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Impact of dialysis modality on survival of new ESRD patients with congestive heart failure in the United States

Austin G. Stack, Donald A. Molony, Noor S. Rahman, Akinsansoye Dosekun, and Bhamidipati Murthy

Division of Renal Diseases and Hypertension, Department of Internal Medicine, University of Texas Health Sciences Center at Houston, Houston, Texas

Impact of dialysis modality on survival of new ESRD patients with congestive heart failure in the United States.

Background. It is hypothesized, but not proven, that peritoneal dialysis might be the optimal treatment for end-stage renal disease (ESRD) patients with established congestive heart failure (CHF) through better volume regulation compared with hemodialysis.

Methods. National incidence data on 107,922 new ESRD patients from the Center for Medicare and Medicaid Services (CMS) Medical Evidence Form were used to test the hypothesis that peritoneal dialysis was superior to hemodialysis in prolonging survival of patients with CHF. Nonproportional Cox regression models evaluated the relative hazard of death for patients with and without CHF by dialysis modality using primarily the intent-to-treat but also the as-treated approach. Diabetics and nondiabetics were analyzed separately.

Results. The overall prevalence of CHF was 33% at ESRD initiation. There were 27,149 deaths (25.2%), 5423 transplants (5%), and 3753 (3.5%) patients lost to follow-up over 2 years. Adjusted mortality risks were significantly higher for patients with CHF treated with peritoneal dialysis than hemodialysis [diabetics, relative risk (RR) = 1.30, 95% confidence interval (CI) 1.20 to 1.41; nondiabetics, RR = 1.24, 95% CI 1.14 to 1.35]. Among patients without CHF, adjusted mortality risk were higher only for diabetic patients treated with peritoneal dialysis compared with hemodialysis (RR = 1.11, 95% CI 1.02 to 1.21) while nondiabetics had similar survival on peritoneal dialysis or hemodialysis (RR = 0.97, 95% CI 0.91 to 1.04).

Conclusion. New ESRD patients with a clinical history of CHF experienced poorer survival when treated with peritoneal dialysis compared with hemodialysis. These data suggest that peritoneal dialysis may not be the optimal choice for new ESRD patients with CHF perhaps through impaired volume regulation and worsening cardiomyopathy.

Recent mortality comparisons of peritoneal dialysis and hemodialysis among new end-stage renal disease (ESRD) patients have suggested that survival on peritoneal dialysis is at least similar to that of hemodialysis if not better within the first 2 years of therapy [1–3]. Accordingly, the general consensus is that peritoneal dialysis and hemodialysis can be viewed as "equivalent therapies" and therefore either modality may be used as primary therapy for most newly diagnosed patients provided there are no contraindications [4]. There has been speculation, however, that the type and nature of dialysis treatment provided to ESRD patients may play a pathogenetic role in enhancing cardiovascular disease progression and cardiovascular mortality, especially among those with preexisting cardiac conditions [5–9].

Given that cardiac disease is the leading cause of death in this population, defining the optimal modality strategy for new ESRD patients, especially those with preexisting cardiac disease, may help reduce future morbidity and mortality. In a recent publication, we have shown that the survival of patients at ESRD onset with known coronary artery disease (CAD) differs with respect to treatment modality [10]. Patients with CAD had significantly poorer survival at 2 years when treated with peritoneal dialysis compared with hemodialysis. These data suggested that peritoneal dialysis, as currently practiced, might not be the optimal choice for new ESRD patients with preexisting CAD possibly because of accelerated cardiovascular disease.

It is widely assumed, but not proven, that ESRD patients with congestive heart failure (CHF) benefit more from peritoneal dialysis than from hemodialysis. Most observations supporting the role of peritoneal dialysis as an efficient volume control therapy have come from single-center studies in the general population [11–15]. These have shown that, among patients with refractory CHF, the choice of peritoneal dialysis is associated with significantly lower hospitalization rates and improved functional status compared with medical therapy. Among ESRD patients with CHF, it is unclear whether peritoneal dialysis confers a survival advantage over hemodialysis. Theoretically, peritoneal dialysis may be superior

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to hemodialysis in regulating volume control and preventing further structural cardiac impairment because of continuous ultrafiltration and fewer hemodynamic consequences. The purpose of this study was to explore the hypothesis that patients new to ESRD with a history of CHF experience greater survival with peritoneal dialysis compared to hemodialysis.

METHODS

Data

This hypothesis was tested in a historical prospective cohort of new ESRD patients in the United States, initiated on dialysis between May 1, 1995 and July 31, 1997. Data sufficient for these analyses were obtained from the Standard Analysis Files (SAFs) of the United States Renal Data System (USRDS). The Medical Evidence SAF is derived from the Center for Medicare and Medicaid Services (CMS) Medical Evidence Form, a government document that is completed for all new patients initiated on dialysis [16]. The CMS form records data on demographic characteristics, comorbid conditions, laboratory indices, date of first dialysis, and type of treatment provided for all incident patients. CHF was defined on the presence or absence of this condition from the Medical Evidence Form. Covariates representing the following conditions were also included: age (modeled as a continuous variable), gender (male vs. female), race (white, black, Asian versus other), ethnicity (Hispanic versus non-Hispanic), diabetes (defined as a cause of ESRD), diabetes (as cause of ESRD or recorded comorbid condition), history of hypertension, CAD (defined as a history of prior CAD, myocardial infarction, angioplasty or coronary artery bypass graft), history of cardiac arrythmia or cardiac arrest, cerebrovascular disease (defined as a history of prior cerebrovascular accident or transient ischemic attack), history of chronic lung disease, tobacco use, malignant neoplasm or cancer, and acquired immunodeficiency syndrome (AIDS). Body mass index (BMI) was calculated from the equation: BMI = weight (kg)/height (m^2). In addition, data were also available for the following laboratory indices: serum creatinine, blood urea nitrogen, serum albumin, and hematocrit. Residual renal function at ESRD initiation was estimated from the Modification of Diet in Renal Disease (MDRD) formula [17].

