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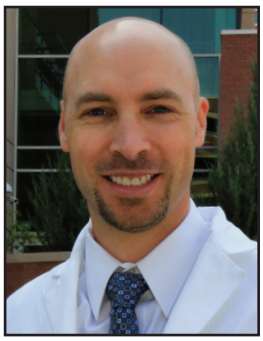
Nutrition Considerations in the Cirrhotic Patient



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Malnutrition is commonly seen in individuals with advanced liver disease, often resulting from a combination of factors including poor oral intake, altered absorption, and reduced hepatic glycogen reserves predisposing to a catabolic state. The consequences of malnutrition can be far reaching, leading to a loss of skeletal muscle mass and strength, a variety of micronutrient deficiencies, and poor clinical outcomes. This review seeks to succinctly describe malnutrition in the cirrhosis population and provide clarity and evidence-based solutions to aid the bedside clinician. Emphasis is placed on screening and identification of malnutrition, recognizing and treating barriers to adequate food intake, and defining macronutrient targets.

INTRODUCTION

The Problem

Individuals with cirrhosis are at high risk of malnutrition for a multitude of reasons. Cirrhotic livers lack adequate glycogen reserves, therefore these individuals rely on muscle breakdown as an energy source during overnight periods of fasting.[1] Well-meaning providers often recommend a variety of dietary restrictions—including limitations on fluid, salt, and total calories—that are often layered onto pre-existing dietary restrictions for those with co-existent conditions such as diabetes or renal disease. Furthermore, different underlying etiologies of liver disease, such as heavy alcohol use and chronic cholestasis, predispose cirrhotic patients to a variety of macro- and micronutrient deficiencies as a consequence of poor intake and altered absorption.

As liver disease progresses, its complications further increase the risk for malnutrition. Large volume ascites can lead to early satiety and decreased oral intake. Encephalopathy also contributes to decreased oral intake and may lead to inappropriate recommendations for protein restriction. Frequent hospitalizations and procedures can lead to periods of prolonged fasting. In combination, the physiology of liver disease and its consequences lead to a prevalence of malnutrition in the cirrhotic population that has been described as nearly universal in those awaiting liver transplantation (LT), and so high in all individuals with cirrhosis that current guidelines recommend anticipating malnutrition, protein depletion, and trace element deficiencies.[1,2]

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The consequences of malnutrition are wide ranging. Sarcopenia can become one of the more obvious and discouraging physical changes patients and families notice. An abundance of evidence links low body mass index (BMI), frailty, and progressive sarcopenia with poor outcomes after liver transplantation.[3,4] Micronutrient deficiencies can lead to a variety of consequences, ranging from anemia to increased bone fracture risk to altered taste. In this setting, identification of malnourished individuals coupled with targeted nutritional interventions are critical to improving quality of life and optimizing clinical outcomes in individuals with cirrhosis.[5]

The Practical Approach to Nutrition in Liver Disease

Screen for Malnutrition

A typical clinical encounter with a patient afflicted by advanced liver disease often requires careful consideration of their primary liver disease, management of liver decompensations, ensuring that appropriate screening of esophageal varices and hepatocellular carcinoma has been completed, and determining whether liver transplantation referral or end-of-life care is appropriate. An important yet often overlooked facet of these complex encounters is consideration of the patient's nutritional risk.

All patients with advanced liver disease should be screened for malnutrition.[6] Decompensated cirrhotics and those with a BMI of ≤ 18.5 kg/m^2 are considered high risk regardless of screening.[6,7] If a patient does not meet either of the aforementioned criteria, multiple screening tools can be used to stratify patients according to their nutritional risk. The Royal Free Hospital-Nutrition Prioritizing (RFH-NP) tool is easy to administer, validated in the cirrhotic population, and has been shown to correlate with disease severity.[8,9] In those identified as moderate or high nutritional risk, a comprehensive nutritional assessment should be conducted by a registered dietitian.[6]

As outlined in Table 1, a comprehensive nutritional assessment should include evaluation for sarcopenia (e.g. lean muscle mass), use of a global assessment tool (GA), and review of the patient's self-reported dietary intake.[6] Sarcopenia, defined as a generalized reduction in muscle mass and function due to age or illness, is likely present when low muscle strength is detected and is confirmed when low muscle quantity or quality is found.[6,10] Handgrip strength has been shown to correlate with strength in other body compartments, and is a cheap, fast, and validated method for evaluating muscle strength.[10] Handgrip strength has also been shown to predict major complications and mortality in the cirrhotic population.[11] An accepted alternative is the chair rise test, defined as the amount of time needed for a patient to rise from a chair five times.[10] The Liver Frailty Index is an increasingly used easy tool that combines hand grip strength, chair rise time, and ability to stand in different positions into a single metric to

