Managing fluid retention in cirrhosis

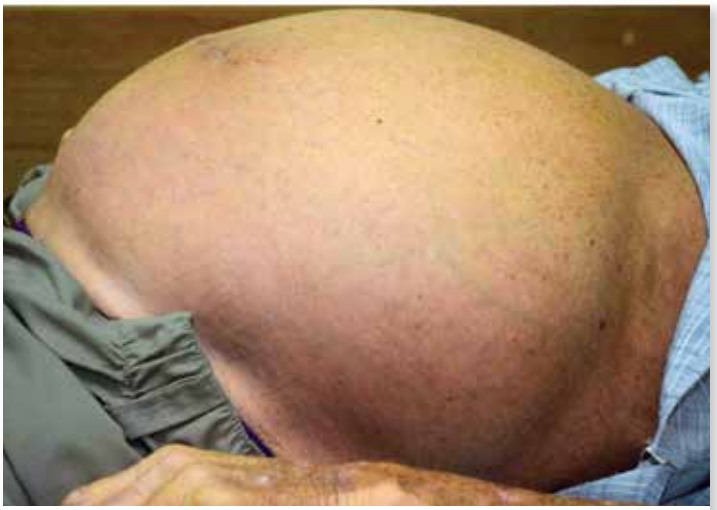

Figure 1. Abdominal distention due to severe ascites.

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Fluid retention in cirrhosis, which most often manifests as ascites, is associated with a poor prognosis. All patients who develop ascites should be referred for specialist hepatology input.

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REMEMBER

- Ascites is the most common complication of cirrhosis (Figure 1), affecting 60% of patients over a 10-year period.[1]
- The presence of ascites is a sign of liver failure and is associated with a five-year mortality of 30%.[2] Hepatic encephalopathy and variceal haemorrhage are other signs of liver failure.
- Signs of fluid retention that are less often observed in patients with cirrhosis include peripheral oedema and hepatic hydrothorax (5 to 10%) and are almost always observed in association with ascites. Hepatic hydrothorax is usually right-sided, but it can be left-sided or bilateral.
- Ascites only occurs on development of portal hypertension and is believed to be due to impaired urinary sodium excretion. Arterial splanchnic vasodilatation results in reduced circulating blood volume, which in turn results in activation of vasoconstrictor and sodium-retaining mechanisms such as the sympathetic nervous system and renin–angiotensin–aldosterone system. These processes lead to increased renal sodium retention with subsequent fluid retention in the form of ascites and peripheral oedema. Despite often being hyponatraemic, patients are usually in a positive total body sodium balance.

ASSESSMENT

- The evaluation of a patient with new-onset ascites should include the following:
  - evaluation of renal and circulatory function (full blood count, electrolytes and renal function)
  - evaluation of liver disease (liver function tests, coagulation profile, abdominal ultrasound and/or CT scan to exclude portal vein thrombus and hepatocellular carcinoma)

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  - diagnostic paracentesis (Figure 2) and ascitic fluid analysis (white cell count and differential count; albumin, protein, glucose and lactate dehydrogenase levels; and cytology)
  - assessment of varices (gastroscopy).
- Ascites is most often due to cirrhosis. However, other causes require exclusion, including heart failure, malignancy, tuberculosis, pancreatitis, Budd–Chiari syndrome and nephrotic syndrome. Other investigations that need to be considered include chest x-ray, echocardiography and measurement of serum B-type natriuretic peptide (BNP).
- Patients with cirrhosis-induced fluid retention, particularly ascites, usually have evidence of muscle wasting, hypoalbuminaemia and features of portal hypertension (e.g. thrombocytopenia, splenomegaly and varices).
- A diagnostic paracentesis should be performed, usually in the hospital setting, in all patients with new onset ascites and in all patients who are hospitalised for worsening of ascites or any complication of cirrhosis. The serum-ascites albumin gradient (SAAG) should be calculated (SAAG = serum albumin [g/L] – ascites albumin [g/L]). A SAAG greater than 11 g/L generally suggests ascites due to portal hypertension with over 97% accuracy, with the most frequent exception being heart failure. A serum BNP level above 364 pg/mL and ascitic protein level of more than 2.5 g/L suggest a diagnosis of heart failure rather than cirrhosis.[3]

MANAGEMENT

- The principles of management in ascites focus on salt restriction, in combination with a high-energy, high-protein diet and diuretic therapy (Table).[4,5]

Alcohol cessation

- Alcohol cessation may have a significant effect within a few months and enable the avoidance of long-term diuretic therapy. The impact of total abstinence can be significant, even in advanced alcohol-related cirrhosis. In a 2002 study of patients with severe alcoholic cirrhosis the three-year survival was found to be 75% in patients who promptly ceased drinking compared with 0% in patients who continued to drink.[6]

Dietary measures

- All patients with ascites should be referred to a dietician and have regular dietetic review for advice regarding a low-salt, high-protein, high-energy diet.
- Due to the advanced nature of their liver disease, patients with ascites are invariably malnourished. Ineffective protein synthesis and low hepatic glycogen stores mean that even overnight fasting results in an early switch of gluconeogenesis from glycogen to amino acids sourced from body protein stores.
- Patients have an excess of total body sodium, which contributes to fluid retention. They need to restrict their sodium intake, aiming for a daily sodium intake of no more than 88 mmol (equivalent to 2 g sodium).
- Patients should be instructed to eat 1.0 to 1.5 g protein/kg per day. In addition to eating three meals each day, patients should be encouraged to eat two or three protein-rich snacks in the form of commercial or dietary supplements. The diet should include a snack at bedtime (such as crackers and cheese or a milkshake).[7]

Figure 2. Diagnostic paracentesis.

