# Protein-Energy Malnutrition in Patients with Liver Cirrhosis

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Protein-energy malnutrition (PEM) is frequently seen in patients with liver cirrhosis. This condition is associated with a poor prognosis and reduced survival. We investigated the protein and energy metabolic status, including serum albumin concentration, and resting energy expenditure (REE) and respiratory quotient (RQ) measured by indirect calorimetry in 23 patients with liver cirrhosis (8 men and 15 women; mean age, 60.3 years). The median value of %REE (measured REE / predicted REE) was highest in Child-Pugh grade A and lowest in grade C, and the range of RQ tended to be highest in Child-Pugh grade A and lowest in grade C, although there were not statistically significant (p=0.871 and 0.664, respectively). Serum triglyceride concentration was significantly lower in patients who had an RQ less than 0.85 than in patients who had an RQ of 0.85 or more, and free fatty acid tended to be higher in patients who had an RQ less than 0.85 than in patients who had an RQ of 0.85 or more. Of the 23 patients, 78.3% were in a state of protein and/or energy malnutrition and 47.8% had PEM. Our results suggest that %REE and RQ were not significantly associated with liver function, but the oxidation rate of fat was increased in advanced liver cirrhosis. A longitudinal study in a large population is needed to determine the efficacy of %REE and RQ measurements for adequate nutritional treatment and improvement of patient outcome.

ACTA MEDICA NAGASAKIENSIA 57: 5−12, 2012

**Keywords:** Respiratory quotient, Indirect calorimetry, Liver cirrhosis, Protein-energy malnutrition

## Introduction

Protein-energy malnutrition (PEM) is a common clinical manifestation of patients with liver cirrhosis.[1-7] Lautz et al.[8] reported that 65% of patients with liver cirrhosis showed some signs of PEM as indicated by low body cell mass, reduced serum albumin concentrations, or abnormal skinfold thickness. This is mainly due to abnormal fuel metabolism including visceral and skeletal muscle protein-catabolic state,[9] increased fat oxidation, and decreased glucose oxidation.[10] This condition is associated with a poor prognosis and reduced survival.[9,11] Therefore, accurate assessments of nutritional status such as measurement of energy expenditure may be of clinical value in cases of liver cirrhosis.[12,13]

Indirect calorimetry is an established method for estimating energy malnutrition, despite being expensive and requiring training to use. Resting energy expenditure (REE) and respiratory quotient (RQ) are the main parameters considered when evaluating energy metabolism by indirect calorimetry.[11] RQ has been reported to decrease after an overnight fast in cirrhotic patients in many studies, but whether increased basal or resting energy expenditure is a constant feature in liver cirrhosis remains controversial.[1,3]

In the present study, we aimed to investigate the protein and energy metabolic statuses, including the measurement of serum albumin concentration, and the measurement of

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Received October 6, 2011; Accepted December 21, 2011

REE and RQ by indirect calorimetry, in patients with liver cirrhosis.

## Patients and Methods

### *Patients*

Of the 150 patients who were admitted to the Department of Gastroenterology and Hepatology, Nagasaki University Hospital, Japan, and who also underwent indirect calorimetry between April 2008 and October 2009, 23 patients with liver cirrhosis (8 men and 15 women; mean age, 60.3 ± 10.3 years) were included in the present study. The medical records of the 23 patients with liver cirrhosis were collected and analyzed. The collected data included sex, age, etiology of liver cirrhosis, Child-Pugh grade (Table 1),[14,15] height, body weight, history of alcohol intake, associated disease such as hypertension, diabetes mellitus, and esophageal varices, and history of branched-chain amino acid (BCAA) treatment. The laboratory data such as peripheral platelet count (PLT), C-reactive protein (CRP), serum levels of albumin (ALB), total bilirubin (TB), aspartate aminotransferase (AST), alanine aminotransferase (ALT), total cholesterol (TC), triglyceride (TG), free fatty acid (FFA), blood urea nitrogen (BUN), creatinine (Cr), sodium (Na), potassium (K), chloride (Cl), calcium (Ca), and phosphorus (P), fasting blood glucose (FBG), immunoreactive insulin (IRI), prothrombin time (PT), ammonia ($NH_3$), and BCAA to tyrosine ratio (BTR) were also collected. Standard biochemical tests were performed on a multichannel autoanalyzer.

