# Ascites in patients with cirrhosis

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*Mr G. is a 79-year-old man with known end-stage alcoholic liver cirrhosis and ascites. He is married and has 3 adult children.*

*Mr G. presented for acute care 3 weeks ago with tense ascites, which was managed with a large volume paracentesis (LVP) of approximately 4 L. He was discharged home with 100 mg/d of spironolactone and 40 mg/d of furosemide to be taken orally. Mr G. was also given a prescription for 0.5 mg of hydromorphone to be taken orally every 4 hours as needed for pain.*

*He is being seen today at home because of a rapid decline in function and escalation of symptoms. Mr G. is taking 0.5 mg of hydromorphone orally 1 to 2 times a day to help control symptoms of increasing abdominal pain and dyspnea. His overall appetite has declined, and this is distressing to his family. Mr G. describes early satiety and persistent nausea but no vomiting. His last bowel movement was 3 days ago.*

*On examination, Mr G. is orientated to time and place. He is afebrile, and measurement of his vital signs reveals a blood pressure of 110/60 mm Hg, a heart rate of 110 beats/min, a respiratory rate of 22 breaths/min, and an oxygen saturation of 97% on room air. Findings from his cardiopulmonary examination are unremarkable. His abdomen is markedly distended with no pain on palpation or rebound tenderness, and testing for shifting dullness reveals positive results of fluid shift. He also has moderate bilateral peripheral edema.*

*Goals and direction of care are discussed with Mr G. while his wife and children are present. Mr G.'s family members express that they had not expected such a rapid decline in just a few weeks following his paracentesis. Mr G. explains that symptom control and being kept comfortable at home are of primary importance to him.*

Cirrhosis is characterized by diffuse fibrosis of liver parenchyma resulting in structurally abnormal liver nodules. In North America, cirrhosis has become the eighth leading cause of death,[1] with alcoholic liver disease, hepatitis C, and nonalcoholic fatty liver disease as the 3 main causes.[2]

The natural history of cirrhotic liver disease progresses from a compensated to a decompensated phase. Ascites is the main complication of cirrhosis,[3] and the mean time period to its development is approximately 10 years.[4,5] Ascites is a landmark in the progression into the decompensated phase of cirrhosis and is associated with a poor prognosis and quality of life; mortality is estimated to be 50% in 2 years.[6]

## Definition, features, and investigation

*Ascites* is defined as the presence of excessive fluid in the peritoneal cavity. Fundamental to the formation of ascites in cirrhosis are portal hypertension, which causes splanchnic vasodilation, and activation of the renin-angiotensin-aldosterone system, further resulting in renal sodium retention.[4,7]

At end-stage cirrhosis, ascites causes symptoms including abdominal distention, nausea and vomiting, early satiety, dyspnea, lower-extremity edema, and reduced mobility. Clinically, on investigation of a full, bulging abdomen, percussion of the flanks and checking for shifting dullness can detect ascites. Radiographically, an abdominal ultrasound is useful in defining the extent of ascites in new-onset or worsening ascites. Abdominal paracentesis, ascitic fluid analysis, and the use of the serum ascites albumin gradient are the most rapid and cost-effective methods of diagnosing the cause of ascites and directing management.[4,8]

## Medical management

Decision making on the management of ascites depends on the severity of symptoms and not the presence of ascites in and of itself. The medical management of ascites includes sodium restriction and use of diuretics.

***Sodium restriction.*** First-line therapy includes sodium restriction. In mild or moderate cases of ascites, sodium restriction of 88 mmol/d (2000 mg of salt per day) is usually advised.[9] As a sodium-restricted diet can be unpalatable, achieving a negative sodium balance while maintaining quality of life for the patient needs to be carefully discussed.

***Diuretics.*** Second-line therapy includes the use of diuretics. Spironolactone is considered the first-line diuretic because aldosterone is the main factor responsible for renal sodium retention in cirrhosis. Dosages of spironolactone typically start at 100 mg/d, increasing stepwise every 7 days by 100 mg, to a maximum of 400 mg daily.[4] Painful gynecomastia and hyperkalemia are the most common side effects. Alternatively, amiloride, starting at 5 mg/d and titrated to 20 mg/d, can be used; however, this option is less

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effective.[10] In patients who do not respond to spironolactone monotherapy, furosemide should be added in an increasing stepwise fashion from 40 mg/d to a maximum of 160 mg/d (in 40 mg/d stepwise dosing).[4] Furosemide enhances the natriuretic response of aldosterone antagonists and is not recommended as a single agent. Common side effects of furosemide include the following: hypokalemia, hypochloremic alkalosis, hyponatremia, and hypovolemia. When used in combination, the side effects of each diuretic alone are generally balanced at the ratio of 100 mg/d of spironolactone to 40 mg/d of furosemide, to a maximum of 400 mg/d and 160 mg/d, respectively.[9]

A common decision-making point is whether to start diuretics as monotherapy or as combined therapy. Studies have shown that spironolactone monotherapy and combination therapy with spironolactone and furosemide are equally effective at relieving ascites.[3,4]

If more rapid symptom control is required, or if the patient has recurrent ascites, then starting combination therapy from the onset should be considered.[10]

Once ascitic fluid is mobilized and symptom control is achieved, the dosage of diuretics needs to be reconsidered with the goal of maintaining symptom control with the lowest dose of diuretics possible in order to prevent diuretic-induced side effects.

