Important factors other than dialysis adequacy associated with inadequate dietary protein and energy intakes in patients receiving maintenance peritoneal dialysis[1–3]

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ABSTRACT

Background: Anorexia that results in inadequate nutrient intake is considered one of the most important causes of malnutrition in dialysis patients.

Objective: The objective was to determine factors other than dialysis adequacy that are associated with inadequate protein and energy intakes in patients receiving continuous ambulatory peritoneal dialysis.

Design: Dietary protein and energy intakes were assessed with a food-frequency questionnaire in 266 patients, and factors other than dialysis adequacy that are potentially associated with reductions in energy and protein intakes were examined.

Results: Only 39% of the patients had protein intakes ≥ 1.2 $g \cdot kg^{-1} \cdot d^{-1}$, and 26% had energy intakes ≥ 126 $kJ \cdot kg^{-1} \cdot d^{-1}$. Other than having a greater total urea clearance and glomerular filtration rate, patients with protein intakes ≥ 1.2, as opposed to < 1.2, $g \cdot kg^{-1} \cdot d^{-1}$ had lower high-sensitive C-reactive protein concentrations and fewer complications with volume overload (29% compared with 46%; $P = 0.006$). Patients with energy intakes ≥ 126, as opposed to < 126, $kJ \cdot kg^{-1} \cdot d^{-1}$ were younger, had lower high-sensitive C-reactive protein concentrations, and had a lower prevalence of diabetes ($P = 0.006$), atherosclerotic vascular disease ($P = 0.020$), and history of volume overload ($P = 0.013$). Multiple regression analysis showed that other than increasing age, diabetes, and total urea clearance, having a history of volume overload was independently associated with a 0.22-$g \cdot kg^{-1} \cdot d^{-1}$decrease in protein ($P = 0.001$) and a 13.07-$kJ \cdot kg^{-1} \cdot d^{-1}$ decrease in energy intake ($P = 0.006$).

Conclusion: An important yet unrecognized association was observed between a history of volume overload and dietary intake in peritoneal dialysis patients. *Am J Clin Nutr* 2003;77:834–41.

KEY WORDS Protein intake, energy intake, volume overload, malnutrition, anorexia, continuous ambulatory peritoneal dialysis

INTRODUCTION

Protein-energy malnutrition is a powerful predictor of morbidity and mortality in dialysis patients (1–3). Its prevalence has been reported to vary from 23% to 76% in hemodialysis patients and from 18% to 56% in patients receiving continuous ambulatory peritoneal dialysis (CAPD) (4–8). Numerous factors contribute to malnutrition in the dialysis population, among which inadequate nutrient intake is regarded to be one of the most important (9, 10). Although hemodialysis and CAPD patients are recommended to have a daily protein intake of ≥ 1.2 g/kg and an energy intake of ≥ 146 kJ/kg body wt (9, 11, 12), nutritional surveys indicate that actual protein and energy intakes are inadequate in most patients receiving maintenance dialysis (13–16). CAPD patients have even more inadequate intakes than do hemodialysis patients (16).

Many factors are responsible for inadequate nutrient intakes in dialysis patients, among which anorexia has been implicated to be one of the most important. Anorexia may be the result of uremic toxin accumulation, underlying illnesses such as diabetes mellitus with impaired gastric emptying, comorbidity, and acute superimposed illnesses such as peritonitis and infections. Persistent uremia due to inadequate dialysis is considered by far the most important anorectic factor for dialysis patients (17). Intraperitoneal injection of uremic toxins with a molecular mass between 1.0 and 1.5 kDa into normal rats suppresses appetite and food intake in a dose-related fashion (18). The CANADA-USA study showed an improvement of appetite with initiation of dialysis in patients with renal failure (19). Our recent study, which showed the significant cross-section relation between the degree of residual renal function as well as total urea clearance and actual protein and energy intakes in CAPD patients (20), provides further evidence that dietary intake is indeed associated with the degree of urea clearance. However, the importance of other clinical factors remains largely undetermined.

This study examined the actual protein and energy intakes among local Chinese CAPD patients and evaluated the importance of the different clinical factors, particularly the presence of comorbidity in relation to dietary intake. Volume overload is a frequent complication in dialysis patients. However, its relation

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with the actual intakes of dialysis patients has never been evaluated.

