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Indication for Dialysis Initiation and Mortality in Patients With Chronic Kidney Failure: A Retrospective Cohort Study

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Abstract

Background—Initiation of maintenance dialysis for patients with chronic kidney failure is a period of high risk for adverse patient outcomes. Whether indications for dialysis initiation are associated with mortality among this population is unknown.

Study Design—Retrospective cohort study.

Setting & Participants—461 patients who initiated dialysis (hemodialysis, 437; peritoneal dialysis, 24) from January 1st, 2004 through December 31st, 2012 and were treated in facilities operated by a single dialysis organization. Follow-up for the primary outcome was through December 31st, 2013.

Predictor—Clinically documented primary indication for dialysis initiation, as categorized into four groups: laboratory evidence of kidney function decline (reference category), uremic symptoms, volume overload or hypertension, and other/unknown.

Outcomes—All-cause mortality

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Contributions: Research idea and study design: MBR, DC, RM; data acquisition: MBR, CHC, AN, DC; data analysis/interpretation: all authors; statistical analysis: MBR, CHC; supervision or mentorship: RM, JH. Each author contributed important intellectual content during manuscript drafting or revision and accepts 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. MBR takes responsibility that this study has been reported honestly, accurately, and transparently; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

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Supplementary Material

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Results—Over a median follow-up of 2.4 years, 183 (40%) patients died. Crude mortality rates were 10.0 (95% CI, 6.8–14.7), 12.7 (95% CI, 10.2–15.7), 21.7 (95% CI, 16.4–28.6), and 12.2 (95% CI, 6.8–14.7) per 100 patient-years among patients initiating dialysis primarily for laboratory evidence of kidney function decline, uremic symptoms, volume overload or hypertension, and other/unknown reason, respectively. Following adjustment for demographic variables, coexisting illnesses, and estimated glomerular filtration rate, initiation of dialysis for uremic symptoms, volume overload or hypertension, or for other/unknown reasons were associated with 1.12 (95% CI, 0.72–1.77), 1.71 (95% CI, 1.03–2.84), and 1.28 (95% CI, 0.73–2.26) times higher risk, respectively, for subsequent mortality compared to initiation for laboratory evidence of kidney function decline.

Limitations—Possibility of residual confounding by unmeasured variables; reliance on clinical documentation to ascertain exposure

Conclusions—Patients initiating dialysis due to volume overload may have increased risk for mortality compared to patients initiating dialysis due to laboratory evidence of kidney function decline. Further studies are needed to identify and test interventions that might reduce this risk.

Keywords

end-stage renal disease (ESRD); hemodialysis; peritoneal dialysis; dialysis initiation; all-cause mortality; symptoms; chronic kidney failure; incident ESRD; volume overload; uremic symptoms; hypertension; indications for renal replacement therapy; clinical decision making

Each year, more than 115,000 patients with chronic kidney failure initiate maintenance dialysis in the United States.¹ This transition period is one of exceptionally high vulnerability for patients; annual mortality rates from chronic kidney disease (CKD) stage 5 through the first year of maintenance dialysis exceed 20%.¹ There is thus a critical need to better understand risk factors for adverse patient outcomes during this high-risk period.

One understudied domain critical to patient-centered care during the transition to dialysis is clinician assessment of the varied signs and symptoms attributable to kidney failure, and the intersection of such assessment with patient and provider shared decision-making regarding dialysis initiation.^{2–4} Current clinical practice guidelines suggest that the decision to initiate maintenance dialysis should be guided primarily by clinical assessment of the constellation of signs and symptoms attributable to the uremic syndrome, including evidence of volume overload refractory to medical therapy.^{5–7} However, there is a paucity of data describing the spectrum of clinical findings present at the initiation of dialysis for patients with chronic kidney failure, and which of these factors may be the primary drivers for patient and provider decisions to initiate renal replacement therapy. To our knowledge, no prior study has examined the relationship between the primary indication for dialysis initiation and subsequent patient-centered clinical outcomes.