Table 1. Comprehensive Nutritional Assessment

Sarcopenia Assessment	Low Strength (sarcopenia probable) **AND** Low Muscle quantity/quality (sarcopenia confirmed) **WITH** Low physical performance (severe sarcopenia)
Global Assessment	RFH-GA **OR** SGA
Dietary Intake Report	1 Day **OR** 3 Day

Table 2. Liver Frailty Index

Handgrip Strength – Jamar Dynamometer
With Dynamometer in 2nd position, take average of 3 attempts with dominant hand
Chair Rise
Record time to do 5 chair stands (1 to 60 secs); If fails, then 0
3 Position Balance
Side-by-side for 0 to 10 secs Semi-tandem stance for 0 to 10 sec Tandem stance for 0 to 10 sec

Table 3. Symptom Based Nutrition Barriers

Symptom	Consideration	Recommendations
Anorexia	Ascites	Ascites management
	Food access	Psychosocial support
	Psychiatric disease	Consultation
Dysguesia	Vit. A, Zinc, Magnesium	Replete deficiencies
	Salt usage	Salt substitutes (careful with potassium containing)
		Lessen salt restrictions
Early Satiety	Ascites	Ascites management
	Meal size	Small meals with snacks
	Gastroparesis	Start a promotility agent
		Calorie dense supplements
Poor Sleep Quality	Sleep hygiene	Optimize environment
		Consider melatonin
	Diuretic timing	Morning diuretic dosing

classify patients as robust, pre-frail, and frail, and has been validated in the liver transplant population (see Table 2; https://liverfrailtyindex.ucsf.edu).[12,13] The second component of a comprehensive nutritional assessment are GA tools, which seek to diagnose varying levels of malnourishment from history and physical. The most common GA tools deployed in clinical practice are the subjective global assessment (SGA) and the Royal Free Hospital-global assessment (RFH-GA).[14] Given that the RFH-GA is time consuming and requires a registered dietitian, the SGA is generally easier to administer and is a reasonable alternative despite weak validation in the cirrhotic population.[1] To complete the nutritional assessment, a review of self-reported dietary intake should be conducted. Dietary intake surveys provide insight into the amount, type, and timing of food consumption and can provide valuable insight into barriers to adequate nutrition.[6]

Barriers and Routes of Feeding

Oral intake is the desired mode of nutrient consumption for a variety of physiologic and psychologic reasons, and consistent messaging regarding the importance of adequate nutrition should be emphasized in all cirrhotic patient encounters. In general, advice should not focus on dietary restrictions, but rather healthy eating patterns that emphasize high vegetable, fruit, protein, and caloric intake.[1,6] Eating a wide variety of enjoyable foods and avoiding the addition of salt or foods with a high sodium content is a reasonable strategy to minimize the consequence of salt restriction's typical negative impact on caloric and protein intake.[1,6] In addition, a variety of disease related barriers are important to consider when discussing nutrition with these patients, each of which has important treatment considerations that can positively impact the patient's nutritional intake (see Table 3).

In cases where oral intake is insufficient to meet caloric demands, enteral nutrition (EN; via naso- and orogastric tubes) or parenteral nutrition (PN) may be required. The most commonly encountered scenario where oral intake is insufficient occurs in hospitalized patients. For patients who do not have evidence of gastrointestinal bleeding, naso- or orogastric tube placement should occur immediately after intubation and can be considered safe regardless of variceal history.[1,6] In those with gastrointestinal (GI) bleeding secondary to esophageal varices, it is prudent to wait 48 to 72 hours after banding prior to placing a gastric tube.[15] In other types of GI bleeding, gastric tube placement is generally reasonable 24 hours

Table 4. Caloric and Protein Goals by Disease State*

	Compensated Cirrhotic[1]	Obese Cirrhotic[2]	Malnourished Sarcopenic Cirrhotic	Pre- & Post-Operative Cirrhotic	Critically Ill Cirrhotic
Calories (kcal/kg/day)	≥35†[3]	25†**	30-35**	30-35†**	≥35-40†
Protein (g/kg/day)	1.2**	2.0-2.5†**	1.5**	1.2-1.5†**	≥1.2†