SUBJECTS AND METHODS

Study population

The study population consisted of all prevalent patients ($n = 266$) receiving maintenance CAPD for ≥ 3 mo in the Prince of Wales Hospital in Hong Kong, except for those with underlying malignancy, those with ongoing systemic inflammatory disease (eg, systemic lupus erythematosus), those with active tuberculosis and still receiving treatment, and those who refused to participate. Informed consent was obtained from all patients. The study protocol was approved by the Human Research Ethics Committee, Chinese University of Hong Kong.

Dietary assessment

All patients completed a 7-d food-frequency questionnaire that was well validated in the Chinese population (21, 22) to estimate the average daily protein and energy intakes. The food-frequency questionnaire was performed by experienced research staff blinded to all clinical and biochemical details of the patients. Estimated protein and energy intakes were normalized to the patients' actual dry body weights, as measured with a weighing scale, after the abdomen had been drained dry of peritoneal fluid. In patients who developed acute intercurrent illness such as infections or peritonitis, dietary assessment was deferred for ≥ 1 mo after resolution of the acute event. Patients were categorized into those with dietary protein intakes ≥ 1.2 or < 1.2 $g \cdot kg^{-1} \cdot d^{-1}$ and those with energy intakes ≥ 126 or < 126 $kJ \cdot kg^{-1} \cdot d^{-1}$.

Indexes of dialysis adequacy

Adequacy of dialysis was determined by measuring total weekly urea clearance and creatinine clearance with the use of standard methods (23). The contribution of urea clearance by peritoneal dialysis (PD urea clearance) and residual renal function was estimated separately. Residual glomerular filtration rate (GFR) was calculated as an average of the 24-h urinary urea and creatinine clearances (24). Creatinine concentration in dialysate was corrected for interference by glucose according to the reference formula determined in our laboratory (25). Total body water was derived by using Watson's formula (26).

Data collection

Information regarding the cause of renal failure, duration of dialysis, smoking history, use of erythropoietin, exit site infection and peritonitis within 6 mo before dietary assessment, and history of diabetes, atherosclerotic vascular disease (AVD), and episodes of volume overload was retrieved from case records and hospitalization records. A single experienced physician further interviewed all patients to confirm the presence of AVD and history of volume overload.

AVD was defined as the presence of any atherosclerotic complication, including ischemic heart disease, with a history of angina, previous myocardial infarction, coronary artery bypass surgery or stenting, cerebrovascular disease, transient ischemic attack, or peripheral vascular disease with or without amputation.

A history of volume overload was defined clinically as the occurrence of one or more episodes of volume overload at any time point between the time of dialysis initiation and the time of dietary assessment. Volume overload was defined as the presence of symptoms and signs of heart failure, such as dyspnea, elevated jugular venous pressure, and basal crepitations together with pulmonary venous congestion or interstitial edema on chest radiograph (27). Radiographic evidence of pulmonary congestion or interstitial edema is an essential criterion for the diagnosis of volume overload and was further confirmed by resolution of symptoms, signs, and radiographic changes with hypertonic PD exchanges.

Echocardiography

Echocardiography was performed with a GE-VingMed System V echocardiographic machine (Horten, Norway) and a 3.5-mHz multiphase-array probe by an experienced cardiologist blinded to all clinical details of the patients. The echocardiographic techniques and calculations of different cardiac dimensions were performed according to recommendations of the American Society of Echocardiography (28, 29). Left ventricular hypertrophy was defined as a left ventricular mass index ≥ 131 g/m^2 in men and ≥ 100 g/m^2 in women, in accordance with the Framingham criteria (30). Systolic dysfunction was defined as those with an ejection fraction (EF) < 45%, whereas diastolic dysfunction was defined according to the guidelines published by the European Study Group on Diastolic Heart Failure (31) with 4 different patterns of diastolic function: normal, impaired relaxation, pseudonormal, and restrictive filling pattern (32).

Biochemical factors

At the time of the dietary assessment, patients had simultaneous venous blood samples taken to determine high-sensitive C-reactive protein (hsCRP), bicarbonate, hemoglobin, calcium, phosphate, and parathyroid hormone concentrations. hsCRP was measured with the use of the Tina-quant CRP (Latex) ultrasensitive assay (Roche Diagnostics GmbH, Mannheim, Germany). A concentration > 2 mg/L is considered to be elevated. Parathyroid hormone was measured with an Immulite immunoassay (Diagnostic Products Corporation, Los Angeles).

