Original Article

Nutritional Assessment in Patients with Cirrhosis: Comparison between Different Methods

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ABSTRACT

Background: Malnutrition is common and is a very important prognostic factor among patients with cirrhosis. The best method for assessing nutritional status in patients with cirrhosis is unclear and there are several limitations and controversies regarding the utility of conventional and sophisticated nutritional assessment methods in this population.

Objective: To determine the prevalence of malnutrition in patients with cirrhosis and to compare the performance of various nutritional assessment methods.

Methods: This cross-sectional study was conducted in Rajavithi Hospital between December 2013 and May 2014. Patients with cirrhosis at outpatient clinic were assessed for their nutritional status several methods including subjective global assessment (SGA), anthropometry [body mass index, tricep skinfold thickness (TST) and mid-arm muscle circumference (MAMC)], hand grip strength dynamometry (HGS), and bioelectrical impedance analysis (BIA).

Results: Eighty-five patients were evaluated, 54.1% were male and mean age were 54.41 ± 11.61 years. Etiology of cirrhosis was chronic hepatitis B 35.29%, chronic hepatitis C 27.05%, and alcohol 21.17% of cases. According to the classification of Child-Pugh, 80% were A, 15.29% were B, and 4.71% were C. The prevalence of malnutrition was varied according to the assessment methods used; 44.71% by SGA, 51.76% by MAMC, 36.47% by HGS, and 15.29% by BIA. The results of statistical analysis in different methods of nutritional assessment revealed slightly agreement between SGA-HGS (Kappa = 0.298, $p < 0.05$) and SGA-BIA (Kappa = 0.291, $p < 0.05$).

Conclusions: There was a relatively high prevalence of malnutrition (15-51%) in patients with cirrhosis even in those with Child-Pugh class A. The frequency of malnutrition in patients with cirrhosis appears to be varied according to the nutritional assessment method used. MAMC was superior to SGA, HGS and BIA in terms of its simplicity and ability detects malnourished cirrhotic patients, therefore MAMC recommended as a screening tool for malnutrition in cirrhosis.

Key words : Cirrhosis, nutritional assessment, hand grip strength, bioelectrical impedance analysis, subjective global assessment, mid-arm muscle circumference

[Thai J Gastroenterol 2014; 15(2):90-98.]

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Introduction

Protein calorie malnutrition (PCM) is common in patients with cirrhosis and its prevalence has been correlated with the severity of liver disease; at least 20% in patients with compensated cirrhosis and 50-100% in patients with decompensated disease[1-5]. Development of malnutrition in patients with cirrhosis is multifactorial but major factors appear to play a major role are poor dietary intake, impaired nutrients digestion or absorption, porto-systemic shunting, hypercatabolic state, and altered nutrient metabolism[6]. Several studies have shown that PCM is associated with a number of complications in cirrhotic patients including development of variceal bleeding and ascites, increased surgical morbidity and mortality, worsening hepatic function, as well as decreased survival[2, 7-13]. Apart from macronutrients, patients with cirrhosis, particularly alcoholic and in those with advanced disease, may also have micronutrient deficiencies, e.g. fat-soluble and water-soluble vitamins, magnesium and zinc deficiencies. Recognition of macro- and micronutrient deficiencies is very important since correction of PCM by appropriated nutritional supplements has been associated with reduced risk of infection and in-hospital complications, improved liver functions and quality of life, and increased patients' survival[14-17].

It is essential to assess the nutritional status for every patient with cirrhosis and identify those at risk of developing preventable complications. The manifestations of malnourishment can vary considerably between patients, even in those with the same cause and severity of illness. As in other conditions, comprehensive nutrition assessment in cirrhosis consists of four main components: historical background, physical examination, biochemical analysis, and anthropometric studies. However, there has been no gold standard nutritional assessment method for patients with cirrhosis and many of typical tools have limitations when applied to patients with decompensated cirrhosis. The presence of fluid in third space from salt and water retention can alter the measurement of body mass index and anthropometry. Several serum markers commonly used for nutritional assessment, such as albumin and retinol-binding protein, are often unreliable in patients with advanced cirrhosis because of impaired hepatic protein synthesis in correlation with the severity of liver dysfunction rather than poor nutritional status. More sophisticated techniques such as bioelectrical impedance analysis (BIA), in vivo neutron activation analysis (IVNAA), and dual energy X-ray absorptiometry (DEXA), seem to be more accurate to quantitate nutritional status in such patients, however the use of these tools are limited, mainly due to availability and cost.