1. In the compensated (i.e. euvolemic) cirrhotic, actual body weight can be used to estimate energy and protein provision
2. Both EASL and ESPEN base energy and protein provision in the obese on ideal body weight (IBW)
3. Caloric provision in the cirrhotic is recommended to be based on resting energy expenditure (REE) as determined by indirect calorimetry (IC). ESPEN recommends providing 1.3 x REE kcal/kg/day; EASL succinctly recommends not less than 35 kcal/kg/day

*Always assess refeeding risk prior to initiating feeding

**ESPEN guideline on clinical nutrition in liver disease (1)

†EASL clinical practice guidelines on nutrition in chronic liver disease (6)

after bleeding cessation. Conversion to post-pyloric feeding should occur in those who cannot tolerate gastric feeding despite efforts to improve tolerance or are at high risk for aspiration.[16] In the outpatient setting, if oral intake is insufficient, feeding tubes can be maintained for considerable periods of time with minimal supervision, although insurance infrequently covers tube-feeding in the pre-transplant population. Percutaneous enteral gastrostomy (PEG) tubes are generally contraindicated in cirrhosis due to bleeding risks (i.e. gastric varices) and infectious complications (especially in the setting of ascites) and should only rarely be employed.[1,6] Parenteral feeding should only be used when enteral feeding cannot meet the patient's energy demands or is contraindicated.[1] In addition to standard trace elements and the multivitamin and mineral supplements provided with PN, all patients requiring PN should receive vitamin K and higher doses of thiamine if actively drinking.

Calorie and Protein Goals and Strategies

Once a patient is determined to be nutritionally at risk or malnourished, they should receive targeted nutritional interventions that provide tailored strategies to achieve proper caloric and protein intake.[5,6]

Caloric and protein intake recommendations are ideally based on indirect calorimetry, but due to limited availability weight-based targets are typically used. Weights taken after a paracentesis or at a time of euvolemia are considered dry weight, and may be used for weight-based energy and protein provision.[1] If no dry weight is available, but the patient is near euvolemia, actual body weight may be used. In decompensated (i.e. hypervolemic) patients, current guidelines are somewhat discordant on the recommended approach. The European Association for Study of the Liver (EASL) recommends using an adjusted body weight based on the amount of ascites and peripheral edema (subtracting 5% if mild ascites, 10% if moderate, and 15% if severe, as well as an additional 5% if pedal edema is present), whereas the European Society for Clinical Nutrition and Metabolism (ESPEN) recommends using the ideal body weight (IBW), which is based on the patient's gender and height.[1,6] When obesity is present, both societies recommend using IBW. With these different approaches in mind, weight-based caloric and protein recommendations can be found in Table 4.

Oral nutrition supplementation and attention to meal timing are important considerations when helping patients achieve recommended protein and calorie goals. Use of protein additives, frequent small meals, and ingestion of high protein foods are common tactics employed in this patient population. Importantly, a late evening snack (LES) has been shown to improve lean muscle mass and should be routinely recommended to cirrhotic patients. The LES should occur between 9pm and 11pm and contain between 500 to 700 kcal with at least 50 grams of carbohydrates.[17,18]

The When and How of Micronutrients

Macronutrient deficiencies are not the only dietary shortfall in cirrhotics. Micronutrients, a broad nutrient class that includes dietary elements (minerals, trace elements) and organic compounds (vitamins) that are required in small

Table 5. Strategies To Avoid Inadequate Caloric and Protein Intake

Inpatient	Outpatient
Avoid/minimize NPO time	Emphasize proper nutrition intake
Add D5 to IVF during NPO periods	Emphasize frequent feedings
Provide bedtime and morning snacks	Recommend bedtime and morning snacks
Utilize calorie dense liquid supplements	Prescribe calorie dense liquid supplements
Optimize glycemic control	Optimize glycemic control; consider endocrinology referral

quantities for normal physiologic function, are also commonly deficient. Assessing many of these micronutrients is challenging and not done in routine clinical practice, as guidelines recommend treating micronutrient deficiencies liberally when suspected or confirmed.[1,6] In this context, it is reasonable to recommend a daily multivitamin (without manganese, as elevated levels observed in cirrhotics may be associated with hepatic encephalopathy), and to consider individual vitamin and mineral deficiencies in the presence of malnourishment or decompensation,[6,19] Among the fat-soluble vitamins requiring consideration, vitamin D should be repleted to a level above 30 ng/ml and vitamin K repleted as needed. Among the water-soluble vitamins, vitamin B1 (thiamine) is routinely deficient and should be aggressively repleted, although other B-vitamins can also quickly become deficient in the setting of decompensation.[1,6] Lastly, zinc repletion may be beneficial in hepatic encephalopathy (HE), and while clinical use increases, data continues to be inconclusive.[20,21]

