Independent effects of residual renal function and dialysis adequacy on dietary micronutrient intakes in patients receiving continuous ambulatory peritoneal dialysis[1–3]

Angela Yee-Moon Wang, Mandy Man-Mei Sea, Ricky Ip, Man Ching Law, Kai Ming Chow, Siu Fai Lui, Philip Kam-Tao Li, and Jean Woo

ABSTRACT

Background: Dialysis patients are at risk of vitamin and mineral deficiencies, not only because of losses during chronic hemodialysis or peritoneal dialysis but also because of low intakes.

Objective: The objective was to determine the importance of urea clearance (calculated as K_t/V) and residual renal function (RRF) in predicting micronutrient intakes in a large cohort of patients receiving continuous ambulatory peritoneal dialysis (CAPD).

Design: We conducted a survey of dietary intakes in 242 CAPD patients and divided them into 3 groups according to their weekly urea clearance and RRF: WD group (n = 84), a urea clearance ≥ 1.7 and a glomerular filtration rate (GFR) ≥ 1 mL • min^{-1} • 1.73 m^{-2}; DD group (n = 71), a urea clearance ≥ 1.7 and a GFR < 1 mL • min^{-1} • 1.73 m^{-2}; and ID group (n = 87), a urea clearance < 1.7.

Results: Most of the patients had intakes of water-soluble vitamins and minerals that were lower than the recommended dietary allowance; most intakes were significantly higher in the WD group than in the DD and ID groups, except those of niacin and calcium. After age, sex, body weight, and the presence of diabetes were controlled for, total weekly urea clearance and the GFR (but not peritoneal dialysis urea clearance) were significantly associated with intakes of vitamins A and C, the B vitamins, and minerals (calcium, phosphate, iron, and zinc). Low intakes of vitamins and minerals with low RRF and urea clearance were the result of reduced overall food intakes, except for thiamine, vitamin B-6, and folic acid, which were deficient in the diet.

Conclusions: Supplementation with most water-soluble vitamins and minerals, including iron and zinc, should be considered in CAPD patients, especially those with low RRF and low urea clearance. The optimal dose needs to be determined. *Am J Clin Nutr* 2002;76:569–76.

KEY WORDS Vitamins, minerals, nutrition, peritoneal dialysis, continuous ambulatory peritoneal dialysis, CAPD, glomerular filtration rate, residual renal function, dialysis adequacy, macronutrient intakes, People's Republic of China

INTRODUCTION

Protein-energy malnutrition is an important complication in dialysis patients and occurs in 20–40% of patients receiving maintenance dialysis (1, 2). Several factors contribute to poor nutritional status, among which inadequate nutrient intake is one of the most important (3) and is considered largely a result of uremia-causing anorexia (4, 5). Indeed, animal experiments showed that the intraperitoneal injection of uremic toxins into healthy rats suppresses appetite and food intake in a dose-related fashion (6). The provision of greater small-solute clearance and better removal of uremic toxins is believed to result in better dietary intakes. Although studies have confirmed a higher weekly urea clearance to be associated with better nutritional status and better patient survival (7, 8), the effect of dialysis adequacy on actual dietary intakes in patients with continuous ambulatory peritoneal dialysis (CAPD) remains largely undetermined. Most importantly, there is no information on the effects of dialysis adequacy on vitamin and mineral nutrition in CAPD patients.

Ensuring adequate intakes of micronutrients other than protein and energy is essential in maintaining good nutritional status. Patients with chronic renal failure are at risk of vitamin and mineral deficiencies because of a restricted diet. The typical diet for patients with renal failure is low in the B vitamins. Uremic factors affect the activities of folate and vitamin B-6. Vitamin C and many of the B vitamins are lost during dialysis (9). On the other hand, renal patients consuming a protein-restricted diet are also at risk of developing deficiencies of trace elements such as iron and zinc (10). Although some investigators recommend vitamin and mineral supplementation for dialysis patients (11–14), the actual dietary intakes of vitamins and minerals in these patients are largely unknown.

This study was undertaken to compare the actual dietary micronutrient intakes of CAPD patients with the recommended dietary allowances (RDAs; 15) and to study vitamin and mineral nutrition in relation to dialysis adequacy and the degree of residual renal function (RRF).

[1] From the Department of Medicine & Therapeutics, Center for Nutritional Studies, Prince of Wales Hospital, Chinese University of Hong Kong.

[2] Supported by the Bristol Myers Squibb Foundation Nutrition Grant Program.

[3] Address reprint requests to AY-M Wang, Department of Medicine & Therapeutics, Prince of Wales Hospital, Chinese University of Hong Kong, Shatin, NT Hong Kong, People's Republic of China. E-mail: awang@cuhk.edu.hk.

Received April 26, 2001.

Accepted for publication September 19, 2001.

SUBJECTS AND METHOD

Patient population

The study population consisted of 242 patients receiving CAPD at the Prince of Wales Hospital for ≥ 3 mo. Patients were excluded from the study if they had received CAPD for < 3 mo or had a recent episode of peritonitis or other infectious complication within 30 d of the dietary assessment. The study protocol was approved by the Human Research Ethics Committee of the Chinese University of Hong Kong, and informed consent was obtained from all patients. The average daily dietary micronutrient intakes and the nutritional status of all patients were assessed on the same day as the indexes of dialysis adequacy were measured.

Dietary survey

Experienced research staff, who were blinded to all of the clinical and biochemical details of the patients, conducted a dietary survey with the use of a 7-d food-frequency questionnaire that had been validated in the local Chinese population (16, 17). The food-frequency questionnaire used allows an estimation of the average daily dietary intakes of protein, energy, fat, carbohydrate, fatty acids, cholesterol, vitamins, and minerals. Dietary protein and energy intakes were normalized to the patients' dry body weight. Intakes of the different micronutrients were compared with the RDAs specified by the National Academy of Sciences, National Research Council, which are similar to the Chinese RDAs compiled by the Standing Committee of the Chinese Nutrition Society. The Chinese food tables do not provide complete information on folic acid, vitamin B-6, and vitamin B-12; only food items with large quantities of these 3 micronutrients are included. Hence, in quantifying the actual intakes of vitamin B-6, vitamin B-12, and folic acid, food items containing ≥ 20% of the RDA for vitamin B-6 and ≥ 25% of the RDA for vitamin B-12 and folic acid were included in the assessment. The dosages of calcium carbonate and vitamin D taken by the patients at the time of the dietary assessment were also recorded.

