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Controlled comparison of hemodialysis and peritoneal dialysis: Veterans Administration multicenter study

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Controlled comparison of hemodialysis and peritoneal dialysis: Veterans Administration multicenter study. We measured mortality and morbidity among 114 patients assigned randomly to home hemodialysis (HD) and home intermittent peritoneal dialysis (IPD). Data were collected during the time of home training and for 12 months after initiation of home dialysis. Training time was shorter for the IPD than for the HD patients ($P < 0.001$) with median time 1.8 months for IPD and 3.9 months for HD. Switching to the alternative mode of treatment was more frequent for the IPD group (29/59 vs. 5/55, $P < 0.001$). Survival time was not different, perhaps because of the modality change. More IPD patients were hospitalized in the first 6 months (20 for IPD vs. 9 for HD, $P = 0.02$), but they had fewer troublesome cardiovascular events in the first year (0 vs. 12, $P < 0.001$). The HD patients maintained better nutritional status as reflected in body weight and arm muscle circumference and possibly in urea appearance rate. Thus, these data suggest that for most patients, IPD is a less satisfactory form of therapy than HD, but certain advantages of IPD did emerge. Applications of this information to the currently more popular mode of CAPD await further study.

Comparaison contrôlée entre l'hémodialyse et la dialyse péritonéale: Étude multicentrique de l'Administration des Veterans. Nous avons mesuré la mortalité et la morbidité chez 114 malades, pris au hasard, en hémodialyse à domicile (HD) ou en dialyse péritonéale intermittente à domicile (IPD). Les données ont été recueillies pendant l'entrainement à domicile et pendant les 12 mois suivant le début de la dialyse à domicile. La durée d'entrainement était plus brève pour les malades en IPD que pour ceux en HD ($P < 0{,}001$), avec un temps médian de 1,8 mois pour l'IPD et de 3,9 mois pour l'HD. Le changement pour l'autre mode de traitement était plus fréquent pour le groupe IPD (29/59 contre 5/55, $P < 0{,}001$). La durée de suivi n'était pas différente, peut-être à cause du changement de modalité. Plus de malades en IPD ont été hospitalisés dans les 6 premiers mois (20 en IPD, contre 9 en HD, $P = 0{,}02$), mais ils ont eu moins d'ennuis cardiovasculaires génants au cours de la première année (0 contre 12, $P < 0{,}001$). Les malades HD conservaient un meilleur état nutritionnel, reflété par le poids corporel, la circonférence musculaire du bras, et probablement la vitesse d'apparition de l'urée. Ainsi ces données suggèrent que pour la plupart des malades, l'IPD est une forme de traitement moins satisfaisante que l'HD, mais certains avantages de l'IPD sont apparus. Les applications de cette information au mode actuellement le plus répandu de CAPD requièrent d'autres études.

In studies to date that compare the outcome of treatment among two or more modes of maintenance dialysis therapy, the evaluations are confounded by the nonrandom assignment of patients to treatment groups. Physicians admittedly tend to select the therapy that may best enhance a patient's outcome potential, whether the potential is real or assumed [1–3]. Recent studies have attempted to circumvent the analytic problems arising from this practice by collating patient characteristics so that later comparisons can be made from demographically similar groups [4, 5]. Those attempts, however, may be only partially successful because the unstated bias in patient assignment likely remains.

To obtain an evaluation based on classic randomization techniques, thus controlling for the extraneous variables of biased selection of subjects, we conducted a nationwide randomized cooperative study in which patients with endstage renal failure were randomly assigned to one of the two major modes of dialysis therapy, hemodialysis (HD), or peritoneal dialysis (PD). Initiated in 1975 and spanning 5 years of data collection at five centers, the study was carried out under the auspices of the Veterans Administration Cooperative Studies Program [6]. This paper presents the results.

Rationale of the study design. The study was designed primarily around the need to control for the selection of patients. However, other considerations guided the design of the study. Home dialysis was chosen as the basis of both modes of therapy because of the impracticality of administering PD in a hospital facility.[1] Moreover, the investigators were proponents of prescribing home dialysis wherever possible. Another design consideration dealt with the problem of treatment dose.

[1] A few patients designated home HD actually cared for themselves in the facility as if they were at home, a process often called "self-dialysis." They are included in the home HD group for the purpose of this report.

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Rather than arbitrarily select treatment schedules in an attempt to normalize theoretical or calculated solute removal rates, we chose to use the standard treatment protocols of the day. For HD, it was single-pass hemodialysis for 10 to 14 hr a week in three treatment sessions. For PD, it was intermittent peritoneal dialysis (IPD) for approximately 35 hr a week in three to four sessions. A final design consideration dealt with physician-investigator discretion in changing treatment modality. We chose to allow complete discretion and to record these decisions as events.

For evaluating outcome, we used a wider selection of outcome measures than the ones usually used. Most other studies, new and old, rely on easily available parametric data, such as the serum concentrations of urea, creatinine, sodium, potassium, bicarbonate, and serum protein values [7–9]. Although similar data were obtained and compared in this study, we also included certain other factors that probably have a stronger influence on both the physicians' and the patients' assessments of outcome: the number of morbid events, their impact on the assessment of well-being, the frequency and duration of hospitalizations (including a semiquantitative assessment of the outcome of events), and the emotional and nutritional status of patients.

In spite of all caution, however, the design of the study suffered two problems. The first was the difficulty of comparing, quantitatively, the dialysis dosages of the two very different treatment techniques. In the absence of knowledge about the specific toxins (or toxin) whose concentrations are presumably being lowered by dialysis, and in the absence of uniform opinions on the adequacy of the dialysis prescription itself, we elected to compare the two therapies in terms of how they were actually being practiced in the community and in the participating hospitals. Even though a common base comparison is difficult, we have provided some comparative data.