Statistical analysis

Statistical analysis was performed with the use of SPSS software (version 10.0; SPSS, Inc, Chicago). Continuous variables were expressed as means ± SDs or medians (interquartile ranges), whereas categorical variables were reported as the number and percentage of subjects. Continuous variables were compared by using Student's t test or the Mann-Whitney U test, where appropriate, whereas categorical variables were compared by using chi-square tests. Dietary protein and energy intakes were then entered into the multiple linear regression model as continuous dependent variables; factors with a P value < 0.25 in univariate analysis were selected into the multivariate regression model. A backward stepwise elimination procedure with a P value > 0.05 to remove was performed to identify factors significantly associated with inadequate dietary protein and energy intakes in CAPD patients. All P values were two-tailed, and a P value < 0.05 was considered significant.

RESULTS

The clinical characteristics of the patients are shown in **Table 1**. Fifty-eight patients had AVD (22%), whereas 104 (39%) patients had a history of volume overload. The daily PD exchange

TABLE 1
Characteristics of the study patients

Characteristics	Value (n = 139 M, 127 F)
Age (y)	55 ± 12[1]
Current smoker or exsmoker (n [%])	100 [38]
Duration of dialysis (mo)	37 ± 29
Diabetes (n [%])	82 [31]
Underlying renal diagnosis (n [%])	
Chronic glomerulonephritis	88 [33]
Diabetic nephropathy	66 [25]
Hypertensive nephrosclerosis	33 [12]
Tubulointerstitial nephritis	8 [3]
Polycystic kidney disease	12 [5]
Obstructive uropathy	13 [5]
Unknown	45 [17]
Received erythropoietin (n [%])	106 [40]
Atherosclerotic vascular disease (n [%])	58 [22]
History of volume overload (n [%])	104 [39]
Total weekly urea clearance	1.81 ± 0.45
Total weekly creatinine clearance (L/1.73 m^2)	57 ± 22

[1] $\bar{x}$ ± SD.

volume was 6.7 ± 1.3 L. Dietary protein and energy intakes were 1.11 ± 0.45 $g \cdot kg^{-1} \cdot d^{-1}$ and 105 ± 38 $kJ \cdot kg^{-1} \cdot d^{-1}$, respectively. The addition of peritoneal glucose energy ($\bar{x}$ ± SD: 17 ± 8 $kJ \cdot kg^{-1} \cdot d^{-1}$) increased total energy input to 121 ± 38 $kJ \cdot kg^{-1} \cdot d^{-1}$ and remained below that recommended for CAPD patients. Only 104 (39%) patients achieved protein intakes ≥ 1.2 $g \cdot kg^{-1} \cdot d^{-1}$. Protein intakes were between 1 and 1.2 $g \cdot kg^{-1} \cdot d^{-1}$ in 44 (17%) patients and < 1 $g \cdot kg^{-1} \cdot d^{-1}$ in 118 (44%) patients. Energy intakes were even more deficient: < 126 $kJ \cdot kg^{-1} \cdot d^{-1}$ and between 126 and 146 $kJ \cdot kg^{-1} \cdot d^{-1}$ in 198 (75%) and 30 (11%) patients, respectively. Even with the addition of peritoneal glucose energy, only 52 (20%) patients achieved the recommended energy input of ≥ 146 $kJ \cdot kg^{-1} \cdot d^{-1}$. This is in contrast with data from our previous 1995 Adult Dietary Survey in 1010 (500 men and 510 women) control subjects with a mean (± SD) age of 46 ± 12 y (21, 22), which showed that the average protein and energy intakes were 1.48 ± 0.55 $g \cdot kg^{-1} \cdot d^{-1}$ and 135 ± 42 $kJ \cdot kg^{-1} \cdot d^{-1}$, respectively. Protein intakes were ≥ 1.2 $g \cdot kg^{-1} \cdot d^{-1}$ in 760 (75%) patients, and energy intakes were ≥ 146 $kJ \cdot kg^{-1} \cdot d^{-1}$ in 433 (43%) control subjects.

