International Journal of Research in Medical Sciences
Vinayakumar KR. Int J Res Med Sci. 2024 Oct;12(10):3997-4005
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20242977

Review Article

Malnutrition and sarcopenia in liver cirrhosis: Indian expert opinion perspective on screening and managements

K. R. Vinayakumar*

Department of Gastroenterology, Ananthapuri Hospitals and Research Institute (AHRI), Thiruvananthapuram, Kerala, India

Received: 16 August 2024
Accepted: 21 September 2024

***Correspondence:**
Dr. K. R. Vijayakumar,
E-mail: drkrvkumara@gmail com

ABSTRACT

Malnutrition and sarcopenia in Liver cirrhosis led to poor outcomes, complications, quality-of-life and increased mortality. This review discusses the prevalence of malnutrition and causative factors from an Indian patient and clinician perspective, nutritional assessment strategies, and management of malnutrition and sarcopenia. A group of experts discussed the dietary and lifestyle factors leading to malnutrition, screening tools and management algorithms to assess severity of malnutrition, and imaging modalities for diagnosing sarcopenia. They discussed the lack of routine screening in cirrhotic patients and advocated the use of quick and practical screening tools such as hand grip strength (HGS), gait speed, and body mass index (BMI) in clinical settings for early assessment of nutritional status and sarcopenia. Following screening and diagnosis of nutritional deficiencies, a comprehensive nutritional management plan consisting of adequate dietary protein and caloric intake, along with multivitamin and BCAA supplementation is recommended and has shown better clinical outcomes. Suitable screening and management strategies were considered essential to improve prognosis of cirrhotic patients.

Keywords: Branched chain amino acids, Malnutrition, Sarcopenia, Nutritional assessment, Liver frailty index

INTRODUCTION

Liver diseases and their complications lead to increased mortality, poor quality of life, increased hospitalizations, and length of stays and development of pre- and post-transplant infections.[1] Depending upon the pattern of hepatocyte damage and structural changes, liver diseases are classified as acute or chronic. Acute liver diseases are often self-limiting and usually resolve without further complications.

Acute viral hepatitis, drug-induced liver injury, and acute fatty liver of pregnancy are common types of acute liver diseases.[2,3] In contrast, chronic liver diseases (CLD) involve progressive deterioration of liver functions and hepatocyte damage that persists for more than six months leading to permanent structural changes in the liver.[3,4] CLDs are quite common problems and are caused by chronic viral hepatitis infections, excessive alcohol consumption, non-alcoholic fatty liver disease (NAFLD), autoimmune diseases, and genetic conditions.4 Repeated inflammation, destruction, and regeneration of liver parenchyma in CLDs leads to fibrosis and ultimately the late and irreversible stage of fibrosis known as cirrhosis or scarring of the liver.[5] In cirrhosis, the tissue architecture is distorted due to formation of interconnected septa and alteration of vascular tissue, blood flow, and portal hypertension that eventually lead to a compromise in liver function.[4]

Multiple hepatic parenchymal and nonparenchymal cell types play a role in the pathogenesis of fibrosis and cirrhosis. Activation of hepatic stellate cells (HSCs) following exposure to inflammatory cytokines, defenestration and capillarization of liver sinusoidal endothelial cells (LSECs), destruction of hepatocytes by Kupffer cells (KC), hepatocyte apoptosis and release of reactive oxygen species, and activation of HSCs are

implicated in the development and progression of cirrhosis. Cytokine-mediated signaling pathways involving platelet-derived growth factor (PDGF), transforming growth factor (TGFβ), tumor necrosis factor alpha (TNFα), interferons, and interleukins also play a role in the pathogenesis of cirrhosis.[6]

A liver disease global burden study showed that of the 2 million deaths globally due to liver diseases, half of them were caused by cirrhosis complications necessitating appropriate measures to diagnose and manage cirrhosis.[7] Cirrhosis was ranked as the 11th leading cause of death in 2015 accounting for 2.1% of total deaths worldwide.[8] In addition to increased mortality, cirrhosis poses a significant economic burden due to increased hospitalizations and impact on health due to high number of disability-adjusted life-years (DALYs).[9]

The prevalence, mortality rate, and causative factors for cirrhosis vary by geographic region, with alcohol and NAFLD being the main causes for cirrhosis in Western and industrialized countries and viral hepatitis being the main cause in China and other Asian countries.[8] In 2010, India accounted for 18.3% or one-fifth of the global cirrhosis death toll with alcohol consumption, hepatitis B and C infections, and metabolic syndrome associated liver diseases.[7,10]

As the liver plays a crucial role in the metabolism of nutrients such as carbohydrates, proteins, and lipids, its malfunction is associated with disturbances in inter-organ nutrient trafficking causing malnutrition. Malnutrition causes a decrease in skeletal muscle volume and strength known as sarcopenia, which is associated with poor prognosis such as unfavorable clinical outcomes and neuropsychiatric problems and post-transplant complications.[11,12] In India, the prevalence of malnutrition and sarcopenia has been seen to vary from 47% to 84% depending upon the assessment tool and severity of liver disease. Hence it is necessary to understand the dietary habits in detail, develop appropriate nutritional strategies, and standardize the use of nutritional assessment tools for the determination of these conditions.

