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Clinical nutritional assessment methods and their progress in hepatocellular carcinoma patients

Guanping Qiu[1]; Yaokai Wen[1]; Yadi Liao[2]*; Yuanfeng Gong[2]

[1]Nan Shan School, Guangzhou Medical University, Jingxiu Road, Panyu District, Guangzhou, 511436, China

[2] Department of Hepatobiliary Surgery, The Affiliated Cancer Hospital & Institute of Guangzhou Medical University, 78 Hengzhigang Road, Yuexiu District, Guangzhou 510095, China

***Corresponding Author(s): Yadi Liao**

Department of Hepatobiliary Surgery, The Affiliated Cancer Hospital & Institute of Guangzhou Medical University, 78 Hengzhigang Road, Yuexiu District, Guangzhou 510095, China

Tel: +86-020-6667-3666; Email: medliaoyd@126.com

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Abstract

Objective: To summarize the nutritional assessment methods of Hepatocellular Carcinoma (HCC) patients and their recent progress, so as to provide reference for reasonable nutritional evaluation and consequent nutritional support for HCC patients.

Methods: We identified eligible studies in PubMed and EMBASE databases in addition to the reference lists of original studies and review articles on this topic.

Results: The effectiveness of individual indicators applied in the traditional nutrition assessment were quite low. The scoring system Subjective Global Assessment (SGA), Mini Nutritional Assessment (MNA), and nutritional risk screening 2002 (NRS-2002) had similar evaluation validity, these three kinds of nutritional assessment methods were more suitable for HCC patients compared with the traditionally nutritional assessment methods.

Conclusion: Clinical nutritional assessment methods such as SGA, MNA, and NRS-2002 should be used in combination with relevant body measurements and laboratory indicators in order to more accurately assess the nutritional status of HCC patients.

Introduction

Hepatocellular Carcinoma (HCC) is the major malignant tumor around the world, particularly in China or Southeast Asia, with poor 5-year survival rate. An estimated 782,500 new cases and 745,500 cancer-related deaths emerge every year, ranking it the sixth among cancer morbidity and the second among cancer mortality [1]. Hepatitis B Virus (HBV) infection is the most important risk factor for HCC in Asia. The only one exception in Asia is Japan, where the prevalence of HCC has been closely associated with hepatitis C virus (HCV) infection. In western countries, however, HCV infection has been observed in about 60% of patients diagnosed with HCC [2].

Previous studies have shown that patients with Hepatocellular Carcinoma (HCC) are at a special increased risk for malnutrition [3]. The majority of them are estimated to have been associated with liver cirrhosis which has been proved to have a negative impact on survivals with these patients [3]. Malnutrition has been neglected by clinicians for a long period, which has severely affected the prognosis of patients with HCC. Thus, a rational nutritional assessment system of HCC patients is essential for improving the clinical outcomes of comprehensive treatment. The most commonly used nutritional assessments applied to HCC patients are summarized as follows.

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Traditional nutritional assessment

Anthropometric measurements

Anthropometric indicators mainly include body mass, Body Mass Index (BMI), Triceps Skin Fold (TSF), Mid-Arm Muscle Circumference (MAMC), Calf Circumference (CC) and so on. These indicators are simple, easy to measure and reliable. So they are generally used as assessment characteristics in comprehensive nutrition assessment. Among them, BMI is the simplest and most direct indicator of body fat and lean tissue mass. However, the body mass changes in the metabolism of various substances in the body, and patients with HCC often have edema, ascites, giant tumors or organ hypertrophy due to digestive tract symptoms and protein metabolism disorders. These symptoms lead to the illusion of excess nutrition. Furthermore, anthropometric indicators are confounding by factors such as gender, age, and measurement errors. According to the study conducted by Schütte*et al*. [3], a significant proportion of patients with HCC was malnourished or at risk for malnutrition. They also found that the calculation of BMI was not suitable to identify malnourished patients. Screening questionnaires and BIA measurement were superior to pure anthropometric measurements to identify the condition that negatively influences survival.

