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A Practical Approach to Nutritional Screening and Assessment in Cirrhosis

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Malnutrition is one of the most common complications of cirrhosis, associated with an increased risk of morbidity and mortality. As a potentially modifiable condition, it is of particular importance to identify malnourished patients so that nutritional therapy can be instituted. Nutrition screening and assessment are infrequently performed in patients with cirrhosis. The reasons for this are multifactorial, including the absence of a validated "rapid" screening tool, multiple definitions of what constitutes malnutrition, and challenges with interpreting body composition and laboratory results in the setting of volume overload and liver dysfunction. This article summarizes the clinically relevant evidence and presents key issues, tools, and clinical options that are applicable to patients with cirrhosis. The definition, etiology, and clinically relevant outcomes associated with malnutrition are reviewed. Rapid nutritional screening is differentiated from more detailed nutritional assessment. Nutritional assessment in special populations, including women and the obese, and the role of inflammation are discussed. Multicenter studies using a common nutritional screening/assessment strategy are the next steps to fast-track adoption and implementation of nutrition-related evaluations into routine clinical practice. (HEPATOLOGY 2017;65:1044-1057).

Malnutrition is one of the most common complications associated with cirrhosis and is diagnosed in anywhere from 5% to 99% of patients depending upon the assessment methods that are used.[1] Malnutrition is associated with increased risk of mortality, higher prevalence of portal hypertension–related complications and infections, as well as longer stays in hospital.[2-4] In mixed populations of malnourished patients, the benefits of nutrition therapy are evidenced by reductions in mortality, infections, systemic inflammatory responses, and hospital length of stay.[5,6] Although cirrhosis-specific studies are limited by cohort size and trial design, nutrition therapy has also shown benefit.[7]

As a potentially modifiable condition, it is of particular relevance to identify malnourished patients so that nutritional therapy can be instituted. Ideally, all patients should first undergo a rapid nutrition screen to determine if they are at risk of malnutrition. Those at risk should complete a more detailed nutritional assessment to confirm the presence and severity of malnutrition.[8] Nutrition screening and assessment are performed infrequently in patients with cirrhosis due to the absence of a validated "rapid" screening tool, multiple definitions of what constitutes malnutrition, and challenges with interpreting body composition and laboratory results in the setting of volume overload and liver dysfunction.

This article presents key issues, tools, and clinical options to enhance the practice of nutrition screening and assessment that are applicable to both outpatients and hospitalized patients with cirrhosis. A PubMed search using the search terms "malnutrition," "nutritional assessment," "cirrhosis," and related terms was carried out in April 2016 and supplemented by articles identified from the gray literature and the

Abbreviations: ASPEN, American Society for Parenteral and Enteral Nutrition; BIA, bioelectrical impedance analysis; BMI, body mass index; CT, computed tomography; ESPEN, European Society for Parenteral and Enteral Nutrition; MRI, magnetic resonance imaging; RFH-NPT, Royal Free Hospital-Nutritional Prioritizing Tool; SGA, Subjective Global Assessment.

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authors' content expertise. Due to the limited evidence in this area, this article also incorporates the authors' opinions and experience to raise awareness and provide a practical approach applicable to the clinical setting. The details of the nutrition prescription, including methods of calculation and nutrient distribution, and the approach to nutritional therapy in patients with cirrhosis are also important topics but fall beyond the scope of the current review.

Defining Malnutrition in the Setting of Cirrhosis

"Malnutrition" can refer to a state of either undernutrition or overnutrition. For the purpose of this review, "malnutrition" will be used synonymously with "undernutrition." Malnutrition is diagnosed following a comprehensive nutritional assessment. Major nutrition and cirrhosis research groups/organizations have proposed expert consensus-based definitions of malnutrition, including the American Society for Parenteral and Enteral Nutrition (ASPEN),[9] the European Society for Parenteral and Enteral Nutrition (ESPEN),[10,11] the International Society for Hepatic Encephalopathy and Nitrogen Metabolism,[1] and a recent guideline in the *American Journal of Gastroenterology*.[6] Some of these guidelines are targeted to a general cohort of adult patients, and others are specific to cirrhosis. Although there is no unifying tool for the diagnosis of malnutrition, there is significant overlap in the components used to objectively define malnutrition, with all societies notably recommending some form of muscle mass assessment (Table 1).

It is accepted that malnutrition increases with worsening liver disease severity. To date, however, in the cirrhosis-specific guidelines, liver disease severity has not been used to stratify patients for their risk of malnutrition. In addition to the well-accepted body mass index (BMI) of <18.5 kg/m^2[10] to define malnutrition, we propose that Child-Pugh C patients are at very high risk of malnutrition and do not need to be "screened" for malnutrition but instead can proceed directly to a nutritional assessment (Fig. 1).

Towards a Practical Approach:

- There is a compelling need for consensus on accurate and readily useable tools to diagnose malnutrition in cirrhosis.
- Cirrhosis patients with a BMI <18.5 or those with Child-Pugh C are at high risk for malnutrition.

