

Comparing Mortality of Elderly Patients on Hemodialysis *versus* Peritoneal Dialysis: A Propensity Score Approach

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Abstract. The objective of this study was to evaluate differences in mortality over the first year of renal replacement therapy (RRT) between elderly patients starting treatment on hemodialysis (HD) *versus* peritoneal dialysis (PD). For the period of 1991 to mid-1996, this study defined an inception cohort of all patients aged >65 yr with new-onset chronic RRT who were New Jersey Medicare and/or Medicaid beneficiaries in the year before RRT and who had been diagnosed with renal disease more than 1 yr before RRT. Propensity scores were calculated for first treatment assignment from a large number of baseline covariates. Mortality was then compared among patients initially assigned to HD *versus* PD using multivariate 90-d interval Cox models controlled for propensity scores and center stratification. Peritoneal dialysis starters had a 16% higher rate of death during the first 90 d of RRT compared with

HD patients (hazard ratio [HR], 1.16; 95% confidence interval [CI], 0.96 to 1.42). Mortality did not differ between day 91 and 180 (HR, 1.03; 95% CI, 0.71 to 1.51). Thereafter, PD starters again died at a higher rate (HR, 1.45; 95% CI, 1.07 to 1.98). These findings were more pronounced among patients with diabetes. Sensitivity analyses using more stringent criteria to ensure that first treatment choice reflected long-term treatment choice confirmed the presence of an association between PD and mortality. In conclusion, compared with HD, peritoneal dialysis appears to be associated with higher mortality among older patients, particularly among those with diabetes, even after controlling for a large number of risk factors for mortality, propensity scores to control for nonrandom treatment assignment, and center stratification.

Various studies have sought to answer the question of whether or not survival on peritoneal dialysis (PD) and hemodialysis (HD) differed. (1–22) These studies vary enormously with regard to population selection criteria, sample size, statistical methodology, definition of treatment, and availability of information on important potential confounders. The various results are conflicting: some studies have found a survival benefit for PD patients (12,16,18,20), others for those on HD (10,11,13), and still others have found mortality not to differ (2–8,14,15,19,21,22).

Many of these previous studies, and all studies on US populations after 1983 have not adequately addressed a key methodologic issue: assessments that start at 4 or 6 mo after onset of RRT are likely to discard relevant events that occur between the first dialysis treatment and the chosen starting

point of such studies, particularly modality switches and deaths. This omission can result in biased estimates of effect. Another important potential source of bias that frequently remained unaccounted for is uncontrolled center effects (23). Furthermore, potentially useful techniques developed to enhance control for nonrandom treatment assignment, such as propensity scores (PS) or g-estimation (24,25), have not been used in comparisons of outcomes between dialysis modalities.

This study evaluates the survival of elderly ESRD patients receiving PD *versus* HD by means of an inception cohort based on the first treatment allocation decision (26). This makes it possible to evaluate patient outcomes in relation to the consequences of that first modality choice. Furthermore, we go beyond previously used methodology by accounting for center effects and introducing PS in an attempt to further reduce bias.

Materials and Methods

Patients

We identified all patients >65 yr of age who began RRT between January 1, 1991, and June 30, 1996, and who had been active participants in either the Medicare or Medicaid programs of the state of New Jersey for at least 12 mo before the initiation of renal dialysis. These patients were identified using the International Classification of Disease (9th revision [ICD-9]) and the Current Procedural Terminology (CPT-4) codes for HD, PD, other dialysis, renal transplantation,

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and other ESRD services. The day of first RRT was considered the index date.

To eliminate patients with acute renal failure, we required a diagnosis of renal insufficiency more than 1 yr before the initiation of RRT, as well as duration of dialysis of at least 1 mo. We further excluded patients, unless they were transplanted, who had >2 mo of survival after their last dialysis claim or who only underwent one dialysis procedure and then survived >1 mo and so may not have had ESRD. We also excluded any patients whose health care providers could not be identified. We furthermore excluded all those patients who underwent renal transplantation during the first month of RRT. The population selection algorithm yielded a total of 2503 incident RRT patients.

Initial Treatment Modality

The study subjects were grouped into HD or PD patients in accordance with their first RRT procedure claim on the index date. Of the 2503 patients in the cohort, 537 patients (21.5%) started RRT on peritoneal dialysis, the remaining 1966 (78.5%) on hemodialysis. For patients who had a procedure code for both HD and PD on the index date ($n = 18$), we assumed the chosen modality was the modality used on the second day of RRT. Patients with a procedure code of “other dialysis” or “ESRD service” ($n = 106$) were assumed to have started on PD if a procedure code for insertion of a peritoneal dialysis catheter was present within 1 mo before or on index date ($n = 31$); otherwise, these individuals were assumed to have started on HD ($n = 75$).

Patient Characteristics

To protect confidentiality, all unique patient identifiers were transformed into anonymous untraceable study numbers in all analyses. For all patients, we assessed age on index date, gender, and race (white/black/other). All other covariates were ascertained within the year before index date. We used membership in the New Jersey Medicaid or the New Jersey Pharmaceutical Assistance for the Aged and Disabled (PAAD) programs as an indicator of low income and, thus, lower socioeconomic status (SES). To be eligible for those programs, patients must demonstrate an income below the federal poverty level (Medicaid) or up to approximately 200% of it (PAAD). We also ascertained a number of covariates from inpatient and outpatient claims using condition or procedure-specific ICD-9 or CPT-4 codes—comorbidities, underlying renal diagnoses, prior medical conditions or procedures, and health care utilization patterns—that might be potentially associated with modality choice or with mortality after initiation of RRT (Table 1).

To control for variations in practice and the associated outcomes among facilities, we identified the provider/facility at which dialysis was started, using information from a database of all US provider codes. For those provider/facility codes that we were unable to identify we created a dummy covariate ($n = 154$ patients), as we did for each identified facility.