The history of alcohol intake was divided into two groups as follows: drinker (at least 70 g/day of alcohol intake for more than 5 years) and non- or light-drinker (less than 70 g/day of alcohol intake for up to 5 years). The diagnosis of liver cirrhosis was based on a compatible clinical history, radiological studies, and/or histopathological examination when available. Patients who were seropositive for hepatitis B surface antigen (HBsAg) were classified as "hepatitis B virus (HBV)-related"; those who were seropositive for antibody to hepatitis C virus (anti-HCV) as "HCV-related"; those who were drinkers and seronegative for HBsAg and anti-HCV as "alcoholic"; and those who were non- or light-drinkers and seronegative for HBsAg and anti-HCV as "others". The body mass index (BMI) was calculated as body weight (kg) divided by height squared ($m^2$).

**Table 1.** Definition and criteria of Child-Pugh classification

| Clinical and laboratory findings | Score | | |
|---|---|---|---|
| | 1 point | 2 points | 3 points |
| Encephalopathy occasionally | None | Mild | Coma |
| Ascites | Absent | Slight | Moderate |
| Serum TB (mg/dL) | <2.0 | 2.0-3.0 | >3.0 |
| Serum ALB (g/dL) | >3.5 | 2.8-3.5 | <2.8 |
| PT (%) | >70 | 40-70 | <40 |

Definition and criteria of encephalopathy and prothrombin time are modified according to the Liver Cancer Study Group of Japan.[14,15] The scores for all findings are totaled, and a final score of 5-6 is assigned a Child-Pugh grade A, score of 7-9 is grade B, and score of 10-15 is grade C. Refer to the text in the Patients and Methods section for abbreviations.

### *Indirect calorimetry*

Indirect calorimetry was carried out in the morning after overnight bed rest and fasting using a Vmax SPECTRA 29n calorimeter (Cardinal Health 207. Inc., Dublin, OH, USA). The equipment was calibrated at the start of each measurement in accordance with the manufacturer's instructions. About 3 or 4 minutes after the patient rested in the supine position in a rigid canopy (placed over the head in which the patient respires freely), oxygen consumption per minute ($VO_2$) and carbon dioxide production per minute ($VCO_2$) were measured during a period of at least 15 minutes. Resting energy expenditure (REE) was calculated using the modified Weir formula[16] as follows: REE (kcal/-day) = [3.9 x $VO_2$ (L/min) + 1.1 x $VCO_2$ (L/min)] x 1440. Respiratory quotient (RQ) was calculated as follows: RQ = $VCO_2$ (L/min) / $VO_2$ (L/min). The predicted REE was estimated from the Harris-Benedict equations[17] as follows: basal metabolic rate (BMR) (kcal/day) for men = 66.47 + 13.75 x body weight (kg) + 5.00 x height (cm) - 6.75 x age (years). The BMR (kcal/day) for women = 655.10 + 9.56 x body weight (kg) + 1.85 x height (cm) - 4.68 x age (years). The %REE was calculated as follows: %REE = measured REE (kcal/day) / predicted REE (kcal/day).

### *Ethical consideration*

This study was performed according to the principles of the Declaration of Helsinki. The study protocol was approved by the Ethical Committee of University of Nagasaki. Informed consent was obtained from all participants in Nagasaki University Hospital.

### *Statistical analysis*

Data were expressed as mean ± standard deviation (SD) or as median (range). Differences between groups were tested for statistical significance using the two-tailed Mann-Whitney U-test, Kruskal-Wallis test followed by Bonferroni's multiple comparison test, chi-square test, or Fisher's exact probability test. All data analyses were performed using IBM SPSS statistics software, version 17.0 (IBM Co., Somers, NY) on a computer with a Windows operating system. A *p*-value less than 0.05 was considered statistically significant.