Etiology and Mechanisms of Malnutrition in Hepatic Cirrhosis

The etiology of malnutrition in cirrhosis involves multiple processes resulting from combined disturbances of oral intake, absorption, and metabolism of nutrients.[12] First, impaired dietary intake is a principal cause of malnutrition and may arise as a consequence of gastrointestinal symptoms, anorexia, dysgeusia, and prescription of unpalatable diets. Anorexia may be triggered by an imbalance between orexigenic and anorexigenic hormones and by the chronic increase in circulating cytokines. Nausea, vomiting, and early satiety are often related to intra-abdominal pressure secondary to ascites. Dysgeusia may result from zinc deficiency, while unpalatability is often the result of rigid sodium-restricted diets.

Second, nutrient malabsorption may occur in patients with cirrhosis due to multiple factors, the mechanisms for which are incompletely understood.[13]

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TABLE 1. Society Guidelines for Defining Malnutrition—Common Components

	Food intake	Weight loss	Muscle mass loss	Subcutaneous fat loss	Fluid accumulation	Functional status	BMI	Inflammation	SGA
General ASPEN[1]	X	X	X	X	X	X		X	
Hospitalized inpatient[2]			X				X		
General ESPEN[3]		X	X				X		
Cirrhosis ESPEN[4]		X	X	X			X		X
Cirrhosis ISHEN[5]	X	X	X		X		X	X	

Abbreviation: ISHEN, International Society for Hepatic Encephalopathy and Nitrogen Metabolism.

Fat malabsorption, secondary to decreased production of bile acids, occurs in cholestatic liver diseases. Intraluminal bile acid deficiency, resulting from decreased bile production and portosystemic shunting, impairs micelle formation and absorption of long chain fatty acids through lymphatics. Pancreatic insufficiency frequently coexists in patients with alcoholic cirrhosis. Portal hypertensive gastropathy and enteropathy, altered intestinal flora, and chronic lactulose use may also lead to malabsorption.

Third, altered macronutrient metabolism is a cornerstone mechanism contributing to malnutrition in cirrhosis. Carbohydrate metabolism is abnormal (e.g., peripheral insulin resistance, hyperinsulinemia, impaired hepatic glycogen synthesis) and promotes gluconeogenesis from amino acids, glycerol, pyruvate, and lactate. These effects are already evident after a short overnight fast and may resemble the catabolic state of healthy subjects undergoing 2-3 days of starvation. Abnormal amino acid metabolism leads to low plasma levels of methionine and branched chain amino acids, which associate with muscle atrophy. Protein catabolism is increased in the postabsorptive state, and protein synthesis that usually occurs in response to a meal is normal or attenuated compared with matched controls. Hypermetabolism is a relatively infrequent feature in stable cirrhosis and is not associated with sex, etiology, or severity of liver disease; however, it may result from up-regulation of the sympathetic nervous system, and hypermetabolism has been reported when energy expenditure is expressed per kilogram of lean body mass. Recent research has also increased our knowledge about molecular mechanisms contributing to the pathophysiology of muscle wasting in patients with cirrhosis, and more information can be derived from a recent review on this topic.[14]

Towards a Practical Approach:

- Malnutrition in cirrhosis is multifactorial.
- Treating malnutrition requires a comprehensive and multidisciplinary strategy and surveillance.

Relationship of Malnutrition and Clinical Outcomes in Cirrhosis

Historically, malnutrition was believed to influence the health outcome of patients with liver cirrhosis. As such, it was included in the 1964 Child-Turcotte classification for the prognosis of patients with cirrhosis undergoing surgery. In 1972, the nutritional status parameter was removed. Since then, many studies on cirrhosis have associated malnutrition with worse health outcomes and lower survival rates (Fig. 2).[2-4,15,16]

Multiple methods have been applied to evaluate malnutrition (e.g., Subjective Global Assessment [SGA], anthropometry, nutritional index, dual X-ray absorptiometry, computed tomography [CT]/magnetic resonance imaging [MRI]), which has led to divergent results. The depletion of muscle mass (commonly termed "sarcopenia") has emerged as the "central core" of the nutrition assessment in cirrhosis. Muscle tissue stores a large proportion of amino acids and proteins, which are mobilized in catabolic conditions. Muscle is crucial for mobility, metabolic regulation of glucose and lipids, heart and respiratory function, immune function, and cytokine activity. Muscle wasting, quantified either by anthropometry or by imaging techniques, is related to a higher rate of mortality in patients with cirrhosis.[3,4,15,16] The strong interplay between malnutrition, sarcopenia, and poor prognosis is further demonstrated by the association of nutritional impairment and liver disease–related complications.[17,18]

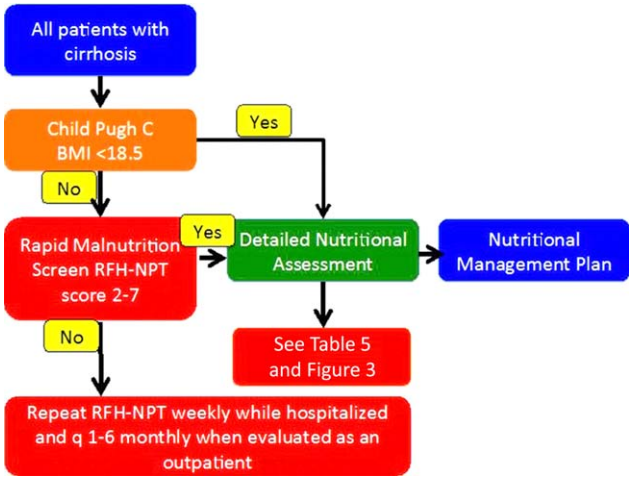

FIG. 1. A proposed algorithm for nutritional screening and assessment in patients with cirrhosis.

