Original Article

Nutrition status and small intestinal bacterial overgrowth in patients with virus - related cirrhosis

Jia Yao MD[1,2], Le Chang MD[2], Lili Yuan MD[2], Zhongping Duan MD[1]

[1]*Artificial Liver Center, Beijing YouAn Hospital, Capital Medical University, Beijing, China*
[2]*Department of Gastroenterology and Hepatology, Shanxi Dayi Hospital, Taiyuan, China*

Malnutrition and small intestinal bacterial overgrowth (SIBO) is frequently present in patients with liver cirrhosis (LC). However, the direct relationship between SIBO and nutrition status in the LC patients has not been elucidated. The aim of this study was to investigate whether there was an association between nutrition status, evaluated by the subjective global assessment (SGA) and SIBO in patients with Hepatitis B virus (HBV) or hepatitis C virus (HCV) related cirrhosis. A total of 120 patients with HBV or HCV-related cirrhosis and 30 healthy controls were included. Nutritional status was determined according to SGA and anthropometry. All patients and healthy controls underwent a glucose hydrogen breath test for SIBO. The prevalence of malnutrition for the patients with HBV or HCV related cirrhosis ranged 19.4%-60% in China. The highest prevalence of malnutrition was detected by SGA, the lowest by triceps skinfold thickness. The frequency of SIBO was significantly higher in the malnourished (SGA-B/C) than in the well-nourished (SGA-A) patients with HBV or HCV related cirrhosis [41/72 (56.9%) vs 12/48 (25.0%) (p=0.001)]. Univariate analysis showed that SIBO, ascites, and Child–Turcotte–Pugh (CTP) class were associated with malnutrition. Multivariate analysis demonstrated that SIBO [odds ratio (OR) 8.10; p=0.002] and ascites (OR 4.56; p=0.022) were independently associated with the occurrence of malnutrition (SGA-B/C) in the same subjects. SIBO is independently related to the occurrence of malnutrition (SGA-B/C) in patients with HBV or HCV cirrhosis. We deduce that SIBO may play an important role in nutrition status in patients with HBV or HCV cirrhosis.

Key Words: nutritional status, small intestinal bacterial overgrowth, hepatitis B, hepatitis C, liver cirrhosis

INTRODUCTION

Malnutrition is a well-known complication in patients with liver cirrhosis (LC), and its presence has important prognostic implications because it is an independent predictor of mortality and is associated with decompensation, complications (ascites, spontaneous bacterial peritonitis, encephalopathy, hepatorenal syndrome) and a poor quality of life.[1] Malnutrition occurs in at least 20% and up to 80% of patients with LC.[2] Its prevalence varies widely depending on which definition of malnutrition is used, which tools are employed to perform the nutritional assessment, and the residual function of the liver, being more common in decompensated cirrhosis.[3] Although there is no gold standard for the assessment of nutritional status in patients with cirrhosis, and it is not practical to attempt detailed nutritional assessment in all patients, several approaches have been investigated with varying degrees of success.[4] The European Society of Clinical Nutrition and Metabolism (ESPEN) 2009 guidelines recommend the use of subjective global assessment (SGA) or anthropometric parameters to evaluate nutritional status and detect the presence of malnutrition.[5]

Small intestinal bacterial overgrowth (SIBO) is a very heterogeneous syndrome characterized by an increased number and/or abnormal type of bacteria in the small bowel.[6] SIBO is frequently found in patients with LC due to various causes, in whom it appears to be related to complications of the disease such as encephalopathy and infections (mainly spontaneous bacterial peritonitis).[7,8] Impaired small bowel motility and intestinal transit time, altered stomach acidity or bile acid composition and alcohol intake are considered to be related to SIBO in cirrhosis.[9]

A variety of mechanisms are considered to contribute to malnutrition in cirrhosis: poor nutrient intake, hypermetabolic state and inadequate synthesis or absorption of micro and macronutrients.[10] Many of these are not fully understood. SIBO is a well recognized cause of maldigestion and malabsorption.[11] Several data suggested that SIBO could play a role in nutritional status of patients. In diabetes mellitus (both types I and II), an increased prevalence of SIBO is also linked to delayed transit[12,13] and appears to result in impaired nutritional status.[12] Marianna Signoretti et al[14] reported that SIBO might affect nutritional status in patients with chronic pancreatitis. Additionally, Klaus J et al[15] reported that SIBO may result in

Corresponding Author: Prof Zhongping Duan, Artificial Liver Center, Beijing YouAn Hospital, Capital Medical University, Beijing, 100069 China.
Tel: 086-010-63291007; Fax: 86-010-63295285
Email: duan2517@163.com
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weight loss in patients with Crohn's Disease. Thus, we deduce that SIBO may play an important role in malnourished patients with cirrhosis.

Hepatitis B virus (HBV) infection, hepatitis C virus (HCV) infection, and alcohol consumption are considered to be the major global etiologies of LC.[16] Probably the most extensive studies of nutritional status in patients with liver disease are in patients with alcoholic liver disease.[17] However, the major cause of liver cirrhosis in China is the hepatitis virus infection, [18] few dates about the nutritional status in patients with virus related cirrhosis in China. Therefore, in this study, we preliminary evaluated the nutrition status in Chinese patients with HBV or HCV related cirrhosis. Additional, association of SIBO with the progression of LC has been reported, and that of malnutrition with LC progression has been reported as well. However, direct relationship between SIBO and malnutrition in the LC patients has not been elucidated. We also investigated whether there was an association between nutrition status, evaluated by the SGA and anthropometry, and SIBO in patients with HBV or HCV related cirrhosis.

