Is Continuous Ambulatory Peritoneal Dialysis Adequate Long-Term Therapy for End-Stage Renal Disease? A Critical Assessment¹ ²

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ABSTRACT

The significant growth in the continuous ambulatory peritoneal dialysis (CAPD) population and the recent interest in the quantitation of dialysis delivered have stimulated much work in the field of kinetic modeling, correlation between model parameters and clinical outcome, and comparison between the long-term benefits of hemodialysis and peritoneal dialysis. A critical assessment of the long-term results of CAPD therapy is made on the basis of clinical results and recent experience with kinetic models including urea and creatinine. The significant differences between the hemodialysis and CAPD techniques have generated hypotheses to allow comparison between the two groups using similar kinetic models. Although CAPD has proven beneficial in the initial treatment of large numbers of patients with ESRD, there is concern about the adequacy of CAPD as long-term therapy for many patients. Prospective, long-term studies applying solute kinetic modeling are necessary to establish the adequacy of CAPD.

Key Words: Continuous ambulatory peritoneal dialysis, adequacy of dialysis, dialysis prescription, peritoneal dialysis kinetics

Remarkable progress has been made in the application of peritoneal dialysis for the treatment of ESRD during the last decade. The increased use of continuous ambulatory peritoneal dialysis (CAPD) and the governmental mandate to quantitate peritoneal dialysis delivery has stimulated much work in the field of kinetic modeling, correlation of results of kinetic modeling with clinical outcome, and comparison between the long-term benefits of hemodialysis and peritoneal dialysis.

The most pertinent issue concerning the ultimate success of CAPD relates to its ability to maintain the patient's health for prolonged periods of time. The only practical frame of reference is hemodialysis. Thus, let us analyze the issue of adequacy of CAPD as chronic therapy on the basis of our knowledge of theoretical and clinical differences between CAPD and hemodialysis, quantitation of dialysis delivered, and clinical outcome.

The goal of optimal dialytic therapy should be to eliminate all signs and symptoms of uremia through normalization of the hematologic, biochemical, neurobehavioral, and nutritional abnormalities. At present, renal transplantation is the only modality available that is capable of reversing all signs and symptoms of uremia. Because all forms of dialytic therapy are incapable of completely reversing the pathophysiologic mechanisms of ESRD, the term "adequacy of dialysis" has been created to describe the clinical efficacy of these modalities. Adequacy of dialysis necessarily implies a compromise between the desired outcome and what is practically achievable. No single formula takes into account all functions of the kidney, and there are physical limitations to the known artificial means of purifying blood.

The available dialytic systems mostly mimic glomerular filtration but provide little or no autoregulation of solute concentration. Artificial means of purifying blood are also limited by their nonphysiologic characteristics such as intermittency of therapy and the toxicity associated with exposure to plastics and dialysis solutions. Insufficient clearance of solutes and ultrafiltration are also evident and variable, ac-
cording to the type of dialysis. Finally, loss of pro-
teins, amino acids, and other nutrients may limit the
prolonged application of certain dialytic methods.

Several approaches to peritoneal dialysis pre-
scriptions can be used. A simple clinical correlation
between patient outcome and prescription, with ad-
justments in prescription according to the patient's
well-being, is the most economical. However, this
method introduces delays in effecting changes in
prescription and fails in preventing uremic manifes-
tations. A more scientific approach is characteriza-
tion of the peritoneal membrane through peritoneal
equilibration tests (PET) and the actual measurement
of solute removal and ultrafiltration through kinetic
modeling.

PERITONEAL SOLUTE TRANSPORT AND THE PET

Knowledge of peritoneal solute transport rates is
fundamental for the prescription of dialysis. In he-
modialysis, all parameters (blood flow, dialysate flow,
ultrafiltration coefficient, diffusion coefficient, and
time) are variable, manipulable, and easily measur-
able. In PD, however, blood flow is unknown in clin-
ical practice, membrane characteristics are fixed, and
and only dialysate flow and time are variable and
manipulable. The use of a "standard" PD regimen is
similar to a hemodialysis prescription, selecting he-
modialyzers at random from a vast selection of un-
abeled filters of various sizes and configurations.

