A Comparison of Mortality Between Patients Treated With Hemodialysis and Peritoneal Dialysis

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ABSTRACT

Patients with ESRD treated with dialysis have a high mortality rate. Controversy exists as to whether this high mortality rate is affected by modality choice. The purpose of this epidemiologic study was to compare mortality in prevalent hemodialysis-treated (HD) and peritoneal dialysis-treated (PD) patients in a large national sample, adjusting for demographic characteristics. Data were obtained from the U.S. Renal Data System for patients prevalent on January 1 of the years 1987, 1988, and 1989, each with 1 yr of follow-up. Patients were censored at transplantation. Death rates per 100 patient years were compared between HD and PD, adjusting for age, race, gender, cause of ESRD (diabetes versus nondiabetes) and <1 yr or >1 yr of prior ESRD, by the use of Poisson regression. There were 42,372 deaths occurring over 170,700 patient years at risk. On average, prevalent patients treated with PD had a 19% higher adjusted mortality risk (relative risk (RR) = 1.19; P < 0.001) than did those treated with HD. This risk was found to be insignificant (P > 0.05) and small for ages <55 and increasingly large and significant for ages >55 y. It was accentuated in diabetics (RR = 1.38; P < 0.001) but was also present in nondiabetics (RR = 1.11; P < 0.001). Although present in both males and females, this risk was accentuated in females (RR = 1.30 versus 1.11; both P < 0.001). In this national study of prevalent U.S. dialysis patients, treatment assignment to PD was associated with a 19% higher all-cause mortality rate than HD. Further studies are necessary to separate the effect of patient selection, differential dose of dialysis, nutrition, patient compliance, and/or medical quality of care from a possible true adverse treatment effect of PD.

Key Words: End-stage renal disease, death rates, continuous ambulatory peritoneal dialysis, continuous cycler-assisted peritoneal dialysis, dialysis, dialysis modality

Over the past decade, the incidence rate of treated ESRD has increased by 8.8% per year in the United States (1), and rapid increases have also been seen in many other countries (2–4). Although renal transplantation is felt to offer the best survival (5) and quality of life (6–9), the majority of ESRD patients at some time in their life are faced with choosing between hemodialysis (HD) or peritoneal dialysis (PD). The best choice of dialytic modality in terms of patient outcome has not been well established. Comparative studies of HD and PD after the introduction of continuous ambulatory peritoneal dialysis (CAPD) in the late 1970s showed no consistent difference in mortality despite the great technical differences inherent in the two modalities (10–15). The choice has therefore usually been made on the basis of the patient's social needs or modality availability, unless a medical contraindication precludes the use of a specific modality. More recent studies show differences in mortality between HD and PD overall or in some subgroups (2,16–22); however, results are conflicting. A large multicenter study performed in Italy found lower mortality for PD among older age groups (18). However, analyses of data obtained from the Michigan Kidney Registry (20) and a large random sample of incident U.S. dialysis patients (21) found a higher risk of mortality associated with PD in older diabetics. The availability of national data on U.S. ESRD patients collected by the U.S. Renal Data System (USRDS) has allowed this epidemiologic study to revisit the question of comparative mortality among patients treated by PD and HD in the United States with sufficient power to detect clinically important differences overall and among major subgroups, a possible limitation of many previous studies.

METHODS

Source of Data and Study Population

Data were obtained from the USRDS, which collects demographic data and clinical information on all treated ESRD patients in the United States who qualify for Medicare and
who survive for a minimum of 90 days on renal replacement therapy (approximately 93% of the total U.S. treated ESRD population) (23). This study included three national cohorts of prevalent patients receiving continuous ambulatory or cycling PD (CAPD/CCPD, subsequently referred to as PD) and center HD on January 1 of 1987, 1988, and 1989, each with 365 days of follow-up. Patients prevalent at the beginning of more than one calendar year contributed to data to more than one cohort. Patients starting ESRD therapy less than 3 months before January 1 were excluded for that year because patient enrollment data are potentially incomplete. Patients with a renal transplant before January 1 of a cohort year were excluded from subsequent cohorts. Patients transplanted during the year were censored on the day of transplantation.