In patients with hepatocellular carcinoma, sarcopenia is an independent prognostic factor decreasing survival[19] and increasing treatment complications and related mortality.[20] Sarcopenia plays a negative prognostic role in candidates for surgical treatment of hepatocellular carcinoma. Malnutrition is also a well-established risk factor in patients with cirrhosis undergoing surgery.

In patients awaiting liver transplantation, muscle depletion is predictive of increased waiting list mortality as the majority of these are patients with decompensated cirrhosis and advanced liver insufficiency.[4] Following transplantation, malnourished patients commonly present with increased length of hospitalization, prolonged intensive care unit stay, longer time of intubation, and higher rate of infections compared with those who are well nourished.[21] Although it is generally accepted that malnourished patients may require greater support in the posttransplantation setting,[22] malnutrition is not currently considered a contraindication to transplantation.

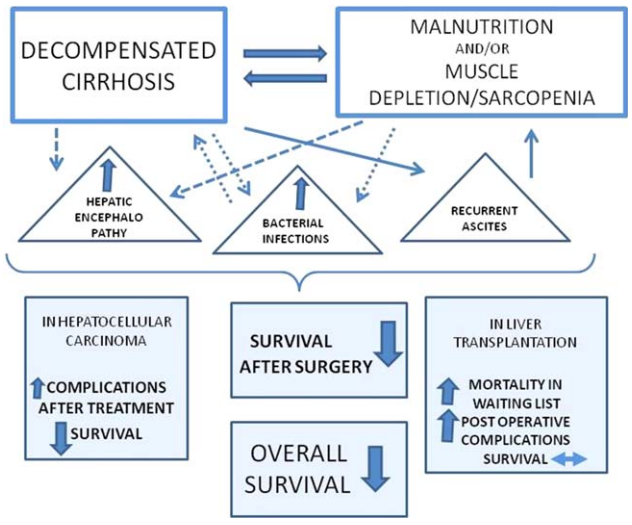

FIG. 2. Overview of the complex relationship between malnutrition, cirrhosis-related complications, transplantation, and survival. Data about the prognostic value of malnutrition for survival after liver transplantation are controversial.

Towards a Practical Approach:

- Evidence suggests that malnutrition is an independent predictor of poor clinical outcomes and lower survival in cirrhosis.
- Loss of muscle mass loss is objectively measureable and has been the most common nutritional variable associated with mortality.

Nutrition Screening and Nutrition Risk

ASPEN defines nutrition screening as a process to identify individuals who are malnourished or at risk of malnutrition for referral to a comprehensive nutritional assessment and intervention if appropriate.[23] ESPEN states that screening should be a rapid and simple process conducted by admitting staff or community health care teams.[24] An ideal screening tool should be usable by an untrained health care professional (or even the patient) and have reasonable sensitivity and specificity.[25] Routine system-wide nutrition screening is not widely practiced, even though it is recommended for high-risk patient groups. As such, patients at risk for malnutrition are often overlooked until they are malnourished and/or have a major health event requiring intervention. By ignoring preventative strategies, malnutrition increases the economic burden of cirrhosis.[26] Nutrition risk acknowledges the interplay between inflammation and malnutrition and is determined by not only nutritional status but also disease severity.[6,27,28] ESPEN defines nutrition risk as "Chances of a better or worse outcome from disease or surgery according to actual or potential nutritional and metabolic status."[8] The literature does not provide a

TABLE 2. Summary of Nutrition Screening Tools

Screening Tool • Care Setting	Advantages	Disadvantages	Tool Components
MUST[6] • Community	High interrater reliability Content and predictive validity for length of hospital stay and mortality Practical	Weight from fluid collections (ascites, peripheral edema) not accounted Disease severity not considered	BMI Unplanned weight loss in past 3-6 months Acutely ill and unable to eat for ≥5 days
NRS-2002[7] • Hospital	Content and predictive validity Moderately reliable Practical Considers disease severity	Weight from fluid collections (ascites, peripheral edema) not accounted	Weight loss Food intake BMI Disease severity
NUTRIC[2] • Critically ill	Externally validated (n = >1,000 patients)	Interleukin-6 not widely available Requires training Classic nutrition parameters not considered	Age APACHE II and SOFA scores Comorbidities Days in hospital pre-ICU Interleukin-6
MNA[8] • Elderly (home-care programs, nursing homes, and hospitals)	Includes physical and mental components plus dietary questionnaire Predictive validity for adverse outcome, social functioning, mortality, and doctor visits Practical	Content validity not reported Interrater reliability modest Weight from fluid collections (ascites, peripheral edema) not accounted Disease severity not considered	GI symptoms Weight loss Mobility Psychological stress/acute disease Neuropsychological problems BMI
SNAQ[9] • Hospital	Simple/practical Facilitates identification and treatment of malnourished inpatients	Weight from fluid collections (ascites, peripheral edema) not accounted Disease severity not considered	Unintentional weight loss Decreased appetite Use of supplements or tube feeding
MST[10] • Hospital	Simple/practical Predictive validity for length of stay Excellent reliability Highly sensitive	Weight from fluid collections (ascites, peripheral edema) not accounted Disease severity not considered	Unintentional weight loss Quantity of weight lost Decreased appetite
RFH-NPT[11] • Ambulatory Hospital	Simple/practicalcirrhosis-specific features Excellent intraobserver and interobserver reproducibility Good external validity Predictive of clinical deterioration and transplant-free survival	Valid in population with cirrhosis only Impact of nutritional therapy based on screening score unknown	Alcoholic hepatitis or tube feeding Considers fluid overload Dietary intake reduction Weight loss + option for assessing diuretic use
CNST[12] • Hospital	Simple/practical Validated against SGA (sensitivity 67%-73%, specificity 80%-86%) High reliability	Weight from fluid collections (ascites, peripheral edema) not accounted Disease severity not considered Symptoms not considered	Unintentional weight loss Dietary reduction

