Chapter 14
Nutrition in Patients with Diseases of the Liver and Pancreas

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Key Points

- Malnutrition is common in patients with cirrhosis. The assessment of this can be challenging but recognition and prompt treatment are essential to improving patient prognosis.
- Dietary protein intake of 1.2–1.5 g/kg/day is recommended for patients with advanced liver disease. Protein restriction should be avoided in cirrhotic patients, even those with hepatic encephalopathy.
- Severe acute pancreatitis can result in significant malnutrition and high rates of mortality. Nutritional support through enteral nutrition is the preferred method of maintaining adequate nutrition.
- Supplemental pancreatic enzymes are of central importance in managing the exocrine insufficiency associated with chronic pancreatitis.

Keywords Protein-calorie malnutrition • Hepatic encephalopathy • Ascites • Pancreatic exocrine function • Steatorrhea

Patients with Liver Disease

The end-stage liver disease of cirrhosis is a serious medical condition with high rates of mortality. The average life expectancy of a patient when diagnosed with cirrhosis is 10 years. Complications of liver disease including ascites, hepatic encephalopathy, or gastroesophageal variceal hemorrhage portend a grim prognosis with a 2-year mortality rate of 50% without liver transplantation [1]. These complications herald the onset of significant portal venous hypertension, where the degree of fibrosis within the cirrhotic liver significantly disrupts blood flow through the splanchnic vasculature. There were 36,400 deaths due to cirrhosis and chronic liver disease in the United States in 2013, with a mortality rate of 11.5 per 100,000 population [2].

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Malnutrition is commonly seen in patients with cirrhosis. The appropriate medical management of patients with cirrhosis must therefore include a focus on nutritional aspects of this disease. The liver's role in metabolic homeostasis has long been recognized and with significant compromise of the liver's function, derangements of metabolism will result. In fact, the prevalence of protein-calorie malnutrition (PCM) has been recognized in up to 90% of patients with cirrhosis [3]. Typically, patients with alcoholic liver disease exhibit the most severe degrees of PCM but other causes of liver disease, including cholestatic liver disease and viral liver disease (i.e., hepatitis) are also complicated by significant rates of PCM. The presence of malnutrition in patients with cirrhosis has been recognized to be a predictor of mortality [4, 5]. The recognition of malnutrition in the patient with cirrhosis, with both an assessment of degrees of malnutrition and interventions designed to lessen its severity, are therefore of paramount importance.

The causes of malnutrition in patients with cirrhosis are multifactorial and include poor appetite, early satiety, nausea, and alterations of metabolism. In addition, cholestasis and small intestinal bacterial overgrowth can result in malabsorption of ingested nutrients [3]. The assessment of nutritional risk must therefore take these factors into account.

The clinical appraisal of malnutrition in the setting of cirrhosis can be difficult. A clinical history can disclose important information about dietary intake although in patients with even preclinical encephalopathy, patient recall may be inaccurate. A physical examination plays an important role in the assessment of malnutrition in the cirrhotic patient although these assessments can also be challenging. Measurements such as body mass index or waist circumference can be skewed due to the presence of ascites and edema. Fluid retention can obscure the loss of adipose tissue in the viscera as well as extremities. Nonetheless, a physical examination can disclose the presence of temporal muscle wasting as well as loss of proximal musculature in the arms and legs; areas that may be less susceptible to fluid retention. Indeed, subjective descriptions of proximal muscle weakness are common in patients with cirrhosis, and body protein stores have been noted to be significantly decreased in patients with cirrhosis [6].

Biochemical evidence of malnutrition by measurements of proteins such as albumin and transthyretin (prealbumin) are imperfect measurements of nutritional status as these levels are affected by the presence of inflammation. Nonetheless, serum levels of albumin have been shown to predict survival in patients with decompensated cirrhosis as a component of the Child-Turcotte-Pugh score [1]. Due to the limitations of individual markers of nutritional status, it is imperative to utilize multiple clinical tools including clinical history, physical examination, and laboratory assessments to gain as thorough an understanding as possible regarding the presence of malnutrition in the cirrhotic patient.

Nutritional support in cirrhotic patients requires that attention be paid to multiple considerations. Recommendations regarding dietary intakes in these patients should consider dry weight of the patient, discounting ascites and edema; an assessment that can be challenging in the setting of significant fluid retention. The total calorie needs of patients should be assessed; it is recommended that an intake of 25–35 kcal/kg/day should be administered to patients with well-compensated cirrhosis. Those patients with more severe illness, including decompensated liver disease and hospitalization, require higher daily caloric intake of up to 30–40 kcal/kg/day in order to combat the development of a catabolic state [7]. Protein intake is of paramount importance in the cirrhotic patient. Prior recommendations that patients with decompensated liver disease should restrict dietary protein intake in order to prevent complications of hepatic encephalopathy have not been supported by clinical studies, and have had the effect of exacerbating malnutrition in cirrhotic patients. Dietary protein intake for patients with cirrhosis should be in the range of 1.2–1.5 g/kg/day to minimize the muscle breakdown that is common in patients with decompensated liver disease [8]. Even in patients who are hospitalized with hepatic encephalopathy, immediate protein restriction has not been found to be clinically useful; a hospital diet that provides 1.2–1.5 g/kg/day of protein should continue to be administered [9].