Laboratory tests

Laboratory testing indicators include Hemoglobin (Hb), Serum Prealbumin (PA), Serum Albumin (Alb), Total Lymphocyte Count (TLC), Creatinine-Height Index (CHI) and so on. Alb is one of the highly reliable indicators of nutritional evaluation. Its half-life is about 21 days, and it mainly reflects chronic protein metabolism. So sustained hypoproteinemia is considered as a reliable indicator of malnutrition [4]. Since the half-life of PA is only 12 h, it is more sensitive to evaluate the acute protein metabolism than Alb. Moreover, it is regarded as a sensitive parameter to determine early liver injury. TLC reflects the body's immune function, however it can be interfered by splenomegaly and hypersplenism due to liver cirrhosis. CHI is generally used to identify the amount of protein in the body. It is closely related to the total muscle mass, body surface area and body weight while exercise and diet have little effect on it. It is not subject to edema and ascites. Previous studies suggested that for patients with normal renal function and no infections, CHI can be used as a sensitive indicator for evaluating malnutrition in patients with HCC under liver cirrhosis [5]. In addition, the reference values of laboratory tests are slightly different, and the lack of a unified cutoff value will lead to differences in the evaluation results. Thus, it is important for us to take into account all indicators to assess the patient's nutritional status.

Traditional nutritional assessment methods also include dietary questionnaires. Nevertheless, dietary questionnaires are not commonly used in clinical practice [6]. Since the intake, digestion and absorption of nutrients in patients with HCC can be severely affected by the liver function. Furthermore, the precise measurement of protein, fat and carbohydrate in meals is difficult to perform as well as the error is great.

Comprehensive nutrition assessment

subjective global assessment (SGA)

The SGA was proposed by Detsky *et al.* in 1984. It consists of medical history and anthropometric measurements. It is a comprehensive nutrition assessment tool recommended by the American Parenteral Nutrition Society and the European Society of Clinical Nutrition and Metabolism for the evaluation of the nutritional status of patients with liver diseases. The SGA is easy to perform, which does not require biochemical tests, and its sensitivity and specificity for assessing malnutrition in liver diseases hasbeen accepted globally. The biggest feature of the SGA compared to the European Nutrition Risk Survey 2000 method (nutritional risk screening 2002, NRS-2002) is that SGA can be used in patients with ascites to reduce the effect of ascites on the body mass of patients, and can be even more effective in reflecting the patients' nutritional status. As a semi-quantitative nutritional assessment tool, SGA is more suitable for nutritional assessment of patients with HCC and chronic liver disease. However, it depends on the clinicians' subjective judgment on related indicators. Furthermore, it is not able to reflect the acute changes of nutritional status in a short term.

PG-SGA

Ottery *et al.* proposed PG-SGA on the basis of the SGA in 1994 [7], which was recognized by the Chinese Anticancer Association and the American Dietitians Association as the standard for nutritional assessment of cancer patients [8]. The PG-SGA scale was subjectively assessed by the patient, and the content was simple and easy to understand. However, systematic training is needed when using the PG-SGA method to screen a large number of patients with digestive tract tumors and advanced malignant tumors [9]. PG-SGA can accurately evaluate the symptoms of HCC patients such as pain, loss of appetite, ascites, jaundice, and diarrhea, which is favorable for comprehensive analysis. Some clinicians have performed nutritional evaluations on 90 patients with tumors using SGA and PG-SGA simultaneously [10]. SGA is an approximate gold standard, with a sensitivity of 97% and a specificity of 86% for PG-SGA. Sharma *et al.*concluded that the accuracy of PG-SGA assessment of nutritional status was not simply comparable to that of SGA, but also enabled rapid identification of malnourished cancer patients and classification of malnutrition [11]. The study showed that PG-SGA combined with CHI can accurately evaluate the nutritional status of HCC patients, and there is a positive correlation between liver function Child-Pugh grade and PG-SGA grade, so the nutritional status was positively correlated with liver function status and clinical outcomes, suggesting that the nutritional status assessment of HCC patients should be emphasized to detect early malnutrition and timely clinical intervention.