Across India, 4 focus-group meetings involving 48 experts in the field of Gastroenterology were conducted to discuss prevalence, etiopathogenesis, and diagnosis of malnutrition and sarcopenia in cirrhotic patients. Nutritional requirements, assessment, management strategies, and guidelines were discussed. Expert opinions from all the meetings were collated and are presented in this paper.

MALNUTRITION AND SARCOPENIA WITH LIVER CIRRHOSIS

Compromise in liver function in patients with cirrhosis impairs nutrient absorption due to increased protein catabolism, decreased glycogen synthesis and increased lipolysis leading to malnutrition.[12] Malnutrition is a measurable change in physical and mental functions secondary to altered body composition and cell mass, resulting in impaired quality of life and poor clinical outcomes.[13,14] Decreased energy and protein intake in cirrhosis due to ascites, salt restrictions, micronutrient deficiencies, loss of appetite, and portal hypertension cause malnutrition. Other factors such as malabsorption and altered metabolism of macro and micronutrients, decreased protein synthesis, hypermetabolism, increased fat utilization and energy expenditure, insulin resistance, disturbances of substrate utilization, hormonal changes, and gut-microbiome dysbiosis are also implicated in malnutrition development.[14,15]

Altered metabolism of carbohydrates, proteins, and lipids due to increased proinflammatory cytokines leads to increased glucogenesis and reduced glycogen synthesis in the liver. This hypermetabolism has been linked to hemodynamic alterations and poor prognosis in post-transplant patients.[16] Although malnutrition is correlated with prognostic outcomes, it is not included in common tools such as the Child-Pugh score and model of end-stage liver disease (MELD) for determination of prognosis. Therefore, it is important to consider the use of validated and specific malnutrition screening tools in addition while assessing patients with cirrhosis.[14]

Sarcopenia is an important malnutrition-related complication characterized by progressive and generalized loss of skeletal muscle mass and strength causing physical disability, poor quality of life, transplant complications. Sarcopenia also causes increased mortality, and tumor recurrence in patients with hepatocellular carcinoma.[17] Dysregulated muscle protein turnover in patients with cirrhosis caused by alteration of key molecular pathways, hyperammonemia-induced increase in myostatin expression and activation of nuclear factor kappa B causing reduced muscle protein synthesis, and reduced levels of testosterone in patients with cirrhosis are implicated in the pathogenesis of sarcopenia.[1,13]

The European Working Group on Sarcopenia in Older People (EWGSOP) uses criteria such as low muscle quality and quantity and low physical performance to diagnose age-related sarcopenia.18 Although there is no defined method or cut-off value to assess sarcopenia in patients with CLD, criteria like those for age-related sarcopenia are generally used. Self-reported questionnaires can be used for screening, followed by assessment of muscle mass using skeletal mass index of the third lumbar vertebra (L3 SMI) using computed tomography (CT) scans, mid arm muscle circumference (MAMC), ultrasound and magnetic resonance imaging scans.

Hand grip strength (HGS) measurements, 6-min walk distance (6MWD), short physical performance battery test (SPPB), and gait speed are practical clinical measures

for measurement of muscle strength and physical performance in patients with CLD.1 Age, gender, and level of physical activity are linked to sarcopenia, with higher incidence of sarcopenia often being reported in older individuals and males.19

Although malnutrition is expected to be highly prevalent in patients with cirrhosis, especially those with the decompensated type, studies have reported that there could be wide variation in its prevalence ranging from 5% to 92%.[5,14] This variation can be explained by lack of proper diagnosis, underreporting, and variation in the methods used for the assessment. According to the consensus statement of the Indian National Association for Study of the Liver (INASL) developed in 2021, malnutrition was found to be higher in Indians compared to the global population.[13]

Because Indians have a lower muscle mass than western populations and Indians primarily follow vegetarian diets, sarcopenia is seen in about half of the patients with chronic advanced liver disease, which is higher compared to other countries.[13,20] Another study reported a 61% prevalence of sarcopenia in Indian patients with CLD, which was associated with hepatic encephalopathy (HE) and ascites.[21] So sarcopenia needs to be assessed properly in Indian patients especially in the late stages.

Changes in protein metabolism, reduced dietary intake, and accelerated starvation in patients with cirrhosis increase their protein and energy requirements such that appropriate nutritional management is crucial. High energy/protein diets, nutritional supplements, and enteral/parenteral nutrition are recommended along with physical exercise to treat malnutrition and sarcopenia.[5] As the protein turnover in cirrhotic patients is high and branched-chain amino acids (BCAAs) are used for energy and detoxification of ammonia, BCAA supplements are often recommended.[13] BCAA supplements have been shown to increase muscle protein synthesis and reduce autophagy in malnourished cirrhotic patients with HE.[22]

The European society of clinical nutrition and Metabolism (ESPEN) and European Association for the Study of the Liver (EASL) have recommended increased energy and protein intake in malnourished and sarcopenic patients along with unrestricted protein intake in those with HE.[23]

This recommendation is in accordance with the INASL guidelines, which have an additional recommendation for calorie intake of 50%-60% from carbohydrates and 20%-30% from fats.[13] Due to inadequate dietary intake and malabsorption, micronutrient deficiency is common in patients with cirrhosis such that most guidelines recommend liberal oral multivitamin supplementation in decompensated patients due to difficulties in diagnosis of vitamin and mineral deficiences.[23,24]