The PET was designed to estimate peritoneal solute
transport rates and to compare peritoneal transport
characteristics of individual patients with the aver-
age or typical patient. The standard protocol for the
PET has been thoroughly described elsewhere (1).
This test has been applied to large populations of
patients for its diagnostic value in screening patients
during early training, for the formulation of a pre-
scription based on their peritoneal transport rates,
and with the help of mathematical modeling, to pro-
vide crude estimates of normalized urea clearance
(KT/V\text{urea}) and protein catabolic rate (PCR) (2–6).
The PET can also serve as a prognostic index through
serial evaluations (7, 8). A significant change in per-
itoneal solute transport rate may herald deterioration
of membrane transport and anatomical changes in the
peritoneal membrane.

Despite the obvious attributes of the PET, we must
recognize its limitations as an index of solute trans-
port rate rather than an absolute quantitative tool to
assess normalized solute removal. The PET metho-
dology has been standardized, but the values are not
adjusted to patient size (surface area or weight). Thus,
significant variations could be expected be-
tween patients with markedly different body mass
and peritoneal surface area. Further research is nec-
essary to match the volume of dialysate to the pa-
tient’s body surface area.

UREA KINETIC MODELING

The great interest in the application of urea kinetic
modeling (UKM) to assess the adequacy of dialysis is
based on the fact that this model can correlate both
the nutritional and the dialytic processes. Application
of this mathematical model can measure the level of dialysis actually received by the patient and
allows comparison with other patients or populations
and correlation between the amount of dialysis, pro-
tein intake, and clinical outcome.

Three major studies served as the foundation for
UKM in hemodialysis and cemented the notion that
UKM can be used to improve the quality of dialysis
and to assess the nutritional status of the dialytic
patient (9–13). The National Cooperative Study was
the first large-scale prospective protocol designed to
study the influence of dialysis duration and time-
averaged urea concentration (TAC\text{urea}) on clinical
outcome. Gotch and Sargent analyzed these data using
the KT/V index and demonstrated the relationship
between KT/V, failure rate, and uremic morbidity
(11, 14).

Similarly, the Mayo Clinic study by Dyck et al.
randomly assigned patients to short (1.5 to 2 h) and
long (3.5 to 4 h) treatment times (12). The urea clear-
ance was 160 mL/min in both groups, and the re-
spective KT/V values were 0.5 and 1.0. The short
dialysis group experienced a shorter observation
period of 6 months, a failure rate of 67%, and a higher
incidence of uremic symptoms. Conversely, the long
dialysis group had a mean observation period of 11
months, a 0% failure rate, and a lower incidence of
symptoms. In a small number of patients, these
symptoms resolved when dialysis duration was pro-
longed.

The experience of Teschan et al. further illustrated
the importance of a uniform minimum dose of di-
laxis in the prevention of uremic signs and symp-
toms and the potential value of UKM in dialysis pre-
scription (13). The meticulous design of their studies
and the incorporation of sophisticated neurobehav-
ioral testing added credence to the observations.
The influence of urea clearance on neurobehavioral ab-
normalities was assessed in an A-B-A study. During
the control periods (A), urea clearance (K) = 3,000
mL/wk/L of body water (KT/V = 1.0), whereas in the
experimental period (B), K = 2,000 mL/wk/L of body
water (KT/V = 0.7). Multiple quantitative neurobe-
havioral indices and an electroencephalogram dis-
riminant score based on spectral analysis of the
electroencephalogram were used. An excellent cor-
relation was observed between the neurobehavioral
score and the dialysis dose. Additionally, the neuro-
behavioral deterioration experienced during the ex-
perimental period was reversed during restitution of
a higher dialysis dose.

The National Cooperative Dialysis Study (NCDS)
demonstrated significant differences in morbidity between patients with high TACurea (≥100 mg/dL) and lower levels (TACurea ≤50 mg/dL), particularly among those patients with lower PCR. It demonstrated the need to maintain a neutral nitrogen balance at a level of urea nitrogen below that associated with uremia by providing a minimal amount of normalized urea clearance and adequate nutrition. On the basis of the vast experience accumulated with UKM in hemodialysis, Teehan et al. have applied these concepts to PD (15). The integration of BUN, PCR, and KT/V may provide a basis for uniform prescription of PD therapy, comparison of treatment between patients and centers, and optimization of dialysis and nutritional therapy.

