increased for each quartile fructose level by 27.0%, 25.0%, 37.4%, and 44.5%, respectively ($P < 0.001$). Each standard deviation increase in fasting serum fructose level was associated with a 60% increased risk of MASLD (odds ratio [OR] 1.60; 95% confidence interval [CI] 1.36–1.88; $P < 0.001$) (37). Excessive fructose consumption increases the risk of MASLD, metabolic dysfunction-associated steatohepatitis (MASH), and hepatic fibrosis independent of calorie intake in a dose-dependent manner (38–40). In addition to the direct hepatic effects of fructose, indirect effects of fructose (i.e., decreased satiety, and alternations in gut barrier function/microbiota, muscle, and adipose tissue) may further lead to acquisition and progression of MASLD.

In contrast to a high-fructose intake, low-fructose diets have emerged as a strategy to mitigate MASLD. A diet low in free sugar can reduce hepatic steatosis and fibrosis while improving glycemic indices (fasting blood glucose and homeostatic measurement of insulin resistance), decreasing the concentrations of biomarkers of inflammation (high sensitivity C-reactive protein, TNF-α, and nuclear factor k B), liver enzymes, and lipids in overweight and obese patients with MASLD (41–47).

A systematic review and meta-analysis of controlled trials of the effect of fructose-containing sugars by food source at different levels of energy control on MASLD markers has been conducted (51 trials, 75 trial comparisons, n = 2,059). The evidence provides a good indication that the addition of excess energy from sugar-sweetened beverages leads to large increases in liver fat and alanine aminotransferase (ALT). However, the evidence is weaker regarding aspartate transaminase (AST) levels on the benefit of the removal of energy from mixed sources including sugar-sweetened beverages.

Finally, the association of simple sugar intake on more severe disease progression/regression was also evaluated in 80 consecutive cirrhotic liver transplant candidates who underwent detailed nutritional evaluations, and who were counseled to follow current nutritional guidelines (48). Compared with the baseline, the model for end-stage liver disease (MELD) score of cirrhotic patients at the end of the 6-month study was decreased, stable, or increased in 36%, 8%, and 56% of patients, respectively. DELTA-MELD was positively and independently correlated with the daily intake of simple sugars (48). Positive associations were present almost exclusively in patients with a visceral fat value above the median value. This is an association study, and future intervention studies are necessary to determine whether patients with cirrhosis with increased visceral adipose tissue benefit from dietary reduction in simple sugars (49).

Key concept

6. Patients with chronic liver disease should be routinely monitored for anorexia or malnutrition resulting from decreased or poor-quality food intake, with appropriate nutritional interventions as needed.

Anorexia is generally defined as the loss of the desire to eat, and it is usually associated with reduced food intake and deterioration of nutritional status (50). Anorexia can also be associated with poor quality of food intake. Alcohol or sugared sodas may replace necessary dietary nutrients. In patients with cirrhosis from any etiology, decreased food intake and anorexia can be multifactorial including gastroparesis resulting from portal hypertension, ascites, dysgeusia from micronutrient deficiency, and reduced taste (51,52). In studies from the Veterans Administration (VA), more than 60% of patients with moderate or severe alcohol-associated hepatitis (AH) had anorexia, and anorexia correlated with the severity of liver disease (33). Dietary protein and calories decreased as liver disease severity increased, and about half of total calories were derived from alcohol. Importantly, protein intake decreased in association with increasing anorexia (Table 6). In an outpatient study of 200 patients from Eastern India, 100% of those with alcohol-associated cirrhosis (AC) reported anorexia (53). A study from China reported that about one-third of patients with cirrhosis had anorexia, and anorexia correlated with the presence of depression. The major cause for cirrhosis in this study was viral-related (hepatitis B or C) (54). Thus, anorexia was observed in patients with different types of liver diseases across the world. Anorexia can also be caused by nutritional deficiencies. A recent study evaluated zinc status and possible symptoms of zinc deficiency in 578 patients with liver disease. Anorexia and taste disorders were associated with liver disease and were most common in patients with the lowest serum zinc levels (55). Anorexia is more common with aging, and patients with advanced liver disease tend to be older (50). Moreover, many of the presumed causes of anorexia of aging, such as inflammatory cytokines, impaired taste, and hormonal dysregulation are present in liver disease (56). Proinflammatory cytokines, such as TNF, are frequently increased in liver disease and can cause anorexia. Similarly, hormones that modulate appetite, such as ghrelin and leptin, are altered in liver disease and are believed to play a role in the anorexia of liver disease. Nausea and bloating are frequent complaints in patients with advanced liver disease and can play a role in anorexia. In a large group of patients with cirrhosis who were not eligible for transplantation, 58% had nausea (57). Gastroparesis is frequent in patients with cirrhosis; indeed, one report showed that 95% of patients with cirrhosis had gastroparesis. Gastroparesis can cause anorexia with decreased and poor-quality food intake (58,59). Patients who have complications of liver disease, such as ascites or HE, are more likely to have anorexia with inadequate food intake. Anorexia with inadequate and possibly poor-quality food intake can affect outcome. For example, in a VA Cooperative Study of 245 inpatients in which 1 month daily caloric intake was available, the calories consumed correlated in a dose-dependent fashion with mortality at 6 months (60).

Key concept

7. Dysbiosis is associated with the development/progression of many forms of liver disease.

Although dysbiosis may not be directly considered as malnutrition, it is highly affected by nutrition and affects nutrition in patients with liver disease and is thus reviewed here. Because treatments for dysbiosis are frequently not nutrients (e.g., antibiotics and phages), treatment will be mentioned but not comprehensively reviewed here. The human gastrointestinal tract contains more than 100 trillion microorganisms including bacteria, fungi, viruses, and archaea that make up the gut microbiome (61). These microorganisms interact in a symbiotic fashion with the gut, liver, and immune system. Dietary factors, such as high-fat diets, alcohol consumption, and other environmental factors including chemicals, can adversely affect microbial communities. This dysbiosis can lead to intestinal barrier dysfunction,