

12 Liver Disorders

Vani Gopalareddy and Joel Rosh

Key Points

1. Always obtain an ultrasound marking of the site prior to abdominal paracentesis to increase the yield.
2. In the setting of cholestasis and coagulopathy always administer vitamin K IM daily for 3 days and recheck INR to evaluate for liver failure.
3. Hepatorenal syndrome can occur in the setting of portal hypertension without ascites.

Key Words: Ascites; fluid; electrolytes; sodium; cirrhosis; liver failure; hepatorenal syndrome

1. ASCITES

The term “ascites” refers to the pathologic accumulation of excess fluid within the peritoneal cavity. With reference to the liver, ascites can result from pre-hepatic, intra-hepatic, or post-hepatic processes. When ascites occurs secondary to intrinsic disease of the liver, it is usually in the setting of advanced cirrhosis and hepatic decompensation (1).

1.1. Pathophysiology of Ascites

There are two proposed theories for the formation of ascites that can be referred to as the “overflow” and the “underfill” theories (Fig. 1). The overflow theory postulates that there is a primary renal tubular retention of sodium that serves to increase the plasma volume and a subsequent extravasation of fluid into the peritoneal cavity. In the underfill theory, a primary decrease in effective arterial blood volume results in renal retention of sodium and the cascade outlined above. Impaired hepatocellular functioning and portal hypertension trigger the release of the endogenous vasodilators such as nitric oxide, glucagon, and prostaglandins. The resulting peripheral vasodilatation leads to a decrease in central blood volume. Decreased plasma volume stimulates the neurohormonal system consisting of the renin–angiotensin–aldosterone (RAAS) pathway, sympathetic nervous system (SNS), and arginine vasopressin (AVP) (antidiuretic hormone). The combined effect leads to renal retention of sodium and water. Cirrhosis is also

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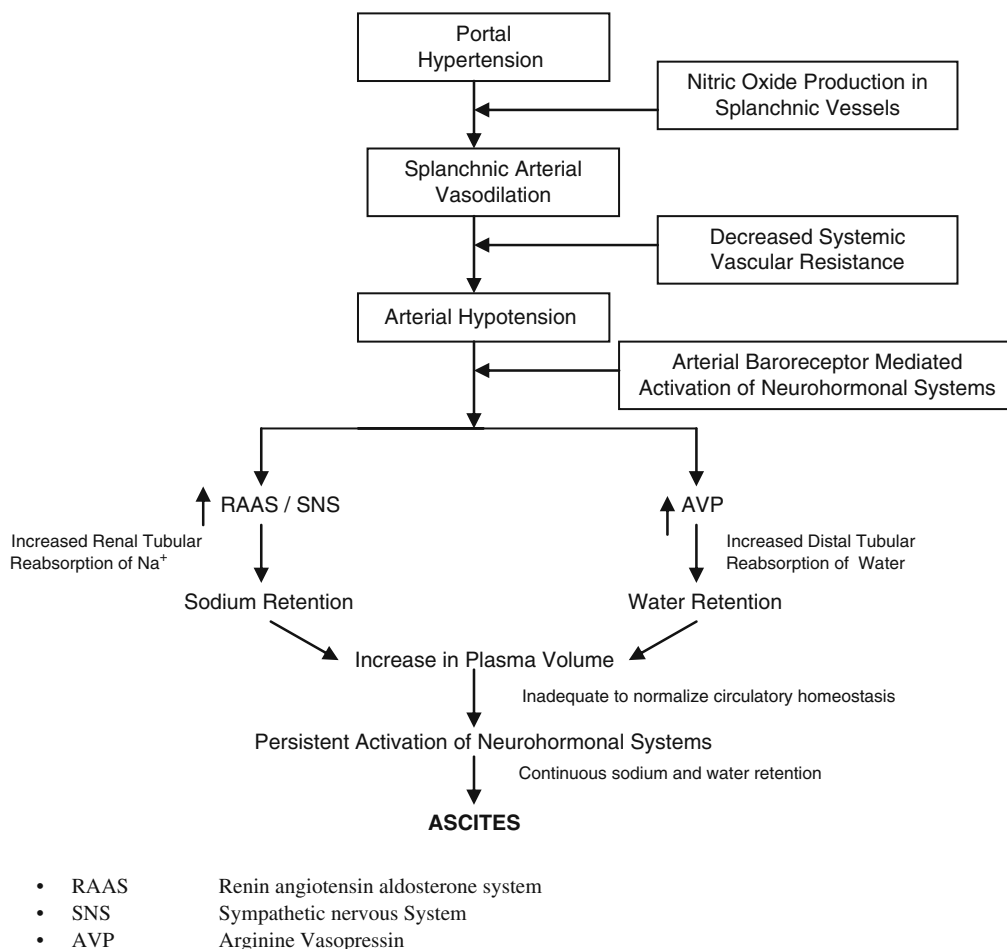


