Advances in Clinical Medicine

Diagnosis and Management of Ascites in the Age of TIPS

Sigurdur Olafsson[1] and Andres T. Blei

In the mid 1990s, radiologists are asked to provide advice on managing patients with cirrhosis and refractory ascites. Liver disease is the most common cause of ascites. However, appropriate management of these patients is based on the ability to exclude other causes as well as knowledge of the physiological abnormalities that result in ascites. The goal of this review is to summarize advances in these areas as well as to discuss therapeutic options.

Although the exact sequence of events in patients with liver disease is unclear, fluid accumulation develops in the presence of portal hypertension, peripheral vasodilatation, and renal sodium retention. Multiple studies continue to examine the mechanisms that account for each abnormality. Diagnosis is made using history and physical examination, but analysis of the ascitic fluid is important in establishing the etiology. The serum–ascites albumin gradient is accurate in determining whether portal hypertension is present. This gradient is superior to the outdated classification of ascites into exudative and transudative types. With regard to therapy of diuretic refractory ascites, large-volume paracentesis is safe but requires multiple procedures. Surgical interventions such as side-to-side portacaval shunting and peritoneovenous shunting provide relief from ascites but are associated with high morbidity and mortality. The recently introduced transjugular intrahepatic portosystemic shunt (TIPS) procedure improves ascites in many patients but is associated with technical complications as well as complications related to portosystemic shunting. Its role in managing refractory ascites is still undefined.

Pathogenesis

Liver disease, especially cirrhosis, is the most common cause of ascites in the United States, accounting for over 80% of cases. Cancer is the second most common cause, with gastrointestinal tumors, hepatoma, and breast and ovarian cancers being the most frequently encountered malignant lesions [1]. Other causes combined account for less than 10% of cases. With improved diagnosis and treatment of cardiac diseases, heart failure due to ischemia, valvular disease, constrictive pericarditis, and chronic pulmonary disease are less commonly associated with ascites than in the past. Infections such as tuberculosis and chlamydia account for a few cases. Rare causes of ascites include those associated with nephrotic syndrome and chronic pancreatitis. Occasionally, ascites of unclear origin is seen in patients on chronic hemodialysis.

Ascites Due to Liver Disease

In cirrhosis, ascites develops in the presence of portal hypertension, peripheral vasodilatation, and renal sodium retention. The three major theories of the pathogenesis of ascites in cirrhosis mainly differ in the sequence of events leading to sodium retention and fluid accumulation. According to the underfill theory [2], the initial event is the intrahepatic obstruction of blood flow leading to elevation of sinusoidal and splanchnic capillary pressures and increased extravasation of fluid into the interstitial spaces. At a com-

Received June 21, 1994; accepted after revision February 13, 1995.
This is another in the continuing series of nonradiology articles concerning recent developments in the clinical and basic sciences. It is designed to help radiologists keep abreast of advances in medicine to ensure that their understanding of disease stays current.
[1]Both authors: Department of Medicine/111E, Lakeside VA Medical Center, 333 E. Huron St., Chicago, IL 60611. Address correspondence to A. T. Blei.

pensated stage, the fluid is returned by the lymphatic vessels into the thoracic duct and systemic circulation. With progression of portal hypertension, the capacity of the lymphatic system is exceeded, resulting in fluid leakage into the peritoneal cavity with formation of ascites. In addition, ascites formation would be further facilitated by hypoalbuminemia resulting in reduced intravascular oncotic forces. By decreasing the intravascular volume, ascites formation would cause sodium and water retention by the kidneys, initiating a cycle of sodium retention and ascites formation.

The overflow theory suggests that urinary sodium retention is the primary event and that ascites formation is a consequence of plasma volume expansion [3]. The initial stimulus for sodium retention may arise from hepatic nerve afferents [4] or from altered hormonal levels as a consequence of liver disease [5]. The third and most recent hypothesis, the peripheral arterial vasodilatation hypothesis [6], combines elements from the previous two. According to this theory, the initial event is peripheral arterial vasodilatation, leading to a reduction in effective arterial plasma volume. Various neurohumoral mechanisms are activated, stimulating the kidneys to retain sodium and water. Total plasma volume is expanded and ascites develops when a critical expansion occurs in the presence of portal hypertension. The peripheral vasodilatation is a part of a generalized hyperdynamic state whose pathogenesis is unclear but appears to be related to increased levels of endogenous vasodilators, including nitric oxide [7]. The source of these substances may lie in the splanchnic bed, gaining access to the systemic circulation via portosystemic shunts.