MATERIALS AND METHODS

Patients

This study involved 30 healthy volunteers and 156 consecutive patients with HBV or HCV related LC. Among them, 120 patients were included and 36 patients were excluded as they fulfilled either one or more of exclusion criteria (Figure 1). Diagnosis of HBV or HCV related cirrhosis was based on clinical, biochemical, and imaging studies, and/or liver histological data.[19] Exclusion criteria included: history of recent (<4 months) alcohol intake; recent (<6 weeks) infection or antibiotic use; recent (<6 weeks) hepatic encephalopathy; recent (<6 weeks) gastrointestinal bleeding; presence of hepatocellular carcinoma.

Ethical considerations

All study participants gave written informed consent, and the Ethics Committee of Shanxi Dayi Hospital approved the study. The study was conducted in compliance with the Declaration of Helsinki.

Nutritional assessment

An initial assessment of nutritional status in all recruited patients was made within 48 h after admission. To avoid possible variation among observers, SGA was performed by trained researchers. Anthropometric data including body weight, height, mid-arm circumference (MAC) and triceps skinfold thickness (TSF) was collected. To minimize operator variability, the averages of 3 consecutive anthropometric measurements were recorded.

Subjective global assessment

SGA is based on history and physical examination and has five components: weight change, dietary intake change, gastrointestinal symptoms, functional capacity, and physical signs of malnutrition (loss of subcutaneous fat, muscle wasting, edema and ascites) (Table 1).[20] After careful assessment, the results were accumulated. If the total number of grade B and C was less than 5, the nutritional status of patients was classified as well nourished. If the total number of grade B was more than 5, the nutritional status of patients was classified as mildly to moderately malnourished. If the total number of grade C was more than 5, the nutritional status of patients was classified as severely malnourished. Therefore, based on the results of SGA, patients were assigned to one of the three categories: A (well nourished), B (mildly to moderately malnourished), or C (severely malnourished).[21]

Anthropometric measurement

Body mass index (BMI) was calculated based on body height and weight. The reference values for malnutrition in patients with cirrhosis are the following: [22] no ascites, BMI $\leq$22 kg/m^2; mild ascites, BMI $\leq$23 kg/m^2; tension ascites, BMI $\leq$25 kg/m^2. MAC and TSF were measured with intertape and adipometer. Mid-arm muscle circum-

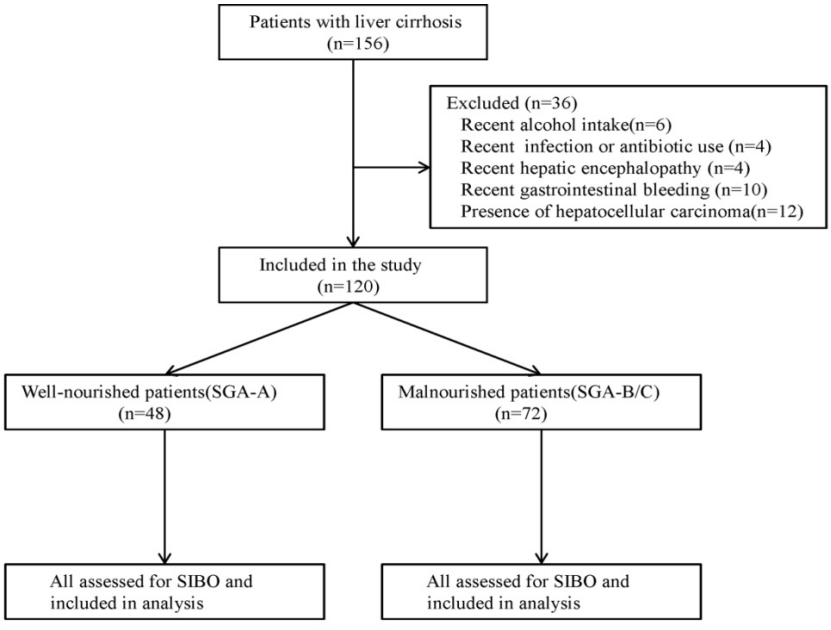

Figure 1. Flow chart of patients in the study

ference (MAMC) was calculated following the formula: MAMC = MAC (mm) –π × TSF (mm). These standards of anthropometric parameters for classifying nutritional status were formulated in accordance with the Chinese Anthropometric Reference Data (Table 2).[23]

Glucose hydrogen breath test (GHBT)

The GHBT was performed according with the criteria suggested by the Rome Consensus Conference.[24] Patients were asked to consume a low-carbohydrate dinner and to avoid milk, dairy products, and bean products on the day before the test. Patients were not permitted to consume food, smoke or do physical exercise within 1 h before the GHBT. In the morning of the test day, patients used a mouthwash with 40 mL 1% chlorhexidine, and defecated. After breath samples were obtained as a baseline, patients ingested 50 g glucose in 250 mL water, and end-expiratory breath samples were collected every 15 min over 2 h and analyzed for breath hydrogen using Gastrolyzer (Bedfont Scientific, Maidstone, Kent, UK). An increase of hydrogen excretion over basal peak of ≥12 parts per million (ppm) was considered as the cutoff value for the test positivity. A value for fasting breath hydrogen >20 ppm, despite adequate preparation, was also recorded as potentially suggesting test positivity.