Patients with protein intakes ≥ 1.2 $g \cdot kg^{-1} \cdot d^{-1}$ (n = 104) were compared with those with intakes < 1.2 $g \cdot kg^{-1} \cdot d^{-1}$ (n = 162) (**Table 2**). Patients with protein intakes ≥ 1.2 $g \cdot kg^{-1} \cdot d^{-1}$ were younger and had a significantly greater prevalence of chronic glomerulonephritis but a lower prevalence of diabetic nephropathy and hypertensive nephrosclerosis as the cause of renal failure. A trend toward more diabetics and a higher prevalence of AVD was noted among patients with the lower protein intake, although the trend was not significant. Forty-six percent of patients with protein intakes < 1.2 $g \cdot kg^{-1} \cdot d^{-1}$ had a history of volume overload compared with 29% of those with intakes ≥ 1.2 $g \cdot kg^{-1} \cdot d^{-1}$ (P = 0.006). The incidences of exit site infection, peritonitis, and hospitalization were not significantly different between the 2 groups. hsCRP was significantly higher in patients with inadequate protein intakes than in those with protein intakes ≥ 1.2 $g \cdot kg^{-1} \cdot d^{-1}$. Patients with the lower protein intakes were significantly more anemic, yet no significant difference was noted in the use of erythropoietin between the 2 groups. Patients with protein intakes ≥ 1.2 $g \cdot kg^{-1} \cdot d^{-1}$ had significantly higher residual GFRs and total urea clearance than did those with inadequate protein intakes. Yet, no difference was noted in the PD urea clearance between the 2 groups. The degree of hyperparathyroidism and acidosis did not differ significantly between the 2 groups.

Patients with energy intakes ≥ 126 $kJ \cdot kg^{-1} \cdot d^{-1}$ (n = 68) were compared with those with intakes < 126 $kJ \cdot kg^{-1} \cdot d^{-1}$ (n = 198) (**Table 3**). Compared with patients with energy intakes < 126 $kJ \cdot kg^{-1} \cdot d^{-1}$, patients with energy intakes ≥ 126 $kJ \cdot kg^{-1} \cdot d^{-1}$ were significantly younger and had a higher prevalence of chronic glomerulonephritis and a lower prevalence of diabetic nephropathy and hypertensive nephrosclerosis as the cause of renal failure. They also had a lower prevalence of diabetes, AVD, and history of volume overload. Patients with energy intakes < 126 $kJ \cdot kg^{-1} \cdot d^{-1}$ had a significantly higher hsCRP concentration and were more anemic despite a similar use of erythropoietin. Residual GFR, renal urea clearance, and resulting total urea clearance were significantly higher in patients with energy intakes ≥ 126 $kJ \cdot kg^{-1} \cdot d^{-1}$ than in those with intakes < 126 $kJ \cdot kg^{-1} \cdot d^{-1}$, despite no significant difference in PD urea clearance.

Multiple regression analysis showed that every 1-y increase in age was associated with a 0.15-$g \cdot kg^{-1} \cdot d^{-1}$ decrease (95% CI: −0.01, −0.001 $g \cdot kg^{-1} \cdot d^{-1}$; P = 0.020) in protein intake and a 0.64-$kJ \cdot kg^{-1} \cdot d^{-1}$ decrease (95% CI: −1.02, −0.26 $kJ \cdot kg^{-1} \cdot d^{-1}$; P = 0.002) in energy intake. The presence of diabetes was associated with a 15.60-$kJ \cdot kg^{-1} \cdot d^{-1}$ decrease in energy intake (95% CI: −25.65, −5.54 $kJ \cdot kg^{-1} \cdot d^{-1}$; P = 0.003). Every 0.25-unit increase in the total weekly urea clearance was associated with a 0.05-$g \cdot kg^{-1} \cdot d^{-1}$ increase in protein intake (95% CI: 0.02, 0.08 $g \cdot kg^{-1} \cdot d^{-1}$; P = 0.002) and a 2.39-$kJ \cdot kg^{-1} \cdot d^{-1}$ increase in energy intake (95% CI: 0.06, 4.85 $kJ \cdot kg^{-1} \cdot d^{-1}$; P = 0.056). A history of volume overload was independently associated with a 0.22-$g \cdot kg^{-1} \cdot d^{-1}$ decrease in protein intake (95% CI: −0.32, −0.09 $g \cdot kg^{-1} \cdot d^{-1}$; P = 0.001) and a 13.07-$kJ \cdot kg^{-1} \cdot d^{-1}$ decrease in energy intake (95% CI: −22.43, −3.72 $kJ \cdot kg^{-1} \cdot d^{-1}$; P = 0.006) (**Table 4**). The lower the dietary protein (P = 0.001) and energy (P = 0.001) intakes, the greater was the prevalence of a history of volume overload (**Figure 1**).

Echocardiographic variables of patients with or without a history of volume overload are shown in **Table 5**. Sixteen patients did not report for the echocardiographic examinations; therefore, results were available for only 250 patients. Patients with a history of volume overload had a significantly greater left ventricular mass index, left ventricular posterior wall thickening, and left ventricular end-diastolic diameter; a lower left ventricular EF and fractional shortening; and a higher prevalence of systolic dysfunction as defined by an EF < 45%. Moreover, a significantly greater prevalence of restrictive diastolic filling pattern was observed in patients with a history of volume overload (P = 0.001).