## Results

### *Clinical characteristics of 23 patients with liver cirrhosis*

The clinical features of 23 patients with liver cirrhosis are shown in Table 2. The etiology of liver cirrhosis was "HBV-related" in 5 patients, "HCV-related" in 9 patients, "alcoholic" in 4 patients, and "others" in 5 patients. Of the 5 patients who were categorized as "others", 3 were diagnosed as primary biliary cirrhosis (PBC), one as autoimmune hepatitis (AIH), and one as PBC-AIH overlapping syn-

**Table 2.** Clinical characteristics of 23 patients with liver cirrhosis

| Feature | Number examined | Result |
|---|---|---|
| Men/women | 23 | 8/15 |
| Age (years) | 23 | 64 (34-76) |
| Etiology* (HBV/HCV/alcohol/others) | 23 | 5/9/4/5 |
| Child-Pugh grade (A/B/C) | 23 | 8/7/8 |
| Height (m) | 23 | 1.53 (1.42-1.75) |
| Body weight (kg) | 23 | 56.4 (37.0-90.0) |
| BMI (kg/m$^2$) | 23 | 24.0 (16.4-29.7) |
| REE (kcal/day) | 23 | 1163 (956-1667) |
| %REE | 23 | 100 (81-126) |
| RQ | 23 | 0.83 (0.72-1.02) |
| $VO_2$ (L/min) | 23 | 0.17 (0.13-0.24) |
| $VCO_2$ (L/min) | 23 | 0.14 (0.12-0.20) |
| PLT (x10$^3$/mm$^3$) | 23 | 12.5 (3.1-35.0) |
| CRP (mg/dL) | 22 | 0.25 (0.02-1.15) |
| ALB (g/dL) | 23 | 3.1 (2.3-4.3) |
| TB (mg/dL) | 23 | 1.4 (0.4-26.7) |
| AST (IU/L) | 23 | 42 (14-156) |
| ALT (IU/L) | 23 | 29 (8-73) |
| FBG (mg/dL) | 16 | 104 (62-166) |
| IRI (μU/mL) | 11 | 8.8 (3.5-107.3) |
| TC (mg/dL) | 14 | 134 (87-377) |
| TG (mg/dL) | 16 | 84 (23-314) |
| FFA (mEq/L) | 13 | 0.73 (0.25-1.57) |
| BUN (mg/dL) | 23 | 17 (4-66) |
| Cr (mg/dL) | 23 | 0.72 (0.42-2.09) |
| Na (mEq/L) | 23 | 137 (125-143) |
| K (mEq/L) | 23 | 4.0 (3.3-4.9) |
| Cl (mEq/L) | 23 | 104 (91-108) |
| Ca (mg/dL) | 13 | 8.7 (8.2-9.8) |
| P (mg/dL) | 10 | 3.3 (1.9-4.6) |
| PT (%) | 23 | 64 (32-120) |
| $NH_3$ (μg/dL) | 18 | 77 (34-174) |
| BTR | 16 | 3.06 (1.32-8.85) |
| History of alcohol intake (non- or light-drinker/drinker/unknown) | 23 | 15/5/3 |
| Diabetes mellitus (absent/present) | 23 | 12/11 |
| Hypertension (absent/present) | 23 | 16/7 |
| Esophageal varices (absent/present) | 23 | 12/11 |
| BCAA treatment (absent/present) | 23 | 13/10 |

*HBV,hepatitis B virus-related; HCV, hepatitis C virus-related.
Refer to the text in the Patients and Methods section for other abbreviations.
Age, height, body weight, body mass index, metabolic parameters, peripheral platelet count, and blood biochemical parameters are expressed as median (range).

drome. Mild hepatic encephalopathy occurred in only one patient. Minimum ascites was observed in 2 patients and moderate ascites was detected in 10 patients. Serum TB was 2.0-3.0 mg/dL in one patient and more than 3.0 mg/dL in 6 patients. Serum ALB was 2.8-3.5 g/dL in 9 patients and less than 2.8 g/dL in 6 patients. Prothrombin time was 40%-70% in 14 patients and less than 40% in 2 patients. The aggregate Child-Pugh score ranged from 5 to 13 points and the median value was 8. Overall, 8 patients were categorized as Child-Pugh grade A, 7 patients as grade B, and 8 patients as grade C.