Treatment modality, hemodialysis or peritoneal dialysis for each patient was determined from the USRDS Treatment History SAF [18]. The USRDS uses a complex analytic process from a variety of data sources to determine dialysis modality at ESRD onset and at any point in time thereafter. These data sources include the Medical Evidence Form, the Quarterly Dialysis File, and the Medicare Claims Files. Any switches in treatment modality, from hemodialysis to peritoneal dialysis or peritoneal dialysis to hemodialysis during follow-up are recorded in the data files and can be used to define the total period for which patients remained on a specific therapy. The definition of switch was based on the 60-day rule as suggested by the USRDS. This rule requires that a patient be on a new modality for at least 60 days before it is considered to be a change in modality [18]. The study start date for all incident patients was defined as *day 90 of ESRD*. The reasons for this are twofold. First, many patients younger than 65 do not become eligible for Medicare for up to 90 days and therefore may have incomplete claims data prior to this. Second, the 90-day rule is important for patients whose final modality is peritoneal dialysis but who have been placed temporarily on hemodialysis until peritoneal dialysis training has been completed. The Medical Evidence Form and Treatment History datasets were merged with mortality and transplantation data from the USRDS. This allowed merging of data on date of death and date of renal transplantation by USRDS identification number for each member of the study.

Patient population

There were 158,685 patients, age 18 years and older, who were initiated on dialysis from May 1, 1995 to July 31, 1997. Patients were excluded from the analysis if they had received a renal transplant within the first 90 days of ESRD initiation, if modality assignment could not be determined at day 90 of ESRD, or if data were missing on demographic, comorbid, and laboratory variables of interest. Following exclusions, there were 107,922 adult patients available for this analysis.

Analytic methods

Time-dependent Cox regression equations compared the mortality risks of hemodialysis with peritoneal dialysis in patients with and without CHF with adjustment for potential confounders. Covariates for adjustment included age at study start, gender (male versus female), race (white versus other race), hypertension, peripheral vascular and cerebrovascular disease, tobacco use, chronic obstructive lung disease, history of cardiac arrest/arrhythmia, AIDS, neoplasm, BMI, serum albumin, hematocrit, estimated glomerular filtration rate (GFR), and pre-ESRD erythropoietin use.

Patient survival times on peritoneal dialysis and hemodialysis were compared at successive 6-month intervals during follow-up and censored at death, loss to follow-up, or at the end of 2 years, whichever came first. "Intent-to-treat" and "as-treated" models evaluated the association of treatment modality with mortality risk in patients with and without CHF. In the "intent-to-treat" analyses, patients were not censored if they changed treatment modality during follow-up and patient death was assigned to the initial treatment modality. In the "as-treated" analyses, patients were censored from contributing additional

Table 1. Characteristics of the study population at end-stage renal disease (ESRD) onset from the Center for Medicare and Medicaid Services (CMS) Medical Evidence Report Form ($N = 107,922$)

Patient characteristics	Study population $N = 107,922$	Hemodialysis $N = 93,900$	Peritoneal dialysis $N = 14,022$
Demographics			
Age of onset of ESRD (mean years ± SD)	61.5 ± 15.3	62.3 ± 15.2	56.5 ± 15.2[f]
Race			
% White	63.4	62.0	73.4[f]
% Black	31.1	32.6	20.8[f]
% Asian	3.7	3.6	4.2[e]
Gender *% male*	53	52.8	53.8[d]
Cause of ESRD *% diabetes*	44.3	44.0	46.1[f]
Laboratory values (mean + SD)			
Serum albumin *g/dL*	3.2 ± 0.7	3.2 ± 0.65	3.4 ± 0.64[f]
Hematocrit *%*	28.1 ± 5.3	27.9 ± 5.3	29.3 ± 5.3[f]
Glomerular filtration rate (MDRD) *mL/min*[a]	7.0 ± 2.8	7.0 ± 2.8	7.3 ± 2.8[f]
Comorbid conditions *% yes*			
Diabetes (history and/or nephropathy)	39.3	39.4	38.7
Hypertension	72.6	72.5	73.2
Coronary artery disease[b]	25.9	26.4	22.7[f]
Myocardial infarction	8.9	9.0	8.4[d]
Cardiac arrest/dysrhythmia	6.4	6.5	5.3[f]
Congestive heart failure	32.7	33.9	24.7[f]
Cerebrovascular disease	8.9	9.3	6.7[f]
Peripheral vascular disease[c]	14.6	15.0	12.1[f]
Chronic obstructive lung disease	6.9	7.3	4.4[f]
Tobacco use	6.2	6.2	6.4
AIDS	0.55	0.57	0.41[d]
Neoplasm	4.9	5.2	3.0[f]
Body mass index (mean kg/m^2 ± SD)	25.7 ± 5.8	25.6 ± 5.9	25.9 ± 5.3[f]