The second problem was the choice of IPD as the representative mode of peritoneal dialysis. Several years after the study was designed, the newer technique of continuous ambulatory peritoneal dialysis (CAPD) began to gain such worldwide popularity that IPD quickly became considered an outdated form of therapy [10]. In spite of this unforeseeable development, however, there was still merit for continuation of the study and for the results to be made available to others. The principal difference between IPD and CAPD is that CAPD provides fluid in the abdomen continuously except during the time of the exchanges. CAPD also has a slower exchange rate (approximately 0.3 to 1.0 liters/hr) than IPD does (4 liters/hr). Because of its relative ease of use, some theoretical advantages [11], and a general consensus that IPD does not provide a satisfactory maintenance therapy, CAPD has become the preferred choice [12–14]. But the current disfavor for IPD is not based on carefully collected evidence. In fact, the medical literature before the ascendance of CAPD suggests that IPD is a very useful form of therapy when carried out with the same enthusiasm usually reserved for hemodialysis [15–18]. Ironically, despite the initial optimism for CAPD, now it, too, is coming under skeptical scrutiny, largely because of reported high patient dropout rate [5, 19].

Thus there were two reasons for continuing the study. The first was that it would represent the only randomized-controlled evaluation for the two predominant modes of dialysis. The second reason for continuation was to allow a more thorough understanding of the analytical advantages and disadvantages of a randomization-based study protocol in the assessment of dialysis treatment.

Methods

The study protocol was approved by the Human Studies Committee at each participating institution and by a central Human Rights Committee at the Veterans Administration (VA) Cooperative Studies Program Coordinating Center at the West Haven VA Medical Center before it was initiated. The study was monitored by an independent Operations Committee[2] and by the Human Rights Committee during the course of the study.

Patient selection. From November, 1975 through November, 1979, at each of the five participating hospitals, all nondiabetic veterans with endstage renal disease who presented for care were screened for possible randomization. Of the 398 patients screened, eight could not be considered further owing to their early death or to plans for transferring them immediately to another institution. Admission criteria [6] excluded 209 others, who were either *ineligible* because they would admit other concomittant conditions or were *rejected* for practical considerations.

Exclusions based on ineligibility were as follows (number of patients in parentheses): female (3); over age 65 (28); the presence of substantial residual renal function, that is, a serum creatinine concentration of less than 8 mg/dl *and* a creatinine clearance of greater than 8 ml/min (13); maintenance dialysis in progress more than 4 months (6), previous bilateral nephrectomy (12), the presence of lupus erythematosis (4); the presence of active malignancy (17), or other major medical problems (20). Although amyloidosis and prior renal transplantation were criteria for ineligibility, no patient fell into these categories.

The reasons for rejection were: an early transplantation was planned (22), full care was needed by the patient (20), a referring physician had made specific recommendations (13), or the physician-investigator felt that IPD was unacceptable (32) or that HD was unacceptable (84). These reasons for rejection were not mutually exclusive.

The remaining 181 eligible and suitable (that is, not *rejected*) patients were asked to participate in the study and to be assigned randomly to one of the two forms of home dialysis. This process of informed consent has been described in detail elsewhere [20]. In brief, the advantages and disadvantages of each type of dialysis were explained; the patients were shown a video tape describing the two forms of therapy and were allowed to review the tape as often as they wished; and a questionnaire was completed after this instruction. The study design allowed randomization to be done before initiating dialysis therapy or within 4 months after its initiation. As a result of these explanations, 67 of the 181 patients chose to

[2] The Operations Committee was comprised of experts in the subject matter of the study, a biostatistician, and other appropriate technical or scientific specialists. The members must not have been participants or consultants in the planning or execution phases of the study. It provided a continuing critical and unbiased evaluation of the study's progress and formulated operational policy consistent with the best current biomedical research practice. Members of the Committee are listed in the **Appendix.**

Table 1. Patient accession at each institution[a]

Institution	Screened *N*	Not considered *N*	Ineligible *N*	Rejected *N*	Refused *N*	Randomized *N*
A	93	1 (1)	9 (10)	32 (34)	24 (26)	27 (29)
B	64	0 (0)	11 (17)	31 (48)	6 (9)	16 (25)
C	114	2 (2)	30 (26)	30 (26)	16 (14)	36 (32)
D	90	5 (6)	35 (39)	22 (24)	11 (12)	17 (19)
E	37	0 (0)	4 (11)	5 (14)	10 (27)	18 (49)
Total	*398*	*8 (2)*	*89 (22)*	*120 (30)*	*67 (17)*	*114 (29)*

[a] Numbers in parentheses are the percent of those screened; *N* is the number of patients in each group.

select one of the therapies rather than enter randomization; of these, 44 selected home HD and 23 selected home PD.

The remaining 114 patients were assigned to one of the two alternative forms of therapy; assignment was based on a table of random numbers. These 114 patients are the subject of this report. Table 1 summarizes their progression through the accession procedure. Treatments were randomized within each institution and each age stratum: age under 50, and age 50 and over; there were 45 patients under age 50 and 69 who were age 50 and over. Fifty-five patients were assigned randomly to HD and 59 to PD.

Table 2 compares the randomized patients with the non-randomized patients (those who refused study participation, those who were ineligible, and those who were rejected) with respect to demographic, clinical, and psychologic status. In evaluating clinical status, we considered the specific features of the patients' condition, including the cause of renal failure, average blood pressure, and residual creatinine clearance before dialysis therapy was required (if the data were available). We also assessed the presence of significant co-morbidity in other organ systems (skin, cardiac, pulmonary, gastrointestinal, hepatic, endocrine, musculoskeletal, central nervous system, psychiatric, and hematologic) by a standard scoring system, which is described under the section on *Clinical and laboratory assessment*. Psychologic status was assessed by the Structured and Scaled Interview to Assess Maladjustment (SSIAM), which is an indicator of the real-life adjustment of the patient in family, social-leisure, marriage, sexual, and working status [21, 22], and by the Multiple Affect Adjective Check List (MAACL), which provides a rapid measure of the mood of the patient [22].

Clinical and laboratory assessment. Survival time from first dialysis was compared in the two treatment groups. A death occurring within 3 months after switching to an alternative form of dialysis was considered a death within the assigned group; however, a death following any transplantation which took place after beginning dialysis treatments was not considered a dialysis-related mortality.

Assessments of outcome including morbidity were carried out at the following intervals: *(1)* at the time of the first regularly scheduled dialysis treatment; *(2)* at the time home-dialysis began; and *(3)* approximately 6 and 12 months later. The precise timing of the 6th and 12th month assessments varied owing to practical considerations, including patient convenience. The average deviation from the precise date of the 6-month follow-up was -3 ± 42 days (SD) for the HD patients and -18 ± 35 days for the IPD patients. The deviations were not significantly different at the 5% level. Similar results were noted at the 12 month follow-up.

