Continuous ambulatory peritoneal dialysis (CAPD) and hemodialysis (HD) both have advantages in the treatment of patients with renal failure. In CAPD, solute removal is sometimes insufficient in patients who have a relatively large muscle mass that produces high levels of creatinine. To compensate for this deficiency, frequent exchanges and large dialysate volumes are required.

We previously reported (1) that once-weekly HD helps CAPD patients who experience insufficient solute removal. In the present study, we followed, for more than 3 years, 9 CAPD patients who underwent additional weekly HD. Add-on HD therapy significantly increased the subjects’ weekly peritoneal creatinine clearance to 45 ± 3 L (mean ± standard deviation); these values rose to more than 60 L over the course of the study.

Our findings suggest that the combined use of CAPD and HD improves solute clearance in CAPD patients who are insufficiently dialyzed.

Key words
CAPD, hemodialysis (HD), weekly creatinine clearance, albumin

Introduction
We previously reported (1) that weekly add-on hemodialysis (HD) therapy can be a useful approach in patients who are on continuous ambulatory peritoneal dialysis (CAPD). In a separate 5-year study (2), we found that 6 of 36 patients who had been exclusively on CAPD had to be switched over to HD because of insufficient solute removal.

Recently, CAPD has been advocated as an initial therapy in patients with end-stage renal disease (3). Several advantages of this approach have been reported, including better preservation of residual renal function, which leads to improved total solute clearance and fluid status (4,5). Ultimately, however, these patients exhibit a decline in residual renal function as indicated by a reduction in total creatinine clearance (CCr)—that is, peritoneal and urinary creatinine excretion combined—that necessitates a switch from CAPD to HD. One problem with this approach is that CAPD patients are transferred to HD despite the availability of their remaining peritoneal function. Among the factors that dictate discontinuation of CAPD, peritoneal transport status—which may be associated with adverse clinical outcome (6,7)—is the most important. An association between peritoneal transport status and weekly CCr has, as expected, been reported (8).

Target guidelines for solute clearance have been developed (9) by the National Kidney Foundation Dialysis Outcomes Quality Initiative (NKF DOQI). The NKF DOQI target for weekly CCr is 60 L or more per 1.73 m² of body surface area. To achieve adequate weekly CCr, several methods are recommended. These methods include the use of automated PD, although no reports have been published concerning the efficacy of that approach. Because one HD session is equivalent to 2 – 3 days of CAPD in terms of its effect on CCr, the addition of HD to a regimen of CAPD in patients who have not achieved their weekly CCr target might be a viable alternative approach. The obstacles to the use of such a regimen are considerable, but most are nonmedical, including physician bias and ingrained conservative policies. In the present study, we followed 9 CAPD patients who underwent once-weekly HD for more than 3 years, retrospectively examining their data.
Patients and methods

Into this study, we enrolled 9 CAPD patients who attended the Kidney Disease Center of Saitama Medical School between 1998 and 2005 (Table I). All patients had a total weekly CCr of less than 45 L. Total weekly CCr was calculated as the sum of weekly residual renal function plus weekly peritoneal CCr. Patients were excluded if they

- were unlikely to survive for 6 months.
- were planning to have an elective living donor transplant.
- were transferring to another renal center within 6 months.

We obtained informed consent from each patient. Baseline data—including age, sex, underlying renal disease, CAPD regimen and its duration, dialysis regimen, and past history of peritonitis—were obtained.

At the beginning of the study, all patients were practicing a standard CAPD regimen with 4 daily exchanges of 1.5 L or 2 L dialysate. During the study, all subjects were asked to maintain their customary dietary and dialysis regimen. Mean daily dietary intake was recorded from individual 24-hour food records during a 3-day period at the start of the study. All subjects consumed between 0.8 g and 1.0 g of protein per kilogram of body weight daily, with a daily energy intake exceeding 25 kcal/kg. Salt intake was restricted to 9 g daily.

