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MINIREVIEWS

Nutritional support in chronic liver disease and cirrhotics

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Abstract

The liver is a major organ and an essential component in maintaining an appropriate nutritional status in healthy individuals through metabolism of protein, carbohydrates, and fat. In individuals with chronic liver disease (CLD), along with a number of other essential functions that the liver serves, its role in nutrition maintenance is severely impaired. Common causes of CLD include hepatitis C, alcoholic liver disease, and non-alcoholic liver disease. Amongst this population, the most common manifestation of impaired nutritional maintenance is protein-calorie malnutrition. Aside from inherent abnormalities in metabolism, such as malabsorption and maldigestion, CLD can be associated with anorexia as well as increased metabolic requirements, all of which contribute to a state of malnutrition. Given the systemic implications and impact on prognosis of malnutrition, proper nutritional assessment is essential and can be achieved through a thorough history and physical, as well as biochemical investigations and anthropometry as needed. Following an appropriate assessment of a patient's nutritional status, an approach to management can be decided upon and is based on the extent of malnutrition which directly reflects the severity of disease. Management options can be grossly separated into enteral and parenteral nutrition. The former is usually sufficient in the form of oral supplements in less severe cases of malnutrition, but as the CLD worsens, parenteral nutrition becomes necessary. With appropriate assessment and early intervention, many of the complications of CLD can be avoided, and ultimately better outcomes can be achieved.

Key words: Chronic liver disease; Cirrhosis; Energy requirements; Nutrition; Malnutrition; Anthropometry; Liver

Core tip: This paper highlights the most recent evidence in the clinical approach to dealing with nutrition in patients with chronic liver disease and cirrhotics.

We will review the pathophysiology of liver disease, etiology, and management of nutrition.

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INTRODUCTION

The liver is a major organ involved in maintaining appropriate nutritional status. Its role includes metabolism of protein, carbohydrates and fat, which are essential sources of nutrition for the body. Accordingly, patients who suffer from chronic liver disease (CLD) often experience debilitating and severe malnutrition that both reflects the severity of the disease, and thereby disease prognosis, but is also an independent predictor of mortality[1,2]. Malnutrition in CLD is a function of multiple factors including, but not limited to, impaired absorption and/or digestion, increased metabolic requirements, as well as anorexia and overall decreased oral intake. The permanent functional deficits in cirrhosis result in nutritional deficiencies with systemic impacts, and coupled with the several mechanisms by which these nutritional deficiencies are realized, approaches to management and support are increasingly complicated[3]. Given the prognostic implications of nutritional status in patients with CLD, further insight into the assessment and therapy of these patients is essential to appropriate management. This literature review aims to summarize a general approach to nutritional support in patients with CLD, including exploring etiology, clinical assessment and key investigations, as well as management.

ETIOLOGY AND PREVALENCE

CLD involves a process of continuous inflammation and regeneration that eventually results in permanent fibrosis and cirrhosis. The most common cause of this condition is hepatitis C virus infection[4]. Other common causes include alcoholic liver disease, non-alcoholic fatty liver disease (NAFLD) and hepatitis B virus infection. Although it is difficult to assess, experts estimate that over 844 million people worldwide have CLD, and this associated with a mortality rate of approximately 2 million deaths per year. Of those affected by CLD, approximately 20% with compensated cirrhosis and 65%-95% with decompensated cirrhosis have protein-calorie malnutrition (PCM)[5]. PCM is a condition involving cachexia due to nutritional deficiencies in calories and protein. This decline in essential macronutrients can lead to extensive body wasting as well as other related sequelae. Micronutrient deficiencies are also present in patients with CLD, albeit with a more subtle presentation than PCM. In the context of cirrhosis, patients with associated malnutrition have higher rates of hepatic encephalopathy, infection, ascites and variceal bleeding[6]. Multiple studies have documented increased complications and overall length of hospital stay in malnourished patients[7]. It is no question that malnutrition complicates patient management significantly, leading to increased rates of morbidity and mortality in CLD patients.