Statistical analysis

The data were presented as the mean ± standard deviation (SD), median value (range) or number (percentage). In the univariate analysis, depending on the data distribution, differences in continuous variables between two groups were analyzed using the Mann–Whitney test or the independent-samples t-test. Categorical variables were analyzed by Pearson Chi-square test. A two-sided p-value of <0.05 was considered statistically significant. A multivariate logistic regression analysis using the block method was performed on variables reaching a significance of $p \leq 0.10$ on univariate analysis to determine the influence on the presence of malnutrition (SGA-B/C). All statistical analyses were performed using SPSS version 15.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

Patient characteristics

Baseline characteristics of the patients are shown in Table 3. There were 120 patients (57 women and 63 men) with HBV or HCV related cirrhosis (mean age: 55.1 years, age range: 42-70 years). Concerning the etiology of liver disease, 72 (60%) patients had HBV related cirrhosis and 48 (40%) had HCV related cirrhosis. According to the Child–Turcotte–Pugh (CTP) classification, 61 (50.8%) patients were Class A, 43 (35.8%) patients were Class B and 16 (13.4%) patients were Class C.

Nutrition status in patients with HBV or HCV related cirrhosis according to different nutrition assessment methods

The prevalence of malnutrition varied widely according

Table 1. Parameters and diagnostic criteria for SGA

Parameters	Grade A	Grade B	Grade C
Food intake	No deficiency	Definite decrease in intake or liquid diet	Severe deficiency in intake or starvation
Weight loss (during the past 6 mo)	No weight loss or weight loss >10% during the past 6 mo but weight gain over the past month	Continuous weight loss of 5%-10%	Continuous weight loss >10%
Gastrointestinal symptoms (nausea, vomit, diarrhea)	None	Mild or moderate GI symptoms for less than 2 week	Continuous severe GI symptoms for more than 2 week
Activities and function	No limitation	Not normal, but able to do fairly normal activities or do not know most things, but in bed or chair for less than half a day	Able to do little activity and spend most of the day in bed or chair; or much bedridden, rarely out of bed
Metabolic stress	No fever	Temperature >37°C and <39°C during the past 72 h	Continuous temperature ≥39°C during the past 72 h
Subcutaneous fat loss	No	Mild to moderate	Severe
Muscle wasting	No	Mild to moderate	Severe
Ankle edema/Ascites	No	Mild to moderate	Severe

SGA: subjective global assessment; GI: Gastrointestinal

Table 2. Classification standards for nutritional parameters in assessing malnutrition

Nutritional parameter	Normal nutrition	Mildly malnourished	Moderately malnourished	Severely malnourished
TSF (mm)				
Men	>10.2	9.04-10.2	6.78-9.03	<6.78
Women	>13.4	11.9-13.4	8.94-11.9	<8.94
MAMC (cm)				
Men	>20.5	18.2-20.5	13.7-18.2	<13.7
Women	>18.8	16.7-18.8	12.5-16.7	<12.5

TSF: triceps skinfold thickness; MAMC: mid-upper arm muscle circumference.

Table 3. Clinical characteristics and univariate analysis of different parameters in well-nourished and malnourished patients with cirrhosis according to SGA

Parameter	All patients	Well-nourished (SGA-A)	Malnourished (SGA-B/C)	*p* value
No. of patients	120	48	72	-
Age (year)	55.1±5.6	52.8±4.9	57.3±4.7	0.073
Women (n, %)	57 (47.5)	21 (43.8)	36 (50.0)	0.502
BMI (kg/ m^2)*	19.5±4.2	20.7±2.3	18.3±3.5	0.002
Etiology (n, %)				0.11
HBV	72 (60)	33 (68.8)	39 (54.2)	
HCV	48 (40)	15 (31.2)	33 (45.8)	
ALT (IU/L)	28.7±5.5	27.2±5.4	30.2±5.7	0.417
AST (IU/L)	32.3±12.9	30.4±6.1	34.8±19.8	0.654
ALB (g/L)*	30.3±6.1	35.7±2.8	24.8±1.8	<0.001
Total bilirubin (μmol/L)	19.5±7.3	18.3±4.3	20.2±5.3	0.432
PT (s)	12.9±4.1	12.5±3.8	13.1±1.8	0.302
INR	1.28±0.21	1.23±0.29	1.32±0.1	0.572
Urea (mmol/L)	5.61±1.4	4.88±1.62	6.35±0.71	0.146
Creatinine (μmol/L)	72.4±20.9	67.1±16.3	77.8±26.3	0.511
Presence of ascites (n, %)*	57 (47.5)	12 (25)	45 (62.5)	<0.001
Presence of SIBO (n, %)*	53 (44.2)	12 (25)	41 (56.9)	0.001
Past history of SBP (n, %)	2 (1.7)	0 (-)	2 (2.8)	0.662
Past history of HE (n, %))	2 (1.7)	0 (-)	2 (2.8)	0.662
Past histories of gastrointestinal bleeding (n, %)	25 (20.8)	9 (18.8)	16 (22.2)	0.646
CTP class (n, %)*				0.005
A	61 (50.8)	32 (66.7)	29 (40.3)	
B/C	59 (49.2)	16 (33.3)	43 (59.7)	