Nutrition assessment

Nutritional status was assessed by experienced research staff, who were blinded to all clinical and biochemical data for the patients, with the use of subjective global assessment. This method was confirmed to be clinically reliable for assessing nutrition in dialysis patients (18). The patients were graded as being well-nourished or as having, mild, moderate, or severe malnutrition (19). While the subjects were shoeless and wearing light clothing, body weight was measured to the nearest 0.1 kg with a scale after the abdomen was drained to be dry of peritoneal fluid; height was measured to the nearest 0.5 cm. Body mass index was calculated as weight in kilograms divided by height squared in meters. Frame size was calculated as the ratio of height (cm) to wrist circumference (cm).

Indexes of dialysis adequacy

The adequacy of dialysis was determined by measuring the total weekly urea and creatinine clearances with the use of standard methods (20). The creatinine concentration of the dialysate was corrected for interference by glucose by using a reference formula developed in our laboratory (21). The contribution of urea clearance by peritoneal dialysis was estimated separately. The residual glomerular filtration rate (GFR) was calculated as an average of the 24-h urinary urea and creatinine clearances (22). Total body water was derived by using Watson's formula (23).

Data collection

Information about age, sex, the cause of renal failure, and the starting date of dialysis was obtained from the case records. The duration of dialysis (in mo) was calculated as the interval between the date of initiation of dialysis and the date of the dietary assessment.

The patients were divided into 3 groups according to their total weekly urea clearance (calculated as K_t/V, where K is a constant, t is time, and V is total body water) and GFR: WD group ($n = 84$), a well-dialyzed group with RRF (urea clearance ≥ 1.7; GFR ≥ 1 mL • min^{-1} • 1.73 m^{-2}); DD group ($n = 71$), a dialysis-dependent group with negligible RRF (urea clearance ≥ 1.7; GFR < 1 mL • min^{-1} • 1.73 m^{-2}); and ID group ($n = 87$), an inadequately dialyzed group (urea clearance < 1.7).

Statistics

Categorical data were expressed as n values and percentages. Continuous data were expressed as means ± SDs or medians and interquartile ranges, depending on the distribution. Categorical data were compared with the use a chi-square test. One-way analysis of variance or the Kruskal-Wallis test was used for between-group comparisons, depending on the distribution of the data. Post hoc analysis was performed with the Bonferroni method. Linear regression analysis was performed to determine the effects of dialysis adequacy and residual GFR on dietary vitamin and mineral intakes after demographic and clinical variables (including age, sex, body weight, and presence of diabetes) were controlled for. Log transformation was performed to normalize data not normally distributed before being entered into the regression model. The statistical analysis was performed with the use of SPSS (version 10.0; SPSS Inc, Chicago) for WINDOWS.

RESULTS

The mean age of the 242 patients (125 men and 117 women), all of Chinese origin, was 55 ± 12 y. The mean duration of CAPD was 37 mo (range: 4–151 mo). The causes of renal failure included chronic glomerulonephritis in 78 patients (32%), diabetic nephropathy in 60 patients (25%), hypertensive nephrosclerosis in 32 patients (13%), obstructive uropathy in 13 patients (5%), polycystic kidney disease in 12 patients (5%), tubulointerstitial disease in 7 patients (3%), and unknown in 40 patients (17%).

The clinical characteristics of the patients are shown in **Table 1**. There were significantly fewer men in the DD group than in the WD and ID groups. The duration of dialysis was significantly shorter in the WD group than in the DD and ID groups. More patients in the ID group than in the 2 other groups were diabetic. The DD group had the highest percentage of women (66%) and the lowest body weight and height, whereas the ID group had the highest percentage of men (62%) and the highest body weight and height.

The indexes of dialysis adequacy are shown in **Table 2**. Significant differences in the total weekly urea and creatinine clearance were noted in the 3 groups. When the total urea clearance was subdivided into that contributed by peritoneal dialysis (PD) and that by residual GFR, significant differences were noted in both PD urea clearance and GFR between the 3 groups. Despite a lower total urea clearance, PD urea clearance was significantly higher in the DD group than in the WD group. PD urea clearance was significantly lower in the ID group than in the WD and DD groups. On the other hand, despite having a

TABLE 1
Clinical characteristics of the 3 groups of patients receiving continuous ambulatory peritoneal dialysis[1]

	WD group (n = 84)	DD group (n = 71)	ID group (n = 87)	P (across groups)
Age (y)	57 ± 12[2]	54 ± 12	56 ± 12	0.350
Men (n [%])	48 [57]	24 [34][3]	54 [62][4]	0.001
Duration of dialysis (mo)	16 (10, 26)	43 (24, 66)[5]	36 (20, 66)[5]	<0.001
Dry weight (kg)	59 ± 11	54 ± 10[6]	61 ± 10[4]	<0.001
Body height (cm)	159 ± 7	155 ± 7[3]	160 ± 8[4]	<0.001
BMI (kg/m^2)	23 ± 4	23 ± 4	24 ± 3	0.346
Frame size[7]	15.8 ± 1.2	15.6 ± 1.2	16.1 ± 1.1[8]	0.009
Diabetes (n [%])	26 [31]	15 [21]	34 [39][9]	0.053
Renal diagnosis (n [%])				
Glomerulonephritis	31 [36.9]	30 [42.3]	17 [19.5][9]	0.028
Diabetic nephropathy	22 [26.2]	11 [15.5]	28 [32.2]	—
Hypertensive nephropathy	12 [14.3]	9 [12.7]	10 [11.5]	—
Tubulointerstitial disease	2 [2.4]	4 [5.6]	1 [1.1]	—
Polycystic kidneys disease	4 [4.8]	2 [2.8]	6 [6.9]	—
Obstructive uropathy	4 [4.8]	1 [1.4]	8 [9.2]	—
Unknown	9 [10.7]	14 [19.7]	17 [19.5]	—

[1] WD, well-dialyzed with residual renal function (urea clearance ≥ 1.7 and a glomerular filtration rate ≥ 1 mL · min^{-1} · 1.73 m^{-2}); DD, dialysis dependent with negligible residual renal function (urea clearance ≥ 1.7 and a glomerular filtration rate < 1 mL · min^{-1} · 1.73 m^{-2}); ID, inadequately dialyzed (urea clearance < 1.7). Urea clearance calculated as K_t/V, where K is a constant, t is time, and V is total body water.
[2] $\bar{x}$ ± SD.
[3,5,6] Significantly different from the WD group (after Bonferroni correction): [3] $P < 0.005$, [5] $P < 0.001$, [6] $P < 0.05$.
[4,8,9] Significantly different form the DD group (after Bonferroni correction): [4] $P < 0.001$, [8] $P < 0.01$, [9] $P < 0.05$.
[7] Ratio of height (cm) to wrist circumference (cm).

higher total urea clearance and PD urea clearance, the DD group had a lower GFR than did the ID group. The difference in body weight between the DD and ID groups explains why the DD group (despite their lower residual GFR and thus their lower total body water) had a higher total urea clearance than did the ID group (Tables 1 and 2).