*Comparison of clinical features among patients who were categorized as Child-Pugh grade A, B, and C*

Except for the laboratory findings included in Child-Pugh classification such as serum TB, ALB, and PT, there were significant differences in serum Na, Ca, TC, and frequency of receiving BCAA treatment among patients who were categorized as Child-Pugh grade A, B, and C. Particularly, BCAA treatment was more common in patients categorized as Child-Pugh grade C (Table 3). There were no significant differences in %REE and RQ among patients who were

**Table 3.** Comparison of clinical features among patients who are categorized as Child-Pugh grade A, B, and C

| Feature | Grade A | Grade B | Grade C | *P* |
|---|---|---|---|---|
| Men/women | 3/5 | 3/4 | 2/6 | 0.866 |
| Age (years) | 65 (46-76) | 65 (49-72) | 51 (34-65) | 0.095 |
| Etiology (HBV/HCV/alcohol/others) | 2/3/1/2 | 1/4/1/1 | 2/2/2/2 | 0.971 |
| Height (m) | 1.52 (1.42-1.64) | 1.55 (1.43-1.67) | 1.52 (1.45-1.75) | 0.675 |
| Body weight (kg) | 56.1 (47.2-63.5) | 59.0 (43.5-68.5) | 56.7 (37.0-90.0) | 0.777 |
| BMI (kg/m$^2$) | 23.2 (20.7-29.4) | 24.0 (18.1-29.7) | 26.0 (16.4-29.4) | 0.838 |
| REE (kcal/day) | 1164 (956-1300) | 1138 (1021-1667) | 1180 (1100-1578) | 0.450 |
| %REE | 103 (90-110) | 101 (81-118) | 97 (81-126) | 0.871 |
| RQ | 0.83 (0.78-1.02) | 0.84 (0.76-0.87) | 0.82 (0.72-0.92) | 0.664 |
| $VO_2$ (L/min) | 0.17 (0.13-0.19) | 0.16 (0.15-0.24) | 0.17 (0.15-0.23) | 0.474 |
| $VCO_2$ (L/min) | 0.14 (0.13-0.17) | 0.13 (0.12-0.20) | 0.14 (0.12-0.18) | 0.646 |
| PLT (x$10^3$/mm$^3$) | 15.3 (6.4-31.2) | 13.6 (6.6-35.0) | 9.1 (3.1-17.6) | 0.204 |
| CRP (mg/dL) | 0.15 (0.02-1.15) | 0.23 (0.05-0.25) | 0.43 (0.17-0.73) | 0.227 |
| ALB (g/dL) | 3.7 (2.9-4.3) | 3.1 (2.7-3.6) | 2.8 (2.3-3.2) | 0.003 |
| TB (mg/dL) | 0.9 (0.4-1.4) | 0.9 (0.5-1.4) | 3.9 (1.5-26.7) | 0.001 |
| AST (IU/L) | 39 (14-74) | 43 (18-63) | 53 (23-156) | 0.342 |
| ALT (IU/L) | 30 (10-53) | 32 (8-39) | 28 (13-73) | 0.742 |
| FBG (mg/dL) | 111 (62-133) | 93.5 (79-166) | 118 (72-144) | 0.934 |
| IRI (μU/mL) | 13.3 (4.2-15.0) | 6.7 (3.5-107.3) | 16.6 (8.6-24.6) | 0.736 |
| TC (mg/dL) | 177 (102-377) | 114 (105-174) | 95 (87-102) | 0.039 |
| TG (mg/dL) | 81 (63-314) | 84 (48-117) | 114 (23-125) | 0.972 |
| FFA (mEq/L) | 0.75 (0.29-1.57) | 0.55 (0.25-1.03) | 0.86 (0.61-1.54) | 0.453 |
| BUN (mg/dL) | 17 (4-23) | 16 (10-66) | 17 (5-48) | 0.856 |
| Cr (mg/dL) | 0.74 (0.42-1.28) | 0.85 (0.56-1.97) | 0.62 (0.43-2.09) | 0.519 |
| Na (mEq/L) | 138 (136-140) | 138 (132-139) | 132 (125-143) | 0.031 |
| K (mEq/L) | 4.3 (3.3-4.7) | 3.9 (3.3-4.9) | 3.9 (3.5-4.9) | 0.606 |
| Cl (mEq/L) | 104 (99-107) | 105 (98-108) | 100 (91-106) | 0.061 |
| Ca (mg/dL) | 9.3 (8.9-9.8) | 8.4 (8.2-8.7) | 8.6 (8.5-9.2) | 0.015 |
| P (mg/dL) | 4.3 (3.4-4.6) | 3.3 (2.6-3.5) | 2.7 (1.9-3.0) | 0.060 |
| PT (%) | 84 (57-120) | 64 (45-70) | 46 (32-67) | 0.002 |
| $NH_3$ (μg/dL) | 71 (60-105) | 115 (62-174) | 83 (34-145) | 0.411 |
| BTR | 3.44 (2.86-7.26) | 3.11 (2.73-4.64) | 2.75 (1.32-8.85) | 0.452 |
| History of alcohol intake (non- or light-drinker/drinker/unknown) | 5/1/2 | 6/0/1 | 4/4/0 | 0.123 |
| Diabetes mellitus (absent/present) | 3/5 | 5/2 | 4/4 | 0.508 |
| Hypertension (absent/present) | 4/4 | 4/3 | 8/0 | 0.073 |
| Esophageal varices (absent/present) | 4/4 | 4/3 | 4/4 | 1.000 |
| BCAA treatment (absent/present) | 8/0 | 4/3 | 1/7 | 0.001 |