Reference ranges are: ALT: alanine aminotransferase (9-50 IU/L); AST: aspartate aminotransferase (15-40 IU/L); ALB: albumin (35-50 g/L); Total bilirubin (5-21 μmol/L); PT: prothrombin time (11-13 s); INR: International Normalized Ratio (0.9-1.2); Urea (2.9-7.1 mmol/L); Creatinine (58-96 μmol/L). BMI: body mass index; SBP: spontaneous bacterial peritonitis; CTP: Child-Turcotte-Pugh; HE: hepatic encephalopathy. *$p<0.05$.

to results obtained by different nutrition assessment methods (Table 4). According to SGA, of the 120 LC patients were assessed, 48 (40.0%) were considered well nourished (SGA-A), 58 (48.3%) moderately malnourished (SGA-B), and 14 (11.7%) severely malnourished (SGA-C). The prevalence of malnutrition (SGA-B/C) in patients with CTP class A was 40.3% (29/72), with CTP class B/C was 59.7% (43/72) (p=0.005) (Table 3).

Prevalence of SIBO in patients with HBV or HCV related cirrhosis and healthy controls according to GHBT

The GHBT positivity rate, defined as a peak over basal of hydrogen excretion ≥12 ppm, was higher in patients with HBV or HCV related cirrhosis than in healthy controls [(44/120 (36.7%) vs 2/30 (6.67%) (p=0.001)]. Taking into account values for basal breath hydrogen >20 ppm as a positive GHBT, this was not significant difference between the two groups (p=0.264). The overall positivity rate calculated, taking into account fasting values, reached 44.2% (53/120) in patients versus 6.67% (2/30) in healthy controls (p<0.001) (Table 5).

The frequency of SIBO was significantly higher in the malnourished (SGA-B/C) than in the well-nourished (SGA-A) patients with HBV or HCV related cirrhosis [41/72 (56.9%) vs 12/48 (25%) (p=0.001)]. The prevalence of SIBO in patients with SGA-A was 12/48 (25.0%), with SGA-B was 51.7% (30/58) and SGA-C was 78.6% (11/14) in SGA-C (p<0.001) (Figure 2).

When stratifying the data by CTP classification, in CTP-A group, no major difference on SIBO positivity rate was observed in patients with SGA-A and SGA-B/C (p=0.91). However, in CTP-B and CTP-C groups, a significant increase in rates of SIBO positivity were observed in malnourished patients (SGA-B/C) (p<0.05) (Figure 3A, 3B, 3C).

Table 4. Nutrition assessment according to SGA and anthropometry

Method	Median value (range)	Prevalence of malnutrition No. (%)
SGA	-	60
BMI	23 (15-30)	25.3
TSF (mm)	11 (6-30)	19.4
MAMC (cm)	22 (11-32)	40

SGA: subjective global assessment; BMI: body mass index; TSF: triceps skinfold thickness; MAMC: mid-upper arm muscle circumference.

Factors affecting the presence of malnutrition (SGA-B/C)

In univariate analysis, patients with malnutrition (SGA-B/C) were more likely to have ascites (p<0.001) and higher frequency of SIBO (p=0.001) than those who were well nourished (SGA-A). Those with malnutrition (SGA-B/C) were more likely to have CTP Class B and C (p=0.005), lower BMI (p=0.002), and lower albumin level (p<0.001), but there were no significant differences between the groups with respect to any of the remaining clinical parameters measured (p>0.05 in each case) (Table 3).

Multivariate logistic regression modeling was performed with adjustments for age, ascites, CTP class and

Table 5. Frequency of SIBO evaluated with HOB and/or values of H_2 basal

	Patients with cirrhosis (n=120)	Healthy controls (n=30)	*p* value
Age	55.1±5.6	56.3±7.9	0.063
Women (n, %)	57 (47.5)	15 (50)	0.806
Hydrogen ≥12 ppm (n, %)	44 (36.7)	2 (6.67)	0.001
H_2 basal >20 ppm (n, %)	9 (7.5)	0 (0)	0.264
HOB ≥12 ppm or H_2 basal >20 ppm (n, %)	53 (44.2)	2 (6.67)	<0.001

HOB: H_2 peak over basal excretion; H_2 basal: basal breath hydrogen

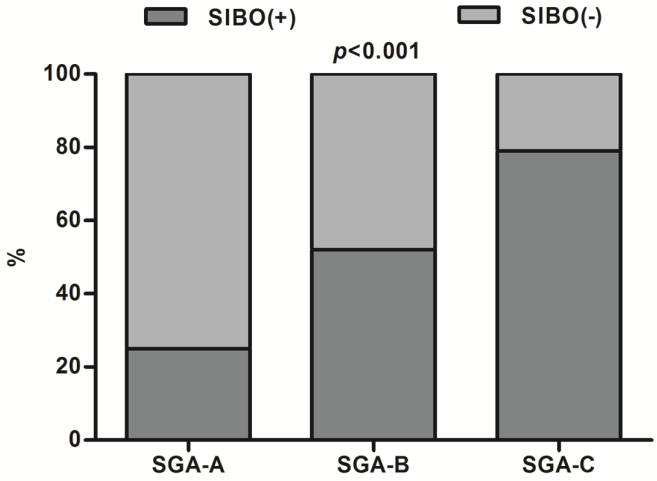

Figure 2. Frequency of SIBO in SGA Class A, B and C

SIBO. Albumin was not included because it was diagnostic parameters for malnutrition. SIBO and ascites were found to be the independent relevant factors for malnutrition according to SGA (Table 6).