In order to maintain an adequate daily calorie and protein intake, as well as to compensate for a poor appetite, early satiety, and hepatic synthetic dysfunction, some modifications to the daily diet

often must be considered. Cirrhotic patients should eat more frequent (4–6), smaller meals daily, including a nocturnal snack that is enriched in protein to help maintain the recommended intake of both calories and protein in the setting of their physiological derangements [3].

An alteration of the ratios of aromatic and branched-chain amino acids may play a role in the pathogenesis of hepatic encephalopathy. Dietary supplementation with branched-chain amino acids (BCAA) is well tolerated by cirrhotic patients. BCAAs are a reasonable supplement, in lieu of other protein sources, in the patient with refractory hepatic encephalopathy. Supplementation with BCAAs may offer additional benefits to cirrhotic patients including improved prognosis [10]. The regular administration of these supplements in the form of "hepatic" enteral supplements has not been demonstrated to be beneficial in routine use.

Vitamin needs should be considered in patients with end-stage liver disease. Fat-soluble vitamins are commonly found to be deficient in cirrhotic patients due to both poor oral intake and malabsorption. Vitamin D deficiency should be assessed regularly with measurement of 25-OH vitamin D levels. Supplementation should be provided to prevent the development of osteomalacia. Vitamin A deficiency can lead to night blindness. Vitamin K deficiency can lead to increased risks of bleeding in the setting of a prolonged prothrombin time. Supplementation of these vitamins is commonly required in cirrhotic patients. A lack of improvement of prothrombin time despite the administration of supplemental vitamin K implies that decreased hepatic synthetic function is responsible for the observed coagulopathy. Thiamine deficiency is commonly seen in patients with alcoholic liver disease and can precipitate neurological consequences such as Wernicke's encephalopathy. Prompt administration of supplemental parenteral thiamine should be performed in patients hospitalized with complications of alcoholic liver disease and maintenance with oral thiamine supplements should be provided thereafter.

Overnutrition and obesity have emerged as among the leading causes of liver disease. Nonalcoholic fatty liver disease (NAFLD) is the hepatic manifestation of insulin resistance. This condition is increasing in prevalence and is the leading cause of cryptogenic cirrhosis [11]. Paradoxically, the presence of protein-calorie malnutrition (PCM) can coexist with cirrhosis due to overnutrition. Clinically useful medications have not yet emerged for NAFLD although clinical trials are ongoing. At present, the mainstay of therapy for NAFLD is gradual weight loss achieved through lifestyle modification. Various diets, including low-calorie diets as well as ketogenic low-carbohydrate diets, have been studied; an optimal diet for the treatment of NAFLD has not been defined. Some studies have suggested that restriction of simple carbohydrates, or modulating certain types of fatty acids in the diet may have an effect on improving hepatic histology but convincing evidence that would allow firm recommendations continues to be lacking [12].

Ascites is the most common of the major complications of cirrhosis and, as mentioned, heralds a 2-year mortality of 50%. The presence of ascites can result in decreased gastric accommodation and resultant early satiety leading to malnutrition. The etiology of ascites is retention of sodium, not water. The fluid that accumulates in ascites and edema is passively associated with retained sodium. The initial therapy of ascites is to decrease dietary sodium intake thereby inducing a negative sodium balance. This can often be accomplished with sodium restriction to 2000 mg/day, a level of intake that is still consistent with a palatable diet. When dietary interventions fail, diuretic therapy with spironolactone as well as furosemide may be required to increase urinary sodium excretion.

Nutritional support for patients who cannot utilize their intestines, either temporarily due to medical or surgical issues or permanently due to gut failure, is by total parenteral nutrition (TPN). While this intervention has been helpful in the maintenance of the patient's nutrition, well-defined hepatic complications of TPN include the development of cholestasis and even of end-stage liver disease in 15% of those receiving long-term TPN [13]. It is unclear what the best treatment options are for liver disease associated with TPN. Recent studies have focused on the potential use of omega-3 fatty acid infusions during TPN administration although a lack of high-quality data prevent firm recommendations from being made [14].

The utility of herbal supplements in patients with cirrhosis is poorly defined. Milk thistle (silymarin) has been used medicinally for centuries and purportedly has beneficial effects on the liver. Despite the fact that milk thistle has been tested in human trials and the general acceptance of the herb's safety, a clinical benefit for its use of has not been established. In the absence of evidence of utility of other herbal remedies, the use of herbal dietary supplements for the treatment of chronic liver disease is not recommended. The potential hepatoxicity of herbal remedies has been long recognized [15] and without clear evidence of safety, the use of these supplements is not recommended in patients with chronic liver disease.

