

Original Research**Nutritional Status and Nutritional Practice of Cirrhotic Patients at Hanoi Medical University Hospital, 2020**

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ABSTRACT *Background and purpose.* Liver cirrhosis (LC) is one of the leading causes of mortality worldwide. Malnutrition frequently imposes a burden on patients with LC, and it is an independent predictor of lower survival. As a result, it is essential to manage LC patients' nutritional status and dietary intake for better treatment. However, in Vietnam, there are limited data regarding this issue. This study aimed to describe the nutritional status, dietary intake, and nutritional practice of cirrhotic patients at Hanoi Medical University Hospital (HMHU) in 2020. *Method.* A cross-sectional study was conducted among 40 patients who were admitted to the HMHU from December 2019 to April 2020. For nutritional status assessment, body mass index (BMI), subjective global assessment (SGA) questionnaire, and muscle strength by handgrip strength (HS) were measured. The 24-hour dietary recall method, as well as some open questions, were also collected for the nutritional practice assessment. *Results.* The prevalence of malnutrition determined by BMI was 12.5%; however, the rate was remarkably high from SGA with 60% and from HS with 75%. The mean energy and protein consumption per ideal body weight (IBW) were 24.6 ± 12.0 kcal/IBWkg and 1.0 ± 0.5 g/IBWkg, respectively. Moreover, 40% of the patients claimed that they restricted animal protein. The percentage of study's patients who had ≥ 4 meals/day and who ate a late evening snack was only 32.5% and 22.5%, respectively. As for those who took an LES, the average energy, carbohydrate, and protein in this study were only 140kcal, 19g, and 5.1g respectively. *Conclusion.* The prevalence of malnutrition in LC patients determined by SGA and HS was remarkably high. Considering this result, HS rather than BMI is a reliable, non-invasive, and effective tool for malnutrition assessment for cirrhotic patients in Vietnam's clinical settings. Consequently, the mean dietary intakes of LC patients were lower than the recommendation; therefore, nutritional education and a late-evening snack diet need to be provided to LC patients.

Key words: Cirrhosis, nutritional status, dietary intake, nutritional practice.

INTRODUCTION

Liver cirrhosis (LC) is one of the leading causes of mortality worldwide, and it is associated with a significant reduction in disabilities-adjusted life-years. In the report of Global Health Estimates (2016), LC was the 11th most common cause of death each year in the world with 2.1% of total deaths(1). According to Institute for Health Metrics and Evaluation (IHME), in 2019, LC ranked 7th among the top 10 most common causes of death in Vietnam with a 47.3% increment from 2009 to 2019(2). The etiologies of LC are most commonly alcohol, hepatitis B, hepatitis C, and non-alcoholic fatty liver disease or sometimes autoimmune hepatitis. Alcoholic liver disease and hepatitis B are the most common causes in most parts of Asia (3). According to the report of the World Health Organization (WHO) on hepatitis B in Vietnam, it is estimated that the number of cases of hepatitis B-related decompensated cirrhosis was 90,704 in 2017 and is projected to increase 10% by 2030(4). Cirrhosis is defined as the histological development of regenerative nodules surrounded by fibrous bands in response to chronic liver injury, which leads to

portal hypertension and end-stage liver disease. In the asymptomatic phase of the disease, usually referred to as compensated cirrhosis, patients may have a good quality of life, and the disease may progress undetected for several years. The decompensation phase is regularly marked by ascites, gastrointestinal bleeding due to esophageal varices, hepatic encephalopathy (HE), and jaundice (5).