DISCUSSION

Inadequate dietary intake is considered the single most important cause of malnutrition in dialysis patients and is largely attributed to uremia secondary to inadequate dialysis (17). The importance of clinical factors other than dialysis adequacy has never been evaluated. This study is the first to show an important association between cardiac comorbidity, particularly a history of volume overload, and dietary protein and energy intakes in CAPD patients. Our results are contrary to the current belief that anorexia in dialysis patients is most commonly the result of uremia secondary to inadequate dialysis (17). We hypothesized that the

TABLE 2
Clinical, biochemical, and dialytic variables for patients with dietary protein intakes ≥ or < 1.2 g·kg^{-1}·d^{-1}

	Dietary protein intake	
	≥1.2 g·kg^{-1}·d^{-1} (n = 104)	<1.2 g·kg^{-1}·d^{-1} (n = 162)
Demographic factors		
Male:female	53:51	86:76
Age (y)	53 ± 14[1]	56 ± 11
Current or exsmoker (n [%])	37 [36]	63 [39]
Duration of dialysis (mo)	35 ± 27	39 ± 30
Renal diagnosis (n [%])[2]		
Chronic glomerulonephritis	44 [42]	43 [27][3]
Diabetic nephropathy	18 [17]	48 [30]
Hypertensive nephrosclerosis	8 [8]	26 [16]
Tubulointerstitial nephritis	2 [2]	6 (4)
Polycystic kidney disease	6 [6]	6 (4)
Obstructive uropathy	7 [7]	6 [4]
Unknown	19 [18]	27 [17]
Presence of comorbidity		
Diabetes (n [%])	26 [25]	56 [35]
Atherosclerotic vascular disease (n [%])	17 [16]	41 [25]
History of volume overload (n [%])	30 [29]	74 [46][4]
Exit site infections (n [%])	46 [44]	68 [42]
Peritonitis (n [%])	38 [37]	49 [30]
Hospitalizations (n)	1 ± 1	1 ± 2
Degree of inflammation		
High-sensitive C-reactive protein (mg/L)[5]	1.61 (0.83–4.74)	3.72 (0.98–11.66)[6]
Degree of anemia		
Hemoglobin (g/dL)	9.55 ± 1.87	9.04 ± 1.58[3]
Received erythropoietin (n [%])	66 [41]	40 [39]
Dialytic indexes		
Residual glomerular filtration rate (mL·min^{-1}·1.73 m^{-2})[5]	0.77 (0–2.35)	0.37 (0–1.82)[3]
Weekly renal urea clearance	0.36 ± 0.50	0.25 ± 0.35[3]
Weekly peritoneal urea clearance	1.53 ± 0.38	1.51 ± 0.37
Total weekly urea clearance	1.89 ± 0.54	1.76 ± 0.38
Total creatinine clearance (L/1.73 m^2)	60 ± 26	55 ± 19
Degree of hyperparathyroidsim		
Calcium × phosphate product	4.34 ± 1.30	4.35 ± 1.42
Parathyroid hormone (pmol/L)[5]	44.0 (16.6–75.3)	39.6 (17.0–68.4)
Degree of acidosis		
Bicarbonate concentration (mmol/L)	28 ± 3	27 ± 3

[1] $\bar{x}$ ± SD.
[2] Percentages may not add up to 100 because of rounding off.
[3,4,6] Significantly different from ≥1.2 g·kg^{-1}·d^{-1}: [3] $P < 0.05$, [4] $P = 0.006$, [6] $P = 0.005$.
[5] Median; interquartile range in parentheses.

hyperosmolality associated with the use of hypertonic exchanges and high fill volume of peritoneal fluid may exert an inhibitory effect on food consumption (33). Inadequate intakes in patients with a history of volume overload may also be partly related to elevated concentrations of tumor necrosis factor (TNF) or other proinflammatory cytokines (34). Elevated TNF concentrations are associated with anorexia and malnutrition in PD patients (35) and with chronic heart failure (36). A study by Anker et al (37) showed peripheral loss of muscle mass in chronic heart failure to be associated with elevated TNF and interleukin 6 concentrations. The chronic inflammatory state is suggested to be the result of bacterial or endotoxin translocation due to bowel wall edema after severe heart failure (38). TNF and interleukin 1 induced anorexia and cachexia by inhibiting the normal adaptive feeding response to energy deficits. They augmented leptin synthesis and release despite the decrease in food intake that would normally suppress leptin expression (39, 40), indicating that hyperleptinemia may be responsible, in part, for preventing the normal compensatory mechanisms in the face of decreased food intake. On the other hand, hyperproduction of intracerebral serotonin secondary to high concentrations of TNF and IL-1 may also be involved in appetite suppression in dialysis patients (41, 42). The significantly higher hsCRP concentrations among patients with the lower protein and energy intakes indicate that inflammation may have a role in appetite suppression, although the exact proinflammatory cytokine and the mechanisms involved require elucidation. On the other hand, higher hsCRP concentrations among the patients with inadequate dietary intakes, indicating a greater degree of inflammation, may also be a marker of the presence of underlying cardiac comorbidity.