MALNUTRITION

Dietary intake

The underlying cause of malnutrition in patients with CLD and cirrhosis is multifactorial, and is typically related to a loss of appetite, malabsorption and increased metabolic requirements. Low dietary intake is commonly found among cirrhotic patients. Davidson *et al*[8] describes the hepatic role in appetite regulation through clearance of chemical mediators like cholecystokinin, which contributes to feelings of satiety. The liver also contributes to splanchnic production of cytokines that reduce the hypothalamic-mediated drive for appetite. Furthermore, considering that ascites is a common complication of CLD, the mechanical compression may possibly lead to a premature feeling of fullness. In addition to a low overall dietary intake, there is an alteration in the pattern of fuel consumption in the body. There is a higher rate of fat oxidation in the fasting state of CLD patients. During an overnight fast, a research study showed that 58% of energy came from fat oxidation in cirrhotics, whereas healthy controls derived 55% of their energy from carbohydrates[9]. This may reflect the low hepatic glycogen stores found in patients with cirrhosis. Additionally, in a study by Nielsen *et al*[10], they demonstrated that body size in cirrhotic patients increased during refeeding therapy. This indicates that the volume of dietary intake was in fact a contributing factor to the decline in body mass and overall malnutrition in CLD patients.

Malabsorption

Malabsorption is also an important consideration in patients who present with malnutrition in the setting of CLD. Liver disease that leads to a decline in the bile-salt pool can contribute to fat malabsorption[11]. This is commonly found in patients who suffer from comorbid biliary and pancreatic disease, as there is a decrease in fat and fat-soluble vitamin absorption. The extent of malabsorption in CLD patients without related cholestatic disease is currently a topic of controversy. Some studies claim that regardless of etiology, CLD patients experience bacterial overgrowth

from small bowel hypomotility and portal hypertension that can contribute to malabsorption[12]. While others have found that neither fat nor protein are noticeably malabsorbed unless there is co-existing biliary or pancreatic disease.

Energy requirements

Whether or not increased metabolic requirements contribute to malnutrition in CLD is considered uncertain, with varying levels of evidence to support this claim. Müller *et al*[13] found that the average resting energy expenditure (REE) in a study of 473 cirrhotic patients was found to be normal. However, 34% of patients had an increased REE of over 120% of the expected value[13]. Various causes for hypermetabolism in CLD have been proposed, including infection, ascites and portal hypertension. The link between energy expenditure and malnutrition in cirrhotics remains unclear and further research on this topic is required. In addition to metabolic changes, the overall protein requirement is also increased in patients with CLD. Druml *et al*[14] credits this to a decrease in the production of protein, and an increase in the rate of protein degradation. Low glycogen reserves in the liver trigger increased rates of gluconeogenesis from amino acids, which are derived from protein breakdown. These elevated protein requirements in cirrhotic patients can contribute to a state of malnourishment.

NUTRITIONAL ASSESSMENT (PHYSICAL EXAM AND SERUM MARKERS)

Considering that PCM and micronutrient deficiencies have major prognostic implications in patients with CLD, it is essential to effectively and regularly assess nutritional status. Clinicians should consider and analyze multiple factors in order to make a comprehensive nutritional assessment. This typically includes a medical history, extensive physical examination, laboratory data and more.

History

A thorough medical history can offer significant insight as a preliminary assessment of nutritional status. Discussing the patient's eating behaviors and dietary intake through 24-h recall can help the clinician identify possible sources of malnutrition. Recent weight loss is also important to review, as it can point towards the severity of nutritional deficit. This can be complicated in cases of decompensated cirrhosis, as water retention and ascites can lead to inappropriate increases in weight. It is also imperative to identify comorbidities, as they can indirectly impact nutritional status. For example, underlying nausea, vomiting, or anorexia can decrease dietary intake and contribute to malnourishment irrespective of the underlying CLD. Additionally, the severity of liver disease should be assessed through various clinical tools like the Child-Pugh score or Model for End-Stage Liver Disease (MELD) score[15]. The clinical suspicion and onset of malnourishment is directly related to the extent of liver disease in patients.