Malnutrition is frequently a burden in patients with LC; it is usually related to the clinical stage of chronic liver disease, increasing from 20% in patients with well-compensated disease to more than 60% in patients with advanced cirrhosis (6). Malnutrition and muscle mass loss (sarcopenia) are associated with a higher rate of complications such as susceptibility to infections, hepatic encephalopathy (HE), and ascites, as well as being independent predictors of lower survival in cirrhosis and in patients undergoing liver transplantation (7). Various mechanisms are considered to contribute to malnutrition in cirrhosis such as poor oral intake, increased intestinal protein loss, decrease protein synthesis, disturbances in substrate utilization,

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hyper-metabolism, and malabsorption(8). Therefore, assessment of nutritional status is essential to increase the number of recovering cases and decrease the mortality rate. It is recommended by the ESPEN guideline that subjective global assessment (SGA) should be used as a “gold standard” for malnutrition assessment in LC patients (6). In addition, handgrip strength (HS) is a reliable, non-invasive, and cost-effective tool to identify malnutrition in cirrhotic patients (9). However, in many of Vietnam’s practical clinics, body index mass (BMI) is still widely used for nutritional assessment though it can be inaccurate due to ascites and/or edema in LC patients. As a consequence, the prevalence of LC patients in Vietnam has not been well-studied.

There has been controversy over the years about the amount of protein intake for LC patients with the old concept restricting the intake in order to limit the synthesis of ammonium and the deamination of protein to aromatic amino acids especially in patients with HE. However, malnourished and sarcopenic cirrhotic patients can experience protein depletion. Increased protein intake is generally well tolerated and safe in cirrhotic patients and ameliorates protein anabolism as shown in previous studies (10, 11). According to ESPEN’s clinical nutrition practice guideline for LC patients in 2019, cirrhotic patients with conditions of increased energy expenditure (i.e. acute complications, refractory ascites) or malnutrition should ingest an increased amount of energy (30-35 kcal/kg/d of energy and 1.2-1.5 g/kg/d of protein (6). Nonetheless, in Vietnam’s clinical setting, a restricted protein-diet is still recommended for LC patients (12).

In addition, several guidelines have recommended short periods of starvation with 4 - 6 meals a day, as well as a 50g carbohydrate and/or 15g protein-containing late evening snack thanks to its benefits to the level of serum albumin, liver enzyme, and nitrogen balance (7, 8, 13, 14). Hence, patients’ practice with regard to food intake is also necessary for the investigation of an adequate supply of food and monitoring food consumption. With Vietnam’s climbing number of new LC cases, it is crucial to evaluate the nutritional status and nutritional practice of these patients; however, there have been relatively limited studies on this issue. For these reasons, we decided to conduct this study to describe the nutritional status, dietary intake, and nutritional practice of cirrhotic patients at Hanoi Medical University Hospital in 2020.

METHODS

Settings and sample. A cross-sectional study was conducted from December 2019 through April 2020 at Hanoi Medical University Hospital (HMHU), a general hospital in Vietnam. All the newly admitted patients (within 0-24 hours) who met the inclusion criteria: (a) diagnosed with cirrhosis of any etiology (alcoholism, hepatitis C, cryptogenic/ NAFLD, autoimmune), (b) age 18 or over, and (c) agreeing to participate in this study were included in this study. The exclusion criteria involved: (a) patients with HE, active gastrointestinal bleeding, acute liver failure, hepatocellular carcinoma, (b) patients with other co-

morbid conditions requiring dietary modification and restrictions for different reasons except for diabetes, hypertension, dyslipidemia, (c) patients with medical conditions that would prevent understanding for food record and/ or providing answers or anthropometric measurements. In the end, 40 patients were enrolled in the study.

Data collection. All the questionnaires were filled out by investigators. The investigators were dietitians who were trained to collect study data. The included information in this study is listed below.

Demographic data. The data were collected from medical records, caregivers, and subjects.

Nutritional status assessment. Bodyweight and height were measured in light clothing and without shoes. Body mass index (BMI) was computed as the ratio of weight (kg) per height squared (m²). A BMI <18.5 kg/m² was considered underweight. 8 patients with ascites and/or edema were excluded from BMI evaluation. Subjective global assessment (SGA) questionnaire was also conducted. Patients with SGA classification A were labeled as well-nourished, and patients with classification B and C were labeled as malnourished (16). Handgrip strength (HS) is a non-invasive, simple, and quick method that has been used for the assessment of nutritional status especially because malnourished patients present with lean mass depletion and low muscle strength. Low handgrip strength is suggested as <26 kg for men and <18kg for women (17).