Data on clinical, laboratory and psychological status 3 months after a patient was permanently re-assigned to the alternative treatment mode were also included in the assessment of the randomly assigned dialysis mode.

Morbidity was assessed at the 6 and 12 month intervals using clinical, laboratory, and psychological parameters. For several clinical assessments, we used a 6-tiered, ordinal scale, referred to here as the *standard scale: Score 1:* Normal or absent; *Score 2:* Borderline normal or possibly present; *Score 3:* Definitely abnormal but of little or no functional significance; *Score 4:* Functionally significant but of slight importance; *Score 5:* Important but not life-determining; *Score 6:* Functionally life-determining.

Morbidity was also assessed by the frequency and duration of hospitalizations. As a part of this assessment, we maintained an inventory of the impact of hospitalization by the use of a six-tiered semiquantitative assessment similar to the standard scale and ranging from *better off* (score 1) to *very seriously ill* (score 6). Additional information was collected for the nature and severity of episodes of dialysis-access failure, myocardial infarction, cerebral vascular accident, peritonitis, and hepatitis. Records were maintained for the number of blood transfusions, the presence of *mild* or *severe* motor and sensory neuropathy (assessed according to vibratory sense), and the patients' general cardiac status (assessed according to criteria set by the New York State Heart Association). Dialysis-related symptomatology was assessed, and scored by the same standard scale, for symptomatic hypotension, muscle cramps, nausea, and post-dialysis lethargy.

Blood and serum parameters were assessed every 3 months by standard clinical laboratory methods. These parameters were hematocrit, serum creatinine, urea nitrogen, uric acid, calcium, phosphorus, alkaline phosphatase, and albumin. A psychologic assessment was carried out at 6- and 12-month intervals by the SSIAM. Nutritional status was assessed by anthropometric studies (estimated dry weight and measured upper arm muscle circumference) [25] and urea generation rate measurements (dialysate loss plus any renal loss) [26]. Arm muscle circumference was calculated by subtracting the tricep skinfold thickness from the mid upper arm circumference.

Also assessed was the time required to achieve home dialysis and the duration of treatment adherence. Those patients randomly assigned to one form of therapy but then, by physician or

Table 2. Characteristics of participants and non-participants in randomized trial of dialysis modality

	Randomized	Non-randomized	*P*
Number of patients	114	276	
Age, *yr*	(114)	(272)	
± SEM	50.3 ± 0.9	51.7 ± 0.7	0.25
Race, %	(114)	(272)	
White	54.4	51.1	
Black	41.2	48.5	
Other	4.4	0.4	0.56
Education, %	(114)	(256)	
<7 years	13.2	14.8	
≥7 but <12 years	42.1	35.9	
High school graduate	21.9	31.3	
Partial college	11.4	11.7	
College graduate	11.4	6.3	0.20
Occupation, %	(113)	(261)	
Officers & managers	23.0	24.5	
Skilled & career enlisted	54.9	50.2	
Semi-skilled	22.1	25.3	0.69
Hometown population, %	(114)	(266)	
<10,000	43.9	33.5	
10,000 to 99,999	31.6	36.5	
≥100,000	24.6	30.1	0.15
No others in home, %	(114)	(261)	
0	4.4	11.9	
1	27.2	39.5	
≥2	68.4	48.7	0.001
Cause of failure, %	(114)	(276)	
Glomerulonephritis	35.1	27.5	
Polycystic kidney disease	10.5	5.4	
Pyelonephritis	0.9	4.3	
Nephrosclerosis	21.9	25.0	
Interstitial nephritis	8.8	8.0	
Nephrolithiasis	0.9	1.8	
Other renal disease	3.5	12.7	
Unknown	18.4	15.2	0.03
Creatinine clearance	(88)	(183)	
Mean ± SEM	4.3 ± 0.4	5.0 ± 0.3	0.09
Systolic pressure, *mm Hg*	(109)	(267)	
Mean ± SEM	144 ± 2	144 ± 1	0.83
Diastolic pressure, *mm Hg*	(109)	(267)	
Mean ± SEM	85 ± 1	84 ± 1	0.82
Co-morbidity severity	(114)	(276)	
% with ≥2 organ systems, each with score >3	48	55	0.20
% with Cardiac or Pulmonary score >3[a]	47	54	0.23
% with Psych. or Neuro. score >3[a]	15	25	0.03
Multiple Affect Adjective Check List[b]	(110)	(223)	
Anxiety	4.88 ± 0.39	5.69 ± 0.30	0.11
Depression	10.62 ± 0.66	11.29 ± 0.48	0.42
Hostility	4.20 ± 0.34	4.23 ± 0.25	0.95
Maladjustment Interview	(110)	(218)	
Overall score[c]	2.72 ± 0.08	2.86 ± 0.06	0.15

Symbol: ( ), indicates number of patients reported.
[a] Scoring is described in **Methods.**
[b] Scoring is described in [21, 22].
[c] Scoring is described in [23].