Ascites Not Associated with Liver Disease

In ascites associated with nonhepatic malignant disease, the pathogenesis depends on the type and location of the tumor [1]. In peritoneal carcinomatosis, the most common cause of malignant ascites, leakage of protein-rich fluid from the malignant cells causes exudation of extracellular fluid into the peritoneal cavity. Large liver tumors pressing on or growing into the portal or hepatic veins can cause portal hypertension and ascites. Obstruction of lymph channels by malignant disease may lead to lymphatic rupture and leakage of chyle into the peritoneum.

In cardiac failure, elevation of pressure in the right side of the heart results in congestion of the hepatic sinusoids and leakage of fluid from the liver surface. In addition, reduction in effective blood volume leads to sodium and water retention by the kidneys [8].

Pancreatic ascites results from rupture of the pancreatic duct or leakage of pancreatic juice from a pseudocyst. Irritation of the peritoneum by the pancreatic juice can cause peritoneal accumulation of a protein-rich exudate. Biliary ascites forms by similar mechanisms. Chylous ascites forms after transection of lymphatics, such as after abdominal surgery, or from obstruction of lymphatic channels by malignant disease, especially lymphoma [9]. Ascites caused by infections such as tuberculosis and chlamydia is probably caused by mechanisms similar to those in peritoneal carcinomatosis. The pathogenesis of ascites in nephrotic syndrome and dialysis-associated ascites is unclear but may be related to volume expansion and abnormal peritoneal permeability.

Diagnosis

History

Cirrhosis is the most common cause of ascites in the United States. Because ascites usually develops in later stages of liver disease as a sign of decompensation, the diagnosis of a specific liver disease has already been established in many patients. However, ascites formation can be the first sign of liver disease, so it is important to obtain a history of risk factors for liver disease, such as alcohol consumption, exposure to blood products, IV drug use, and family history of liver diseases. Sudden development of ascites in a previously stable patient with cirrhosis raises suspicion of hepatoma.

A history of heart failure and pericardial disease should alert the physician to the possibility of cardiac ascites. A history of cancer, especially gastrointestinal, breast, and ovarian carcinoma and lymphoma, may suggest malignant ascites [1]. Tuberculous ascites should be suspected in immigrants from endemic areas [10], in the presence of known extraabdominal tuberculosis, and in immunocompromised persons. In patients with pancreatic ascites, there is usually a history of chronic pancreatitis, most commonly due to alcoholism.

The same patient may have more than one disease predisposing to ascites. In patients with alcoholic cirrhosis, other causes such as tuberculosis or pancreatitis may be overlooked. An IV drug user may have liver disease from viral hepatitis and infectious or malignant ascites related to AIDS. Patients with renal disease may have cirrhosis from hepatitis viruses, nephrotic syndrome, or both.

Physical Examination

Abdominal distention can also be caused by tumors and cysts, bowel obstruction, and excessive intestinal gas. The accuracy of physical examination in detecting ascites depends largely on the amount of fluid present. The diagnosis may be obvious in patients with massive ascites, but when only a small or moderate amount is present, physical assessment is only about 50% accurate, even by experienced gastroenterologists [11]. Flank dullness, which is present in over 90% of patients, is the most sensitive physical sign of ascites. However, this sign is also nonspecific. Shifting dullness on percussion is more specific but less sensitive than flank dullness. Although the presence of a fluid wave was found to be a relatively specific sign of ascites, it is cumbersome to elicit and has low sensitivity [11]. The puddle sign, reported to detect as little as 120 ml of fluid, requires the patient to be in the knee–hand position during examination.

Physical examination can provide clues to the pathogenesis of ascites in a given patient. Signs of liver disease, such as jaundice, palmar erythema, and spider nevi, should be sought. Splenomegaly and large abdominal collateral veins

may indicate portal hypertension. Patients with a supradiaphragmatic cause of ascites have prominent jugular veins. Collaterals in the back indicate caval obstruction, as seen with membranous obstruction of the inferior vena cava.

