Energy intake and expenditure profile in chronic peritoneal dialysis patients complicated with circulatory congestion

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ABSTRACT

Background: Circulatory congestion is an adverse predictor of mortality in peritoneal dialysis (PD) patients.

Objective: This study evaluated the nutritional status, energy intake, and expenditure profile of PD patients with and without previous circulatory congestion.

Design: We conducted a cross-sectional study in 244 PD patients, of whom 92 had previous circulatory congestion. We estimated dietary energy intake by using a locally validated 7-d food-frequency questionnaire and by assessing resting energy expenditure (REE) and total energy expenditure (TEE) with indirect calorimetry and a locally validated physical activity questionnaire, respectively.

Results: In comparison with those without circulatory congestion, patients with previous circulatory congestion were more malnourished by subjective global assessment (59% compared with 36%; \( P < 0.001 \)), had lower handgrip strength, had lower midarm muscle circumference, had lower dietary protein (0.98 ± 0.45 compared with 1.19 ± 0.44 g·kg\(^{-1}·d^{-1}; \ P < 0.001 \)), and had lower energy intake (92.5 ± 37.0 compared with 110.9 ± 35.7 kJ·kg\(^{-1}·d^{-1}; \ P < 0.001 \)) but had higher C-reactive protein (\( P = 0.025 \)) and higher REE (\( P < 0.001 \)). However, no difference in TEE was noted between the 2 groups, which indicated lower activity energy expenditure among patients with previous circulatory congestion. The resulting energy balance was significantly more negative for patients with previous circulatory congestion than for those without previous circulatory congestion (\( P = 0.050 \)). Furthermore, the prevalence of malnutrition increased with increasing episodes of circulatory congestion (\( P = 0.017 \)).

Conclusions: Patients with previous circulatory congestion had significantly more inflammation, more muscle wasting, and higher REE but lower activity energy expenditure and energy and protein intakes in keeping with an anorexia-cachexia syndrome. The mechanisms of increased REE and reduced energy intake among patients with previous circulatory congestion warrant further investigation. Am J Clin Nutr 2009;90:1179–84.

INTRODUCTION

Cardiovascular disease is the leading cause of death in dialysis patients, accounting for 40% of the total mortality (1, 2). Of the different complications, circulatory congestion or extracellular volume overload is considered one of the most frequent. In peritoneal dialysis (PD) patients, sodium and water retention is an important predictor of mortality and cardiovascular death (3). The clinical manifestation of circulatory congestion is indistinguishable from that of heart failure in dialysis patients. The prevalence of heart failure was reported to be \( \approx \)31% on initiation of dialysis, 56% of whom had a recurrence. Among patients with no previous heart failure, 25% developed subsequent heart failure, at a rate of 7%/y (4).

The presence of heart failure at initiation of dialysis and its recurrence were both adverse prognostic indicators of mortality for patients receiving maintenance dialysis (5, 6). Malnutrition, a powerful predictor of mortality and morbidity, may partly contribute to the adverse outcomes associated with heart failure (7, 8). Indeed, up to 60% of nonrenal failure patients with chronic heart failure were malnourished (9). However, the nutritional status of chronic PD patients complicated with previous circulatory congestion or heart failure has not been determined. Furthermore, factors contributing to malnutrition in patients with circulatory congestion are not known.

Given this background, the current study was conducted to evaluate the nutritional status, degree of inflammation, and components of energy balance (including energy input and energy expenditure profile) in PD patients with and without previous circulatory congestion.

SUBJECTS AND METHODS

Study population and procedures

The study protocol was approved by the Human Research Ethics Committee of the Chinese University of Hong Kong.

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Informed consent was obtained from all patients before study entry. The study was of a cross-sectional design and was performed at a single regional dialysis center in Hong Kong between August 1998 and February 2001.