Patient characteristics including age, race (black or white), gender, dialysis modality (PD or HD), time on ESRD therapy (<1 yr versus >1 yr), and cause of ESRD (diabetic nephropathy versus all others) were classified at the beginning of each cohort year. This allowed a more accurate reflection of the effect of covariates that change in a given patient from one cohort year to another (age, modality, duration of ESRD). Patients switching dialytic modality during the 60 days before January 1 were excluded for that cohort year. Switches in dialytic modality during the 365 days of follow-up were not considered, yielding an "intent-to-treat" type of analysis for each year. Each cohort was monitored for deaths, cause of death, and days at risk of death.

Data Analysis

The total number of patient deaths and years at risk for the three cohorts were available in aggregated form, enhancing the stability of the estimated death rates (DR). The all-cause DR were computed as the total number of deaths divided by the total number of patient years at risk for the three cohorts and were expressed as deaths per 100 patient years at risk. DR for PD and HD were compared by use of Poisson regression, which allowed adjustment for age, gender, race, cause of ESRD, and duration of ESRD therapy (<1 yr or >1 yr). The calculated DR ratio (RR) represents the adjusted rate of death in PD-treated as compared with HD-treated patients. To determine if the all-cause RR varied by demographic characteristics (e.g., by gender), interaction terms were then included in a regression model. If an interaction term was found to be present (P < 0.05), a PD/HD RR was calculated for each subgroup (e.g., for males and females). Statistical analysis were performed with the PROC LOGISTIC procedure of SAS v6.07 (Cary, NC).

Because of the large sample size, many results fall within the realm of what is traditionally referred to as "highly statistically significant," thus ruling out random variation as a potential explanation. Thus, in this report, especially, evaluation of the magnitude (clinical significance) of an association, examination of the likely causes of an association, and careful review of potential sources of bias are more important considerations than is the P value.

RESULTS

In this study population of prevalent dialysis patients, there were 42,372 deaths occurring over 170,700 patient years at risk. Demographics of the study population are presented in Table 1. Blacks were less frequently treated by PD than were whites, and PD-treated patients were on average younger than HD-treated patients. Diabetics were equally distributed among HD- and PD-treated patients.

The all-cause DR was 19% higher for PD-compared with HD-treated patients (RR = 1.19; P < 0.001) when adjusted for age, race, gender, diabetic versus nondiabetic ESRD, and duration of ESRD. Figure 1 shows DR for patients with the average characteristics of the total study population among HD-treated patients (21.3 per 100 patient years) and among PD treated patients (25.3 per 100 patient years). This indicates that there are, on average, four more deaths per 100 patient years on PD as compared with HD.

Further analysis based on an interaction between modality and a linear age term showed that the RR varied significantly by age (P < 0.001). It was close to 1.00 and statistically insignificant (P > 0.05) for ages <55 and increasingly large and significant for ages >55 (Figure 2). Although the quantitative age effect is...
Figure 2. Adjusted all-cause DR modeled by age for PD- and HD-treated patients. The PD/HD RR varies significantly by age (P < 0.001), as reflected by the different slopes. The DR are significantly different above the age of 55. DR are for patients with the average characteristics of the total study population. Adjustments are for age, race, gender, diabetes, and duration of prior ESRD (less than or more than 1 yr).

unlikely to be truly linear, the results presented here show the qualitative result that the RR is larger for older patients than for young patients. In addition, the higher RR for PD patients was significantly accentuated (P < 0.001) among patients with diabetes as a cause of ESRD (RR = 1.38) and females (RR = 1.30), although it was also present in nondiabetics and males (both RR = 1.11) (Figure 3). There was no statistically significant effect of race on the PD/HD RR (P = 0.07).

The RR of PD/HD among patients on dialysis for less than 1 yr was lower (1.14) and significantly different (P = 0.045) from the RR among those treated for more than 1 year (1.21), as shown in Table 2. To enable comparisons of results with those of other studies, the effect of duration of ESRD was also analyzed for diabetics and nondiabetics separately. Among the diabetic subgroup, a nonsignificant (P = 0.30) trend by increasing duration of ESRD was observed (RR for <1 yr was 1.28 and for >1 yr was 1.43). In the nondiabetic subgroup, the PD/HD RR increased with longer duration of ESRD (P = 0.036). The RR for patients treated <1 yr (at start of follow-up) was not significantly different from 1.00. The PD/HD RR for patients treated >1 yr was 1.13 (different from 1.00; P < 0.001).