To address these gaps in knowledge, we conducted a retrospective cohort study using detailed information from electronic medical record abstraction to describe the symptom burden and clinical indication for dialysis initiation among a cohort of patients with chronic kidney failure, and to examine the association of these factors with subsequent mortality risk.

METHODS

Study Population and Data Source

The study cohort comprised all patients aged 18 years or older who initiated maintenance dialysis from January 1, 2004 through December 31, 2012 with a primary nephrologist affiliated with the University of Washington (UW), and who received outpatient dialysis treatment at one of 14 dialysis facilities operated by the Northwest Kidney Centers. A total of 508 patients were initially identified for inclusion through dialysis facility electronic medical records. Of these, 47 patients were excluded for initiation of dialysis at a non-UW-affiliated hospital or under the care of a non-UW-affiliated nephrologist and thus relevant data on dialysis initiation decision-making were not available. The final cohort included 461 patients.

Inpatient and outpatient provider documentation, laboratory data, and procedure notes were identified and abstracted utilizing the UW electronic health record system. Patient demographics were ascertained from dialysis facility records, as was the date of initiation of maintenance dialysis. The UW electronic health record was used to abstract the remainder of the clinical and laboratory data, and all record review and abstraction was performed by one of two physician study investigators (M.B.R., C.H.C.). During the abstraction process, study investigators were blinded to the primary study outcome (patient all-cause mortality). Documentation used for abstraction included nephrology provider notes, inpatient admission and discharge summary notes, clinical laboratory data, and surgical procedure notes. Abstracted data included insurance status at the time of initiation of dialysis, etiology of chronic kidney failure, coexisting illnesses, clinical setting of dialysis initiation (inpatient versus outpatient), initial dialysis modality, and type of vascular or peritoneal access used at time of dialysis initiation. Laboratory data within 30 days prior to dialysis initiation was abstracted if available, and included serum potassium, bicarbonate, serum urea nitrogen, creatinine, phosphorus, albumin, and blood hemoglobin.

Using clinical documentation available within 30 days prior to the date of dialysis initiation, signs and/or symptoms present immediately prior to initiation of dialysis were abstracted. The following sign/symptom categories were used: lower extremity edema, pulmonary edema or pleural effusion, shortness of breath, pericarditis or pericardial effusion, cognitive or neurologic dysfunction, pruritus, nausea or vomiting, anorexia, diarrhea, constipation, fatigue, muscle weakness, muscle cramps, musculoskeletal pain, sleep disturbance, sexual dysfunction, depressive symptoms or anxiety, altered taste, hiccups, and dizziness or lightheadedness.

Assessment of Primary Exposure

Possible indications for dialysis initiation were defined *a priori* by the study investigators. The following categories were used: uremic symptoms, uremic pericarditis, clinical evidence of volume overload or hypertension, laboratory evidence of decline in kidney function, hyperkalemia, metabolic acidosis, other electrolyte derangements (disturbances in serum calcium, phosphorus, or magnesium), protein-energy wasting or failure to thrive, patient preference, other, and unknown or unable to ascertain. Ascertainment of the primary

indication for dialysis initiation for each patient was made based on the clinical indication and reasoning documented by the nephrologist in the outpatient or inpatient consultation or progress notes most proximal to the initiation event, and within 30 days of the date of initiation (Table S1, available as online supplementary material). When more than one major factor prompting dialysis initiation was described by the treating nephrologist, further progress notes and complementary notes from other providers up to 7 days before and 30 days after the event date were used as supplementary data to assign the primary indication for dialysis initiation. If after these procedures no one primary indication was identified explicitly by the nephrologist or another provider, the indication mentioned most frequently by the nephrologist or other providers was assigned as primary. Following completion of the abstraction process, indications for dialysis initiation were collapsed into four categories for analytic purposes: laboratory evidence of kidney function decline, uremic symptoms, volume overload or hypertension, and other/unknown. To assess the precision of ascertainment of indications for initiation of dialysis, a random sample of 10% of records reviewed by each primary abstractor were independently reviewed by an additional study investigator. The percentage of agreement ranged from 87% to 95% across exposure categories (Table S2). The κ statistic ranged from 0.71 (95% confidence interval [CI], 0.47–0.95), signifying moderate agreement among chart reviewers, to 0.89 (95% CI, 0.74–1.00), signifying near-perfect agreement.⁸