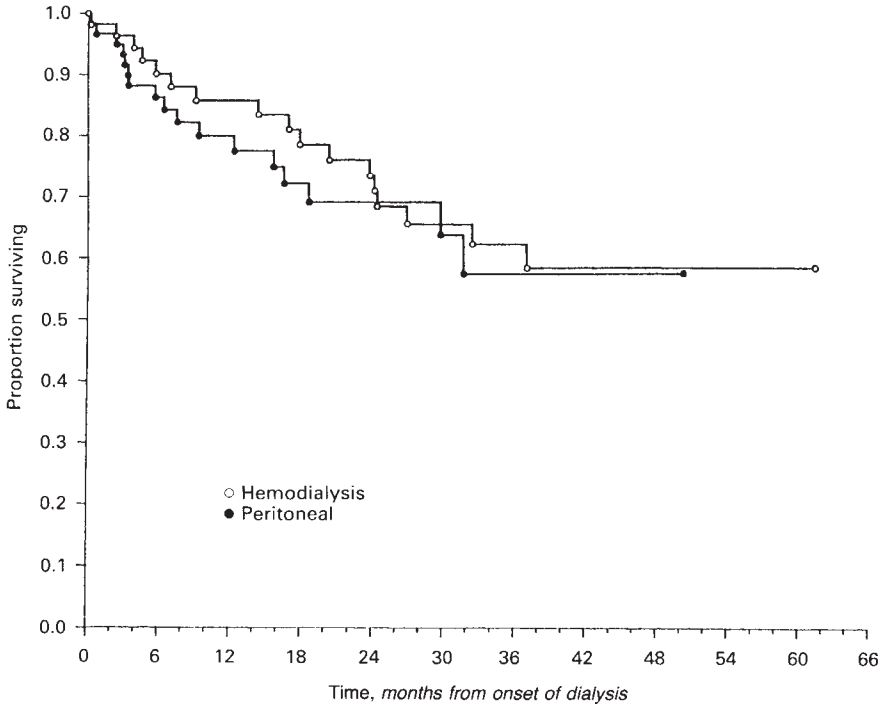

Fig. 1. *Survival curves for patients assigned randomly to hemodialysis and peritoneal dialysis.* Data 3 months after the change of dialysis therapy are excluded from analysis *(censored)*. No significant difference in survival time was observed.

patient judgement, reassigned permanently to the other form of therapy were classified as withdrawals from the study.

Statistical methods. Three types of statistical analysis were used: *(1)* Hypothesis of equal proportions or identical distributions for categorical data were tested by the chi-square test statistic with appropriate degrees of freedom [27]. Fisher's exact test was used whenever the expected value in a cell of 2 × 2 table was five or less; *(2)* hypothesis of equal means for continuous variables were tested with the t-statistic [27]; *(3)* curves for HD and IPD were constructed by the product-limit method of Kaplan-Meier [28] for each of the following variables: Survival time from first dialysis, duration from first dialysis to completion of home-care training, and duration of adherence to assigned therapy after achieving home-care. The generalized Wilcoxon test [29] was used for comparison of the curves between HD and IPD. The approach proposed by Cox [24] was also adopted to test the treatment effect after adjusting for age.

The probability under the sampling distribution that the test statistic was equal to or more extreme than the observed value was calculated for each of these tests. The level of significance was set at 5%.

Results

Characteristics of randomized and non-randomized patients. As noted earlier, we excluded certain groups of patients from the randomization process. In view of the possible application of these results to other patients we compared selected characteristics (Table 2) between the aggregate non-randomized group (consisting of the *rejected, ineligible,* and *refused* subgroups) and the randomized group. The two groups were similar in the following categories: age, race, education, occupational experience, size of hometown, and residual renal function. The randomized group differed from the non-randomized aggregate group in that they had slightly larger families at home, higher frequency of glomerulonephritis, and less neuropsychiatric co-morbidity. Other characteristics not listed in Table 2 were also compared. No difference was noted for the presence or severity of dyspnea, angina, cardiac enlargement, or motor strength. As expected the patients randomized to HD and IPD were similar with respect to all the characteristics considered.

Dialysis dosage. The patients assigned to home HD were treated 11.5 ± 1.6 (SD) hr a week. The HD patients used blood

Table 3. Causes of treatment change for randomized patients

	Transfer from		
	HD to IPD	IPD to HD	*P*
Before home-care	2/55 (3.6%)	5/59 (8.5%)	0.28
After home-care[a]	3/42 (7.1%)	24/47 (51.5%)	<0.001
Total	*5/55 (9.1%)*	*29/59 (49.2%)*	*<0.001*
Principal reason			
Medical	3[b]	14[c]	
Technical	1	5	
Patient and/or family	1	3	
Staff-initiated	0	3	
None given	0	4	

[a] There were reasons for discontinuing assigned therapy before achieving home-care other than transfer to alternate therapy. Of 55 assigned to HD home-care, two received a renal transplant, four died, three were unwilling or unable to complete training and two were alive but not yet finished training at the end of the study. Of 59 assigned to peritoneal dialysis, four died, one was unwilling to complete training and two were on dialysis for a short duration and then required no dialysis for the next 3 years.

[b] One reported two principal reasons, including medical.

[c] Four reported two principal reasons, including medical.

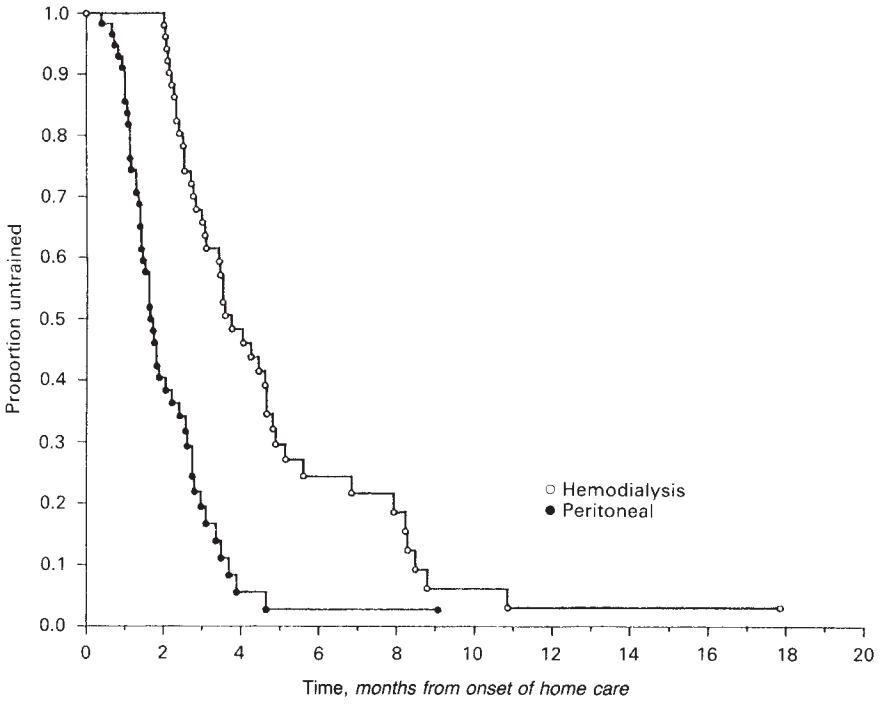

Fig. 2. *Actuarial curves for time required to complete home training.* The median training time was approximately 2 months shorter for peritoneal dialysis patients and the difference was significant.