Nutritional practice. Assessment of individual patients’ oral energy and protein intake was determined by 24 h diet recall one day before their hospitalization. The average intakes of energy and protein were recorded in calories and grams per day and grams per ideal body weight (IBW) per day, respectively. In addition, a 7-day food frequency and some open questions regarding nutritional practice were also collected.

Data analysis. Input data were entered into REDcap software. Stata version 15.0 was used for data analysis. Data were expressed as mean \pm SD, median, interquartile range (IQR). For comparison of categorical variables, chi-square was used, and for continuous variables, Student’s t-test and Wilcoxon sign rank test were used, as appropriate. The probability level of $p < 0.05$ was set for statistical significance.

RESULTS

The total participants of the study were 40 patients, of which 35 (87.5%) were males and 5 (12.5%) were female. Figure 1 shows the prevalence of malnutrition according to BMI was 12.5% (4/32); at the same time, from HS 75% (30/40) of the patients were malnourished, and from SGA 60% (24/40).

The mean energy and protein consumption based on IBW were 24.6 ± 12.0 kcal/IBWkg and 1.0 ± 0.5 g/IBWkg (Table 1), respectively. Furthermore, males’ intake was higher than females’, though only the protein index was statistically significant. Regarding vitamins, dietary vitamin B1 was 1.2 mg/d. As for mineral intake, the mean intake of iron from meals was 9.6 mg/d and the median intake of zinc was 8.0 mg/d.

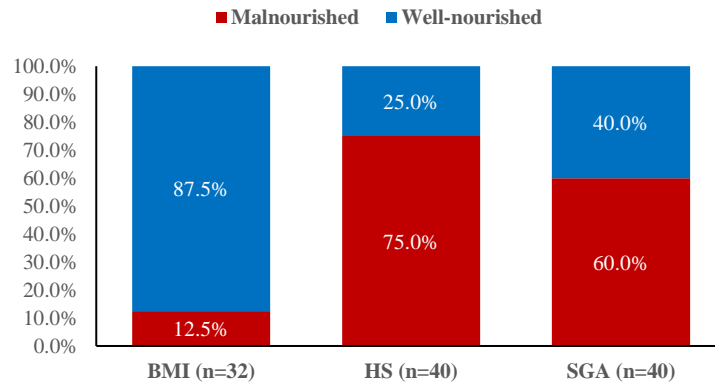


Fig 1. Nutritional status of LC patients by different methods *8 patients with edema and/or ascites were excluded from BMI evaluation

In general, the mean intakes of energy, protein, vitamins, and minerals by malnourished patients and well-nourished patients classified by BMI and HS were not significantly different (Table 2).

Nevertheless, in SGA classification, the mean intakes of energy, protein, carbohydrate, lipid, iron, and zinc by well-nourished patients were significantly higher than by malnourished patients.

Table 1. Dietary intake of LC patients (N = 40)

Dietary intake	Total	ESPEN guidelines2019	Vietnamese recommendation 2016
	Mean \pm SD	Median (IQR)	
Energy (kcal/IBWkg)	24.6 \pm 12.0	25 -35	30 -35
Protein (g/IBWkg)	1.0 \pm 0.5	1.2-1.5	Compensated: 1.0-1.2 Decompensated: 0.8-1.0
Carbohydrate (g/IBWkg)	4.0 \pm 0.3	50-60% of total energy	50-60% of total energy
Lipid (g/IBWkg)	0.45 (0.3; 0.6)	-	15-25% of total energy
Fiber (g/d)	5.6 (2.4; 7.7)	-	20-30
Fe (mg/d)	9.6 \pm 5.7	-	Male: 7.9mg/day Female: 6.7mg/day
Zinc (mg/d)	8.0 (5.3; 11.4)	-	Male: 10.0mg/day Female: 8.0mg/day
Vitamin B1 (mg/d)	1.2 (0.7; 1.6)	-	Male: 1.2mg/day Female: 1.0mg/day