Assessment of Clinical Outcomes

Follow-up for the primary outcome of all-cause mortality was available for study participants through December 31, 2013. Dates of death were obtained from the Centers for Medicare & Medicaid Services End-Stage Renal Disease Death Notification Form 2746. Additional outcomes included transplantation, transfer to a non-affiliated dialysis facility, and withdrawal from dialysis, and event dates for these outcomes were obtained from dialysis facility electronic records.

Statistical Analyses

Baseline data were summarized, stratified by primary indication for dialysis initiation. Data were complete for age at dialysis initiation, sex, race, primary insurance status, comorbid conditions, location of dialysis initiation, initial dialysis modality, dialysis access type, serum potassium, serum urea nitrogen, and creatinine at time of dialysis initiation. Data for serum albumin, body mass index, and blood hemoglobin were missing for <2% of the cohort; data for serum phosphorus were missing for 32%. Missing data were imputed using multiple imputation by chained equations with 10 repetitions. Missing values were modeled as continuous variables using linear regression with independent variables age, gender, race, body mass index, coexisting diabetes, congestive heart failure, coronary artery disease, other cardiac disease, cerebrovascular disease, peripheral vascular disease, year of dialysis incidence, estimated glomerular filtration rate (eGFR) at dialysis initiation, and initial dialysis access type. Level of eGFR at initiation of dialysis was estimated on the basis of each patient's last recorded serum creatinine measurement within 30 days prior to dialysis initiation using the CKD-EPI (CKD Epidemiology Collaboration) creatinine equation.⁹ Scatter plots were created and Pearson's correlation coefficients calculated to summarize the relationship between eGFR at initiation of dialysis and number of signs/symptoms present.

Mortality rates, follow-up time, and 95% CIs estimated using the bootstrap method were calculated separately for groups defined by the primary indication for dialysis initiation. Unadjusted Kaplan-Meier event curves for the primary outcome of all-cause mortality, stratified by primary indication for dialysis initiation, were created and superimposed. Equality of the survivor functions was tested using the log-rank test.

For the primary analysis, time-to-event survival analyses were performed using Cox proportional hazards regression to determine the association of the primary indication for dialysis initiation with all-cause mortality over study follow-up. Censoring reasons included transplantation, discharge to a facility operated by another dialysis provider, discontinuation of dialysis, and administrative censoring at end of follow-up (Table S3). The proportional hazards assumption was confirmed by examining log-log plots of survival, and through analysis of Schoenfeld residuals.¹⁰ Four nested hierarchical models were examined: (1) unadjusted; (2) adjusted for age, sex, and race/ethnicity; (3) additionally adjusted for coexisting diabetes, congestive heart failure, coronary artery disease, other cardiac disease, cerebrovascular disease, peripheral vascular disease, year of dialysis incidence, and eGFR at initiation of dialysis; and (4) additionally adjusted for serum albumin and dialysis access type at initiation of dialysis. Model (3) was used as the primary analytic model. For all analyses, the referent group comprised patients who initiated dialysis primarily based on laboratory evidence of kidney function decline. The pre-determined level of significance (α) was set at 0.05.

Three *a priori* defined subgroup analyses were performed to assess for heterogeneity of effects. First, the association of indication for initiation of dialysis with mortality was determined within subgroups defined by initial dialysis access. Second, analyses were performed within subgroups according to urgency of dialysis initiation. Routine initiation was defined as initiation in the outpatient setting or during a planned inpatient admission. Urgent initiation was defined as initiation during an unplanned hospital admission. Finally, the association of indication for initiation of dialysis with mortality was examined within groups defined by location of dialysis initiation. As for the primary analysis, the referent group in all subgroup analyses comprised the group of patients who initiated dialysis primarily for laboratory evidence of kidney function decline. For each subgroup analysis, multiplicative interaction terms were created to test for effect modification. We evaluated statistical significance of each interaction term by the likelihood ratio test comparing nested models with or without inclusion of the interaction term.