Therefore, the present study was aimed to evaluate the prevalence of malnutrition in patients with cirrhosis by several assessment methods, as well as to identify amongst the available methods for prevalence, low cost and easily reproducible, which one offer a safe and efficient nutritional diagnosis, which may help the clinical practice and allow an early intervention in all cirrhotic patients.

Materials and Methods

Patients

This cross-sectional study was conducted in a single tertiary care hospital (Rajavithi Hospital, Bangkok, Thailand) between December 2013 and May 2014. Consecutive adult patients (age >18 years) with a diagnosis of cirrhosis were enrolled. The study protocol was approved by the Ethics Committee for Research at Rajavithi Hospital and all patients provided written informed consent prior to enrollment.

Exclusion criteria were hepatocellular carcinoma or others malignancy, acquired immunodeficiency syndrome, malabsorption syndrome, end stage renal disease, psychiatric disease, hepatic encephalopathy grade 3 or 4, disability or involuntary participant.

Diagnostic criteria for cirrhosis

Cirrhosis was diagnosed based on a combination of clinical features, biochemical profile radiological imaging and/or liver biopsy compatible with cirrhosis. Clinical features suggesting the presence of cirrhosis were cutaneous liver stigmata (palmar erythema, spider nevi, parotid gland enlargement, gynecomastia and testicular atrophy), signs of portal hypertension (ascites, superficial vein dilatations, ascites, splenomegaly, and gastroesophageal varices). Biochemical profile included evidence of reversed albumin-to-globulin ratio, thrombocytopenia and/or coagulopathy. Radiological features, either with transabdominal ultrasound or computerized tomography, demonstrated a small shrunken liver, nodular surface, increased left-to-right lobe ratio, splenomegaly, and/or intra-abdominal col-

lateral vessels and varices. Severity of liver disease was graded according to Child-Pugh score with grades A (mild; score 5-6), B (moderate; score 7-9), and C (severe; score 10-15) indicating degree of hepatic reserve and function.

Nutritional assessment

Nutritional assessment methods were performed including: anthropometry, subjective global assessment (SGA), bioelectrical impedance analysis (BIA), and dynamometry (hand grip strength, HGS). All interviews and measurements were taken in the same day by the same two investigators (one for SGA, anthropometry, and HGS; and one for BIA) who are unaware of the patient's clinical data, in order to avoid possible bias and inter-performer variation.

Anthropometry

All patients in the study had a baseline body mass index (BMI) was calculated using the standard formula: BMI = wt(Kg)/Ht(M)^2. Patients with BMI less than 18.5 Kg/m^2 were categorized as malnutrition. Further anthropometric measurements included the following: mid-arm circumference (MAC), tricep skinfold thickness (TST), mid-arm muscle circumference (MAMC). MAC was measured to the nearest centimeter with a graduated, non-retracting, flexible measuring tape that measured between the tip of the shoulder and the tip of the elbow (olecranon process and the acromion process). TST, a standard measurement of fat stores, was measured to the nearest millimeter using skin calipers at the level of the mid-point between the acromial (lateral edge of the acromion process, e.g. bony tip of shoulder) and the radial (proximal and lateral border of the radius bone, approximately the elbow joint), on the mid-line of the posterior (back) surface of the arm (over the triceps muscle). Mid-arm muscle circumference (MAMC), a standard measurement of muscle protein mass, was calculated from MAC and TST using a standard formula: MAMC = MAC - (3.1415xTST). MAMC was used to classified for nutrition status along with the patient's age and gender, at 5 percentile as malnutrition according to the reference parameter of Frisancho *et al*[18].

