concentration into normal and zinc deficient subjects. Those with hypozincemia had significantly higher liver enzymes and lower albumin, suggesting that hypozincemia may play a role in the development of early-stage ALD (202). Himoto et al (203) used polaprezinc as an antifibrotic therapy in patients with chronic hepatitis C and showed a decrease in noninvasive fibrosis markers. Subsequently, Matsuoka et al treated chronic hepatitis C virus patients for 3 years with polaprezinc, 150 mg bid. Zinc therapy was associated with improvement of AST and ALT (204).

Zinc deficiency has been associated with PSE, and zinc supplementation has been postulated to improve PSE (185,205). Severe zinc deficiency *per se* has been reported to cause mental disturbances and encephalopathy (185,206). In 100 patients with minimal HE, zinc deficiency predicted overt HE and mortality in patients with liver cirrhosis (205). Zinc metabolism is highly linked to ammonia metabolism, and zinc supplementation improved hepatic nitrogen clearance in patients with advanced cirrhosis (207,208). In a meta-analysis including 4 trials with 247 cirrhotic patients, zinc supplementation combined with lactulose improved number connection tests in patients with mild PSE compared with lactulose monotherapy (209). This is consistent with a previous meta-analysis of 4 trials that concluded that oral zinc improved this psychometric test but did not decrease PSE (210). If used, zinc supplementation at a dose of ≤50 mg elemental zinc orally per day should be taken with a meal to decrease the potential side effects of nausea and copper deficiency.

Recommendation

4. We suggest coffee consumption, preferably ≥2 cups per day, in patients with chronic liver disease to reduce risk of hepatic fibrosis progression or HCC development (conditional recommendation, low quality of evidence).

Over the past approximately 2 decades, there have been multiple publications ranging from animal data to human meta-analyses that have suggested positive health outcomes associated with regular coffee consumption. Public opinion on coffee is evolving, and it is now perceived by many to be a health-promoting beverage. Data specifically on the effects of coffee on liver health are especially compelling. It has been shown that coffee consumption is inversely related to fatty liver, advanced hepatic fibrosis, and even HCC (211–224). Studies in experimental animals have evaluated potential mechanisms, but the data are unclear (225). Individual studies and meta-analyses of data from diverse patient groups show a decrease in hepatic steatosis with coffee consumption (212–215,226). Recent data from the National Health and Nutrition Examination Survey database show that coffee consumption is associated with lower hepatic fibrosis, and the fibrosis findings are supported by other studies (216–219,221,227–229). The risks for cirrhosis and HCC also seem to be lower in coffee consumers based on large epidemiologic studies (220,223,224,230–232). It is debated whether caffeine, among more than 1,000 ingredients in coffee, is the critical ingredient for these beneficial effects (225). Some studies have reported positive effects even with decaffeinated coffee, suggesting that ingredients other than caffeine may be mediating the beneficial effects on the liver (233). Caffeine is metabolized in the liver, and reduced levels of breakdown products of caffeine correlate with the severity of liver disease (234). Thus, if caffeine metabolites were the beneficial ingredients as suggested by some studies, patients with liver disease would benefit less. Coffee consumption also is associated with epigenetic effects that may confer liver health (235). Biologically active polyphenols, such as chlorogenic acid, are present in coffee, and these polyphenols have antioxidant and anti-inflammatory properties that may play a role in the hepatic health effects of coffee (236). It seems that a wide variety of types of liver diseases derive benefit from coffee, ranging from hepatitis C to MASLD to ALD. Importantly, although coffee seems to protect against HCC, it does not protect against many other common types of cancers. There seems to be some dose-response relation, with 2 to 4 cups, often suggested as optimal amounts (233). Further studies are required to define mechanisms and dose thresholds for the hepatic benefits.

Key concepts

15. Lifestyle modification with diet and exercise decreases adverse clinical outcomes in patients with MASH and should be encouraged independent of MASH disease severity.
16. Data suggesting that lifestyle modification is associated with reversal of hepatic fibrosis are limited.

Fibrosis in the presence of MASH is the primary predictor of clinical outcomes (237). Lifestyle modification with diet and exercise can improve liver histology and potentially alter natural history for disease progression. Lifestyle modification is the foundation of treatment not only for MASLD/MASH but also for its associated metabolic comorbidities and improved cardiometabolic health (238). Achieving ≥10% weight loss through life-style modification may resolve steatohepatitis and improve hepatic fibrosis (239–241). Although most patients may be able to achieve modest degrees of weight loss, few patients (≤10%) achieve effective weight loss at 1 year, despite structured interventions. Importantly, fewer than half of these maintain the lost weight at 5 years after the intervention (239,242), highlighting the need for ongoing nutrition support and lifestyle modification.

Exercise independent of weight loss has a beneficial effect on MASLD/MASH. Regular moderate exercise at least 5 times a week for a total of 150 minutes per week or an increase in physical activity by more than 60 minutes per week can prevent her improve MASLD/MASH (238,243–245). More vigorous exercise is needed for resolution of MASH, with even higher intensity exercise demonstrated to reduce hepatic fibrosis (239,246).

Studies combining diet with increases in physical activity consistently demonstrate reduction in liver fat proportional to the intensity of the intervention (247–249). Even in those patients with MASH-related advanced hepatic fibrosis or cirrhosis, regular physical activity has been demonstrated to reduce portal pressure (250), improve frailty, sarcopenia, and quality of life (251). Using National Health and Nutrition Examination Survey Data (n = 3,548 participants), a dose-dependent, nonlinear association of physical activity (volume and intensity) was associated with all-cause mortality and a dose-dependent, linear association of diet quality with all-cause mortality (252). Both physical activity and diet quality were associated with lower cardiovascular risk in US adults with MASLD (252).

Key concept

17. In patients with cirrhosis and evidence of fluid retention (ascites and/or edema), free water restriction may be needed when serum sodium is below 126 mEq/L.