Physical examination

An appropriate physical examination is a critical component of an effective nutritional status assessment. Macronutrient and micronutrient deficiencies can have a variety of unique physical manifestations. Common examples include pallor in iron deficiency, dermatitis in vitamin A deficiency, bruising in vitamin K or C deficiency and many more[16]. Of particular importance is being able to recognize and assess sarcopenia, which is the generative loss of skeletal muscle mass. Sarcopenia is the most common complication of cirrhosis and so will often be the initial or only presentation of someone with malnutrition secondary to CLD[17]. One of most notable and effective measures of nutritional assessment in clinical practice is known as the subjective global assessment (SGA). The SGA is a standardized array of questions and physical exam findings that are collectively scored to provide a comprehensive rating of nutritional status[18]. In the medical history component, patients are asked a variety of questions about weight changes, dietary intake, associated symptoms, and functional capability. The physical examination includes an assessment of muscle wasting, peripheral edema, ascites, and fat loss. They are then graded with a letter score: Grade A - well nourished, Grade B - Moderately malnourished, Grade C - Severely malnourished. The SGA has been found to serve as a good prognostic indicator in post-liver transplant and chronic dialysis patients[19]. Unfortunately, the SGA is a subjective assessment and it has been found to underestimate the severity of malnutrition in cirrhotic patients compared to the handgrip strength (HG) tool[20]. However, despite being a subjective assessment, there is an 80% inter-rater reproducibility of SGA results[19]. A variation of the SGA includes Royal Free Hospital Global Assessment (RFHGA) tool. This assessment tool adds anthropometric measurements and incorporates gender differences into its final rating of nutritional status[3].

Serum markers

In addition to an appropriate history and physical, there are various laboratory markers that help evaluate the nutritional status of a patient. Currently, various plasma proteins, vitamin levels, and creatinine are considered useful for nutritional assessment. Albumin, pre-albumin, and occasionally transferrin are major plasma proteins that are included in biochemical investigations. Prealbumin, also known as

transthyretin, is a hepatic protein that has been found to correlate well with the body protein status. With a half-life of approximately 2 d, its serum concentration closely reflects recent dietary intake. Production is measurably decreased roughly 14 d following insufficient dietary protein intake, which is less than 60% of the required amount[21]. Devoto *et al*[22] found that prealbumin levels correlated well with the Detailed Nutritional Assessment (DNA) tool, which was used as a reference standard for detecting PCM. They concluded that prealbumin is a good screening tool for protein malnutrition. Furthermore, low prealbumin levels as a nutritional marker have been shown to correlate with higher rates of complications and mortality[21]. In an independent study of dialysis patients, prealbumin was found to be the best nutritional predictor of survival in comparison to serum albumin, cholesterol and creatinine[23]. A serum level less than 15 mg/dL denotes concern for malnutrition[21]. Limitations to the use of prealbumin include inappropriate fluctuations after an alcoholic binge, prednisone use, or active infection and inflammation[24].

In addition to prealbumin, serum albumin was historically considered a good nutritional marker for protein status. However, recent studies have placed significant doubt on this claim and reported no significant link between albumin levels and nutritional status[25]. In malnourished patients, albumin levels were effectively maintained despite the clinical presence of severe PCM. Furthermore, albumin has a half-life of 20 d, making it a particularly slow tool for use in tracking clinical improvement or decline[25]. The serum concentration is also heavily impacted by active inflammation, where hepatic protein synthesis is reduced in order to prioritize the production of acute phase reactants[26]. Several studies have therefore recommended against the use of albumin for nutritional assessment, claiming that it does not serve as a marker for PCM. Similar to albumin, transferrin is also major hepatic protein that was historically measured to assess nutritional status. Transferrin functions as a transport protein for iron. Its use as a marker for protein status is limited because of the large number of factors that influence serum levels[27].

Finally, another major serum marker that has historically been used as a measure of protein status includes creatinine. Researchers hypothesized that urinary creatinine can be used as a serum indicator because it is almost entirely derived from processes in muscle tissue. A creatinine-height index (CHI) was developed as a method of assessing protein status[28]. However, this tool requires 24-h urine measurements and this can serve as a limitation to clinical application. Nevertheless, studies have shown that CHI as a nutritional marker serves as a better prognostic indicator than total body protein and serum albumin.

In terms of micronutrient malnutrition, serum measurements of various vitamins and minerals can serve as a rough measure of total body stores. The specific micronutrients that warrant clinical attention can depend on the etiology of cirrhosis. For example, alcoholic liver cirrhosis is often associated with a thiamine deficiency and cholestatic liver disease can include deficiencies in fat-soluble vitamins.