This study was approved by the University of Washington Institutional Review Board as exempt from informed consent (Human Subjects Application #47502). All analyses followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.¹¹ Statistical analyses were performed using STATA, version 11 (StataCorp LP, College Station, TX).

RESULTS

Descriptive Characteristics

Overall, the largest percentage of the cohort, 47%, initiated dialysis primarily due to development of uremic symptoms; 21% initiated due to volume overload or hypertension; 18%, due to laboratory evidence of kidney function decline; and 6%, due to hyperkalemia. Fewer than 2% of the cohort initiated dialysis primarily due to metabolic acidosis and only 1% because of electrolyte abnormalities other than hyperkalemia. There were few differences in the characteristics of patients who initiated dialysis primarily due to uremic symptom burden compared to patients who initiated dialysis primarily due to laboratory evidence of kidney function decline (Table 1). In contrast, patients who initiated dialysis primarily based on evidence of volume overload or hypertension were more likely to have diabetes or cardiovascular comorbidity, and had lower serum albumin, creatinine, blood hemoglobin, and eGFR. Additionally, they were more likely to initiate dialysis urgently and be treated with in-center hemodialysis.

Signs and Symptoms at Dialysis Initiation

Overall, there was a high burden of clinical signs and symptoms consistent with advanced kidney disease among study patients (Table 2). The mean number of signs and symptoms present at the time of dialysis initiation was 5.1 ± 2.1 (standard deviation). The most prevalent signs or symptoms present in the full cohort were lower extremity edema (71%), fatigue (48%), nausea or vomiting (46%), and shortness of breath (40%). Compared to patients initiating dialysis primarily for uremic symptoms, patients initiating dialysis for volume overload or hypertension had a greater prevalence of lower extremity edema, pulmonary edema, and shortness of breath; conversely, they had a lower prevalence of cognitive dysfunction, nausea or vomiting, fatigue, and anorexia. Among all patients, there was poor correlation between eGFR at the time of dialysis initiation and the number of signs and symptoms present ($r = 0.06$; $P = 0.49$; Figure S1).

Indications for Dialysis Initiation and Patient Outcomes

Over a median follow-up of 2.4 years, 183 patients in the full cohort died, 49 received a kidney transplant, and 53 transferred to a non-affiliated dialysis facility (Table 3 and Table S1). The crude mortality rates for patients initiating dialysis due to laboratory evidence of kidney function decline alone compared with those initiating primarily because of uremic symptoms and volume overload or hypertension were 10.0 (95% CI, 6.8–14.7), 12.7 (95% CI, 10.2–15.7), and 21.7 (95% CI, 16.4–28.6) per 100 patient-years, respectively (Table 3). Figure 1 shows unadjusted Kaplan-Meier survival curves for patients stratified by the four grouped primary indications for dialysis initiation.

In an unadjusted analysis, initiation of dialysis for volume overload or hypertension was associated with a significantly higher risk for all-cause mortality (hazard ratio [HR], 2.20; 95% CI, 1.37–3.54) compared to initiation for laboratory evidence of kidney function decline (Table 4). Following adjustment for demographic factors, comorbidities, year of dialysis incidence, and eGFR at the time of initiation of dialysis, this association remained significant (HR, 1.69; 95% CI, 1.02–2.80). In an additional model adjusting for access type

and serum albumin at the time of dialysis initiation, this association was attenuated to a non-significant level (HR, 1.42; 95% CI, 0.87–2.44). In contrast to these findings, patients who initiated dialysis primarily due to uremic symptom burden did not have increased risk for death, irrespective of level of adjustment for potential confounders or mediators (Table 4).

