

Comparing the Risk for Death with Peritoneal Dialysis and Hemodialysis in a National Cohort of Patients with Chronic Kidney Disease

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Background: The influence of type of dialysis on survival of patients with end-stage renal disease (ESRD) is controversial.

Objective: To compare risk for death among patients with ESRD who receive peritoneal dialysis or hemodialysis.

Design: Prospective cohort study.

Setting: 81 dialysis clinics in 19 U.S. states.

Patients: 1041 patients starting dialysis (274 patients receiving peritoneal dialysis and 767 patients receiving hemodialysis) at baseline.

Measurements: Patients were followed for up to 7 years and censored at transplantation or loss to follow-up. Cox proportional hazards regression stratified by clinic was used to compare the risk for death with peritoneal dialysis versus hemodialysis.

Results: Twenty-five percent of patients undergoing peritoneal dialysis and 5% of hemodialysis patients switched type of dialysis. After adjustment, the risk for death did not differ between patients undergoing peritoneal dialysis and those undergoing hemodialysis during the first year (relative hazard, 1.39 [95% CI, 0.64 to 3.06]), but the risk became significantly higher among those

undergoing peritoneal dialysis in the second year (relative hazard, 2.34 [CI, 1.19 to 4.59]). After stratification, the survival rate was no different for patients who had the highest propensity of being initially treated with peritoneal dialysis. Results were consistent with adjustment based on a propensity score model and in sensitivity analyses that used as-treated models and models in which switches in type of dialysis were treated as treatment failures. Results were similar but stronger in analyses that were restricted to patients who were treated only in clinics offering both types of dialysis.

Limitations: Patients were not randomly assigned to their initial type of dialysis. Also, more patients undergoing peritoneal dialysis than hemodialysis switched type of dialysis over time, and the reason for switching was often a consequence of the technique.

Conclusions: The risk for death in patients with ESRD undergoing dialysis depends on dialysis type. Further studies are needed to evaluate a possible survival benefit of a timely change from peritoneal dialysis to hemodialysis.

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The burden of end-stage renal disease (ESRD) in the United States has increased dramatically over the past 30 years, with the number of patients treated for ESRD with dialysis or transplantation reaching more than 400 000 by the end of 2001 (1). The number of patients requiring renal replacement therapy is projected to exceed 2 million patients by 2030 (1). Although kidney transplantation remains the best treatment option for eligible patients with ESRD (2), rates of kidney donation have not kept pace with the number of cases, leading to an increase in the number of patients on waiting lists (1). Thus, most patients with ESRD, including those eligible for kidney transplantation, must select a type of dialysis for renal replacement therapy.

Since the introduction of peritoneal dialysis in the mid-1970s, several studies have tried to assess differences in survival between patients undergoing peritoneal dialysis and those undergoing hemodialysis, but the influence of type of dialysis on survival of patients with ESRD or subgroups of these patients remains controversial. Limitations of previously published studies include the enrollment of patients who had been receiving dialysis therapy for different amounts of time after the onset of ESRD (3), noncontemporary cohorts of patients undergoing incident dialysis (3–6), short follow-up (1 to 2 years) (3, 7–12), and limited

information on comorbid conditions (3, 6, 7, 9, 13). Furthermore, many of these studies used only intention-to-treat analyses that do not account for switches in type of dialysis that occur over time (3–5, 7–9, 13).

We performed a comprehensive comparative study of survival in patients undergoing peritoneal dialysis and those undergoing hemodialysis.

METHODS

Study Design and Sample

We conducted a national prospective cohort study of patients undergoing incident dialysis. Eligibility criteria for

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enrollment into the Choices for Healthy Outcomes in Caring for ESRD (CHOICE) study included ability to provide informed consent for participation, age older than 17 years, and ability to speak English or Spanish. Median time from initiation of dialysis to enrollment was 45 days; 98% of patients enrolled within 4 months of initial dialysis. Enrolled patients were oversampled for peritoneal dialysis to allow statistical comparisons by type of dialysis. The institutional review boards of Johns Hopkins University and the clinical centers approved the study protocol, and all participants gave written informed consent.

From October 1995 to June 1998, 1041 participants from 19 U.S. states were enrolled at 81 dialysis clinics associated with Dialysis Clinic, Inc., Nashville, Tennessee (923 patients), and New Haven Continuous Ambulatory Peritoneal Dialysis (86 patients) or St. Raphael's Hospital, New Haven, Connecticut (32 patients).

Data Collection

Demographic and Clinical Data

At baseline, patients used a questionnaire to self-report demographic characteristics, health behaviors, work history, medical history, preparation for dialysis, social support, and distance to dialysis unit. Baseline data on routine care were available for serum albumin level, hemoglobin level, calcium-phosphate product, and total cholesterol level. High-sensitivity C-reactive protein was measured at a median of 5.0 months from initiation of dialysis by using a colorimetric competitive enzyme-linked immunosorbent assay (coefficient of variation, 8.9%). Residual urine output was defined as the ability to produce at least 250 mL of urine daily; this information was obtained from the baseline self-report questionnaire. Glomerular filtration rate before initiation of dialysis was estimated from the Modification of Diet in Renal Disease equation by using the serum creatinine concentration obtained from the ESRD Medical Evidence Report (Form 2728) (14).