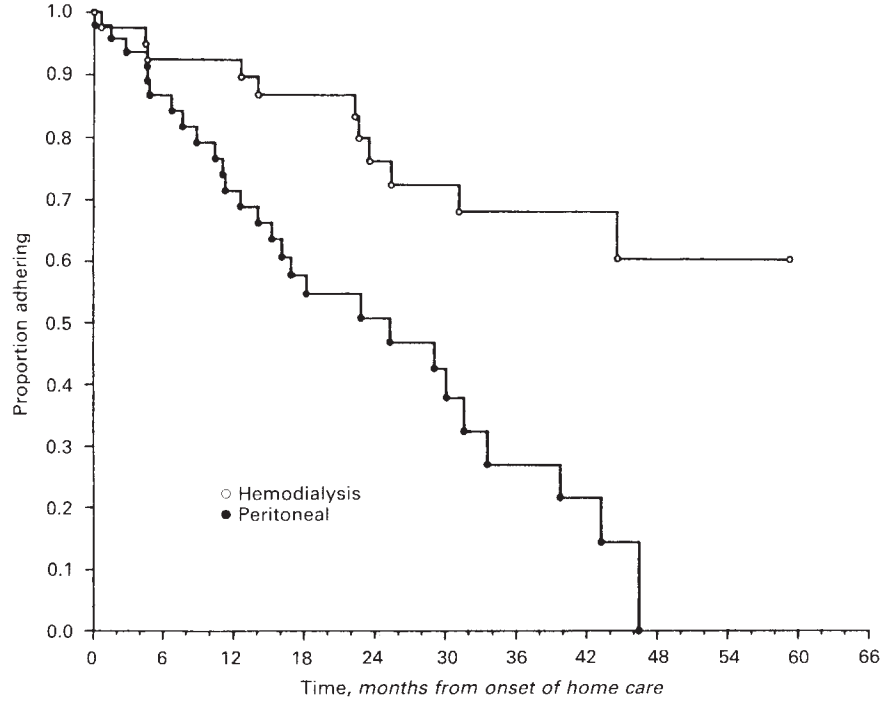

Fig. 3. *Actuarial curves for duration of adherence to assigned therapy.* Patients randomly assigned to peritoneal dialysis dropped out of this dialysis therapy approximately 10 months earlier than those assigned to hemodialysis and the difference was significant.

flows of 180 to 250 ml/hr, with dialysate rates of 500 ml/min. Dialyzers with nominal urea clearance of 97 to 175 ml/min at blood flow rates of 200 ml/min were used. The calculated dialysis urea clearance were between 59 and 133 liters/week (average: 104 ± 19 liters/wk).

All patients assigned to home IPD used automated equipment that exchanged peritoneal fluid at a rate of 4 liters/hr. Treatment duration was 34.9 ± 7.2 (SD) hr/wk, usually in three to four sessions a week. Assuming that average urea clearance was 25 ml/min, the average weekly urea clearance was approximately 52 ± 11 liters/week.

Study results. Of the 114 patients randomly assigned to either home HD (55) or home IPD (59), all but one actually entered their assigned therapy; he died before starting therapy. Of those

Table 4. Major morbidity after achieving home care

	First 6 months		Second 6 months	
	HD	IPD	HD	IPD
At risk (beginning of period)	42	47	38	38
Hospitalization				
No. admissions[a]	9	30[b]	20	28
No. of patients admitted > 1 time	0	7[c]	6	8
Average duration ± SEM for those hospitalized, *days*	16.3 ± 3.2	18.3 ± 2.8	24.0 ± 5.8	28.4 ± 5.8
Dialysis access malfunction requiring surgical revision				
No. events (no. patients)	7 (4)	9 (6)	2 (2)	7 (5)
No. with moderate morbidity or greater	3	5	0	3
No. deaths	1	0	0	0
Not requiring surgical revision	3	2	2	3
No. deaths	0	0	1	0
Cardiac incidents				
Arrhythmia	1	0	2	0
Angina (new or worse)	0	0	1	0
Myocardial infarction	0	0	0	0
Cardiac decompensation	2	0	3	0
Pericarditis	1	0	2	0
Total no. incidents[a]	4	0[b]	8	0[b]
No. with moderate morbidity or greater	1	0	1	0
Peritonitis				
No. events[a]	1	21[c]	0	17[c]
No. patients	1	13[c]	0	10[d]
No. with moderate morbidity or greater	0	9[c]	0	8[c]

[a] Student's *t* test was used.
[b] $P < 0.05$.
[c] $P < 0.01$.
[d] $P < 0.001$.

who entered therapy, 89 (42 HD patients, 47 IPD patients) successfully completed training for dialysis at home or for dialysis in the facility done entirely by themselves *self-care)*. Older patients (≥50 years) achieved home-care as frequently (36/45 = 80%) as younger patients did (53/69 = 77%).

Survival curves from first dialysis (Fig. 1) were not significantly different between HD and IPD ($P = 0.40$). The median survival time was greater than 61 months for HD, and greater than 50 months for IPD. The treatment effect was not significant after adjusting for age ($P = 0.53$) by the Cox method [24]. The survival curves were also not significant between the two groups after achievement of home-care status ($P = 0.96$). The median survival time was greater than 59 months for HD and greater than 49 months for IPD. The treatment effect after adjusting for age was also not significant ($P = 0.99$).

The time from initiation of dialysis treatment to achievement of home-care dialysis status was significantly shorter for the IPD group ($P < 0.001$) with median duration 3.9 months for HD and 1.8 months for IPD (Fig. 2). But the duration of adherence to the assigned therapy after achieving home-care status was considerably greater or longer for the HD group ($P < 0.01$) with median duration for HD greater than 60 months, while the median duration for IPD was 25.4 months (Fig. 3). The treatment effect was also significant after adjusting for age ($P < 0.001$). Overall, 29 of the 59 patients randomized originally to IPD were transferred to HD, and five of them did so before achieving home-care status (Table 3). In contrast, only five of those randomized to HD transferred to IPD ($P < 0.001$). The reasons for transfer were given as "medical" in most cases, regardless of which change was made. Temporary assignment to the alternate form of dialysis was required during hospitalization of five IPD patients for between 25 and 47 days; and for two HD patients for 22 and 36 days.