[a] At first dialysis per MDRD formula [17]
[b] Includes history of coronary artery disease, myocardial infarction, coronary artery bypass surgery, angioplasty or abnormal angiography
[c] Includes a history of peripheral vascular disease amputation, intermittent claudication or absent pulses
[d] $P < 0.05$; [e] $P < 0.01$; [f] $P < 0.001$ for bivariate comparisons

time at risk when they switched from one modality of treatment to another. Moreover, the "as-treated" data allowed us to evaluate the mortality risks of patients who switched from one modality to another during the follow-up period by comparing survival times of patients who switched from peritoneal dialysis to hemodialysis (HD_{new}) and from hemodialysis to peritoneal dialysis (PD_{new}) with those remaining on peritoneal dialysis (PDo) or hemodialysis (HDo) since ESRD start. Diabetics and nondiabetics were analyzed in separate models as prior studies have shown nonproportional hazards. Statistic analyses were performed using SAS statistical software (Version 8.0 SAS Institute, Cary, NC, USA).

RESULTS

Baseline characteristics of the study cohort

The study cohort consisted of 107,922 patients who were initiated on dialysis between May 1, 1995 and July 31, 1997. Table 1 illustrates the characteristics of the entire cohort at study entry and according to the initial mode of dialysis. Hemodialysis was the initial modality for 93,900 (87%), peritoneal dialysis for 14,022 (13%) and the prevalence of CHF was 33%. The average age at onset of ESRD was 61.5 ± 15 years, 63% were white, 53% were male, and 44% had ESRD from diabetes. The demographic and clinical characteristics of patients excluded as a result of incomplete or missing data were nearly identical to those of the study population. At baseline, patients on peritoneal dialysis differed from those on hemodialysis with respect to demographic and comorbid characteristics. Patients treated with peritoneal dialysis were younger in age and had fewer comorbid conditions than their hemodialysis counterparts. Overall, peritoneal dialysis patients had significantly lower prevalence of CAD (22.7% versus 26.4%), CHF (24.7% versus 33.9%), cerebrovascular disease (6.7% versus 9.3%), peripheral vascular disease (12.1% versus 15.0%), chronic lung disease (4.4% versus 7.3%), and cancer (3.0% versus 5.2%). Moreover, peritoneal dialysis–treated patients had significantly higher hematocrit (29.3% ± 5.3% versus 27.9% ± 5.3%), and albumin levels (3.4 g/dL ± 0.64 g/dL versus 3.2 g/dL ± 0.65 g/dL) and greater residual renal function at ESRD onset compared to patients treated with hemodialysis (7.3 mL/min ± 2.8 mL/min versus 7.0 mL/min ± 2.8 mL/min). Table 2 compares the characteristics of patients with and without CHF by treatment modality. The distribution of patients characteristics among patients without CHF treated with peritoneal dialysis were similar to that of the overall peritoneal dialysis cohort with fewer comorbid conditions and better laboratory indices among these peritoneal dialysis patients com-

Table 2. Characteristics of patients with and without congestive heart failure (CHF) by treatment modality at end-stage renal disease (ESRD) onset (N = 107,922)

	CHF present (N = 35,285)		CHF absent (N = 72,637)	
Patient characteristics	Hemodialysis (N = 31,824)	Peritoneal dialysis (N = 3461)	Hemodialysis (N = 62,076)	Peritoneal dialysis (N = 10,561)
Demographics				
Age of onset of ESRD (mean years ± SD)	67.1 ± 12.4	63.5 ± 12.6[e]	59.8 ± 15.9	54.3 ± 15.3
Race				
% White	68.2	79.8[e]	58.7	71.3[e]
% Black	27.4	16.4[e]	35.3	22.3[e]
% Asian	3.0	2.6	4.7	4.0[d]
Gender *% male*	49.5	53.5[e]	54.6	53.9
Cause of ESRD *% diabetes*	54.1	60.4[e]	38.8	41.7[e]
Laboratory Values (mean + SD)				
Serum albumin *g/dL*	3.1 ± 0.61	3.3 ± 0.60[e]	3.2 ± 0.67	3.5 ± 0.65[e]
Hematocrit %	28.3 ± 5.1	29.8 ± 5.2[e]	27.7 ± 5.4	29.2 ± 5.4[e]
Glomerular filtration rate (MDRD) *mL/min*[a]	7.7 ± 2.9	8.2 ± 3.0[e]	6.7 ± 2.6	7.0 ± 2.6[e]
Comorbid Conditions (% yes or suspected)				
Diabetes (history and/or nephropathy)	50.8	53.3[d]	33.5	33.9
Hypertension	79.2	78.8	69.0	71.4[e]
Cardiac arrest/dysrhythmia	12.5	12.9	3.4	2.8[d]
Coronary artery disease	46.3	49.3[d]	16.2	14.0[e]
Cerebrovascular disease	12.6	11.2[c]	7.6	5.3[e]
Peripheral vascular disease[b]	24.9	25.4[c]	10.0	7.8[e]
Chronic lung disease	12.4	9.5[e]	4.6	2.7[e]
Tobacco use	6.5	6.1	6.4	6.1
AIDS	0.18	0.23	0.78	0.47[d]
Neoplasm	5.1	3.6[e]	5.3	2.8[e]
Body mass index (mean kg/m^2 ± SD)	25.7 ± 5.9	25.8 ± 5.3	25.6 ± 5.9	25.9 ± 5.3[e]