IBW: Ideal body weight; *p<0.05

Table 2. The dietary intake of LC patients as their nutritional status

Dietary intake	BMI (n=32)		HS (n = 40)		SGA (n = 40)	
	Malnourished (n = 4)	Well-nourished (n = 28)	Malnourished (n = 30)	Well-nourished (n = 10)	Malnourished (n = 24)	Well-nourished (n = 16)
	Mean \pm SD; Median (IQR)					
Energy (kcal/IBWkg)	19.0 \pm 7.3	28.4 \pm 2.0	24.2 \pm 1.8	25.9 \pm 5.4	19.4 \pm 2.1	32.4 \pm 2.5*
Protein (g/IBWkg)	0.8 \pm 0.3	1.1 \pm 0.1	1.0 \pm 0.1	1.1 \pm 0.2	0.8 \pm 0.1	1.3 \pm 0.1*
Carbohydrate (g/IBWkg)	2.8 \pm 1.0	4.7 \pm 0.3	3.9 \pm 0.7	4.0 \pm 0.4	3.2 \pm 0.4	5.3 \pm 0.4*
Lipid (g/IBWkg)	0.4 (0.1; 0.8)	0.5 (0.4; 0.6)	0.45 (0.3; 0.6)	0.49 (0.1; 1.0)	0.4 (0.2; 0.5)	0.6 (0.4; 0.8)*
Fiber (g/d)	1.7 (1; 5.1)	6 (4.1; 7.8)	5.1 (3.0; 7.6)	6.0 (2.4; 7.8)	4.8 (1.7; 7.4)	6.1 (4.2; 7.7)
Fe (mg/d)	8.5 \pm 6.7	11.1 \pm 5.1	9.3 \pm 5.0	10.5 \pm 7.6	8.2 \pm 5.4	11.8 \pm 5.6*
Zinc (mg/d)	5.3 (3.6; 10.3)	9.4 (6.5; 11.5)	7.3 (5; 10.7)	10.5 (5.5; 15.1)	5.9 (3.3; 9)	11 (8.2; 13.5)*
Vitamin B1 (mg/d)	1.2 (0.6; 1.7)	1.4 (1.1; 1.7)	1.1 (0.7; 1.6)	1.6 (0.3; 1.6)	1.1 (0.6; 1.6)	1.3 (1.1; 1.6)

*8 patients with edema and/or ascites were excluded from BMI evaluation.

Figure 2 shows that alcohol, animal protein, and fat/oil had the highest number of patients who were restricted in eating them: 67.5%, 40%, 35%, respectively. Meanwhile, LC patients reportedly increased their intake of vegetables (25%), fruits (37.5%), and dairy (40%), and only 5% increased legumes. Most of the patients continued their intake of starch (87.5%) and confectionery/soft drinks (77.5%).

Figure 3 reveals that only 32.5% of patients had ≥ 4 meals/day and the number of respondents who had a late-evening snack (LES) was only 9 (22.5%). Moreover, the mean energy, carbohydrate, and protein of the late-evening snack were 140.4 ± 60.7 kcal; 19.1 ± 9.0 g; 5.1 ± 2.5 g respectively (Table 3)