Statistical Analyses

Treatment Model. For each patient, we used logistic regression to calculate the estimated propensity score (PS) for being assigned to PD versus HD as first dialysis modality. The PS is defined as the estimated probability of being assigned to one treatment over another given the observed baseline covariates from such a logistic regression model. PS are an efficient way of condensing the information from many covariates into a single variable. It has been demonstrated that observed characteristics are balanced between treatment groups, con-

ditional on each level of the PS (24,27,28). As it is recommended that covariates be introduced generously into such a PS model, we included a large number of pretreatment covariates independent of significance thresholds or other selection criteria. Furthermore, we generously employed interaction and higher order terms. The full list of covariates in the PS model can be found in Table 1. In addition, we used indicator variables for individual centers to predict treatment assignment ($n = 56$). Predictive performance of the treatment models was assessed using the c statistic, which can assume values from 0.5 for chance prediction to 1.0 for perfect prediction (29).

Outcomes Model. We built several multivariate Cox proportional hazards models, with death being the outcome of interest. Patients were censored at the earliest of loss to follow-up, renal transplantation, end of study period, or at 365 d after first RRT. Multivariate models including first modality as the parameter of interest were further adjusted for age, race (white/black/other), gender, socioeconomic status, and all comorbid conditions. We used age as a continuous covariate, as it demonstrated no significant deviation from linearity. Having restricted our cohort to patients >65 yr, we tested for significance of several interactions that had been found to be important in previous studies, most prominently the diabetes-modality interaction. Similarly, we tested for any deviations from the proportional hazards assumption by introducing interactions of time on RRT with all covariates.

After scrutiny of appropriateness of model specification, we introduced the estimated PS (dummy-coded for quintiles of PS) into our final model. We analyzed important subgroups of patients to evaluate the sensitivity of our findings. Finally, we built outcomes models that accounted for PS and included information about individual centers, additionally stratifying the Cox models by center to account for possible variations in baseline mortality rates across centers.

In addition, we matched all PD patients with one HD patient each on PS. We used a publicly available matching algorithm (“greedy match”) (30) that was recently used for a similar analysis (31). A Kaplan-Meier actuarial survival plot from the resulting cohort was created using the SAS LIFETEST procedure. A Kaplan-Meier plot from such a cohort is essentially unconfounded by covariates used to create the propensity score, because the baseline covariate vectors are nearly identical. We found that whether we used PS as covariate adjustment in multivariate models or analyzed cohorts of PS-matched patients did not change the results materially. Therefore, to capitalize on all information available and to increase statistical efficiency, we decided to show results from models that adjusted for quintiles of PS.

All statistical analyses used the SAS system for UNIX, version 8.2, statistical analysis software (SAS Institute, Inc., Cary, NC).

Results

The frequency and distribution of important patient characteristics are presented in Table 2. Patients starting RRT on PD were less likely to be black, low SES, or to have undergone major abdominal surgery. Furthermore, PD patients were more likely to have coronary artery disease, congestive heart failure, and mental disease other than depression compared with those starting on HD, whereas the latter group tended to have more peripheral vascular disease, and a significantly higher proportion had history of alcohol and/or substance abuse. Health care utilization patterns were also different between patients starting on PD versus HD.

For the outcomes analysis, we first built a Cox proportional hazards model that contained all demographic covariates, co-

Table 1. Covariates used to estimate propensity scores for initial dialysis modality

Demographic covariates <ul style="list-style-type: none"> ● age, age², age³ ● race (white/black/other) ● gender ● socioeconomic status (SES)^a 	Comorbidities ^b <ul style="list-style-type: none"> ● hypertension ● diabetes ● coronary artery disease (CAD) ● congestive heart failure ● cerebrovascular disease (CVD) ● peripheral vascular disease (PVD) ● malignancy ● gastrointestinal erosion/ulcer (without surgery) ● abdominal hernia (with or without surgical repair) ● major abdominal surgery ● diverticulosis of colon ● severe liver disease ● obesity ● Chronic obstructive pulmonary disease ● HIV⁺/AIDS ● dementia ● depression ● alcohol or substance abuse ● other mental disease
Renal underlying disease ^b <ul style="list-style-type: none"> ● acute (glomerulo)nephritis ● polycystic kidney disease ● diabetic nephropathy ● hypertensive kidney disease ● chronic pyelonephritis ● obstructive nephropathy ● renovascular disease ● miscellaneous ● chronic renal disease not otherwise specified 	
Health care utilization ^b <ul style="list-style-type: none"> ● late versus early nephrologist referral^c ● number of nephrologist visits (0 to 3; 4 to 9; 10+) ● presence of primary care visits ● presence of medical subspecialist visits^d ● presence of surgical consultations ● number of hospital days (0; 1 to 7; 8 to 28; 29+) ● presence of nursing home stay 	Interaction terms <ul style="list-style-type: none"> ● age * gender, race (2 terms), SES ● race * gender (2 terms), SES (2 terms) ● diabetes * CVD, CAD, PVD

^a Assessed using enrollment in Medicaid or the New Jersey Pharmaceutical Assistance for the Aged and Disabled program within the year before first renal replacement therapy as a proxy for lower socioeconomic status.

^b All covariates were assessed within the year before first renal replacement therapy. Covariates were binary (absent/present) unless specifically noted otherwise.

^c Late referral, first nephrologist visit ≤ 90 d before first renal replacement therapy; early referral, first nephrologist visit > 90 d before first renal replacement therapy.