Dialysis Technique

Dialysis technique at baseline was defined as the type of dialysis being used at 4 weeks after enrollment in the study (an average of 10 weeks after starting dialysis) and was obtained from clinic records. All forms of peritoneal dialysis (continuous ambulatory peritoneal dialysis, continuous cycling peritoneal dialysis, and intermittent cycling peritoneal dialysis) were combined as a single category. Patients were considered to have switched technique when they changed from one type of dialysis to another and continued to use the new technique for at least 30 days.

Assessment of Comorbid Conditions

Comorbid conditions were assessed by using the Index of Coexistent Disease, a medical record-derived index that has been demonstrated to predict death in patients undergoing dialysis (15, 16). Scores on this index range from 0

Context

Does dialysis method affect survival of patients with end-stage renal disease?

Contribution

At 81 clinics in 19 states, 25% of the patients receiving peritoneal dialysis and 5% of those receiving hemodialysis switched methods at least once within 7 years. Patients initiating treatment with peritoneal dialysis appeared healthier and of higher socioeconomic status than did those receiving hemodialysis. Analyses that adjusted for baseline differences found statistically significantly higher risks for death among patients receiving peritoneal dialysis compared with those receiving hemodialysis during the second, but not first, year of treatment.

Cautions

This prospective study of incident dialysis was not a randomized trial.

—The Editors

(no comorbid condition) to 3 (highest severity of comorbid conditions). The Index of Coexistent Disease aggregates the presence and severity of comorbid conditions within 2 scales: the Index of Disease Severity and the Index of Physical Impairment. The Index of Disease Severity consists of 19 categories of medical conditions (ischemic heart disease, congestive heart failure, arrhythmias, other heart disease, hypertension, cerebrovascular disease, peripheral vascular disease, diabetes mellitus, respiratory disease, cancer, hepatobiliary disease, gastrointestinal disease, non-vascular neurological disease, musculoskeletal disease, hematologic disease, HIV or AIDS, anticoagulation, urogenital disease, and ophthalmologic disease), with 4 levels of severity for each condition. Information for the Index of Disease Severity was abstracted from dialysis unit records, hospital discharge summaries, medication lists, consultation notes, diagnostic imaging, and cardiac imaging reports. These data were collected at each dialysis unit, photocopied, and sent to New England Medical Center for abstraction and scoring. The Index of Physical Impairment is an observer-based assessment of 11 functional domains (circulation, respiration, neurologic function, mental function, urinary elimination, bowel elimination, feeding, ambulation, vision, hearing, and speech), each with 3 severity levels. The Index of Physical Impairment was completed by a local dialysis nurse who was familiar with the patient's level of functioning, with input from a family member or caregiver if necessary.

Two dialysis nurses with previous training and experience in using the Index of Coexistent Disease reviewed and scored all charts. The reliability of data abstraction and severity scoring was assessed by using a masked recoding of 45 charts. Interrater reliability, as assessed by the κ statistic,

was excellent for Index of Disease Severity score ($\kappa = 0.93$), maximum Index of Disease Severity score ($\kappa = 0.84$), and maximum Index of Physical Impairment score ($\kappa = 1.0$).

Statistical Analysis

We compared characteristics of patients undergoing peritoneal dialysis with those of patients undergoing hemodialysis by using analysis of variance for continuous variables and the Pearson chi-square test for categorical variables. The C-reactive protein level was log-transformed to reduce skewness of distribution.

Patients were followed for death for up to 7 years. We used survival analysis to assess the presence, direction, strength, and independence of an association between dialysis technique and death. We used stratified Cox proportional hazards models to assess the risk for death among patients undergoing peritoneal dialysis versus those undergoing hemodialysis, independent of differences in demographic characteristics (age, sex, ethnicity, and employment status), clinical factors (smoking status, score on the Index of Coexistent Disease, diabetes status, history of cardiovascular disease, primary cause of renal failure, late referral to a nephrologist [<4 months from first evaluation by a nephrologist to initiation of dialysis], body mass index, and baseline residual urine output), and laboratory values (serum albumin level, hemoglobin level, calcium-phosphate product, total cholesterol level, C-reactive protein level, and creatinine concentration). We censored patients at transplantation or loss to follow-up.

As the main analysis, we used intention-to-treat models based on the type of dialysis at baseline. Within the limitations of an observational study, this analysis was an attempt to replicate the intention-to-treat analysis in a clinical trial. If we could have adjusted for all of the factors that determine the choice of initial treatment technique, our results would mirror those of a randomized, controlled trial. We believe that this is the most important matter from the clinical point of view, because the real therapeutic choice for the clinician and the patient occurs primarily at the time of initiation of dialysis, whereas future switches may be motivated by treatment failures over which clinicians have little control.

For the intention-to-treat models, we used multivariate Cox models that included all covariates, as well as models that incorporated dialysis technique and a technique propensity score. The propensity score, an established method used to address selection bias due to observed factors, is the estimated probability of being treated initially with peritoneal dialysis rather than hemodialysis. This propensity score, which was derived from a separate logistic regression model that predicts initial type of dialysis by using patients' baseline characteristics, is the single summarized confounding covariate used in the Cox model (17). The propensity score was calculated separately for each adjustment model.