In order to facilitate the application of UKM to PD, several assumptions must be made: (1) TACurea in the stable CAPD patient is analogous to a random BUN. The validity of this assumption is questionable, given the marked differences in hemodialysis and peritoneal membrane permeabilities and the steady state provided by CAPD, favoring a higher BUN level at comparable or less toxicity among CAPD patients. (2) BUN or TACurea is directly proportional to nitrogen intake (protein intake) and inversely proportional to nitrogen removal. Thus, if protein intake and nitrogen removal are equal, BUN remains constant and neutral nitrogen balance is maintained. (3) Urea achieves virtual equilibration between dialysate and plasma at the conclusion of an exchange in most CAPD patients (dialysate/plasma [DIP] urea ≈ 1). Thus, drain volume (DV) is analogous to urea nitrogen removal (KT).

Teehan et al. have applied UKM to the CAPD patient based on these assumptions. They have formulated useful nomograms based on these concepts, expressing the relationships between DV, residual renal urea nitrogen clearance, and body weight for CAPD patients with a target BUN of 70. They have also proposed a dialysis index (DI) describing the ratio of actual daily DV to prescribed DV. The relationship between DI, BUN, and PCR can be plotted in graphic form similar to the relationship between KT/V, PCR, and BUN for hemodialysis cohorts.

This approach to UKM is convenient and helpful as a general measure to decide the adequacy of PD regimen. Because CAPD is limited by dialysis flow rates, this simple model can be used to decide which patient should continue on a standard CAPD regimen, which one should be transferred to a high-flow rate of CAPD, and which one should be referred to a more efficient modality of therapy in order to maintain a neutral nitrogen balance. However, many assumptions are made with this approach, including full equilibration of urea between dialysis and plasma, without actually measuring urea concentrations. This may introduce a significant error. Furthermore, the estimation of urea volume of distribution is more difficult in CAPD than in hemodialysis. This is because in hemodialysis there is a sawtooth profile of BUN with respect to time allowing reliable estimates of volume kinetically. Conversely, in CAPD, the steady-state BUN makes this approach impossible. Most investigators have used the Hume and Weyers formula for this estimation (16). It would be of interest to apply other techniques such as urea infusion and/or bioelectrical impedance techniques to evaluate volume in CAPD (17). Formal UKM is recommended in prospective studies designed to correlate dialysis dose with nutritional status and patient outcome.

COMPARISON WITH HEMODIALYSIS

Membrane Characteristics

The use of urea as an index of adequacy of dialysis in PD and hemodialysis is perhaps unfair, and at best difficult, because the peritoneal system clearance is most inefficient in clearing low-molecular-weight solutes. The peritoneal membrane is more permeable and provides higher clearances of larger molecules. The latter may explain the marked differences in the magnitude of KT/V between these therapies while achieving similar patient outcome.

Steady-State BUN Levels

CAPD provides a steady state, whereas hemodialysis results in wide fluctuations in BUN concentrations. Application of UKM has demonstrated that hemodialysis and CAPD have the same TACurea at the same KT/V; however, BUN in hemodialysis exceeds TAC for approximately 50% of the time, whereas in PD, BUN ≈ TAC. Keshaviah et al. have proposed a Peak Concentration Hypothesis that states that the peak, rather than the TACurea, relates to uremic toxicity (18). A higher KT/V is then required in hemodialysis to achieve a peak concentration at or below the steady state of CAPD. The hypothesis predicts a weekly KT/V of 1.7 or a daily KT/V of 0.24 for CAPD as equivalent to a weekly hemodialysis KT/V of 2.6 or 0.87 per treatment. Long-term studies applying these concepts to PD patients, similar to those of the NCDS, are necessary in order to establish the validity of UKM in PD.