Expert opinion

Experts discussed the causes of high prevalence of cirrhosis-related malnutrition in Indian clinical settings, suggested methods for assessment of malnutrition and sarcopenia in the routine practice and expressed their views on nutritional support and supplementation. The prevalence of malnutrition in clinical practice was seen to vary from 15% to 70% with a higher rate amongst patients with alcoholic liver disease and decompensated cirrhosis. According to experts, dietary habits in India involving the avoidance of protein-rich foods and consumption of vegetarian and vegan diets, lack of exercise and limited food intake were linked to higher levels of malnutrition especially in alcohol abuse patients.

Non-alcoholic steatohepatitis (NASH) is also observed increasingly in the clinical practice now as a cause of advanced liver disease. In India definite etiological differences could be observed between rural and urban populations, with NASH cirrhosis being more common in urban areas and alcoholic cirrhosis in the rural population.

Experts agreed on the lack of nutritional assessment and sarcopenia diagnosis in patients with cirrhosis and attributed it to untrained manpower and lack of time. They suggested the use of quick and practical tools such as HGS, gait speed, hemodynamic parameters and body mass index (BMI) in clinical and hospital settings to determine muscle mass and strength. Integration of L3 SMI measurements with routine CT scans in cirrhotic patients was suggested for more objective sarcopenia assessment. However, when the CT scans and MELD scores were compared with liver frailty index (LFI), the experts felt that LFI was superior for assessment of sarcopenia and frailty.

In addition, LFI values were an important criterion for liver transplant. Candidates with LFI of 4-5 along with clinical and nutritional assessment were considered better suitable for transplant.

The importance of nutritional assessment and advice as an integral part of a management strategy to result in better transplant outcomes was emphasized by experts. They also recommended protein intake via nasogastric feeding tubes to pre-transplant patients for 2-3 weeks to improve transplant outcomes.

Although there was some debate on the role of ammonia and ammonia-lowering therapies in cirrhotic patient, the experts reached a consensus supporting the use of BCAAs as ammonia scavengers for decelerating sarcopenia when included in the early course of treatment in patients with HE. Overall, the experts advocated systematic nutritional assessment and advice for all patients with cirrhosis in accordance with the severity of the disease and transplant requirements.

ASSESSMENT OF NUTRITIONAL STATUS

The high prevalence of malnutrition in patients with cirrhosis and malnutrition-related complications that result in poor outcomes and mortality makes it necessary to use a comprehensive nutritional assessment protocol to improve prognosis.25,26 Nutritional screening and assessment are important for determining the risk of malnutrition and severity of existing malnutrition that can guide the overall management of cirrhotic patients. The absence of a gold standard tool for malnutrition assessment and inaccurate measurements of weight and BMI due to edema and ascites that are common in cirrhotic patients makes malnutrition assessment challenging.15 A combined approach that incorporates recommendations from practice guidelines, published reports, and clinical judgement is used for nutritional assessment.

Figure 1 is a schematic diagram of the screening and assessment protocol recommended for patients with cirrhosis. Rapid pre-screening of all cirrhotic patients is recommended, and malnutrition assessment and risk stratification are performed based on calculated CP score and BMI using validated tools. Patients with CP score C category or those with BMI of <18.5 kg/m2 are assumed to have a high risk for malnutrition and are subjected to detailed nutritional and sarcopenia assessment.13,24 For all other groups, scoring tools such as the Royal Free Hospital-Nutritional Prioritizing Tool (RFH-NPT), Nutrition Risk Screening 2002 (NRS-2002), and the Liver Diseases Undernutrition Screening Tool (LDUST) are utilized for risk categorization.

RFH-NPT is a preferred tool that discriminates patients into high, medium, and low categories using variables such as alcoholic hepatitis, fluid overload, dietary intake, BMI, unplanned weight loss, and dietary reduction.[13,24] It has been shown to correlate with liver-related complications such as HE, ascites and hepatorenal syndrome. In a study on cirrhotic patients, the RFH-NPT was found to be an independent predictor of clinical deterioration, complications, and transplant-free survival.[27]

Other tools such as the NRS-2002 that considers parameters such as weight loss, food intake, and BMI along with disease severity are also used for nutritional screening, but do not account for fluid retention, which is common in advanced cirrhotic patients. Malnutrition universal screening tool (MUST) that is recommended for use by societies also incorporates BMI and weight loss, which are affected by fluid retention resulting in unreliable scoring. Patients' subjective assessment of symptoms using patient-directed questions is used in the LDUST tool, which is convenient but requires validation with clinical outcomes to be used reliably.[28] Thus, it is necessary to utilize screening tools that are validated and simple enough to integrate into clinical practice.

Following the screening, patients with medium nutritional risk are recommended to undergo a detailed nutritional assessment and those in the high-risk category undergo nutritional and sarcopenia assessment. Nutritional assessment and lifestyle interventions are advocated in patients with BMI ≥30 kg/m2. As nutritional assessments are comprehensive and lengthy, it is necessary to have expert dieticians to perform them on a routine basis for effective patient management.