Nutritional status was significantly different between the 3 groups (P = 0.003; **Figure 1**). Moderate-to-severe malnutrition was more prevalent in the ID group (29%) than in the WD (13%) and DD (10%) groups (P = 0.012). On the other hand, 66% of the WD group, 65% of the DD group, and 41% of the ID group were well nourished (P = 0.012). No significant difference in nutritional status was noted between the WD and DD groups.

The patients' average daily intakes of vitamins and minerals in relation to the corresponding RDAs of the National Academy of Sciences are shown in **Table 3**. Intakes of vitamins A, B-12, C, and D met the RDAs in > 50% of the patients. However, intakes of folic acid, all of the B vitamins (except vitamin B-12), and the minerals calcium, phosphate, iron, and zinc were below the RDA in most patients. Calcium carbonate and aluminum phosphate binder were used by 213 (88%) and 46 patients (19%), respectively. With the addition of calcium supplements, the total daily calcium intake far exceeded the RDA in > 80% of our patients.

The dietary intake of the fat-soluble vitamins was significantly higher in the WD group than in the DD and ID groups. The daily intake of the water-soluble vitamins thiamine, riboflavin, vitamin B-6, vitamin B-12, folic acid, and vitamin C showed a significant trend across the 3 groups in that the lower the total urea clearance, the lower the intakes of these vitamins (**Table 4**). The average daily dietary intakes of minerals are shown in **Table 5**. The WD group had significantly higher iron, phosphate, and zinc intakes than did the DD and ID groups. A trend toward higher dietary calcium intake in the WD group than in the DD and ID groups was noted, although the trend was not significant. The protein intakes of all 3 groups of patients were below the intake of 1.4 g · kg^{-1} · d^{-1} recommended by the Dialysis Outcomes Quality Initiative (DOQI) for peritoneal dialysis patients.

Nutrient densities for vitamin A; riboflavin; vitamins B-1, C, and D; and the minerals calcium, phosphate, iron, and zinc were not significantly different between the 3 groups (**Table 6**). This indicates that lower vitamin and mineral intakes with lower urea clearance values were related to an overall reduction in daily energy

TABLE 2
Indexes of dialysis adequacy in the 3 groups of patients receiving continuous ambulatory peritoneal dialysis[1]

	WD group (n = 84)	DD group (n = 71)	ID group (n = 87)	P (across groups)
PD exchanges (L/d)	6.21 ± 0.97	6.90 ± 1.26[2]	6.63 ± 1.06[3]	<0.001
Weekly total urea clearance	2.23 ± 0.46	1.97 ± 0.22[2]	1.46 ± 0.17[2,4]	<0.001
Weekly PD urea clearance	1.48 ± 0.31	1.91 ± 0.24[2]	1.32 ± 0.24[4,5]	<0.001
GFR (mL · min^{-1} · 1.73 m^{-2})	3.13 ± 1.75	0.21 ± 0.31[2]	0.62 ± 0.79[2]	<0.001
Weekly creatinine clearance (L · wk^{-1} · 1.73 m^{-2})	82 ± 26	49 ± 7[2]	47 ± 9[2]	<0.001

[1] $\bar{x}$ ± SD. WD, well-dialyzed with residual renal function [urea clearance ≥ 1.7 and a glomerular filtration rate (GFR) ≥ 1 mL · min^{-1} · 1.73 m^{-2}]; DD, dialysis dependent with negligible residual renal function (urea clearance ≥ 1.7 and a GFR < 1 mL · min^{-1} · 1.73 m^{-2}); ID, inadequately dialyzed (urea clearance < 1.7); PD, peritoneal dialysis. Urea clearance calculated as K_t/V, where K is a constant, t is time, and V is total body water.
[2,3,5] Significantly different from the WD group (after Bonferroni correction): [2] $P < 0.001$, [3] $P < 0.05$, [5] $P = 0.001$.
[4] Significantly different from the DD group, $P < 0.01$ (after Bonferroni correction).

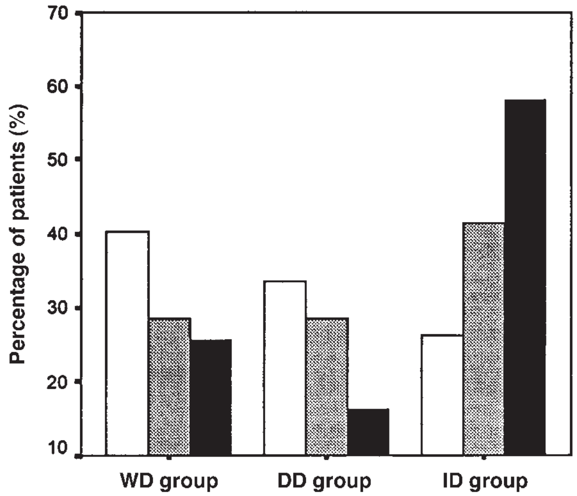

FIGURE 1. Nutritional status of patients receiving continuous ambulatory peritoneal dialysis who had different degrees of urea clearance (calculated as K_t/V, where K is a constant, t is time, and V is total body water) and residual renal function: WD group ($n = 84$), a urea clearance ≥ 1.7 and a glomerular filtration rate (GFR) ≥ 1 mL • min^{-1} • 1.73 m^{-2}; DD group ($n = 71$), a urea clearance ≥ 1.7 and a GFR < 1 mL • min^{-1} • 1.73 m^{-2}; and ID group ($n = 87$), a urea clearance < 1.7. On the basis of subjective global assessment, patients were classified as having normal (□), mild (■), or moderate-to-severe (■) malnutrition. Nutritional status was significantly different between the 3 groups, $P = 0.003$.

intake but not with any particular dietary pattern in the DD and ID groups. In contrast, nutrient densities for thiamine, vitamin B-6, and folic acid were significantly higher in the WD group than in the DD and ID groups, indicating a truly reduced dietary content of thiamine, vitamin B-6, and folic acid not attributable to a reduction in energy intake in the DD and ID groups. Indeed, intakes of thiamine and vitamin B-6 in our patients were significantly lower than the RDA (Table 3).