Fig. 1. Pathogenesis of ascites and hyponatremia.

associated with an increase in both atrial and ventricular atrial natriuretic peptide (ANP) release. Currently, support for the underfill theory seems most common (2).

In addition to the above theories, there are several other physiologic factors that contribute to the development of ascites. Individuals with late-stage liver disease often have hypoalbuminemia secondary to poor nutrition and synthetic liver dysfunction. The hypoalbuminemia leads to a significant decrease in vascular oncotic pressure and subsequent sodium and water retentive state through RAAS and AVP as reviewed above. Additionally, portal hypertension serves to facilitate localization of this excessive amount of fluid to the peritoneal space.

1.2. Diagnosis and Treatment

Ascites may be graded as grades 1–3 or as mild, moderate, or severe (Table 1). When patients no longer respond to maximum doses of spironolactone (400 mg/day) and

Table 1
Grading of Ascites

<i>Grade</i>	<i>Definition</i>
Grade I (mild)	Normally detectable only by ultrasound examination
Grade II (moderate)	Manifest clinically by symmetric distension of the abdomen
Grade III (severe)	Gross tense ascites with marked abdominal distension

furosemide (160 mg/day) or they develop serious side effects that prohibit continued use of diuretic therapy, they are said to have untreatable (refractory) ascites.

Clinical findings of massive ascites include abdominal distension with shifting dullness and/or fluid thrill with associated lower-extremity edema and can accompany other clinical findings of chronic liver disease. Dietary restriction of sodium to about 2 g/day in adult patients (90 mEq/day), diuretic therapy with spironolactone alone or in combination with furosemide is standard practice (Figs. 2, 3, 4)

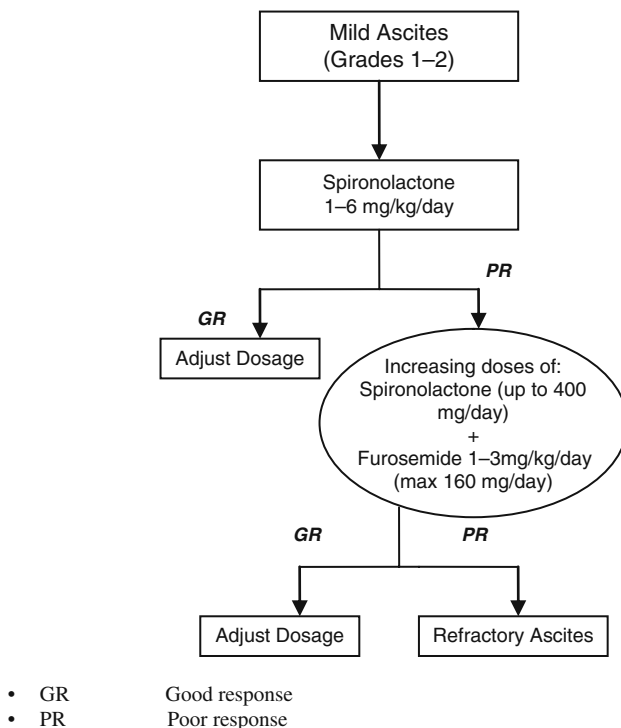
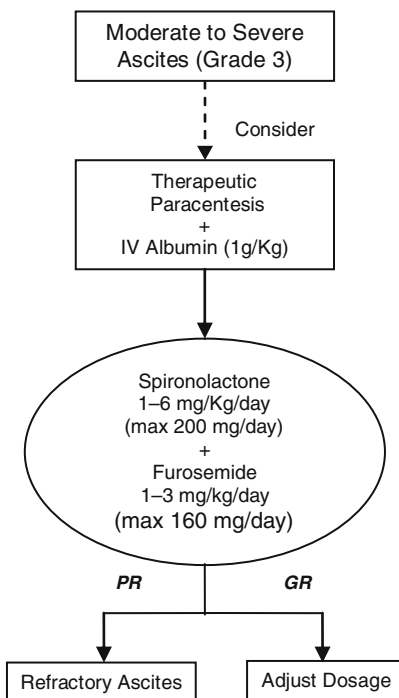