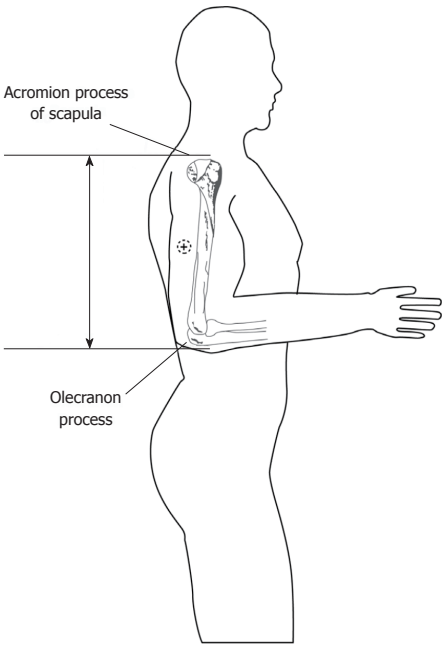

Figure 1 Position for mid-arm muscle circumference measurement[49].

Anthropometry

The mainstay of nutritional assessment almost always involves a history, physical and biochemical investigation. However, patients with a more complicated picture of malnutrition can undergo anthropometric ancillary tests to better characterize their nutritional status. One of the simplest methods of anthropometric assessment includes the body mass index (BMI). BMI evaluates patient height and weight to determine if they are underweight, normal, or overweight. However, the use of BMI in liver disease is very limited as patients often have volume overload complications, which can lead to an overestimation of nutritional status[29]. An anthropometric test that is less affected by fluid status is known as mid-arm muscle circumference (MAMC). MAMC can be used as a measurement of lean tissue levels and muscle bulk (Figure 1). Multiple studies have demonstrated that MAMC correlates well with various other markers in estimating muscle mass[18]. Specifically, it has been shown to correlate well with body cell mass (BCM) measurement, which is a proven marker for PCM in CLD patients. There is also prognostic value to MAMC measurements, as it is associated with mortality risk in CLD patients[1]. In addition to MAMC, triceps skinfold

Figure 2 Position and technique for triceps skinfold thickness measurement[49].

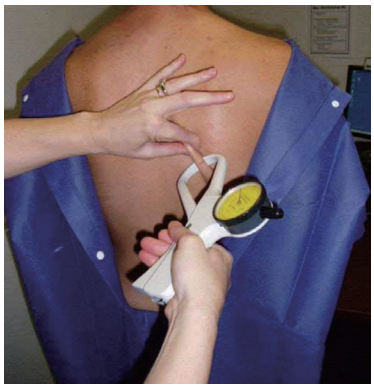

Figure 3 Position and technique for subscapular skinfold thickness measurement[49].

thickness (ST) is another anthropometric test that uses a caliper to measure fat reserve (Figure 2). ST was found to correlate with DEXA scan as a marker of body fat stores. Both ST and MAMC compare results on a percentile score, with values below the 5th percentile indicating severe malnutrition[20]. Anthropometric measurements are widely available, inexpensive and easy to complete. This makes them quite invaluable as bedside tools for nutritional status assessment. However, a major limitation to the use of anthropometric measurements as nutritional markers includes poor inter-rater reproducibility of results[30] (Figure 3) .

Functional measurements have also gained popularity as tools to assess nutritional status in CLD patients. In particular, HG has been shown to be a strong predictor of malnutrition. In a study by Alvares-da-Silva *et al*[20], HG was found to be more sensitive than SGA in predicting malnutrition and the incidence of major complications at 1-year in cirrhotic patients. This functional assessment is completed with a dynamometer and is useful for tracking clinical change in patients. Refer to Table 1 for a summary of these anthropometric measurements and their unique limitations.

Miscellaneous

Less commonly used tests for nutritional status assessment include a DEXA scan, bioelectrical impedance analysis, and *in vivo* neutron activation analysis (IVNAA). These tests are rarely used, primarily due to their limited availability and high cost[30]. DEXA scans can accurately assess the fat mass in CLD patients. Sarcopenia is the most common complication of cirrhosis and DEXA scans can also be used to assess skeletal muscle mass[31]. Additionally, CT and MRI scans can be used to measure the extent of sarcopenia as they both can determine muscle cross-sectional area. These two tests are not used as commonly as DXA scans would be in assessment of sarcopenia however because CT scans are expensive and expose the patient to significant radiation, while MRI scans are also expensive and less available[17]. Bioelectrical impedance analysis uses electrodes to accurately estimate fat content. IVNAA is used to measure total body protein and can serve as a good indicator of PCM[30]. Nevertheless, these are not typical tools used in a standard nutritional assessment.