After age, sex, body weight, and presence of diabetes were controlled for, the total weekly urea clearance remained significantly and independently associated with actual dietary intakes of vitamin A, thiamine, riboflavin, niacin, and vitamin B-12. A significant association was also noted between urea clearance and dietary phosphate, iron, and zinc intakes (**Table 7**). On the other hand, the GFR showed significant and independent effects on actual intakes of vitamin A, thiamine, riboflavin, vitamin B-12, folic acid, niacin, vitamin C, calcium, phosphate, iron, and zinc.

DISCUSSION

This was the largest single-center survey of actual dietary intakes of vitamins and minerals in CAPD patients. Deficiencies of thiamine, vitamin B-6, vitamin C, folic acid, and zinc reported in CAPD patients were largely based on low blood concentrations (12, 24, 25). This survey confirmed that the actual intakes of most water-soluble vitamins, except vitamin B-12, and minerals (including iron and zinc) were low in most of the CAPD patients. This finding provides further support for the recommendation that CAPD patients be supplemented with vitamins and minerals (9, 11–13, 24, 26).

Thiamine and vitamins B-6 deficiencies, as a result of protein restriction or anorexia (9, 10, 12, 14, 24, 26), have been reported in many CAPD patients who were not taking supplements (12, 24). In the present study we showed a novel relation of dialysis adequacy and RRF with dietary intakes of the B vitamins. A low intake of B vitamins in patients with a low urea clearance and low

TABLE 3
Average daily dietary intakes of micronutrients in patients receiving continuous ambulatory peritoneal dialysis in relation to the recommended dietary allowance (RDA; 15)

	Actual dietary intake of men (n = 125)[1]	Actual dietary intake of women (n = 117)[1]	RDA[2]	
			Men	Women
Fat-soluble vitamins				
Vitamin A (mg)	2.24 (0.12–12.67) [80.2]	2.03 (0.08–14.10) [75.7]	1.00	0.8
Vitamin D (μg)	13.24 (0–110.36) [64.3]	6.11 (0–61.31) [41.7]	5	5
Total vitamin D (μg)[3]	13.35 (0–111.61) [64.6]	6.26 (0–61.31) [41.7]	5	5
Water-soluble vitamins				
Thiamine (mg)	0.64 (0.19–2.52) [5.6]	0.49 (0.06–1.20) [4.3]	1.2	1.0
Riboflavin (mg)	0.67 (0.19–1.80) [4.0]	0.55 (0.13–1.67) [1.7]	1.4	1.2
Vitamin B-6 (mg)[4]	0.29 (0–1.04) [26.0]	0.22 (0–0.98) [21.7]	0.40	0.32
Vitamin B-12 (μg)[5]	1.34 (0–6.93) [82.7]	1.05 (0–8.10) [68.7]	0.5	0.5
Folate (μg)[5]	48.65 (0–331.95) [35.4]	44.00 (0–261.30) [35.7]	50	45
Niacin (mg)	12.52 (3.26–36.73) [23.0]	10.03 (0.89–35.36) [20.9]	15	13
Vitamin C (mg)	91.12 (10.84–354.00) [66.7]	73.91 (4.05–261.50) [50.4]	60	60
Minerals				
Calcium (mg)	322 (107, 820) [0.8]	264 (58, 802) [0.9]	800	800
Total calcium (mg)[6]	1984 (119, 4929) [91.3]	1677 (85, 4875) [80.0]	800	800
Phosphate (mg)	752 (186–1711) [38.1]	612 (199–1446) [19.1]	800	800
Iron (mg)	10.38 (3.96–25.97) [47.6]	8.29 (2.62–20.06) [26.1]	10	10
Zinc (mg)	8.07 (2.69–62.90) [3.2]	6.27 (2.27–17.24) [3.5]	15	12

[1] The percentage of subjects whose intake met the RDA is in parentheses.
[2] For healthy adults aged ≥50 y (15).
[3] Dietary plus supplemental vitamin D.
[4] Includes only those food items with ≥20% of the RDA of the vitamin.
[5] Includes only those food items with ≥25% of the RDA of the vitamin.
[6] Includes calcium phosphate binder.

TABLE 4
Average daily dietary intakes of fat-soluble and water-soluble vitamins in the 3 groups of patients receiving continuous ambulatory peritoneal dialysis in relation to the recommended dietary allowance (RDA; 15)[1]

	WD group (n = 84)	DD group (n = 71)	ID group (n = 87)	RDA[2] Men	RDA[2] Women	P (across groups)
Fat-soluble vitamins						
Vitamin A (mg)	1.87 (1.14, 3.29)[3]	1.62 (0.93, 2.36)	1.41 (0.92, 2.36)[4]	1.00	0.8	0.047
Vitamin D (μg)	5.07 (1.20, 16.35)	3.12 (0, 11.72)	4.57 (0, 12.54)			0.042
Vitamin D supplement (μg)	0 (0, 0.01)	0 (0, 0.29)	0 (0, 0.25)			0.005
Total vitamin D (μg)[5]	5.48 (1.22, 16.35)	3.41 (0.23, 12.28)	4.81 (0.25, 12.54)	5	5	0.070
Water-soluble vitamins						
Thiamine (mg)	0.66 ± 0.36[6]	0.53 ± 0.24[4]	0.52 ± 0.29[7]	1.2	1.0	0.003
Riboflavin (mg)	0.67 ± 0.32	0.60 ± 0.29	0.56 ± 0.28[4]	1.4	1.2	0.047
Vitamin B-6 (mg)[8]	0.25 (0.07, 0.30)	0.19 (0.07, 0.30)[4]	0.17 (0.07, 0.33)[7]	0.40	0.32	0.003
Vitamin B-12 (μg)[9]	1.04 (0.60, 1.85)	0.79 (0.50, 1.59)	0.88 (0.41, 1.27)[4]	0.50	0.50	0.049
Folic acid (μg)	44.71 (21.16, 85.49)	29.65 (16.05, 51.02)[4]	28.77 (11.17, 60.17)[7]	50	45	0.003
Niacin (mg)	12.49 ± 6.07	10.58 ± 5.31	10.86 ± 6.94	15	13	0.111
Vitamin C (mg)	93.59 ± 53.53	82.64 ± 44.24	72.53 ± 59.96	60	60	0.038

[1] WD, well-dialyzed with residual renal function (urea clearance ≥ 1.7 and a glomerular filtration rate ≥ 1 mL · min^{-1} · 1.73 m^{-2}); DD, dialysis dependent with negligible residual renal function (urea clearance ≥ 1.7 and a glomerular filtration rate < 1 mL · min^{-1} · 1.73 m^{-2}); ID, inadequately dialyzed (urea clearance < 1.7). Urea clearance calculated as K_t/V, where K is a constant, t is time, and V is total body water.