Patients eligible for study inclusion were those stable on chronic PD for ≥3 mo. We excluded patients with underlying active malignancy, active systemic inflammatory disease, such as systemic lupus erythematosus, active infections, chronic liver disease, and chronic obstructive airways disease because these conditions confound nutritional status. All patients underwent assessment of dietary intake, nutritional status, assessment of resting energy expenditure (REE) and total energy expenditure (TEE), inflammation, and dialysis adequacy as well as estimation of energy input from peritoneal glucose absorption. In patients who developed any acute intercurrent illness, such as peritonitis, exit site infection, pneumonia, or acute myocardial infarction, the above assessments were deferred for ≥1 mo after resolution of the acute illness.

Data collection

Demographic data including age, sex, cause of end-stage renal disease, duration of dialysis, presence of diabetes mellitus (DM), background atherosclerotic vascular complications (AVD), circulatory congestion, number of previous hospitalizations (as a result of circulatory congestion), and PD regimen at the time of entry. The study was of a cross-sectional design and was performed at a single regional dialysis center in Hong Kong between August 1998 and February 2001.

Background AVD was defined as the presence of ischemic heart disease, stable or unstable angina, previous myocardial infarction with or without coronary artery bypass surgery or stenting, and ischemic cerebrovascular event or peripheral vascular disease with or without revascularization or amputation.

Circulatory congestion was defined as such to include only episodes that were clearly documented to require hospitalization. It was diagnosed based on the presence of 3 clinical criteria: 1) presence of symptoms and signs of heart failure, including dyspnea, raised jugular venous pressure and basal crepitations; 2) radiographic evidence of pulmonary venous congestion or interstitial edema (4, 10); and 3) resolution of symptoms, signs, and radiographic changes with hypertonic PD exchanges. This was assessed by direct patient inquiry and by reviewing the computerized Clinical Management System of the Hong Kong Hospital Authority and the Renal Registry Database. They were developed and maintained by the Hong Kong Hospital Authority, who keep a detailed record of all episodes of hospital admissions. A plain chest X-ray was routinely performed in all patients requiring hospitalization, including patients with suspected circulatory congestion.

Nutrition assessment

Dry weight was measured to the nearest 0.1 kg by a weighing scale with the patient’s abdomen drained dry of PD fluid. Body height was measured to the nearest 0.5 cm. Body mass index was calculated as weight (in kg) divided by height squared (in m). Subjective global assessment (SGA) was used to evaluate the overall protein-energy nutritional status (11, 12). Patients were graded to have normal nutrition or mild or moderate-to-severe malnutrition (12). Triceps skinfold (TSF) thickness was measured with a Harpenden caliper on the nondominant arm of patients. Midarm muscle circumference (MAMC) was derived from TSF and midarm circumference (MAC) as follows: MAMC = MAC – (π × TSF). Handgrip strength (HGS) was measured by using the Smedley handy dynamometer. Patients were instructed to apply as much handgrip pressure as possible using the nondominant hand. The measurements were repeated 3 times, and the highest score was recorded in kilogram. All nutritional measurements were performed by experienced research staff blinded to all clinical and biochemical data and grouping of patients.

Estimation of daily total energy input

A locally validated 7-d food-frequency questionnaire (13, 14) was administered to all study patients to estimate average daily dietary protein, carbohydrate, fat, and energy intakes. The food-frequency questionnaire was performed by experienced research staff blinded to all clinical and biochemical data and grouping of patients. The estimated dietary protein and energy intakes were normalized to the patient’s actual dry body weight.

Average daily energy input from peritoneal glucose absorption was calculated by using Grodstein’s formula (15). Average daily total energy input was calculated as the sum of energy derived from peritoneal glucose absorption and dietary energy input estimated from the food-frequency questionnaire.

Estimation of daily TEE and REE

A locally validated physical activity questionnaire (16) was administered to all study subjects on the same day that REE was assessed to estimate the average daily TEE. The questionnaire was based on the modified Yale Physical Activity Survey questionnaire (17). It provides a useful estimation of the average daily habitual energy expenditure of local Chinese population.