Subjective global assessment

Subjective global assessment (SGA) is a simple evaluation tool that allows physicians to assessment of nutrition status. The SGA has been shown to be a valid and useful clinical nutritional assessment tool for patients of various medical conditions[19]. The SGA used in this study was modified from the standard English-language version which was previously validated for using in Thai patients with chronic liver disease. [Supplementary document] Several general and nutritional aspects were integrated in the checklists including history data of ponderous loss, reduced daily caloric ingestion, gastrointestinal symptoms, functional capacity, physical signs of malnutrition (edema, ascites) and serum albumin. The patients were classified as: well nourished (A), with moderate malnutrition (B) and severe malnutrition (C), according to the method scores[20].

Bioelectrical impedance analysis (BIA)

Biospace, InBody720 model, Gangnam-gu, Seoul, Korea was used to assessment of nutritional state. The patient was tested following standard instructions of machine. The electrical current used in the measurement at frequency 50 kHz, which enables to measure resistance and reactance and obtain the phase angle (PA) value. The PA derives from two segments of corporal composition, calculated by PA = tangent arc (Xc/R) x 180/3.1416, proposed by Barbosa-Silva et al. The PA result enables to classify the patient according his/her nutrition status. The PA result enables to classify the patient according cirrhotic patients nutrition status by cutoff point 5.44°[21].

Dynamometry

A digital hand grip dynamometer was used to assess the hand grip strength (HGS). The patient sat on a chair without armrest and with the plantar region on the floor; the appraiser adjusted the dynamometer handle to place the patient's hand comfortably during the test, and was kept far from the body and chair. The patients were asked to compress the handle with as much strength as possible with the non-dominant hand. Five measurements were made, with an interval of more than 15 seconds between each measurement. The highest and lowest results were omitted, then the mean of the middle three measurements was recorded and classified for nutrition status along with the patient's age and gender, according to the reference parameter from a population-based study by Massy-Wastropp *et al*[22]. Malnutrition was defined as a result below 2 standard deviations from the mean value.

Statistical analysis

A descriptive analysis was performed through mean values and standard deviation for continuous variable of symmetric distribution, or median value and interquartile amplitude for continuous variables of asymmetric distribution, and absolute and relative frequency for categorical variables. Kappa coefficient of agreement was used to assess the agreement between each different methods of nutritional assessment. The significance level of 5% was considered and the analyses were performed using Statistical Packages for the Social Sciences (SPSS) version 22.0 (Chicago, Illinois, USA) software.

Results

Patients

From a total number of 130 patients were screened during the study period, 85 patients who met the inclusion and exclusion criteria were recruited in this analysis. The details of enrollment and study flow are shown in the Figure 1.

The clinical characteristics of the cirrhotic patients are summarized in Table 1. The mean age was 54.41 years (± 11.61 years, ranging from 30 to 77 years); 46 (54.1%) were male and 39 (45.9%) were female. The most common etiology of cirrhosis were chronic hepatitis B (n=30, 35.3%), chronic hepatitis C (n=23, 27.1%) and alcoholic liver disease (n=18, 21.2%). According to the Child-Pugh system, most patients were classified as Class A (n=68, 80%), whereas 13 patients were class B (15.3%), and 4 patients were class C (4.7%). BMI was not different between gender or Child-Pugh stage, but appeared to be increased in older patients; 23.8±4.3 for age 20-39 years, 25.4±3.1 for age 40-49, 25.6±3.6 for age 50-59, and 23.4±3.8 for age ≥60 years.

Nutrition assessment

According to the standard cutoff values of each methods, malnutrition was documented in 4/85 (4.71%) by BMI, 38/85 (44.71%) by SGA, 31/85 (36.47%) by HGS, 44/84 (51.76%) by MAMC, and 13/85 (15.29%) by BIA, as shown in Figure 2. There was no statistically significant difference in the prevalence of mal-

