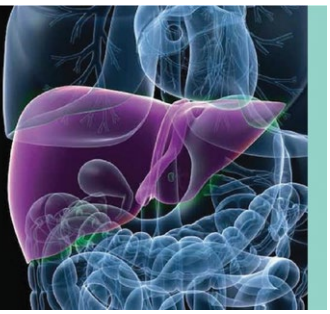

Assessment and Management of Nutrition Status in the Hospitalized Patient With Cirrhosis

Christopher Moore, M.D., and Adam C. Stein, M.D.

CASE

Inpatient consult for a 55-year-old woman with primary biliary cirrhosis (PBC) admitted with recurrent encephalopathy. Her Model for End-Stage Liver Disease (MELD)-Na score is 16, and body mass index (BMI) is 30. What are the recommendations for nutrition support while she is admitted?

BODY

Progression from compensated to decompensated cirrhosis reflects a change in average mortality from 12 to 2 years, respectively. This fact is correlated with a number of parameters: (1) the primary disease state, (2) comorbid conditions, and (3) patient behaviors.[1,2] These factors are dynamic and at times mutually reenforcing. Nutrition status, in quantitative and qualitative terms, is one such factor both impacted by and impacting upon the natural history of decompensated cirrhosis.[3] Invariably, decompensating events will require hospitalization of patients, such as with our case. Therein, an opportunity arises for assessment and management of these issues, including underlying functional and nutrition status. Identification of admitted patients with or at risk for malnutrition (defined vaguely as any deviation from the normal values of nutrition) allows for targeted nutrition intervention.

Overall it makes intuitive sense to improve nutrition in the setting of decompensated cirrhosis, both in the short-term (hospital) and long-term (outpatient) states. Unfortunately, there is a paucity of compelling high-quality evidence to suggest that nutrition interventions have any positive impact in chronically ill states in general, let alone in the decompensated cirrhotic state.[4,5] Although there are some equivocal data in critically ill patients, none are specific to cirrhosis, and the fundamentally heterogeneous nature of malnutrition itself hinders precise inquiry and generalization of results. Nonetheless, it is our contention that nutrition status in patients with cirrhosis, and in

Abbreviations: BMI, body mass index; HE, hepatic encephalopathy; INR, international normalized ratio; MELD, Model for End-Stage Liver Disease; NPO, *nihil per os*; PBC, primary biliary cirrhosis; PN, parenteral nutrition.

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particular within the decompensated state, should not be marginalized, but rather proactively optimized.[6]

In this review, we focus our recommendations for the short-term (hospitalized) patient cohort, as referenced in our case. Nutrition support in decompensated cirrhosis should start with a focused nutrition assessment to identify patients both with malnutrition and at-risk features. The tenets of a focused nutrition assessment can be done during a standard intake history and physical and supplemented with laboratory markers. On interview, attention should be paid to factors that affect nutrition intake and overall metabolism (Table 1), weight loss, and functional status (frailty, activities of daily living). Physical examination should include evaluation of muscle mass/distribution, strength, swelling, and specific features of micronutrient deficiencies. Additionally, validated tools can be used to define both current nutrition level and risk for malnutrition for patients in general; some examples include (but are not limited to) the Nutrition Risk in the Critically Ill, Subjective Global Assessment, and Nutrition Risk Screening 2002. This assessment is best administered by a trained nutrition support clinician, such as a registered dietitian or a physician with specific training and/or experience in nutrition.[7] Although these tools are useful in generating an overall assessment, none are specific to cirrhosis and are therefore fundamentally limited in generating a comprehensive nutrition evaluation. Regardless, attention should be paid to liver-specific nutrition serum biomarkers. We recommend checking micronutrients at admission or shortly thereafter.[8] (Table 2) The mechanisms for such deficiencies in cirrhosis are multifactorial in nature and outside the scope of this review. Repletion and supplementation strategies for micronutrients should take into account the relationship to liver clearance as well as potential risks associated with toxicity (Table 2).