Patient Survival

It is generally accepted that CAPD/continuous cyclic peritoneal dialysis (CCPD) and hemodialysis patients have comparable survival rates (19–36). However, technique survival rates for CAPD patients have been repeatedly reported as lower than those for hemodialysis patients (22,23,26,31,32, 36–38) (Table 1). Although the criteria used for technique
survival varies among these studies, each series applied the same criteria to the hemodialysis and CAPD cohorts. In most of these series, the data are insufficient to determine the flux of patients from hemodialysis to CAPD, and vice versa (19-48). However, it is very possible that because the technique survival for CAPD patients was lower, more patients transferred from CAPD to hemodialysis. If that is the case, is the hemodialysis cohort being penalized with the higher rates of mortality provided by the CAPD failures?

Table 1. Patient and technique survival for CAPD and hemodialysis

<table>
<thead>
<tr>
<th>Authors (Ref. No.)</th>
<th>Time (yr)</th>
<th>Patient Survival (%)</th>
<th>Technique Survival (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schriel et al. (37)</td>
<td>2</td>
<td>80</td>
<td>76 (C and HHD)</td>
</tr>
<tr>
<td>Blagg et al. (39)</td>
<td>2</td>
<td>90</td>
<td>80 (C and HHD)</td>
</tr>
<tr>
<td>Shapiro and Umen (40)</td>
<td>2</td>
<td>100</td>
<td>94 (C and HAD)</td>
</tr>
<tr>
<td>Khanna et al. (41)</td>
<td>2</td>
<td>90</td>
<td>98 (HHD)</td>
</tr>
<tr>
<td>Mion et al. (36)</td>
<td>2</td>
<td>89</td>
<td>90 (C and HHD)</td>
</tr>
<tr>
<td>Wing et al. (42)</td>
<td>1</td>
<td>89</td>
<td>90 (C and HHD)</td>
</tr>
<tr>
<td>Nolph et al. (43)</td>
<td>1</td>
<td>94</td>
<td>94 (HHD)</td>
</tr>
<tr>
<td>Kramer et al. (44)</td>
<td>2</td>
<td>90</td>
<td>92 (CHD)</td>
</tr>
<tr>
<td>Capelli et al. (19)</td>
<td>2</td>
<td>59</td>
<td>85 (HHD)</td>
</tr>
<tr>
<td>USA CAPD Registry (45)</td>
<td>2</td>
<td>66</td>
<td>66 (CHD)</td>
</tr>
<tr>
<td>Rubin et al. (38)</td>
<td>2</td>
<td>80</td>
<td>80 (C and HHD)</td>
</tr>
<tr>
<td>Charytan et al. (20)</td>
<td>2</td>
<td>84</td>
<td>84 (HHD)</td>
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<tr>
<td>Burton and Walls (21)</td>
<td>2</td>
<td>45</td>
<td>45 (C and HHD)</td>
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<tr>
<td>Gokal et al. (22)</td>
<td>4</td>
<td>62</td>
<td>74 (HHD)</td>
</tr>
<tr>
<td>Gokal et al. (23)</td>
<td>2</td>
<td>83</td>
<td>84 (HHD)</td>
</tr>
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<td>6</td>
<td>41</td>
<td>41 (C and HHD)</td>
</tr>
<tr>
<td>Tranaeus et al. (46)</td>
<td>2</td>
<td>81</td>
<td>81 (C and HHD)</td>
</tr>
<tr>
<td>Serkes et al. (31)</td>
<td>4</td>
<td>60</td>
<td>60 (C and HHD)</td>
</tr>
<tr>
<td>Diabetics</td>
<td>2</td>
<td>60</td>
<td>60 (C and HHD)</td>
</tr>
<tr>
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<td>83</td>
<td>83 (C and HHD)</td>
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<td>40 (±)</td>
<td>40 (±)</td>
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<td>60 (C and HHD)</td>
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<tr>
<td>Maiorca et al. (33)</td>
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<td>75</td>
<td>75 (C and HHD)</td>
</tr>
<tr>
<td>Capalli et al. (34)</td>
<td>3</td>
<td>71</td>
<td>71 (C and HHD)</td>
</tr>
</tbody>
</table>

likely to switch to hemodialysis (15.6%) than hemodialysis patients to CAPD/CCPD (4.4%). In the same population, death on the first modality contributed fractions for hemodialysis (14.7%) similar to those for CAPD/CCPD (15.2%).