MANAGEMENT - ENTERAL AND PARENTERAL

Therapeutic interventions to maintain adequate nutritional status in CLD patients can be divided into enteral or parenteral forms. The indications and contraindications for each mode of therapy vary widely depending on the patient and the extent of disease.

Generally speaking, guidelines suggest that the required energy intake for cirrhotic patients is 35-40 kcal/kg-BW per day and a protein intake of 1.2-1.5 g/kg-BW per day[32,33]. The dietary plan for an average 70 kg adult does not significantly differ from a practically "normal" diet, as long as the above caloric and protein intake guidelines are met (usually through protein supplementation). In fact, the diet of CLD patients is largely based on a standard diet with added supplements as needed[31]. It is however important to discuss variations in a patient's condition, as they may concomitantly have hepatic encephalopathy or hepatic-renal syndrome, and these must be addressed as well. With regards to hepatic encephalopathy, the general recommendation currently is to simply continue usual diet, while maximizing appropriate treatment with lactulose rifaximin, and so on[33]. In hepato-renal syndrome, there do not appear to be any recommendations as per the current literature to adjust nutrition, and the current approach remains to address the underlying mechanism causing HRS (*e.g.*, correcting hypovolemia with albumin infusions)[34].

Note that CLD can arise through different pathologies, including NAFLD. This is of particular importance because the pathophysiology through which NAFLD arises is metabolic syndrome and diet/

Table 1 Anthropometric techniques: Benefits and limitations

Technique	Benefits	Limitations
BMI	Weight (kg)/height (m^2) Indicator of choice for chronic undernutrition in adults Probability of misclassifying nutritional status on basis of BMI considered to be very small	Confounded in cirrhotics with ascites and peripheral edema
Mid-arm muscle circumference	Measured in centimeters using flexible measuring tape (halfway between olecranon and acromion process) Less influenced by patient fluid status (upper limbs less commonly edematous) Recognize malnutrition earlier relative to BMI Better at recognizing mild-moderate malnutrition	Possibly significant inter-observer variability Poorly recognizes patients with severe malnutrition
Skinfold thickness (triceps, biceps, subscapular, suprailiac)	Measured in millimeters using skinfold caliper Less influenced by patient fluid status Recognize malnutrition earlier relative to BMI Better at recognizing mild-moderate malnutrition	Possibly significant inter-observer variability Poorly recognizes patients with severe malnutrition
Handgrip strength	Measured in kilogram force, using hydraulic dynamometer adjusted to patient hand size Highly sensitive indicator of functional impairment, reflective of protein-calorie malnutrition Correlates with severity of clinical outcome in different disease states	Requires certain equipment to measure which may not be widely available

BMI: Body mass index.

lifestyle is largely implicated[35]. Given this, addressing diet in patients with CLD from NAFLD is of utmost importance. General recommendations are to reduce total fat, saturated fats, trans fats, and fracture, while simultaneously increasing intake of polyunsaturated fats, and monosaturated fats[35]. These changes will likely benefit any patient with CLD but are especially important in those with NAFLD.

As prognosis is closely linked to nutrition in patients with chronic liver pathology, the goal of any therapeutic measure is to achieve the recommended intake amount.

Enteral

Enteral means of nutritional administration implies that food is absorbed primarily through the digestive processes of the gastrointestinal tract. The intake of nutritional substances can be done orally, directly into the stomach, or from the rectum. In the setting of comorbidities or inability to consume food orally, a nasogastric (NG) or percutaneous endoscopic gastrostomy (PEG) tube can be inserted for direct gastric administration.

Oral

The content and distribution of diet must be regulated to ensure adequate nutritional intake in CLD and cirrhotic patients. The general diet recommendation is to have multiple (5-6) small meals that are rich in complex carbohydrates, while lipids may compose 20%-30% of the overall caloric intake[32]. Initially, it was thought that protein restriction was essential as it was shown to decrease the incidence of encephalopathy in end-stage liver disease. However, recent insight into the value of protein restriction has shown that there is minimal impact on the onset of encephalopathy and rather that overall protein intake should be increased since requirements are higher[36]. A diet low in protein should therefore be avoided.