Results of the detailed statistical analysis of morbidity of the randomized patients after they achieved home-care status are presented in Tables 4 and 5. In the first 6 months, there were 30 hospitalizations of 20 IPD patients, a sharp contrast with the only nine hospitalizations, each for a separate patient, during that time for the HD patients ($P < 0.001$). In the second 6-month period, with fewer IPD patients at risk, the frequency distribution of hospitalizations was similar. The duration of hospitalization for those hospitalized was not statistically different in either 6-month period.

Dialysis-access malfunction for both forms of dialysis was compared for frequency and severity. Two HD patients died as a result of dialysis-access malfunction (one of endocarditis and the other, of pulmonary edema after dialysis was delayed) but the proportion of difficulties requiring surgical revision seemed, if anything, less in this group (9.5% for HD and 12.8% for IPD), though the difference was not significant statistically. In over

Table 5. Other outcome features for randomized patients after achieving home care[a]

	First 6 months		Second 6 months	
	HD	IPD	HD	IPD
No. of patients at onset	42	47	38	38
Clinical parameters				
No. of patients	41	45	36	36
Pts. receiving transfusions	6	7	6	8
Avg. units blood rec'd	3.7 ± 0.8	5.6 ± 1.9	7.3 ± 3.4	5.9 ± 3.0
Systolic BP, *mm Hg*	148 ± 2	152 ± 3	154 ± 4	147 ± 3
Diastolic BP, *mm Hg*	83 ± 2	87 ± 2	86 ± 2	85 ± 2
Use of anti-hypertensive agents (No. of patients)	10	23[c]	12	20
Avg. weight gain, *kg* between treatments	3.7 ± 0.3	6.0 ± 0.4[e]	4.5 ± 0.5	5.3 ± 0.5
Swelling of ankles (No. of patients)	5	15[c]	5	11
Dialysis symptoms				
Muscle cramps	26 (63%)	18 (40%)[c]	26 (72%)	16 (44%)[c]
Moderate or worse	6 (15%)	6 (13%)	8 (22%)	4 (11%)
Nausea	19 (46%)	4 (9%)[e]	17 (47%)	2 (6%)[e]
Moderate or worse	6 (15%)	2 (4%)	8 (22%)	2 (6%)[c]
Hypotension	16 (39%)	11 (24%)	12 (33%)	8 (22%)
Moderate or worse	5 (12%)	3 (7%)	4 (11%)	2 (6%)
Nutritional parameters				
Pre-dialysis weight, *kg*	71 ± 2 (37)	70 ± 2 (40)	71 ± 2 (32)	71 ± 2 (29)
Change in body weight[b]	+0.4 ± 0.7 (35)	−0.8 ± 1.1 (33)	−0.0 ± 0.8 (30)	−3.5 ± 1.1[c] (26)
Arm circum. corrected, *cm*	28.4 ± 0.6 (37)	28.3 ± 0.5 (40)	28.4 ± 0.6 (32)	28.3 ± 0.6 (29)
Change in arm circum.[b]	0.7 ± 0.3 (35)	−0.3 ± 0.4[c] (33)	0.1 ± 0.4 (30)	−1.0 ± 0.4[c] (26)
Urea appearance rate	8.5 ± 0.6 (36)	6.8 ± 0.4[c] (37)	8.4 ± 0.4 (31)	7.3 ± 0.5 (34)
Laboratory parameters				
Number of patients	41	44	36	37
Hematocrit, %	24.1 ± 0.7	25.2 ± 0.9 (43)	24.6 ± 0.9	24.2 ± 0.8
Serum urea nitrogen, *mg/dl*	78 ± 3	75 ± 3	81 ± 3	81 ± 3
Serum creatinine, *mg/dl*	14.9 ± 0.7	16.5 ± 0.8	15.5 ± 0.7	17.7 ± 0.8[c]
Serum uric acid, *mg/dl*	8.4 ± 0.3 (40)	9.2 ± 0.3[c]	8.3 ± 0.3	8.8 ± 0.2
Serum albumin, *g/dl*	4.0 ± 0.1	3.5 ± 0.1[e]	4.0 ± 0.1	3.5 ± 0.1[e]
Serum calcium, *mg/dl*	9.5 ± 0.1	8.8 ± 0.2[e]	9.5 ± 0.2	8.8 ± 0.2[d]
Serum phosphorus, *mg/dl*	5.0 ± 0.2	5.5 ± 0.3	5.3 ± 0.3	6.0 ± 0.3
Psychosocial parameters				
Multiple affect adjective checklist				
Number of patients	35	34	27	25
Anxiety	3.89 ± 0.63	3.62 ± 0.57	4.63 ± 0.84	3.32 ± 0.72
Depression	8.80 ± 0.92	7.15 ± 0.86	10.44 ± 1.53	8.32 ± 1.12
Hostility	3.09 ± 0.39	3.09 ± 0.47	4.11 ± 0.84	4.00 ± 1.06
Maladjustment interview				
Number of patients	36	35	28	26
Overall	2.53 ± 0.14	2.37 ± 0.15	2.68 ± 0.17	2.42 ± 0.15

[a] All values are mean ± SEM.
[b] Changes were calculated between the first and the last values in each period. The last observation within each period was used for the other parameters.
[c] $P < 0.05$.
[d] $P < 0.01$.
[e] $P < 0.001$.

one-half of the recorded instances of peritoneal-access malfunction, the problem was associated with "moderate or worse" morbidity. A malfunction that did not require surgical revision was relatively less frequent and of similar distribution in the two groups.

An inventory of cardiac incidents revealed a statistically significant disproportionate number of events in the second 6-month period among patients assigned to HD. Three of the 12 cardiac incidents were a source of moderate morbidity during the first year in the HD group.

Peritonitis, as expected, was virtually confined to IPD patients and was associated with 20 of 58 hospitalizations (>5

days) during the first year for this group. In addition, there were 13 incidents of peritonitis which led to shorter hospitalizations and five episodes treated as outpatients. In 31 of the 38 episodes, the associated morbidity was moderately severe or worse.

Only one patient (HD group) had a cerebral vascular event during the first year after achieving home-care status. No patient from either group developed hepatitis.