REE was determined by indirect calorimetry by using Datatrac TMII, MBM-200, Metabolic monitor (Datex, Helsinki, Finland) on the morning before dietary and nutritional assessment. It was conducted under standardized conditions in the morning after the subjects fasted overnight for ≥10 h. REE was measured for ~30 min while the patients were lying supine at complete physical rest, alone, and undisturbed in a quiet room. Energy expenditure was determined from the rate of oxygen consumption and carbon dioxide production. Readings from the first 5 min were discarded. An average was taken from the subsequent readings of 25 min of steady state and was used to calculate REE. The intrapatient variance of REE in our laboratory was 3.2%.

Estimation of daily energy balance

Daily energy balance was calculated as the difference between daily total energy input and TEE estimated from the physical activity questionnaire.

Biochemical measures

Fasting venous blood samples were collected immediately before nutritional assessment for measurement of blood hemoglobin, fibrinogen, serum urea, creatinine, serum albumin, and C-reactive protein (CRP). CRP was measured with an immunomassay kit (Beckman Instruments Co, Fullerton, CA). Fibrinogen was
Assessment of indexes of dialysis adequacy

Adequacy of dialysis was determined by measuring total weekly urea clearance (KrV) and creatinine clearance (CrCl) by using a standard method (18). Contribution by PD was estimated separately. The residual glomerular filtration rate (GFR) was calculated as an average of 24-h urinary urea and CrCl (19).

Statistical analysis

Data were presented as mean ± SD or median (interquartile range; IQR). Between-group comparisons were made by Student’s t test or Mann-Whitney U test for continuous data, depending on the distribution and by the chi-square test for categorical data. Multiple regression analysis was performed to determine the associations between previous circulatory congestion and nutritional status, dietary intake, and REE with adjustment for confounding covariates. A P value <0.05 was considered to be statistically significant. Statistical analysis was performed by using SPSS 16.0 (SPSS Inc, Chicago, IL) for Windows software.

RESULTS

Of the 244 chronic PD patients (127 men and 117 women) who participated in the study, 92 (37.7%) had previous circulatory congestion. The average duration of PD was 37.5 (range: 4–151) mo. A positive smoking history was reported in 36.5% of patients. Causes of end-stage renal disease included chronic glomerulonephritis (n = 76; 31%), diabetic nephropathy (n = 59; 24%), hypertensive nephrosclerosis (n = 34; 14%), obstructive uropathy (n = 13; 5%), polycystic kidney disease (n = 12; 5%), tubulointerstitial nephritis (n = 7; 3%), and unknown (n = 43; 18%). Seventy-four (30%) patients had DM, and 56 (23%) patients had background AVD. Ninety-eight (40%) patients received regular subcutaneous erythropoietin therapy. The clinical characteristics of patients with and without previous circulatory congestion are compared in Table 1.

Of the 244 patients, 136 (55.7%) were normally nourished, 68 (27.9%) were mildly malnourished, and 40 patients (16.4%) were moderately to severely malnourished by SGA. Fifty-nine percent of patients with previous circulatory congestion compared with 36% of patients with no previous circulatory congestion were malnourished by SGA (P < 0.001; Figure 1). In addition, the prevalence of malnutrition increased with increasing number of previous hospitalizations for circulatory congestion (P = 0.017; Figure 2). Nutritional, biochemical, dialysis, and echocardiographic data of patients with and without previous circulatory congestion are shown in Table 2. Of the 244 patients, those with CRP ≥10 mg/L (n = 35) had a significantly lower energy intake (91 ± 26 compared with 106 ± 38 kJ · kg⁻¹ · d⁻¹; P = 0.027) and a trend toward a lower protein intake (0.98 ± 0.35 compared with 1.13 ± 0.47 g · kg⁻¹ · d⁻¹; P = 0.07) than did those with CRP <10 mg/L (n = 209).