^d Cardiology, endocrinology-diabetology, gastroenterology-hepatology, hematooncology, infectious diseases, pulmonology, and rheumatology.

morbidity, and renal diagnoses listed in Table 1. We omitted the covariates for diabetic nephropathy and hypertensive kidney disease due to their expected high collinearity with the respective comorbidities. The covariate depicting late versus early nephrologist referral was also included. This model revealed that patients who started their RRT with PD had a 24% higher rate of death during the first year of treatment compared with those starting on HD (hazard ratio [HR], 1.24; 95% confidence interval [CI], 1.09 to 1.41). However, we found the modality-time interaction term to be highly significant ($P < 0.001$), thus violating this assumption of the Cox proportional hazards model. We therefore proceeded with building interval-Cox models, stratifying our analyses into 90-d intervals. Table 3 describes the four interval-cohorts with regard to number of enrollees, person-time accrued, and the number of deaths observed.

Figure 1 shows that patients initially assigned to PD had a 23% higher mortality rate than HD patients during the first 90 d after initiation of RRT (HR_{months1–3}, 1.23 [1.04 to 1.46]), whereas there was no mortality differential in the second 3-month

period (HR_{months4–6}, 1.05 [0.76 to 1.45]). The relative death rate thereafter increased again (HR_{months7 to 9}, 1.28; (0.90 to 1.83)). In the fourth quarter-year of RRT, the mortality rate of PD patients was again higher compared with HD patients. Individuals who had started RRT on PD died at a 57% higher rate than did HD patients during that interval (HR_{months9–12}, 1.57 [1.05 to 2.36]).

We next attempted to control for center effects in two ways: first, by introducing dummy covariates for each treatment site into the PS model. The PS including center identification did particularly well in distinguishing future PD from HD patients, with a c statistic of 0.82 (29). Second, we adjusted for potential differences in the underlying background death rate among centers by using center as a blocking variable in the proportional hazards models.

The results obtained from applying either or both of these techniques were not substantially different. Controlling for center in either of these ways attenuated the effect estimates slightly (Figure 1). However, confidence intervals were wider than in the models that did not block by center or use PS.

Table 2. Patient characteristics by treatment modality on index date

Covariate ^a	Hemodialysis Patients (n = 1966)		Peritoneal Dialysis Patients (n = 537)		P χ^2 or t test
	n	%	n	%	
Age (categorical)					
66 to 74 yr	981	49.9	277	51.6	
75 to 84 yr	838	42.6	225	41.9	
>85 yr	147	7.5	35	6.5	0.66
Gender					
male	1092	55.5	298	55.5	
female	874	44.5	239	44.5	0.98
Race					
white	1516	77.1	449	83.6	
black	371	18.9	65	12.1	
other	79	4.0	23	4.3	0.001
Socioeconomic status					
lower	675	34.3	142	26.4	
higher	1291	65.7	395	73.6	<0.001
Hypertension	1610	81.9	446	83.1	0.53
Diabetes	951	48.4	274	51.0	0.28
Coronary artery disease	1452	73.9	414	77.1	0.13
Congestive heart failure	1315	66.9	388	72.3	0.02
Peripheral vascular disease	384	19.5	91	17.0	0.18
Cerebrovascular disease	478	24.3	127	23.7	0.75
Malignancy	486	24.7	123	22.9	0.38
Upper GI erosion/ulcer (without surgery)	515	26.2	129	24.0	0.31
Major abdominal surgery	87	4.4	14	2.6	0.06
Abdominal hernia (with or without surgery)	111	5.6	40	7.5	0.12
Diverticulosis/-itis of colon	182	9.3	40	7.5	0.19
Severe liver disease	51	2.6	12	2.2	0.64
Massive obesity	32	1.6	7	1.3	0.59
Chronic obstructive pulmonary disease	526	26.8	150	27.9	0.59
HIV ⁺ /AIDS	25	1.3	7	1.3	0.95
Dementia	84	4.3	24	4.5	0.84
Depression	109	5.5	32	6.0	0.71
Alcohol or substance abuse	143	7.3	26	4.8	0.05
Other mental disease	206	10.5	70	13.0	0.09
Nursing home admission	27	1.4	8	1.5	0.84
First nephrologist visit \leq 90 d before index	676	34.4	177	33.0	0.54
Nephrologist visits					
0 to 3	876	44.6	232	43.2	
4 to 9	573	29.2	164	30.5	
\geq 10	517	26.3	141	26.3	0.80
Hospital days					
none	308	15.7	66	12.3	
1 to 7	457	23.3	126	23.5	
8 to 28	675	34.3	184	34.3	
\geq 29	526	36.8	161	30.0	0.19
Family/primary care physician office visit (\geq 1)	674	34.3	209	38.9	0.05
Medical subspecialist office visit (\geq 1)	541	27.5	179	33.3	0.008
Surgical specialist office visit (\geq 1)	295	15.0	89	16.6	0.37

^a Measured on or during year prior to index date.

Table 3. Distribution of individuals, person-time, and deaths by time interval and modality

Time Interval	Modality	Sample Size	Person-Years	Number of Deaths
Days 1 to 90	HD	17966	385.7	576
	PD	537	99.2	185
	Total	2503	484.9	761
Days 91 to 180	HD	1330	242.8	174
	PD	339	60.2	47
	Total	1669	303.0	221
Days 181 to 270	HD	1127	182.5	132
	PD	282	43.0	41
	Total	1409	225.5	173
Days 271 to 365	HD	956	128.2	89
	PD	237	28.9	33
	Total	1193	157.1	122

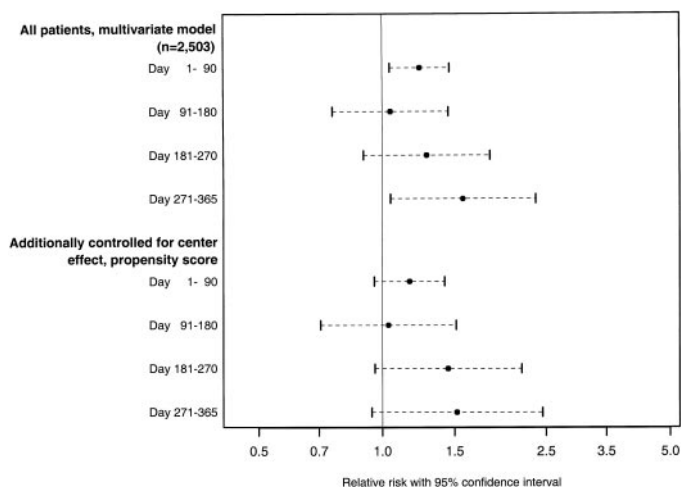


Figure 1. Relative death rates of peritoneal dialysis (PD) versus hemodialysis (HD) patients (hazards ratios [95% CI]).