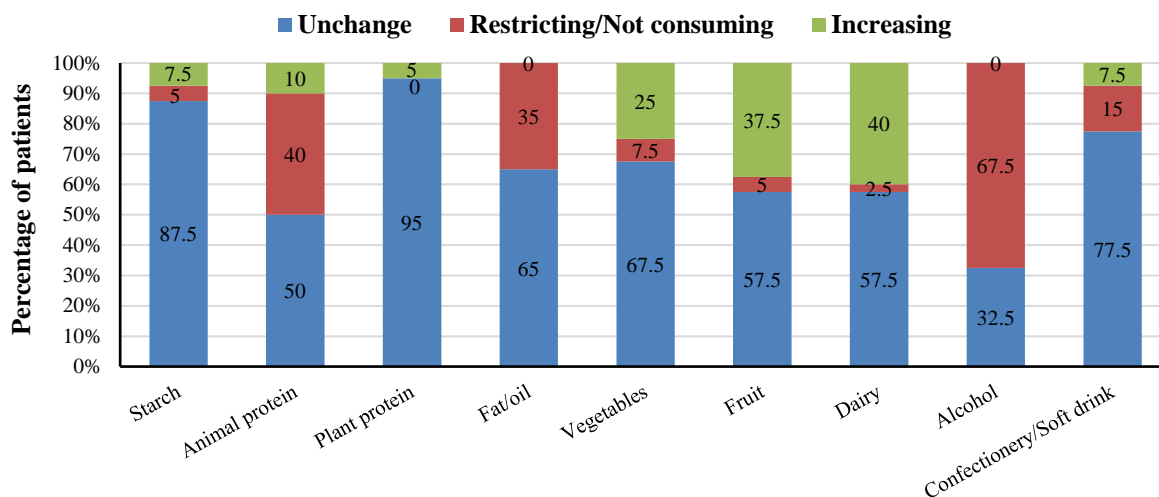


Fig 2. Nutritional practice characteristics of LC patients after being diagnosed with LC (N = 40)

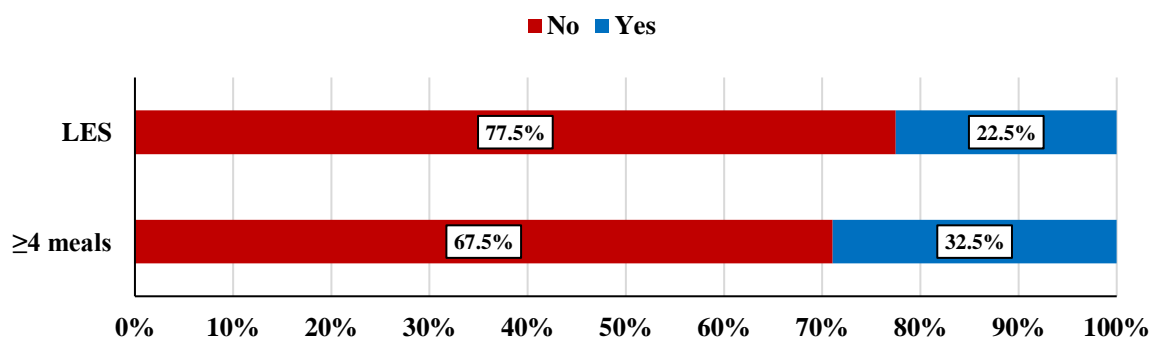


Fig 3. The number of meals/day that LC patients had and late-night snacks (LES) (N = 40)

Table 3. The energy intake of the late-evening snacks (LES) (n = 9)

	Male (n = 7)	Female (n = 2)	All (n = 9)	p
Energy (kcal)	151.7 ± 65.1	101 ± 11.3	140.4 ± 60.7	0.33
Carbohydrate (g)	19.0 ± 10.4	19.6 ± 1.6	19.1 ± 9.0	0.94
Protein(g)	5.8 ± 2.4	2.7 ± 1.6	5.1 ± 2.5	0.13

DISCUSSION

With the increasing burden of liver diseases on the world's and Vietnam's mortality, proper nutrition for hepatic patients has become a challenge, in order to achieve that appropriate nutritional assessment methods are also needed. In many international guidelines, SGA is considered as the "gold standard" for nutritional assessment and

should be used for LC patients instead of BMI (6, 7). Unlike BMI, which is only considered about patients' anthropometry, SGA is relied on not only the aforementioned but also the process of losing weight, patients' dietary decrement, hypermetabolism, and clinical symptoms also (16). However, in most Vietnamese hospitals, BMI is the main method of malnutrition screening and