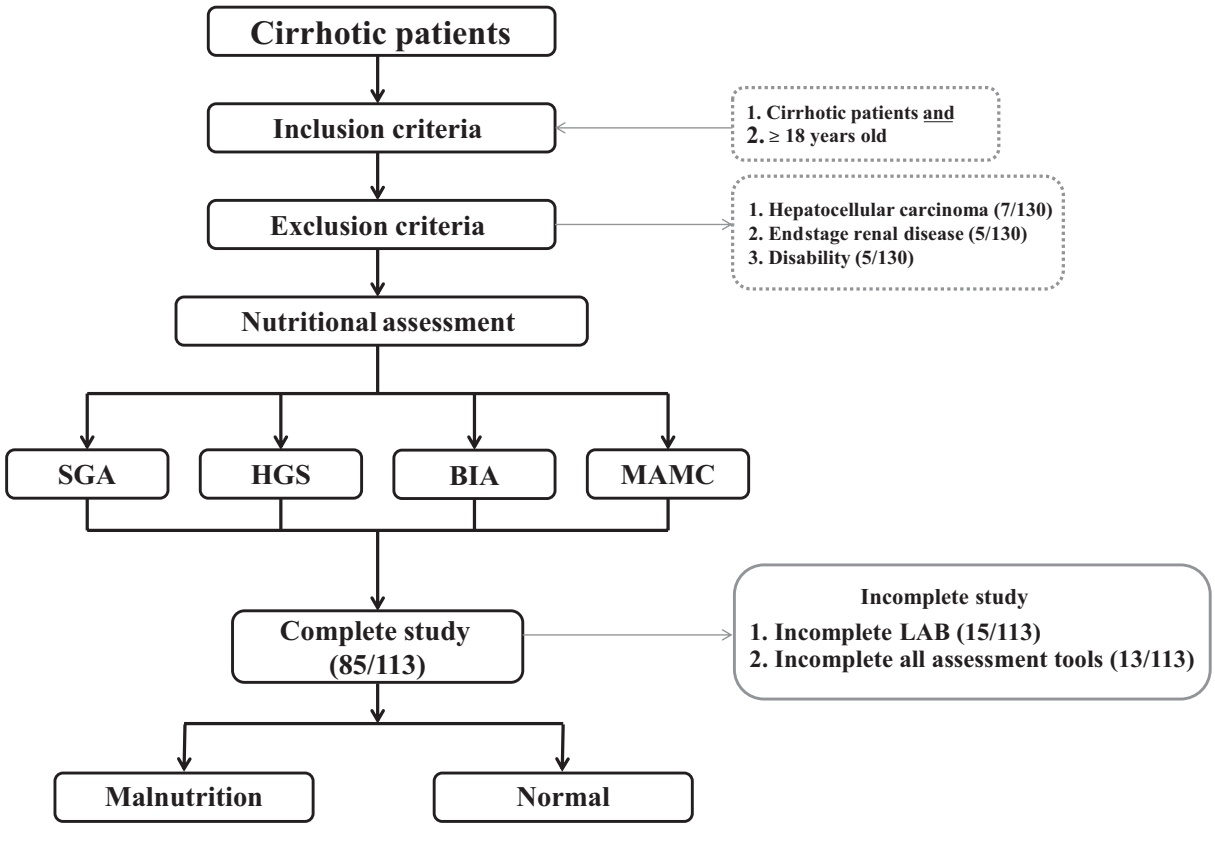

Figure 1. Schematic diagram of study.

Table 1. Characteristic of 85 patients with cirrhosis.

Characteristics	Values
Age	
Mean (SD)	54.41 (±11.61)
Median (range)	55 (30-77)
Age <40 years	12 (14.1%)
Age between 40-59 years	47 (55.3%)
Age ≥60 years	26 (30.6%)
Gender	
Male	46 (54.1%)
Female	39 (45.9%)
Region	
BMA[#]	39 (%)
Central	36 (%)
Northeast	7 (%)
North	1 (%)
Myanmar	2
Child- Pugh classification	
A	68
B	13
C	4
Etiology of cirrhosis	
Chronic hepatitis B	30
Chronic hepatitis C	23
Alcohol	18
Autoimmune liver disease	3
Cryptogenic	11
BMI (Kg/m^2)	
Mean (SD)	54.41 (±11.61)
Obesity: BMI >25	40 (47.1%)
Overweight:	41 (48.2%)
Malnourished: BMI <18.5	4 (4.7%)

[#]BMA: Bangkok metropolitan area (Bangkok, Nontaburi, Samutprakarn, Samutsakorn, Pathumthani, and Nakornpathom)

nutrition detected by SGA, HGS, and MAMC (p>0.05), whereas the prevalence of malnutrition was significantly lower when detected by BMI and BIA (p≤0.05).