Abbreviations: APACHE II, Acute Physiology and Chronic Health Evaluation II; CNST, Canadian Nutrition Screening Tool; GI, gastrointestinal; MNA, Mini Nutritional Assessment; MST, Malnutrition Screening Tool; MUST, Malnutrition Universal Screening Tool; NRS-2002, Nutritional Risk Screening 2002; NUTRIC, Nutrition Risk in Critically Ill; SNAQ, Short Nutritional Assessment Questionnaire; SOFA, Sequential Organ Failure Assessment.

unanimous definition for nutrition screening, and there is no consensus regarding the concept of nutrition risk.[8]

Nutritional Risk Screening 2002[28] and the Nutrition Risk in Critically Ill[27] are examples of two scoring systems to determine nutrition risk. Other validated nutrition screening tools can be used as general screens for malnutrition (Table 2).[29] Although many tools demonstrate sensitivity and specificity values over 70% (minimally accepted prerequisite), flaws in the validation processes have been observed,[25] including the use of expert trained professionals and lack of validation of tool administration by nonexperts (e.g., nutrition assistants, diet technicians, or nurses). Importantly, to date, none of the frequently recognized nutrition screening tools (Table 2) have been validated in the setting of cirrhosis.

Which Nutrition Screening/ Nutrition Risk Tool(s) Can Be Used in Cirrhosis?

Cirrhosis-specific tools have been developed. The Royal Free Hospital-Nutritional Prioritizing Tool (RFH-NPT) was developed by validation against the

Royal Free Hospital SGA (Supporting Fig. S1).[1] It takes ~3 minutes to complete; discriminates patients into low, medium, and high-risk categories; and includes the variables of alcoholic hepatitis, fluid overload and impact on dietary intake, BMI, unplanned weight loss, and reduced dietary intake (Supporting Fig. S2). Importantly, the Malnutrition Universal Screening Tool (recommended by ESPEN as the preferred screening tool for outpatients) is incorporated within the RFH-NPT in patients who do not have fluid overload. In a series of 148 patients, the RFH-NPT was identified as an independent predictor of clinical deterioration and transplant-free survival.[30] The content validity of this tool in a population with cirrhosis is promising and encompasses features of clinical and metabolic risk, along with classical nutritional variables that may influence response to nutrition therapy. Additionally, although it includes BMI as a variable, this is only considered in the absence of fluid overload.

A second liver-specific nutrition screening tool is the Liver Disease Undernutrition Screening Tool (Supporting Fig. S3). This tool uses a series of six patient-directed questions covering the domains of nutrient intake, weight loss, subcutaneous fat loss, muscle mass loss, fluid accumulation, and decline in functional status to determine whether undernutrition is present or absent. This tool was based on the Academy of Nutrition and Dietetics and ASPEN consensus statements for identifying malnutrition[31] and may have limitations as it relies on the patient's subjective judgment of each of the measured parameters. Preliminary data comparing it against a dietitian's nutrition assessment in a setting of cirrhosis (n = 22) suggest that the Undernutrition Screening Tool had a high positive predictive value (93%) but a low negative predictive value (37.5%), leading to the conclusion that a negative screen was unable to reliably rule out undernutrition. As with the RFA-NPT, further validation is needed with comparison to clinical outcomes in patients with cirrhosis.

Towards a Practical Approach:

- Screening tools including either weight or BMI have limited clinical value in cirrhosis due to known fluctuations in body water.
- The cirrhosis-specific nutrition risk screening tool, RFH-NPT, is currently preferred as it considers metabolic and nutritional parameters.

Overview of the Components of a Detailed Nutritional Assessment

Once patients with cirrhosis have been screened, a detailed nutrition assessment should be performed in patients at high nutritional risk to confirm the nutrition risk assessment, characterize nutrition status, and identify modifiable variables for nutrition support. Repeated assessments can monitor the effects of nutrition therapy. As nutritional assessment is more comprehensive, is time-consuming, and requires interpretation of multiple nutrition indicators, it is preferable but not mandatory to have this performed by a registered dietitian or a dedicated person with specialized knowledge.

In patients with cirrhosis whose screen results indicate a high risk for malnutrition, we suggest that each component be assessed and documented every 1-6 months in outpatients as well as inpatients at admission and periodically throughout their hospital stay. Regardless of which tools are used, clinically relevant information is obtained and awareness of nutrition risks is raised by repeating the assessments in patients with cirrhosis to improve quality of health care.