Nevertheless, the overall pattern of survival differences remained robust: patients starting on PD died at a 16% higher rate during the first 90 d of treatment (HR_{months1–3}, 1.16; (0.96 to 1.42)), whereas there was no difference in the second 3-mo interval. Thereafter, those who began dialysis with PD demonstrated a higher mortality again. A Kaplan-Meier actuarial survival plot by modality from the propensity score-matched cohort can be found in Figure 2.

Because the hazard ratios observed in the third and fourth interval were similar, we conducted a post hoc analysis combining those intervals. We found a statistically significant 45% higher mortality rate among patients initially assigned to PD compared with HD in the interval from 7 to 12 mo after treatment assignment (HR_{months7–12}, 1.45; [1.07; 1.98]). The detailed results for all models assessing the stratified relative interval death rates on PD versus HD in the overall cohort are shown in Table 4.

Subgroup and Sensitivity Analyses

We did not find any statistically significant interactions between patients with or without diabetes ($P > 0.30$ in all

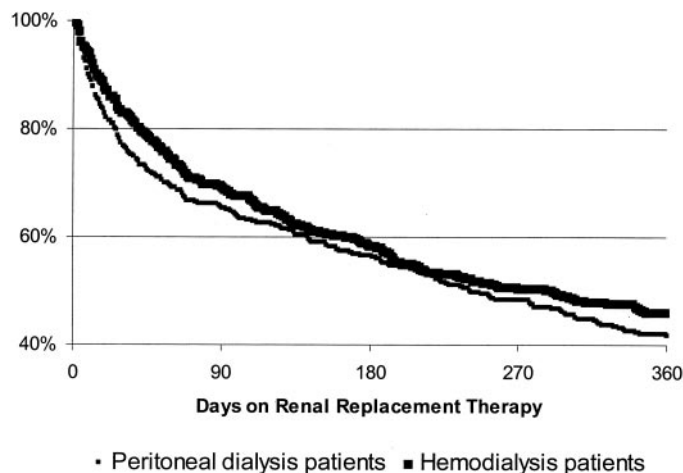


Figure 2. Kaplan-Meier survival plot in propensity score matched pairs ($n = 1062$).

interval Cox models). However, previous reports have suggested that such effect modification may in fact be present (2,6,8–10,20). We therefore conducted separate analyses (including PS and center adjustment) among patients with diabetes and those without a diagnosis of diabetes (Figure 3). Although the finding of higher mortality in the first 90 d among PD starters was present in patients with and without diabetes, we found that the excess death rate observed beyond 180 d of RRT was solely driven by patients with diabetes. In this later time period, mortality was not different between patients without diabetes who started RRT on PD versus HD.

We repeated all analyses on a population subset excluding those patients who switched modality at least once during the first month of RRT ($n = 182$) and also those for whom we were unable to identify the first treatment modality without making inference from presence of peritoneal dialysis catheters ($n = 106$). These results were essentially unchanged when compared with the full cohort (Figure 4). We also evaluated the effect of modality choice on survival among those patients who first consulted a nephrologist more than 90 d before onset of

Table 4. Results from multivariate interval Cox regression models for overall population using propensity scores and center stratification

Covariate	Hazards Ratio (95% Confidence Interval)			
	1 to 90 d	91 to 180 d	181 to 270 d	271 to 365 d
Age	1.04 (1.03 to 1.05)	1.02 (1.00 to 1.05)	1.05 (1.02 to 1.07)	1.02 (0.99 to 1.06)
Male gender	1.04 (0.89 to 1.21)	0.94 (0.71 to 1.25)	0.93 (0.67 to 1.28)	0.87 (0.59 to 1.30)
Black race	0.79 (0.62 to 1.01)	0.65 (0.41 to 1.01)	0.82 (0.51 to 1.33)	0.99 (0.56 to 1.75)
Other race	0.65 (0.40 to 1.04)	1.35 (0.71 to 2.54)	0.68 (0.24 to 1.90)	1.15 (0.44 to 2.98)
Lower socio-economic status	0.92 (0.77 to 1.09)	1.11 (0.81 to 1.51)	0.89 (0.62 to 1.29)	0.79 (0.50 to 1.25)
Hypertension	0.65 (0.54 to 0.78)	0.77 (0.53 to 1.12)	0.61 (0.40 to 0.94)	0.48 (0.29 to 0.79)
Diabetes	0.95 (0.81 to 1.11)	1.35 (1.01 to 1.82)	1.31 (0.94 to 1.84)	1.17 (0.78 to 1.76)
Congestive heart failure	2.01 (1.65 to 2.45)	1.56 (1.11 to 2.19)	1.55 (1.06 to 2.27)	1.70 (1.08 to 2.67)
Coronary artery disease	1.15 (0.94 to 1.40)	1.01 (0.70 to 1.44)	1.12 (0.75 to 1.68)	1.57 (0.94 to 2.64)
Malignancy	1.14 (0.96 to 1.34)	1.44 (1.06 to 1.96)	0.94 (0.64 to 1.36)	1.34 (0.87 to 2.05)
Cerebrovascular disease	1.22 (1.03 to 1.44)	1.03 (0.75 to 1.42)	1.36 (0.95 to 1.96)	1.19 (0.75 to 1.89)
Peripheral vascular disease	1.44 (1.21 to 1.71)	1.11 (0.78 to 1.58)	1.06 (0.72 to 1.58)	1.26 (0.78 to 2.04)
Late referral	1.56 (1.34 to 1.81)	1.28 (0.94 to 1.73)	0.94 (0.65 to 1.35)	1.32 (0.87 to 1.99)
Peritoneal dialysis	1.16 (0.96 to 1.42)	1.03 (0.71 to 1.51)	1.45 (0.96 to 2.18)	1.52 (0.94 to 2.45)