Radiologic Studies

Radiologic studies are used if the presence of ascites needs to be confirmed. They also may be helpful in determining the cause of fluid accumulation. However, the cause is most often elicited by history, physical examination, and ascitic fluid analysis.

Abdominal sonography may detect as little as 100 ml of ascites [12]. This study may help determine the cause of ascites; the appearance of the liver may suggest cirrhosis, a pancreatic pseudocyst can be visualized, and intraabdominal tumors can be detected in the case of malignant ascites. Doppler sonography can detect thrombosis of the portal or hepatic veins. Furthermore, sonography helps localize a safe site for insertion of a paracentesis needle in patients with a small amount of ascites or in cases in which the ascites is compartmentalized. Sonography is relatively inexpensive, noninvasive, and can be performed at the bedside if needed. CT is also a sensitive tool in detecting ascites and may provide information that can be difficult to obtain by sonography, such as evidence of peritoneal carcinomatosis, abscesses, and focal liver lesions.

Diagnostic Paracentesis

Abdominal paracentesis performed to obtain a sample of fluid for analysis is the single most important procedure in evaluating the patient with ascites. The procedure should be performed in all patients with newly onset ascites and whenever deterioration occurs in a patient with known ascites. Although an early, retrospective study reported a 2.9% rate of major complications, such as bowel perforation and severe hemorrhage [13], a more recent, prospective study found the procedure to be safe [14]. Transfusion-requiring hematomas developed in only 0.9% of patients and smaller hematomas in another 0.9%. This was in spite of the fact that two thirds of the patients, most of whom had cirrhosis, had prolonged prothrombin time; 21% had a prolongation of 5 sec or more. Therefore, it is unnecessary to routinely administer fresh frozen plasma and/or platelets to cirrhotic patients who have a coagulopathy before performing paracentesis. Concerns regarding the introduction of bacterial peritonitis are also unfounded [14]. Because the midline caudad to the umbilicus is usually relatively avascular, this site is recommended for paracentesis [13, 14]. If a midline surgical scar is present, either of the lower quadrants should be used. The bowel may adhere to the abdominal wall near surgical scars, and a needle inserted close to a scar may enter the intestine. In cases in which the presence of ascites is uncertain or where there are multiple surgical scars, sonography should be used for guidance.

Analysis of the Ascites Fluid

The gross appearance may be helpful in determining the pathologic process. Uncomplicated ascitic fluid is slightly yellow and transparent. A common cause of cloudy ascites in patients with portal hypertension is the presence of neutrophils, but this is not specific. Chylous ascites typically has a milky appearance. Bloody fluid can be caused by a traumatic tap, malignant tumors, or tuberculosis. Dark-brown fluid may indicate the presence of bile.

Ascites was formerly classified as exudative or transudative according to total protein concentration. However, the serum–ascites albumin gradient has been found to be more helpful than the exudate–transudate concept in the differential diagnosis of ascites [15, 16]. The gradient is obtained by subtracting the ascitic fluid albumin level from the serum level. A gradient of ≥1.1 g/dl indicates, with 97% accuracy [15], that the patient has portal hypertension. The gradient correlates directly with portal pressure; an increasing hydrostatic pressure between the portal vasculature and ascitic fluid is balanced by a corresponding difference in oncotic forces. When the portal hypertensive patient has another potential cause of ascites, or mixed ascites, the gradient is preserved [16].

The cell count is probably the single most important ascitic fluid test. An elevated ascitic fluid WBC count is seen in malignant diseases and in all inflammatory processes. The differential diagnosis is important; in spontaneous bacterial peritonitis (SBP), polymorphs predominate; in tuberculosis and peritoneal carcinomatosis, lymphocytes often predominate. Culture of ascitic fluid for bacteria should be obtained routinely in patients with cirrhotic ascites, in whom SBP is common. For optimal results, ascitic fluid should be inoculated at the bedside into blood culture bottles [17]. Gram's stain of the fluid is of little help in diagnosing SBP even in centrifuged specimens but is likely to be positive in secondary peritonitis. In tuberculous peritonitis, acid-fast smear is rarely positive and culture is positive in only 50% of cases [18]. Ascitic glucose concentration may drop to zero in severe infections such as secondary peritonitis or late-stage SBP.