Diuretic therapy

- Hyperaldosteronism contributes to sodium retention in cirrhosis, and so an aldosterone antagonist such as spironolactone is the diuretic of choice.[8] Patients with their first presentation of moderate ascites can be commenced on spironolactone 100 mg daily as single agent therapy. Patients should be encouraged to weigh themselves daily and report weight loss of more than 0.5 kg/day because this rate of diuresis may precipitate renal impairment and electrolyte disturbances.
- Spironolactone has a slower onset of action than frusemide. Patients with slow weight loss and patients who develop hyperkalaemia should have frusemide 40 mg daily added to the regimen. Recommending elimination of foods high in potassium (e.g. banana, orange juice, tomato, spinach) and salt substitutes may help avoid hyperkalaemia.
- In patients who do not lose weight, the diuretic doses can be uptitrated to a maximum of spironolactone 400 mg/day (increasing by 100 mg every five days) and a maximum of frusemide 160 mg/day (increasing by 40 mg every five days). Dose adjustments should be made in consultation with the treating specialist. Very few patients with cirrhosis-induced ascites tolerate these doses because of renal or electrolyte disturbances.
- A patient's renal function and electrolyte levels (looking for hyponatraemia, hyperkalaemia or kidney injury) should be monitored at three- to five-day intervals from the start of treatment and whenever doses are changed. In patients on established stable doses of diuretics, monthly renal function and electrolyte testing is appropriate.

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TABLE. GRADING OF ASCITES: FEATURES AND MANAGEMENT

Grade	Features	Treatment strategies
1	Ascites present on ultrasound or CT scan only Diffusely thickened gallbladder wall on imaging Not clinically palpable	Restriction of sodium intake High-energy, high-protein diet
2	Moderate ascites resulting in symmetrical abdominal distension	High-energy, high-protein and low-salt diet Diuretic therapy
3	Large or tense ascites	High-energy, high-protein and low-salt diet Diuretic therapy Large volume paracentesis Transjugular intrahepatic portosystemic shunt (TIPSS) Liver transplantation

* There is no role for fluid restriction in the first-line management of cirrhosis-induced ascites in the absence of hyponatraemia.

- To minimise complications, diuretic doses should be reduced at the earliest opportunity upon resolution of ascites. Splitting a daily dose into two doses, to be taken first thing in the morning and at midday, may be used, although this may affect compliance.
- Amiloride (10 mg to 40 mg daily) has a role in patients who do not tolerate spironolactone due to painful gynaecomastia.[9] However, it is not as efficacious as spironolactone.
- Diuretics should be ceased in patients with a serum sodium level below 125 mmol/L, worsening renal function, hepatic encephalopathy or severe muscle cramps. Significant hypokalaemia (serum potassium below 3 mmol/L) can be managed by withholding frusemide. Aldosterone antagonists should be stopped in patients with recurrent significant hyperkalaemia (serum potassium over 6 mmol/L).
- There is no role for fluid restriction in first-line management of cirrhosis-induced ascites. Use of diuretics and dietary sodium restriction is effective in the majority (>90%) of patients.[10] The addition of fluid restriction may result in acute kidney injury in the outpatient setting and is recommended only in patients with significant hyponatraemia (serum sodium <125 mmol/L) who have a normal serum creatinine level.

Other treatment options

- Patients with tense ascites or significant discomfort from their ascites benefit from paracentesis. Referral for large-volume paracentesis with intravenous albumin supplementation to prevent post-paracentesis circulatory dysfunction is recommended;[11] this can be performed in a hospital or day procedural setting.
- Some patients fail to respond to maximal doses of diuretics (refractory ascites) or develop electrolyte disturbances or worsening renal function from diuretics (diuretic intolerance). In these patients, treatment usually involves serial therapeutic paracenteses. Selected patients may benefit from transjugular intrahepatic portosystemic shunt (TIPSS) or liver transplantation.
- For patients with hepatic hydrothorax, a high-protein, low-sodium diet and diuretic therapy are the management of choice. However, dyspnoeic patients may require a therapeutic thoracentesis. Selected patients may benefit from TIPSS if the hepatic hydrothorax is refractory to medical management.

FINAL COMMENTS

- Fluid retention in cirrhosis most often manifests as ascites. It is the most common complication of cirrhosis and is associated with a poor quality of life, increased risk of infections and poor long-term outcome (five-year mortality of 30%).
- Patients with ascites have advanced liver disease and usually have evidence of muscle wasting. Dietary measures form an integral component of their management, and referral to a dietitian for advice regarding a high-energy, high-protein and low-salt diet is crucial. Patients should be encouraged to eat frequent snacks between meals, and a bedtime snack.
- Management of fluid retention is largely directed at dietary salt restriction in conjunction with diuretic therapy. Regular monitoring of a patient's electrolytes and renal function is imperative.
- All patients who develop ascites should be referred for specialist hepatology input. MT

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A list of references is included in the website version (www.medicinetoday.com.au) and the iPad app version of this article.

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