Nutritional assessments involve detailed assessments of dietary intake using patient-reported food diaries and analysis by dieticians to understand food routines, fasting periods, protein source information, and any nutritional deficiencies. Global assessment tools such as Royal Free Hospital-Global Assessment (RFH-GA) and subjective global assessment (SGA) use dietary history and metabolic and physical examination parameters to rate patients into malnourishment categories. Although the RFH-GA tool shows a better correlation with nutritional status and post-transplant outcomes than the SGA, its subjective nature and gender generalizability are debatable.[24,29] Anthropometric measurements that are not affected by fluid retention such as MAMC and triceps skin fold can also be used to evaluate nutritional status in end-stage liver disease patients.[15]

It is important to include an assessment of sarcopenia in patients identified as high risk following nutritional screening using measurements of muscle mass, muscle strength, physical performance, and frailty. Imaging techniques such as CT scans, magnetic resonance spectroscopy, and dual-energy X-ray absorptiometry (DEXA) can be used to determine total body weight, fat mass, lean muscle mass, and bone mineral density.[13] The most common muscle mass measurement using CT is the cross-sectional area of L3 SMI, which incorporates the measure of the psoas, paraspinal, and abdominal muscles at L3.[1,13] Because abdominal CT scans are routinely performed in transplant candidates, the L3 SMI measure is commonly used without the need for additional investigations.

Body composition can be analyzed by bioimpedance analysis (BIA) that allows for quick determination of lean mass and is an attractive option because of its convenience, absence of radiation exposure, and low cost. However, both DEXA and BIA are subject to inaccurate results in cases of fluid retention and have limited accessibility, thus making CT scans preferable for sarcopenia diagnosis. Because muscle mass of Indians is lower than that of Caucasians, adjustments of cut-off values for sarcopenia diagnosis are necessary and normative values from Western populations are not recommended for use. The INASL has developed CT SMI cut-off values of <42 cm2/m2 and <38 cm2/m2 for Indian men and women, respectively, which are lower than cut-off values in Western countries.[13,30] HGS is used to determine muscle strength. It is a simple and cost-effective technique that can be performed with a

handheld dynamometer and is found to correlate with mortality.[13,31] Impaired physical performance can be used to diagnose sarcopenia by tests such as gait speed, 6MWD, SPPB, and LFI. The link between cirrhosis and physical frailty and their impact on adverse outcomes such as wait-list mortality makes it necessary to use frailty tools to assess muscle strength in an objective manner. The LFI test includes a combination of tests to assess frailty such as HGS (measure of nutritional status), balance testing (measurement of neuromuscular function), and chair stands (marker of lower extremity weakness). It is a practical test that can be performed at the bedside or in an outpatient setting.[13,32] Therefore, nutritional assessment and diagnosis of malnutrition and sarcopenia are critical elements for the management of cirrhotic patients and should be performed in a comprehensive manner to enable recommendations for nutritional therapy.

Expert opinion

Experts emphasized the importance of nutritional assessment and treatment as an integral part of liver cirrhosis management. Different tools to assess nutritional status and sarcopenia were presented from the perspective of cirrhosis and liver transplant patients.

Experts discussed the lack of routine screening in cirrhotic patients and agreed upon the use of simple tests such as BMI, HGS, walk test, and sit-ups for nutritional assessment. The validated RHF-NPT tool was suggested to be used for screening, but with cut-off values specific for the Indian population. Experts recommended the use of CT scans for critically ill patients, whereas LFI was suggested to be used routinely in clinical practice for assessment of muscle mass or sarcopenia. In addition to screening tests, clinician judgement, patient history, and serum albumin levels were considered important to gain information on baseline nutritional status, which would help to determine the efficacy of nutritional treatment.

Challenges faced in the assessment of nutritional status included improper patient history, loss to follow-up, and lack of periodic assessment, which led to inaccurate data. Early assessment of nutritional status and sarcopenia was highlighted as an important factor in improving prognosis especially in obese patients with NASH and in patients awaiting liver transplant. Overall, experts supported the assessment of all patients and use of practical tools or subjective and clinical assessments that would be suitable to handle heavy patient volumes.

In addition to the challenges with diagnosis, lack of physician intent and awareness was quoted as being an important reason for the absence of routine testing. To make screening available at all centers, experts suggested the organization of dedicated teams with dieticians and support staff that would enable routine screening for liver transplant and out-patient department patients. Awareness programs to train gastroenterologists on the availability and use of tools was recommended.

Following the testing, the experts agreed on the importance of tailoring dietary supplementation and nutritional intake as per patients' needs that could be performed by junior doctors and multidisciplinary staff. Micronutrient supplementation was recommended to be given based on clinical evaluation to improve treatment outcomes and patient's quality-of-life.

TREATMENT OF MALNUTRITION AND SARCOPENIA

Malnutrition in cirrhosis is attributed to aggravated starvation due to decreased dietary intake (protein and energy) caused by dysgeusia, anorexia, salt and protein restricted food, portal hypertension causing disturbances in gut motility, nutrient malabsorption, prolonged periods of fasting during hospitalization and diagnostic procedures, encephalopathy, and gastrointestinal bleeding.[5,33] Various factors such as increased muscle proteolysis, increased gluconeogenesis, and impaired muscle biosynthesis are implicated in the development of sarcopenia in cirrhotic patients. As several mechanisms are involved in malnutrition and sarcopenia, a combination of nutritional, physical, and pharmacological treatments is suggested to improve prognostic outcomes in patients.