The most common explanation given for the high rate of abandonment of therapy among CAPD patients is peritonitis (50). In favor of peritonitis being responsible for the low technique survival rates among CAPD patients is the experience of those Italian centers using Y-set systems and reporting very low peritonitis rates and excellent technique survival rates (27-29, 33, 34). Maiorca et al. have recently reported their experience with hemodialysis and CAPD patients in six Italian centers (33). Four hundred eighty CAPD and 373 hemodialysis patients were studied. The 7-yr patient survival rate was not significantly different for the two modalities of therapy. Technique survival was significantly different in the six centers and was better for hemodialysis.
However, when adjustments were made for peritonitis, no statistically significant difference between CAPD and hemodialysis technique survival was noted.

Cavalli et al. have reported similar technique survival rates for CAPD and hemodialysis after 3 yr of follow-up (34). Analysis of their data also suggests a negative influence of peritonitis on CAPD technique survival. Thus, it is very possible that reduction in the rate of peritonitis by means of better CAPD systems may improve technique survival. Some authors have related peritonitis to malnutrition (low albumin serum concentrations) whereas others have failed to correlate the two conditions (51).

Nutritional Considerations

Malnutrition is a great concern in long-term CAPD therapy. It is well known that serum albumin and total protein concentrations in blood are lower in CAPD than in hemodialysis populations (26, 52). This is likely the result of large protein losses through the dialysate effluent (averaging 8 to 10 g/day in stable patients and much higher during peritonitis) and a reduced PCR (53).

The relationship between KT/V and PCR has been validated for both PD and hemodialysis (54–63). It is generally accepted that within the range of KT/V usually applied to hemodialysis patients, an increase in KT/V results in proportional increases in PCR. LeFebvre et al. have reported improvement in PCR among CAPD patients transferred to hemodialysis and reversal to lower levels of PCR upon reinstitution of CAPD (59). Similarly, Lindsay and Spanner have increased KT/V by either increasing the number of CAPD exchanges or supplementing these with hemodialysis and observing a further increase in PCR proportional to the increment in KT/V (56). Those authors also compared the relationship between KT/Vurea and the type of dialysis used. The comparison consisted of hemodialysis with cellulose acetate membranes and more porous membranes (AN69-S; Hospal, Basle, Switzerland) versus CAPD. Surprisingly, CAPD patients required more KT/V than hemodialysis patients to achieve the same PCR. This phenomenon could be attributed to decreased appetite due to the large glucose load supplied by the PD solution or the increased intra-abdominal pressure associated with infusion of peritoneal dialysate.

Lysaght et al. observed a strong linear correlation between estimated daily protein intake and KT/V for both hemodialysis and CAPD patients. The correlation was virtually the same for both modalities of therapy, with the slope slightly favoring CAPD (55). Bergström et al. analyzed pooled data from nitrogen balance studies in patients of their own and in those studied by Blumenkrantz et al. (53, 62). They again found a good correlation between PCR and KT/V between CAPD and hemodialysis patients, but the regression PCR on KT/V had a steeper slope in the CAPD group than in the hemodialysis group. Their results imply that increasing the dose of dialysis has a more salutory effect on appetite in CAPD than in hemodialysis patients.

Gotch has described the kinetic logic involved in comparing CAPD and hemodialysis with respect to KT/V and has proposed an empiric formula to determine the equivalency of KT/V for both modalities of therapy (63). The equivalent KT/V for CAPD is corrected upwards to the KT/V required with hemodialysis to maintain the same control of peak BUN. In a current prospective study of CAPD patients, he has found a strong correlation between normalized protein catabolic rate (NPCR) and KT/V and a virtually identical dependence of NPCR on KT/V in hemodialysis and CAPD patients.

