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Survival Comparison between Hemodialysis and Peritoneal Dialysis Based on Matched Doses of Delivered Therapy

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Abstract. Several studies have recently confirmed that hemodialysis (HD) and continuous ambulatory peritoneal dialysis (CAPD) survival is highly associated with delivered therapy Kt/V_{urea}. A direct comparison of equivalently dosed CAPD and HD has not previously been performed. A total of 968 incident HD patients at the Regional Kidney Disease Program from 1987 to June 1995 were studied, and these results were compared with those of the Canadian–United States prospective trial (CANUSA) consisting of 680 incident CAPD patients from September 1990 to December 31, 1992, with follow-up through December 31, 1993. All patients had quantitation of urea nitrogen for a total delivered dialysis session. On HD, *in vivo*, 2-pool, pre– and post–blood urea nitrogen kinetic modeling was performed with residual renal function determined every 6 mo. Patients were characterized by age, gender, race, renal diagnosis, and comorbid conditions. A Cox proportional hazards model was used to evaluate the effect of the individual comorbid conditions and the effect of dialysis therapy in the time-dependent method. The mean total Kt/V, both residual renal function and dialytic therapy in the HD patients, was 1.59. The CANUSA-delivered weekly Kt/V was 2.38 at the beginning of the baseline period and 1.99 after 24 mo of follow-up. When the peak concentration hypothesis was used, a Kt/V of 1.59 on HD was equivalent to a weekly CAPD dose of 2.1 to 2.2. A 1-unit increase in Kt/V was associated with 7% lower risk of death on HD and with a similar 8% lower risk of death while on CAPD. Patients with diabetes aged 46 to 60 yr had virtually identical 2-yr survival estimates on HD (83 to 90%), compared with CAPD (83 to 89%), with Kt/V ranges from 0.84 to 1.70 in HD and from 1.6 to 2.2 weekly Kt/V on peritoneal dialysis. Comparisons between HD and CAPD in older patients with diabetes yielded comparable results. Patient survival is highly influenced by delivered dialysis in both HD and peritoneal dialysis. Carefully matching of the therapies with delivered Kt/V demonstrates little differences in the survival outcome of HD and peritoneal dialysis patients, in contrast to some previous reports.

Several studies (1–9) have confirmed that for both hemodialysis (HD) and continuous ambulatory peritoneal dialysis (CAPD), patient survival improves with increased doses of delivered therapy. For HD, the Kt/V_{urea} index and for peritoneal dialysis (PD), the Kt/V_{urea} indices, as well as the weekly creatinine clearance per 1.73 m^2, are significant predictors of patient survival. Yet most of the survival comparisons between these two modalities have not been controlled for the delivered dose of dialysis. These studies have controlled for other significant predictors of survival (*e.g.*, age, diabetic status, history of cardiovascular disease [CVD]) but have ignored the solute removal in the populations being compared. Such survival comparisons must therefore be interpreted cautiously because the differences in survival elicited by the analyses may not be related to the therapy modality *per se* but may be a consequence of differences in the delivered dose of dialysis.

HD is an intermittent therapy with peaks and valleys of small solute concentrations over the duration of the week; concentrations fall steeply during the period of dialysis, then rise gradually over the interdialytic period as a result of solute generation within the body. In the case of CAPD, such wide swings of solute concentration are not typically observed because of the continuous nature of the therapy. The solute concentration profiles are relatively flat over the duration of the week, with solute removal being matched by solute generation. The peak concentration hypothesis (10) has provided a basis for matching an intermittent therapy such as HD with a continuous therapy such as CAPD by determining the dose of dialysis for the continuous therapy that results in a steady-state solute concentration that matches the peak solute concentration of the intermittent therapy rather than the time-averaged concentration.

We compared the survival of patients on HD and CAPD, controlling for dose of delivered dialysis; the doses of dialysis were matched on HD and CAPD by means of the peak concentration approach. We matched the Kt/V_{urea} per HD session with the weekly Kt/V_{urea} for CAPD. For each dialysis modal-

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ity, we selected a relatively large number of dialysis patients who had actual measurements of delivered therapy (inclusive of residual renal function) and that had achieved patient survival results that were documented to be better than those seen in North America.