One of the largest topics of study in patients with liver disease includes the possible benefits of oral supplement use. More specifically, there have been multiple research studies on the use of branched chain amino acids (BCAAs) for nutritional support. BCAAs include leucine, isoleucine, and valine, which cannot be synthesized in the body and must be obtained through diet[37]. Patients with CLD or cirrhosis are known to have low levels of BCAAs, which impacts a variety of bodily functions including ammonia detoxification. Furthermore, inadequate levels have been shown to worsen hepatic encephalopathy and ultimately contribute to a worsened clinical outcome[36]. Multiple research studies have demonstrated benefits of using BCAA supplementation for patients with severe liver disease. A randomized clinical trial showed that long-term supplementation with oral BCAAs helped prevent progressive hepatic failure[37]. They have also been noted to improve cases with pre-existent hepatic encephalopathy. In addition to BCAAs, usage of a controlled diet with nutritional supplements like casein-based protein mixtures were associated with lower bilirubin levels, improved prothrombin time and an overall reduction in infection[37]. A 2012 systematic review by Koretz *et al*[32] identified that the use nutritional supplements in oral feeding for patients with liver disease were associated lower rates of ascites, infection and hepatic encephalopathy. Finally, multivitamins are also recommended but there is

limited research on the benefits in CLD patients.

Increasing numbers of patients with CLD are being found to have coexisting celiac disease and this introduces an additional barrier with regards to tailoring feeds to achieve appropriate nutrition[38-40]. Given that general recommendations for diet include meals that are rich in complex carbohydrates, it is essential that patients with concomitant celiac disease ensure the carbohydrates that they intake are gluten-free. Many BCAA supplements do not contain gluten, and further supplementation with protein mixtures can be achieved by ensuring the protein mixture acquired is gluten-free[41]. Although celiac disease does in fact introduce an additional barrier, much of it can be overcome with a fastidious approach to which foods are consumed. These principles apply to other methods of nutritional intake explored below as well.

Tube feeding

If it is evident that nutritional requirements cannot be met through oral feeding, the next line of therapy is tube feeding. In regards to the use of a NG or PEG tube, clinicians are often concerned about the possibility of an NG tube causing gastrointestinal bleeding. However, literature has found that the risk of GI bleeding in NG tube placement is quite low and should not deter clinicians away from this form of tube feeding[42]. The European Society for Parenteral and Enteral Nutrition (ESPEN) guidelines originally indicated that tube feeding could be used in patients who were not able to maintain adequate nutritional status through oral intake, even in the presence esophageal varices. Though, this was modified shortly after the results of a small-randomized trial identified the possibility of tube feeding causing recurrence of bleeding[42]. The guidelines were then changed to state that tube feeding in patients with esophageal varices is dangerous, and that patients should be closely monitored should this therapy be initiated[42].

When NG tubes are needed for extended periods of time, smaller diameter NG tubes are recommended to avoid irritation of the nasal mucosa when in use for extended periods of time. However, in cases where long term enteral tube feeding is needed, there is typically discussion on the merits of using a PEG tube. Major problems with using PEG tubes in this patient population are that there are various instances in liver disease where PEG tubes are contraindicated; specifically in the setting of ascites, bleeding varices, coagulopathy or other sequela of decompensated cirrhosis[43]. Due to this, clinicians are rarely inclined to use a PEG tube for CLD or cirrhotic patients.

Research comparing oral diets to enteral-tube feeding has shown variable results in determining which mode of nutrition provides better outcomes. Studies by Kearns *et al*[44] and Cabre *et al*[45] have shown significant clinical improvements in serum albumin, Child's score, and a reduction in mortality with patients who were on enteral-tube feeding compared to oral diet controls[46]. Accordingly, a recent multicenter trial in 99 cirrhotic patients randomly placed half on enteral tube-feeding for 4 wk, followed by oral supplements for 8 wk while the other half was kept on a strict oral diet[47]. Using short-term enteral tube feeding allowed investigators to achieve the recommended caloric intake in 70% of patients, but there was no difference in 1-year survival, or other liver parameters between the 2 groups[47]. Considering the multitude of studies on the topic of oral nutrition *vs* tube feeding, Hasse *et al*[48] performed an extensive review of enteral nutrition in the setting of liver disease. This review indicated that evidence for starting a patient on oral or tube feeding is currently inconclusive, as the majority of data show highly variable results[48]. However, the discussion of when to use oral or tube feeding is typically not a matter of preference, but more so what a patient is able to tolerate. Currently, this review of enteral nutrition outlines that patients should maximize oral intake with a targeted diet and supplements initially. At this stage, individuals should be closely monitored to see if oral feeding is able to achieve the desired caloric and nutrient intake. If nutritional status continues to decline, it is recommended that patients begin tube feeding within 1 wk of inadequate oral intake[42,48]. Delaying the onset of tube feeding is associated with worse outcomes and delayed improvement in nutritional status. NG tubes are recommended, since PEG tubes are often contraindicated in CLD patients.