Refer to the text in the Patients and Methods section and Table 2 for abbreviations.
Age, height, body weight, body mass index, metabolic parameters, peripheral platelet count, and blood biochemical parameters are expressed as median (range)

categorized as Child-Pugh grade A, B, and C, but the median value of %REE was highest in Child-Pugh grade A and lowest in grade C. Moreover, the range of RQ tended to be highest in Child-Pugh grade A and lowest in grade C, although there were not statistically significant (Fig. 1).

*Comparison of clinical features between patients who had a respiratory quotient less than 0.85 and patients who had a respiratory quotient of 0.85 or more*

Because an RQ of 0.85 was reported to be the point at which substrate for thermogenesis turned from carbohydrate dominant (RQ>0.85) to fat dominant (RQ<0.85), and survival rate was significantly lower in patients with low RQ (<0.85) than in patients with scores above 0.85,[3] we conducted a comparison of clinical features between patients who had an RQ less than 0.85 and patients who had RQ of 0.85 or more (Table 4). Height was significantly higher in patients who had an RQ less than 0.85 than in patients who had an RQ of 0.85 or more. Serum TG was significantly lower in patients who had an RQ less than 0.85 than in patients who had an RQ of 0.85 or more, and FFA

**Table 4.** Comparison of clinical features between patients who have a respiratory quotient less than 0.85 and patients who have a respiratory quotient of 0.85 or more