To further investigate the influence of initial dialysis access type on the association between initiation of dialysis for volume overload and subsequent mortality risk, stratum-specific survival analyses were performed among subgroups of dialysis access type. The crude mortality rate for patients initiating dialysis due to volume overload was 13.2 (95% CI, 6.3–27.8) per 100 patient-years for individuals with a permanent dialysis access (either arteriovenous access or a peritoneal dialysis catheter) compared to 24.2 (95% CI, 18.0–32.6) per 100 patient-years for individuals with a central venous catheter (Table S4). In patients initiating dialysis using a permanent dialysis access, initiation of renal replacement therapy due to volume overload or hypertension was associated with an 8-fold higher risk for death compared to initiation due to laboratory evidence of kidney function decline (HR, 8.01; 95% CI, 1.62–39.6; Figure 2). In contrast, among patients initiating dialysis with a central venous catheter, there was no evidence of significant increased adjusted risk associated with initiation for volume overload or hypertension (HR, 1.38; 95% CI, 0.79–2.41). Although these stratum-specific risk estimates were substantially different, the statistical interaction was not significant (P for interaction = 0.3). There was no evidence of heterogeneity of risk by vascular access type for patients who initiated dialysis for uremic symptoms or for other or unknown indications.

Examination of subgroups defined by urgency or location of dialysis initiation also suggested heterogeneity of effects (Figure 2). Among patients initiating dialysis in a routine fashion, there was a higher adjusted risk for death with initiation of dialysis for volume overload or hypertension compared to initiation for laboratory evidence of kidney function decline (HR, 13.5; 95% CI, 2.61–70.2; Figure 2). In contrast, this elevated risk was not seen among patients who initiated dialysis urgently, although formal testing did not reveal evidence of a statistical interaction (P for interaction = 0.3). Similarly, although higher mortality risk with initiation of dialysis for volume overload was also observed among patients who initiated dialysis in a hospital setting but not among those who initiated dialysis in an outpatient dialysis facility, there was no evidence of a statistical interaction (P for interaction = 0.2).

DISCUSSION

In this study, we comprehensively described the burden of signs and symptoms present at initiation of dialysis in a cohort of patients with chronic kidney failure, and examined mortality risk associated with indications for dialysis initiation amongst this group. The results of this study allow us to make several novel observations. First, irrespective of the primary indication for dialysis initiation, the burden of signs and symptoms attributable to kidney failure in patients initiating dialysis is substantial and wide-ranging. Second, among the possible indications prompting initiation of renal replacement therapy, initiation of dialysis for evidence of volume overload or hypertension is associated with the greatest risk for subsequent all-cause mortality. Third, this mortality risk persists after accounting for

potential confounders such as demographic factors and coexisting illnesses, but is attenuated significantly with adjustment for initial dialysis access type and serum albumin. Finally, the risk of death associated with initiation of dialysis for volume overload or hypertension may vary among subgroups, and may be as much as 13-fold higher for patients initiating dialysis with permanent dialysis access or who initiate dialysis in a routine outpatient setting.

Our analysis is the first to comprehensively describe the symptom burden and clinical indications prompting the initiation of dialysis therapy among patients with chronic kidney failure. Our results show that patients initiating dialysis due to evidence of volume overload or hypertension had higher risk for subsequent death compared to patients initiating dialysis prompted solely by laboratory evidence of kidney function decline, even after accounting for potentially confounding comorbid conditions such as a history of heart failure. Prior studies have shown that volume overload, whether determined clinically, through assessment of laboratory biomarkers, or using bioimpedance spectroscopy, is associated with kidney disease progression and mortality risk among patients with advanced CKD.^{12–15} Similarly, among patients with chronic kidney failure undergoing maintenance dialysis, accumulating evidence suggests that high interdialytic weight gains and volume overload are associated with loss of residual kidney function and all-cause mortality, particularly in the first year after the transition to dialysis therapy.^{16–20} One explanation for these observations is that volume overload either prior to or in the early period following initiation of renal replacement therapy may be a marker of abrupt or rapid decline in residual kidney function, which has been shown to predict early death after initiation of maintenance dialysis.²¹ Additionally, volume overload in CKD leads to left ventricular hypertrophy, which over time may predispose to subendocardial ischemia, left ventricular dilation and subsequent impairment in systolic function.^{22–24} Thus, evidence of volume overload prompting initiation of dialysis in patients without a preceding diagnosis of heart failure may represent the first clinical manifestation of previously subclinical disease.^{25,26} Another potential pathway by which volume overload in the period surrounding dialysis initiation may lead to adverse clinical outcomes is through pro-inflammatory endothelial activation. Inflammation may subsequently lead to accelerated atherogenesis^{27,28}, predisposition to cardiac arrhythmias²⁹, or increased risk for infection.^{30,31} Finally, it is possible that volume overload might be an indicator of dietary or medication non-adherence, and thus may serve as a marker of behavioral patterns predisposing to increased risk for adverse clinical outcomes.