The daily energy input (from diet and PD glucose absorption) and expenditure profile in chronic PD patients with and without previous circulatory congestion are shown in Table 3. After control for age, sex, duration of dialysis, DM, CRP, residual GFR, and total KrV in the multiple regression analysis, patients with previous circulatory congestion were independently associated with 2.44-fold more malnourishment by SGA (95% CI: 1.37, 4.32; P = 0.002), a 2.71 g/L lower serum albumin concentration (95% CI: -4.03, -1.40 g/L; P < 0.001), a 0.77-mm lower MAMC (95% CI: -0.41, -0.11 mm; P = 0.022), and a 1.40-g/L lower serum albumin concentration (95% CI: -2.23, -0.58 g/L; P = 0.006). After adjustment for body weight and height in addition to the same confounding covariates as above, patients with previous circulatory congestion were independently associated with a 371-kJ higher REE (95% CI: 161, 581 kJ; P < 0.001).

DISCUSSION

This study, for the first time, showed an increased prevalence of malnutrition and increased muscle wasting complicated by

| TABLE 1 Clinical characteristics of chronic peritoneal dialysis patients with and without previous circulatory congestion* |
|-------------|-----------------------------|-----------------------------|---------|
|              | Previous circulatory congestion (n = 92) | No previous circulatory congestion (n = 152) | P²  |
| Age (y)      | 56 ± 11¹ | 55 ± 12 | 0.52 |
| Sex (male/female) | 48/44 | 79/73 | 0.98 |
| Dialysis duration (mo) | 26 (13–49) | 30 (16–55) | 0.015 |
| Smoking status [n (%)] | Never 57 (62) | 98 (63) | 0.91 |
| Ex-smoker | 24 (26) | 36 (24) | |
| Current | 11 (12) | 18 (12) | |
| Diabetes mellitus [n (%)] | 43 (47) | 31 (20) | <0.001 |
| Hypertension [n (%)] | 86 (94) | 122 (80) | 0.005 |
| Underlying renal diagnosis [n (%)] | Chronic glomerulonephritis 21 (23) | 55 (36) | |
| Diabetic nephropathy | 38 (41) | 21 (14) | |
| Hypertensive nephropathy | 12 (13) | 22 (15) | |
| Polycystic kidney disease | 3 (3) | 9 (6) | |
| Obstructive uropathy | 2 (2) | 11 (7) | |
| Tubulointerstitial disease | 2 (2) | 5 (3) | |
| Unknown | 14 (15) | 29 (19) | |
| Background AVD [n (%)] | 39 (42) | 17 (11) | <0.001 |
| Use of erythropoetin [n (%)] | 42 (46) | 56 (37) | 0.17 |
| Use of ACEI or ARB [n (%)] | 33 (36) | 28 (18) | 0.002 |
| Use of β-blockers [n (%)] | 51 (55) | 78 (51) | 0.53 |

¹Percentages may not add up to 100 because of rounding off of decimal places.
² χ² test, or chi-square test for data expressed as means ± SDs, data expressed as medians (interquartile ranges), and categorical data, respectively.
³ Mean ± SD (all such values).
⁴ Median; interquartile range in parentheses (all such values).
circulatory congestion in PD patients. The association was independent of well-known factors for malnutrition, including dialysis adequacy and residual renal function (20–22). In addition, reduced dietary intake, increased REE, and inflammation were all significant contributing factors to malnutrition and muscle wasting in these patients.