[a] At first dialysis per MDRD formula [17]
[b] Includes a history of peripheral vascular disease amputation, intermittent laudication or absent foot pulses
[c] $P < 0.05$; [d] $P < 0.01$; [e] $P < 0.001$ for bivariate comparisons in each CHF category

pared to hemodialysis patients. In contrast, among patients with CHF, the distribution of comorbid conditions in peritoneal dialysis and hemodialysis-treated patients were similar with some exceptions. CAD (49.3% versus 46.3%), peripheral vascular disease (25.4% versus 24.9%), and diabetes (53.3% versus 50.8%) were more common in the peritoneal dialysis group.

Patient survival

The median follow-up was 12 months; 27,149 (25.2%) patients died, 5423 (5%) were transplanted, and 3753 (3.5%) patients were lost to follow-up within the 2-year period. Adjusted Cox survival curves were estimated for peritoneal dialysis and hemodialysis-treated patients in each CHF category as shown in Figures 1 and 2. Overall survival was significantly poorer for new ESRD patients with CHF compared to those without CHF in both the diabetic (Fig. 1) and nondiabetic (Fig. 2) cohorts. For diabetic patients with CHF, the survival curves begin to diverge at 6 months and continue thereafter with significantly poorer survival for peritoneal dialysis–treated patients. For diabetics without CHF, there was an early increased hazard for hemodialysis patients (during the first 9 months of therapy); however, survival curves crossed after 9 months with a less favorable outcome for peritoneal dialysis patients observed thereafter. For nondiabetics with CHF, the estimated survival functions were almost identical to those for diabetic CHF patients.

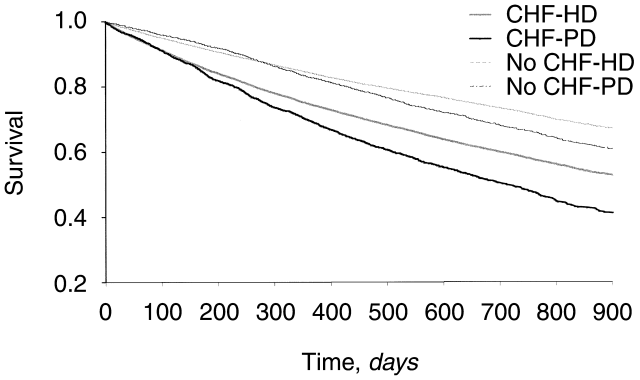

Fig. 1. Adjusted Cox survival curves for new diabetic end-stage renal disease (ESRD) patients with and without congestive heart failure (CHF) treated with peritoneal dialysis (PD) versus hemodialysis (HD). Adjusted for age at study start, gender, race, cause of ESRD, hypertension, coronary artery disease (CAD), peripheral vascular and cerebrovascular disease, tobacco use, chronic lung disease, acquired immunodeficiency syndrome (AIDS), neoplasm, serum albumin, body mass index (BMI), hematocrit, estimated glomerular filtration rate (GFR), and pre-ESRD erythropoietin use. For CHF, PD/HD comparison, $P < 0.0001$; no CHF PD/HD comparison, $P < 0.01$.

In contrast, among nondiabetic patients without CHF, survival curves were almost superimposed.

Mortality risk predictors in new ESRD patients

The relationship between treatment modality and subsequent mortality risk was explored for the entire cohort and the unadjusted and adjusted hazard ratios with 95%

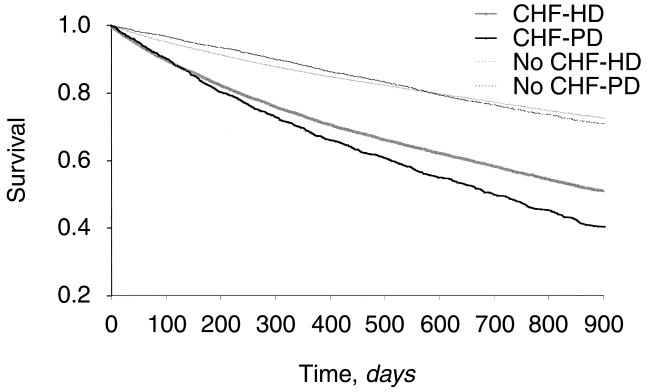

Fig. 2. Adjusted Cox survival curves for new nondiabetic end-stage renal disease (ESRD) patients with and without congestive heart failure (CHF) treated with peritoneal dialysis (PD) versus hemodialysis (HD). Adjusted for age at study start, gender, race, cause of ESRD, hypertension, coronary artery disease (CAD), peripheral vascular and cerebrovascular disease, tobacco use, chronic lung disease, acquired immunodeficiency syndrome (AIDS), neoplasm, serum albumin, body mass index (BMI), hematocrit, estimated glomerular filtration rate (GFR), and pre-ESRD erythropoietin use. For CHF, PD/HD comparison, $P < 0.0001$; no CHF PD/HD comparison, P = NS.