In pre-defined subgroup analyses, we observed greater estimates of risk associated with initiation of dialysis for volume overload among patients with permanent dialysis access compared to those initiating dialysis with a central venous catheter. One explanation for this finding is that patients initiating dialysis via a catheter are less likely to have undergone adequate preparation for the transition to dialysis, and are more likely to have had rapid decline in kidney function obviating the possibility for permanent access placement.³² Based on these factors, these patients are thus at higher risk for adverse outcomes in the peri-initiation period, irrespective of the specific indication prompting the initial dialysis session. Thus, in our study, the increased risk associated with indwelling catheter use may have obscured subtler variations in risk associated with different indications prompting initiation of dialysis.

Despite its strengths, our study should be interpreted in light of some limitations. Investigator assessment of symptoms present and determination of the primary indication for dialysis initiation relied on clinical documentation, and, while extensive, such documentation may be incomplete. Patients who initiated dialysis in the inpatient setting but did not survive to outpatient dialysis, or who were referred to a non-affiliated dialysis facility, were not included in the study cohort. Additionally, this study was limited to patients seen by nephrologists affiliated with two academic medical centers, and this may limit generalizability. As with any observational study, we cannot exclude the possibility of residual confounding due to unmeasured or incompletely measured factors. Finally, data were not available for clinical outcomes other than mortality such as infectious events, non-fatal cardiovascular events, or hospitalizations, and thus we were unable to examine these outcomes among the study cohort.

In conclusion, there is a significant burden and a wide-ranging spectrum of clinical signs and symptoms of advanced kidney disease present in patients with chronic kidney failure, and there is heterogeneity within these findings among patients initiating dialysis for different indications. Furthermore, among patients with chronic kidney failure, initiation of dialysis for volume overload is associated with the greatest risk for subsequent mortality. Improved understanding of symptoms and clinical decision-making at the time of the transition to dialysis has the potential to lead to innovation in identifying the optimal timing for the initiation of maintenance dialysis. Additionally, further studies are needed to determine whether modification of symptoms or volume overload attributable to advanced kidney disease in this patient population leads to improved patient-centered outcomes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1. Unadjusted Kaplan-Meier event curve for all-cause mortality, by primary indication for dialysis initiation

Log rank test for equality of survivor functions: $P = 0.002$.

Figure 2. Subgroup analyses - Association of indication for initiation of dialysis with risk for all-cause mortality, by initial dialysis access, clinical urgency, and location

Referent category for all subgroup analyses comprises individuals who initiated dialysis for laboratory evidence of kidney function decline. Hazard ratios are from Cox regression models adjusted for age, sex, race/ethnicity, coexisting diabetes, CHF, coronary artery disease, other cardiac disease, cerebrovascular disease, peripheral vascular disease, and eGFR at initiation of dialysis. Abbreviations: CVC, central venous catheter; P_{interaction}, P value for significance of multiplicative interaction term (potential effect modifier [2 levels])*(dialysis initiation indication [4 groups]).

