Recent Progress of Nutritional Management for Liver Cirrhosis

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Summary Evidence-based Clinical Practice Guidelines for Liver Cirrhosis were updated in 2021 by The Japanese Society of Gastroenterology/Japan Society of Hepatology. In the guidelines, the flowchart for nutritional therapy was revised based on accumulated evidence. In particular, sarcopenia is incorporated as an assessment for nutritional status. In addition, late evening snack is repositioned as a 1st-line nutritional therapy. Furthermore, recent study demonstrated unforeseen pharmacological actions of branched-chain amino acids including improving sarcopenia and prognosis. In this mini-review, we summarize the updated points for nutritional therapy for patients with liver cirrhosis.

Key Words liver cirrhosis, albumin, sarcopenia, late evening snack, branched-chain amino acids

Evidence-based Clinical Practice Guidelines for Liver Cirrhosis were updated in 2021 by The Japanese Society of Gastroenterology/Japan Society of Hepatology (1, 2). In the guidelines, the flowchart for nutritional therapy was revised based on accumulated evidence. Furthermore, a recent study demonstrated the usefulness of the flowchart for stratifying the mortality risk and providing effective nutritional interventions in malnourished patients with liver cirrhosis (3). In this review, we summarize the updated points for nutritional therapy for patients with liver cirrhosis.

Nutritional assessment

The initial step of nutritional therapy is assessment. Nutritional status is evaluated by the following three criteria: 1) serum albumin level ≥3.5 g/dL, 2) Child-Pugh class B or C, 3) presence of sarcopenia. Patients who fulfill any of the above three criteria are considered as having malnutrition (Fig. 1).

Diagnosis of sarcopenia

In the guidelines, the diagnosis of sarcopenia is based on handgrip strength and skeletal muscle mass. A feature of the diagnostic criteria for sarcopenia is no requirement of evaluation for walking speed. All patients with slow walking speed are known to show low handgrip strength (4). Thus, grip strength is a suitable proxy for walking speed in patients with liver cirrhosis. Sarcopenia is highly prevalent in patients with liver cirrhosis (1, 2). In addition, sarcopenia is an independent prognostic factor and should be paid attention to (5).

Late evening snack (LES)

For cirrhotic patients with malnutrition, the 1st-line nutritional therapy is divided meal/LES (1, 2). LES was originally developed for the improvement of nocturnal starvation (6). Nocturnal starvation is frequently seen in cirrhotic patients while asleep and is associated with disease progression. A pathogenesis for nocturnal starvation is a decrease in hepatic glycogen, which results in an energy shortage while asleep, whereas LES acts as an energy source like hepatic glycogen and maintains blood glucose concentration while asleep, leading to the improvement of nocturnal starvation. In addition, a meta-analysis demonstrated that LES exerts beneficial effects on hepatic biochemical parameters including albumin, ammonia, and prothrombin time (7). LES also suppresses the development of ascites and hepatic encephalopathy, and improves survival in patients with liver cirrhosis (7, 8).

Branched-Chain Amino Acids (BCAAs)

A low ratio of plasma BCAAs to aromatic amino acids is a hallmark of liver cirrhosis (9) and the 2nd-line nutritional therapy is oral BCAA-related agents (1, 2). There are two types of oral BCAA-related agents in Japan, namely BCAA granules and BCAA-enriched supplementation (10, 11). BCAA granules consist of L-isoleucine, L-leucine, and L-valine, and are approved for hypoalbuminemia in decompensated cirrhotic patients with sufficient energy intake (12). BCAA-enriched supplementation consists of BCAAs, other amino acids, lipids, carbohydrates, minerals, and vitamins (13). BCAA-enriched supplementation is approved for malnutrition in patients with chronic liver failure accompanying hepatic encephalopathy (14).

BCAAs are not only protein constituents. BCAAs act as pharmacological nutrients (9) (Fig. 2). For instance, BCAAs promote albumin synthesis in rat primary hepatocytes through an up-regulation of the mammalian target of rapamycin signaling (15). BCAAs also increase the amount of reduced human serum albumin, leading to the restoration of albumin function in cirrhotic patients (16). Besides effects on albumin,
BCAAs stimulate the secretion of hepatocyte growth factor from hepatic stellate cells (17). BCAAs also improve the dendritic cell function (18). In addition, BCAAs improve insulin resistance, which is associated with hepatocarcinogenesis in patients with liver cirrhosis (9). Furthermore, BCAAs improve the function of the intestinal tight junction and suppress hepatic translocation of microbiota in a mouse model of liver cirrhosis (19). These findings suggest that BCAAs promote hepatic regeneration, improve immunity, and suppress the onset of hepatocellular carcinoma (HCC) and bacterial translocation. In fact, large-scale, multicenter studies demonstrate that BCAAs inhibit the development of life-threatening events including the development of hepatocellular carcinoma, and prolong the overall survival of patients with liver cirrhosis (8, 20, 21).

BCAAs are unique in the metabolism site. Unlike most amino acids, BCAAs are catabolized mainly in the muscle. In patients with liver cirrhosis, BCAAs are used to promote the detoxification of ammonia in muscles. BCAAs also increase protein synthesis and cause the anabolism of muscle. BCAA supplementation reverses impaired mammalian target of rapamycin signaling and increased autophagy in the muscle, leading to the suppression of sarcopenia in patients with liver cirrhosis (22–24).

Carnitine/zinc/vitamin D

Deficiency of carnitine, zinc, and vitamin D is frequently seen in patients with liver cirrhosis (1, 2). This issue is not included in the flowchart for nutritional therapy due to a lack of sufficient evidence. However, previous studies showed that supplementation of these nutrients improves hepatic function and sarcopenia as well as the survival of patients with liver cirrhosis (25–27).

Conclusion

In this review, we summarize the updated points for nutritional therapy for patients with liver cirrhosis. Recent evidence has clearly demonstrated that nutritional therapy improves not only hepatic function but also survival and quality of life in patients with liver cirrhosis. Thus, regular assessment and nutritional intervention are crucial in the management of patients with liver cirrhosis.

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REFERENCES