assessment for LC patients. In this study, as per SGA, 60% of Vietnamese LC patients were malnourished; however, as per BMI, only 12.5% of patients were found to be undernourished. This result was similar to Huisman and et al.'s study in 2011, in which the prevalence of malnutrition was 5% by modified BMI for ascites and/or edema patients, 58% by SGA, and 67% by HS (18). Furthermore, 75% of patients had impaired HS, a reliable, non-invasive, and cost-effective tool to identify malnutrition in cirrhotic patients (9, 19). The mean HS in this study was $20.7 \pm 7.92\text{kg}$ (based on the Asian Working Group for Sarcopenia (AWGS) criteria), in which the means for males ($21.5 \pm 7.98\text{kg}$) and females ($15.2 \pm 5.19\text{kg}$) were both below the cut-off value ($<26\text{ kg}$ for males and $<18\text{ kg}$ for females), so their handgrip strength was classified as low (17). The mean value of HS in this study was roughly equal to that of D. K. Daphnee and colleagues ($20.2 \pm 7.9\text{kg}$), which was used as the study's cut-off point, and 99% of patients were considered to have impaired HS (9). The correlation between HS and mortality is expected, as reduced intake is associated with reduced body protein mass and affects muscle function (19). Given these points, SGA and HS are considered to be the recommended assessment methods of malnutrition for LC patients rather than BMI in Vietnam's clinical facilities.

Despite the high prevalence of malnutrition, the calorie intakes of LC patients were lower than the recommended calorie intake ($24.6 \pm 12.0\text{kcal/kg/d}$ vs 35kcal/kg/d of energy) from ESPEN's latest clinical nutrition practice guideline for LC patients (2019) (6). Cirrhotic patients are usually in conditions of increased energy expenditure as cirrhosis is a catabolic disease, possibly associated with hypermetabolism (6). The fact that most patients had low-calorie intake confirms what the literature has shown, that chronic liver disease patients have a decreased food intake due to the disease's symptoms and dietary restrictions. The mean total daily energy intake of LC patients in this study was quite the same as a study in 2017 by D.K. Daphnee and et al. on 93 LC patients ($1445.9 \pm 727.7\text{kcal/d}$ and $1540.7 \pm 309.3\text{kcal/d}$) (9).

The mean protein intake per ideal body weight of the study's subjects ($1.0 \pm 0.5\text{g/IBWkg}$) was lower than ESPEN's recommendation ($1.2 - 1.5\text{g/IBWkg}$) (6). In the past, there has been controversy about whether patients who had advanced cirrhosis or HE should undergo a transient restriction in protein intake, in order to limit the synthesis of ammonium and the deamination of protein to aromatic amino acids. However, increased protein intake is generally well tolerated and safe in cirrhotic patients and ameliorates protein anabolism, as shown in previous studies (10, 11). Thus, the recommended protein intake in patients with a diagnosis of liver cirrhosis is $1.2-1.5\text{g/kg.BW/d}$ to prevent loss of muscle mass and reverse muscle loss in those who are sarcopenic (6, 7). However, in Vietnam's clinical practice, LC patients' protein intake is still recommended within $0.8-1.2\text{g/kg.BW/d}$ (12). Considering the high prevalence of impaired HS, a sign of sarcopenia, it is essential to reconsider the protein intake recommendation for Vietnamese LC patients in future studies. Nonetheless, the low intake of protein can be the result of low energy intake; therefore, it is possible that LC patients with a proper energy intake can

consume more protein. In future studies, how to increase energy and protein intake in Vietnamese LC's patients needs to be addressed.

As for the minerals, reduced zinc levels are quite common in cirrhotic patients, especially those with an alcoholic origin. Zinc deficiency leads to hyperammonemia, anorexia, and altered taste, which contributes to decreased intake and consequent malnutrition. In contrast to zinc, iron intake in cirrhotic patients needs to be treated cautiously as their iron regulation may be disturbed, and overdosing on iron could result in poisoning. However, the dietary iron of the study's respondents was higher than the RDA in both genders. This result can be due to the fact that the proportion of red meat (like beef and pork) and seafood (like fish, shrimp...) in their meals was high. Furthermore, vitamin B1 is also most likely to be reduced in liver diseases. This study's subjects' intakes of vitamin B1 intake met the requirement.