Weekly assessments of residual renal function (in liters) were estimated from the mean of the subjects’ renal and urea clearances as determined daily from 24-hour urine collections. Weekly peritoneal CCr was calculated from 24-hour spent dialysate collections. Serum and peritoneal creatinine concentrations were both measured. The CCr by HD was calculated using this formula:

$$\text{creatinine concentration} \times (\text{dialysate flow} \times \text{duration of dialysis} + \text{fluid removed})$$

All subjects had used the same dialyzer for a duration of 3.5 years. The CCr by HD was found to be 2000 – 2400 mg.

If a subject’s systolic blood pressure (SBP) exceeded 140 mmHg, or if diastolic blood pressure (DBP) exceeded 90 mmHg, antihypertensive therapy was initiated.

During the study period, the subjects were treated with recombinant human erythropoietin (rHuEPO) as necessary, and their hemoglobin levels were maintained at 8 – 10 g/dL. Subjects were given oral iron supplementation if they were diagnosed with iron deficiency.

Subjects with parathyroid hormone levels above 200 pg/mL were treated with 1,25(OH)2D3 and CaCO3 supplements, and patients with levels below 70 pg/mL were treated with CaCO3 to reduce their degree of hyperphosphatemia. Doses were adjusted based on serum levels of calcium and phosphate. Lipid-lowering drugs, primarily statin derivatives, were administered if serum cholesterol levels exceeded 240 mg/dL.

Every 6 months, laboratory data were collected from each subject. At those times, we measured blood urea nitrogen, serum creatinine, electrolytes, calcium,

| TABLE I Three-year follow-up of laboratory and dialysis data in 9 patients |
|---------------------------------------------|------------------|------------------|------------------|------------------|
|                                             | Start            | Year 1           | Year 2           | Year 3           |
| Systolic blood pressure (mmHg)              | 140.8±4.7        | 135.3±3.6        | 131.7±3.0        | 132.1±5.5        |
| Diastolic blood pressure (mmHg)             | 72.3±3.8         | 69.5±4.1         | 70.3±3.6         | 70.5±3.6         |
| Serum creatinine (mg/dL)                    | 13.5±0.8         | 13.6±0.5         | 12.7±1.0         | 12.9±0.9         |
| Blood urea nitrogen (mg/dL)                 | 76.4±7.8         | 70.7±3.0         | 63.8±4.5         | 67.6±2.8         |
| Serum albumin (g/dL)                        | 3.66±0.25        | 3.78±0.25        | 4.12±0.18        | 4.03±0.2         |
| Serum calcium (mg/dL)                       | 8.49±0.46        | 9.05±0.55        | 9.72±0.25        | 8.84±0.51        |
| Serum phosphate (mg/dL)                     | 7.2±0.7          | 7.6±0.6          | 6.5±0.7          | 7.5±0.7          |
| Serum potassium (mEq/L)                     | 4.8±0.3          | 4.7±0.3          | 4.3±0.2          | 4.5±0.3          |
| Total cholesterol (mg/dL)                   | 164.6±7.6        | 162.0±7.6        | 146.2±9.3        | 158.0±9.5        |
| Hemoglobin (g/dL)                           | 7.7±0.6          | 8.2±0.3          | 8.6±0.4          | 8.7±0.5          |
| Intact PTH (mg/dL)                          | 386±124          | 388±138          | 512±266          | 366±299          |

* $p < 0.05$ as compared with start values.
phosphate, alkaline phosphatase, hemoglobin, hematocrit, parathyroid hormone level (intact molecule assay), and serum cholesterol.

Statistical analysis
All data are presented as mean ± standard deviation. Comparisons between starting values and values obtained at one of the other time points of the study were made using the Student t-test, with a p value less than 0.05 accepted as statistically significant. Regression analyses were performed to compare levels of serum albumin and hemoglobin, with weekly CCr being the independent variable.

Results

Patient characteristics
At the beginning of the study, our 9 subjects (8 men, 1 women) had a mean age of 58 ± 7 years and a mean CAPD duration of 3.6 ± 0.2 years. The underlying renal diseases in the group were chronic glomerulonephritis (n = 6), nephrosclerosis (n = 1), diabetes mellitus (n = 1), and Bechet disease (n = 1). All subjects survived beyond the 3 years of the study, and none were transferred to HD alone. Parathyroidectomy was performed in 1 patient because his serum parathyroid hormone level exceeded 1000 mg/dL; this subject was subsequently found to have had multiple parathyroidal adenomas.