Although the assessment provided below focuses on macronutrient deficiencies, patients with advanced liver disease are also at risk of micronutrient deficiencies. Zinc deficiency may be observed as a consequence of diuretic use and restricting animal protein intake. Hypomagnesemia may arise secondary to diuretic use. Frequently, fat-soluble vitamin deficiencies, particularly of vitamins A and D, are encountered. Considering the high prevalence of micronutrient deficiencies in this population, it is reasonable to incorporate basic micronutrient screening into the broader nutrition assessment. There are few guidelines to reference regarding the frequency of micronutrient screening. At a minimum, our group would recommend 6-monthly testing of serum magnesium, serum 25-hydroxyvitamin D_3 and vitamin A, and serum zinc levels.

#1 DIETARY ASSESSMENT

Dietary Intake

A detailed assessment of dietary intake (i.e., food, fluids, and supplements) may include a 3-day food diary. Notably, this method is only useful if patients are

provided with standardized instructions to understand how to complete the diary properly. Although this formal assessment may be burdensome for the patient, the diary is preferred over a 24-hour dietary recall, which is simple to use but heavily reliant on recall skills and may not accurately represent routine food choices and behaviors.

With the exception of dietitians, most health care providers have insufficient "food" knowledge to incorporate, analyze, and interpret these tools during routine clinical practice. At a minimum, patients should be asked if their relative food intake has changed and, if so, over what duration. Although it requires validation in cirrhosis, parts of the abridged scored Patient-Generated SGA, developed and validated in oncological patients (Supporting Fig. S4),[32] may be useful to initiate nutritional intake discussions with patients who have cirrhosis. Given the detrimental effects of fasting in cirrhosis, additional questions should be asked, such as the duration of fasting between meals, snacking routines, and use of nutritional supplements. Inadequate protein intake is linked to sarcopenia and has also been independently associated with mortality in patients with cirrhosis[33]; therefore, inquiry into adequate protein sources is important.

Barriers to Dietary Intake

To effectively address oral intake, it is also essential to delve into the factors that may compromise intake (e.g., dysgeusia, taste fatigue, low-sodium diet, early satiety, socioeconomic factors). Tools such as the abridged scored Patient-Generated SGA[32] can be useful. Validation of such tools is required in cirrhosis, but engaging dietetic staff is helpful in assessing this information.

#2 BODY COMPOSITION ASSESSMENT WITH A FOCUS ON MUSCLE MASS

Body composition is an important parameter for evaluation in nutrition assessment; however, choosing a modality can be challenging, and one needs to consider feasibility, cost, and level of accuracy or precision that is required in practice. Body size by weight or BMI provides a crude classification of patients in the underweight, normal weight, overweight, or diverse obese categories. There is no well-validated means of adjusting BMI for the fluid retention that occurs in cirrhosis. Similarly, bioelectrical impedance analysis (BIA) offers the opportunity for quick and easy determinations of lean mass; however, BIA is highly influenced by fluid shifts, especially edema, and its use in longitudinal evaluations in this population have been deferred. Studies have varied in their estimation of dry weight BMI using either the postparacentesis body weight or by subtracting a percentage of weight based upon severity of ascites (mild, 5%; moderate, 10%; severe, 15%), with an additional 5% subtracted if bilateral pedal edema was present.[4,34,35] More advanced tools quantify specific body composition compartments (such as adipose tissue depots [e.g., visceral adiposity] and/or skeletal muscle) with varying accuracy and specificity (Table 3). These tools are important in nutrition practices as they relate to poor metabolic, clinical, and functional outcomes and will be the focus of this section.[3,4,15,16]

Importantly, in addition to quantifying body composition compartments, CT imaging can be used to evaluate the potential infiltration of fat into muscle by examining changes in Hounsfield units, which crudely reflect the density of muscle tissue. Similarly, the use of echogenicity with ultrasonography may provide similar measures of changes in muscle density, which may reflect fatty infiltration or muscle damage. These measures may provide additional insight on possible relationships and mechanisms of poor muscle function and health[36] but require validation before routine use in clinical settings.

Special Considerations in Body Composition—Identifying Patients With Low Muscle Mass

Cutoff points for low muscle mass in a cirrhosis population have yet to be clearly defined or validated using CT, MRI, or ultrasonography. This and standardized landmarks are needed to identify patients with low muscle mass and compare results from different studies (Table 4).

Special Considerations in Body Composition—Understanding Sources of Error

Understanding and controlling potential sources of both modifiable errors (e.g., anatomical landmarking, skill of tester) and nonmodifiable errors (i.e., base assumptions incorporated into calculations) affect the interpretation of results (Table 3). These errors are particularly important in cirrhosis as patients frequently present with fluid retention or shifts, ascites, or edema,

TABLE 3. Characteristics of Diverse Body Composition Modalities That Have Been Used in Liver Cirrhosis