Nutritional support and supplementation form an integral component of management of cirrhotic patients due to reduced dietary intake. This approach is based on maintenance of a nutritional equilibrium between the energy supply and the total energy expenditure, which includes resting energy expenditure, food-related thermogenesis, and physical activity. Gluconeogenesis causes an increase in REE in cirrhotic patients, and energy utilization from proteins and lipids is increased necessitating frequent feeding and increased protein intake along with micronutrient supplementation.[13] Late evening snacks, early morning breakfasts, and nocturnal feedings have been recommended to shorten periods of fasting. One study has shown an increase in body protein stores equivalent to 2 kg of lean tissue sustained over 12 months in cirrhosis patients receiving nighttime feeds.[34]

Table 1 contains various guideline recommendations for nutritional management of cirrhotic patients that focus on dietary intake, frequency of meals, nocturnal feeding, and BCAA and other supplements. In addition to these, administration of enteral nutrition when required, avoiding, or minimizing salt and food, physical exercise, and nutritional counseling should accompany guideline recommendations to improve outcomes. Sarcopenia management involves pharmacological therapies such as vitamin D supplementation, ammonia lowering treatments (L-carnitine), and testosterone treatments to preserve muscle mass, bone mass, and hemoglobin levels and to decrease inflammation.35-37 Immunonutrition,

i.e., activation of the immune system by nutrients such as amino acids (glutamine, arginine), omega-3 fatty acids, and nucleotides can also be applied for sarcopenia management.[38]

Alterations in protein metabolism and reduced dietary intake require adequate protein intake in cirrhotic patients to prevent muscle catabolism. Recent guidelines have specified quantities of proteins to be consumed along with emphasis on removal of protein restrictions except temporary restrictions in patients with HE. The type of protein, animal, vegetable, or dairy has been shown to be important in terms of their effect on protein synthesis and status in cirrhotic patients with HE.[39] Although some studies have shown improvement in, HE, mental status, and nitrogen balance with vegetable proteins compared to animal proteins, the evidence is not robust enough to claim superiority of vegetable versus animal proteins. Thus, INASL guidelines recommend a combination of increased intake of vegetable proteins along with supplementation with BCAA, eggs, and lean meats to meet protein requirements and calcium, iron, and energy needs.[13,24]

Serum concentrations of BCAAs such as leucine, isoleucine, and valine levels have been shown to be decreased in patients with liver cirrhosis, resulting in amino acid imbalance that causes disease progression and HE. Dietary oral BCAA supplementation is important to counteract the effects of hyperammonemia in patients with liver cirrhosis by facilitating ammonia detoxification and supporting muscle glutamine synthesis and muscle mass. The role of BCAAs in liver cirrhosis is multifactorial and includes induction of mitochondrial biogenesis and inhibition of reactive oxygen species, stimulation of albumin and glycogen synthesis, inhibition of liver apoptosis and stimulation of liver regeneration, and improved insulin resistance.[40]

Several clinical studies have demonstrated a positive effect of BCAAs in advanced cirrhosis via improvement of prognostic outcomes such as decreased hospital admission rate and length of stay, and improvement in Child-Pugh scores, nutritional parameters, and liver function tests.41Additionally long-term BCAA supplementation was found to be associated with improvement in prognostic markers (MELD score, Child-Pugh score, serum albumin, total bilirubin), and improvement in muscle strength and volume when combined with walking exercises.[42-44] A Cochrane meta-analyses that evaluated the effect of BCAAs in patients with HE (n=16 trials) showed a beneficial effect on HE manifestations when administered orally without any significant effect on mortality, quality of life, or nutritional parameters.[45]

In a cross-sectional, questionnaire-based survey conducted with gastroenterologists pan India regarding BCAA use in clinical practice, a high percentage of physicians considered Fischer ratio (related to amino acid imbalance) and long-term BCAA supplementation (>6 months) an important treatment option for the management of patients with HE. In addition, one-third of the participating physicians observed an improvement in quality of life, reduced HE episodes, and increased muscle mass in 40%-60% of their patients receiving BCAA supplementation.[46] Therefore, a comprehensive nutritional management plan involving adequate protein and calorie intake, nutritional supplements, and BCAA supplementation is important for prevention or correction of malnutrition and sarcopenia in patients with end-stage liver disease or HE.

Expert opinion

The experts discussed the causative factors leading to starvation in cirrhosis, guideline recommendations on type of food, meal frequency, and energy and protein supplementation. The role of BCAAs for nutritional management in cirrhosis and clinical studies evaluating their efficacy were presented.

The importance of nutritional management in cirrhotic patients with evaluation of regular dietary habits prior to recommendation of protein and calorie requirements and supplementation was discussed. Late night snacks of proteins and complex carbohydrates such as banana shakes, and energy bars were suggested to prevent prolonged periods of fasting. There was conflicting advice on the use of testosterone and growth hormones, whereby some panelists supported the use of testosterone and growth hormones, whereas others stated that more studies were necessary to assess the efficacy and safety of anabolic steroids in liver cirrhosis. Experts advised avoiding severe salt restrictions and including a diuretic instead to prevent food avoidances. Limited liquid intake was also advocated to prevent ascites. Dietary advice, counseling, and physical exercise were suggested to be important particularly in patients with cirrhosis due to NASH and needed to be included in the management plan by a multidisciplinary team.

