Diagnosis and management of ascites and hepatorenal syndrome (acute kidney injury) in cirrhosis

Kevin Moore

Abstract

The development of ascites and/or the hepatorenal syndrome in liver disease signifies the beginning of the end of liver function (decompensation). Patients with this condition need careful medical management to reverse these abnormalities, and identify any precipitating cause, such as spontaneous bacterial peritonitis or other causes of sepsis leading to acute kidney injury (AKI) or hepatorenal syndrome (HRS). Once ascites develops, all patients should be considered for liver transplantation because the long-term prognosis is poor. For those with alcoholic cirrhosis who stop drinking alcohol there is a large capacity for recovery. Likewise, treatment of newly presenting autoimmune hepatitis or chronic viral hepatitis (if tolerated) may improve liver function sufficiently to enable resolution of ascites without the need for diuretics. Patients should start a no-added-salt diet, and spironolactone as the first-line diuretic drug.

The development of acute kidney injury or HRS is most commonly secondary to sepsis. Pathologically, HRS is due to a combination of vasodilatation causing a lowering of blood pressure, activation of the sympathetic nervous system, impairment of cardiac functional reserve, and increased synthesis of vasoactive mediators. Patients developing hepatorenal syndrome should be managed with volume expansion, terlipressin, and antibiotics.

Keywords acute kidney injury in cirrhosis; AKI; hepatorenal syndrome; paracentesis; renal failure in/and cirrhosis; spontaneous bacterial peritonitis; transjugular intra-hepatic portosystemic shunt (TIPSS)

What's new?

- In patients with hepatorenal syndrome (HRS), cardiac output is inadequate to maintain normal blood pressure and this may be secondary to cirrhotic cardiomyopathy
- The most common trigger for the development of type 1 HRS is bacterial infection
- Renal function and survival in HRS can be improved by pharmacological therapy

Introduction and pathophysiology

Fifty percent of patients with compensated cirrhosis develop ascites within 10 years of the onset of cirrhosis. Ascites occurs only in patients with chronic liver disease and portal hypertension. It results from the sodium and water retention that follows activation of arterial and cardiopulmonary volume receptors, and homeostatic activation of the sympathetic nervous system and the renin–angiotensin–aldosterone system, secondary to arterial splanchnic vasodilatation and decreased effective arterial blood volume (Figure 1). Expansion of the extracellular fluid in the presence of portal hypertension enhances formation of hepatic lymph, extravasation of peritoneal fluid and formation of ascites and oedema. The European Association for the Study of the Liver (EASL) has recently published more extensive clinical guidelines than are presented here.[1]

The development of ascites is associated with a poor prognosis in patients with cirrhosis, because these patients may develop spontaneous bacterial peritonitis (SBP) or the hepatorenal syndrome (HRS), with an increased risk of variceal bleeding or sepsis.

The probability of death at 2 and 5 years after the appearance of ascites in patients with cirrhosis is estimated at 35% and 65% respectively,[1] and the development of ascites has a marked impact on quality of life. However, prognosis is considerably better in patients with alcoholic cirrhosis if they stop drinking alcohol. Low serum sodium concentration is the most powerful predictor of mortality, and 50% of patients presenting with ascites have a serum sodium concentration less than 135 mmol/litre.[2] Thus, patients with ascites should always be considered for referral for liver transplantation.

While the majority of cases (75%) of patients who present with ascites have underlying cirrhosis and portal hypertension, the remaining 25% have causes other than liver disease, such as malignancy (10%) or tuberculosis (3%) (Table 1).

Diagnosis of ascites

A full history, physical examination, measurement of liver and renal function, and urine electrolytes, as well as an analysis of the ascitic fluid, should be undertaken in all patients at the time of admission. The presence of liver disease is often evident from the history or physical examination. The presence of jaundice, spider naevi, palmar erythema, hepatomegaly and/or splenomegaly suggests underlying cirrhosis as a cause of ascites. Patients should be asked about a history of cancer, tuberculosis and heart disease with careful examination of the jugular venous pressure. An abdominal ultrasound scan is needed to confirm the presence of ascites and a nodular or coarse-looking heterogeneous liver, and to screen for hepatocellular carcinoma (or other malignancy) and portal vein thrombosis; it may even reveal dilated hepatic veins suggesting a cardiac cause, or thrombosis of the hepatic veins (Budd–Chiari syndrome). Portal vein thrombosis in the absence of cirrhosis does not usually cause ascites