Dialysis technique was not balanced by center; in addition, patient characteristics varied by center and dialysis technique in our cohort. Therefore, confounding by clinic is possible. To account for this problem, all Cox models were stratified by clinic. With stratification, risk is assessed separately in each stratum and then pooled across all strata, a method that corresponds to a conditional, fixed-effects model. This analysis addresses the question of whether hemodialysis provides better survival than does peritoneal dialysis once a patient enters a specific clinic.

We also evaluated the sensitivity of our findings in several ways. To address the effect of peritoneal dialysis or hemodialysis once the patient is undergoing that treatment regardless of treatments used in the past, we examined 2 extreme scenarios: as-treated models incorporating changes in dialysis technique over time, and models in which switches were counted as treatment failures. For the as-treated models, survival time was attributed to current rather than baseline type of dialysis. For example, if a patient switched from hemodialysis to peritoneal dialysis, the period of survival before the switch would be attributed to hemodialysis; the patient would then be censored at the date of switch and reenter the study as a patient undergoing peritoneal dialysis at that date. This second survival period would last until a survival event (death or censoring for transplantation or loss to follow-up) or another switch in type of dialysis. As-treated models are most favorable to peritoneal dialysis because patients who switch from peritoneal dialysis to hemodialysis may be at increased risk for death. In this case, the assumption of noninformative censoring may be violated. Models in which switches were treated as treatment failures are most unfavorable for peritoneal dialysis because more patients switched from peritoneal dialysis to hemodialysis than vice versa. Because not all clinics offered both types of dialysis, a risk for bias exists in the way in which patients were selected for their initial type of dialysis. To examine this matter, we performed additional sensitivity analyses on the subgroup of patients treated only in clinics offering both techniques.

We also examined whether the risk for death was similar among persons with different clinical characteristics by performing Cox regression analyses in subgroups based on age, diabetes mellitus status, history of cardiovascular disease, and baseline residual urine output. Furthermore, patients were sorted into 3 tertiles of propensity score that were calculated as described above, such that patients in the first tertile had the lowest probability and those in the third tertile had the highest probability of being treated initially with peritoneal dialysis. The demographic, clinical, and laboratory characteristics of patients in each of the tertiles were determined. We formally tested for interactions that had been found to be significant in previous studies by including interaction terms and testing their statistical significance in the full-sample models. Furthermore, we tested for deviations from the proportional hazards assumption by examining the global test of Schoenfeld resid-

Table 1. Baseline Characteristics of Patients, by Initial Type of Dialysis

Characteristic	Patients Undergoing Peritoneal Dialysis*	Patients Undergoing Hemodialysis†	P Value‡
Demographic			
Mean age, y	53.7, SD 14.8	59.3, SD 14.8	<0.001
Female, %	44.5	46.3	>0.2
White, %	77.4	63.1	<0.001
High school graduate, %	82.6	66.3	<0.001
Married, %	67.5	52.8	<0.001
Employed, %	27.0	8.6	<0.001
Living >30 miles from clinic, %	28.9	8.4	<0.001
Clinical			
Ever a smoker, %	61.3	60.4	>0.2
Index of Coexistent Disease score, %			<0.001
≤1 (none to mild)	50.7	30.3	
2 (moderate)	25.2	38.0	
3 (severe)	24.1	31.6	
Diabetes mellitus, %	55.0	51.2	>0.2
Primary cause of renal failure, %			<0.001
Diabetes mellitus	46.9	46.4	
Hypertension	9.6	20.2	
Glomerulonephritis	18.8	15.3	
Other	24.7	18.1	
Cardiovascular disease, %	49.3	59.9	0.003
Mean body mass index, kg/m ²	26.5, SD 5.7	27.3, SD 7.0	0.101
Late referral, %§	19.8	32.9	<0.001
Residual urine output at baseline, %	88.0	81.1	0.015
Mean glomerular filtration rate at start of dialysis, mL/min/1.73 m ²	7.1, SD 2.6	7.3, SD 2.4	>0.2
Laboratory			
Mean serum albumin level, g/L	36.3, SD 4.9	35.0, SD 4.7	<0.001
Mean hemoglobin level, g/L	113, SD 14	106, SD 12	<0.001
Mean calcium-phosphate product, mmol ² /L ² (mg ² /dL ²)	3.78, SD 0.99 (46.8, SD 12.3)	4.01, SD 1.02 (49.6, SD 12.6)	0.002
Mean total cholesterol level, mmol/L (mg/dL)	5.37, SD 1.38 (207.3, SD 53.3)	4.76, SD 1.16 (183.8, SD 44.9)	<0.001
Median log C-reactive protein level (interquartile range), mg/L	3.18 (1.34–6.24)	3.92 (1.76–10.26)	0.005
Mean creatinine concentration, μmol/L (mg/dL)	648, SD 238 (7.33, SD 2.69)	640, SD 220 (7.24, SD 2.49)	>0.2

* For peritoneal dialysis, *n* = 274 for all characteristics except education (*n* = 236), marital status (*n* = 249), distance from center (*n* = 225), primary cause of renal failure (*n* = 271), body mass index (*n* = 257), late referral (*n* = 207), residual urine output at baseline (*n* = 234), albumin level (*n* = 260), hemoglobin level (*n* = 258), calcium-phosphate product (*n* = 259), cholesterol level (*n* = 229), C-reactive protein level (*n* = 168), and creatinine concentration (*n* = 264).