Materials and Methods

For this matched-dose comparison of patient survival, we selected the database of the Regional Kidney Disease Program (RKDP) in Minneapolis, Minnesota, for HD and the Canadian–United States prospective trial (CANUSA) database (3) for CAPD. In the RKDP database, we included 968 incident HD patients who had entered the HD dialysis program between January 1, 1987, and December 31, 1994, and who were followed until June 30, 1995. Only patients with measurements of Kt/V_{urea} on dialysis, residual renal function, and serum albumin were included in the analysis. Delivered single-pool $(Kt/V)_{urea}$ was quantitated by the Daugirdas equation (11) with laboratory-measured values pre- and post–blood urea nitrogen. Urine was collected over the interdialytic period for quantifying the residual urea clearance and its contribution to total delivered Kt/V_{urea}. The quantity of Kt/V_{urea} contributed by the residual renal function in HD was determined by the Gotch method (11).

The CANUSA database included a prospective cohort of 680 patients commencing continuous PD in 14 centers in Canada and the United States between September 1, 1990, and December 31, 1992, with follow-up until December 31, 1993. In these patients, the dose of dialysis was quantitated by 24-h collection of effluent dialysate and urine, with representative aliquots from these collections assayed for urea nitrogen to determine the total delivered Kt/V_{urea}. To compare the CAPD and HD survival at each level of Kt/V_{urea}, estimated survival curves were developed that were based on specific patient profiles.

Each database of HD (RKDP) and PD (CANUSA) patients was analyzed separately. The patient and therapy variables were analyzed in a Cox regression model in a stepwise manner. The independent variables included age, gender, race, comorbidity, and the 6-mo data on mean Kt/V_{urea} from both the dialysis therapy and residual renal function. A time-dependent analysis was used to define the effect of dialysis therapy and residual renal function on mortality risk.

The Cox proportional hazards model (12) was used to compare patient survival in the two therapy modalities. In this comparison, age, diabetes mellitus as primary renal disease, history of CVD, serum albumin, and Kt/V were the selected covariates. Age was stratified into 3 categorical groups: 45 yr or less, 46 to 60 yr, and 61 yr or more. Kt/V and serum albumin were treated as continuous variables. In the survival predictions, the population average serum albumin was used. The doses of delivered dialysis, measured as total Kt/V_{urea}, were matched on the basis of the peak concentration hypothesis.

In the RKDP population, history of CVD included atherosclerotic heart disease, defined as a history of angina, previous acute myocardial infarction detected by electrocardiogram or enzymes, history of coronary artery bypass operation, percutaneous transluminal coronary angioplasty, or angiographic evidence; congestive heart failure; or peripheral vascular disease, defined as bruits in vessels, steal syndromes from vascular accesses, aneurysms, poor extremity pulses, and amputations. The CANUSA definition of CVD was less broad and only included patients with one of the following: angina, myocardial infarctions, New York Heart Classifications grades III to IV congestive heart failure, and amputation as a result of vascular disease. Results of the analyses were compared both with and without peripheral vascular disease to evaluate the effect of this condition.

Table 1. Population descriptive statistics[a]

Parameter	RKDP (HD)	CANUSA (PD)
n	968	680
Mean age (yr)	60.1	54.3
DM as primary renal diagnosis (%)	40%	30%
CVD history (%)	60%	36%
Mean serum albumin	35.3 g/L	34.9 g/L
Mean total therapy Kt/V (dialytic and RRF combined)	1.59 (per HD)	2.38 (per wk at baseline) 1.99 (per wk at 24 mo)

[a] RKDP, Regional Kidney Disease Program; HD, hemodialysis; CANUSA, Canadian/United States prospective trial; PD, peritoneal dialysis; DM, diabetes mellitus; CVD, cardiovascular disease; RRF, residual renal function.

Results

The two populations being compared are described in Table 1. The mean age of the HD population is approximately 6 yr older, with a higher percentage of patients with diabetes as primary renal disease. The much larger percentage of patients in the RKDP population with CVD may be related to the broader definition of CVD in the RKDP database. The mean serum albumin is comparable in the two populations. The mean total Kt/V per session is 1.59 in the RKDP HD population, and in the CANUSA group, it varies between a weekly value of 2.38 at baseline and 1.99 after 24 mo of follow-up.