Other outcome features are shown in Table 5 and are divided into clinical, nutritional, laboratory, and psychological categories. Only selected clinical observations are shown in the tables and will be reviewed here along with many which are not shown. There was no difference in the number of blood transfusions in the two groups of patients. Average systolic and diastolic blood pressure values were similar, but fewer HD patients were treated with antihypertensives, a difference which was significant statistically in the first 6 months. Interdialytic weight gains (presumably fluid weight) were higher in the IPD group, and again this difference was significant in the first 6 months. Related to this, was the observation of peripheral edema in more IPD than HD patients in the first 6-months ($P = 0.03$), but there was no difference in the second 6 months ($P = 0.10$). The use of digitalis or antiarrhythmic drugs, the frequency of abnormal electrocardiogram, and the frequency or severity of dyspnea, angina, or arrhythmia were not different in the two groups. Nor was there a difference in the frequency of weakness or sensory abnormalities between the two groups.

Dialysis-related symptoms tended to be more common among the HD patients and the difference for "muscle cramps" was significant during the second 6-month period. Nausea, in particular, was a feature of HD patients' dialysis symptomatology.

We also assessed selected parameters intended to reflect changes in the patients' nutritional status. Whereas the average pre-dialysis body weight (selected as a useful surrogate measure of *dry weight* changes because patients were more likely to record these weights) was similar in both groups, the IPD patients who completed the surveillance period lost dry weight, a statistically significant ($P = 0.01$) difference in the second 6-month period. The absence of a statistical difference between the average weight of the IPD patients at the beginning and end of the second period is explained by the fact that patients dropping out of IPD before the end of the period were lighter at the beginning than those remaining (63.7 ± 2.8 vs. 74.4 ± 2.6 kg, $P < 0.05$). Trends and statistical comparisons of the *corrected* arm circumference were similar. Protein intake as reflected by urea appearance rate [26] appeared to be lower among the IPD patients during the first 6 months and probably lower during the second 6 months, though it did not reach statistical significance.

Except for a slightly but significantly lower serum concentration of albumin and calcium in the IPD group, laboratory parameters were essentially the same in both groups throughout the study. Of special note was the absence of a difference in hematocrit values between the two groups. Psychological status appeared to be similar in both groups and unchanged from one assessment period to the other.

Discussion

In interpreting the results of the study, one must keep in mind the study design and its possible impact on the study outcome. In particular, these results cannot be extrapolated to expected outcome of current CAPD patients in comparison to hemodialysis patients. The present data suggest that survival times are the same for patients assigned to home hemodialysis and home intermittent peritoneal dialysis where modality re-assignment was available. Re-assignment was permitted when the attending physician and patient concluded that the patient's clinical status was unsatisfactory and might improve with modality change. The interpretation of morbidity data is more complex. Hospitalization was excessive among the IPD patients, largely due to peritonitis. Control of fluid accumulation and hypertension was more difficult among the IPD patients. On the other hand, dialysis symptomatology, especially nausea, was greater among the HD patients. Moreover, the HD group seemed to have more frequent and more severe cardiovascular morbidity including two deaths associated with vascular access problems. The most apparent overall differences in outcome between the two modes of therapy were that *(1)* the period of training needed to achieve home-care was relatively shorter with IPD, *(2)* the dropout rate and change of therapy was greater among the IPD patients, and *(3)* the nutritional status was relatively poorer for the IPD group, as reflected in the decreased body mass.

The shorter training time for IPD is due to the reduced complexity of the procedure and the relative lack of anxiety about it. This is in contrast with the anxiety and critical need for mastery of safety precautions when extra-corporeal blood circulation is required.

The higher dropout among IPD patients is explained less easily. Since the participating physicians were experienced and comfortable with home IPD, dropout probably does represent a genuine concern for the patients' condition and not a program bias. No doubt, the frequent episodes of peritonitis and the higher hospitalization rates contributed to this concern. Therefore the comparison of dropout rates is of some interest. Other comparative data seem to reflect only small differences in outcome. However, these differences would probably have been greater had the study not allowed patients to transfer out of their assigned treatment modality. Physicians, in fact, encouraged the transfer of patients who were not doing well. Because of this, the nutritional assessments, for example, probably underestimate the degree to which patients assigned to IPD were losing body mass. The urea appearance rate of the IPD patients was lower than that of the HD patients, an observation which also suggests that nutritional status of the IPD patients was relatively impaired. However, the lower rate may also be explained by peritoneal losses of protein and amino acids (unmeasured in this study) [31]. Other studies comparing selected patients assigned to HD and PD have found that PD patients have significantly, but not dramatically, lower serum albumin concentration [26, 32, 33]. Our data in randomized patients confirm this observation but leave unaddressed its relationship to nutritional status.

In contrast to many other [5, 7–9, 16–18, 32, 33], but not all studies [15], our PD patients did not have higher hematocrits than the HD patients. Serum phosphorus has also been said to be lower [5, 8], but we and others [7, 9] did not find this difference. Perhaps the lack of difference in these areas is simply due to our use of a random assignment process which minimized the selection bias.

Only two other studies [4, 5] have made a comprehensive effort to compare clinical outcomes of matched HD and PD patients. Although they did not use a randomizing protocol as we did, the care in their design and the breadth of their outcome measures invite special attention.

Roxe et al [4] used a prospective pairing procedure to obtain groups comparable in age, sex, race, body size, blood pressure, cause of renal disease, residual renal function, and a number of other features. Their patients ($N = 32$) had been on maintenance dialysis for nearly 2 years preceding the study and might therefore be regarded as *survivors* and therefore not representative of patients just starting dialysis therapy. In contrast, we studied new patients. Their treatment schedule for IPD was slightly shorter than ours, but the difference may be insignificant. They monitored a larger number of biochemical parameters than we did and found few differences. Unlike our results, they found a small but significantly lower serum potassium among IPD patients. They emphasized an apparent early rise in hematocrit values in the IPD patients as compared to the HD patients, but this difference was unsustained by the end of 6 months. Our analysis of hematocrit was not carried out in the same fashion. Included in their comparison were quantitative assessments of computerized electroencephalographic (EEG) records and visual evoked and photic driving responses, which were somewhat more abnormal among HD patients [34]. As in our study, they compared hospitalization and morbidity, but found little or no difference except for the expected increase in peritonitis in patients treated by IPD. Their lack of excessive hospitalization for IPD patients, which contrasts with our findings, may be an artifact from using dialysis-experienced *survivors* of chronic illness. In support of this proposed explanation, our data do not show excess hospitalization among the IPD patients in the second 6th month period.