† For hemodialysis, *n* = 767 for all characteristics except education (*n* = 736), marital status (*n* = 758), employment (*n* = 766), distance from center (*n* = 729), Index of Coexistent Disease score (*n* = 765), diabetes (*n* = 765), primary cause of renal failure (*n* = 763), body mass index (*n* = 716), late referral (*n* = 621), residual urine output at baseline (*n* = 725), albumin level (*n* = 748), hemoglobin level (*n* = 744), calcium-phosphate product (*n* = 746), cholesterol level (*n* = 598), C-reactive protein level (*n* = 699), and creatinine concentration (*n* = 747).

‡ By analysis of variance (continuous variables) or chi-square test (categorical variables) for peritoneal dialysis at baseline versus hemodialysis at baseline.

§ Less than 4 months from first evaluation by a nephrologist to initiation of dialysis.

|| Estimated by using the Modification of Diet in Renal Disease equation.

uals, both overall and within each following year. We also used multiple imputation to impute values for missing covariates (18).

Statistical analyses were performed by using Stata software, version 8.1 (Stata Corp., College Station, Texas), and SAS system for Windows, version 8.1 (SAS Institute, Inc., Cary, North Carolina). A *P* value less than 0.05 was considered statistically significant.

Role of the Funding Sources

The funding organizations had no role in the design and conduct of the study; collection, analysis, and interpretation of the data; or preparation, review, or approval of the manuscript.

RESULTS

Patient Characteristics

The age, sex, and ethnicity of the CHOICE study participants were similar to that of the contemporary (1997) U.S. population undergoing dialysis (19). Table 1 shows baseline characteristics of the sample. Twenty-six percent of the 1041 patients undergoing incident dialysis were receiving peritoneal dialysis, and 74% were receiving hemodialysis. Patients undergoing peritoneal dialysis had a significantly better case-mix profile at the start of dialysis than did patients undergoing hemodialysis. Overall, 68 (24.8%) of the 274 patients undergoing peritoneal dialysis and 38 (5%) of the 767 patients undergoing hemodialysis switched type of dialysis at least once.

Table 2. Baseline Characteristics of Patients by Initial Type of Dialysis, within Tertile of Propensity Score for Peritoneal Dialysis

Characteristic*	Lowest Tertile		Intermediate Tertile		Highest Tertile	
	Peritoneal Dialysis (n = 26)	Hemodialysis (n = 321)	Peritoneal Dialysis (n = 59)	Hemodialysis (n = 288)	Peritoneal Dialysis (n = 189)	Hemodialysis (n = 157)
Demographic						
Mean age, y	60.8, SD 13.6	63.3, SD 13.3	61.8, SD 13.6	59.2, SD 14.2	50.4, SD 14.0	51.3, SD 15.4
Female, %	42.3	48.0	35.6	46.2	47.1	43.3
White, %	46.2	47.4	83.1	70.1	79.9	82.2
High school graduate, %	59.1	59.6	79.3	69.1	86.3†	76.2†
Married, %	63.6	50.2	66.7	55.9	67.6†	53.2†
Employed, %	0.0	1.6	10.2	7.6	35.5†	25.6†
Living >30 miles from clinic, %	13.6	5.2	38.8‡	10.2‡	27.3‡	12.2‡
Clinical						
Ever a smoker, %	54.6	58.4	66.0	60.7	60.7	63.6
Index of Coexistent Disease score, %						
≤1 (none to mild)	19.2	17.5	28.8	28.9	61.9	59.2
2 (moderate)	38.5	45.9	39.0	39.7	19.1	19.1
3 (severe)	42.3	36.6	32.2	31.4	19.1	21.7
Diabetes mellitus, %	65.4	53.8	52.5	59.2	48.7	49.7
Primary cause of renal failure, %						
Diabetes mellitus	56.0	40.0	50.9	51.8	44.4	49.4
Hypertension	24.0	33.8	10.5	12.2	7.4	7.1
Glomerulonephritis	4.0	12.8	24.6	14.3	19.6	21.8
Other	16.0	13.4	14.0	21.7	28.6	21.8
Cardiovascular disease, %	61.5	65.0	64.4	58.9	42.9	51.0
Mean body mass index, kg/m ²	26.6, SD 6.0	27.5, SD 7.4	27.3, SD 5.6	27.4, SD 6.6	26.3, SD 5.8	27.0, SD 6.9
Late referral, %§	42.1	43.0	13.2†	30.9†	18.0	16.7
Residual urine output at baseline, %	77.3	73.1	86.5	85.3	90.0	89.8
Mean glomerular filtration rate at start of dialysis, mL/min/1.73 m ²	7.85, SD 3.16	7.44, SD 3.26	7.64, SD 3.15	7.44, SD 3.01	7.40, SD 2.53	7.42, SD 3.32
Laboratory						
Mean serum albumin level, g/L	35.3, SD 3.2	34.1, SD 5.0	35.3, SD 4.8	35.2, SD 4.2	36.7, SD 5.0	36.3, SD 4.5
Mean hemoglobin level, g/L	99, SD 13	101, SD 12	109, SD 11	108, SD 12	116, SD 14†	112, SD 11†
Mean calcium-phosphate product, mmol ² /L ² (mg ² /dL ²)	4.14, SD 0.95 (51.3, SD 11.8)	4.24, SD 1.05 (52.5, SD 13.0)	3.90, SD 1.15 (48.3, SD 14.3)	3.86, SD 0.97 (47.8, SD 12.0)	3.69, SD 0.94 (45.7, SD 11.6)	3.80, SD 0.94 (47.0, SD 11.6)
Mean total cholesterol level, mmol/L (mg/dL)	4.62, SD 1.03 (178.4, SD 39.9)	4.45, SD 0.93 (171.9, SD 35.8)	4.73, SD 1.36 (182.7, SD 52.6)	4.82, SD 1.14 (186.0, SD 44.0)	5.66, SD 1.33 (218.5, SD 51.4)†	5.30, SD 1.41 (204.6, SD 54.6)†
Median log C-reactive protein level (interquartile range), mg/L	5.1 (1.9, 11.8)	4.9 (2.2, 14.5)	3.8 (1.7, 8.3)	3.6 (1.8, 6.2)	2.7 (1.1, 5.6)	3.2 (1.3, 5.5)
Mean creatinine concentration, μmol/L (mg/dL)	671, SD 265 (7.59, SD 3.00)	643, SD 217 (7.27, SD 2.46)	630, SD 232 (7.13, SD 2.63)	624, SD 215 (7.06, SD 2.43)	648, SD 255 (7.33, SD 2.66)	666, SD 233 (7.53, SD 2.64)