| Feature | RQ≧0.85 | RQ≧0.85 | *P* |
|---|---|---|---|
| Men/women | 7/7 | 1/8 | 0.086 |
| Age (years) | 62.5 (34-76) | 64 (46-72) | 0.728 |
| Etiology (HBV/HCV/alcohol/others) | 4/7/3/0 | 1/2/1/5 | 0.009 |
| Child-Pugh grade (A/B/C) | 5/4/5 | 3/3/3 | 0.484 |
| Height (m) | 1.55 (1.45-1.75) | 1.46 (1.42-1.67) | 0.012 |
| Body weight (kg) | 56.1 (43.5-90.0) | 59.0 (37.0-68.5) | 0.753 |
| BMI (kg/m$^2$) | 22.2 (18.1-29.4) | 25.7 (16.4-29.7) | 0.176 |
| REE (kcal/day) | 1163 (1021-1667) | 1179 (956-1402) | 0.614 |
| %REE | 101 (81-126) | 98 (90-111) | 0.592 |
| $VO_2$ (L/min) | 0.17 (0.15-0.24) | 0.17 (0.13-0.20) | 0.256 |
| $VCO_2$ (L/min) | 0.14 (0.12-0.20) | 0.14 (0.13-0.17) | 0.313 |
| PLT (x10$^3$/mm$^3$) | 12.2 (3.1-35.0) | 13.0 (6.4-31.2) | 0.925 |
| CRP (mg/dL) | 0.42 (0.08-0.73) | 0.23 (0.02-1.15) | 0.306 |
| ALB (g/dL) | 3.0 (2.4-4.2) | 3.5 (2.3-4.3) | 0.218 |
| TB (mg/dL) | 1.3 (0.5-26.7) | 1.4 (0.4-5.4) | 0.548 |
| AST (IU/L) | 44 (20-85) | 33 (14-156) | 0.450 |
| ALT (IU/L) | 29 (10-53) | 29 (8-73) | 0.636 |
| FBG (mg/dL) | 97 (62-166) | 129 (99-151) | 0.079 |
| IRI (μU/mL) | 11.1 (3.5-107.3) | 8.6 (4.5-14.5) | 0.683 |
| TC (mg/dL) | 114 (102-177) | 196 (87-377) | 0.205 |
| TG (mg/dL) | 81 (23-114) | 125 (80-314) | 0.015 |
| FFA (mEq/L) | 0.77 (0.25-1.57) | 0.53 (0.45-0.61) | 0.277 |
| BUN (mg/dL) | 17 (5-44) | 17 (4-66) | 0.925 |
| Cr (mg/dL) | 0.79 (0.43-2.09) | 0.58 (0.42-1.97) | 0.549 |
| Na (mEq/L) | 137 (125-143) | 137 (126-140) | 0.751 |
| K (mEq/L) | 4.0 (3.3-4.9) | 4.0 (3.3-4.9) | 0.411 |
| Cl (mEq/L) | 104 (91-108) | 103 (94-107) | 1.000 |
| Ca (mg/dL) | 8.5 (8.2-9.3) | 9.3 (8.6-9.8) | 0.122 |
| P (mg/dL) | 3.3 (2.6-4.6) | 3.1 (1.9-4.3) | 0.793 |
| PT (%) | 60 (32-85) | 66 (32-120) | 0.284 |
| $NH_3$ (μg/dL) | 77 (34-174) | 91 (48-145) | 1.000 |
| BTR | 2.98 (2.51-7.26) | 5.47 (1.32-8.85) | 0.275 |
| History of alcohol intake (non- or light-drinker/drinker/unknown) | 8/5/1 | 7/0/2 | 0.131 |
| Diabetes mellitus (absent/present) | 9/5 | 3/6 | 0.214 |
| Hypertension (absent/present) | 10/4 | 6/3 | 1.000 |
| Esophageal varices (absent/present) | 5/9 | 7/2 | 0.089 |
| BCAA treatment (absent/present) | 7/7 | 6/3 | 0.669 |

Refer to the text in the Patients and Methods section and Table 2 for abbreviations.
Age, height, body weight, body mass index, metabolic parameters, peripheral platelet count, and blood biochemical parameters are expressed as median (range).

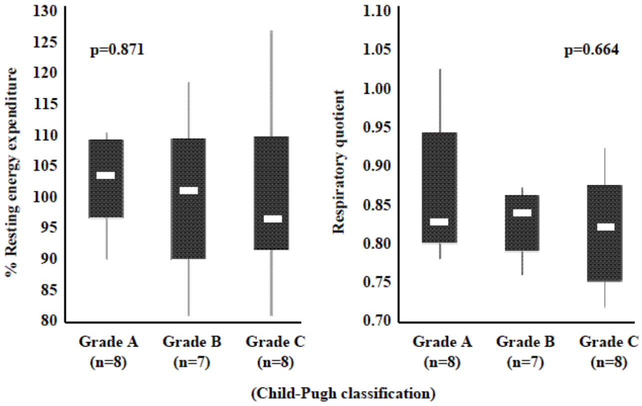


**Figure 1.** Comparison of % resting energy expenditure and respiratory quotient among patients who are categorized as Child-Pugh grade A, B, and C

tended to be higher in patients who had an RQ less than 0.85 than in patients who had an RQ of 0.85 or more (Fig. 2). Patients with "HCV-related" cirrhosis were more common, and patients with autoimmune-related ("others") cirrhosis were less common in the group of RQ<0.85. Child-Pugh grade and %REE were similar in patients who had an RQ less than 0.85 and patients who had an RQ of 0.85 or more.