HGS assessment through digital dynamometry, decreasing values as the age increased were observed in female patients above 40 years old while similar finding was observed in male above 50 years old, as shown in Table 2. A trend of decreasing HGS with increasing age was clearly seen in both genders when the patients were above 60 years.

The results of nutritional assessment through MAMC according to age group and gender are summarized in Table 3.

Table 4 summarized the number of cirrhotic patients with different etiology categorized by different diagnostic methods. The highest prevalence related to the etiology of cirrhosis in malnourished patients, according to SGA and BIA is virus C. In contrast to HGS and MAMC, Chronic hepatitis B was found to be the most etiology.

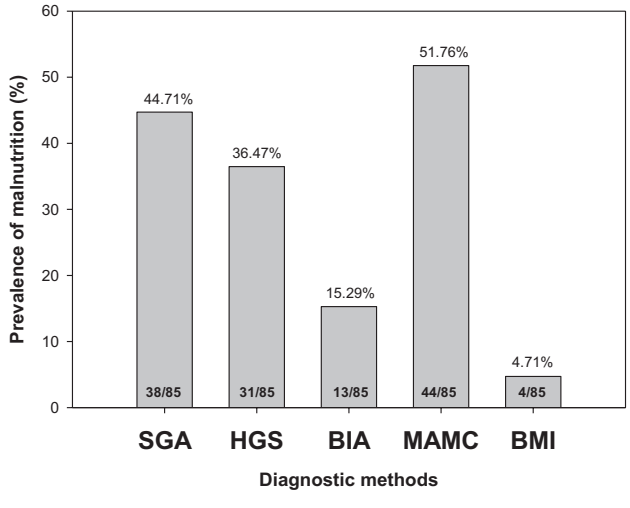

Figure 2. Prevalence of malnutrition according to different nutritional assessment methods.

Table 2. Evaluation through HGS (unit: Kg/F) by age and gender.

Age group	Number of cirrhotic patients		Mean and SD values of HGS	
	Men	Women	Men	Women
20-39	7	5	32.89 (8.81)	17.31 (4.25)
40-49	11	5	28.33 (4.05)	20.76 (7.61)
50-59	11	15	28.50 (6.52)	17.36 (4.97)
≥60	17	14	23.40 (8.89)	14.77 (4.42)
Total	**46**	**39**	**27.21 (7.90)**	**16.86 (5.24)**

Table 3. Evaluation through MAMC by age group and gender.

Age group	Number of cirrhotic patients		Mean and SD values of MAMC	
	Men	Women	Men	Women
18-18.9	0	0	-	-
19-24.9	0	0	-	-
25-34.9	3	2	22.53 ± 3.11	17.64 ± 0.08
35-44.9	9	3	20.95 ± 2.63	17.63 ± 1.68
45-54.9	12	11	22.22 ± 2.71	21.49 ± 2.62
55-64.9	11	16	22.21 ± 2.54	21.65 ± 3.19
65-74.9	10	7	23.08 ± 2.50	19.26 ± 3.47
≥75	1	0	20.60	-
Total	**46**	**39**	**22.14 ± 2.59**	**20.66 ± 3.17**

Table 4. Association of cirrhotic etiology with malnutrition assessed through different methods of nutritional assessment.

Etiology	Total sample	Assessment method				
		SGA	HGS	MAMC	BIA	BMI
Chronic hepatitis B	30	11	12	16	2	2
Chronic hepatitis C	23	15	6	11	5	2
Alcohol	18	6	7	8	3	0
Autoimmune	3	2	1	2	1	0
Cryptogenic	11	4	5	7	2	0

Table 5. Association of cirrhotic Child-Pugh classification with malnutrition assessed through different methods of nutritional assessment.

Child-Pugh	Total sample	Assessment method				
		SGA	HGS	MAMC	BIA	BMI
A	68	21	23	35	5	3
B	13	13	7	6	6	1
C	4	4	1	3	2	0

Table 6. The values of reliability *(Kappa coefficient - k)* for the assessment of agreement between different diagnostic methods.