DISCUSSION

Poor nutritional status and SIBO have been shown in various patient groups with hepatic disorders, and particularly in patients with alcoholic cirrhosis. To our knowledge, no study has evaluated the direct relationship between nutrition status and SIBO in HBV or HCV related cirrhosis. The present study revealed the prevalence of malnutrition for the patients with HBV or HCV related cirrhosis ranged 19.4%-60% in China. The highest prevalence of malnutrition was detected by SGA, the lowest by TSF. Meanwhile, the results of this study confirm the higher prevalence rate of SIBO in malnourished (SGA-B/C) compared to well-nourished (SGA-A) patients with HBV or HCV related cirrhosis. Moreover, multivariate analysis showed that SIBO was independently related to the occurrence of malnutrition (SGA-B/C) in the same group of subjects.

In the present study, malnutrition was found in 19.4% by TSF, in 40% by MAMC, in 25.3% by BMI and in 60% by SGA. In the literature, Liboredo JC et al[25] reported that malnutrition was present in 66.7% of the LC patients due to any cause according to SGA**.** Vieira PM et al[26] reported that malnutrition was diagnosed in 61.5% (SGA), 16.7% (BMI), 93.6% (TSF), 62.8% (MAC) and 38.5% (MAMC) of the LC patients due to any cause. Compared to the previous studies, the prevalence of malnutrition was slightly lower in our study. We speculate that this difference is due to the number of assessed patients and etiology of disease. Some studies have shown that alcoholic cirrhosis was associated with a poorer nutritional state compared with virus-associated cirrhosis.[27] However, evidence concerning the impact of etiology (of cirrhosis) on malnutrition is conflicting. Other studies have shown no difference in prevalence and severity of malnutrition in patients with viral and alcohol related cirrhosis who were abstinent.[28,29] Kawabe N et al[30] showed in patients with LC due to HCV, the prevalence of malnutrition was found in 11 (12.8%) patients by TSF, 15 (17.4%) by MAMC, 22 (25.6%) by SGA. The prevalence of malnutrition in our study was higher. We speculate that this difference is due to the patient populations studied, which included more patients with Child B/C in our study.

Similar to previous studies that SIBO was more prevalent in alcoholic cirrhosis compared to controls,[31,32] in the current study, the GHBT positivity rate also significantly increased in patients with HBV or HCV related cirrhosis compared with healthy volunteers. In previous studies, the rate of SIBO in populations of LC patients was highly variable, ranging from 17% to 60% using either GHBT or jejunal aspirate culture.[33] Using the same diagnosis standard and test methods, Pande et al showed SIBO was present in 49% of patients with cirrhosis due to any cause.[34] Our study showed the positivity rate of SIBO (44.2%) in our study was lower. We speculate that this difference is due to only including patients with virus related cirrhosis in our study. It is known that alcohol consumption was a strong risk factor for SIBO.[35]

Furthermore, we found that the frequency of SIBO was higher in malnourished (SGA-B/C) than in well-nourished (SGA-A) LC patients. Moreover, we found that SIBO was more prevalent in patients with SGA-C than