Dietary intake was deliberately not assessed at the time of volume overload but rather some time after the resolution of volume overload. Dietary intake continued to be inadequate long after resolution of volume overload. This suggested that either the episode of volume overload induced a persistent appetite-suppressive effect or that these patients remained in subclinical volume

TABLE 3
Clinical, biochemical, and dialytic variables for patients with dietary energy intakes ≥ or < 126 kJ · kg^{-1} · d^{-1}

	Dietary energy intake	
	≥126 kJ · kg^{-1} · d^{-1} (n = 68)	<126 kJ · kg^{-1} · d^{-1} (n = 198)
Demographic factors		
Male:female	36:32	103:95
Age (y)	51 ± 15[1]	56 ± 11[2]
Current or exsmoker (n [%])[3]	25 [37]	75 [38]
Duration of dialysis (mo)	33 ± 25	39 ± 30
Renal diagnosis (n [%])[3]		
Chronic glomerulonephritis	29 [43]	58 [29][4]
Diabetic nephropathy	9 [13]	57 [29]
Hypertensive nephrosclerosis	5 [7]	29 [15]
Tubulointerstitial nephritis	1 [2]	7 [4]
Polycystic kidney disease	6 [9]	6 [3]
Obstructive uropathy	4 [6]	9 [5]
Unknown	14 [21]	32 [16]
Presence of comorbidity		
Diabetes (n [%])	12 [18]	70 [35][5]
Atherosclerotic vascular disease (n [%])	8 [12]	50 [25][4]
History of volume overload (n [%])	18 [27]	86 [43][4]
Exit site infections (n [%])	27 [40]	87 [44]
Peritonitis (n [%])	21 [31]	66 [33]
Hospitalizations (n)	1 ± 1	1 ± 2
Degree of inflammation		
High-sensitive C-reactive protein (mg/L)[6]	1.42 (0.85–3.93)	3.54 (0.95–10.95)[4]
Degree of anemia		
Hemoglobin (g/dL)	9.64 ± 1.76	9.12 ± 1.68[4]
Received erythropoietin (n [%])	24 [35]	82 [41]
Dialytic variables		
Residual glomerular filtration rate (mL · min^{-1} · 1.73 m^{-2})[6]	0.98 (0.37–2.37)	0.35 (0–1.83)[2]
Weekly renal urea clearance	0.42 ± 0.45	0.25 ± 0.40[5]
Weekly peritoneal urea clearance	1.51 ± 0.39	1.52 ± 0.37
Total weekly urea clearance	1.93 ± 0.53	1.77 ± 0.42[4]
Total weekly creatinine clearance (L · wk^{-1} · 1.73 m^{-2})	61 ± 27	55 ± 20
Degree of hyperparathyroidism		
Calcium × phosphate product	4.38 ± 1.43	4.33 ± 1.35
Parathyroid hormone (pmol/L)[6]	42.4 (15.6, 80.9)	40.1 (17.3, 66.9)
Degree of acidosis		
Bicarbonate concentration (mmol/L)	28 ± 4	27 ± 3

[1] $\bar{x}$ ± SD.
[2,4,5] Significantly different from ≥126 kJ · kg^{-1} · d^{-1}: [2] $P \leq 0.002$, [4] $P < 0.05$, [5] $P = 0.006$.
[3] Percentages may not add up to 100 because of rounding off.
[6] Median; interquartile range in parentheses.

overload status. It is, however, important to caution that because of the cross-sectional design of the study and because of the retrospective diagnosis of volume overload, we were unable to assign a cause and effect relation between volume overload, inflammation, and dietary intake. Further prospective longitudinal study is needed to clarify the exact interrelations between volume overload, proinflammatory cytokines, and appetite suppression in dialysis patients.