BCAA supplementation and high protein intake were extensively discussed and considered to be important in patients with HE, decompensated cirrhosis, and refractory ascites. According to experts, early and long-term treatment with BCAAs would help reduce complication rates and decompensation but discussed limitations of its use due to high cost and unpalatability. Formulation with food or liquids was recommended to prevent compliance and palatability issues with BCAA. BCAA supplements were recommended for use in patients who were unable to achieve dietary protein intake and for hospitalization time only, whereas plant-based proteins and non-vegetarian protein sources were deemed adequate for all other patients. Vitamin supplements were also recommended along with periodic assessments of micronutrient levels to prevent toxicity issues.

Ryles tube feeding was believed to have a place for patients with alcoholic cirrhosis and sick patients with anorexia who could not maintain sufficient dietary intake. Further studies evaluating the efficacy of protein and calorie supplementation, physical exercise, and BCAA were considered necessary to determine the efficacy of each intervention separately in the management of malnutrition and sarcopenia.

Table 1: Guideline recommendations for nutritional management in cirrhosis patients.

Guideline	Energy	Protein	BCAA	Multinutrients and vitamins	Other recommendations
EASL	For non-obese: 35 kcal/kg/d For obese: 500-800 kcal/day	For non-obese: ≥ 1.2-1.5 g/kg/d For obese: >1.5 g/kg/d	Recommended in decompensated cirrhotic patients	Vitamin D supplements in patients with levels <20 ng/ml to reach serum levels >30 ng/ml. Sodium restriction to 80-120 mmol/day	Late evening oral supplementation and breakfast in decompensated patients. Enteral nutrition in case of insufficient oral intake. Increase in physical activity and lifestyle program in obese cirrhotic patients
ESPEN	For malnourished: 30-35 kcal/kg/d For obese: 25 kcal/kg/d (obese)	For non-malnourished: 1.2 g/kg/d For malnourished and sarcopenic: 1.5 g/kg/d For obese cirrhotic: 2-2.5 g/kg/d	Long-term BCAA (0.25 g/kg/d)	Micronutrient supplements in case of clinically suspected deficiency	Consumption of 3-5 meals/day and late evening snack. No protein restriction in HE patients
INASL	For cirrhosis patients: 30-35 kcal/kg/d	For cirrhosis patients: 1.2-1.5 g/kg/d	Leucine-rich BCAA supplementation recommended in patients with HE	Fat-soluble and water-soluble vitamin supplementation is recommended for deficiencies identified by laboratory tests	Multiple small frequent meals (4-6 h) with complex-carbohydrate bedtime snack and protein-rich breakfast. Nasogastric tube or parenteral nutrition in patients with advanced HE or protected airways

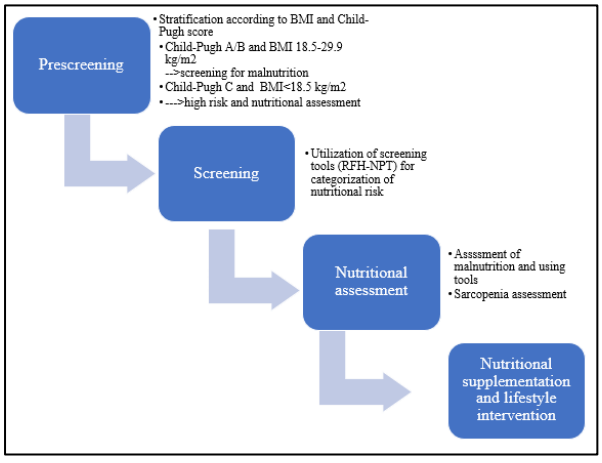

Figure 1: Nutritional screening and assessment algorithm according to EASL guidelines and INASL consensus statement.

CONCLUSION

Altered dietary intake, malabsorption, and impaired metabolism result in malnutrition and muscle wasting or sarcopenia in patients with liver cirrhosis. Malnutrition and sarcopenia can cause complications such as HE, ascites, and post-transplant issues that affect prognostic outcomes and have negative effects on quality of life, increased mortality, and higher economic burden. Thus, diagnosis of nutritional deficiencies, muscle strength and mass, and physical performance is crucial to be able to manage these conditions in a timely manner and prevent disease progression.

A thorough assessment of nutritional status by a multidisciplinary team of gastroenterologists and dieticians must be performed in accordance with the risk profile of the patient. Following screening and diagnosis of nutritional deficiencies, a comprehensive nutritional management plan consisting of adequate dietary protein and caloric intake and multivitamin and BCAA supplementation is recommended according to various guideline recommendations. Studies have shown that BCAA supplementation in the treatment of malnutrition and sarcopenia along with dietary adjustments is an optimal treatment and has shown better clinical outcomes.