Caution with Restrictions

One of the more challenging barriers to maintaining adequate nutrition occurs in response to direct advice or orders from providers caring for these patients. Given the many comorbidities commonly associated with advanced liver disease, other dietary restrictions are often present (e.g. heart-healthy, carbohydrate controlled, and renal diets), and providers should offer clear guidance for dietary strategies in these patients. Protein restrictions are never wise and should be avoided in these individuals. Historically, protein restriction was advised in cirrhotics with HE, but subsequent studies have demonstrated normal and high protein intake does not precipitate or worsen HE, and may actually improve mental status.[22,23] Fluid restriction is only recommended for individuals who experience significant hyponatremia (less than 125mEq/L).[24] Sodium restriction is important in managing ascites and hypervolemia, although providers should recommend a variety of strategies to ensure compliance without increasing the risk of malnutrition.[1] Table 5 offers strategies to avoid poor nutritional intake in both the in- and outpatient settings.

Special Groups/Problems

Several subpopulations and groups warrant special considerations regarding nutritional recommendations. These include the following:

Acute Liver Failure (ALF)

By definition, individuals with ALF do not have underlying cirrhosis and are not malnourished at the time of disease onset. Regardless, nutritional support in this population is vital and should be initiated early to prevent metabolic derangements, namely protein catabolism, and potentially decrease risks of gastrointestinal bleeding. Nasogastric tube placement should be performed once patients are intubated to provide EN.

Alcoholic Hepatitis

Most patients with alcoholic hepatitis are malnourished and require nutritional support, with the goal to provide adequate calories and protein as well as micronutrients including vitamins (namely folate and thiamine) and minerals (namely magnesium and phosphate). Calorie counts should be initiated early and, when oral intake cannot be maintained, enteral feeding is preferred over parenteral nutrition.

Hepatic Encephalopathy

Individuals with HE should not have their protein intake restricted. To prevent a catabolic state and resultant ammonia production, these individuals should be instructed to eat small frequent meals and ensure a late-night snack. Some data suggests benefit of branched-chain amino acids (either intravenous or oral) in individuals with HE, including a meta-analysis of 16 trials showing no benefit in mortality but a beneficial effect on manifestations of HE.[6,25] Due to costs and conflicting evidence on relatively heterogeneous cohorts, IV infusions are generally not recommended and oral supplements only recommended in protein intolerant individuals.

Hospitalized Patients

Individuals with cirrhosis are commonly kept NPO in the hospital for a variety of reasons and frequently fail to meet caloric goals. Practitioners should prioritize advancing their diet as early as possible, avoiding prolonged fasting, and placing an NG tube for EN at the time of intubation.

Sarcopenic Obesity

As cirrhosis progresses, individuals with obesity are also at risk of muscle catabolism and sarcopenia. Providers must balance preserving muscle mass and function with weight loss goals. Reasonable recommendations include a calorie-restricted, but high protein diet, in combination with an exercise regimen with the goal of achieving greater than 5-10% weight loss.[6]

CONCLUSION

Malnutrition is a ubiquitous problem in the cirrhotic patient population, negatively impacting quality of life and clinical outcomes. Current guidelines recommend screening for malnutrition, and, if present or at moderate risk, providing comprehensive dietary assessments and targeted dietary interventions. These interventions should focus less on dietary restrictions and more on adequate caloric and protein intake from diverse, healthy sources. Attention to disease-specific symptoms can maximize the impact of these interventions, with an ultimate goal to prolong and improve the cirrhotic patient's life. ■