confidence intervals (95% CI) for each covariate are given in Table 3. The relative risk of death for peritoneal dialysis versus hemodialysis varied significantly over time. The unadjusted analysis found a lower risk of death for peritoneal dialysis compared to hemodialysis-treated patients up to 12 months' follow-up, an equalization of risk at between 12 and 18 months and significantly higher risk of death during 18 to 24 months [relative risk (RR) = 1.11, 95% CI 1.01 to 1.21]. With adjustment, however, the benefit of peritoneal dialysis over hemodialysis was observed only in the first 6 months of dialysis, after which peritoneal dialysis patients experienced significantly higher mortality risk compared to their hemodialysis counterparts (RR = 1.15, 1.28, and 1.37 at each 6-month interval, respectively, $P < 0.001$).

Mortality risks of peritoneal dialysis and hemodialysis in patients with and without CHF: Intent-to-treat

The finding of significant interactions between treatment modality, CHF, and survival, as well as treatment modality, diabetes, and survival ($P < 0.001$ for each) permitted us to investigate these relationships further in a series of time-dependent Cox regression models stratified by diabetes and CHF. The unadjusted and adjusted RR estimates are presented in Table 4.

Among diabetics with CHF, the unadjusted mortality risk of peritoneal dialysis versus hemodialysis varied over time and was significantly higher for peritoneal dialysis patients between 6 and 24 months of follow-up. With adjustment for differences in demographic factors, measures of nutrition, and cardiovascular conditions between peritoneal dialysis and hemodialysis, an even stronger relationship was evident with significantly higher mortality risk for peritoneal dialysis–treated patients (RR = 1.14, 1.37, 1.50, and 1.39 at each successive 6-month time period, respectively). A similar pattern in risk was observed among diabetics without CHF with higher death risk between 6 and 24 months of follow-up.

Among nondiabetics, the modality × CHF interaction with mortality was also highly significant ($P < 0.0001$), indicating that the impact of dialysis treatment on survival was different in patients with and without CHF. In the stratified analysis, patients with CHF treated with peritoneal dialysis had significantly higher adjusted mortality risk compared to those who received hemodialysis between 6 and 24 months of follow-up (RR = 1.11, 1.28, 1.35, and 1.47 at each successive 6-month interval, respectively). Similarly, the hazard ratios of peritoneal dialysis versus hemodialysis in nondiabetic patients without clinical CHF also varied over time but in contrast peritoneal dialysis–treated patients experienced a lower mortality risk during the first 6 months, similar risk between 6 and 12 months, and significantly higher risk between 12 and 24 months compared to hemodialysis-treated patients (RR = 0.79, 1.01, 1.20, and 1.36 at each successive 6-month period, respectively).

Mortality risks of peritoneal dialysis and hemodialysis in patients with and without CHF: As-treated analysis

The results of the time-dependent as-treated analyses mirrored those of the intent-to-treat analysis and are presented in Table 5. Among diabetics with CHF, the adjusted mortality risk was significantly higher for peritoneal dialysis patients who remained on this therapy during follow-up (PDo/HDo = 1.29, $P < 0.0001$) and for patients who switched therapies either from peritoneal dialysis to hemodialysis (HD_{new}/HDo = 1.50, $P < 0.0001$) or from hemodialysis to peritoneal dialysis (PD_{new}/HDo = 1.72, $P < 0.0001$) compared to those who remained on hemodialysis from ESRD start. For diabetics without CHF who did not switch; survival was similar either on PDo or HDo (RR = 1.02, P = NS), while those who switched from peritoneal dialysis to hemodialysis and from hemodialysis to peritoneal dialysis had substantially higher mortality risks, by 72% and 39%, respectively. Among nondiabetics stratified by CHF, the results of the as-treated analysis again paralleled those of the intent-to treat analysis. In the CHF subgroup, PDo patients experienced a 21% higher mortality risk compared to HDo patients during follow-up, while those who switched therapies had substantially greater risks, 54% (HD_{new}) and 45% (PD_{new}), respectively. In contrast, PDo patients in the non-CHF group had a 10% lower mortality risk compared to HDo patients following adjustment, while those who switched had significantly greater risks, 46% for HD_{new} and 28% for PD_{new}.