The term *volume overload* encompasses not only episodes due to extracellular fluid overload but also episodes due to true cardiac dysfunction, because in practical terms it is very difficult to distinguish the 2 entities in dialysis patients. Although patients with a history of volume overload had more severe left ventricular hypertrophy and left ventricular dilatation as well as a lower EF, only 8% had systolic dysfunction as defined by an EF < 45%, whereas 80% had diastolic dysfunction. This is in keeping with the results of a recent study in which EF was not low in patients with hypertensive pulmonary edema and that pulmonary edema occurred as a result of exacerbation of diastolic but not of systolic dysfunction (43). The greater prevalence of restrictive filling pattern indeed indicated more severe diastolic dysfunction among those patients with a history of volume overload (44). On the other hand, 90% of the patients with a history of volume overload had normal systolic function, whereas 20% had normal diastolic function. These findings suggest that volume overload also occurred as a result of poor ultrafiltration or fluid noncompliance without ventricular dysfunction.

Although the CAPD patients were recommended to have protein intakes ≥ 1.2 g · kg^{-1} · d^{-1} and energy intakes ≥ 146 kJ · kg^{-1} · d^{-1} (11), up to 60% of our patients failed to reach the target protein intake. Energy intake was even more inadequate; only 14% of our patients had energy intakes ≥ 146 kJ · kg^{-1} · d^{-1}. Even with additional energy from peritoneal glucose absorption, the total energy input remained < 146 kJ · kg^{-1} · d^{-1} in 80% of the patients. Of more concern was the considerably lower energy intake than protein intake. This phenomenon was also observed in other surveys, which showed an average protein intake of 1 g · kg^{-1} · d^{-1} and an average energy intake of 96–100 kJ · kg^{-1} · d^{-1} in CAPD patients (45–47).

TABLE 4
Multiple regression analysis showing important factors associated with dietary protein and energy intakes in patients receiving continuous ambulatory peritoneal dialysis

	Protein intake		Energy intake	
Factors	Regression coefficient (95% CI)	*P*	Regression coefficient (95% CI)	*P*
Age (y)	−0.15 (−0.01, −0.001)	0.020	−0.64 (−1.02, −0.26)	0.001
Diabetes mellitus	—	—	−15.60 (−25.65, −5.54)	0.003
Total weekly urea clearance	0.20 (0.07, 0.33)	0.002	9.56 (0.24, 19.38)	0.056
History of volume overload	−0.22 (−0.32, −0.09)	0.001	−13.07 (−22.43, −3.72)	0.006

Studies suggest that the intake of carbohydrates was suppressed in these patients because of an adaptive mechanism in response to obligatory peritoneal glucose absorption (48). Whether this explains the markedly lower energy than protein intake requires further evaluation. In the current study, 126 $kJ \cdot kg^{-1} \cdot d^{-1}$ was used as the minimum daily energy requirement instead of 146 $kJ \cdot kg^{-1} \cdot d^{-1}$ because peritoneal glucose energy (average: 17 $kJ \cdot kg^{-1} \cdot d^{-1}$) had not yet been taken into account.

Persistent uremia due to inadequate dialysis is considered to be one of the most important anorectic factors in dialysis patients (49). Spontaneous reduction in protein intake was noted with progression of renal failure, indicating that decreased clearance of uremic substances was associated with progressive anorexia at all stages of renal failure (50). Our results showed that total urea clearance and residual GFR, but not PD urea clearance, were associated with protein and energy intakes in CAPD patients. The CANADA-USA study showed that low urea clearance was associated with low protein intake (19). Although higher protein intakes and a better nutrition status were observed among patients with higher weekly urea clearance (20, 51), the prospective analysis by Harty et al (51) showed that the dependence of protein intake on urea clearance was mainly in those patients with a reduction in clearance due to loss of residual renal function. An increase in the PD urea clearance to offset such losses was not accompanied by improvements in protein intake. This was consistent with our recent findings (20) that PD and renal urea clearance are not equivalent in terms of their solute removal and that residual renal function had a significant contribution to the overall urea clearance and nutrition status of PD patients (52).