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References

1. Plauth M, Bernal W, Dasarathy S, et al. ESPEN guideline on clinical nutrition in liver disease. Clinical nutrition (Edinburgh, Scotland). 2019;38(2):485-521.
2. McClave SA, Taylor BE, Martindale RG, et al. Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.). JPEN J Parenter Enteral Nutr. 2016;40(2):159-211.
3. Dick AA, Spitzer AL, Seifert CF, et al. Liver transplantation at the extremes of the body mass index. Liver Transpl. 2009;15(8):968-77.
4. Englesbe MJ, Patel SP, He K, et al. Sarcopenia and mortality after liver transplantation. J Am Coll Surg. 2010;211(2):271-8.
5. Iwasa M, Iwata K, Hara N, et al. Nutrition therapy using a multidisciplinary team improves survival rates in patients with liver cirrhosis. Nutrition (Burbank, Los Angeles County, Calif). 2013;29(11-12):1418-21.
6. EASL Clinical Practice Guidelines on nutrition in chronic liver disease. Journal of hepatology. 2019;70(1):172-93.
7. Cederholm T, Bosaeus I, Barazzoni R, et al. Diagnostic criteria for malnutrition - An ESPEN Consensus Statement. Clinical nutrition (Edinburgh, Scotland). 2015;34(3):335-40.
8. Borhofen SM, Gerner C, Lehmann J, et al. The Royal Free Hospital-Nutritional Prioritizing Tool Is an Independent Predictor of Deterioration of Liver Function and Survival in Cirrhosis. Digestive diseases and sciences. 2016;61(6):1735-43.
9. Arora S, Mattina C, Catherine M, et al. PMO-040 The development and validation of a nutritional prioritising tool for use in patients with chronic liver disease. Gut. 2012;61:A90-A.
10. Cruz-Jentoft AJ, Bahat G, Bauer J, et al. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing. 2019;48(4):601.
11. Alvares-da-Silva MR, Reverbel da Silveira T. Comparison between handgrip strength, subjective global assessment, and prognostic nutritional index in assessing malnutrition and predicting clinical outcome in cirrhotic outpatients. Nutrition (Burbank, Los Angeles County, Calif). 2005;21(2):113-7.
12. Lai JC, Covinsky KE, Dodge JL, et al. Development of a novel frailty index to predict mortality in patients with end-stage liver disease. Hepatology. 2017;66(2):564-74.
13. Wang CW, Lebsack A, Chau S, et al. The Range and Reproducibility of the Liver Frailty Index. Liver Transpl. 2019;25(6):841-7.
14. Morgan MY, Madden AM, Soulsby CT, et al. Derivation and validation of a new global method for assessing nutritional status in patients with cirrhosis. Hepatology. 2006;44(4):823-35.
15. McClave SA, Chang WK. When to feed the patient with gastrointestinal bleeding. Nutrition in clinical practice : official publication of the American Society for Parenteral and Enteral Nutrition. 2005;20(5):544-50.
16. McClave SA, DiBaise JK, Mullin GE, et al. ACG Clinical Guideline: Nutrition Therapy in the Adult Hospitalized Patient. The American journal of gastroenterology. 2016;111(3):315-34; quiz 35.
17. Tsien CD, McCullough AJ, Dasarathy S. Late evening snack: exploiting a period of anabolic opportunity in cirrhosis. Journal of gastroenterology and hepatology. 2012;27(3):430-41.
18. Plank LD, Gane EJ, Peng S, et al. Nocturnal nutritional supplementation improves total body protein status of patients with liver cirrhosis: a randomized 12-month trial. Hepatology. 2008;48(2):557-66.
19. Hauser RA, Zesiewicz TA, Martinez C, et al. Blood manganese correlates with brain magnetic resonance imaging changes in patients with liver disease. Can J Neurol Sci. 1996;23(2):95-8.
20. Takuma Y, Nouso K, Makino Y, et al. Clinical trial: oral zinc in hepatic encephalopathy. Alimentary pharmacology & therapeutics. 2010;32(9):1080-90.
21. Katayama K, Saito M, Kawaguchi T, et al. Effect of zinc on liver cirrhosis with hyperammonemia: a preliminary randomized, placebo-controlled double-blind trial. Nutrition (Burbank, Los Angeles County, Calif). 2014;30(11-12):1409-14.
22. Gheorghe L, Iacob R, Vădan R, et al. Improvement of hepatic encephalopathy using a modified high-calorie high-protein diet. Rom J Gastroenterol. 2005;14(3):231-8.
23. Cordoba J, Lopez-Hellin J, Planas M, et al. Normal protein diet for episodic hepatic encephalopathy: results of a randomized study. Journal of hepatology. 2004;41(1):38-43.
24. Runyon BA. Introduction to the revised American Association for the Study of Liver Diseases Practice Guideline management of adult patients with ascites due to cirrhosis 2012. Hepatology. 2013;57(4):1651-3.
25. Gluud LL, Dam G, Les I, et al. Branched-chain amino acids for people with hepatic encephalopathy. The Cochrane database of systematic reviews. 2017;5(5):Cd001939.