* By analysis of variance for continuous variables or chi-square test or Fisher exact test for categorical variables.

† P values were as follows: intermediate tertile and late referral, 0.025; highest tertile and high school graduate, 0.021; highest tertile and married, 0.007; highest tertile and employed, 0.050; highest tertile and hemoglobin level, 0.007; and highest tertile and total cholesterol level, 0.028.

‡ P < 0.001.

§ Less than 4 months from first evaluation by a nephrologist to initiation of dialysis.

|| Estimated by using the Modification of Diet in Renal Disease equation.

Patients in the highest tertile of propensity for initially receiving peritoneal dialysis had a better case-mix profile than did patients in the lowest tertiles in terms of age ($P < 0.001$), comorbid conditions ($P < 0.001$), residual urine output ($P < 0.001$), and most laboratory data (albumin,

cholesterol, hemoglobin, and C-reactive protein level and calcium-phosphate product, $P < 0.001$). The patients in the highest tertile were also more likely to be white ($P < 0.001$), high school graduates ($P < 0.001$), married ($P = 0.034$), employed ($P < 0.001$), and living more than 30

miles from the clinic ($P < 0.001$) and to have been referred earlier to a nephrologist ($P < 0.001$). However, within each tertile, patients undergoing peritoneal dialysis differed little from those undergoing hemodialysis (Table 2), except that within the highest tertile of propensity score, patients undergoing peritoneal dialysis were more likely to be high school graduates, married, and employed.

Risk for Death among All Patients

At the mean follow-up of 2.4 years, crude mortality rates were 21.2% for patients undergoing peritoneal dialysis and 24.4% for patients undergoing hemodialysis ($P > 0.2$). In the unadjusted analyses, the risk for death was not significantly greater in patients undergoing peritoneal dial-

ysis than those undergoing hemodialysis. However, after adjustment for demographic characteristics, clinical and treatment factors, and laboratory values, the risk for death was significantly greater in patients undergoing peritoneal dialysis (Table 3).

Because the risk for death by dialysis technique appeared to be nonproportional in these adjusted models, we used the same models to assess separately the risk for death associated with dialysis technique during the first and second years of follow-up. For the latter analysis, deaths in the first year of follow-up were censored. Table 3 shows the risk for death during the first 2 years of follow-up. The risk for death did not differ significantly between patients undergoing peritoneal

Table 3. Relative Hazard of Death Associated with Peritoneal Dialysis versus Hemodialysis, from Intention-to-Treat Cox Proportional Hazards Analysis*