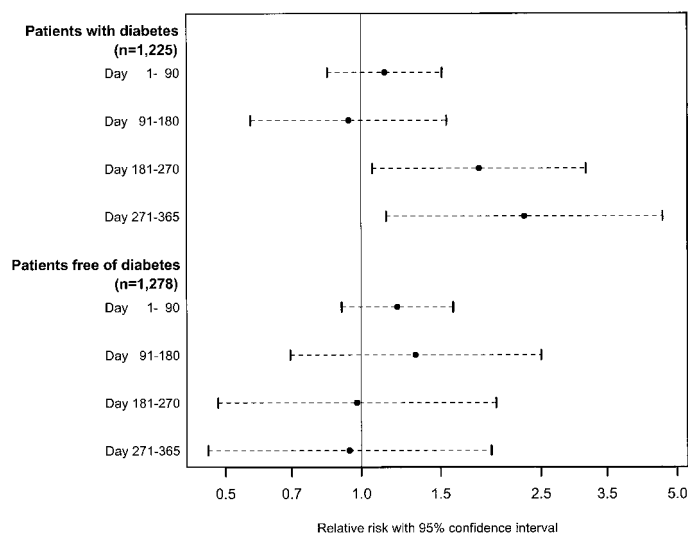


Figure 3. Subgroup analysis of patients with *versus* without diabetes (hazards ratios [95% CI]).

RRT *and* who did not switch during the first month of therapy. In this group of patients, who could be assumed to have made an educated decision *and* to have had sufficient time to be prepared for treatment, we found an even more pronounced result (Figure 4).

Discussion

In this large cohort of elderly ESRD patients followed during their first year on RRT, we found that patients initially assigned to PD had a higher overall mortality rate than patients initially assigned to HD (HR, 1.24; 95% CI, 1.09 to 1.41). We furthermore found that the relative survival pattern between treatment modalities changed over time (Figure 1). Stratifying by 3-mo intervals, we found that patients starting RRT on PD

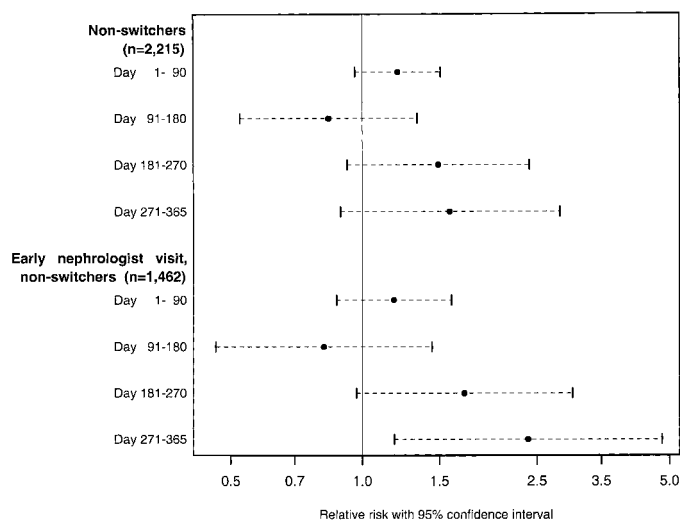


Figure 4. Sensitivity analysis (hazards ratios [95% CI]).

were 16% more likely to die during the first 3 mo of treatment (HR, 1.16 [0.96 to 1.42]). Between 3 and 6 mo after beginning of RRT, we observed similar mortality rates among patients assigned to PD and HD (HR, 1.03; 95% CI, 0.71 to 1.51). However, in the final 6 mo of the first year of RRT, patients initially assigned to PD had a 45% higher mortality rate than HD patients (HR, 1.45 [1.07 to 1.98]). These results were robust in multivariate models that controlled for a large number of demographic, medical, and health care utilization characteristics. Additional bias-reduction was introduced with the use of propensity scores, as well as by controlling for center effects.

This analysis of the death rates of patients starting RRT on HD *versus* PD was more detailed than previous analyses. To study the relative mortality between these two treatment modalities, we selected from a large database a historic cohort of

incident ESRD patients whose kidney disease had developed chronically, rather than occurring acutely. The experiences of those patients were then followed prospectively in light of their first treatment assignment.

Our finding that patients starting RRT on PD were at a higher mortality risk within the first 3 mo of treatment has to our knowledge not been described before. Most earlier studies did not test for or failed to detect violations of the proportional hazards assumption, and thus chose to present effect estimates that were aggregated over time. Alternatively, many analyses, especially in the United States, omitted the first few months of RRT from analysis entirely. Interestingly, we found no difference in survival between patients assigned to PD or HD in the period from 4 to 6 mo after initial treatment allocation. This finding may be explained by depletion of susceptibles: (32) many patients who did not fare well on PD died, and those still alive had accommodated to the treatment.

Previous reports have suggested that mortality between PD and HD patients differed across important patient subgroups, most prominently with regard to age and presence of diabetes (2,6,8–10,20). Results for patients with and without diabetes were very similar in our study when we did not control for PS or center effects (not shown). However, when introducing such techniques, we found the effects of modality choice on mortality among patients with diabetes to be more pronounced but not present for patients free of diabetes. This is consistent with previous findings that demonstrated that patients with diabetes had higher mortality when on PD rather than HD, which was not the case among patients without diabetes (8,9).