Diagnostic methods	HGS	BIA	MAMC
SGA	0.298 ($p = 0.005$)	0.264 ($p = 0.002$)	-0.069 ($p = 0.524$)
HGS		0.131 ($p = 0.157$)	0.172 ($p = 0.097$)
BIA			-0.078 ($p = 0.318$)
MAMC			

We observed, BIA method had a statistic significant in diagnosed malnourished patients with cirrhosis Child-Pugh A comparing to other methods.

The results of statistical analysis in different methods of nutritional assessment revealed slightly agreement between SGA-HGS (Kappa = 0.298, $p < 0.05$) and SGA-BIA (Kappa = 0.291, $p < 0.05$).

DISCUSSION

It has been well-established that malnutrition is common and is a very important prognostic factor among patients with cirrhosis. However, the best method for assessing nutritional status in patients with cirrhosis remains unclear, which is largely due to some limitations in interpreting the results of standard methods in cirrhotic setting. Unfortunately, there have been few studies comparing various nutritional assessment methods in patients with cirrhosis which yielded heterogeneous results[18-23]. Apart from the disease itself, it should be noted that ethnics, geographical areas, local foods and cultures are also key factors affecting nutritional status. From this reason, studies from other parts of the world may be quite difficult to apply for Thai population and studies conducted in Thailand are more preferable. In the present study, we assessed nutritional status of Thai cirrhotic patients by various methods in an outpatient clinic setting which included a sensible number of patients with cirrhosis from various etiologies, mostly viral hepatitis and alcoholic liver disease. The majority of patients were clinically classified as Child-Pugh A. The prevalence of malnutrition in this study varies between 15-51% according to the methods used, with somewhat agreement between the methods when a statistical analysis was applied. This finding underlines that malnutrition is commonly seen in Thai patients with cirrhosis, even with Child-Pugh class A.

Previous study supported the utility of the SGA in Asian patients with cirrhosis[23]. Although anthropometric, hand grip strength, and BIA are known to be better predictors of malnutrition in adult patients with cirrhosis[24,25]; these tools are not practical use, high cost, and unavailable for everyday use. SGA compared to standard anthropometry, is much more applicable in clinical practice and has previously been demonstrated to be highly predictive of malnutrition in advanced cirrhosis.

This study demonstrated the prevalence of malnutrition, defined by SGA, was 44.71 %; same as in the study conducted by Roongpisuthipong *et al*[20] with a high percentages of malnutrition and similar population. Moreover, this study demonstrated that SGA has significant slightly agreement to HGS and BIA for detection malnourished in patients with cirrhosis. Thus, only SGA or a combination of SGA with either HGS or BIA may be used as nutritional assessment tool in patients with cirrhosis.

By MAMC, 51.19% patients were diagnosed as malnourished. Moreover, due to non-availability of reference standard for MAMC for healthy Thai or Asian population, values described by healthy North Americans were used[18]. Studied demonstrated the mean (± SD) of MAMC with age group and gender that no statistic significant compared the reference parameters for MAMC, validated by Frisancho AR *et al*[18] except male 35-44.9 years, female 45-54.9 years, and female 55-64.9 years. Another limitation, both gender had no cutoff in age ≥ 75 years that found 1 patient in this study. Thus, it seem to be used MAMC from this study to reference cut off parameter to diagnosed malnourished Asian/Thai patients with cirrhosis.

Hand grip strength (HGS) can also be used to assess nutrition status; it has been found to identify 63% of malnourished cirrhotic patients, which is superior to the SGA[24]. In contrast, this study demonstrated no statistical different in percentages of nutritional risk of malnutrition could not be observed between diagnostic methods of HGS and SGA with similar result in values of reliability (Kappa coefficient - k) for the assessment of agreement between HGS and SGA.

This study used the reference parameters for HGS, validated by Westropp *et al*[22] that different from other study that validated by Alvares-da-Silva *et al.* A discrepancy was observed when comparing it to the values found in the population of patients with cirrhosis, a factor that might have contributed to over/underestimated proportion of cirrhotic patients.