It is worthwhile to note the important limitations in laboratory assessments. Regarding the international normalized ratio (INR): (1) Its value will indeed be elevated by vitamin K deficiency (for which the body has small storage capacity, especially revealed during critical illness); (2) it will also reflect coagulation factor deficiencies (cirrhotic synthetic dysfunction); and/or (3) coagulation factor inhibitors (iatrogenic or pathological). Regarding the protein markers albumin and prealbumin: (1) They are also limited by the synthetic capacity of the liver; (2) their values can change quickly in the setting of acute illness; and (3) they and other proteins can be low, despite appropriate intake and metabolism, in the setting of gastrointestinal losses (e.g., protein-losing enteropathies) or kidney disease (e.g., nephrotic syndrome).[9]

Patients who have limited oral intake, including both fluid and nutrition (protein, calories, fat), should be assessed regarding cause, if possible by a registered dietitian with experience in liver disease. In patients who are

TABLE 1. FACTORS AFFECTING NUTRITION STATUS IN PATIENTS WITH CIRRHOSIS

1. Quantity and quality of oral `intake	a. Socioeconomic limitations to food b. Dietary excesses (e.g., alcohol intake or salt) c. Dietary restrictions d. Poor dentition e. Dysgeusia f. Nausea (and vomiting) g. Early satiation (ascites related in some cases) h. Altered mentation (e.g., recurrent hepatic encephalopathy episodes or intoxicants)
2. Maldigestion/absorption, losses	a. Altered gut motility b. Bowel resection (e.g., patients with inflammatory bowel disease) c. Bowel edema (portal hypertension related) d. Protein-losing enteropathies e. Bile acid insufficiency/cholestatic disease (e.g., primary biliary cholangitis) f. Pancreatic insufficiency (e.g., chronic pancreatitis) g. Altered gut microbiota h. Increased bowel movements (iatrogenic or otherwise) i. Proteinuria/nephrotic syndrome
3. Metabolic abnormalities	a. Glucose intolerance b. Decreased glycogenic storage c. Increased gluconeogenesis, lipolysis d. Sarcopenia e. Ascites per se as a hypercatabolic state (and with paracenteses losses of vitamins, minerals, and proteins) f. Electrolyte abnormalities related to altered dietary intake, iatrogenic medications (e.g., diuretics), and degrees of kidney injury

TABLE 2. MICRONUTRIENTS FOR POTENTIAL ASSESSMENT IN PATIENTS WITH CIRRHOSIS AND CONSIDERATIONS FOR REPLETION

Micronutrient	Potential Impact in Cirrhosis	Considerations for Repletion
Vitamin A	Symptoms including night blindness; potential role in disease progression in cholestatic liver disease	Fat soluble. Avoid toxicity; serum levels do not necessary correlate with tissue levels.
Vitamin D	Relationship with hepatic osteodystrophy	Fat soluble. Serum level potentially influenced by inflammation. Check 1,25-dihydroxy vitamin D with concomitant renal disease.
Vitamin E	Potential role in nonalcoholic steatohepatitis, antioxidant	Dosing guidance remains unclear.
Vitamin K	Elevated INR seen in cirrhosis; potential for improvement if deficient	No clear evidence of toxicity in adults.
Thiamine	Deficiency is common in cirrhosis; association with Wernicke–Korsakoff syndrome	If increased risk for Wernicke–Korsakoff syndrome, give thiamine repletion prior to sugar-containing fluids.
Folate	Potential source of anemia	Toxicity rare but can cause neurological problems.
Zinc	Deficiency potentially associated with hepatic encephalopathy	Oral zinc could interfere with copper absorption. High doses can sometimes cause gastrointestinal symptoms.
Vitamin B_{12}	Potential source of anemia	Replete sublingual or intramuscular.
Selenium		Toxicity rare but can cause neuropathy and mental status changes.
Copper	Deficiency seen with zinc repletion/supplementation	Biliary excretion; avoid toxicity.

not taking in adequate fluid and nutrition, enteral rather than parenteral strategies should be used whenever possible.[6] Parenteral nutrition (PN) in the setting of cirrhosis has increased risk for complications, including PN-associated liver disease, infection, and line-associated clot.[6]