A central purpose of this study was to model and analyze the consequences of real-life baseline decision-making. However, we could not automatically assume that the modality used for the first dialysis was in congruence with the decision that had been made by the patient and her/his physician, due to inadequately late nephrologist consultation or to complications during the preparation process. For example, it may have been decided to use HD as the modality for long-term treatment, but at the time of first dialysis the shunt had not sufficiently matured, resulting in this interval being bridged using PD. Other scenarios might go in the opposite direction. To minimize such “misclassification,” we also presented results on a subset of patients who did not switch modality during the first month of RRT, assuming that their initial modality corresponded to their choice for long-term maintenance treatment. For this step, we excluded all first-month switchers as well as those patients for whom we had to make any inference regarding their first treatment modality from the presence or absence of claims for insertion of a PD catheter. In a second step, we took this point even further and eliminated those patients who had not consulted with a nephrologist until ≤ 3 mo from RRT. Seeing a nephrologist earlier gives the patient a considerably better chance to make an educated decision about which modality to use as well as sufficient preparation time for a smooth initiation of treatment. However, even applying such restriction criteria did not change our findings.

Most previous studies have not assessed treatment modality at baseline, but rather at an arbitrary later point in time, most

often 90 or 120 d after first dialysis. In the United States, this is for one practical reason: availability of data that are collected from medical claims. The large nationwide registry of patients with ESRD, the United States Renal Data System (USRDS), is based on the medical claims submitted to Medicare as the predominant payor of ESRD services. However, Medicare does not become a principal payor until day 90 of RRT, which leaves the experiences of ESRD patients during the first 90 d of treatment in obscurity. For the purpose of comparing outcomes of initial therapy, this can be highly problematic, because it is of paramount importance to assess treatment assignment from the first day of treatment. Only if such left-censoring were completely noninformative, *i.e.*, nondifferential with regards to all exposure and confounder characteristics, could an analysis starting at a later point potentially be unbiased. This is usually not the case, and certainly not in the ESRD population as demonstrated here and in earlier work (33). In the present context, such biases would tend to favor PD. First, the relatively more numerous early deaths among PD starters would be ignored, and their more frequent modality switches discarded (33). Second, studies of the survival of HD versus PD patients assessed after day 90 would be conducted in a population that was unrepresentative of all new RRT starters. Such information would overestimate the benefits of PD and understate those of HD. Third, by ignoring the number and direction of earlier modality switches, a substantial proportion of individuals labeled as “HD patients” at 3 mo would be misclassified with regard to their original treatment choice. It is in this way that the present study differs from previous studies that used interval analyses but assessed treatment on day 90 (20).

Two statistical aspects of the present study are also noteworthy. The present analysis went beyond the multivariate modeling and stratification that had been done before by the introduction of PS to further control for nonrandom treatment assignment and by adjusting for center effects. The value of PS lies in their ability to efficiently control for baseline differences between treatment groups using a single scalar (27,28). This is particularly appealing when prediction of treatment assignment is complex and correct model specification would require introduction of multiple interaction or higher-order terms. This may lead to difficulties in interpretability when one wishes to evaluate and estimate main effects. However, although introduction of PS reduces bias introduced by imbalances of observed covariates, it does nothing to reduce bias caused by unobserved confounders.

Prediction of choice of dialysis modality could be expected to be poor in the absence of information on factors known to be important for this decision, such as financial incentives for providers of RRT, educational deficits in the health care team, and/or patient, physician bias, resource availability, social mores, and cultural habits (34). However, it seemed reasonable that some of this predictive power could be captured by including information into the PS model that identified the individual dialysis facility. Indeed, the *c* statistic increased substantially from 0.64 to 0.82 when facility covariates were added into the model (29). A number of recent articles have

shown that various outcomes are highly associated with center-specific factors even after adjustment for individual patient characteristics and that center characteristics can be even stronger predictors of outcomes than individual patient predictors (35–37). This dominance of center-specific factors also expressed itself in the large improvement of the *c* statistic of our propensity score model when entering dummy covariates for each center. This clearly indicates that center policies regarding modality assignment were important determinants of treatment choice beyond individual patient characteristics. When adding quintiles of estimated PS into the survival models, the results did not change very much in the overall population; we found marginal to moderate attenuation in the effect estimates toward the null value (Figure 1).

Outcomes such as mortality are also correlated with the center where treatment is received. Mortality among ESRD patients is highly variable across centers, but clustered within centers, even when controlling for patient characteristics (36,37). Failure to account for this phenomenon may lead to biased effect estimates and reduced power (23). Various analytical techniques are available to control for such center-effects. We decided to account for such effects in our analysis by blocking on center. Such methodology permits efficient estimation of common relative mortality rates among strata of individuals, but allows baseline rates to vary by center (23).

These findings should be considered in light of the study's limitations. Although its findings are externally valid for patients aged 66 or older, they are probably not generalizable to the ESRD population <66 yr of age, and their generalizability to other geographic regions is also unclear. The present study may also suffer from shortcomings inherent in all claims database research: missing data, miscoding, as well as residual confounding arising from overly crude categorization of confounding conditions such as comorbidities or socioeconomic status. Furthermore, we do not have any information on clinical and biologic parameters, patient compliance with treatment, or dose of dialysis prescribed or delivered. It is also not clear whether the findings from the early and mid-1990s are representative of current patient outcomes. The techniques of both HD and PD are evolving over time, and associations between outcomes and delivered dose of dialysis were discovered earlier for HD compared with PD (38–40). Although we did not find any significant trends over time, our findings will still need to be confirmed in more recent cohorts of patients.

Finally, the value of this analysis to patients, health care providers, and policymakers depends on whether the modality chosen at baseline reflected actual long-term treatment decisions. We believe that our population selection algorithm and the robustness of our findings after application of stringent criteria regarding timely nephrologist care and early modality switching in sensitivity analyses make a compelling argument that this was actually the case.