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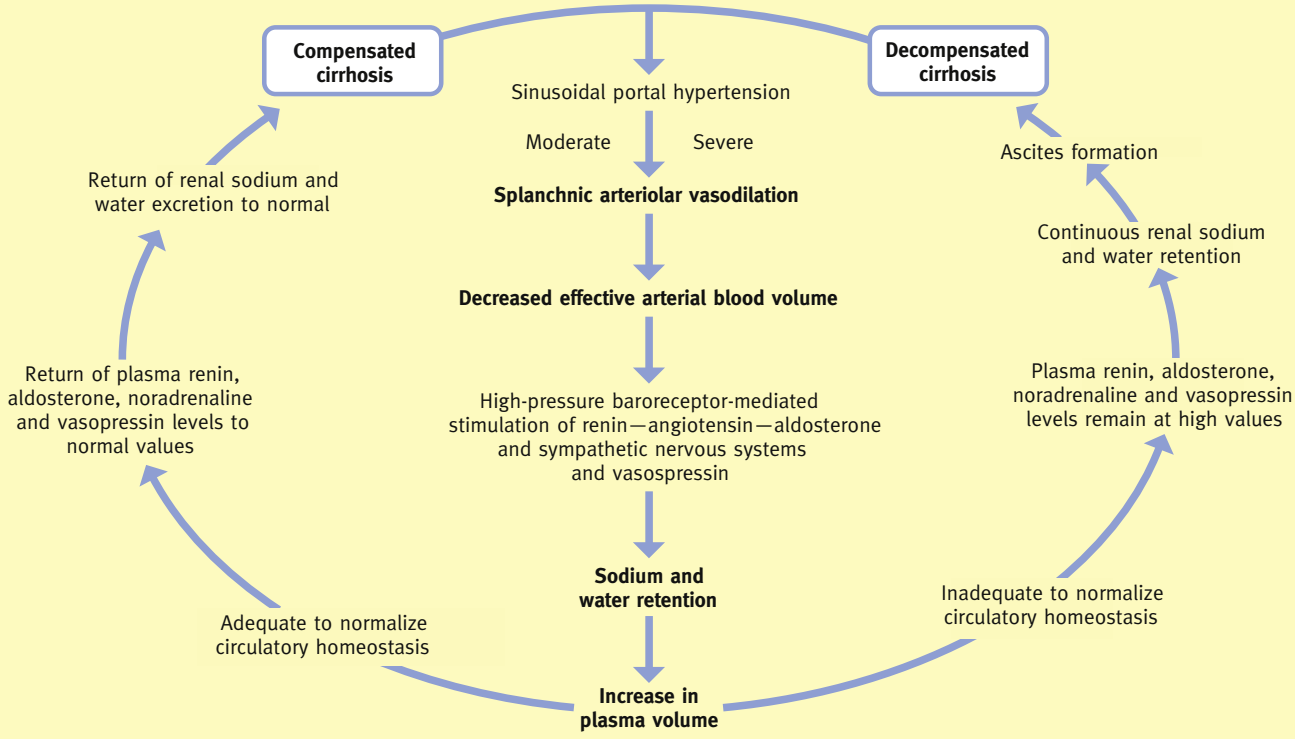
Pathogenesis of salt and water retention in cirrhosis



The development of portal hypertension leads to system vasodilatation of the splanchnic vascular bed, decreased effective arterial volume, leading to activation of the sympathetic nervous system and renion—angiotensin system, and subsequently increased sodium and water retention.

Figure 1 From Schrier R.W. et al.,[3] with kind permission of John Wiley & Sons.

unless there is a major insult such as gastrointestinal (GI) bleeding.

A diagnostic paracentesis with an appropriate ascitic fluid analysis is essential in all patients investigated for ascites, before any therapy, to diagnose SBP and look for other causes of ascites. When the diagnosis of cirrhosis is not clinically evident, ascites due to portal hypertension can be differentiated from ascites due to other causes by means of the serum:ascites albumin gradient (SAAG). This is calculated by subtracting the ascitic albumin concentration from the serum albumin. An SAAG of 11 g/litre or more identifies portal hypertension as the cause with 97% accuracy. Measurement of ascitic protein is markedly inferior to measurement of albumin for diagnostic purposes, but a low ascitic protein concentration (<15 g/dl) increases the risk of developing SBP.

Portions of the ascitic fluid should be put into a plain plastic tube or EDTA tube for examination by microscopy, and inoculated into a blood culture bottle. An ascitic polymorphonuclear (PMN) leucocyte count over 250/mm^3 is diagnostic of SBP, in the absence of abdominal surgical sources of infection. Coulter counter counts of white blood cells (WBCs) may be unreliable at low but significantly elevated PMN leucocyte counts. Ascitic fluid amylase activity should be measured to diagnose pancreatic ascites. A clinical suspicion of alternative causes of ascites, suggested by lymphocytosis or SAAG under 11 g/litre, justifies other tests, such as cytology, polymerase chain reaction (PCR) and culture for mycobacteria.

Causes of ascites

- Cirrhosis and portal hypertension 75%
- Malignancy 10%
- Pancreatic ascites 2%
- Tuberculous ascites 2%
- Cardiac causes 3%
- Miscellaneous 8%

Table 1

Management of ascites

Mild or moderate ascites: patients with mild or moderate ascites can generally be treated as outpatients. They should be advised to reduce their sodium intake with a no-added-salt diet, and to avoid foods with a high salt content (e.g. prepared meals). Patients with moderate ascites will usually benefit from an aldosterone antagonist such as spironolactone to increase urinary sodium excretion. Loop diuretics should be avoided unless ascites is difficult to treat.