Compared with patients without circulatory congestion, those with circulatory congestion had significantly lower dietary protein and energy intakes. The intake was far below the recommended protein intake of ≥1.2 g·kg⁻¹·d⁻¹ and energy intake of ≥146 kJ·kg⁻¹·d⁻¹ for PD patients (23). Even with additional energy input from peritoneal glucose absorption, total daily energy input remained significantly lower in patients with previous circulatory congestion than in those without. This suggests that either the episode of circulatory congestion may induce a persistent anorexic effect or they may have ongoing subclinical circulatory congestion. The exact mechanism whereby circulatory congestion induces appetite suppression is not known. Suggested factors include hepatic congestion, hypoxia, delayed gastric emptying, and gut hypomotility (24). Inflammation may be one such factor that induces appetite suppression in patients with previous circulatory congestion. Infusion of recombinant interleukin-1 increased plasma interleukin-6, acute phase protein production, and decreased food intake in animal models (25). Increased tumor necrosis factor is present in heart failure patients (26) and is associated with anorexia and poor nutritional status in PD patients (27). Our current findings of higher CRP among patients with previous circulatory congestion and an inverse relation between CRP and dietary energy and protein intake were all in keeping with this hypothesis. Normally, a greater systemic inflammatory response requires a higher dietary protein and energy intake to maintain normal nutrition (28, 29). This suggests that the actual protein and energy intakes of our PD patients with previous circulatory congestion were inadequate given the presence of a systemic inflammatory response. Sympathetic overactivity, which is associated with the presence of diseased native kidneys (30), has also been invoked as a potential cause of anorexia-cachexia syndrome in patients with end-stage renal disease (31). Despite being more malnourished, as evidenced by various nutritional indexes, including SGA, handgrip strength, MAMC, and serum albumin, patients with previous circulatory congestion had a significantly greater body weight and body mass index. This suggests an ongoing subclinical extracellular fluid overload in patients with previous circulatory congestion. The lower serum albumin concentration may be partly explained by hemodilution secondary to fluid overload.

The other important novel finding was the significantly high REE among PD patients with than in those without previous circulatory congestion. REE accounts for 60–80% of the TEE, and its increase may contribute to cachexia in patients with heart failure (32). Indeed, increased REE has been reported in both acute (33) and chronic heart failure (34) in nonrenal failure patients and was attributed to the increased work of breathing (34). A graded increase in REE was observed with increased severity of heart failure symptoms as reflected by the New York Heart Association Classification (35), indicating that the clinical severity of illness corresponds to the magnitude of increase in resting energy demand. The higher REE observed among patients with previous circulatory congestion raised the possibility that these patients may still have subclinical circulatory congestion and heart failure. Daily TEE consists of REE, thermic effect of meals, and energy expenditure from physical activity (36). Despite having a higher REE, daily TEE showed no significant difference between patients with and without previous circulatory congestion, which suggests a lower activity EE among patients with previous circulatory congestion. Decreased physical activity in patients with previous circulatory congestion may further contribute to skeletal muscle atrophy and exercise intolerance (37, 38) and is evidenced by the lower handgrip strength and MAMC among these patients. Our results indicate that cachexia in patients with previous circulatory congestion was not due to increased daily TEE, in keeping with other studies in nonrenal failure patients (39). Rather, it was due to increased REE and inflammation with increased muscle wasting as well as inadequate protein and energy intakes (40–42). Thus, repleting nutritional intake alone may be insufficient to reverse cardiac cachexia. Rather, targeting immune activation and hypercatabolism may be more successful, and this deserves further evaluation.

In this study, the energy intake and expenditure profile and nutritional status were deliberately not assessed during the acute phase of circulatory congestion but rather when patients appeared to be clinically stable and any intercurrent illness had resolved for ≥1 mo. This enabled us to show the long-lasting effect of
previous circulatory congestion on the habitual energy intake and expenditure profile of PD patients. A significantly higher prevalence of DM and AVD was seen among patients with previous circulatory congestion, which suggests that these comorbidities may also predispose to an increased risk of cardiac dysfunction and circulatory congestion. The lower hemoglobin concentration among patients with previous circulatory congestion may be partly explained by hemodilution. It may also be possible that these patients were more malnourished with greater degrees of inflammation and became relatively resistant to erythropoietin. No association was observed between smoking status and previous circulatory congestion. The apparent protective effect of chronic glomerulonephritis is worth noting. It may be explained by a higher percentage of diabetic nephropathy among patients with circulatory congestion. This raised the percentage of chronic glomerulonephritis among those without circulatory congestion.