Patient Group†	Multivariate Model		Propensity Score Model	
	Total Cohort in All Clinics	Subcohort in Clinics Offering Both Techniques	Total Cohort in All Clinics	Subcohort in Clinics Offering Both Techniques
All patients (n = 1041/609)				
Unadjusted	1.10 (0.80–1.51)	1.45 (0.98–2.15)	1.10 (0.80–1.51)	1.45 (0.98–2.15)
Adjusted				
Demographic characteristics‡	1.25 (0.91–1.73)	1.46 (0.94–2.24)	1.33 (0.96–1.84)	1.64 (1.08–2.48)
Plus clinical/treatment factors§	1.35 (0.97–1.87)	1.56 (1.00–2.44)	1.57 (1.12–2.18)	1.91 (1.25–2.91)
Plus laboratory values	1.61 (1.13–2.30)	2.02 (1.23–3.32)	1.74 (1.23–2.46)	2.14 (1.38–3.32)
By year of follow-up				
First year (n = 1041/609)				
Unadjusted	0.75 (0.37–1.54)	0.77 (0.33–1.81)	0.75 (0.37–1.54)	0.77 (0.33–1.81)
Adjusted				
Demographic characteristics‡	0.92 (0.45–1.89)	0.77 (0.31–1.88)	0.97 (0.47–2.00)	0.94 (0.39–2.26)
Plus clinical/treatment factors§	1.06 (0.51–2.19)	0.84 (0.33–2.14)	1.33 (0.64–2.77)	1.29 (0.52–3.22)
Plus laboratory values	1.39 (0.64–3.06)	1.18 (0.41–3.43)	1.47 (0.69–3.15)	1.55 (0.60–3.96)
Second year (n = 795/478)				
Unadjusted	1.06 (0.59–1.90)	1.25 (0.59–2.64)	1.06 (0.59–1.90)	1.25 (0.59–2.64)
Adjusted for				
Demographic characteristics‡	0.77 (0.31–1.88)	0.77 (0.31–1.88)	1.23 (0.67–2.27)	1.44 (0.66–3.16)
Plus clinical/treatment factors§	0.84 (0.33–2.14)	0.84 (0.33–2.14)	1.47 (0.80–2.72)	1.87 (0.85–4.14)
Plus laboratory values	2.34 (1.19–4.59)	2.52 (0.90–7.04)	2.05 (1.07–3.92)	2.96 (1.25–6.97)
By patient subgroup				
Age < 65 years (n = 664/408)¶	1.67 (1.01–2.75)	1.69 (0.89–3.21)	1.88 (1.16–3.06)	1.74 (1.00–3.05)
Age ≥ 65 years (n = 377/201)¶	1.66 (0.93–2.97)	2.32 (0.84–6.44)	1.67 (0.96–2.90)	2.24 (0.98–5.13)
$P_{interaction}$	>0.2	>0.2	>0.2	>0.2
No diabetes mellitus (n = 480/264)¶	2.78 (1.36–5.68)	3.11 (1.07–9.06)	2.15 (1.09–4.25)	2.84 (1.17–6.91)
Diabetes mellitus (n = 561/345)¶	1.23 (0.79–1.94)	1.28 (0.65–2.50)	1.41 (0.91–2.19)	1.72 (0.97–3.05)
$P_{interaction}$	>0.2	0.096	>0.2	>0.2
No history of cardiovascular disease (n = 447/268)¶	0.83 (0.38–1.81)	1.60 (0.54–4.74)	1.11 (0.54–2.26)	1.44 (0.58–3.60)
History of cardiovascular disease (n = 594/341)¶	2.10 (1.36–3.25)	2.19 (1.17–4.07)	1.74 (1.15–2.65)	1.99 (1.15–3.45)
$P_{interaction}$	0.157	0.086	>0.2	0.033
No residual urine output at baseline (n = 181/107)¶	3.78 (1.33–10.7)**	2.17 (0.55–8.55)**	2.91 (1.04–8.12)	2.38 (0.37–15.1)
Residual urine output at baseline (n = 860/502)	1.15 (0.80–1.64)**	1.59 (0.98–2.59)**	1.69 (1.16–2.48)	2.60 (1.58–4.27)
$P_{interaction}$	>0.2	>0.2	>0.2	>0.2

* All Cox proportional hazards models are stratified by clinic. Multivariate model results are based on Cox models with individual terms for each covariate; propensity score model results are based on Cox models with terms for type of dialysis and propensity score for receiving peritoneal dialysis initially.

† Patients in all clinics/patients in clinics offering both techniques.

‡ Age, sex, ethnicity (white, black, or other), and employment status (employed or not employed).

§ Smoking status (ever smoker or never smoker), Index of Coexistent Disease score, diabetes mellitus status, baseline history of cardiovascular disease, primary cause of renal failure (diabetes, hypertension, glomerulonephritis, or other), late referral to nephrologist (<4 months from first evaluation by nephrologists to initiation of dialysis), body mass index (quartiles), and baseline residual urine output.

¶ Baseline serum albumin level, hemoglobin level, calcium–phosphate product, log C-reactive protein level, total cholesterol level (quartiles), and creatinine concentration.

¶ Models include all demographic, clinical or treatment, and laboratory values.

** Because of the small numbers of events in the subgroups for residual urine output, parsimonious models with only the most influential confounders (age, ethnicity, Index of Coexistent Disease score, and albumin level) were used, to prevent inflation of the estimates.

dialysis and those undergoing hemodialysis during the first year of follow-up. However, after adjustment, the risk for death in patients undergoing peritoneal dialysis was approximately twice that of patients undergoing hemodialysis during the second year of follow-up (Table 3).

Risk for Death, by Tertile of Propensity Score

Within patient subgroups based on tertile of propensity for receiving peritoneal dialysis as the initial treatment, the unadjusted risk for death did not differ between patients undergoing peritoneal dialysis and those undergoing hemodialysis in the highest tertile of propensity (data not shown). After adjustment, among patients in the highest tertile of propensity for receiving peritoneal dialysis (which includes those with an overall better case-mix profile), the risk for death did not differ between those undergoing peritoneal dialysis and those undergoing hemodialysis (relative hazard, 1.17 [95% CI, 0.57 to 2.40]). However, the risk for death was greater in patients undergoing peritoneal dialysis than those undergoing hemodialysis in the lowest and intermediate tertiles of propensity (relative hazard, 2.24 [CI, 0.89 to 5.68] and 2.21 [CI, 1.07 to 4.59], respectively), but the association was statistically significant only for the intermediate tertile. The association of peritoneal dialysis with death did not significantly differ between the lowest and highest tertiles (P for interaction = 0.141) or between the middle and lowest tertiles (P for interaction > 0.2).