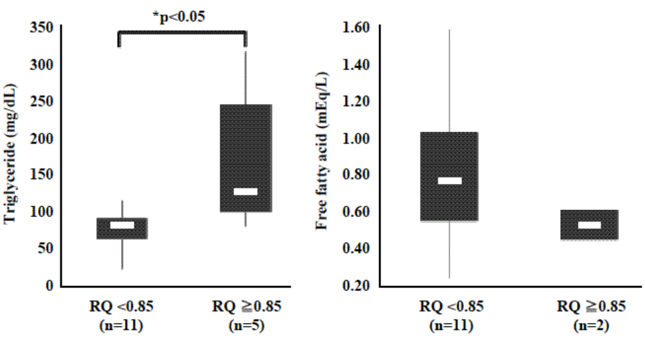


**Figure 2.** Comparison of serum triglyceride and free fatty acid concentration between patients who have a respiratory quotient less than 0.85 and patients who have a respiratory quotient of 0.85 or more

*Frequency of protein-energy malnutrition in patients with liver cirrhosis*

Of the 23 patients with liver cirrhosis, 11 patients (47.8%) had an RQ less than 0.85 and serum ALB less than 3.5 g/dL, suggesting PEM (Table 5). The frequencies of patients with PEM were 25.0% (2 out of 8 patients) in Child-Pugh grade A, 57.1% (4 out of 7 patients) in Child-Pugh grade B, and 62.5% (5 out of 8 patients) in Child-Pugh grade C.

**Table 5.** Number and frequency of protein-energy malnutrition in patients with liver cirrhosis

| | Serum albumin <3.5 g/dL | Serum albumin ≧3.5 g/dL |
|---|---|---|
| RQ ≧ 0.85 | 4 (17.4%) | 5 (21.7%) |
| RQ < 0.85 | 11 (47.8%) | 3 (13.0%) |

RQ, respiratory quotient.

## Discussion

Resting energy expenditure, the amount of calories required by a body for a 24-hour period of inactivity (lying in bed at rest in a comfortable environment), is a marker of metabolic status. To eliminate the effects of age, sex, height, and body weight on REE, the predicted REE is calculated by the Harris-Benedict equations.[17] A %REE (measured REE/predicted REE) of more than 1.1 is usually considered to be a hypermetabolic status.[3] For example, %REE is reported to increase in patients with cancer because the competition for nutrients between the tumor and the host can lead to an accelerated starvation state that promotes metabolic disturbances (alterations in carbohydrate, lipid, and protein metabolism) in the host, including hypermetabolism, which leads to decreased energy efficiency.[18,19] The patients with liver cirrhosis also showed some signs of PEM, but whether increased basal or resting energy expenditure is a constant feature remains controversial.[1,3,12,20-22] Kato et al.[1] reported that the basal energy expenditure in liver cirrhosis was elevated with decreased oxidation rates of carbohydrate and protein and an increased oxidation rate of fat. They also reported that REE was higher in patients with more advanced disease such as Child-Pugh grades B and C.[1] In the present study, however, the median value of %REE was just 100%, and there was no significant difference in %REE among patients who were categorized as Child-Pugh grade A, B, and C. Moreover, the median value of %REE was highest in Child-Pugh grade A and lowest in grade C. The reason for these discrepancies is unclear. Some of the possible explanations would be heterogenous patients populations and methodologic problems associated with the measurement of energy expenditure because REE could not be accurately predicted by using Harris-Benedict equations.[19] In the cirrhotic patients with peripheral edema and/or ascites, the predicted REE is sometimes over-estimated. In fact, 52.2% of our patients (12 out of 23 patients) had ascites.

