generalization of our results to a broad US population. We do acknowledge some limitations of the study, including the retrospective nature of the study and the potential for residual confounding. Given that the CMS death notification form may be completed by non-medical personnel, there is the potential for inaccurate coding.[12-14] Additionally, the USRDS database does not have patient-identified

reasons for deciding to stop dialysis, and we do not know definitively the reasons why peritoneal dialysis patients discontinued treatment less often than hemodialysis patients or why dialysis discontinuation rates have been increasing in more recent years. We are also unable to capture factors such as existential distress and spirituality.[15] Qualitative or mixed methodological studies may be needed to capture the true associations or drivers of this complex decision. Finally, we do not have data surrounding important factors such as decisional capacity, cognitive status, or the presence of frailty, dementia, or mental health comorbidities, all of which may play an important role in determining the likelihood of discontinuation of therapy.

In conclusion, the decision to discontinue dialysis among patients in non-acute settings is more common among those who initiated treatment more recently in our study and is associated with a host of additional risk factors that deserve further investigation. In addition, factors associated with early discontinuation of dialysis in this population appear similar to those associated with discontinuation throughout their treatment course. Future multi-center studies that capture the granular reasons for why some patients decide to discontinue dialysis are needed to understand how to optimize the quality and delivery of palliative care when appropriate. This may equip kidney care teams with the ability to anticipate which patients are most likely to decide to discontinue therapy and ensure a patient-centered decision-making process.

Disclosures

All authors have nothing to disclosure.

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All authors contributed intellectual content during the writing or revision of the manuscript and accept accountability for the overall work by ensuring that questions pertaining to the accuracy or integrity of any portion of the work are appropriately investigated and resolved.

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Table 1. Cohort Characteristics

	Discontinued Dialysis* (N = 29,212)	Total Cohort (N = 1,175,252)
Age at first dialysis initiation, median (IQR) in years	75.0 (66.0, 81.0)	64.0 (54.0, 75.0)
Sex (%)		
Male	53.0	56.8
Female	47.0	43.2
Race (%)		
Non-Hispanic White	78.1	53.6
Non-Hispanic Black	13.6	27.7
Hispanic	5.7	13.4
Other	2.5	5.3
Primary Cause of Renal Failure (%)		
Diabetes Mellitus	43.6	45.8
Hypertension	32.8	29.4
Glomerulonephritis	5.6	8.0
Cystic kidney disease	1.2	1.9
Other	16.8	14.8
Modality Switching (%)		
HD to PD	5.1	6.3
PD to HD	3.1	3.6
HD, No Change	89.8	86.2
PD, No Change	2.1	3.8
Region (%)		
West	18.0	19.9
Midwest	28.7	21.3
South	38.3	41.3
Northeast	15.0	17.5
Insurance Status (%)		
Insured**	98.0	93.2
Uninsured	2.0	6.8
First Year of Dialysis (%)		
2005-2008	34.1	34.9
2009-2012	38.8	36.5
2013-2015	27.1	28.6
Comorbidities (%)		
Stroke	13.4	9.2
Heart Failure	37.1	31.5
Smoker	5.9	6.3
Hypertension	86.1	85.9
Drug Dependence	0.6	1.3
Peripheral Vascular Disease	17.1	12.6
Coronary Artery Disease	26.2	19.1
Malignancy	11.9	7.4
Diabetes Mellitus	54.5	55.3

ESRD, end-stage renal disease; IQR, interquartile range; HD, hemodialysis; PD, peritoneal dialysis

** When compared to patients who did not discontinue dialysis, p for all categories < 0.001*

*** Insured comprises patients with both public and private insurance*

Table 2. Association between Demographic Factors and Risk of Discontinuation in the Overall Cohort and Risk Factors for Early Discontinuation

	Overall Cohort Hazard Ratio (95% CI)	Early Discontinuation* Hazard Ratio (95% CI)
Treatment Modality		
PD only (vs. HD only as reference)	0.45 (0.42-0.49)	0.37 (0.33-0.41)
HD to PD (vs. HD only as reference)	1.02 (0.97-1.07)	0.74 (0.67-0.82)
PD to HD (vs. PD only as reference)	2.73 (2.46-3.03)	3.22 (2.72-3.81)
Age at Dialysis Onset (years)		
18-29	Reference	Reference
30-64	4.11 (3.25-5.20)	3.68 (2.55-5.32)
≥ 65	15.85 (12.54-20.03)	14.63 (10.15-21.10)
Sex		
Male	Reference	Reference
Female	1.16 (1.13-1.19)	1.17 (1.13-1.21)
Race/Ethnicity		
Non-Hispanic White	Reference	Reference
Non-Hispanic Black	0.32 (0.31-0.33)	0.31 (0.30-0.33)
Hispanic	0.29 (0.27-0.30)	0.27 (0.25-0.29)
Other	0.30 (0.28-0.32)	0.27 (0.24-0.31)
Region		
West	Reference	Reference
Midwest	1.16 (1.12-1.21)	1.12 (1.06-1.17)
South	1.04 (1.01-1.08)	1.03 (0.98-1.08)
Northeast	0.77 (0.74-0.80)	0.71 (0.67-0.75)
Median Income in Zip Code	0.97 (0.97-0.98)	0.97 (0.96-0.98)
Primary Cause of Renal Failure		
Diabetes Mellitus	Reference	Reference
Hypertension	1.04 (1.01-1.08)	1.12 (1.07-1.17)
Glomerulonephritis	0.81 (0.77-0.86)	0.89 (0.82-0.97)
Cystic Kidney Disease	0.67 (0.60-0.75)	0.52 (0.43-0.63)
Other/Unknown Cause	1.02 (0.99-1.07)	1.35 (1.28-1.42)
Year of Dialysis Initiation		
2005-2008	Reference	Reference
2009-2012	1.22 (1.18-1.25)	1.16 (1.12-1.21)
2013-2015	1.61 (1.56-1.66)	1.55 (1.49-1.62)
Uninsured (vs. Insured)	0.57 (0.53-0.62)	0.53 (0.46-0.61)
Comorbidity (vs. without condition)		
Stroke	1.42 (1.37-1.47)	1.46 (1.39-1.53)
Diabetes Mellitus	1.01 (0.97-1.04)	0.96 (0.92-1.00)
Hypertension	0.92 (0.89-0.95)	0.83 (0.80-0.87)
Heart Failure	1.20 (1.17-1.23)	1.28 (1.23-1.32)
Coronary Artery Disease	1.09 (1.06-1.12)	1.06 (1.02-1.11)
Peripheral Vascular Disease	1.20 (1.16-1.24)	1.22 (1.16-1.27)
Malignancy	1.42 (1.37-1.48)	1.49 (1.42-1.56)
Smoking	1.13 (1.07-1.18)	1.05 (0.98-1.13)
Drug Dependence	1.03 (0.88-1.20)	1.31 (1.06-1.62)

**Analysis limited to 1.9 years of follow-up (median time to discontinuation of dialysis for overall cohort)*
HD, hemodialysis; PD, peritoneal dialysis