	Modality	Measures	Relative Accuracy and Precision	Level of Training	*Merits* and Limitations
Increased Practicality and Applicability	Anthropometrics	*Overall body size:* weight, height for BMI; MAC *Predicted Muscle:* MAMC *Predicted visceral adiposity:* WC, W:H, skinfold	*Accuracy:* Low *Precision:* Low	Minimal	*Highly feasible, accessible, and inexpensive for large patient populations and clinics* Results need to be interpreted cautiously as these are crude and predictive
	BIA	Prediction equations to calculate lean and fat mass	*Accuracy:* Moderate *Precision:* High	Minimal to moderate	May present inaccuracies in patients with ascites and/or edema *Feasible as a bedside tool and relatively inexpensive to moderately expensive* Proper positioning of inpatients or patients who have a larger body size may be challenging Equations are used to predict whole-body lean tissue based on same device and population
	Ultrasound imaging	Muscle thickness and CSA Subcutaneous adipose tissue Echogenicity for tissue integrity	*Accuracy:* Moderate to high *Precision:* Moderate to high	Ultrasonographer may be helpful	*Moderately feasible and accessible in clinics* Prediction equations for whole-body lean or skeletal muscle mass are needed Cutoff points for low muscularity have not been developed for cirrhosis
	CT or MRI	CSA and integrity of specific muscle and adipose tissue groups	*Accuracy:* High *Precision:* High	Certified medical radiologist	*Can capture specific lean and adipose tissue deposits* Not performed on all patients Only capture a single or few slice(s), and prediction equations are needed for whole-body lean mass Specific cutoff points have not been established in cirrhosis
	Dual-energy X-ray absorptiometry	Whole-body and regional fat, lean, and bone mineral content Bone mineral density	*Accuracy:* High *Precision:* High	Certified medical radiologist	*Low-dose radiation for prospective studies* *Can perform regional analysis* May not be available in clinic Cannot specifically distinguish between different tissue compartments

Abbreviations: CSA, cross-sectional area; MAC, mid-arm circumference; MAMC, mid-arm muscle circumference; WC, waist circumference; W:H, weight to height ratio.

factors that may confound single-point and longitudinal assessments. For example, although a patient's weight may not change over time, muscle and adipose tissue changes (i.e., fat and muscle loss) may be masked by fluid retention or ascites. Although there are tools (e.g., bioimpedance spectroscopy) to discriminate fluid shifts from body composition changes, these devices are not widely available due to cost. Further, repeated CT or MRI scanning is limited by the expense, availability, and, in the case of CT, significant risk of ionizing radiation and contrast exposure to the patient.[37] Preliminary data are available for thigh ultrasound as a predictor of sarcopenia in cirrhosis, but this requires the development of a universal approach as well as validation in cirrhosis and correlation with clinical outcomes.[34]

#3 FUNCTIONAL ASSESSMENT

The quality of lean tissue, particularly skeletal muscle, is optimally evaluated through functional measures. Several studies have demonstrated that muscle strength deteriorates more quickly than mass, suggesting that it may be a more sensitive measure of "muscle health."[38-40] Moreover, in patients with cirrhosis, functional measures (e.g., handgrip, 6-minute walk, physical frailty,

TABLE 4. Methods of Identifying Low Muscularity Using Various Body Composition Modalities and Low Muscle Strength Using Hand Grip

Modality	Calculations Required	Cutoff Point for Low Muscularity/Strength	Population in Which Cutoff Point Was Derived
MAMC[13,14]	MAMC (cm) = MAC (cm) − (3.14 × TSF [cm])	Females: <19.2 cm Males: <21.1 cm	≥80 years old
BIA	Skeletal muscle mass (kg) = [(Ht^2 [m^2]/R (Ohms) × 0.401) + (sex [M = 1, F = 0] × 3.825) + (age × –0.071)] + 5.102[15] Skeletal muscle index (kg/m^2) = skeletal muscle mass (kg)/$height^2$ (m^2)	Females: 5.76-6.75 kg/m^2 associated with moderate physical disability ≤5.75 kg/m^2 associated with high physical disability Males: 8.51-10.75 kg/m^2 associated with moderate physical disability ≤8.50 kg/m^2 associated with high physical disability	Multiethnic ≥60 years old[16]
Ultrasound	None	None for the 4-site protocol	Liver cirrhosis and ICU Cancer[17,18]
CT or MRI	Muscle index =cross-sectional area at L3 (cm^2) / $height^2$ (m^2)	Females: <39 cm^2/m^2 Males: <54 cm^2/m^2	
Dual-energy X-ray absorptiometry	Appendicular lean mass index = sum of lean mass in upper and lower limbs (kg)/$height^2$ (m^2)	Females: <5.45 kg/m^2 Males: <7.26 kg/m^2	Young and elderly[19]
Handgrip strength	None	Males: BMI ≤24: ≤29 kg BMI 24.1-28: ≤30 kg BMI >28: ≤30 kg Women: BMI ≤23: ≤17 kg BMI 23.1-26: ≤17.3 kg BMI 26.1-29: ≤18 kg BMI >29: ≤21 kg	≥65 years of age, community-dwelling participants in the Cardiovascular Health Study[20]

Abbreviations: ICU, intensive care unit; MAC, mid-arm circumference; MAMC, mid-arm muscle circumference; TSF, triceps skinfold.

and volume of O_2 peak tests) have been associated with clinical decompensation.[41-43] These measures are complemented with body composition assessments to better understand the metabolic integrity of the muscle and its ability to perform its tasks.

#4 GLOBAL ASSESSMENT TOOLS IN CIRRHOSIS

As a supplement to the performance of a detailed nutritional assessment, we are aware of two global assessment tools that incorporate some of the above nutritional assessment parameters.