Table 1
Baseline characteristics at time of dialysis initiation, by primary indication for dialysis initiation

Characteristic	Total (N = 461)	Primary Indication for Dialysis Initiation				P value ^d
		Lab Evidence of Kidney Function (n = 83)	Uremic Symptoms (n = 216)	Volume Overload / HTN (n = 95)	Other/ Unknown (n = 67)	
Age (y)	55 ± 15	53 ± 16	55 ± 15	57 ± 15	56 ± 13	0.2
Male Sex	63	61	63	66	63	0.3
Body mass index (kg/m ²)	28 ± 8	28 ± 7	28 ± 8	29 ± 9	28 ± 7	0.3
Insurance status						0.2
Medicare	31	29	29	38	36	
Medicaid	36	33	35	40	39	
Private/other	33	39	37	22	25	
Race/Ethnicity						0.06
White	39	37	38	46	37	
African American	28	30	30	23	22	
Asian	13	7	14	16	13	
Hispanic	7	6	9	5	4	
Other/Unknown	13	20	9	9	22	
Primary etiology of kidney disease						0.2
Diabetes mellitus	42	34	40	56	36	
Hypertension	15	17	17	8	13	
Glomerulonephritis	17	23	14	18	19	
Other/Unknown	27	27	29	18	30	
Coexisting illnesses						
Diabetes mellitus	52	47	50	64	46	0.05
Hypertension	82	86	83	82	73	0.2
Congestive heart failure	25	16	20	45	19	<0.001
Coronary heart disease	20	11	17	34	19	0.001
Other cardiac disease	21	12	21	31	16	0.03
Cerebrovascular disease	13	11	13	16	12	0.8

Characteristic	Total (N = 461)	Primary Indication for Dialysis Initiation				P value ^a
		Lab Evidence of Kidney Function (n = 83)	Uremic Symptoms (n = 216)	Volume Overload / HTN (n = 95)	Other/ Unknown (n = 67)	
Peripheral vascular disease	10	10	6	14	15	0.2
Viral hepatitis	22	23	21	21	25	0.9
Cancer	9	8	9	7	9	0.9
Blood lab results (pre- initiation)						
Potassium (mEq/L)	4.6 ± 0.8	4.5 ± 0.7	4.6 ± 0.7	4.5 ± 0.7	5.0 ± 1.1	0.01
Bicarbonate (mEq/L)	20 ± 5	20 ± 5	20 ± 5	21 ± 5	18 ± 6	0.01
Serum urea nitrogen (mg/dL)	94 ± 39	89 ± 42	94 ± 40	91 ± 33	105 ± 43	0.1
Creatinine (mg/dL)	8.4 ± 4.8	8.4 ± 4.8	8.6 ± 5.1	7.0 ± 2.7	9.7 ± 5.5	<0.001
Phosphorus (mg/dL)	7.1 ± 2.5	7.2 ± 2.4	6.9 ± 2.5	6.8 ± 1.9	7.9 ± 2.8	0.08
Albumin (mg/dL)	2.8 ± 0.8	2.8 ± 0.7	2.9 ± 0.8	2.5 ± 0.7	2.8 ± 0.8	<0.001
Hemoglobin (g/dL)	9.4 ± 1.7	9.6 ± 1.5	9.6 ± 1.8	8.8 ± 1.6	9.4 ± 1.7	0.001
eGFR (mL/min/1.73m ²)	8.0 ± 4.2	8.2 ± 4.4	7.9 ± 4.4	8.9 ± 3.8	7.0 ± 4.1	0.02
Clinical setting						<0.001
Inpatient	70	57	61	88	85	
Outpatient	30	43	39	12	15	
Modality						0.01
In-center hemodialysis	95	87	95	99	98	
Peritoneal dialysis	5	13	5	1	2	
Access type used at dialysis initiation						<0.001
AV fistula	22	17	27	17	19	
AV graft	7	11	6	4	7	
Tunneled cuffed CVC	55	48	55	64	49	
Temporary uncuffed CVC	12	11	7	14	24	
PD catheter	5	13	5	1	1	
Urgency of dialysis initiation						<0.001
Routine	31	45	37	12	19	
Urgent	69	55	62	88	80	

Abbreviations: eGFR, estimated glomerular filtration rate; AV, arteriovenous; CVC, central venous catheter; HTN, hypertension; Lab, laboratory; PD, peritoneal dialysis