Several sensitivity analyses evaluated the robustness of our observations. First, we repeated the regression

Table 3. Predictors of all-cause mortality in new end-stage renal disease (ESRD) patients in the United States ($N = 107,922$)

Patient characteristics	Unadjusted relative risk[a]	95% CI	Adjusted relative risk[a]	95% CI
Demographics				
Age of onset of ESRD *years*	1.04	1.035–1.037[h]	1.03	1.030–1.032[h]
White race (nonwhite)	1.53	1.49–1.57[h]	1.25	1.22–1.29[h]
Male gender (female)	1.02	0.99–1.04	0.99	0.97–1.02
Diabetic ESRD (all other causes)	1.10	1.08–1.13[h]	1.08	1.05–1.11[h]
Laboratory values				
Serum albumin *per 1 g/dL*	0.75	0.73–0.76[h]	0.72	0.71–0.73[h]
Hematocrit *per 1%*	1.02	1.015–1.020[h]	1.01	1.010–1.014[h]
Glomerular filtration rate (MDRD) *per mL/min*[b]	1.08	1.07–1.08[h]	1.05	1.046–1.055[h]
Comorbidity (yes or suspected versus no)				
Coronary artery disease[c]	1.68	1.64–1.73[h]	1.11	1.08–1.14[h]
Cardiac arrest/dysrhythmia	1.86	1.78–1.93[h]	1.18	1.14–1.23[h]
Congestive heart failure	1.72	1.68–1.76[h]	1.26	1.23–1.29[h]
Cerebrovascular disease	1.58	1.53–1.64[h]	1.18	1.13–1.22[h]
Peripheral vascular disease[d]	1.66	1.61–1.71[h]	1.18	1.14–1.22[h]
Chronic obstructive lung disease	1.82	1.75–1.90[h]	1.24	1.19–1.29[h]
Tobacco use	1.01	0.96–1.07	1.03	0.98–1.09
AIDS	2.62	2.33–2.95[h]	4.91	4.37–5.52[h]
Neoplasm	1.81	1.73–1.90[h]	1.42	1.36–1.49[h]
Body mass index (per kg/m^2)	0.963	0.960–0.965[h]	0.98	0.974–0.978[h]
Pre-ESRD care				
Erythropoeitin use (yes vs no)	0.90	0.87–0.93[h]	0.86	0.84–0.89[h]
Dialysis modality				
Peritoneal dialysis versus hemodialysis (reference)[e]				
0–6 months	0.69	0.65–0.73[h]	0.92	0.87–0.98[h]
6–12 months	0.91	0.86–0.97[g]	1.15	1.08–1.23[h]
12–18 months	1.06	0.99–1.13	1.28	1.19–1.38[h]
18–24 months	1.11	1.01–1.21[f]	1.37	1.25–1.51[h]
0–24 months	0.83	0.80–0.87[h]	1.11	1.07–1.16[h]

[a] Unadjusted and adjusted relative risks for all covariates in the study population
[b] At first dialysis per MDRD formula [17]
[c] Includes history of coronary artery disease, myocardial infarction, coronary artery bypass surgery, angioplasty, or abnormal angiography
[d] Includes a history of peripheral vascular disease amputation, intermittent claudication, or absent foot pulses
[e] Relative risks for peritoneal dialysis versus hemodialysis were estimated at each successive 6-month interval. A separate model found significant interactions between modality × congestive heart failure (CHF) ($P < 0.0001$) and modality × diabetes ($P < 0.0001$) when included in the adjusted model.
[f] $P < 0.05$; [g] $P < 0.01$; [h] $P < 0.001$ compared to a relative risk of 1.00

Table 4. Relative risk of death for peritoneal dialysis (PD) versus hemodialysis (HD) among incident end-stage renal disease (ESRD) patients with and without preexisting congestive heart failure (CHF): Intent-to treat analysis

	CHF relative risk (PD/HD)		No CHF relative risk (PD/HD)	
Time *months*	Unadjusted	Adjusted (95% CI)	Unadjusted	Adjusted (95% CI)
Diabetic population				
0–6	1.05 (0.94, 1.18)	1.14 (1.01, 1.28)[a]	0.68 (0.60, 0.78)[c]	0.93 (0.82, 1.07)
6–12	1.28 (1.12, 1.46)[c]	1.37 (1.20, 1.57)[c]	1.07 (0.94, 1.21)	1.31 (1.16, 1.49)[c]
12–18	1.45 (1.25, 1.69)[c]	1.50 (1.29, 1.75)[c]	1.17 (1.02, 1.34)[a]	1.39 (1.21, 1.61)[c]
18–24	1.35 (1.09, 1.65)[a]	1.39 (1.12, 1.72)[b]	1.12 (0.93, 1.34)	1.32 (1.09, 1.60)[b]
0–24	1.21 (1.12, 1.31)[c]	1.30 (1.20, 1.41)[c]	0.86 (0.80, 0.93)[c]	1.11 (1.02, 1.21)[a]
Non diabetic population				
0–6	0.96 (0.85, 1.09)	1.11 (0.98, 1.26)	0.53 (0.48, 0.58)[c]	0.79 (0.71, 0.87)[c]
6–12	1.12 (0.97, 1.29)	1.28 (1.10, 1.48)[b]	0.73 (0.65, 0.81)[c]	1.01 (0.90, 1.13)
12–18	1.18 (0.99, 1.41)[a]	1.35 (1.13, 1.61)[c]	0.93 (0.83, 1.05)	1.20 (1.06, 1.35)[b]
18–24	1.36 (1.10, 1.68)[b]	1.47 (1.18, 1.83)[c]	1.07 (0.93, 1.22)	1.36 (1.18, 1.57)[c]
0–24	1.07 (0.99, 1.16)	1.24 (1.14, 1.35)[c]	0.69 (0.65, 0.74)[c]	0.97 (0.91, 1.04)