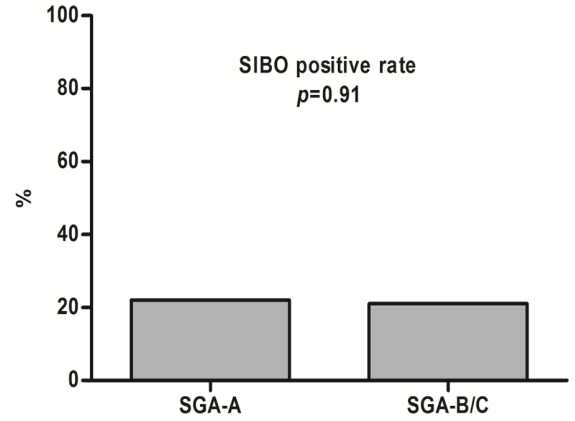

Figure 3A. Difference frequency of SIBO between SGA-A and SGA-B/C in CTP-A group

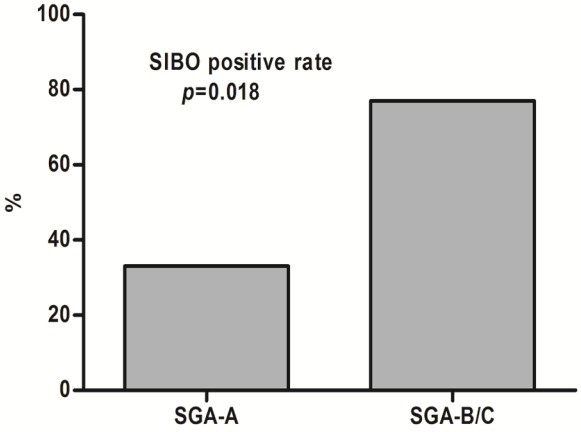

Figure 3B. Difference frequency of SIBO between SGA-A and SGA-B/C in CTP-B group

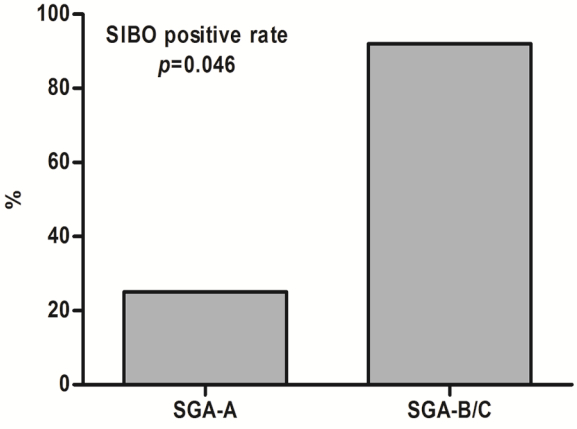

Figure 3C. Difference frequency of SIBO between SGA-A and SGA-B/C in CTP-C group

SGA-B cirrhosis. Its frequency increased with increase in severity of malnutrition. The explanation for the phenomenon is that SIBO induces inflammatory changes in the bowel mucosal membrane, and the bacteria might interfere with the enzymatic, absorptive and metabolic actions of the body.[15] Thus, excess of bacteria can lead both to increased consumption of carbohydrates and of some fat-soluble vitamins and proteins, and to the bacterial deconjugation of bile salts and to a decreased absorption of micronutrients.[36] Meantime, SIBO itself is associated with gastrointestinal symptoms including abdominal distension, increased flatus, abdominal pain, and diarrhea.[6]

In previous studies, malnutrition was more prevalent in patients with CTP Class B and C than Class A cirrhosis.[37] In our study, our result was similar to the previous studies. In order to eliminate the influence of the severity of disease, we stratified the data by CTP classification, in CTP-A group, no major difference on SIBO positivity rate was observed in patients with SGA-A and SGA-B/C. However, in CTP-B and CTP-C groups, a significant increase in rates of SIBO positivity ($p<0.05$) was observed in malnourished patients (SGA-B/C) respectively. For further identifying the relationship between SIBO and malnutrition (SGA-B/C), the adjusted OR for SIBO and ascites reached 8.10 and 4.56, respectively, after adjusting for other factors. Therefore, we considered SIBO and ascites in LC patients were independently associated with the presence of malnutrition (SGA-B/C). As a cross-sectional study in which a convenient sample was analyzed, we cannot determine the causality from our results. However, SIBO may aggravate malnutrition through reducing the availability of nutrients. Thus, it seems reasonable to speculate that SIBO plays an important role on nutrition status in LC patients. We believe that this information could help with prevention of the progression of malnutrition by targeting therapy against bacterial overgrowth in malnourished patients with LC.

There were some limitations to our study. First, we did not use jejunal fluid cultures for making a diagnosis of SIBO, which is considered the gold standard. However, GHBT has remained the most frequent noninvasive test for diagnosis of SIBO. Second, accurate assessments of nutritional status are not easily obtained in patients with cirrhosis. SGA uses clinical information obtained during history taking and examination to determine nutritional status without objective measurements in patients with cirrhosis. However, SGA is still a strong and easy-to-perform predictor of malnutrition in patients with cirrhosis. Third, as a cross-sectional study in which a convenient sample was analyzed, we cannot clearly determine the causality from our results.

In conclusion, our study showed that SIBO was signifi-

Table 6. Adjusted odds ratios of effects of ascites, SIBO, and CTP class on malnutrition (SGA-B/C)

Variable	aOR	95% CI	*p* value
Age	1.54	0.35-6.28	0.435
SIBO (absent versus present)	8.10	2.15-30.5	0.002
Ascites (absent versus present)	4.56	1.25-16.7	0.022
CTP class (A versus B/C)	1.63	0.47- 5.69	0.444

aOR: adjusted odds ratio; SIBO: small intestine bacterial overgrowth; CTP: Child-Turcotte-Pugh.

cantly higher in malnourished (SGA-B/C) compared with well-nourished (SGA) patients with HBV or HCV cirrhosis. Moreover, SIBO was found to independently relate to malnutrition (SGA-B/C) in the same group of subjects. Further prospective studies are needed to document improvement of nutritional status by targeting therapy against bacterial overgrowth in patients with liver cirrhosis.

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AUTHOR DISCLOSURES

The authors declare no conflicts of interest.