We confined our analysis to the description of associations between treatment assignment and mortality in a 1-yr follow-up. The present study stopped short of describing the different causes of deaths, evaluating the effects of center size on outcomes, or providing an analysis beyond the first year of

RRT. We found that the population at hand was too small to answer more detailed questions or to assess outcomes further down the road in a meaningful way.

Conversely, there are several characteristics of this study that address problems inherent in past studies with similar objectives. Most important of these is its use of an inception cohort of new starters of RRT, drawn from a variety of settings in an entire state. Thus, the important biases arising from follow-up after a later point in time are not present, and the results are representative of patients receiving care in typical settings. Furthermore, we were able to assemble information on more patient characteristics than had been available in previous studies. From such information we calculated PS, which enabled us to reduce distortions originating from selection bias even further in this observational study. By including information on centers, we improved prediction of treatment assignment considerably and we controlled for variations in treatment practices across institutions (23). Such control for center effects had been infrequent in analyses of mortality in RRT (11). Furthermore, analysis of data stratified by time took account of the fact that mortality hazards between treatment modalities varied over time. This provided important insights into the time course of excess risks among PD patients. Overall, this study complements and confirms earlier analyses that have shown that older patients with diabetes are at an increased mortality risk on PD compared with HD (19,20).

Conclusions

These data suggest that elderly patients who start RRT on peritoneal dialysis are at a higher risk of death both in the very early phase as well as during later courses of treatment, compared with comparable patients who begin their RRT on hemodialysis. We confirm earlier studies that found excess mortality among older patients, especially those with diabetes on PD (19,20). Our findings are based on the experience of a large and typical cohort of incident ESRD patients aged >65 in a large eastern state of the United States rather than of a single center with above-average experience with PD (2,15,22), or from populations with higher overall utilization of PD relative to HD than is seen in the United States that may not be representative of the way renal health care is delivered in this country (4,6,11,17,21). If replicated in other studies, these results may be relevant to the decision of patients nearing ESRD and their physicians in making decisions about which treatment to choose for long-term RRT. Other important considerations for such treatment decision are quality of life, access and availability, and the associated costs. Application of similar approaches to large and nationally representative prospective inception cohorts of ESRD patients seems important to confirm our findings.