On analyzing dietary restriction patterns, 35% of the respondents were restricting fats in their diet. This figure was higher in the study of Nguyen Thanh Liem (2013), in which almost all the subjects had a good practice of restricting fat (83.3%) and avoiding greasy food (95%) (20). 67.5% of participants had a good practice of restricting alcohol. While only 5% of patients claimed to increase the intake of vegetable protein like beans and legumes, 40% of the patients reported that they restricted their animal protein intake as they believed that protein, in general, was harmful to the liver. In any case, the mean intake of protein by the current study's patients was still below the recommendation, which can be caused by the over-restriction of protein. When asked the reason for doing so, the answer was because of the advice of their relatives, friends, and/or from the media. As a result, nutritional education is ensured to deliver the correct information to the patients.

Not only is meal composition important, but also the number of meals that LC patients eat, which is preferably from four to six meals per day with three main meals and three snacks, especially a late evening snack (LES). A meta-analysis proved that LES intervention helped to improve liver biochemical parameters for albumin, ammonia, and prothrombin time, and liver enzymes including aspartate aminotransferase and alanine aminotransferase (21). LES also decreased skeletal muscle proteolysis (14); therefore it may help to reverse sarcopenia. In addition, increasing the number of meals can also help to increase the amount of dietary intake in LC patients. In a systematic review, Tsien et al. recommended a 200kcal with 50g carbohydrate late evening snack to minimize gluconeogenesis and preserve muscle mass (14), as well as 15g of protein (13). However, the practice of this aspect is poor among the study's patients as most of the subjects believed that a nocturnal snack would make them gain more fat mass and overwork their liver, as night is the time for the liver to rest. As for those who ate a LES, the average energy, carbohydrate, and protein in this study were only 140kcal, 19g, and 5.1g respectively, which were lower than the recommendation, and in a cohort study in Japan (22). In a Vietnamese hospital, the nutritional intervention regimen for LC patients consists only of 3 main meals (breakfast, lunch, and dinner). Owing to this fact, in future

studies, it is necessary to estimate the effect of an appropriate LES on Vietnamese LC patients' dietary intake, nutritional status and liver function.

There were several limitations in this cross-sectional study. The dietary intake of patients was collected by the 24-hour recall for only 1 day; however, a 7-day food frequency was used to help to reduce the non-representativeness. Moreover, the sample size of the study was limited due to the impact of the Covid19 pandemic.

In conclusion, the prevalence of malnutrition in Vietnamese LC patients was remarkably high from SGA with 60% and from HS with 75%. Considering this result, HS is a reliable, non-invasive, and effective tool for malnutrition assessment for cirrhotic patients in Vietnam's clinical settings rather than BMI. Consequently, the mean dietary intakes of LC patients were lower than the recommendation with many Vietnamese LC patients restricting their protein intake, while few of them ate a late-evening snack. In future studies, appropriate nutritional management with a late-evening snack included in the menu to increase dietary intake needs to be provided to LC patients.