The peak concentration matching of the Kt/V per session for HD with the weekly Kt/V for CAPD is shown in Table 2. Note that the mean Kt/V of 1.59 for the HD population is equivalent to a weekly Kt/V for CAPD of between 2.1 and 2.2, which is within the range of actual measured values (1.99 to 2.38). The National Kidney Foundation–Dialysis Outcomes Quality Initiative (NKF-DOQI) recommendation (13) of a single-pool Kt/V of 1.2 for HD corresponds to a weekly Kt/V of 1.9 for CAPD (Table 2). This is fairly consistent with the NKF-DOQI recommendation of a weekly Kt/V of 2.0 for CAPD.

Table 2. $(Kt/V)_{HD}$ per session and weekly $(Kt/V)_{PD}$ matched on the basis of the peak concentration hypothesis

$(Kt/V)_{HD}$ Single Pool	$(Kt/V)_{PD}$
0.84	1.6
0.95	1.7
1.07	1.8
1.20	1.9
1.35	2.0
1.52	2.1
1.70	2.2

Table 3. Results of the Cox analysis of relative risks for hemodialysis

Risk[a]	Relative Risk	P[b]
Age <45 y	1.00	Reference group
Age 45–60 y	1.57	0.13
Age >60 y	3.48	0.0001
DM (primary disease)	1.26	0.11
CVD history	1.20	0.13
Serum albumin (increase of 1 g/L)	0.83	0.0001
Kt/V (increase of 0.1 per session)	0.93	0.002

[a] DM, diabetes mellitus; CVD, cardiovascular disease.
[b] P value is compared with the reference group.

Table 4. Results of the Cox analysis of relative risks for hemodialysis

Risk[a]	Relative Risk	P[b]
Age <45 y	1.00	Reference group
Age 45–60 y	1.50	0.32
Age >60 y	2.40	0.02
DM (primary disease)	1.10	0.60
CVD history	2.40	0.0002
Serum albumin (increase of 1 g/L)	0.93	0.001
Kt/V (increase of 0.1 per week)	0.92	0.0009

[a] DM, diabetes mellitus; CVD, cardiovascular disease.
[b] P value is compared with the reference group.

The relative risk associated with the covariates chosen for this analysis, along with corresponding P values, are shown in Tables 3 and 4 for HD and CAPD, respectively. Note that diabetes as a primary disease is not a significant risk factor in either group when adjustments for comorbidity, serum albumin, and dialysis therapy are included in the model. The relative risk of CVD is more pronounced in the CAPD population, possibly a consequence of the more stringent definition of CVD in the CANUSA population. Being older than 60 appears to be associated with a slightly higher relative risk on HD than on CAPD. A 1-g/L increase in serum albumin is associated with a 17% lower risk of death on HD and a 7% lower risk of death on CAPD. A 0.1-unit increase in Kt/V is associated with a 7% lower risk of death on HD and a similar 8% lower risk of death on CAPD.

On the basis of the relative risk associated with each 0.1-unit change in Kt/V, representative 2-yr patient survival estimates on HD and CAPD are compared in Tables 5 to 8. The comparisons shown are for different age groups with and without diabetes mellitus and with or without CVD. The various combinations of age, diabetes mellitus, and CVD would result in a total of 12 comparative tables. However, only four tables have been chosen to illustrate what appears to be a consistent theme—that survivals are similar in HD and CAPD if the dose of dialysis is matched. In these 4 tables, the matching doses of Kt/V and the 2-yr survival rates at those doses of Kt/V are shown for both treatment modalities. Although Kt/V has a significant effect on survival in the older, sicker patients, it has much less effect in the younger, healthier patients. For example, the 2-yr survival on HD increases from 58 to 74% as Kt/V per session increases from 0.84 to 1.70 in patients older than 61 with diabetes and CVD. In patients younger than 45 without

Table 5. Predicted 2-yr percent survival (mean ± SEM) *versus* Kt/V: Age >61 yr, diabetes mellitus as primary disease, cardiovascular disease present