## Management of refractory ascites

Refractory ascites occurs in patients who do not respond to diuretic therapy, who have diuretic-induced complications, or for whom ascites recurs rapidly after therapeutic paracentesis.[4,9,11] Once ascites becomes refractory, survival decreases to 50% at 1 year.[12] Management options in refractory ascites include LVP, serial therapeutic paracentesis, indwelling peritoneal catheters, and transjugular intrahepatic portosystemic shunts (TIPSs).

***Large volume paracentesis.*** Large volume paracentesis is effective and viewed as a safe procedure, with a local complication rate of less than 1%.[13] Up to 5 L of fluid can be withdrawn at one time without the use of a postparacentesis colloid infusion.[4] If more than 5 L of ascites volume is extracted, intravenous administration of plasma expanders such as albumin are recommended to prevent paracentesis-induced circulatory dysfunction.[4] Serial LVP can be tolerated every 2 weeks, but variables in determining the frequency of paracentesis include the patient's time to recurrence of ascites, symptoms, tolerability, and practicality of the procedure. As LVP does not treat the underlying cause of ascites, salt restriction and diuretic therapy to slow down the rate of reaccumulation should be continued.

***Indwelling peritoneal catheters.*** The decision whether to continue serial therapeutic paracentesis versus considering a permanent indwelling catheter is guided by the patient and his or her burden of disease, prognosis, and goals of care. Indwelling catheters, such as a pigtail catheter or a pleural catheter, are an option for those patients who require frequent paracenteses. Tunneled catheters are preferred over pigtail catheters owing to stability and lower rates of infection.[14] The advantages to having an indwelling catheter include convenience for the patient, avoidance of the risk of complications of repeat paracenteses, and cost. Permanent catheters can be under continuous or intermittent drainage, with the frequency determined by the patient in accordance with symptom control. There is no literature to inform the daily maximum of fluid drainage with indwelling peritoneal catheters; however, it is common practice to drain 1 to 2 L/d and to not surpass 5 L/d in order to avoid complications.[15] The main consideration against an indwelling catheter is the risk of infection. What the exact risk of infection posed by an indwelling catheter is and whether or not patients require prophylactic antibiotics is not well defined in the literature.

***Transjugular intrahepatic portosystemic shunt.*** A TIPS is a shunt between the portal vein and the hepatic vein, designed to reduce portal hypertension and improve renal sodium excretion by directly bypassing the cirrhotic parenchymal tissue. Multiple meta-analyses have shown that a TIPS is much more effective for managing refractory ascites than serial LVP is.[5,16,17] More recently, use of a TIPS has been shown to provide some survival advantage in carefully selected patients. However, limiting the use of TIPSs in palliative care is the high incidence of hepatic encephalopathy, up to 30%,[18] in patients undergoing this procedure.

## Back to the case

*Mr G. has a second LVP of approximately 4.5 L, which is arranged on an outpatient basis. Doses of his diuretics are increased to 200 mg/d of spironolactone and 80 mg/d of furosemide taken orally. He is given an enema with good results, and then starts taking 2 senna tablets orally once daily at bedtime.*

*Within 7 days, Mr G.'s ascites returns, along with abdominal discomfort, decreased oral intake, exertional dyspnea, and nausea. He is afebrile. Mr G. is taking an average of 4 to 5 breakthrough doses of hydromorphone daily. He agrees to have a permanent indwelling catheter inserted. Every 1 to 2 days, Mr G.'s wife is able to drain approximately 200 mL of his ascites. Despite this, Mr G.'s abdominal pain persists. A 0.5-mg oral dose of hydromorphone is started every 8 hours, with a 0.5-mg oral dose of hydromorphone available every hour as needed to help control his pain and dyspnea. A 10-mg oral dose of metoclopramide is started 3 times daily before meals and a fourth dose at bedtime.*

*Mr G. becomes progressively somnolent, taking only small sips of fluid. He is no longer able to swallow his medications including his diuretics. Mr G.'s hydromorphone and metoclopramide doses are given subcutaneously at the same dose and frequency with good effect. Mr G. dies comfortably in his home.*

## Conclusion

Management of patients with ascites in end-stage cirrhosis is becoming more common in palliative care. Decision making should be influenced by best practices and the patient's goals of care, prognosis, and burden of disease.

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**Competing interests**
None declared

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## BOTTOM LINE

- Ascites is the main complication of cirrhosis. It is a landmark of the progression into the decompensated phase of cirrhosis and is associated with a poor prognosis and quality of life; mortality is estimated to be 50% in 2 years.
- Management of patients with ascites in end-stage cirrhosis is becoming more common in palliative care. Decision making should be influenced by best practices, as well as the patient's goals of care, prognosis, and burden of disease.
- Management of ascites includes sodium restriction and use of diuretics. Large volume paracentesis, indwelling peritoneal catheters, or transjugular intrahepatic portosystemic shunts can be considered in refractory ascites.

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