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References

- Nolph KD: Comparison of CAPD and HD. *Kidney Int* 24[suppl]: S123–S131, 1988
- Maiorca R, Vonesh E, Cancarini GC, Cantaluppi A, Manili L, Brunori G, Camerini C, Feller P, Strada A: A six-year comparison of patient and technique survivals in CAPD and HD. *Kidney Int* 34: 518–524, 1988
- Wolfe RA, Port FK, Hawthorne VM, Guire KE: A comparison of survival among dialytic therapies at choice: In-center hemodialysis versus continuous ambulatory peritoneal dialysis at home. *Am J Kidney Dis* 15: 433–440, 1990
- Serkes KD, Blagg CR, Nolph KD, Vonesh EF, Shapiro F: Comparison of patient and technique survival in continuous ambulatory peritoneal dialysis (CAPD) and hemodialysis: a multicenter study. *Perit Dial Int* 10: 15–19, 1990
- Lunde NM, Port FK, Wolfe RA, Guire KE: Comparison of mortality risk by choice of CAPD versus hemodialysis among elderly patients. *Adv Perit Dial* 7: 68–72, 1991
- Maiorca R, Vonesh EF, Cavalli P, De Vecchi A, Giangrande A, La Greca G, Scarpioni LL, Bragantini L, Cancarini GC, Cantaluppi A, Castelnovo C, Castiglioni A, Poiseti P, Viglino G: A multicenter, selection-adjusted comparison of patient and technique survivals on CAPD and hemodialysis. *Perit Dial Int* 11: 118–127, 1991
- Gentil MA, Carriazo A, Pavon MI, Rosado M, Castillo D, Ramos B, Algarra GR, Tejuca F, Banasco VP, Milan JA: Comparison of survival in continuous ambulatory peritoneal dialysis and hospital hemodialysis: A multicenter study. *Nephrol Dial Transplant* 6: 444–451, 1991
- Nelson CB, Port FK, Wolfe RA, Guire KE: Comparison of continuous ambulatory peritoneal dialysis and hemodialysis patient survival with evaluation of trends during the 1980s. *J Am Soc Nephrol* 3: 1147–1155, 1992
- Held PJ, Port FK, Turenne MN, Gaylin DS, Hamburger RJ, Wolfe RA: Continuous ambulatory peritoneal dialysis and hemodialysis: comparison of patient mortality with adjustment for comorbid conditions. *Kidney Int* 45: 1163–1169, 1994
- Bloembergen WE, Port FK, Mauger EA, Wolfe RA: A comparison of mortality between patients treated with hemodialysis and peritoneal dialysis. *J Am Soc Nephrol* 6: 177–183, 1995
- Locatelli F, Marcelli D, Conte F, Limido A, Lonati F, Malberti F, Spotti D: 1983 to 1992: Report on regular dialysis and transplantation in Lombardy. *Am J Kidney Dis* 25:196–205, 1995
- Fenton S, Desmeules M, Copleston P, Arbus G, Froment D, Jeffery J, Kjellstrand C: Renal replacement therapy in Canada: A report from the Canadian Organ Replacement Register. *Am J Kidney Dis* 25: 134–150, 1995
- Disney APS: Demography and survival of patients receiving treatment for chronic renal failure in Australia and new Zealand: Report on dialysis and renal transplantation treatment from the Australian and New Zealand Dialysis and Transplant registry. *Am J Kidney Dis* 25: 165–175, 1995
- Marcelli D, Spotti D, Conte F, Tagliaferro A, Limido A, Lonati F, Malberti F, Locatelli F: Survival of diabetic patients on peritoneal dialysis or hemodialysis [Supplement]. *Perit Dial Int* 16: S283–S287, 1996
- Maiorca R, Cancarini GC, Zubani R, Carnerini C, Manili L, Brunori G, Movilli E: CAPD viability: a long-term comparison with hemodialysis. *Perit Dial Int* 16: 276–287, 1996
- Fenton SSA, Schaubel DE, Desmeules M, Morrison HI, Mao Y, Copleston P, Jeffery JR, Kjellstrand CM: Hemodialysis versus peritoneal dialysis: A comparison of adjusted mortality rates. *Am J Kidney Dis* 30: 334–342, 1997
- Foley RN, Parfrey PS, Harnett JD, Kent GM, O’Dea R, Murray DC, Barre PE: Mode of dialysis therapy and mortality in end-stage renal disease. *J Am Soc Nephrol* 9: 267–276, 1998
- Schaubel DE, Morrison HI, Fenton SSA: Comparing mortality rates on CAPD/CCPD and hemodialysis. The Canadian experience: Fact or fiction? *Perit Dial Int* 18: 478–484, 1998
- Vonesh EF, Moran J: Mortality in end-stage renal disease: A reassessment of differences between patients treated with hemodialysis and peritoneal dialysis. *J Am Soc Nephrol* 10: 354–365, 1999
- Collins AJ, Hao W, Xia H, Ebben JP, Everson SE, Constantini EG, Ma JZ: Mortality risks of peritoneal dialysis and hemodialysis. *Am J Kidney Dis* 34: 1065–1074, 1999
- Murphy SW, Foley RN, Barrett BJ, Kent GM, Morgan J, Barre P, Campbell P, Fine A, Goldstein MB, Handa SP, Jindal KK, Levin A, Mandin H, Muirhead N, Richardson RMA, Parfrey PS: Comparative mortality of hemodialysis and peritoneal dialysis in Canada. *Kidney Int* 57: 1720–1726, 2000
- Tanna MM, Vonesh EF, Korbet SM: Patient survival among incident peritoneal dialysis and hemodialysis patients in an urban setting. *Am J Kidney Dis* 36: 1175–1182, 2000
- Localio AR, Berlin JA, Ten Have TR, Kimmel SE: Adjustments for center in multicenter studies: and overview. *Ann Intern Med* 135: 112–123, 2001
- Rosenbaum PR, Rubin DB: The central role of the propensity score in observational studies for causal effects. *Biometrika* 70: 41–55, 1983
- Robins JM, Blevins D, Ritter G, Wulfsohn M: G-estimation of the effect of prophylaxis therapy for *Pneumocystis carinii* pneumonia on the survival of AIDS patients. *Epidemiology* 3: 319–336, 1992
- Maclure M, Schneeweiss S: Causation of bias: The episcopo. *Epidemiology* 12: 114–22, 2001
- D’Agostino RB Jr: Tutorial in biostatistics. Propensity score methods for a bias reduction in the comparison of a treatment to a non-randomized control group. *Statist Med* 17: 2265–2281, 1998
- Joffe MM, Rosenbaum PR: Invited commentary: Propensity scores. *Am J Epidemiol* 150: 327–333, 1999
- Ash AS, Shwartz M: Evaluating the performance of risk-adjustment methods: Dichotomous outcomes. In: *Risk Adjustment for Measuring Health Care Outcomes*. 2nd edition, edited by Iezzoni LI, Chicago, Health Administration Press, 1997
- Parsons LS: Reducing bias in a propensity matched-pair sample using greedy matching techniques. Available at: <http://www2.sas.com/proceedings/sugi26/p214-26.pdf>, Accessed on February 19, 2002
- Gum PA, Thamilarasan M, Watanabe J, Blackstone EH, Lauer MS: Aspirin use and all-cause mortality among patients being evaluated for known or suspected coronary artery disease: A propensity analysis. *JAMA* 286:1187–1194, 2001
- Yola M, Lucien A: Evidence of the depletion of susceptibles effect in non-experimental pharmacoepidemiologic research. *J Clin Epidemiol* 47: 731–737, 1994
- Winkelmayer WC, Glynn RJ, Levin R, Owen W, Avorn J: Late referral and modality choice in end-stage renal disease. *Kidney Int* 60: 1547–1554, 2001

34. Nissenson AR, Prichard SS, Cheng IK, et al.: ESRD modality selection into the 21st century: The importance of non-medical factors. *ASAIO J* 43: 143–150, 1997
35. Fink JC, Blahut SA, Briglia AE, Gardner JF, Light PD: Effect of center- versus patient-specific factors on variations in dialysis adequacy. *J Am Soc Nephrol* 12: 164–169, 2001
36. Lowrie EG, Teng M, Lacson E, Lew N, Lazarus JM, Owen WF: Association between prevalent care process measures and facility-specific mortality rates. *Kidney Int* 60: 1917–1929, 2001
37. McClellan WM, Soucie JM, Flanders WD: Mortality in end-stage renal disease is associated with facility-to-facility differences in adequacy of hemodialysis. *J Am Soc Nephrol* 9: 1940–1947, 1998
38. Owen WF Jr, Lew NL, Liu Y, Lowrie EG, Lazarus JM: The urea reduction ratio and serum albumin concentration as predictors of mortality in patients undergoing hemodialysis. *N Engl J Med* 329: 1001–1006, 1993
39. Maiorca R, Brunori G, Zubani R, Cancarini GC, Manili L, Camerini C, Movilli E, Pola A, D'Avolio G, Gelatti U: Predictive value of dialysis adequacy and nutritional indices for mortality and morbidity in CAPD and HD patients. A longitudinal study. *Nephrol Dial Transplant* 10: 2295–2305, 1995
40. CANUSA Peritoneal Dialysis Study Group: Adequacy of dialysis and nutrition in continuous peritoneal dialysis: Association with clinical outcomes. *J Am Soc Nephrol* 7: 198–207, 1996