Fig. 2. Management of mild ascites.



- IV Intravenous
- GR Good response
- PR Poor response

Fig. 3. Management of moderate ascites.

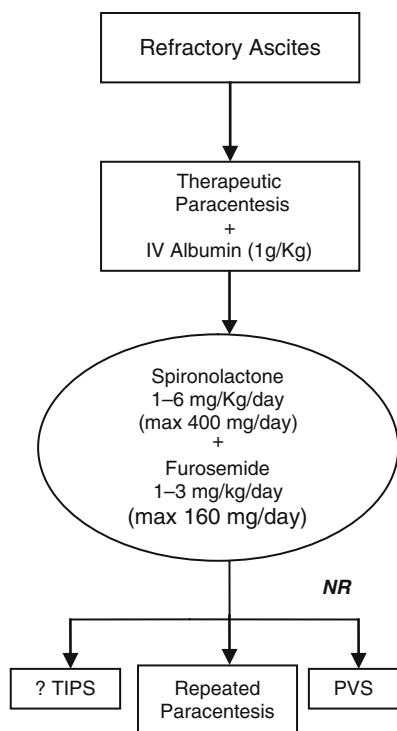
2. HEPATORENAL SYNDROME

Hepatorenal syndrome (HRS) is a state of functional renal failure in a patient with end-stage liver disease and occurs despite structurally normal kidneys. While relatively rare in pediatric patients, it can occur in 18–39% of adult cirrhotics over a 1–5 year interval without liver transplantation (2).

The syndrome is characterized by persistent oliguria (<500 ml/day), urine osmolality greater than plasma osmolality, urine–plasma creatinine ratio greater than 30:1, an elevated serum creatinine level, and urinary sodium excretion of <10 mEq/L, with a fractional excretion of sodium (FENa) < 1%. The oliguria does not respond to plasma volume expansion alone.

2.1. Pathophysiology

HRS is a severe complication of cirrhosis occurring as a consequence of an intense vasoconstriction of the renal circulation, resulting from a loss of renal autoregulation. This leads to reduced renal perfusion and a reduced glomerular filtration rate.



- IV Intravenous
- PVS Peritoneovenous Shunt
- TIPS Transjugular Intrahepatic Portosystemic Shunt
- NR No response

Fig. 4. Management of refractory ascites.

2.2. Management

Patients with HRS are usually candidates for liver transplantation if no other contraindications are present. Volume expansion and large volume paracentesis have been used for acute control of HRS. Volume expansion increases mean arterial pressure and paracentesis increases cardiac output and decreases renal venous pressure. The net effect of this is an increase in renal perfusion pressure and the renal flow. This leads to temporary improvement in renal function in patients with HRS. Vasodilators such as dopamine, or shunt procedures such as LeVeen (peritoneovenous), TIPS (transjugular intrahepatic portosystemic stent shunt), or orthotopic liver transplantation may be required for long-term improvement.

3. ACUTE LIVER FAILURE

The broadest definition of fulminant hepatic failure (FHF) is the development of hepatic necrosis leading to loss of liver function occurring within weeks of onset of liver disease (3).

Ascites in acute liver failure is the result of acute portal hypertension, vasodilatation, poor vascular integrity, and reduced oncotic pressure. Possible fluid and electrolyte imbalances that should be anticipated include

- Hypo/hyperkalemia.
- Hypo/hyponatremia.
- Hypophosphatemia: It should be noted that there is a risk for hypophosphatemia with hepatic regeneration and ATP synthesis.
- Hypoglycemia due to decreased production and increased utilization: Defective gluconeogenesis and inadequate hepatic uptake of insulin.