$(Kt/V)_{HD}$[a]	$(Survival)_{HD}$	$(Survival)_{PD}$	$(Kt/V)_{PD}$[a]
0.84	58 ± 6	48 ± 9	1.6
0.95	60 ± 5	51 ± 9	1.7
1.07	62 ± 5	54 ± 8	1.8
1.20	65 ± 4	56 ± 8	1.9
1.35	68 ± 3	59 ± 7	2.0
1.52	71 ± 3	61 ± 7	2.1
1.70	73 ± 3	64 ± 7	2.2

[a] $(Kt/V)_{HD}$ and $(Kt/V)_{PD}$ were matched on the basis of the peak concentration hypothesis.

Table 6. Predicted 2-yr percent survival (mean ± SEM) *versus* Kt/V: Age >61 yr, diabetes mellitus as primary disease, cardiovascular disease absent

$(Kt/V)_{HD}$[a]	$(Survival)_{HD}$	$(Survival)_{PD}$	$(Kt/V)_{PD}$[a]
0.84	66 ± 8	74 ± 7	1.6
0.95	68 ± 7	75 ± 6	1.7
1.07	70 ± 6	77 ± 6	1.8
1.20	72 ± 6	78 ± 6	1.9
1.35	75 ± 5	80 ± 5	2.0
1.52	77 ± 4	81 ± 5	2.1
1.70	80 ± 4	83 ± 5	2.2

[a] $(Kt/V)_{HD}$ and $(Kt/V)_{PD}$ were matched on the basis of the peak concentration hypothesis.

Table 7. Predicted 2-yr percent survival (mean ± SEM) *versus* Kt/V: Age 46–60 yr, diabetes mellitus as primary disease, cardiovascular disease absent

$(Kt/V)_{HD}$[a]	$(Survival)_{HD}$	$(Survival)_{PD}$	$(Kt/V)_{PD}$[a]
0.84	83 ± 4	83 ± 5	1.6
0.95	84 ± 4	84 ± 5	1.7
1.07	85 ± 3	85 ± 4	1.8
1.20	86 ± 3	86 ± 4	1.9
1.35	88 ± 3	87 ± 4	2.0
1.52	89 ± 2	88 ± 3	2.1
1.70	90 ± 2	89 ± 3	2.2

[a] $(Kt/V)_{HD}$ and $(Kt/V)_{PD}$ were matched on the basis of the peak concentration hypothesis.

Table 8. Predicted 2-yr percent survival (mean ± SEM) *versus* Kt/V: Age ≤45 yr, diabetes mellitus not primary disease, cardiovascular disease absent

$(Kt/V)_{HD}$[a]	$(Survival)_{HD}$	$(Survival)_{PD}$	$(Kt/V)_{PD}$[a]
0.84	91 ± 3	95 ± 1	1.6
0.95	91 ± 3	90 ± 3	1.7
1.07	92 ± 2	91 ± 3	1.8
1.20	93 ± 2	91 ± 3	1.9
1.35	93 ± 2	87 ± 4	2.0
1.52	94 ± 2	93 ± 3	2.1
1.70	95 ± 1	93 ± 2	2.2

[a] $(Kt/V)_{HD}$ and $(Kt/V)_{PD}$ were matched on the basis of the peak concentration hypothesis.

diabetes or CVD, the same increase in Kt/V from 0.84 to 1.70 is associated with a much smaller survival improvement—from 91 to 95%. So not only is the 2-yr survival much higher in the younger, healthier patient, but it is also less influenced by changes in Kt/V.

Discussion

The Cox proportional hazards model clearly indicates that age, history of CVD, serum albumin, and Kt/V are significant predictors of patient survival for both HD and CAPD. Although the magnitude of the risks is different, the direction and significance of the risks are the same. A more direct comparison of risks was not possible because of the observational nature of the study. Differences, if any, may reflect severity of disease or acceptance rates. After adjustment for other risk factors, this study shows that diabetes mellitus as primary renal disease does not appear to pose any additional risk in either HD or CAPD, particularly when albumin and dialysis therapy are taken into consideration. We confined our analysis to patients with diabetes as a primary disease, excluding those with other etiologies of renal disease.