[2] For healthy adults aged ≥50 y (15).

[3] Median; interquartile range in parentheses.

[4,7] Significantly different from the WD group (after Bonferroni correction): [4] $P < 0.05$, [7] $P < 0.01$.

[5] Dietary plus supplemental vitamin D.

[6] $\bar{x} \pm$ SD.

[8] Includes only those food items with ≥20% of the RDA of the vitamin.

[9] Includes only those food items with ≥25% of the RDA of the vitamin.

RRF was largely the result of an overall low energy or food intake. Nutrient densities of thiamine, vitamin B-6, and folic acid were significantly lower in the ID group than in the DD and WD groups, indicating a truly low intake of these vitamins that was not simply the result of a low energy intake in patients with a urea clearance < 1.7 and low RRF. The main source of folic acid is vegetables, whereas meat, legumes, and dairy products are not only rich sources of thiamine and vitamin B-6 but also of protein and phosphate. Intakes of these food items is low in patients with low RRF and low urea clearance as a result of diets that are low in protein and phosphate. This is in keeping with the findings of a previous study that showed a spontaneous reduction of dietary protein intakes in patients with chronic renal failure as renal function worsened and uremia increased (27). On the other hand, significant and independent associations between RRF (but not PD urea clearance) and intakes of the different B vitamins indicate that the contribution of PD urea clearance and RRF to dietary intakes of vitamins in CAPD patients is not equivalent.

Previous studies noted that 11–40% of nonsupplemented CAPD patients have low plasma folic acid concentrations (12, 24). Actual dietary intakes of folic acid in hemodialysis patients were often below the RDA (28, 29). Our survey showed that dietary folic acid intakes were below the RDA in two-thirds of our CAPD patients and that the lower the RRF, the lower the folic acid intakes.

TABLE 5
Average daily dietary intakes of protein, energy, and minerals in the 3 groups of patients receiving continuous ambulatory peritoneal dialysis in relation to the recommended dietary allowance (RDA; 15)[1]

	WD group (n = 84)	DD group (n = 71)	ID group (n = 87)	RDA[2] Men	RDA[2] Women	P (across groups)
Protein (g/kg)	1.23 ± 0.47[3]	1.12 ± 0.49	0.99 ± 0.40[4]	1.1–1.2	1.1–1.2	0.002
Energy (kJ/kg)[5]	114 ± 37	100 ± 36[6]	96 ± 35[7]	164	164	0.002
Calcium (mg)	313 ± 130	295 ± 134	276 ± 134	—	—	0.187
Calcium supplement (mg)	1677 ± 942	1406 ± 999	1528 ± 929	—	—	0.208
Total calcium (mg)[8]	1991 ± 962	1703 ± 1013	1803 ± 950	800	800	0.175
Phosphate (mg)	746 ± 268	665 ± 240	647 ± 273[9]	800	800	0.036
Iron (mg)	10.39 ± 3.91	8.83 ± 3.42[9]	8.86 ± 3.86[9]	10	10	0.011
Zinc (mg)	7.15 (5.62, 8.69)	6.19 (4.67, 7.97)	6.10 (4.53, 8.28)[9]	15	12	0.023

[1] WD, well-dialyzed with residual renal function (urea clearance ≥ 1.7 and a glomerular filtration rate ≥ 1 mL · min^{-1} · 1.73 m^{-2}); DD, dialysis dependent with negligible residual renal function (urea clearance ≥ 1.7 and a glomerular filtration rate < 1 mL · min^{-1} · 1.73 m^{-2}); ID, inadequately dialyzed (urea clearance < 1.7). Urea clearance was calculated as K_t/V, where K is a constant, t is time, and V is total body water.

[2] For healthy adults aged ≥50 y (15).

[3] $\bar{x} \pm$ SD.

[4,6,7,9] Significantly different from the WD group (after Bonferroni correction): [4] $P < 0.001$, [6] $P < 0.05$, [7] $P < 0.005$, [9] $P < 0.05$.

[5] Does not include energy from peritoneal glucose absorption.

[8] Dietary plus supplemental calcium.

TABLE 6

Nutrient densities of different vitamins and minerals in the 3 groups of patients receiving continuous ambulatory peritoneal dialysis[1]

	WD group (n = 84)	DD group (n = 71)	ID group (n = 87)	P (across groups)
Fat-soluble vitamins				
Vitamin A (mg/MJ)	0.31 (0.20, 0.48)[2]	0.30 (0.18, 0.50)	0.27 (0.19, 0.38)	0.314
Vitamin D (μg/MJ)	1.19 (0.17, 2.43)	0.54 (0, 2.25)	0.60 (0, 2.20)	0.089
Water-soluble vitamins				
Thiamine (mg/MJ)	0.10 ± 0.04[3]	0.10 ± 0.04	0.09 ± 0.03[4]	0.046
Riboflavin (mg/MJ)	0.10 ± 0.03	0.11 ± 0.05	0.10 ± 0.03	0.153
Vitamin B-6 (mg/MJ)	0.04 (0.03, 0.07)	0.03 (0.02, 0.06)	0.03 (0.02, 0.06)[4]	0.024
Vitamin B-12 (μg/MJ)	0.18 (0.11, 0.27)	0.15 (0.10, 0.26)	0.15 (0.08, 0.22)	0.244
Folic acid (μg/MJ)	7.22 (3.90, 12.56)	5.00 (2.68, 9.73)	5.45 (2.46, 9.46)[4]	0.031
Niacin (mg/MJ)	1.91 ± 0.59	1.91 ± 0.73	1.90 ± 0.97	0.998
Vitamin C (mg/MJ)	15.19 ± 8.63	15.37 ± 8.08	12.62 ± 7.98	0.058
Minerals				
Calcium (mg/MJ)	49.7 ± 17.7	54.2 ± 20.7	48.2 ± 14.0	0.088
Phosphate (mg/MJ)	116 ± 24	121 ± 31	114 ± 28	0.359
Iron (mg/MJ)	1.63 ± 0.43	1.60 ± 0.43	1.56 ± 0.38	0.528
Zinc (mg/MJ)	1.13 (1.04, 1.35)	1.15 (1.03, 1.38)	1.12 (1.01, 1.29)	0.373