REFERENCES

1. Moctezuma-Velazquez C, Garcia-Juarez I, Soto-Solis R, Hernandez-Cortes J, Torre A. Nutritional assessment and treatment of patients with liver cirrhosis. Nutrition. 2013;29: 1279-85. doi: 10.1016/j.nut.2013.03.017.
2. Cheung K, Lee SS, Raman M. Prevalence and mechanisms of malnutrition in patients with advanced liver disease, and nutrition management strategies. Clin Gastroenterol Hepatol. 2012;10:117-25. doi: 10.1016/j.cgh.2011.08.016.
3. Periyalwar P, Dasarathy S. Malnutrition in cirrhosis: contribution and consequences of sarcopenia on metabolic and clinical responses. Clin Liver Dis. 2012;16:95-131. doi: 10.1016/j.cld.2011.12.009.
4. Juakiem W, Torres DM, Harrison SA. Nutrition in cirrhosis and chronic liver disease. Clin Liver Dis. 2014;18:179-90. doi: 10.1016/j.cld.2013.09.004.
5. Plauth M, Cabre E, Campillo B, Kondrup J, Marchesini G, Schutz T et al. ESPEN Guidelines on Parenteral Nutrition: hepatology. Clin Nutr. 2009;28:436-44. doi: 10.1016/j.clnu. 2009.04.019.
6. Bures J, Cyrany J, Kohoutova D, Forstl M, Rejchrt S, Kvetina J et al. Small intestinal bacterial overgrowth syndrome. World J Gastroenterol. 2010;16:2978-90. doi: 10.3748/wjg.v16.i24.2978.
7. Gupta A, Dhiman RK, Kumari S, Rana S, Agarwal R, Duseja A et al. Role of small intestinal bacterial overgrowth and delayed gastrointestinal transit time in cirrhotic patients with minimal hepatic encephalopathy. J Hepatol. 2010;53: 849-55. doi: 10.1016/j.jhep.2010.05.017.
8. Bauer TM, Steinbruckner B, Brinkmann FE, Ditzen AK, Schwacha H, Aponte JJ et al. Small intestinal bacterial overgrowth in patients with cirrhosis: prevalence and relation with spontaneous bacterial peritonitis. Am J Gastroenterol. 2001;96:2962-7. doi: 10.1111/j.1572-0241. 2001.04668.x.
9. Wiest R, Lawson M, Geuking M. Pathological bacterial translocation in liver cirrhosis. J Hepatol. 2014;60:197-209. doi: 10.1016/j.jhep.2013.07.044.
10. Tsiaousi ET, Hatzitolios AI, Trygonis SK, Savopoulos CG. Malnutrition in end stage liver disease: recommendations and nutritional support. J Gastroenterol Hepatol. 2008;23: 527-33. doi: 10.1111/ j.1440-1746.2008.05369.x.
11. Quigley EM. Small intestinal bacterial overgrowth: what it is and what it is not. Curr Opin Gastroenterol. 2014;30:141-6. doi: 10.1097/mog.0000000000000040.
12. Faria M, Pavin EJ, Parisi MC, Lorena SL, Brunetto SQ, Ramos CD et al. Delayed small intestinal transit in patients with long-standing type 1 diabetes mellitus: investigation of the relationships with clinical features, gastric emptying, psychological distress, and nutritional parameters. Diabetes Technol Ther. 2013;15:32-8. doi: 10.1089/dia.2012.0158.
13. Rana S, Bhansali A, Bhadada S, Sharma S, Kaur J, Singh K. Orocecal transit time and small intestinal bacterial overgrowth in type 2 diabetes patients from North India. Diabetes Technol Ther. 2011;13:1115-20. doi: 10.1089/dia. 2011.0078.
14. Signoretti M, Stigliano S, Valente R, Piciucchi M, Delle Fave G, Capurso G. Small intestinal bacterial overgrowth in patients with chronic pancreatitis. J Clin Gastroenterol. 2014; 48(Suppl 1):S52-5. doi: 10.1097/mcg.0000000000000238.
15. Klaus J, Spaniol U, Adler G, Mason RA, Reinshagen M, von Tirpitz CC. Small intestinal bacterial overgrowth mimicking acute flare as a pitfall in patients with Crohn's Disease. BMC Gastroenterol. 2009;9:61. doi: 10.1186/1471-230x-9-61.
16. Schuppan D, Afdhal NH. Liver cirrhosis. Lancet. 2008;371: 838-51. doi: 10.1016/s0140-6736 (08)60383-9.
17. McClain CJ, Barve SS, Barve A, Marsano L. Alcoholic liver disease and malnutrition. Alcohol Clin Exp Res. 2011;35: 815-20. doi: 10.1111/j.1530-0277.2010.01405.x.
18. Wang X, Lin SX, Tao J, Wei XQ, Liu YT, Chen YM et al. Study of liver cirrhosis over ten consecutive years in Southern China. World J Gastroenterol. 2014;20:13546-55. doi: 10.3748/wjg.v20.i37.13546.
19. Haozhu Chen. Practice of internal medicine. Beijing: People's Medical Publishing House; 2005. (In Chinese)
20. Detsky AS, McLaughlin JR, Baker JP, Johnston N, Whittaker S, Mendelson RA et al. What is subjective global assessment of nutritional status? JPEN J Parenter Enteral Nutr. 1987;11:8-13. doi: 10.1177/014860718701100108.
21. Wu BW, Yin T, Cao WX, Gu ZD, Wang XJ, Yan M et al. Clinical application of subjective global assessment in Chinese patients with gastrointestinal cancer. World J Gastroenterol. 2009;15:3542-9. doi: 10.3748/wjg.15.3542.
22. Campillo B, Richardet JP, Bories PN. Validation of body mass index for the diagnosis of malnutrition in patients with liver cirrhosis. Gastroenterol Clin Biol. 2006;30:1137-43. doi: 10.1016/S0399-8320 (06)73491-1.
23. Cao WX. The new concept and new technical in clinical nutrition. Beijing: People's Military Medical Press; 2002. (In Chinese).
24. Gasbarrini A, Corazza GR, Gasbarrini G, Montalto M, Di Stefano M, Basilisco G et al. Methodology and indications of H2-breath testing in gastrointestinal diseases: the Rome Consensus Conference. Aliment Pharmacol Ther. 2009;29 (Suppl 1):1-49. doi: 10.1111/j.1365-2036.2009.03951.x.
25. Liboredo JC, Vilela EG, Ferrari Mde L, Lima AS, Correia MI. Nutrition status and intestinal permeability in patients eligible for liver transplantation. JPEN J Parenter Enteral Nutr. 2015;39:163-70. doi: 10.1177/0148607113513465.
26. Vieira PM, De-Souza DA, Oliveira LC. Nutritional assessment in hepatic cirrhosis; clinical, anthropometric, biochemical and hematological parameters. Nutr Hosp. 2013; 28:1615-21. doi: 10.3305/nh.2013.28.5.6563.
27. Caly WR, Strauss E, Carrilho FJ, Laudanna AA. Different degrees of malnutrition and immunological alterations according to the aetiology of cirrhosis: a prospective and sequential study. Nutr J. 2003;2:10. doi: 10.1186/1475-28 91-2-10.
28. Caregaro L, Alberino F, Amodio P, Merkel C, Bolognesi M, Angeli P et al. Malnutrition in alcoholic and virus-related cirrhosis. Am J Clin Nutr. 1996;63:602-9.
29. Thuluvath PJ, Triger DR. Evaluation of nutritional status by using anthropometry in adults with alcoholic and nonalcoholic liver disease. Am J Clin Nutr. 1994;60:269-73.