There are various formulas that are suitable for tube-feeding depending on the individual patient disease. They may typically be a standard formula that is protein rich, or nutrient-dense in those who are on fluid restrictions. These can also be hydrolyzed for those who have impaired digestion, include more BCAAs or offer immune complexes for patients that are immunocompromised. These formulas are highly variable and can be altered for individual patient needs.

Parenteral

Parenteral nutrition therapy is an intervention in which feeding is done entirely through an intravenous line. In patients with liver disease, parenteral nutrition is often recommended when caloric and nutritional intake is insufficient through either oral or enteral means. It can also be considered in short-term situations where patients must undergo prolonged fasts for procedural considerations. It is also a consideration in patients with compromised airways, encephalopathy or impaired swallowing reflexes that would make oral and sometimes tube feeding difficult.

Cirrhotic patients require a caloric intake that is

approximately 1.2-1.3 times the REE[43]. Nutrient intake is divided into carbohydrates, lipids, proteins and micronutrients. Through parenteral nutrition, carbohydrates are provided in the form of glucose to make up for approximately 50%-60% of non-protein energy requirements. Lipids are provided as emulsions of unsaturated fatty acids that make up approximately 40%-50% of non-protein energy requirements. Protein requirements are met through an infusion of amino acids that ranges from 1.2-1.5 g/kg per day depending on the patient's current disease severity[43]. These amino acid solutions typically contain a larger proportion of BCAAs and a lower fraction of aromatic amino acids[16]. The inclusion of micronutrients into parenteral formulas is a topic of controversy as many studies have failed to show actual therapeutic benefits. Nevertheless, various water and fat-soluble vitamins, and electrolytes are included in the overall infusion by clinicians. This is primarily because CLD is often associated with significant micronutrient deficiencies, specifically those that have an alcohol-related etiology[44]. Once again, the recommendations for beginning parenteral nutrition are when oral and enteral means have been tried and failed.

There are a variety of complications involved with parenteral nutrition. Since it often requires chronic vascular access, there is risk of catheter infection and clotting. Furthermore, there is risk of total parenteral nutrition (TPN) induced liver disease, particularly due to interactions between linoleic acid (major lipid source of calories) and the liver parenchyma[43]. Furthermore, patients may experience severe hunger pains because TPN use completely bypasses the GI system. Refeeding syndrome is also a consideration in patients with severe cirrhosis or CLD that have been experiencing severe nutrient deficiencies for a prolonged period of time[9].

CONCLUSION

In summary, given the essential role of the liver in maintaining appropriate nutritional status, the importance of prompt recognition of nutritional deficiency in patients with CLD cannot be understated given the immense implications it has on overall morbidity and mortality. The etiology of this malnutrition is multifactorial, including decreased intake, increased metabolic requirements, and malabsorption/maldigestion. Recognizing and assessing nutritional deficiencies can be challenging in patients with CLD. Although a history and physical examination can prove helpful, often they are insufficient and further investigations in the form of serum markers and anthropometry are required for proper assessment. Ultimately, management is in the form of enteral or parenteral nutrition, with the appropriate choice being reflective of disease severity. Although enteral nutrition in oral form with appropriately selected supplements can be sufficient in managing the majority of patients with CLD and malnutrition, often with worsening disease and malabsorption/maldigestion, a step-wise approach moving from oral, to tube feeding, and if necessary, parenteral nutrition is required. Early recognition and intervention is beneficial as the systemic implications of malnutrition greatly impact the prognosis and can limit management options as the disease progresses. With an appropriate approach to malnutrition in CLD, many of the associated complications can be avoided and overall improve the outcomes in this patient population.

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