ACKNOWLEDGEMENTS

The authors acknowledge Namita Kunal Dalal for medical writing support and editorial assistance.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Allen SL, Quinlan JI, Dhaliwal A, Armstrong MJ, Elsharkawy AM, Greig CA, et al. Sarcopenia in chronic liver disease: mechanisms and countermeasures. Am J Gastrointest Liver Physiol. 2021;320:241-57.
2. Shah NJ, Royer A, John S. Acute liver failure. In: StatPearls. Treasure Island (FL): StatPearls Publishing. 2023. Available at: https://www.ncbi.nlm.nih.gov. Accessed on 17 May 2024.
3. Das J. Liver disease: managing the complications. Pharm J. 2011. Available at: https://pharmaceutical-journal.com/article/ld/liver-disease. Accessed on 17 May 2024.
4. Sharma A, Nagalli S. Chronic liver disease. [Updated 2023 Jul 3]. In: StatPearls [Internet]. Treasure Island (FL):2024. Available at: https://www.ncbi.nlm.nih.gov.
5. Meyer F, Bannert K, Wiese M, Esau S, Sautter LF, Ehlers L, et al. Molecular mechanism contributing to malnutrition and sarcopenia in patients with liver cirrhosis. Int J Mol Sci 2020;21:5357.
6. Zhou W-C, Zhang Q-B, Qiao L. Pathogenesis of liver cirrhosis. World J Gastroenterol 2014;20:7312-24.
7. Mokdad AA, Lopez AD, Shahraz S, Lozano R, Mokdad AH, Stanaway J, et al. Liver cirrhosis mortality in 187 countries between 1980 and 2010: A systematic analysis. BMC Med. 2014;12:145. doi: 10.1186/s12916-014-0145-y.
8. Asrani SK, Devarbhavi H, Eaton J, Kamath PS. Burden of liver diseases in the world. J Hepatol 2019;70:151-71.
9. Devarbhavi H, Asrani SK, Arab JP, Nartey YA, Pose E, Kamath PS. Global burden of liver disease: 2023 update. J Hepatol 2023;79:516-37.
10. Mukherjee PS, Vishnubhatla A, Amarapurkar DN, Das K, Sood A, Chawla YK, et al. Etiology and mode of presentation of chronic liver diseases in India: a multi centric study. PLoS One 2017;12:e0187033. doi: 10.1371/journal.pone.0187033.
11. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, et al. Sarcopenia: European consensus on definition and diagnosis: Report of the European Working Group on Sarcopenia in Older People. Age Ageing 2010;39:412-23.
12. Bémeur C, Butterworth RF. Nutrition in the management of cirrhosis and its neurological complications. J Clin Exp Hepatol 2014;4:141-50.
13. Puri P, Dhiman RK, Taneja S, Tandon P, Merli M, Anand AC. Nutrition in chronic liver disease: Consensus of the Indian National Association for Study of the Liver. J Clin Exp Hepatol 2021;11:97-143.
14. Traub J, Reiss L, Aliwa B, Stadlbauer V. Malnutrition in patients with liver cirrhosis. Nutrients 2021;13:540. doi: 10.3390/nu13020540.
15. Bémeur C, Desjardins P, Butterworth RF. Role of nutrition in the management of hepatic encephalopathy in end-stage liver failure. J Nutr Metab 2010;2010:489823.
16. Müller MJ, Böttcher J, Selberg O, Weselmann S, Böker KH, Schwarze M, et al. Hypermetabolism in critically stable patients with liver cirrhosis. Am J Clin Nutr. 1999;69:1194-201.
17. Chang KV, Chen JD, Wu WT, Huang KC, Hsu CT, Han DS. Association between loss of skeletal muscle mass and mortality and tumor recurrence in hepatocellular carcinoma: a systematic review and meta-analysis. Liver Cancer. 2018;7:90-103.
18. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, et al. Sarcopenia: European consensus on definition and diagnosis. Age Ageing. 2010;39:412-23.
19. Kim G, Kang SH, Kim MY, Baik SK. Prognostic value of sarcopenia in patients with liver cirrhosis: a systematic review and meta-analysis. PLoS One. 2017;12:186990.
20. Thyloor KS, Sharma S, Kumar M, Ghuman SS, Arora A, Ranjan P. A Prospective Study of Prevalence and Impact of Sarcopenia on Short-term Mortality in Hospitalized Patients with Liver Cirrhosis. J Clin Exp Hepatol. 2023;13(6):946-954.
21. Gajula U, Murugan N. Assessment of sarcopenia in patients with chronic liver disease. J Clin Exp Hepatol. 2018;8:67.
22. Bunchorntavakul C, Reddy KR. Review article: malnutrition/sarcopenia and frailty in patients with cirrhosis. Ailment Pharmacol Ther. 2020;51:64-77.
23. Cederholm T, Barazzoni R, Austin P, Ballmer P, Biolo G, Bischoff SC, et al. ESPEN guidelines on definitions and terminology of clinical nutrition. Clin Nutr. 2017;36:49-64.
24. Merli M, Berzigotti A, Zelber-Sagi S, Dasarathy S, Montagnese S, Genton L, et al. EASL clinical practice guidelines on nutrition in chronic liver disease. J Hepatol. 2019;70:172-93.
25. Molfino A, Johnson S, Medici V. The challenges of nutritional assessment in cirrhosis. Curr Nutr Rep. 2017;6:274-80.
26. Mendenhall CL, Andersen S, Weesner RE, Goldberg SJ, Crolic KA. Protein-calorie malnutrition associated with alcoholic hepatitis. Veterans Administration Cooperative Study Group on Alcoholic Hepatitis. Am J Med. 1984;76:211-22.
27. Borhofen SM, Gerner C, Lehmann J, Fimmers R, Görtzen J, Hey B, et al. The Royal Free Hospital-Nutritional Prioritizing Tool is an independent predictor of deterioration of liver function and survival in cirrhosis. Dig Dis Sci. 2016;61:1735-43.
28. McFarlane M, Hammond C, Roper T, Mukarati J, Ford R, Burrell J, et al. Comparing assessment tools