REFERENCES

- World Health Organization. Global health estimates 2016: deaths by cause, age, sex, by country and by region, 2000-2016. 2018.
- Institute for Health Metrics and Evaluation (IHME). Vietnam profile [online]. Available at <http://www.healthdata.org/Vietnam>. (Accessed 01 Dec 2019).
- Sumeet K. Asrani¹, Harshad Devarbhavi, John Eaton, et al. Burden of liver diseases in the world. *Journal of Hepatology*. 70(1), 151–171. 2019.
- Van Thi Thuy Nguyen, Quang Dai Tran, Anh Thu Nguyen, et al. Estimates and projection of disease burden and economic analysis for hepatitis B in Viet Nam. *Journal of Viral Hepatitis*. 2018.
- Schuppan, D., & Afdhal, N. H. Liver cirrhosis. *Lancet*. 371(9615):838–851. 2018.
- Plauth M, Bernal W, Dasarathy S, et al. ESPEN guideline on clinical nutrition in liver disease. *Clin Nutr*. 38(2):485-521. 2019.
- European Association for the Study of the Liver. European association for the study of the liver: EASL clinical practice guidelines on nutrition in chronic liver disease. *J Hepatol*. 70(1):172–193. 2019.
- Maharshi, S., Sharma, B.C., Srivastava, S. Malnutrition in cirrhosis increases morbidity and mortality. *J Gastroenterol Hepatol*. 30(10):1507–1513. 2015.
- Daphnee, D.K., John, S., Vaidya, A., Khakhar, A., Bhuvaneshwari, S., Ramamurthy, A. Handgrip strength: a reliable, reproducible, cost-effective tool to assess the nutritional status and outcomes of cirrhotics awaiting liver transplant. *Clinical Nutrition ESPEN*. 19:49–53. 2017.
- Nielsen K, Kondrup J, Martinsen L, Døssing H, Larsson B, Stilling B, et al. Longterm oral refeeding of patients with cirrhosis of the liver. *Br J Nutr*. 74(4):557-567. 1995.
- Swart GR, Zillikens MC, van Vuure JK, van den Berg JW. Effect of a late evening meal on nitrogen balance in patients with cirrhosis of the liver. *BMJ*. 299(6709):1202-1203. 1989.
- Huong Thi Le, Nguyet Thi Phuc Tran. *Dinh dưỡng lâm sàng – tiết chế*, Nhà xuất bản Y học. 2016.
- El-Kalla FS, Mansor LO, El-Bassat HA, Mishaal S, Attia JF. The effect of a late-evening protein-containing snack on nitrogen balance in cirrhotic patients. *Tanta Med J*. 42:47-52. 2014.
- Tsien CD, McCullough AJ, Dasarathy S. Late evening snack: exploiting a period of anabolic opportunity in cirrhosis. *J Gastroenterol Hepatol*. 27(3):430-441. 2012.
- Ministry of Health and National Institute of Nutrition. Recommended dietary allowances for Vietnamese. 2016.
- Detsky, A.S., McLaughlin, J.R., Baker, J.P., Johnston, N., Whittaker, S., Mendelson, R.A., Jeejeebhoy, K.N. What is subjective global assessment of nutritional status? *JPEN J Parenter Enteral Nutr*. 11(1):8–13. 1987.
- Liang-Kung Chen, Li-Kuo Liu, Jean Woo, et al. Sarcopenia in Asia: consensus report of the Asian working group for sarcopenia. *JAMDA*. 15(2):95-101. 2014.
- Huisman, E.J., Trip, E.J., Siersema, P.D., van Hoek, B., van Erpecum, K.J. Protein-energy malnutrition predicts complications in liver cirrhosis. *Eur J Gastroenterol Hepatol*. 23(11):982–989. 2011.
- Alvares-da-Silva, M., Silveira, T. Hand-grip strength or muscle mass in cirrhotic patients: who is the best? *Nutrition*. 22(2):218–219. 2006.
- Liêm N.T., Mai H.X. Khảo sát thực hành dinh dưỡng và một số yếu tố liên quan của bệnh nhân xơ gan tại khoa nội tiết tiêu hoá bệnh viện đa khoa trung ương Cần Thơ. *Y học thực hành*. 12(899):28-30. 2013.
- Chen, C.-J., Wang, L.-C., Kuo, H.-T., Fang, Y.-C., Lee, H.-F. Significant effects of late evening snack on liver functions in patients with liver cirrhosis: A meta-analysis of randomized controlled trials. *J Gastroenterol Hepatol*. 34(7):1143-1152. 2019.
- Hanai, T., Shiraki, M., Imai, K., Suetsugu, A., Takai, K., Shimizu, M. Late evening snack with branched-chain amino acids supplementation improves survival in patients with cirrhosis. *Journal of Clinical Medicine*. 9(4):1013.20.