The 2-yr survival comparisons demonstrate that, although Kt/V is a significant predictor of patient survival, once Kt/V is controlled for, 2-yr patient survivals are similar in the 2 modalities being compared, independent of patient age, diabetic status, history of CVD, and the absolute differences in the value of the other risks. This appears to be the first time these observations have been demonstrated. Previous analyses by Bloembergen *et al.* (7) have suggested a 19% higher risk of death in CAPD relative to HD, this difference being even more pronounced in patients with diabetes, who had a 38% higher risk of death on CAPD. There are three major differences between our analysis and that of Bloembergen *et al.* We analyzed an incident dialysis population, whereas Bloembergen *et al.* analyzed point-prevalent patients with varying time on dialysis ("vintage"). Because dialysis dose and residual renal function vary over vintage, this issue should be more carefully considered. The dose of dialysis was not quantitated or controlled for in the Bloembergen *et al.* analysis, nor did the analysis adjust for comorbidity.

To resolve the results of the Bloembergen *et al.* (7) analysis with our results, one would have to account for the influence of vintage, dose, and comorbidity in the Bloembergen *et al.* analysis. Fenton *et al.* (14) have shown that for an incident population of 11,970 patients with end-stage renal disease from the Canadian Organ Replacement Register, the mortality rate ratio for CAPD–continuous cycling PD relative to HD was 0.73, based on a Poisson regression. The lower mortality on PD relative to HD was applicable to all subgroups defined by age and the presence of diabetes. However, when the analysis was repeated using prevalent patients, CAPD no longer had a lower mortality risk ratio (rate ratio = 1.01). These same observations were also confirmed by Collins *et al.* (15) in a US population of HD and PD patients.

Regarding dose, one would have to postulate that if the typical CAPD patient is being less adequately dialyzed then the typical HD patient, one might expect a higher risk of death on CAPD, particularly if vintage on dialysis therapy is a surrogate for residual renal function. This postulate may not be completely unreasonable. Studies on the adequacy of CAPD are relatively recent—less than a decade old—whereas HD adequacy has been a subject of interest for almost three decades. This is not surprising when one considers that CAPD is a much newer therapy than HD. Clinicians have therefore not paid as much attention to CAPD therapy prescription practices as they have to HD prescriptions.

In addition, surveys (16) indicate that the majority of CAPD patients receive the standard prescription of 2-L exchanges 4 times a day without regard to body size or residual renal function. It has been calculated (17) that this standard regimen of CAPD cannot provide an adequate dose of dialysis in even average-sized patients without residual renal function. It has been recommended (18) that the volume of the CAPD exchange be tailored to the size of the patient, with average-sized patients using 2.5-L exchanges and larger patients using 3-L exchanges. If the patients in the Bloembergen *et al.* (7) population underwent dialysis with the standard 2-L, 4-times-a-day exchange regimen and had no significant residual renal function, it is likely that these patients were underdialyzed and therefore had a higher risk of death. The 19% higher risk of death in the Bloembergen *et al.* analysis may therefore have been a consequence not only of uncontrolled vintage but also of the dose of dialysis delivered rather than the modality.

The 2-yr survival data in younger (<45 yr), healthier (no diabetes mellitus, no CVD) patients indicate a relatively high survival rate (approximately 90%) with a consequently lesser effect of Kt/V on survival. This is probably a testimonial to the resilience of young, healthy patients. However, this should not be misinterpreted as suggesting that one should deliver less adequate dialysis in these patients.

The peak concentration hypothesis is approximately a decade old and is, by its very nature, not easy to test directly. The results of this analysis provide an indirect verification of this hypothesis and indicate that it may be a reasonable basis for comparing a continuous therapy with an intermittent one.

To our knowledge, this comparative analysis of HD and CAPD survival is the first to control for the delivered dose of

dialysis. The analysis shows clearly that for both HD and CAPD, dose of dialysis as measured by the Kt/V index is a significant predictor of survival. Furthermore, our study demonstrates that when dose of dialysis is matched, HD and CAPD provide comparable 2-yr survival rates, independent of age, diabetic status, and history of CVD. These results are an indirect confirmation of the peak concentration hypothesis.

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