Recommendation

5. In patients with cirrhosis and ascites who are managed with diuretic therapies, we cannot recommend for or against strict sodium restricted diets (Insufficient evidence, no recommendation).

Portal hypertension in patients with cirrhosis with consequent splanchnic pooling of blood leads to a decrease in effective circulating blood volume. Cardiac compensation with an increase in cardiac output attempts to maintain the effective circulating blood volume and renal blood flow. With increasing severity of liver disease naturally or due to a precipitant event (gastrointestinal bleeding, portal vein thrombosis, or dehydration), the cardiac compensation may not be enough, and this results in activation of renin angiotensin system with an increase in aldosterone levels, leading to active sodium and passive fluid retention. About 50% of patients with decompensated cirrhosis have fluid retention with ascites and/or edema of the feet, the most common complication of cirrhosis (253). Moderate to severe fluid retention in patients with cirrhosis is a common cause for recurrent hospitalization and utilization of resources. Hence, optimal outpatient management of patients with ascites is critical to improve patient-reported outcomes including patient survival (254).

The American Association for the Study of Liver Diseases recommends moderate dietary sodium restriction to 2,000 mg/d of salt (88 mEq of sodium) with diuretics (spironolactone with or without furosemide) as a first step in the management of clinically evident ascites in patients with cirrhosis (255). As sodium restricted diets are not very palatable and can potentially lead to malnutrition, randomized studies have been performed to examine what is the maximum sodium intake which can be allowed to these patients (254). In a multicenter study on 140 outpatients with AC, unrestricted sodium intake (n = 74) was compared with 483 mg (21 mmol) of sodium intake (n = 66) in the management of ascites. At 14 days there was a greater weight loss, decrease in abdominal girth, and improved appetite in the sodium restricted arm, but this difference was not seen at the 90-day evaluation. Furthermore, there was a trend for improved patient survival, $P = 0.09$ (256). In another randomized clinical trial, sodium restriction of 40 mmol/d (n = 62) was compared with 120 mmol (n = 53), with a stepped-up approach in use of diuretics in both arms. The more restricted sodium intake did not add to the 93% successful reduction in ascites with optimal diuretic treatment (257). In a more recent study from China, sodium restriction of up to 5,000 mg/d (n = 102) was compared with unrestricted sodium intake (n = 98) among hospitalized patients with cirrhosis, with use of diuretics in both the arms. The unrestricted sodium arm had higher rate of ascites disappearance and a shorter time to ascites control/discharge from hospital. Furthermore, the sodium restricted group had lower serum sodium and renal impairment during the hospitalization (258). In a larger randomized study on 328 patients managed in outpatients or during admission, 6 arms were studied with use of diuretics and other modes for management of ascites, and sodium restriction up to 500 mg/d in 5 arms and unrestricted sodium intake in the sixth arm. No statistically significant difference was seen on ascites control across the 6 arms in the study (259). Although the available evidence shows some benefit from sodium restricted diet, the contradictory studies with limited data call for larger well-designed studies to definitively examine the limit of sodium restriction in patients with cirrhosis and fluid retention.

Regarding fluid restriction, there are no high-quality randomized studies in the management of ascites and fluid retention in patients with cirrhosis. Fluid restriction is not required in the management of ascites because the fluid retention in patients with cirrhosis is passive along with sodium retention. Hence, adequate sodium control combined with optimal diuretic dose is enough in the management of ascites. However, when the serum sodium falls below 125 mEq/L due to dilutional or isotonic hyponatremia, fluid restriction is recommended by most organizations including the American Association for the Study of Liver Diseases (255).

Recommendation

6. We suggest not restricting dietary protein in patients with decompensated cirrhosis and HE (conditional recommendation, very low quality of evidence).

Protein and caloric malnutrition is common in patients with cirrhosis, and adversely affects the clinical outcomes. Ammonia plays a central role in the occurrence of HE, a common complication in patients with decompensated cirrhosis. Ammonia synthesized by the gut bacteria from the dietary proteins is cleared by conversion to urea in the liver. However, in patients with decompensated cirrhosis, impaired liver function cannot perform this metabolic function leading to risk of HE. Hence, protein restriction to reduce the availability of substrate has been practiced minimizing ammonia synthesis (260,261). Indeed, as recently as 2001, the ACG Practice Guidelines on Hepatic Encephalopathy recommend that for cirrhotics with acute encephalopathy, protein intake should be started at 0.5 g/kg/d with a progressive increase to 1.0–1.5 g/kg/d, depending on patient tolerance (262). However, restricting proteins worsen malnutrition and sarcopenia that can potentially worsen hyperammonemia due to reduced skeletal muscle ammonia disposal (118). In a study on 30 patients with decompensated cirrhosis who were hospitalized with HE, subjects were randomized to receive protein restricted diet with progressive increment or normal protein diet for 2 weeks. The outcome of HE in the 2 groups was not different, with similar stage and severity of HE at days 7 and 14. Furthermore, patients in the low-protein intake group had higher protein breakdown compared with normal protein intake (263). In another study on 6 healthy subjects and 14 patients with biopsy proven cirrhosis (6 decompensated), plasma levels of amino acids were similar in the 3 groups after 20 g protein meal, except for greater increase in the levels of isoleucine, leucine, and tyrosine in patients with cirrhosis compared with healthy subjects. However, none of the patients with cirrhosis developed covert HE as evaluated by the number connection test (264). A large clinical trial at 8 Department of Veterans Affairs Medical Centers analyzed food intake including protein consumption and encephalopathy over time. Sixty-three percent of patients had some degree of HE at entry, which decreased over time. Time-dependent regression analysis found low-protein intake to be independently associated with worsening HE. Similarly, less malnutrition at study entry was independently associated with improved HE (265).