3.1. Management

1. Maintain hydration without inducing fluid overload. Often 2/3 routine maintenance fluids are used to maintain urine output >0.5 cc/kg/h.
2. Restrict sodium <0.5 mEq/kg/day.
3. Diuretics spironolactone (1–6 mg/kg/day) with or without furosemide.
4. Hypoglycemia: Addition of 10% dextrose to intravenous fluids may be necessary. Frequent monitoring of blood glucose levels. Maintain blood glucose >70 mg/dL.
5. Sodium: 0.5–1 mmol/kg/day.
6. Potassium: 3–6 mmol/kg/day.
7. Phosphorus: Give IV potassium phosphate if hypophosphatemic.
8. Decreased renal perfusion (hepatorenal syndrome): State of intravascular hypovolemia hence at risk for oliguria; may need to maintain renal perfusion with
 - High-dose loop diuretics: furosemide 1–3 mg/kg q 6 h.
 - Dopamine: 2–5 μ g/kg/min and FFP.
 - Hemofiltration or dialysis for severe oliguria.

CASE SCENERIO: 1

A 16-year-old male with a known diagnosis of cryptogenic cirrhosis and awaiting liver transplantation is brought to the hospital in a confused state with decreased urine output over the last 2 days. His medical condition was also complicated by marked ascites and fatigue for the last few weeks. His oral maintenance medications include lactulose given as 30 ml three times a day, spironolactone 50 mg three times a day, and ursodeoxycholic acid 300 mg twice a day.

On examination, he was afebrile with icteric sclera. His laboratory results revealed sodium of 120 mEq/L, BUN of 80 mg/dL, creatinine of 2.0 mg/dL. His serum albumin was 2.5 g/dL and conjugated bilirubin was 6.0 mg/dL.

What Is the Assessment of This Patient?

It is important to establish a diagnosis. With no history of recent medications causing nephrotoxicity, this represents acute renal deterioration in a patient with end-stage liver disease. Make sure the patient does not have excessive diarrhea and dehydration related to lactulose or diuretic therapy. The diagnosis of true hepatorenal syndrome (HRS) is

made by having an appropriate level of suspicion while excluding other potential precipitating factors.

What Is the Next Step in Management?

Obtain urinary electrolytes and creatinine to determine fractional excretion of sodium (FE_{Na}). Central vascular pressure monitoring can be considered to help assess intravascular volume status although, in this compromised host, the risk of infection from this intervention must be carefully considered. An $FE_{Na} < 1\%$ is consistent with the diagnosis of HRS.

How Will You Treat This Patient?

1. *Hyponatremia*: Fluid restriction to 75% maintenance fluid with normal saline to correct hyponatremia. Dialysis may be required in this patient. Rapid correction with hypertonic saline is contraindicated as it may lead to pulmonary edema, worsening ascites, and central pontine myelinolysis. In asymptomatic patients, the target rate of rise of the serum sodium should not exceed 2–4 mEq/L every 4 h or about 20 mEq/L in 24 h.
2. *Hypoalbuminemia and Oliguria*: Large volume paracentesis with concomitant albumin infusion can be considered. Alternative to this may be a trial of albumin infusion followed by a high dose of a loop diuretic like furosemide. A low-dose infusion of dopamine may be helpful as well by stimulating renal dopaminergic receptors leading to renal vasodilatation. If these measures fail to induce an adequate diuresis, then dialysis should be considered pending procurement of a suitable liver donor and transplantation.

CASE SCENERIO: 2

A 15-year-old boy with end-stage liver disease due to primary sclerosing cholangitis has just undergone orthotopic liver transplantation. The patient's intra-operative course was remarkable for a significant transfusion requirement of 15 units of packed red cells, 10 L of crystalloid, and 4 L of coagulation products. Postoperatively, he demonstrates good liver graft function; however, he has had a 15 kg weight gain and a decreased urine output to 10 cc/h for last few hours.

What Is the Assessment of This Patient?