Risk for Death in Patient Subgroups

Among patients with cardiovascular disease, the risk for death was approximately twice as high in those undergoing peritoneal dialysis than in those undergoing hemodialysis; however, among patients without cardiovascular disease, no increased risk for death was observed among patients undergoing peritoneal dialysis (P for interaction = 0.157) (Table 3). Similarly, we found no significant interaction by age, diabetes mellitus status, or residual urine output (P for interaction > 0.05) (Table 3). In all analyses, results were consistent across all models (Table 3).

Sensitivity Analyses

We conducted a sensitivity analysis to examine the effect of switching from one type of dialysis to another. In the as-treated model, in which events were assigned to the current treatment in a time-dependent manner, the risk for death was greater in patients undergoing peritoneal dialysis than in those undergoing hemodialysis in the overall sample (relative hazard, 1.41 [CI, 1.00 to 1.98]). Likewise, when we considered the alternative extreme scenario in which all switches in type of dialysis were treated as treatment failures, the risk for death among patients undergoing peritoneal dialysis compared with hemodialysis was even greater (relative hazard, 2.81 [CI, 2.04 to 3.86]). In addition, in analyses that were restricted to patients treated only in clinics offering both types of dialysis, the risk for death was slightly greater compared with the whole cohort

in the as-treated model (relative hazard, 1.56 [CI, 1.00 to 2.45]) and in the model in which switches were considered as treatment failures (relative hazard, 3.35 [CI, 2.21 to 5.07]). Results in the intention-to-treat models were similar (Table 3).

Because patients undergoing peritoneal dialysis in the highest tertile of propensity were more likely to be high school graduates, married, and employed, we ran an additional analysis in which marital status and education were added as predictors of the propensity score (employment was already included). The results for the overall sample and for patients attending clinics offering both types of dialysis were consistent with our main results that were adjusted for propensity score (relative hazard, 1.84 [CI, 1.30 to 2.61] and 2.25 [CI, 1.44 to 3.52]), respectively.

DISCUSSION

In this national prospective cohort study of patients undergoing incident dialysis, those who received peritoneal dialysis had a better case-mix profile at initiation of dialysis than did those who received hemodialysis. After adjustment, the risk for death did not differ between patients undergoing peritoneal dialysis and those undergoing hemodialysis during the first year of treatment. However, after the second year, the risk for death was significantly higher in patients undergoing peritoneal dialysis than in those undergoing hemodialysis.

Several explanations have been proposed for the increased risk for death over time in patients undergoing peritoneal dialysis. First, residual renal function facilitates the regulation of fluid and electrolyte balance and has been linked with improved nutritional status and survival (20–22). Loss of residual renal function and urine output over time in patients undergoing peritoneal dialysis has been associated with an increased mortality rate, possibly because of inadequate dialysis or volume overload (21, 22). Second, loss of ultrafiltration due to increased peritoneal membrane transport characteristics can eventually lead to fluid overload and associated complications, such as hypertension and congestive heart failure (23, 24). Finally, because patients undergoing peritoneal dialysis are usually seen less frequently by their nephrology providers, they may receive less recognition of and attention to comorbid diseases than do patients undergoing hemodialysis. These findings of an increased risk for death over time in nationally recruited patients undergoing peritoneal dialysis compared with patients undergoing hemodialysis are consistent with those of previous studies outside the United States (6, 25) and a geographically limited study within the United States (8).

The increased risk for death in patients undergoing peritoneal dialysis is not uniformly distributed among patients with ESRD. This fact is best demonstrated by our findings based on tertiles of propensity score, or the esti-

mated probability of being treated initially with peritoneal dialysis. The propensity score, an established technique used to address selection bias, helped to further identify patients at increased risk for death while receiving peritoneal dialysis compared with hemodialysis. After stratification by tertile of propensity, the risk for death was higher in patients undergoing peritoneal dialysis than in those undergoing hemodialysis in the lowest and intermediate tertiles, although it was statistically significant only in the intermediate tertile. Of note, patients who had the highest propensity of being treated initially with peritoneal dialysis had an overall better case-mix profile regardless of dialysis technique, and survival did not differ between patients undergoing peritoneal dialysis and those undergoing hemodialysis in this subgroup. The major contributors to the highest propensity of being treated initially with peritoneal dialysis were white ethnicity, employment, lower comorbidity score, higher residual urine output at baseline, and higher serum albumin level at start of dialysis.

We did not confirm the findings of previous studies that reported an increased risk for death associated with peritoneal dialysis among diabetic patients compared with nondiabetic patients and among older patients compared with younger patients (4, 9). This inconsistent result might be related to use of a noncontemporary cohort of patients undergoing dialysis (4), shorter duration of follow-up, and limited adjustment for comorbid conditions in the previous studies (4, 9). However, our finding of no difference in the risk for death between diabetic and nondiabetic patients is supported by more recent studies from Lombardy (26), Canada (6), and the United States (11, 27, 28). Similar to our results, after stratification by age, Foley and colleagues reported no significant difference in the risk for death conferred by peritoneal dialysis versus hemodialysis (6).