30. Kawabe N, Hashimoto S, Harata M, Nitta Y, Murao M, Nakano T et al. Assessment of nutritional status of patients with hepatitis C virus-related liver cirrhosis. Hepatol Res. 2008;38:484-90. doi: 10.1111/j.1872-034X.2007.00300.x.
31. Casafont Morencos F, de las Heras Castano G, Martin Ramos L, Lopez Arias MJ, Ledesma F, Pons Romero F. Small bowel bacterial overgrowth in patients with alcoholic cirrhosis. Dig Dis Sci. 1996;41:552-6. doi: 10.1007/BF02282340.
32. Morencos FC, de las Heras Castano G, Martin Ramos L, Lopez Arias MJ, Ledesma F, Pons Romero F. Small bowel bacterial overgrowth in patients with alcoholic cirrhosis. Dig Dis Sci. 1995;40:1252-6. doi: 10.1007/BF02065533.
33. Lakshmi CP, Ghoshal UC, Kumar S, Goel A, Misra A, Mohindra S et al. Frequency and factors associated with small intestinal bacterial overgrowth in patients with cirrhosis of the liver and extra hepatic portal venous obstruction. Dig Dis Sci. 2010;55:1142-8. doi: 10.1007/s10620-009-0826-0.
34. Pande C, Kumar A, Sarin SK. Small-intestinal bacterial overgrowth in cirrhosis is related to the severity of liver disease. Aliment Pharmacol Ther. 2009;29:1273-81. doi: 10.1111/j.1365-2036.2009.03994.x.
35. Gabbard SL, Lacy BE, Levine GM, Crowell MD. The impact of alcohol consumption and cholecystectomy on small intestinal bacterial overgrowth. Dig Dis Sci. 2014;59:638-44. doi: 10.1007/s10620-013-2960-y.
36. Gubergrits NB, Linevskiy YV, Lukashevich GM, Fomenko PG, Moroz TV, Mishra T. Morphological and functional alterations of small intestine in chronic pancreatitis. JOP. 2012;13:519-28. doi: 10.6092/1590-8577/656.
37. Naqvi IH, Mahmood K, Salekeen S, Akhter ST. Determining the frequency and severity of malnutrition and correlating it with the severity of liver cirrhosis. Turk J Gastroenterol. 2013;24:415-22.

Original Article

Nutrition status and small intestinal bacterial overgrowth in patients with virus - related cirrhosis

Jia Yao MD[1,2], Le Chang MD[2], Lili Yuan MD[2], Zhongping Duan MD[1]

[1]*Artificial Liver Center, Beijing YouAn Hospital, Capital Medical University, Beijing, China*
[2]*Department of Gastroenterology and Hepatology, Shanxi Dayi Hospital, Taiyuan, China*

病毒相关肝硬化患者营养状态和小肠细菌过度生长关系的研究

肝硬化患者常常合并营养不良和小肠细菌过度生长（SIBO），但是，营养状态和SIBO是否直接相关并未阐明。因此，本研究旨在探讨乙型肝炎（HBV）或丙型肝炎（HCV）相关的肝硬化患者的营养状态和SIBO的关系。本研究入组HBV或者HCV相关的肝硬化患者120名，健康对照30名。根据主观全面营养评估法（SGA）和人体测量学评价入组肝硬化患者的营养状态。所有入组患者及健康对照组均进行氢呼气检测。HBV或者HCV相关的肝硬化患者在中国的营养不良患病率率为19.4%~60%。SGA检测法的营养不良检测率最高，三头肌皮褶厚度检测法的营养不良检测率最低。在营养不良（SGA-B/C）的肝硬化患者中的SIBO的发生率明显高于营养良好（SGA-A）患者[41/72 (56.9%) vs 12/48 (25.0%) (p=0.001)]。单因素分析显示：SIBO、腹水和Child–Turcotte–Pugh（CTP）分级与营养不良相关。多因素分析显示：SIBO [OR 8.10，p=0.002]和腹水(OR 4.56，p=0.022)是营养不良的独立危险因素。因此，在HBV或者HCV相关的肝硬化患者中，SIBO与营养不良（SGA-B/C）独立相关。从而，我们认为SIBO对于病毒相关的肝硬化患者的营养状态可能有重要的影响。

关键词：营养状态、小肠细菌过度生长、乙型肝炎、丙型肝炎、肝硬化