Comorbid factors—including advanced age, diabetes, and AVD—were predictive of higher mortality (53) and increased risk of malnutrition in dialysis patients (5). Our current study showed that age was an important factor associated with inadequate protein and energy intakes. More patients with diabetic or hypertensive nephropathy had inadequate protein and energy intakes, which may have been related to the higher prevalence of cardiac comorbidity in these patients. The presence of diabetes was

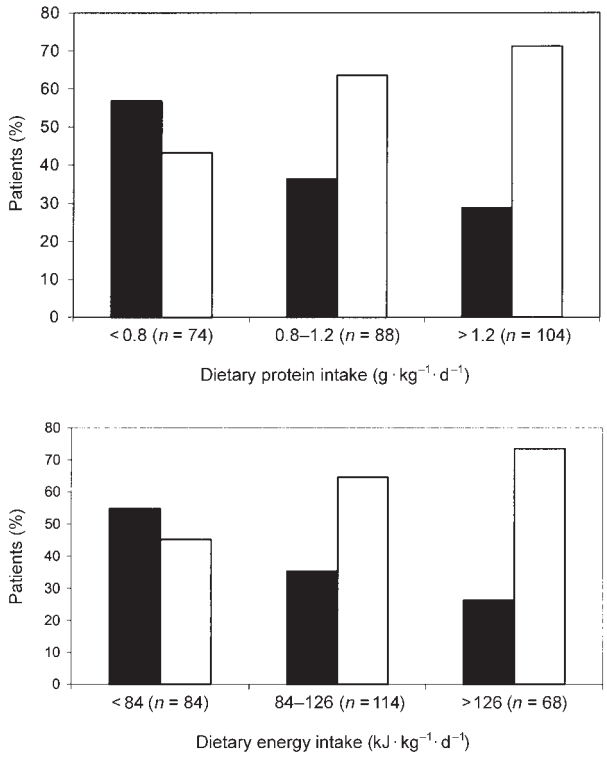

FIGURE 1. Prevalence of a history (■) or no history (□) of volume overload in relation to daily dietary protein and energy intakes in patients receiving continuous ambulatory peritoneal dialysis. As protein and energy intakes increased, the percentage of patients with a history of volume overload decreased ($P < 0.01$).

TABLE 5
Echocardiographic variables for patients with or without a history of volume overload[1]

	History of volume overload (n = 98)	No history of volume overload (n = 152)
LVH (n [%])	95 [96.9]	136 [89.5][2]
LV mass index (g/m^2)	262 ± 89[3]	205 ± 75[4]
LV end-diastolic diameter (cm)	5.29 ± 0.82	4.84 ± 0.79[4]
LV end-systolic diameter (cm)	3.70 ± 0.93	3.16 ± 0.76[4]
LV posterior wall thickness in diastole (cm)	1.37 ± 0.36	1.28 ± 0.23[2]
IVS end-diastolic thickness (mm)	1.60 ± 0.49	1.42 ± 0.30[5]
LV EF	0.65 ± 0.13	0.71 ± 0.11[4]
LV fractional shortening	0.31 ± 0.09	0.35 ± 0.08[4]
Systolic function (n [%])		
LV EF < 45%	8 [8.2]	4 [2.6][2]
LV EF ≥ 45%	90 [91.8]	148 [97.4][2]
Diastolic function (n [%])		
Normal	28 [22]	38 [21][4]
Abnormal relaxation pattern	55 [61]	112 [77]
Pseudonormal	1 [1]	0 [0]
Restrictive filling pattern	14 [16]	2 [2]

[1] LVH, left ventricular hypertrophy; LV, left ventricular; IVS, interventricular septal; EF, ejection fraction.
[2,4,5] Significantly different from history of volume overload: [2] $P < 0.05$, [4] $P \leq 0.001$, [5] $P = 0.002$.
[3] $\bar{x}$ ± SD.

significantly associated with an inadequate energy but not protein intake. Low energy intakes in diabetic patients indicate that either these patients have an incorrect perception of their daily energy intake allowance and have been brainwashed to have a lower energy intake or that they experience more anorectic symptoms and hence have a poorer intake. Patients with AVD had significantly lower energy intakes and a trend toward lower protein intakes than did those with no AVD. The degree of metabolic acidosis and hyperparathyroidism showed no significant relation with protein or energy intake. This finding indicates that these conditions increased malnutrition by promoting protein catabolism, as suggested by other studies (54, 55), rather than inducing a direct appetite-suppressive effect.

In summary, intakes of protein and energy were inadequate in most of the CAPD patients. Other than showing an association between dietary intakes and total urea clearance, residual renal function, increasing age, and diabetes was observed, we showed an important yet unrecognized association between inadequate protein and energy intakes and a history of volume overload in CAPD patients. The appetite-suppressive effect for protein and energy intakes persists long after resolution of the episode of volume overload. Our data suggest that preventing volume overload may be important in ensuring adequate dietary intakes of protein and energy and in preventing malnutrition in peritoneal dialysis patients. The exact mechanisms underlying the association between volume overload and persistent anorexia in dialysis patients require further elucidation.

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