The patient is in acute renal failure in the postoperative period (Fig. 5). The origin of renal failure in this patient may be due to a variety of factors such as post-operative acute tubular necrosis (ATN), intravascular volume depletion with pre-renal azotemia, and less likely, post-renal causes such as obstructive uropathy. A component of acute nephrotoxicity from immunosuppressive medications should be considered especially if calcineurin inhibitors are being administered. Since ATN is a salt-wasting entity, patients with ATN usually have granular casts present in the urine, high urinary sodium, and an $FE_{Na} > 1\%$. A normal renal ultrasound will usually exclude any obstructive uropathy. Central vascular monitoring may be necessary to exclude pre-renal causes such as volume depletion.

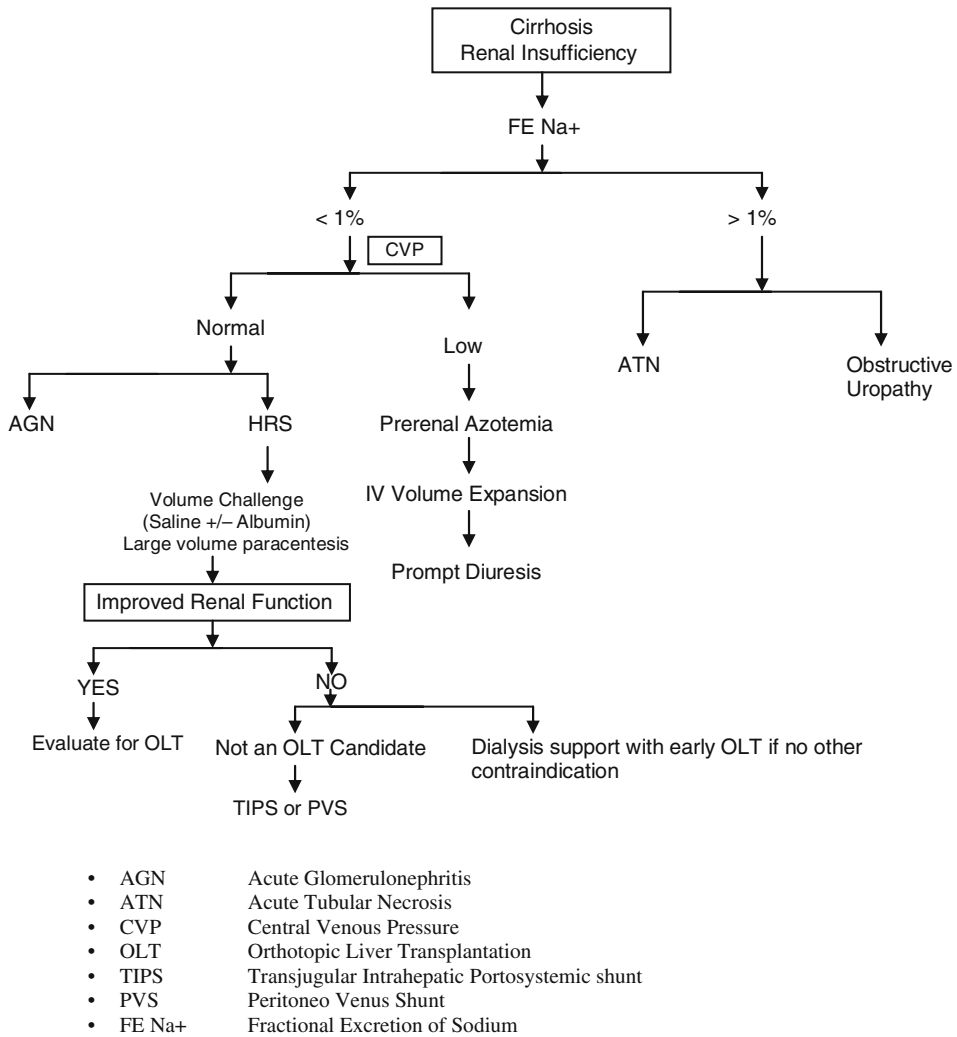


Fig. 5. Algorithm to approach a patient with cirrhosis and impaired renal function.

How Will You Treat This Patient?

Carefully evaluate the patient to assess possible etiology for renal failure as in Fig. 5. Reassess intravascular volume and total body fluid status. Once this is determined, volume expansion or slow diuresis with careful monitoring of calcineurin inhibitor levels can be instituted.

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