The RQ, the ratio of the volume of carbon dioxide produced to the volume of oxygen consumed during respiration, is a useful marker to estimate energy metabolism and can be used to determine which nutrients are being used as an energy source.[11] During aerobic respiration, the respiration of fat gives an RQ of 0.7, the respiration of protein gives an RQ of 0.8, and the respiration of carbohydrate gives an RQ of 1.0. Usually, the RQ ranges from 0.7 to 1.0 and averages around 0.82 in a healthy person. In cases of liver cirrhosis, the RQ is reported to be lower than in healthy subjects.[7] Enhanced lipid oxidation and reduced glucose oxidation can be responsible for the decrease in RQ. Reduced glucose oxidation is due to the lower production rate of glucose from glycogen, the decrease in peripheral glucose use, and the decrease in hepatic glycogen stores.[3] Kato et al.[1] also reported that the basal oxidation rate of fat was increased in patients with liver cirrhosis and therefore, the RQ was significantly lower in patients with liver cirrhosis than in healthy volunteers. In our present study, the median value of RQ was 0.83 and there were no significant differences in RQ among Child-Pugh grade A, B, and C. However, the range of RQ tended to be highest in Child-Pugh grade A and lowest in grade C, although there were not statistically significant.

Tajika et al.[3] reported that an RQ of 0.85 was the point at which substrate for thermogenesis turned from carbohydrate dominant (RQ>0.85) to fat dominant (RQ<0.85), and the survival rate was significantly lower in patients with liver cirrhosis with a low RQ (<0.85) than in patients with RQ scores above 0.85. Therefore, we conducted a comparison of clinical features between patients who had an RQ less than 0.85 and patients who had an RQ of 0.85 or more. As a result, Child-Pugh grade and %REE were similar in patients who had an RQ less than 0.85 and patients who had an RQ of 0.85 or more.

It is not surprising that there was a significant difference in serum TC but not TG among patients who were categorized as Child-Pugh grade A, B, and C. However, serum TG was significantly lower in patients who had an RQ less than 0.85 than in patients who had an RQ of 0.85 or more, and FFA tended to be higher in patients who had an RQ less than 0.85 than in patients who had an RQ of 0.85 or more. These results may suggest that serum TG concentration reflects the status of fat metabolism but not liver function, and also, that the increase in FFA in liver cirrhosis might be due to enhanced lipolysis. Plasma FFA oxidation rate has been reported to increase in cirrhosis. This can suppress the syntheses of TG and very low density lipoprotein (VLDL) in liver, and therefore, decreases serum concentration of TG-rich lipoproteins such as VLDL.[23]

Albumin synthesis appears to parallel liver function and skeletal muscle protein synthesis is diminished in liver cirrhosis.[9] Normal protein nutrition state can be defined as serum ALB concentrations above 3.5 g/dL.[3] In the present study, 78.3% of patients were in a state of protein and/or energy malnutrition: 17.4% had protein malnutrition alone (RQ of 0.85 or more and serum ALB of less than 3.5 g/dL), 13.0% had energy malnutrition alone (RQ of less than 0.85 and serum ALB of 3.5 g/dL or more), and 47.8% had PEM (RQ of less than 0.85 and serum ALB of less than 3.5 g/dL). Our data were in line with the previously reported results of Tajika et al.[3] that 87% of patients with liver cirrhosis were in a state of either protein or energy malnutrition. Moreover, PEM was more frequently observed at advanced stages of liver cirrhosis such as Child-Pugh grade B (57.1%) and grade C (62.5%) than grade A (25.0%) in our patients, as previously described.[6,8]

In conclusion, our results revealed that %REE and RQ were not associated with liver function, but the distribution of RQ tended to be highest in Child-Pugh grade A and lowest in grade C, suggesting that the oxidation rate of fat was increased in advanced liver cirrhosis. Overall, 78.3% of patients were in a state of protein and/or energy malnutrition. In our patients, 43.5% (10 out of 23 patients) received oral BCAA treatment, particularly patients with Child-Pugh grade C or an RQ less than 0.85. Oral supplementation with BCAA is reported to be effective not only in treating hepatic encephalopathy but also in improving protein malnutrition.[1,24] Because the PEM state in liver cirrhosis leads to a poor prognosis, adequate nutritional support is very important.[2] A longitudinal study in a large population is needed to determine the efficacy of %REE and RQ measurements by indirect calorimetry for adequate nutritional treatment and improvement of patient outcome.

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