DISCUSSION

This study has found a higher mortality risk associated with PD compared with HD, except among younger patients, which is significantly different from 1.0 for ages over 55. It is accentuated in diabetics but is also present in nondiabetics. Although present in both males and females, it is shown to be accentuated in females. The RR for PD increased with duration of ESRD.

These results differ from some previous comparisons of mortality among PD- and HD-treated patients. Most early comparisons found no statistically significant differences in dialysis patient survival (10-15). More recently, differences in survival by modality have been reported overall or among subgroups of patients; however, these have not been consistent and differ in some aspects from this study’s results (2,18-22). Maiorca et al. (18), in a multicenter study performed in Italy, found no difference in mortality between HD- and PD-treated groups overall but showed for older age groups that CAPD patients had a lower mortality than HD patients, in direct contrast to our study. Consistent with our study results, Nelson et al. (20) found a higher risk of death associated with CAPD in
older diabetics, but among patients aged less than 52 yr, diabetic CAPD patients had a lower risk of death compared with corresponding HD patients (19). These studies from the Michigan Kidney Registry found no difference in mortality between PD and HD among nondiabetics. Our analysis does suggest the possibility of a lower risk of death with PD compared with HD in the younger ages (Figure 2); however, these differences were not significant. Most recently, Held et al. (21) also found no difference in nondiabetics, whereas in diabetics, PD-treated patients had a higher risk of mortality than did HD-treated patients. This finding was also accentuated among older ages. The difference in the results of this current and previous studies may be the result of differences in the patient populations, study design, and analytic methodologies.

Our study included prevalent patients, whereas many others, including the USRDS Special Study of Case Mix Severity by Held et al. (21), were of incident patients. Our choice was made on the basis of the availability of data on a large national sample, the size of which would ensure sufficient power to detect clinically important differences in mortality, a possible limitation of previous studies. It would also allow adequate sample size to compare cause-specific mortality between PD- and HD-treated patients (see companion article (24)). Survival curves depicted in a number of previous studies (7–9,11,12,14–16) indicate that the RR of mortality among PD- compared with HD-treated patients may vary by duration of ESRD. Although some of these studies suggest worse survival with HD as duration of ESRD increases (overall or in major subgroups) (12,14,19), the survival curves of the majority of studies suggest nonsignificant trends toward lower survival with PD (10,11,15,17,18). In the USRDS Case-Mix Study (21), survival curves of PD- and HD-treated patients were similar among diabetics in the first year but appeared to diverge thereafter, with survival in PD becoming relatively worse than that in HD. This may be related to a potential protective effect of greater residual renal function in PD patients that is eventually lost over time (25), causing a reduction in the total clearance of uremic solutes. In that same study, the survival curves for nondiabetic CAPD and HD patients were virtually superimposed.

In view of these observations, we evaluated the PD/HD relative risk by duration of ESRD separately for diabetics and nondiabetics. The RR of PD/HD was higher with longer duration of ESRD (>1 yr) among both diabetic and nondiabetic patients. We found that PD was associated with a significantly higher mortality rate than HD except in nondiabetics treated for less than 1 yr. The apparent discrepancy with the USRDS Case-Mix Study could be related to the adjustments for comorbidity, smaller sample size, or different definition of time of treatment. Our study labeled patients as being on dialysis for <1 yr on January 1, with follow-up for 365 days thereafter. Therefore, deaths attributed to these patients may have actually occurred up to 2 yr after the initiation of therapy. The Case-Mix Study survival curves were calculated with data from patients monitored for only 2.25 to 4.25 yr. Our results of analyses among prevalent patients raise the possibility that, also among nondiabetic patients, a difference in mortality occurs after prolonged treatment with ESRD therapy.

Most previous comparative studies did not discuss sample size requirements to detect a difference in mortality and may be limited by inadequate patient numbers. In order to detect a four-percentage-point (i.e., 20 vs 24 deaths/100 patient years or 20%) difference in 1-yr survival between PD and HD (RR = 1.2) with 90% power, a sample size of 1,400 patients per group (total N = 2,800) and a follow-up period of 2 yr would be required. To detect incrementally smaller differences in 1-yr survival, which arguably are also of clinical importance, would require even larger sample sizes. For example, a total of 4,600 patients would be required to detect a three-percentage-point (15%) difference. No previous studies have been of this magnitude. This national study of over 170,000 dialysis patient years and 42,000 deaths is by far the largest comparative study of PD and HD to date.

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<sup>a</sup> Tests if RR is significantly different from 1.00.