for detecting undernutrition in patients with liver cirrhosis. Clin Nutr ESPEN. 2018;23:156-61.
29. Tandon P, Raman M, Mourtzakis M, Merli M. A practical approach to nutritional screening and assessment in cirrhosis. Hepatology. 2017;65:1044-57.
30. Anand A, Saraya A. Assessment of sarcopenia in chronic liver disease: Indian perspective. Clin Liver Dis (Hoboken). 2021;18:164-7.
31. Sinclair M, Chapman B, Hoermann R, Angus PW, Testro A, Scodellaro T, et al. Handgrip strength adds more prognostic value to the model for end-stage liver disease score than imaging based on measures of muscle mass in men with cirrhosis. Liver Transpl. 2019;25:1480-7.
32. Lai JC, Covinsky KE, Dodge JL, Boscardin WJ, Segev DL, Roberts JP, et al. Development of a novel frailty index to predict mortality in patients with end-stage liver disease. Hepatology. 2017;66:564-74.
33. Plauth M. Basics in clinical nutrition: nutritional support in liver disease. e-SPEN. 2010:104-6.
34. Plank LD, Gane EJ, Peng S, Muthu C, Mathur S, Gillanders L, et al. Nocturnal nutritional supplementation improves total body protein status of patients with liver cirrhosis: a randomized 12-month trial. Hepatology. 2008;48:557-66.
35. Carey EJ, Lai JC, Sonnenday C, Tapper EB, Tandon P, Duarte-Rojo A, et al. A North American expert opinion statement on sarcopenia in liver transplantation. Hepatology. 2019;70:1816-29.
36. Hiramatsu A, Aikata H, Uchikawa S, Ohya K, Kodama K, Nishida Y, et al. Levocarnitine use is associated with improvement in sarcopenia in patients with liver cirrhosis. Hepatol Commun. 2019;3:348-55.
37. Sinclair M, Grossmann M, Hoermann R, Angus PW, Gow PJ. Testosterone therapy increases muscle mass in men with cirrhosis and low testosterone: a randomized controlled trial. J Hepatol. 2016;65:906-13.
38. Calder PC. Immunonutrition in surgical and critically ill patients. Br J Nutr. 2007;98:133-9.
39. Eghtesad S, Poustchi H, Malekzadeh R. Malnutrition in liver cirrhosis: the influence of protein and sodium. Middle East J Dig Dis. 2013;5:65-75.
40. Tajiri K, Shimizu Y. Branched-chain amino acids in liver diseases. World J Gastroenterol. 2013;19:7620-9.
41. Marchesini G, Bianchi G, Merli M, Amodio P, Panella C, Loguercio C, et al. Nutritional supplementation with branched-chain amino acids in advanced cirrhosis: a double-blind randomized trial. Gastroenterology. 2003;124:1792-801.
42. Park JG, Tak WY, Park SY, Kweon YO, Jang SY, Lee YR, et al. Effects of branched-chain amino acids (BCAAs) on the progression of advanced liver disease: a Korean nationwide, multicentre, retrospective, observational, cohort study. Medicine (Baltimore). 2017;96:65-80.
43. Hiraoka A, Michitaka K, Kiguchi D, Izumoto H, Ueki H, Kaneto M, et al. Efficacy of branched-chain amino acid supplementation and walking exercise for preventing sarcopenia in patients with liver cirrhosis. Eur J Gastroenterol Hepatol. 2017;29:1416-23.
44. Tejavath AS, Mathur A, Nathiya D, Singh P, Raj P, Suman S, et al. Impact of branched chain amino acid on muscle mass, muscle strength, physical performance, combined survival, and maintenance of liver function changes in laboratory and prognostic markers on sarcopenic patients with liver cirrhosis (BCAAS study): A randomized clinical trial. Front Nutr. 2021;8:7157-95.
45. Gluud LL, Dam G, Les I, Marchesini G, Borre M, Aagaard NK, et al. Branched-chain amino acids for people with hepatic encephalopathy. Cochrane Database Syst Rev. 2017;5:19-39.
46. Bhargava V, Sarda K, Das S. Current practice of branched chain amino acids administration in patients with liver cirrhosis: a physician survey. J Clin Diag Res. 2021;15:44-8.

Cite this article as: Vinayakumar KR. Malnutrition and sarcopenia in liver cirrhosis: Indian expert opinion perspective on screening and managements. Int J Res Med Sci 2024;12:3997-4005.