If the data of Bergström et al. are adjusted for KT/V equivalency, as suggested by Gotch, and adjustments are made for protein and amino acid losses in dialysate effluent in the data of Blumenkrantz et al., then the relationship between NPCR and KT/V is very similar in the CAPD and hemodialysis patients.

Finally, in a recent study of 44 patients on CAPD, Nolph and Moore observed a significant correlation between PCR and KT/Vurea (P < 0.01; r = 0.61) (64). The slope of this regression (PCR = 0.31 KT/V + 0.22) is more than twice that reported for the relationship of PCR to weekly KT/V in hemodialysis patients, once again supporting the hypothesis that KT/Vurea requirements are related to peak concentration control rather than time-averaged BUN. The authors state that CAPD patients are more likely to have a PCR ≥0.8 if weekly KT/Vurea ≥2.0.

An international study designed to assess the nutritional status of CAPD patients in Europe and North America found a 40.6% incidence of malnutrition with 21 variables derived from history and physical examination, anthropometry, and biochemical analysis (65). It is also common to observe low PCR or daily protein intake (DPI) values of <0.8 among CAPD patients. We must conclude then, on the basis of the aforementioned relationships between PCR and KT/Vurea, that many CAPD patients are not receiving enough KT/V to maintain the goal protein intake of ≥1.0 g/kg-day.

An additional artifact may influence the interpretation of these data. Although some investigators normalize PCR for kilogram of ideal body weight, others use actual body weight and still others have proposed body water. Corrections for these differences will obviously change the relationship to a modest degree.

The concern with nutrition is further emphasized by a recent report by Lowrie and Lew correlating
serum albumin concentrations and mortality among hemodialysis patients (66). A minimal drop in serum albumin from 4.0 to 3.5 g/dL resulted in a twofold increase in the relative risk of death and a further drop to 3.0 g/dL raised the risk of death by fivefold. Are CAPD patients at the same risk?

A single but most interesting study by Kaysen and Schoenfeld on albumin homeostasis in patients undergoing CAPD raises the question of whether albumin is an adequate index of nutrition in the CAPD population (67). The authors studied albumin and protein removal rates and albumin distribution and turnover among patients undergoing CAPD. The total albumin loss was 4.23 ± 1.42 g/1.73 m²/24 h, and total protein removed was 8.79 ± 4.21 g/1.73 m²/24 h. Although these values were well within the range for severe nephrosis, serum albumin concentrations remained near normal at 3.7 ± 0.5 g/dL. The plasma albumin mass and total albumin mass did not differ significantly from those in the control group. Compared with the control group, patients had reduced albumin catabolism and increased albumin synthesis. The serum albumin concentration correlated negatively with albumin losses. The authors concluded that the CAPD patients maintained albumin homeostasis through decreased albumin catabolism and increased synthesis. The patients were able to maintain the major albumin pools despite massive albumin losses.

This study raises the question of the validity of serum albumin concentrations as an adequate index of nutrition among CAPD patients. On the other hand, if CAPD patients had the ability to compensate for their protein losses through increased synthesis and decreased catabolism, why did they reset homeostasis at a lower serum concentration rather than at normal values? We also wonder if the phenomenon observed is a transient or acute compensation that cannot be maintained on a chronic basis. We must question the ability of the CAPD patient to maintain homeostasis during episodes of peritonitis associated with massive protein losses and sepsis when protein synthesis may be impaired and catabolism increased. These issues deserve further study.

EFFECT OF RESIDUAL RENAL FUNCTION

Various groups have reported better preservation of residual renal function (RRF) in CAPD than in hemodialysis patients (55, 68–74). The proposed explanations for this difference include: (1) stable and high BUN levels; (2) absence of acute fluid shifts; (3) hemodynamic stability and prevention of glomerular ischemia; (4) reduced dietary protein; (5) protein losses in dialysate; and (6) absence of cytokine-mediated responses to extracorporeal membrane treatment. If indeed CAPD patients maintain a significantly better RRF for a longer period of time than hemodialysis patients, then it is imperative to consider this variable (Kt) in any reported survival and comparison between hemodialysis and PD patients.