[a] $P < 0.05$; [b] $P < 0.01$; [c] $P < 0.001$ compared to a relative risk of 1.00

analyses in which we adjusted only for objective measures of disease at ESRD onset, namely, serum albumin (an index of cumulative comorbidity), hematocrit, residual renal function, and BMI. Second, as we recently have shown an effect modification between dialysis modality and CAD with mortality, it is possible that a high correlation of CAD with CHF could give rise to similar results and therefore bias our analyses [10]. For this reason we repeated our analyses in another series of statistic models excluding patients with a history of CAD from the original cohort. Finally, we considered the possibility of selection bias due to differences in the rates of renal transplantation between peritoneal dialysis and hemodialysis groups, differences that may result in "healthier" peritoneal dialysis patients receiving a renal transplant while leaving a relatively "sicker" fraction on peritoneal dial-

Table 5. Relative risk of death for peritoneal disease (PD) versus hemodialysis (HD) among incident end-stage renal disease (ESRD) patients with and without preexisting congestive heart failure (CHF): As-treated analysis[a]

	CHF relative risk		No CHF relative risk	
Modality	Unadjusted	Adjusted	Unadjusted	Adjusted
Diabetic population				
HDo (reference) [1]	1.00	1.00	1.00	1.00
PDo[a]	1.20[f]	1.29[f]	0.78[f]	1.02
PD > HD_{new}[b]	1.38[f]	1.50[f]	1.35[f]	1.72[f]
HD > PD_{new}[c]	1.58[f]	1.72[f]	1.22[d]	1.39[f]
Nondiabetic population				
HDo (reference)[a]	1.00	1.00	1.00	1.00
PDo[a]	1.05	1.21[d]	0.62[f]	0.90[e]
PD > HD_{new}[b]	1.32[e]	1.54[f]	1.14[d]	1.46[f]
HD > PD_{new}[c]	1.34[f]	1.45[f]	1.03	1.28[f]

[a] The as-treated analyses compared the mortality risks of patients who switched from one modality to another during the follow-up with those remaining on PD (PDo) or HD (HDo) since ESRD start

[b] (HD_{new}), patients who switched from PD to HD

[c] (PD_{new}), patients who switched from HD to PD. Model adjusted for all covariates listed in Table 2.

[d] $P < 0.05$; [e] $P < 0.01$; [f] $P < 0.001$ compared to a relative risk of 1.00

ysis. In each additional analysis, the association of peritoneal dialysis with higher mortality risk among patients with CHF persisted (data not shown).

DISCUSSION

Despite the widely held opinion that peritoneal dialysis might be the better choice for new ESRD patients with CHF given its positive effect on hemodynamic stability and volume regulation, this study suggests the contrary. Compared with hemodialysis, the selection of peritoneal dialysis was associated with significantly higher mortality risks among new ESRD patients with a history of CHF. The results were consistent in both diabetic and nondiabetic subgroups, remained significant even after a comprehensive adjustment for differences in measurable baseline comorbidity and differences in transplantation rates, and were confirmed in both "intent to treat" and "as-treated" analyses. Moreover, this study demonstrates that switches in modality therapy occurring after dialysis initiation, independent of the direction of switch, are associated with a worsened survival. These findings suggest that the utilization of peritoneal dialysis among ESRD patients with documented CHF may adversely affect patient survival.

The increased mortality risk among CHF patients treated with peritoneal dialysis was not constant over time but increased with follow-up. Among diabetics with CHF, the risk increased from 14% during the first 6 months to almost 40% at the end of the final 6 months of the 2-year observation period. Similarly, for nondiabetics with CHF, the relative risk of death increased from 11% in the first 6 months to 47% in the final 6 months. These findings suggest that the deleterious effect of peritoneal dialysis on survival of ESRD patients with CHF is a time-dependent phenomenon and suggest that the mechanism(s) through which this increased mortality occurs may also be a function of time. The negative impact of peritoneal dialysis on survival was also observed in the diabetic group without CHF, at least in the "intent-to-treat" analysis. However, the finding of similar survival in the "as-treated" model suggests that the negative impact of peritoneal dialysis in the "intent-to treat" may be due to crossovers from hemodialysis who are doing poorly and argue against a selective peritoneal dialysis disadvantage. Moreover, the finding of a survival advantage among nondiabetic patients without CHF in favor of peritoneal dialysis (albeit modest) suggests that peritoneal dialysis is at least comparable to hemodialysis for a large segment of the incident ESRD population.

Previous comparisons of peritoneal dialysis- and hemodialysis-treated patients have not compared survival outcomes in high-risk subgroups, especially those with preexisting cardiovascular disease. Given the epidemic of cardiovascular disease among newly diagnosed ESRD patients, defining the optimal modality strategy in these groups might reduce future morbidity and mortality [19, 20]. The current study demonstrates a very significant effect modification between dialysis modality, CHF, and mortality in the nonrandomized observational setting. This study does not, however, provide evidence for the mechanism of increased mortality among peritoneal dialysis–treated patients. There are, however, several possibilities. First, the apparent short-term benefit of peritoneal dialysis in maintaining volume control in CHF patients through ultrafiltration may be offset by the long-term negative impact of peritoneal dialysis on cardiac performance. Prospective comparisons of peritoneal dialysis and hemodialysis patients have shown significantly more left ventricular hypertrophy and poorer left ventricular function among peritoneal dialysis–treated patients [5, 6, 21]. These deleterious consequences may in part be due to alterations in peritoneal transport patterns occurring over time in peritoneal dialysis–treated patients resulting in inadequate regulation of fluid balance