The second of these two comparison studies was done more recently to compare home HD patients to home CAPD [5], but made no attempt to randomize or prospectively pair the patients. The investigators did, however, retrospectively pair subsets of patients whose demographic and medical backgrounds were similar, a process which left them with relatively small numbers of patients for comparison ($N = 8$). In this study, Rubin et al found that the transfer of patients from one mode of dialysis to another and the frequency of hospitalization were greater in the CAPD patients, a finding which remained true even in the comparison of the retrospectively matched subsets. They noted that peritonitis was more common among those of lower socio-economic status. Many biochemical differences were noted and yielded findings which were similar to those of other less comprehensive comparisons [7–9, 32, 33].

Our own study presents problems in drawing conclusions as well. The data are limited to an older form of peritoneal dialysis, IPD, which has been said to be a less effective form of dialysis than CAPD and therefore more likely to allow malnutrition to occur [35]. In addition, we relied, in part, on subjective and semiquantitative assessments of patient well-being. Even though these assessments lack rigid definitions and easily validated measurements, they focus on features of patient status that are often more meaningful to both the staff and patients than are the more easily measured and calculated laboratory assessments. We acknowledge more than the usual uncertainty of these data, however. Finally, as the data collection turned out to be limited to men who had a slightly better family and medical background, which might allow them to undertake home dialysis more easily, the results may not apply to the remaining patients screened for this study or to other disadvantaged persons. Encouragingly, the patients who participated in this randomized study had a poor educational background and yet trained successfully for home dialysis.

Taken together, our study and the other two studies cited in detail [4, 5] suggest (with due regard to the drawbacks of each study) that hospitalization frequency may be excessive, for peritoneal dialysis, especially early in the course of treatment. Much of the excess hospitalization may be due in part to peritonitis and may also be the cause of a higher dropout rate [5, 19]. Subtle malnutrition appears to be another problem with IPD patients [35]. While this problem is allegedly less likely to occur in patients on CAPD [36], little solid evidence is available. The principal advantage of peritoneal dialysis, appearing in all three studies is the shorter training time. Our study further suggests that additional important advantages of IPD are the lower incidence of cardiac morbidity (including arrhythmia, pericarditis, and cardiac edema), the absence of vascular access problems which can be fatal, and the lower incidence of dialysis-related symptoms. We found no psychological advantage to IPD. Although others have contended that CAPD offers an opportunity for better psychological rehabilitation, this suggestion failed to be supported by the observations of Evans, Manninen, Garrison, Hart, Blagg, Gutman, Hull, and Lowrie (submitted for publication) in their cross-sectional evaluation of various modalities of therapies.

The planning and execution of this study itself invite some discussion with regard to design of future studies. The study results could be viewed as moot since it was carried out during a state of flux in the technique of peritoneal dialysis and is being published after the widespread use of IPD has ceased and been replaced by CAPD. However, as it was a randomized study, we can be secure that the outcome differences were strongly related to the inherent differences in technique, especially the cardiovascular difficulties on the one hand and the high drop-out rates on the other. This last point remains germane in view of the early reports of high drop-out rates for patients assigned to CAPD [5, 19]. Should a study of CAPD be designed along similar lines? Our multicenter randomized study was conceived and carried out in the same scientific spirit [2] which stimulates this question. Perhaps the same outcome differences could have been nearly as convincingly demonstrated by using a "comprehensive system of prognostic stratification" [3] wherein patients non-randomly assigned to each therapy are compared on the basis of their inherent clinical strengths and weaknesses. Such group comparisons are possible if we become able to reliably measure clinical status, a process Feinstein calls "clinimetrics" [37]. This possibility must be considered in planning further evaluation of "unstable therapy" because, while random allocation study design is appealing, this and other studies often border on being infeasible [37].

Appendix

This study was organized as follows under the auspices of the VA Cooperative Studies Program: *Study Chairman:* F. K. Curtis, Seattle, WA; *Associate Chairman:* Jack W. Coburn,

Los Angeles; *Coordinator:* M. J. Blumenkrantz, Los Angeles (Wadsworth), CA.

Participating Stations, Investigators, and Staff Assistants. Charleston, SC: C. Thomas Tucker, Frances Ennis; Durham, NC: Robert Gutman, Lucille Hardison; Hines, IL: C. Gandhi, Janet Luby; Little Rock, AK: Galen Barbour, Gayle Pitts, Debbie Pitts; Seattle, WA: Fu Shen, Kristin Vandehey; Chicago, IL: Peter Ivanovich, Susan White (terminated April, 1977); Los Angeles (Wadsworth), CA: James Shinaberger, Darlene Friday (terminated October, 1977); West Haven, CT: John Goffinet, Helen Losnes (terminated October, 1977).

Executive Committee. F. K. Curtis, (Chairman) Seattle; Jack W. Coburn, Los Angeles (Assoc. Chairman); M. J. Blumenkrantz, Los Angeles (Coordinator); Yick-Kwong, Chan, West Haven (Biostatistician); Galen Barbour, Little Rock; Robert Gutman, Durham, NC; Ben Murawski, Boston (Consultant).

Biostatistics and Research Data Processing. West Haven Cooperative Studies Program Coordinating Center (CSPCC). Chief: Yick-Kwong Chan; Study Biostatistician: Yick-Kwong Chan; Programmers: Irene Voynick, Dorothea Collins, Gary R. Johnson; Statistical Assistants: Joyce Pritchett, Patricia Ferrucci, Roxane Posteraro (Former); Keypunch Operators: Stella Marcinauskis, Velma Williams.

Special Laboratories. Manfred Morris (Lipid Laboratory), Little Rock.

Operations Committee. George A. Porter (Chairman), Portland; Colin White, New Haven; Christopher Blagg, Seattle; Frank A. Gotch, San Francisco. *Human Rights Committee.* Margaret Flower (Chairman), West Haven; Jack H. Evans, New Haven; Margaret A. Farley, New Haven (to 6/81); Barbara A. Kathe, West Hartford (7/81–); Willis Pritchett, New Haven.

Cooperative Studies Program Central Administration. James A. Hagans, Chief; Ping C. Huang, Staff Assistant.

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