The risk for death associated with peritoneal dialysis compared with hemodialysis seemed to be higher in patients with cardiovascular disease at start of dialysis than in those without cardiovascular disease, after adjustment. These results are consistent with findings from retrospective studies that were based on administrative data (11, 28). Several mechanisms have been proposed to explain this increased risk. Accelerated atherosclerosis may occur in patients undergoing peritoneal dialysis because serum levels of lipoprotein(a) (29, 30) and homocysteine (31) and hyperlipidemia (30, 32) are reported to be higher in these patients than in those undergoing hemodialysis. Furthermore, loss of residual renal function and loss of the ultrafiltration capacity of the peritoneal membrane over time in patients undergoing peritoneal dialysis may lead to inadequate dialysis and fluid overload (22–24). In that setting, patients undergoing long-term peritoneal dialysis have been shown to have a higher risk for death from stroke (33) and an increased prevalence of severe left ventricular hypertrophy with hypertension (24, 34, 35) than do patients undergoing hemodialysis.

Our study has limitations. A measure of delivered di-

alysis dose at baseline was available for 76.3% of patients undergoing hemodialysis but only for 26.3% of patients undergoing peritoneal dialysis. The mean delivered dialysis dose (urea kinetics) at baseline was 2.06 (recommended dose of at least 2.0 per week) in patients undergoing peritoneal dialysis and 1.27 (recommended dose of at least 1.2 per session) in patients undergoing hemodialysis. Although our results reflect the doses delivered in routine dialysis practice as part of an effectiveness study rather than adherence to a strict protocol in a randomized clinical trial measuring efficacy, the lack of dialysis dose is a clear limitation. We did not study home hemodialysis performed at a frequency similar to in-center hemodialysis because less than 1% of U.S. dialysis patients use this method (19). Daily home and nocturnal hemodialysis are receiving greater attention and merit rigorous, comparative study. Although a randomized clinical trial would largely overcome other limitations inherent to observational studies, such a study has not yet been feasible, in part because of a very low enrollment rate and other substantial logistic difficulties (36). One such limitation is the extent to which patient outcome reflects differences in treatment versus center. To address this important issue, we ran stratified Cox proportional hazards analyses in which each clinic cluster was its own stratum. Finally, switching of patients from one type of dialysis to another complicates the analysis. The as-treated model would suffer from selection bias if the causes of switches were nonmedical; however, in the CHOICE study, most patients switched type of dialysis because of a specific medical reason (for example, most patients switched from peritoneal dialysis to hemodialysis after peritonitis or ultrafiltration failure, whereas most patients switched from hemodialysis to peritoneal dialysis because of vascular access failure). Another limitation of the as-treated model was that covariates were not available at the time of changes in type of dialysis.

Notwithstanding these limitations, the CHOICE study represents one of the most comprehensive prospective studies to date that compares survival between patients undergoing incident peritoneal dialysis and patients undergoing hemodialysis in the United States. We overcame several limitations reported in other studies by obtaining detailed and precise information on demographic characteristics, clinical and treatment factors, and laboratory values directly from patients, providers, and a systematic chart review process. Furthermore, by studying patients undergoing incident dialysis, we avoided the incidence-prevalence bias seen in cohort studies of prevalent patients. Also, because residual renal function contributes to improved patient survival, the issue of lead-time bias remains important when comparing risk for death between patients undergoing peritoneal dialysis and patients undergoing hemodialysis. Most previous studies have not taken into account baseline residual renal function at initiation of dialysis, with the exception of a recent study from the Netherlands (25). Our data suggest no lead-time

bias because residual renal function at start of dialysis did not differ between patients undergoing peritoneal dialysis and those undergoing hemodialysis. Results were consistent and robust in overall cohort and subgroup analyses across models.

In considering choice of dialysis technique, other issues must be considered. Recent reports suggest that patients undergoing peritoneal dialysis are more satisfied with their care than are patients undergoing hemodialysis and that quality of life is better in some domains for patients undergoing peritoneal dialysis and better in other domains for patients undergoing hemodialysis (37, 38). This finding suggests that tradeoffs may exist among overall satisfaction, quality of life, and survival for patients who choose peritoneal dialysis. Patients should be informed about these tradeoffs and actively participate in decisions about choice of dialysis technique.

In conclusion, results of the CHOICE study suggest that the risk for death does not differ between patients undergoing peritoneal dialysis and those undergoing hemodialysis during the first year of dialysis and that the risk for death with peritoneal dialysis is not uniformly distributed among patients with ESRD. In patients with ESRD who had a better case-mix profile and the highest propensity for initially receiving peritoneal dialysis, survival did not differ by dialysis type. In subgroups, the relative hazard of death with peritoneal dialysis versus hemodialysis was somewhat higher among patients with a history of cardiovascular disease; however, because the interaction between dialysis technique and cardiovascular disease was not statistically significant in all models, we should interpret these results with caution. Further work is needed to define effective therapeutic approaches, such as the use of angiotensin-converting enzyme inhibitors to preserve residual renal function, particularly in patients undergoing peritoneal dialysis (39), and to evaluate a possible survival benefit of a timely switch from peritoneal dialysis to hemodialysis as an integrated approach to dialysis (40).

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APPENDIX

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