<sup>b</sup> Different from each other, P < 0.001.

<sup>c</sup> Patients classified on January 1 with follow-up for 365 days thereafter.

<sup>d</sup> Different from each other, P = 0.046.

<sup>e</sup> Not significantly different from each other, P = 0.30.

<sup>f</sup> Different from each other, P = 0.036.

<sup>*</sup> Significant differences in 1-yr survival, which arguably are also of clinical importance.
ity, a unique analytic consideration is the issue of how to deal with patients who switch among modes of dialysis. The appropriate analysis to be performed is subject to debate. The major limitation for all analytic techniques is the result of the high rate of modality switching, especially for PD to HD. Most previous studies have used the “intent-to-treat” approach where deaths among patients who switch are attributed to the initial therapy, regardless of the duration of time the patient used this treatment and/or the treatment history approach wherein patient follow-up is censored at or after the time of switch in therapy. Because the frequency of “switches” is high, the latter approach excludes a substantial part of the ESRD population experience. Our USRDS data included a tabulation of deaths and person years by various demographic variables. Time at risk was ascribed to the modality that the patient was receiving on January 1, allowing new assignment in the following year (January 1) if the patient switched dialytic modalities. This design may therefore better reflect the actual cumulative use of each of the two modalities than other strict “intent-to-treat” studies. Deaths after a switch in therapy were included and attributed to the therapy used at the beginning of the calendar year, unless a change occurred within the 60 days before January 1, in which case patients were excluded (avoiding the attribution of mortality to the new therapy during the transition phase). If patients are more likely to switch from one treatment to another before death, this analytic technique may introduce a bias in favor of PD because switches from PD to HD are more common.

As the result of patient selection, patients treated with PD differ from those treated with HD in terms of demographics and comorbid conditions, which are known to influence survival on chronic dialysis. Although adjustments were made in this study for several demographic variables, this study is limited by the lack of adjustment for comorbid factors, because these data are not recorded in the USRDS data base for all patients. A number of studies have found higher comorbidity in patients treated with PD (12,14,15,17,18). However, the USRDS Case-Mix Study, at the present largest, most rigorously designed evaluation of comorbidity differences between HD and PD, found among incident patients only a higher relative chance of peripheral vascular disease (RR = 1.2) and actually a lower chance of cerebrovascular accidents (RR = 0.66), inability to independently ambulate (RR = 0.57), and amputation due to peripheral vascular disease (RR = 0.66, p = 0.05) among PD-treated as compared with HD-treated patients (26). There was no significant difference in history of congestive heart failure or coronary heart disease. These results would suggest that the absence of adjustment for comorbid conditions in this study does not threaten the overall validity of our study results. It should be mentioned, however, that, in the USRDS Case-Mix Study (26), only the presence and not the severity of comorbid conditions was measured and compared. It is possible that, in a comparison where severity is also considered, overall comorbidity would be greater in PD-treated patients, in which case, the results of our study would be biased against PD. Similar to previous comparative studies, this study lacks adjustment for probable differences in social circumstances, education, patient preferences, patient health attitudes, and beliefs between HD- and PD-treated patients. It is clear that, regardless of the number of baseline characteristics that are controlled for, there will remain possible unknown differences between patients who choose PD and those who choose HD. The issue of selection bias in a comparative study of HD and PD can only be resolved by undertaking a randomized trial.

This study has found a higher risk of death associated with treatment with PD than with HD except among younger patients. There are several technical features of PD that may predispose a dialysis patient to death, including the obligatory dialysate protein loss, the excess absorption of glucose, and the risk of infection associated with the PD catheter. The differences in solute removal between PD and HD may also be critical in terms of mortality.

On the other hand, the higher DR observed in PD compared with HD may be the result of a lower delivered dose of dialysis in PD. Several studies have shown that higher doses of dialysis are associated with lower mortality in HD patients (27–31). More recently, this association has also been found among PD-treated patients (32,33). Relative dose of dialysis may therefore be important in comparative studies. However, because of the differences in the solute clearance of these modalities, it is difficult to compare dialysis dose. It is known that urea clearances are in general much less in PD-treated patients (34).

There is evidence from a national sample of HD patients that, at a time corresponding to this study sample (1987 to 1989), prescribed HD dose was inadequate and that delivered dose was substantially lower than prescribed (35). Since then, dose of HD has increased nationally, which would be expected to increase the difference in PD and HD relative DR. However, recently, much more interest has also developed in the measurement and individualization of PD dose (36,37). It is unclear how these changes in dose of PD and HD will affect relative mortality rates.