Subjective Global Assessment

The SGA[44] (Supporting Fig. S5) divides patients into three categories based on five historical parameters (weight change, dietary intake relative to usual, gastrointestinal symptoms, functional capacity, and metabolic stress of underlying diagnosis) and three physical examination parameters (loss of subcutaneous fat, loss of muscle mass, and edema/ascites). The components are combined to obtain a rating of A, well nourished; B, moderately malnourished; or C, severely malnourished. The SGA correlates well with adverse postoperative outcomes in patients without cirrhosis[44] but underestimates the prevalence of sarcopenia.[34] In a recent study, of 69 patients identified to have sarcopenia by CT or MRI, only 46% were identified by the SGA as being moderately or severely malnourished. Moreover, in the setting of cirrhosis, unlike more objective measures, the SGA has had a limited capacity to predict clinical outcomes.[34,41]

Royal Free Hospital SGA

Recognizing the limitations of the traditional SGA in the setting of cirrhosis, Morgan et al. devised the Royal Free Hospital SGA, a global scheme incorporating both subjective and objective variables.[35] This algorithm includes BMI (estimated dry body weight),

mid-arm muscle circumference, and dietary intake (Supporting Fig. S1). Notably, although nutritional status as diagnosed by the Royal Free Hospital SGA was significantly associated with a shorter survival in men, it was not found to be prognostic in women, raising questions about its generalizability to both sexes. The subjective interpretation required for scoring two of the three variables, estimated dry body weight BMI and dietary intake, may also raise some challenges. Additional external validation is required before this tool can be widely accepted.

Toward a Practical Approach

- In cirrhosis, we suggest a minimum baseline and longitudinal assessment of a 3-day food diary, barriers to intake (question 3 of the patient-generated global SGA), estimated dry weight BMI, and mid-arm muscle circumference (Tables 4 and 5).
- Additional muscle health measures can be used based on clinic capacity (budget, training, etc.)
- Repetition of the base measures is essential to inform clinical practice.

Special Considerations

IS THERE A DIFFERENCE IN NUTRITIONAL ASSESSMENT BETWEEN THE SEXES?

As a major objective component of malnutrition, low muscularity or sarcopenia differs in men and women. This may result from the different prevalence of autoimmune or cholestatic disease in women, but it is likely that other factors also play a role. Usually women have greater fat stores than men, while a progressive depletion in muscle tissue is more evident in men.[45] Moreover, the prognostic implications of low muscle mass and function are less clear in female than in male patients.[16] It has been suggested that hypogonadism and testosterone deficiency in men with cirrhosis may lead to chronic muscle depletion even before malnutrition is clinically evident.[46]

TABLE 5. Minimum Components of a Detailed Nutritional Assessment For Patients With Cirrhosis

1. Inflammation & cirrhosis severity
• Non-elective hospitalization or Child-Pugh C?
• Severe cirrhosis and/or complications?
2. Dietary intake & possible barriers
• Estimate dietary intake versus recommended
• Identify barriers to intake (taste, food access, symptoms)?
3. Weight loss & BMI
• Interpretation limited with fluid retention or ascites.
• Estimate percent weight loss in past 1-3 months
• Estimate BMI using dry weight
• If obese (BMI ≥30), consider specific nutritional advice
4. Muscle assessment
• Mass change: at a minimum use mid-arm muscle circumference (MAC)
• Function change: at a minimum use hand grip strength
• ***Lower sensitivity for females

INFLAMMATION

Recognizing the importance of inflammation in promoting catabolism, Jensen and colleagues, as part of the international clinical nutrition support community,[47] proposed an etiology-based diagnosis of adult starvation and disease-related malnutrition. They incorporated the concept of inflammation, as an energy demanding condition, to define three different categories of malnutrition. Across the categories, energy needs progressively increase and the response to nutritional therapy decreases: (1) pure chronic starvation without inflammation (e.g., anorexia nervosa), (2) chronic diseases or conditions that impose sustained inflammation of a mild to moderate degree (e.g., organ failure, pancreatic cancer), and (3) acute disease or injury with a marked inflammatory response (e.g., major infection, burns). At present, the evidence suggests that patients with cirrhosis are conservatively designated as having mild to moderate inflammation. Hospitalized patients with acute-on-chronic liver failure are elevated to category 3.[48] The use of specific inflammatory markers (i.e., C-reactive protein or procalcitonin) to further refine the categorization and predict the responsiveness to nutritional supplementation requires evaluation.

OBESITY

The epidemic of obesity and the association between nonalcoholic steatohepatitis and cryptogenic cirrhosis have significantly increased the number of obese and