[1] WD, well-dialyzed with residual renal function (urea clearance ≥ 1.7 and a glomerular filtration rate ≥ 1 $mL \cdot min^{-1} \cdot 1.73\ m^{-2}$); DD, dialysis dependent with negligible residual renal function (urea clearance ≥ 1.7 and a glomerular filtration rate < 1 $mL \cdot min^{-1} \cdot 1.73\ m^{-2}$); ID, inadequately dialyzed (urea clearance < 1.7). Urea clearance was calculated as K_t/V, where K is a constant, t is time, and V is total body water.

[2] Median; interquartile range in parentheses.

[3] $\bar{x}$ ± SD.

[4] Significantly different from the WD group, $P < 0.05$ (after Bonferroni correction).

However, it remains unknown whether the hyperhomocysteinemia in dialysis patients is partly due to low dietary folic acid intakes subsequent to low RRF. Folic acid supplementation resulted in an average reduction in homocysteine concentrations of 30–40% in hemodialysis patients (30–32) but never normalized it. Our data, together with current available evidence (26, 33), suggest that folic acid supplementation should be considered in CAPD patients with reduced intakes subsequent to low RRF. However, the optimal dose of supplementation needs to be determined.

Dialysis patients are at risk of vitamin C deficiency (24, 34) as a result of restricted intakes of fruit and leafy vegetables and increased dialysate losses (12). Prolonged soaking and boiling of vegetables to reduce the potassium content also inactivates vitamin C (26). We noted that the intake of vitamin C was below the RDA in nearly one-half of our patients and was especially deficient in those with low RRF and low total urea clearance. In keeping with previous studies (12, 24, 26, 35), our results suggest the need for vitamin C supplementation in all dialysis patients, especially those with low RRF and low total urea clearance (< 1.7). On the other hand, > 80% of our patients had dietary intakes of vitamins A and B-12 that met the RDA; therefore, routine supplementation with these vitamins is not necessary (26).

Dietary intakes of iron and zinc also decreased secondary to the loss of RRF and decreased urea clearance. Iron intakes below the

TABLE 7

Linear regression analysis showing independent effects of total weekly urea clearance (for every 0.25-unit increase) and residual renal function (for every 1-unit increase) on dietary micronutrient intakes in patients receiving continuous ambulatory peritoneal dialysis after control for age, sex, body weight, and diabetes

	Total weekly urea clearance		Residual renal function	
Dependent variable	Estimated mean (95% CI)	P	Estimated mean (95% CI)	P
Protein ($g \cdot kg^{-1} \cdot d^{-1}$)	0.052 (0.023, 0.081)	<0.001	0.04 (0.01, 0.07)	0.012
Energy ($kJ \cdot kg^{-1} \cdot d^{-1}$)	2.385 (0.205, 4.569)	0.015	3.60 (1.26, 1.42)	0.003
Fat-soluble vitamins (%)				
Vitamin A[1]	6.05 (−0.05, 12.53)	0.053	7.25 (0.73, 14.19)	0.028
Water-soluble vitamins (%)[1]				
Thiamine	3.82 (0.22, 7.55)	0.039	6.40 (2.51, 10.43)	0.001
Riboflavin	3.67 (0.32, 7.13)	0.032	4.08 (0.40, 7.57)	0.030
Vitamin B-6	3.76 (−2.46, 11.37)	0.240	5.34 (−0.87, 11.94)	0.092
Vitamin B-12	9.12 (3.09, 15.50)	0.003	8.11 (1.94, 14.66)	0.011
Folic acid	1.59 (−6.53, 10.65)	0.680	11.52 (3.11, 20.61)	0.007
Niacin	4.92 (1.23, 8.74)	0.010	4.92 (1.08, 8.90)	0.014
Vitamin C	4.89 (−0.12, 10.16)	0.057	8.33 (2.95, 13.99)	0.003
Minerals				
Calcium (mg/d)	7.91 (−1.26, 17.09)	0.091	10.28 (0.57, 19.80)	0.038
Phosphate (mg/d)	26.77 (8.91, 44.63)	0.003	24.04 (5.17, 42.92)	0.013
Iron (mg/d)	0.31 (0.05, 0.57)	0.018	0.35 (0.08, 0.63)	0.011
Zinc (%)[1]	3.20 (0.31, 6.18)	0.030	3.15 (0.16, 6.23)	0.040

[1] Data were log transformed before being entered into the regression model.

TABLE 8
Recommendations concerning vitamins and minerals for patients receiving continuous ambulatory peritoneal (CAPD) dialysis[1]

	Recommendation
Fat-soluble vitamins	
Vitamin A	None
Vitamin D	Individualize on the basis of serum calcium, parathyroid hormone, and alkaline phosphatase concentrations
Water-soluble vitamins	
Thiamine	2–5 mg/d
Riboflavin	1.2–1.4 mg/d (RDA)
Vitamin B-6	10 mg/d
Vitamin B-12	None
Folic acid	5 mg/d
Niacin	13–15 mg/d (RDA)
Vitamin C	60 mg/d (RDA)
Minerals	
Calcium	Given for phosphate binding
Phosphate	None
Iron	To maintain a serum ferritin concentration > 100 ng/mL and transferrin saturation > 20%
Zinc	10 mg/d (RDA) if deficient

[1] Recommendations based on our own local survey of dietary intakes in CAPD patients and on relevant studies (11–14, 24, 26, 28, 30, 33–37). RDA, recommended dietary allowance (15).