[22]. Second, the loss of residual renal function and urine volume over time among peritoneal dialysis–treated patients may further compromise overall volume regulation and explain in part the deleterious effect of peritoneal dialysis on survival [23, 24]. Indeed the time-dependent increase in death risk with peritoneal dialysis as shown in our study might correlate with the known rates of decline in residual renal function and membrane transport characteristics that are seen in peritoneal dialysis–treated patients [25, 26]. Finally, it is also possible that several other factors such as accelerated atherosclerosis, increased infection rates, or specific differences in aspects of delivered clinical care between peritoneal dialysis and hemodialysis might be responsible for the observed mortality differences. Whatever the mechanism, our results shown that despite the putative benefits of peritoneal dialysis, the choice of hemodialysis confers a significant survival advantage.

The optimal study design for comparing peritoneal dialysis and hemodialysis treatment modalities would be a randomized controlled clinical trial. This choice of experimental design would ensure that any differences in outcomes seen on follow-up would be solely due to one treatment or the other. In the ideal setting, this experimental design would virtually remove "treatment by indication" bias or "selection bias" described above insuring that the patients assigned to the respective treatment modalities are approximately equivalent with respect to all extraneous factors, regardless as to whether these factors are known to the researcher [27, 28]. However, given the logistic, feasibility, methodologic, and financial concerns in designing and executing such a study, the nonrandomized observational approach provides a reasonably robust alternative scientific strategy. However, such a study has inherent limitations. First, it cannot replace the randomized controlled clinical trial and therefore comparisons based on observational data may be subject to several biases and lead to conflicting results [1, 29–33]. These include selection bias between hemodialysis and peritoneal dialysis, survival bias from analyses of "prevalent" over "incident" cohorts, and statistic bias that fail to account for time-dependent effects of treatment modality on mortality [34, 35]. In an attempt to overcome some of these limitations and permit unbiased comparisons, we based our analyses on a nationally representative cohort of newly diagnosed patients. We adjusted for several baseline differences present between comparison groups. Indeed, our analyses show that patients assigned to peritoneal dialysis had on average lower comorbidity levels, better laboratory values, and greater residual renal function at ESRD onset than those assigned to hemodialysis, favoring greater survival in the peritoneal dialysis group. Finally, we have based our observations on both "intent-to treat" as well as "as-treated" analyses, thereby reducing bias resulting from switches in treatment modalities during follow-up.

An additional concern in our study was the possible underreporting of comorbid conditions from the CMS Evidence Form, especially CHF, as this was our principal stratifying variable [36]. In addition, differential reporting of medical conditions in hemodialysis and peritoneal dialysis–treated patients may lead to insufficient adjustment in multivariate analysis and bias modality comparisons. In response to these concerns, we demonstrated that the prevalence of CHF in this study was 33%, similar to reported estimates from several other nationally representative studies [19, 37]. Moreover, sensitivity analyses, adjusting only for objective measures of comorbidity (BMI, hematocrit, serum albumin, and estimated GFR), yielded estimates that were consistent with the overall results. Finally, our study lacked prospective data on residual renal function, delivered dose of dialysis, anemia management, nutritional indices, and other clinical indicators that may have varied with treatment modality and time and influenced survival outcome.

To our knowledge this is the first comparative analysis of hemodialysis and peritoneal dialysis survival among new ESRD patients with CHF and has important implications. First, it demonstrates significantly poorer overall survival in patients with CHF treated with peritoneal dialysis as compared to hemodialysis, an observation that was present in both diabetic and nondiabetic patients. Second, it shows that negative impact of peritoneal dialysis on survival is time-dependent, occurring as early as 6 months after ESRD start and increasing as time progresses. Although selection bias may explain the detrimental impact of peritoneal dialysis on survival, the persistence of this finding after comprehensive adjustment for potential confounding factors suggests that this reduced survival may represent a true adverse peritoneal dialysis–treatment effect. Nonetheless, this observation may be due to differences in dialysis dose, rates of decline in residual renal function, and cardiac risk factor profiles between peritoneal dialysis and hemodialysis patients. Finally, this study shows that for patients who do not have CHF at ESRD onset, the choice of peritoneal dialysis has similar survival outcomes compared with hemodialysis. Taken together, these findings suggest that peritoneal dialysis, as is currently practiced, may not be a suitable choice for new ESRD patients with CHF and that hemodialysis may be preferred therapy. Given the epidemic of cardiovascular disease and alarmingly high prevalence of CHF in new ESRD patients, there is an urgent need for detailed prospective studies comparing peritoneal dialysis to hemodialysis in this population.

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Reprint requests to Austin G. Stack M.B., B.Ch., M.S., M.R.C.P.I. Assistant Professor in Internal Medicine, Division of Renal Diseases and Hypertension, University of Texas Health Science Center at Houston, 6431 Fannin St, MSB 4.148, Houston, TX 77030.
E-mail: Austin.Stack@uth.tmc.edu

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