The eventual loss of RRF may influence the aforementioned higher rate of technique failure among CAPD patients and may affect the nutritional status of the CAPD patient. A recent international study on nutritional assessment of CAPD patients sheds light on the interrelationship between these parameters (65). Eight percent of the patients were considered severely malnourished, 33% were moderately malnourished, and 59% did not show evidence for malnutrition. There was a higher incidence of malnutrition in diabetics than in nondiabetics. Loss of RRF correlated with muscle wasting and length of CAPD therapy. Loss of RRF contributed to anorexia and symptoms of malnutrition.

CLINICAL CORRELATION

There are very few studies on the influence of UKM on clinical outcome among CAPD patients. However, some of the published studies suggest a lack of correlation between the two (60, 75). In a prospective, uncontrolled study, Blake et al. analyzed the effect of KT/V and NPCR on 76 new patients at the beginning of CAPD and at 6-month intervals (60). Dialysis index, KT/V, and PCR all tended to decrease with time on CAPD. DI and KT/V highly correlated with each other, and both correlated with PCR. None of the indices correlated with levels of hemoglobin, parathyroid hormone concentration, alkaline phosphatase, albumin, nerve conduction velocity, or clinical outcomes including death, technique failure, hospital days, peritonitis rates, and subjective indices of well-being. The authors concluded that UKM was not predictive of clinical outcomes among CAPD patients. Unfortunately, no formal UKM studies were performed, dialysis dose was assigned by the individual physicians on the basis of clinical observations, alterations in dialysis dose occurred during the period of observation, and the range of KT/V was both limited and unusually high compared with standard CAPD regimens in most centers.

Pederson and Smith reported their observations on changes from empiric CAPD prescriptions to UKM-based prescriptions in short-term studies (75). Although UKM-based prescriptions increased KT/V and DI among their patients, there was no significant effect on complications, sleep patterns, appetite, activity patterns, PCR, peritonitis rates, or biochemical parameters.

Teehan et al. analyzed the clinical outcome of 51 patients studied over a 5-yr period as a function of urea kinetic parameters (76). They selected three outcome parameters: survival, blood transfusion
rates, and hospitalization rates. Ten potential predictive factors that could have affected the three outcome parameters were also studied. The predictive factors included urea kinetic parameters (KT/V, DI, BUN, and NPCR) as well as other parameters including serum albumin and comorbidity factors. This study showed that both KT/V and NPCR were significant predictors of clinical outcome; however, no single parameter proved to be an isolated predictor.

A most interesting finding in the study by Teehan et al. was that both KT/V and serum albumin levels fit the model as negative predictors of death. However, serum albumin was a predictor four times more powerful than KT/V. Analysis of the data (by stepwise variable selection) to identify which predictors influenced serum albumin levels showed KT/V and BUN as the most important factors, whereas NPCR did not fit the model.

The authors concluded that urea kinetic parameters do affect clinical outcome in CAPD patients but that these factors tend to act in concert, rather than as individual predictors. Their findings in CAPD patients are consistent with the observations by Lowrie and Lew (66) in hemodialysis patients that serum albumin is a powerful predictor of death. They also extend previous observations by Lysaght et al. and Lindsay and Spanner, who reported a linear correlation between KT/V and PCR, to include a correlation between KT/V and albumin concentration (55, 56).

SEARCH FOR ALTERNATE KINETIC MODELS

Extensive experience with PET in some centers has shown a fairly good correlation between creatinine transport curves and clinical outcomes for CAPD/CCPD patients. These observations have led Twardowski to recommend a minimum total creatinine clearance (Kp + Kt) of 6 to 7 L/day or 40 to 50 L/wk per 1.73 m² (77). Unfortunately, significant overlap between D/P creatinine at 4 h and clinical response occurred in these studies, resulting in a decreased usefulness of this ratio in determining the adequacy of dialysis. Furthermore, despite the predictive values of PET, it is well known that the simple estimation of peritoneal solute transport rates is a crude measurement that may not reflect actual delivery of dialysis. In an attempt to strengthen the predictive value of D/P creatinine in terms of clinical response, Brandes et al. have suggested an efficacy number (EN) calculated from the data obtained from PET for creatinine (78, 79). They have developed the following expression:

\[
EN = \int [D/P] \times V_{24} + \text{ACP}_{PD}
\]