Follow-up physical and laboratory data
During the 3 years of the study, the patients’ DBP, serum creatinine, blood urea nitrogen, potassium, calcium, phosphate, and total cholesterol did not vary significantly from starting values (Table I). However, SBP, serum albumin, and hemoglobin gradually rose, with the difference in values from baseline reaching statistical significance in years 2 and 3 (p < 0.05).

Changes in drain volume and weekly CCr
Drain volume and weekly CCr both increased significantly by year 1 (p < 0.05) and remained elevated over the subsequent 2 years (Figures 1 and 2).

Correlation between weekly CCr and serum albumin and hemoglobin levels
We observed a significant correlation (p < 0.05) between CCr and serum albumin (Figure 3), but not between CCr and hemoglobin or SBP.
Peritonitis
The incidence of peritonitis decreased dramatically to 0.09 episodes/patient–year from 0.13 episodes/patient–year (\(p < 0.05\)) during the 3-year study.

Dose of rHuEPO
Before the start of add-on HD therapy, the average monthly dose of rHuEPO required by our patients was 5500 ± 600 IU. However, because hemoglobin levels increased gradually in response to the treatment regimen, subjects required reduced doses of rHuEPO (5000 ± 600 IU).

Antihypertensive medication
The blood pressure of 5 subjects decreased after the start of add-on HD therapy, and their antihypertensive treatment regimen was reduced.

Discussion
In this retrospective study, add-on HD therapy in CAPD patients increased their serum albumin levels, hemoglobin concentration, drain volume, and weekly CCr, and decreased their SBP. In a previous report (1), we demonstrated that add-on HD therapy in CAPD patients increased weekly CCr and drain volume over a 3-month period. For the present study, we followed 9 CAPD patients for more than 3 years after the start of add-on HD.

According to NKF DOQI guidelines (9), weekly CCr should be maintained above 60 L per 1.73 m² body surface area. Alternatively, Szeto et al. (10) proposed a cut-off value for weekly CCr that was more than 50 L, but not more than 60 L. After the start of add-on HD therapy, the weekly CCr of our subjects rose above 60 L, resulting in an elevation in their serum albumin and hemoglobin levels and a fall in their SBP. Moreover, rHuEPO dose and antihypertensive medications were reduced in 4 and 5 subjects respectively. Our subjects’ weekly CCr correlated with their serum albumin levels, but not with their hemoglobin concentration or SBP. The absence of a correlation of CCr with SBP or hemoglobin was probably because these parameters are affected by drug treatment, which was reduced in the case of hemoglobin (rHuEPO) in 4 patients, for example.

Elevated levels of serum albumin were closely associated with increased weekly CCr. It is well known that serum albumin correlates with morbidity and mortality in CAPD (11) and HD (12) patients alike. The practical significance of this correlation remains unclear, although it is likely that low serum albumin is a marker rather than a direct cause of morbidity and may result from malnutrition. Low serum albumin levels are not simply a consequence of inadequate dialysis because they do not correlate with either Kt/V urea or CCr (11,12). And the lower serum albumin values seen in CAPD and HD may be attributable to different causes. For example, in addition to inadequate dialysis in HD patients, dietary restriction of vegetables, fruits, and salt might play a role. In CAPD patients, reduced protein intake might be the cause, as suggested by Young et al. (13).

In the present study, elevations in both weekly CCr and serum albumin might be attributable to the add-on HD therapy. Subjects that received PD and HD in combination did not restrict their intake of vegetables and fruits and were adequately dialyzed.

All subjects acknowledged that their quality of life had improved after they began add-on HD therapy. Unfortunately, we did not evaluate quality of life before and after the study. This subjectively assessed improved quality of life may have contributed to the increase in serum albumin. Alternatively, the subjects’ underdialysis before the study may have resulted in the reduced serum albumin levels seen at the start of the study.

Conclusions
The present retrospective study suggests that add-on HD therapy in CAPD patients corrects underdialysis. The fact that the low serum albumin levels in these patients can be corrected by this approach suggests that it may improve prognosis and possibly obviate a need for full HD therapy.

References

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