Nutrition status and deviations from it naturally link to the concept of frailty, and as such it will be briefly discussed. Frailty is conceived of as a diminished capacity to handle stressors as a result of anatomic and physiological changes.[10] Although frailty was traditionally assessed within the general geriatric population, it is quite obviously and broadly observed in patients with cirrhosis. Importantly, there is increasing appreciation for associations between frailty and morbidity and mortality in those awaiting and even recovering from liver transplantation. These facts, combined with the inherent limitations in the MELD score to optimally capture 90-day mortality, have prompted investigators to sharpen frailty as an instrument of prognosis and metric for interventions.[10-13] Frailty can be assessed anatomically, through the concept of sarcopenia, defined as the loss of muscle mass. Current assessments, which are not standardized or widely implemented (in part due to cost), involve quantitative radiological analysis of the *psoas* muscle, among others.[4] Complementarily, and more commonly, frailty is assessed physiologically through standardized and aggregated performance-based testing, such as gait speed, grip strength, and chair stands. Such tasks are easily implemented, quantifiable, and longitudinally implemented.[11] As such, these data have prompted increasing appreciation for physical therapy interventions ("prehabilitation") and a renewed urgency in discussing with patients and providers optimization of exercise patterns and nutrition status.

The risk for malnutrition, and/or the worsening of it, in the hospital should not be understated.[14] Efforts should be employed to minimize prolonged periods of *nihil per os* (NPO), for example, during the numerous procedures patients undergo for an expedited liver transplantation evaluation. Patients should be encouraged to engage oral nutrition when able. If it is determined that the patient requires periods of NPO or is unable to maintain appropriate nutritional intake by mouth, assisted enteral nutrition (e.g., Dobhoff tube) or PN should be considered.[15] Ultimately, the nutrition assessment (status and risk for malnutrition) should be routinely performed during the hospitalization to both reflect the patient's condition and gauge ongoing interventions for safety and (when possible) for effectiveness. Interventions should always be specific and goal directed.

Therefore, in this vignette, a number of nutrition concerns should be addressed and optimized. Cholestatic diseases, such as PBC, require attention to fat-soluble vitamin deficiencies and their clinical sequelae.[16] (Table 2) Regarding hepatic encephalopathy (HE), there are many interrelated issues. Recurrent HE episodes, in altering cognition and thus behavior, can fundamentally affect the nutritional intake processes (Table 1). Sarcopenia should

be identfied in such patients, noting that skeletal muscle provides a mechanism for ammonia catabolism (glutamine synthetase pathway), beyond its obvious mechanical function. Moreover, it is becoming increasingly appreciated that increased ammonia levels may actually inhibit muscle protein synthesis and activate proteolysis, thus further exacerbating HE episodes. The BMI is 30, which defines "obesity" status generally, and yet in patients with cirrhosis, this can be misleading. Is the BMI elevated due to fat (and less often muscle), as one would presume, or is there a significant portion (as noted by clinical examination and imaging) that is in fact fluid (e.g., edema, ascites)? From this assessment the requisite corrective therapies can be initiated in the hospital, not the least of which is education to the patient regarding these nuances. Interventional targets will include (1) testing for and repletion of nutritional deficiencies (Table 2); (2) optimizing bowel movements through standard medical therapies to offset the frequency and intensity of HE upon nutritional intake and exercise maintenance; (3) assessing frailty and engaging in longitudinal physical therapy sessions; and (4) understanding the nature of weight (and BMI) and the effects that, e.g., volume overload can have on nutritional status, and also the basic ability to engage in daily healthy activities. It is important to note that interventional efficacy in these domains will not be seen in days, but on the order of weeks to months, and expectations and resources should be tailored to that end.

In the natural history of the patient with decompensated cirrhosis, it is not at all uncommon for there to be increasingly frequent, prolonged, and complex hospitalizations. Nutrition status represents a key factor that both reflects and affects this natural history. Despite the lack of compelling published evidence for nutrition interventions in this scenario, we nonetheless support their thoughtful use to both mitigate malnutrition and preserve overall health.

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