MNA

MNA is a simple and quick method proposed by Guigoz *et al.* in 1997 for the screening of nutritional status and assessment of nutritional status in elderly patients, surgical patients and patients with chronic diseases [12]. It is based on anthropometric, dietary and subjective evaluations to conclude a comprehensive assessment. At present, MNA has been widely used to evaluate the nutritional status of HCC patients, and it can correctly analyze the relationship between tumor cachexia characteristics and multiple prognostic indicators of patients. Tsai *et al*. found that the results of MNA were correlated with Hb, Alb, C-reactive protein (CRP), γ- glutamyltranspeptidase (γ-GT), liver function classification, TNM staging, etc [13]. Another study showed that MNA can screenpatients at nutritional risk more intensively than PG-SGA, which facilitates early intervention and improves prognosis [14]. Of course, the MNA questionnaire also has several limitations to be strengthened. In 2001, Rubenstein *et al.* developed a short form mini nutritional assessment (MNA-SF) based on MNA based on 881 elderly malnourished patients

[15]. MNA-SF is not only highly relevant to MNA, but also easy to perform. Kaiser *et al.* investigated 2032 patients with malignant tumors and found a significant correlation between MNA-SF and MNA [16]. At present, the application of MNA-SF of malignancy in China is not widespread. Further research is still needed on whether MNA-SF is suitable for nutritional screening of HCC patients.

NRS-2002

NRS-2002 was developed by the European Society of Parenteral Nutrition (ESPEN) in 2002 and is a method for the screening of in-patient nutritional risk [17]. It is also recommended by Chinese enteral nutrition association and Chinese medical association for the assessment of nutritional risk in patients with liver disease. The NRS-2002 total score is the sum of the impaired nutritional status and the severity of the disease. The evaluation method is simple, fast, and can be finished within 3 minutes. Clinicians have confirmed the feasibility of NRS-2002 in the nutritional evaluation of cirrhosis patients. Kim *et al.* used NRS-2002 for nutritional evaluation of 1057 cancer patients with PG-SGA as reference. The results showed that NRS-2002 was more sensitive and specific, 72.9% and 81.9% respectively [18]. Moreover, NRS-2002 can be used to predict the nutrition-related prognosis of patients with malignant tumors and the effect of nutritional intervention. However, there are some limitations as follow. It can be affected by the subjective judgment of clinicians, and it cannot apply to long-term, bedridden or severe hepatic encephalopathy patients, and also the score is also affected by fatigue and loss of appetite in HCC patients.

Summary

In summary, the malnutrition status in patients with HCC is common. The study showed that the main causes of progressive malnutrition in patients with hepatocellular carcinoma and cirrhosis were fewer intakes, energy depletion, and change in metabolic pathways. At present, there are many methods and indicators for assessing malnutrition in patients with HCC, but so far, no method or standard has been defined as a "gold standard". Basically, several subjective assessment tools such as SGA, MNA, and NRS-2002 have been used in combination with relevant anthropometric and laboratory indicators to comprehensively evaluate patients with HCC. Comprehensive nutritional assessment software is on the rise to integrate the nutrition screening, nutrition assessment, and prescription planning automatically. If necessary, the comprehensive nutritional assessment software can also track the results and improve the prognosis.

Previous studies have confirmed the nutritional support for the treatment of patients with HCC, such as improving the nutritional status of patients, promoting postoperative recovery, reducing the incidence of complications, shortening the hospital stay, and reducing treatment costs. A number of studies have shown that nutritional intervention can effectively improve the nutritional status or the prognosis. Therefore, the accurate nutritional assessment, early detection and diagnosis of malnutrition, the development of a reasonable and individualized nutritional support program, timely and reasonable nutrition support and nutritional conditioning, can improve the quality of life of patients with HCC and improve prognosis.

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