Patient compliance to the dialysis procedure is another possible factor contributing to the mortality differences observed. Compliance to HD treatments is easily measured and has been previously studied (38). However, relatively little is known regarding the compliance of PD patients. A recent report suggests that it may be a substantial problem (39). Frequent missed exchanges would be almost certain to adversely affect long-term outcomes. Information on patient compliance is not available in this study and has not been reported in previous HD/PD comparative studies.

This epidemiologic study is a comparison of mortal-
ility of HD and PD as practiced nationally in the United States. It has been suggested by the results of some studies (10,11,14,16–18) that, in dialysis programs where there is a considerable interest in PD, it has the potential to equal or exceed HD in terms of patient survival, particularly in some patient subgroups. The low percentage of patients receiving PD in the United States may indicate inexperience and a relative lack of interest in the use of this modality among nephrologists in this country as compared with in other countries. These results may therefore not be generalizable to individual centers or to other countries where PD receives greater use. Furthermore, this study reflects the practice of PD and HD from 1987 to 1989 (as well as any carryover effects from previous years). Clinical experience with the technical aspects of PD has increased, and there have been changes in catheter design, connection devices, and exchange systems with improvements in infection rates. However, changes have also occurred in the practice of HD. There has been greater attention to nutrition and dose of dialysis in both PD and HD to varying degrees. Therefore, it is unclear if more recent mortality rates for PD and HD would reflect dramatically different relative risks of mortality. The USRDS 1993 and 1994 annual data reports present unadjusted DR for PD and HD for 1988 to 1990 and 1989 to 1991, respectively. There has been an improvement in overall unadjusted DR for both PD and HD that has been greater for PD. By specific age groups, however, DR have increased among PD-treated patients in the younger age groups and for the 65 to 70 age group, whereas for HD, they have consistently decreased or remained the same. On the other hand, in many age groups, the magnitude of improvement is larger in the PD-treated patients. It is therefore difficult to draw conclusions without an adjusted analysis.

As outlined in the Methods, patients starting dialysis less than 3 months before January 1 were excluded for that year because patient enrollment is likely to be less complete during this period. This was done to avoid the bias that might be introduced by basing an analysis on the distinguished patients whose data are available during the first 90 days. In addition, the cohort scheme did not allow the capture of data on incident patients who did not survive to the first of a calendar year. If the effect of modality was significantly different in these excluded patients than in those included in the study, the overall effect of modality may be different. In fact, PD was associated with higher mortality than HD among patients with both shorter (<1 yr) and longer (>1 yr) duration of ESRD. This suggests that the exclusion of some incident patients is unlikely to substantially alter the study results. However, the results of this study should rightfully be generalized only to patients similar to those included.

CONCLUSIONS

This large national study of prevalent U.S. dialysis patients questions the assumption held by many nephrologists that PD and HD are comparable in terms of patient outcome. Except among the younger dialysis population, it has found mortality rates associated with PD to be higher than those for HD, particularly among diabetics, but also among nondiabetics. Several technical features of PD or their consequences may contribute to excess mortality. However, similar to all other studies that have compared mortality in patients treated with these modalities, baseline differences in PD- and HD-treated patients, which have not been accounted for, are almost certain to exist. Therefore, although these results may represent a true adverse treatment effect, the selection to PD of patients who are at greater risk of death may also account for the results obtained. It is unlikely that this issue of selection bias will ever be fully resolved in this comparison of dialytic modalities unless patients are randomly assigned to PD or HD. Alternate explanations of these findings include possible differential dose of dialysis, compliance of PD and HD patients to their dialytic regimen, or differences in the medical quality of care given to PD and HD patients. This study therefore again emphasizes the requirement for a large prospective study with standardization of treatments and close monitoring of compliance to resolve this question of comparative mortality in PD and HD, despite the significant cost and complexities this may entail. It would be essential for such a study to also measure and compare other important outcomes such as morbidity and quality of life to enable patients starting dialysis to make informed decisions regarding modality choice. In the interim, more attention to an adequate delivered dialysis dose, compliance, nutrition, and overall medical care will likely benefit patients using both dialytic modalities.

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REFERENCES

6. Churchill DN, Torrance GW, Taylor DW, et al.: Measure-