RDA in nearly two-thirds of our patients explains the high incidence of iron deficiency and confirms the need for iron supplementation in these patients. Although patients with better-preserved RRF and a higher urea clearance had higher dietary zinc intakes than did those with low RRF, zinc intakes remained largely below the RDA in most of the patients. This occurred because of anorexia or because of restricted intakes of foods rich in these trace elements, eg, meat and seafood. Low plasma zinc concentrations were reported in predialysis and dialysis patients (25) and may explain many of the symptoms associated with renal failure (eg, loss of appetite and altered taste and smell), which improved after zinc supplementation (36). Our results suggest the need for zinc supplementation in most CAPD patients with deficient dietary intakes of zinc. However, studies are needed to better define ways to detect zinc deficiencies and guidelines for giving zinc supplement. Although dietary calcium intakes were low in most of the CAPD patients, total daily calcium intakes were well above the RDA in most of the patients, because of additional calcium taken for phosphate binding, and may predispose to a higher risk of calcific complications in the presence of hyperparathyroidism.

Current daily vitamins requirements are not well defined for the dialysis population and are largely based on the RDA for the general population. Although dietary intakes of most water-soluble vitamins and minerals, including zinc and iron, were lower than the RDA, none of our patients had obvious clinical vitamin deficiency syndrome. However, one cannot exclude the possibility of mild deficiency syndrome because clinical symptoms may not be obvious and blood vitamins concentrations are needed to confirm the deficiencies. Normalization of blood vitamin concentrations was shown after supplementation with vitamin B-6, vitamin C, and folic acid (12, 37, 38). However, it remains to be determined whether vitamin or mineral supplementation make any clinical difference in persons with mild deficiencies. On the basis of our own survey and the findings of others, we have formulated a recommendation for vitamin and mineral supplementation in CAPD patients. These recommendations not only take into account low intakes but also account for increased losses of some of the vitamins (**Table 8**).

Although the current DOQI working group recommends a minimum weekly urea clearance target of 2.0 for CAPD patients (39), a total weekly urea clearance of 1.7 was used as the cutoff for adequate dialysis in this study. This cutoff is based on previous epidemiologic studies showing that Asian CAPD patients had better clinical outcomes despite having urea clearance values that were lower than standards for whites (40, 41). The 2-y patient survival was 83% in Chinese patients (41) and 78% in the Canada-United States study (7); the average urea clearance values were 1.75 and 2.1, respectively. Our recent study confirmed that providing a total weekly urea clearance of ≥ 1.7 resulted in an average dietary protein intake of 1.2 $g \cdot kg^{-1} \cdot d^{-1}$ in the Chinese patients (42).

The estimation of total body water varies significantly depending on the method of calculation and results in significant variation in urea clearance. One study suggested that Watson's formula provides a reliable estimation of total body water in peritoneal dialysis patients (43), although other studies warned about significant underestimation of total body water with the use of Watson's formula, especially in lean and obese peritoneal dialysis patients with overhydration (44, 45). Watson's formula was used to estimate total body water in the present study, as recommended by the DOQI guidelines (46), because it provides a reasonable and acceptable approximation based on ease of determination.

In summary, we showed the importance of performing a detailed dietary assessment in dialysis patients to detect not only protein-energy malnutrition but also micronutrient malnutrition. Significant and independent effects of RRF and dialysis adequacy on actual intakes of the B vitamins, vitamin C, and minerals—including calcium, phosphate, iron, and zinc—were observed. Our results support the recommendation that CAPD patients be supplemented with most water-soluble vitamins, except vitamin B-12, and minerals such as iron and zinc; this recommendation holds especially for those patients with low dietary intakes of these nutrients subsequent to loss of RRF and a resulting decrease in total urea clearance.

We acknowledge the valuable assistance of Ly-Mee Yu (Center of Clinical Trials and Epidemiologic Research) for providing statistical support.

REFERENCES

1. Young GA, Kopple JD, Lindholm B, et al. Nutritional assessment of continuous ambulatory peritoneal dialysis: an international study. Am J Kidney Dis 1991;17:462–71.
2. Hakim RM, Levin N. Malnutrition in hemodialysis patients. Am J Kidney Dis 1993;21:125–37.
3. Blumenkrantz MJ. Nutrition. In: Daugirdas JT, Ing T, eds. Handbook of dialysis. 2nd ed. Boston: Little Brown, 1995:284–302.
4. Bergstrom J. Appetite in CAPD patients. Perit Dial Int 1996;16: S181–4.
5. Bergstrom J. Regulation of appetite in chronic renal failure. Miner Electrolyte Metab 1999;25:291–7.
6. Bergstrom J, Mamoun H, Anderstam B, Sodersten P. Middle molecules (MM) isolated from uremic ultrafiltrate (UF) and normal urine induce dose-dependent inhibition of appetite in the rat. J Am Soc Nephrol 1994;5:488 (abstr).
7. Canada-USA (CANUSA) Peritoneal Dialysis Study Group. Peritoneal dialysis study group: adequacy of dialysis and nutrition in continuous peritoneal dialysis: association with clinical outcomes. J Am Soc Nephrol 1996;7:198–207.