Where,

\[
D/P^\ominus = \text{PET-derived dialysate/plasma}
\]

\[
V_{24} = \text{volume of creatinine at 4 h prescribed for 24 h}
\]

\[
\text{ACP}_{PD} = \text{adjusted creatinine production based on daily dialysate creatinine appearance}
\]

The authors divided their patients into three groups according to clinical outcome as good, intermediate, or poor. EN and KT/V_{urea} were applied to all three groups of patients. Although there was a significant correlation between the good and poor outcome groups and KT/V_{urea}, the EN was a more sensitive index of prediction of clinical outcome, with statistically significant differences between all three groups. The authors concluded that the EN appears to be more useful than the D/P ratio alone or UKM in determining the adequacy of CAPD.

Because of the marked differences in the magnitude of KT/V_{urea} between PD and hemodialysis and the fact that PD is much more efficient in clearing middle molecules than hemodialysis, interest has been expressed in kinetic modeling for middle molecules. For typical CAPD exchanges lasting 4 to 6 h, the clearance of solutes with molecular weights of approximately 1,300 approaches 50% of dialysate flow rates. Assuming typical weekly drain volumes of 84 L, a middle molecule clearance of 42 L is obtained. This significantly exceeds the average 30 L/wk obtained with hemodialysis. On the basis of the 30-L/wk standard recommendation for the average hemodialysis patient described by Scribner and Babb, the typical CAPD patient with a Kt = 3 mL/min will satisfy the middle molecular clearance requisite without any drain volume (80, 81). Thus, this approach is impractical and does not meet the criteria for nitrogen balance.

CLOSING REMARKS

CAPD has proven most beneficial in the initial treatment of a large number of patients with ESRD or as an alternative to hemodialysis for variable periods of time. However, there is concern about the adequacy of CAPD as long-term therapy for most patients. The basis for this concern rests on the relatively high rate of technique failure after the first 2 yr of therapy and the possible development of progressive protein malnutrition. Peritonitis, the Achilles heel of CAPD (and sometimes the scapegoat), has been preferentially blamed for both of these problems.
ducible tool with which to assess peritoneal transport. The clinical application of PET has been useful in diagnosing peritoneal abnormalities (both anatomic and functional) in the formulation of CAPD prescriptions and in the serial evaluation of membrane performance. However, the PET, although standardized for methodology, has not been standardized for patient size or, thus, for the peritoneal membrane effective area of the individual patient. Therefore, its accuracy as a predictor of dialysis efficiency or magnitude is uncertain at best.

UKM has been applied to CAPD as a potential tool to provide a quantitative approach to the formulation of proper prescription. Marked differences in the magnitude of KT/V between hemodialysis and PD are evident. Hypotheses to explain these differences have been proposed based on the mechanical and physiologic differences between hemodialysis and CAPD, often ignoring the influence of selection criteria for the group studied. The clinical observation of low PCR among CAPD patients, the progressive malnutrition observed with reduction in RRF, and the relatively low KT/V provided by CAPD for anuric individuals with large body mass suggests that "standard" regimens of CAPD are not adequate under many circumstances.

Prospective, long-term studies applying urea and alternate solute kinetic modeling are necessary to establish the adequacy of CAPD. In the meantime, current knowledge suggests that alterations in the PD prescription, based on the body mass and RRF of the patient, are necessary in order to improve solute clearance and nutrition. "High-flow" PD regimens at competitive cost are likely to be developed in the near future to satisfy the need for more efficient CAPD.

In the meantime, alternate solute kinetic modeling are necessary to circumvent the patient, are necessary in order to improve solute clearance and nutrition. "High-flow" PD regimens at competitive cost are likely to be developed in the near future to satisfy the need for more efficient CAPD. Therefore, its accuracy as a predictor of dialysis efficiency or magnitude is uncertain at best.

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59. LeFebvre JM, Lindsay RM, Spanner E, Hodson A, Allison M. Protein catabolic rate is de-