In clinical practice, it is very important to identify cirrhotic patients that are approaching the state of malnutrition by simple, fast, and reproducible methods. In addition, the preferred malnutrition screening methods should be able to detect malnutrition at the early stages in order to provide early nutritional support to improve the patient's clinical outcomes maximally. According to our findings, BMI has a low sensitivity and in which it should not be used as malnutrition screening tool as it can detect only severely mal-

nourished patients. Further, it seems that the three other conventional nutritional assessment methods (SGA, HGS, and MAMC) are sensibly correspond to each other and are all acceptable for determining malnutrition in patients with cirrhosis. MAMC appeared to be slightly superior to SGA, HGS and BIA in terms of its simplicity and ability detect malnourished cirrhotic patients, and is therefore recommended as a screening tool for malnutrition in cirrhosis. However, BMI, SGA and HGS are also simple, inexpensive, and quick to perform so that any of these methods can be utilized as well depending on availability and center's preference. The role of more sophisticated methods for determining nutritional status in patients with cirrhosis is controversial. In the present study, BIA was not associated with significantly increased benefit for the detection of malnutrition. Further, patients with advanced liver disease, particularly those with encephalopathy, may have some restrictions to perform the test such as inability to stand securely and invalid measurement from tremors.

Regarding the utilization of BIA, studies demonstrated the correlation of the phase angle as a good prognostic indicator in severe clinical situations[29,30]. BIA had a statistically significant correlation with each patient's Child-Pugh score[21]. Although possibly not readily available in all institutions, the BIA is considered to be an accurate tool in cirrhosis patients without ascites[26]. The BIA sends a small amount of electrical current through the body. Percent fat, lean body mass and body water are calculated based on the water content of different types of tissue and the speed at which the current passes through them. For example, adipose tissue has low water content, and therefore, the electrical current slows down passing through it, whereas it passes quickly through muscle because of its high water content. It is because of BIA's reliance on body water, that it will not accurately determine body composition in patients with ascites and/or presence of fluid in the third space.

A previous study by Fernandes et al., has demonstrated a correlation of phase angle 5.440, measuring by BIA, as cutoff point to characterize malnutrition in patients with cirrhosis[21]. In the present study, we observed that BIA had a statistically significant lower performance in diagnosing malnutrition in patients with cirrhosis Child-Pugh A when compared to other methods, whereas the diagnostic performance of BIA seems to be comparable to other methods in patients with cirrhosis Child-Pugh B and C. However, due to the low number of patients with cirrhosis Child-Pugh B and C in this study, the latter finding is difficult to conclude and more subjects with advanced cirrhosis are needed.

The Royal Free Hospital-SGA, a sequential combination of conventional nutritional assessment methods (BMI, MAMC, and dietary intake), is simple, reproducible, and has shown to provide predictive validity for patient outcomes[27]. Thus, it has recently been endorsed by the International Society for Hepatic Encephalopathy and Nitrogen Metabolism Consensus as a method of choice of assessing nutritional status in patients with cirrhosis[28]. Though our findings have supported this recommendation, this combined method needs further validations in Thai population.

Limitations of the present study were absence of non-cirrhotic controls, lack of long-term follow up for clinical outcomes, and small number of subjects from some subgroups such as patients with advanced cirrhosis and autoimmune liver disease. It should also be noted that there was no gold standard method, universally-accepted guideline or cutoff points for determining malnutrition in patients with cirrhosis so that it is quite difficult to compare and interpret the results between different methods. To our best, we performed several conventional nutritional assessment methods, as well as a sophisticated method (BIA) and used specific cutoff points taken from selected studies with good methodology and large sample size that were conducted in Asian populations. Despite limitations, this study provided several useful information regarding nutritional assessment and status which are currently lacking among patients with cirrhosis especially among Thai population.

Conclusions

Malnutrition is common in patients with cirrhosis, even in those with Child-Pugh class A. However, the assessment of the nutritional status of patients with cirrhosis and the comparison with different methods show significant discrepancies, with the prevalence of malnourished patients with cirrhosis ranging from 4.71% to 51.19%. MAMC is simple and detected a highest number of malnourished patients.

However, more studies with a larger sample and control group are required to substantiate these findings, particularly expanding the number of cases patients with Child-Pugh B and C.

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