8. Randerson DH, Chapman GV, Farrell PC. Amino acid and dietary status in CAPD patients. In: Atkins RC, Farrell PC, Thomson N, eds. Peritoneal dialysis. Edinburgh: Churchill Livingstone, 1981:171–91.
9. Makoff R. Vitamin replacement therapy in renal failure patients. Miner Electrolyte Metab 1999;25:349–51.
10. Gilmour ER, Hartley GH, Goodship THJ. Trace elements and vitamins in renal disease. In: Mitch WE, Klahr S, eds. Handbook of nutrition and the kidney. 3rd ed. Philadelphia: Lippincott-Raven, 1998: 107–22.
11. Kopple JD, Mercurio K, Blumenkrantz MJ, et al. Daily requirement for pyridoxine supplements in chronic renal failure. Kidney Int 1981; 19:694–704.
12. Blumberg A, Hanck A, Sander G. Vitamin nutrition in patients on continuous ambulatory peritoneal dialysis. Clin Nephrol 1983;20: 244–50.
13. Mydlik M, Derzsiova K, Valek A, Szabo T, Dandar V, Takac M. Vitamins and continuous ambulatory peritoneal dialysis (CAPD). Int Urol Nephrol 1985;17:281–6.
14. Gentile MG, Manna GM, D'Amico G, Testolin G, Porrini M, Simonetti P. Vitamin nutrition in patients with chronic renal failure and dietary manipulation. Contrib Nephrol 1988;65:43–50.
15. National Research Council. Recommended dietary allowances. 10th ed. Washington, DC: National Academy Press, 1989.
16. Woo J, Leung SSF, Ho SC, Lam TH, Janus ED. A food frequency questionnaire for use in the Chinese population in Hong Kong: description and examination of validity. Nutr Res 1997;17:1633–41.
17. Leung SF, Woo J, Ho S, Lam TH, Janus ED. Hong Kong adult dietary survey 1995. Aust J Nutr Diet 1998;55:S11–3.
18. Enia G, Sicuso C, Alati G, Zoccali C. Subjective global assessment of nutrition in dialysis patients. Nephrol Dial Transplant 1993;8: 1094–8.
19. Detsky AS, McLaughlin JR, Baker JP, et al. What is subjective global assessment of nutritional status? JPEN J Parenter Enteral Nutr 1987; 11:8–13.
20. Nolph KD, Moore HL, Twardowski ZJ, et al. Cross-sectional assessment of weekly urea and creatinine clearances in patients on continuous ambulatory peritoneal dialysis. ASAIO J 1992;38: M139–42.
21. Mak TW, Cheung CK, Cheung CM, Leung CB, Lam CW, Lai KN. Interference of creatinine measurement in CAPD fluid was dependent on glucose and creatinine concentrations. Nephrol Dial Transplant 1997;12:184–6.
22. Van Olden RW, Krediet RT, Struijk DG, Arisz L. Measurement of residual renal function in patients treated with continuous ambulatory peritoneal dialysis. J Am Soc Nephrol 1996;7:745–8.
23. Watson PE, Watson ID, Batt RD. Total body water volumes for adult males and females estimated from simple anthropometric measurements. Am J Clin Nutr 1980;33:27–39.
24. Boeschoten EW, Schrijver J, Kredict RT, Schreurs WHP, Arisz L. Deficiencies of vitamins in CAPD patients: the effect of supplementation. Nephrol Dial Transplant 1988;2:187–93.
25. Thomson NM, Stevens BJ, Humphrey TJ, Atkins RC. Comparison of trace elements in peritoneal dialysis, hemodialysis, and uremia. Kidney Int 1983;23:9–14.
26. Chazot C, Kopple JD. Vitamin metabolism and requirements in renal disease and renal failure. In: Kopple JD, Massry SG, ed. Nutritional management of renal disease. Baltimore: Williams & Wilkins, 1997: 415–77.
27. Pollock CA, Ibels LS, Zhu FY, et al. Protein intake in renal disease. J Am Soc Nephrol 1997;8:777–83.
28. Allman MA, Truswell AS, Tiller DI, et al. Vitamin supplementation of patients receiving haemodialysis. Med J Aust 1989;150:130–3.
29. Ramirez G, Chen M, Boyce HW Jr, et al. Longitudinal follow-up of chronic hemodialysis patients without vitamin supplementation. Kidney Int 1986;30:99–106.
30. Stanford JL, Molina H, Phillips J, Kohlman-Trigoboff D, Moore J, Smith BM. Oral folate reduces plasma homocysteine levels in hemodialysis patients with cardiovascular disease. Cardiovasc Surg 2000;8:567–71.
31. Sunder-Plassmann G, Fodinger M, Buchmayer H, et al. Effect of high dose folic acid therapy on hyperhomocysteinemia in hemodialysis patients: results of the Vienna multicenter study. J Am Soc Nephrol 2000;11:1106–16.
32. Chauveau P, Chadefaux B, Coude M, Aupetit J, Kamoun P, Jungers P. Long-term folic acid but not pyridoxine supplementation lowers elevated plasma homocysteine level in chronic renal failure. Miner Electrolyte Metab 1996;22:106–9.
33. Clarke R, Armitage J. Vitamin supplements and cardiovascular risk: review of the randomized trials of homocysteine-lowering vitamin supplements. Semin Thromb Hemost 2000;26:341–8.
34. Sullivan JF, Eisenstein AB. Ascorbic acid depletion in patients undergoing chronic hemodialysis. Am J Clin Nutr 1970;23: 1339–46.
35. Stein G, Sperschneider H, Koppe S. Vitamin levels in chronic renal failure and need for supplementation. Blood Purif 1985;3:52–62.
36. Sprenger KB, Bundschu D, Lewis K, Spohn B, Schmitz J, Franz HE. Improvement of uremic neuropathy and hypogeusia by dialysate zinc supplementation: a double blind study. Kidney Int Suppl 1983;16: S315–8.
37. Ross EA, Shah GM, Reynolds RD, Sabo A, Pichon M. Vitamin B6 requirements of patients on chronic peritoneal dialysis. Kidney Int 1989;36:702–6.
38. Henderson IS, Leung AC, Shenkin A. Vitamin status in continuous ambulatory peritoneal dialysis. Perit Dial Bull 1984;4:143–5.
39. National Kidney Foundation, Dialysis Outcome Quality Initiative, Peritoneal Dialysis Work Group. Clinical practice guidelines for peritoneal dialysis adequacy. Am J Kidney Dis 1997;30:S67–136.
40. Lo WK, Jiang Y, Cheng SW, Cheng IK. Survival of CAPD patients in a center using three two-liter exchanges as standard regime. Perit Dial Int 1996;16:S163–6.
41. Szeto CC, Wong TYW, Leung CB, et al. Importance of dialysis adequacy in mortality and morbidity of Chinese CAPD patients. Kidney Int 2000;58:400–7.
42. Wang AY, Sea MM, Ip R, et al. Independent effects of residual renal function and dialysis adequacy on actual dietary protein, calorie, and other nutrient intake in patients on continuous ambulatory peritoneal dialysis. J Am Soc Nephrol. 2001;12:2450-7.
43. Arkouche W, Fouque D, Pachiaudi C, et al. Total body water and body composition in chronic peritoneal dialysis patients. J Am Soc Nephrol 1997;8:1906–14.
44. Cooper BA, Aslani A, Ryan M, et al. Comparing different methods of assessing body composition in end-stage renal failure. Kidney Int 2000;58:408–16.
45. Wong KC, Xiong DW, Kerr PG, et al. Kt/V in CAPD by different estimations of V. Kidney Int 1995;48:563–9.
46. National Kidney Foundation. Dialysis Outcomes Quality Initiative clinical practice guidelines. Am J Kidney Dis 1997;30:S122–3.