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Note: Values for categorical variables are given as percentage; for continuous variables, as mean $\pm$ standard deviation. Data are complete (N = 461) for all variables with the exception of the following: serum albumin (n = 455), body mass index (n = 453), blood hemoglobin (n = 457), and serum phosphorus (n = 313). Conversion factors for units: creatinine in mg/dL to $\mu\text{mol/L}$, $\times 88.4$; phosphorus in mg/dL to $\mu\text{mol/L}$, $\times 0.3229$; serum urea nitrogen in mg/dL to mmol/L , $\times 0.357$;

_p P value from test for heterogeneity among groups

Table 2
Signs and symptoms present at dialysis initiation, by primary indication for dialysis initiation

	Total (N = 461)	Primary Indication for Dialysis Initiation			P value ^a
		Lab Evidence of Kidney Function (n = 83)	Uremic Symptoms (n = 216)	Volume Overload / HTN (n = 95)	
Sign or symptom					
Lower extremity edema	71	73	67	89	<0.001
Pulmonary edema	37	22	27	74	<0.001
Pericarditis or pericardial effusion	2	0	4	0	0.1
Shortness of breath	49	40	40	80	<0.001
Cognitive/neurologic dysfunction	31	25	35	23	0.2
Pruritus	26	18	30	22	0.3
Nausea or vomiting	54	46	68	37	<0.001
Anorexia	53	33	72	41	<0.001
Diarrhea	15	8	18	14	0.1
Constipation	9	8	7	15	0.2
Fatigue	58	48	70	42	<0.001
Muscle cramps	8	10	9	6	0.05
Pain	38	39	40	33	0.9
Sleep disturbance	22	16	28	23	0.04
Sexual dysfunction	2	1	3	1	0.5
Depressive symptoms or anxiety	9	10	13	3	0.2
Altered taste	8	10	10	4	0.4
Muscle weakness	6	4	6	5	0.6
Hiccups	4	2	6	3	0.5
Dizziness or lightheadedness	3	4	4	2	0.9
No. of signs/symptoms	5.1 ± 2.1	4.2 ± 2.0	5.6 ± 2.0	5.2 ± 1.9	4.4 ± 2.1

^aP value from test for heterogeneity among groups

Note: Values for categorical variables are given as percentage; for continuous variables, as mean ± standard deviation.

HTN, hypertension; Lab, laboratory

Table 3

Crude event numbers and mortality rates, by primary indication for dialysis initiation

Indication for dialysis initiation	Patient- years of F/U	Events	Mortality Rate ^a (95% CI)
Lab Evidence of Kidney Function	260	26	10.0 (6.8–14.7)
Uremic Symptoms	655	83	12.7 (10.2–15.7)
Volume Overload/HTN	231	50	21.7 (16.4–28.6)
Other/Unknown	197	24	12.2 (6.8–14.7)
Total	1341	183	13.6 (11.8–15.8)

^aMortality rate reported as rate per 100 patient-years

CI, confidence interval; F/U, follow-up; HTN, hypertension; Lab, laboratory

Table 4

Association of primary indication for dialysis initiation and risk for all-cause mortality

Indication for dialysis initiation	Model 1 ^a	Model 2 ^b	Model 3 ^c	Model 4 ^c
Uremic Symptoms	1.23 (0.79–1.92)	1.16 (0.74–1.81)	1.12 (0.72–1.77)	1.26 (0.80–2.01)
Volume Overload/HTN	2.20 (1.37–3.54)	1.80 (1.11–2.92)	1.69 (1.02–2.80)	1.42 (0.87–2.44)
Other/Unknown	1.20 (0.69–2.08)	1.15 (0.66–2.01)	1.28 (0.73–2.26)	1.26 (0.70–2.26)

Note: Associations are given as hazard ratio (95% confidence interval). Laboratory evidence of kidney function used as referent category for all models. HTN, hypertension

^aModel 1 is unadjusted

^bModel 2 adjusted for age, sex, race/ethnicity

^cModel 3 additionally adjusted for coexisting diabetes, congestive heart failure, coronary artery disease, other cardiac disease, cerebrovascular disease, peripheral vascular disease, year of dialysis incidence, and estimated glomerular filtration rate at initiation of dialysis

^dModel 4 additionally adjusted for dialysis access type and serum albumin at initiation of dialysis