Patients with Pancreatic Disease

Acute pancreatitis is characterized by marked abdominal pain with nausea and vomiting and associated elevations of serum levels of amylase and lipase. Abdominal imaging with computed tomography can also be used to secure a diagnosis. Typically, abdominal pain is exacerbated by eating which has been attributed to stimulation of the inflamed pancreas that occurs during the digestion process. Acute pancreatitis is characterized as mild when edema of the pancreas is noted on abdominal imaging. Discontinuation of eating is typically one of the first measures taken in a bout of acute pancreatitis along with administration of intravenous fluids and analgesics. In cases of mild acute pancreatitis, abdominal pain typically abates over a few days. Upon improvement of pain, oral intake can be resumed. As oral intake is only delayed by a few days, it is not felt that bouts of mild acute pancreatitis pose a significant nutritional risk to patients.

Severe acute pancreatitis is associated with the development of the systemic inflammatory response system that can result in a high risk of morbidity and mortality. Pancreatic necrosis can result from organ failure; resultant infected pancreatic necrosis can entail mortality rates as high as 30% [16]. Mortality rates are high when adequate nutritional support is lacking because of the marked negative nitrogen balance, hypermetabolism, and catabolism that are characteristic of severe acute pancreatitis. The standard management of patients with severe acute pancreatitis was, for many years, to avoid oral intake so as to prevent further stimulation of the inflamed pancreas. When nutritional support was necessary, this was typically provided by TPN. This approach, however, was found to be associated with high rates of infectious complications due to bacterial overgrowth and translocation of bacteria via the intestines [17]. The use of enteral nutritional support has resulted in improved outcomes from severe acute pancreatitis. It is necessary to initiate nutritional support within 48 h of admission for pancreatitis in order to combat the metabolic distress of the condition [16]. Enteral nutrition improves the structural integrity of the intestinal mucosa, preventing bacterial translocation and infectious complications.

Nutritional support is best administered via a nasojejunal feeding tube, which has the advantage of delivering nutrition distal to the pancreas thereby avoiding further stimulation of the pancreas. Interestingly, studies have demonstrated that there is no significant difference in outcomes between nasojejunal and nasogastric feedings [18]. Therefore, enteral nutrition should not be delayed if deep intestinal intubation is not obtained with a feeding tube. There is no convincing evidence that any particular type of enteral tube feeding is superior [19]. There is no evidence that the administration of probiotics yields any improvement in clinical outcomes and clinical trials have actually yielded contradictory data as to whether mortality rates may be affected by the administration of probiotics [19]. Until clear evidence emerges, no recommendations about specific enteral formulations can be made, other than that enteral nutritional support is superior to parenteral nutrition, as well as superior to no nutrition at all.

Chronic pancreatitis is the condition where progressive inflammatory changes in the pancreas result in structural changes of the pancreatic duct as well as fibrosis and calcification of the pancreatic body. Over time, both endocrine and exocrine functions of the pancreas become compromised. The most common cause of chronic pancreatitis is long-standing abuse of alcohol, which may be

accompanied by nutritional deficits irrespective of associated pancreatic disease. Chronic pancreatitis is a cause of pain that can lead to anorexia and resultant malnutrition. Maldigestion of food results from deficient pancreatic exocrine function. When the functional mass of the pancreas declines to the point that pancreatic enzymes including lipase and trypsin are reduced to less than 10% of baseline, steatorrhea indicative of poor fat digestion can occur [20].

Maintaining adequate caloric intake is the nutritional goal of patients with chronic pancreatitis but can be limited by chronic pain. Multiple modalities often need to be utilized to treat the chronic pain. There is some evidence that elemental diets, fat avoidance, supplemental pancreatic enzymes, and lifestyle modification including alcohol avoidance and tobacco cessation may improve symptoms of pain in chronic pancreatitis [21]. In addition to conservative measures to improve the pain, the judicious use of analgesics, as well as surgical and endoscopic therapies may improve pain and anorexia in selected patients [21].

While avoidance of dietary fat will result in improvement of steatorrhea, this intervention can result in an inadequate intake of fat-soluble vitamins. Therefore, the use of supplemental pancreatic enzymes (SPE) along with a normal fat diet is the preferred means of treatment of steatorrhea [22]. The administration of 25,000–75,000 IU of pancreatic lipase ingested concurrently with meals allows for the proper digestion of dietary fat and amelioration of steatorrhea [20]. As the effect is greatest if the enzymes properly mix with ingested food, it is therefore important that the SPE be taken during the meal and not before or after it. SPE should be taken with all ingested foods though the amount taken can be reduced for snacks. Some types of SPE are susceptible to inactivation by gastric acid; medical control of gastric acidity may therefore be required for full effectiveness. Fat-soluble vitamin supplementation (A, D, E, and K) should be offered to all patients with chronic pancreatitis in whom maldigestion or steatorrhea is seen.

In the rare patient in whom weight loss and steatorrhea persist despite the use of SPE, medium-chain triglycerides can be used as a dietary supplement [20]. They are absorbed by the intestine in a lipase-independent manner and can provide adequate fat-derived calories despite the lack of sufficient pancreatic function. The use of TPN is generally not required in patients with chronic pancreatitis though rare indications may be discovered.

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Suggested Further Reading

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