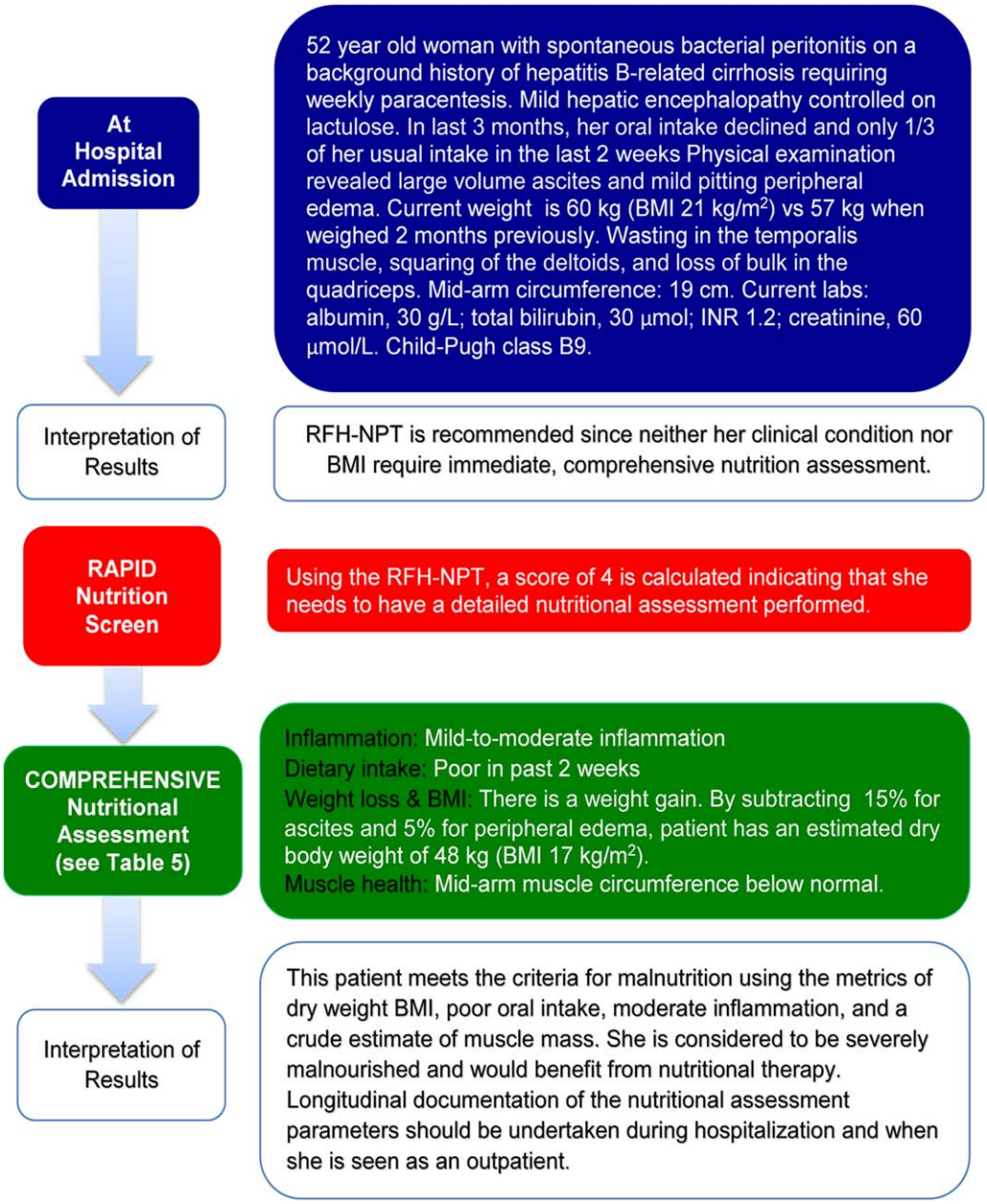

FIG. 3. A case example using the proposed algorithm for nutritional screening and assessment. Abbreviation: INR, international normalized ratio.

morbidly obese patients with cirrhosis. As evidence, nonalcoholic fatty liver disease is becoming a leading indication for liver transplantation. Obese patients typically exhibit low inflammation, muscle and hepatic insulin resistance, dyslipidemia, and/or other comorbidities. The combination of cirrhosis and obesity exacerbates complications that may require specific nutrition advice. Skeletal muscle atrophy may be masked by adiposity when using BMI and BIA. In ultrasound, distinguishing between the muscle and subcutaneous adipose tissue border may also be challenging in obese individuals, decreasing accuracy and reliability of ultrasound. While CT and MRI may distinguish between muscle and adipose tissue deposits, many obese individuals may not be scanned due to the size restrictions of the scanner.

Generally, obesity increases the rate of clinical decompensation in patients with cirrhosis,[49] and morbid obesity (BMI >35) has been associated with decreased survival after liver transplantation.[50] Given the limitations of existing bedside tools in these patients and the practical issues associated with repeated CT/MRI-based imaging, further data are needed before recommendations can be made about the ideal approach to nutritional assessment in obese patients.

Towards a Practical Approach:

- The implications of female sex, inflammation, and obesity on the assessment of nutritional status are complex and poorly understood.
- All cirrhosis patients are considered to have mild to moderate inflammation.

Conclusion

Malnutrition, regardless of definition, is an independent predictor of poor clinical outcomes in cirrhosis. There is uncertainty in the areas of nutritional screening and nutritional assessment in the population of patients with cirrhosis. The approach to patient management highlighted here is based on a combination of the literature evidence, practice guidelines, and clinical experience. A case example using the proposed approach is presented in Fig. 3. Although common sense indicates that adoption of even the minimal elements of nutrition screening and assessment outweighs the issues associated with the absence of validated tools and consensus in this area, there is still much room for refinement. Future studies need to assess the implications of sex, volume status, inflammation, and obesity on nutritional screening and assessment algorithms. The proposed approach for nutritional screening and assessment requires prospective validation and refinement, preferably in a multicenter network. Practitioner and patient education is also needed to increase awareness of and need for surveillance of nutrition factors to prevent and/or mitigate poor health outcomes, especially as these are potentially modifiable. This approach will eventually result in a practical, validated, and unified nutritional screening/assessment strategy, which can be implemented into routine clinical practice.

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