Our study had several limitations. First, circulatory congestion not only included episodes due to extracellular volume overload but also probably ventricular dysfunction, because it is extremely difficult to distinguish between the 2 entities in dialysis patients in practical terms. It is possible that patients with very mild subclinical volume overload who do not require hospitalization may be misclassified as having no previous circulatory congestion, and the true prevalence of previous circulatory congestion may have been underestimated in our PD population. Second, the diagnosis of circulatory congestion was reviewed retrospectively by direct patient inquiry and review of previous computerized hospitalization records. Third, volume status was not assessed in this study. Thus, it remains a hypothesis to test whether patients with previous circulatory congestion continued to have subclinical circulatory congestion at the time of nutritional assessment. Nevertheless, our novel findings indicate the need for more detailed nutritional evaluation in PD patients with previous circulatory congestion.

In conclusion, PD patients with a history of previous circulatory congestion have an increased prevalence of malnutrition and muscle wasting due to a combination of different factors, including reduced intake, increased REE and inflammation, and reduced activity energy expenditure. The role of inflammation in the anorexia-cachexia syndrome and the mechanisms of increased REE in PD patients with previous circulatory congestion warrants further investigation.

### TABLE 2

<table>
<thead>
<tr>
<th>Nutritional data</th>
<th>Previous circulatory congestion (n = 92)</th>
<th>No previous circulatory congestion (n = 152)</th>
<th>P²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight (kg)</td>
<td>60 ± 11</td>
<td>57 ± 9</td>
<td>0.016</td>
</tr>
<tr>
<td>Body height (m)</td>
<td>1.59 ± 0.08</td>
<td>1.58 ± 0.08</td>
<td>0.40</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>23.7 ± 3.9</td>
<td>22.7 ± 3.0</td>
<td>0.028</td>
</tr>
<tr>
<td>Triceps skinfold thickness (mm)</td>
<td>16.65 ± 9.77</td>
<td>15.43 ± 8.41</td>
<td>0.30</td>
</tr>
<tr>
<td>MAMC (cm)</td>
<td>20.82 ± 2.84</td>
<td>21.60 ± 2.59</td>
<td>0.029</td>
</tr>
<tr>
<td>Handgrip strength (kg)</td>
<td>15.61 ± 9.48</td>
<td>19.43 ± 10.01</td>
<td>0.004</td>
</tr>
</tbody>
</table>

### TABLE 3

<table>
<thead>
<tr>
<th>Daily energy input</th>
<th>Previous circulatory congestion (n = 92)</th>
<th>No previous circulatory congestion (n = 152)</th>
<th>P²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dietary protein intake (g · kg⁻¹ · d⁻¹)</td>
<td>0.98 ± 0.45</td>
<td>1.19 ± 0.44</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Dietary fat intake (g · kg⁻¹ · d⁻¹)</td>
<td>0.75 ± 0.36</td>
<td>0.87 ± 0.38</td>
<td>0.017</td>
</tr>
<tr>
<td>Dietary carbohydrate intake (g · kg⁻¹ · d⁻¹)</td>
<td>3.01 ± 1.32</td>
<td>3.45 ± 1.31</td>
<td>0.012</td>
</tr>
<tr>
<td>Total energy intake (kJ · kg⁻¹ · d⁻¹)</td>
<td>92.5 ± 37.0</td>
<td>110.9 ± 35.7</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

All values are means ± SDs. *P* values were calculated with Student’s *t* test for data expressed as means ± SDs or by Mann-Whitney *U* test for data expressed as medians (interquartile ranges).

*² Between-group comparisons were made by Student’s *t* test for data expressed as means ± SDs or by Mann-Whitney *U* test for data expressed as medians (interquartile ranges).

¹ Mean ± SD (all such values).

² Median; interquartile range in parentheses (all such values).
The authors’ responsibilities were as follows—AY-MW: contributed to the concept of the study, study design, data collection, data analysis, and writing and review of the manuscript; MM-MS: contributed to the measurement of nutritional data; CWL and IH-SC: contributed to the measurements of all biochemical data in the study and review of manuscript; NT: contributed to the use of the indirect calorimetry and review of the manuscript; S-FL and JES: contributed to the critical review of the manuscript; and JW: contributed to the concept of the study, study design, and final critical review of the manuscript. None of the contributing authors had any financial or personal interest in any company or organization sponsoring the research.

REFERENCES