Ascitic fluid lactate dehydrogenase originates from blood and from the breakdown of WBCs in the ascitic fluid. Severalfold increase over serum levels may be seen in secondary peritonitis (an identified intraabdominal source of infection) [19]. Triglyceride levels should be measured if chylous ascites is suspected. Measurement of ascitic fluid amylase is useful when pancreatic ascites is suspected. If there is a suspicion of perforation of the biliary tree and/or the fluid is dark brown, the bilirubin concentration should be measured. Cytology studies are appropriate whenever there is evidence of a malignant tumor, or when a nonmalignant cause of ascites is not obvious. A large volume of ascites (500 ml) is recommended for better results.

Laparoscopy

With the availability of new imaging techniques, the need for laparoscopy in determining the cause of ascites has decreased [20]. The cause of ascites is usually easily determined by history and physical examination and by one or more of the tests described above. However, if the diagnosis is still unclear, laparoscopy for direct visualization of the peritoneum may be indicated. Tuberculous peritonitis can often be diagnosed by laparoscopy only; the procedure

should be performed promptly if the clinical picture and analysis of ascitic fluid suggest this disease [10]. Typical peritoneal tubercles are found in most patients and peritoneal biopsies show caseating granulomas in all and acid-fast bacilli in 74% of biopsy material [21]. Chlamydial peritonitis may have a similar appearance. This procedure is rarely needed to detect peritoneal carcinomatosis because of the sensitivity of cytology [1].

Complications of Ascites

Spontaneous Bacterial Peritonitis

By definition, SBP results from spontaneous bacterial infection of the ascitic fluid without an apparent intraabdominal source. Most cases are seen in patients in whom ascites is due to cirrhosis of the liver and portal hypertension. SBP is diagnosed by routine paracentesis in 10–20% of patients with cirrhotic ascites upon hospital admission [22].

The mechanism by which the ascitic fluid becomes infected is unclear. The risk of SBP is increased in patients with low protein concentration in the ascitic fluid [23] and in patients with ascitic fluid deficient in opsonic activity [24]. Gastrointestinal bleeding [25] is a common antecedent, suggesting a role for bacterial translocation. Ascitic fluid may become infected from spontaneous bacteremia, which is common in patients with cirrhosis, possibly because of depressed phagocytic activity in the reticuloendothelial system [26].

Although most patients have signs and symptoms, these can be subtle and nonspecific. The most common signs and symptoms are fever and abdominal pain [19], but patients may have encephalopathy alone or a deterioration in general health without abdominal symptoms. The diagnosis of SBP is made on the basis of the clinical picture and an analysis of the ascitic fluid. The most important finding in the ascitic fluid is an elevated polymorphonuclear count. A count of 250 cells/mm^3 is often considered diagnostic [27]. Gram-negative enteric bacteria, usually a single organism, are responsible for most episodes [28]. *Streptococcus pneumoniae*, the second most common cause, is likely to arise from hematogenous spread. Secondary peritonitis, such as from a perforated gut, is suspected if the ascitic fluid is polymicrobial or if a patient with presumed SBP does not respond to antibiotic therapy.

Patients with clinical signs and symptoms suggestive of SBP and/or an ascitic polymorphonuclear count greater than 250 cells/mm^3 should be treated empirically with antibiotics. Broad-spectrum antibiotics should be used and adjusted to culture results. Aminoglycosides should be avoided because of increased risk of nephrotoxicity in patients with cirrhosis [29]. Cefotaxime, a third-generation cephalosporin, is the best-studied antibiotic for treating SBP. It has proved superior to older regimens, is not nephrotoxic, and covers 98% of the bacterial flora [30]. It does not provide coverage for *Enterococcus* species. The development of SBP is a serious event. Although in-hospital mortality appears to be decreasing in recent series, 70% of patients have another episode within 1 year, and the 1-year survival rate is 38% [31]. Prophylactic treatment with antibiotics may prevent recurrence but has not proved to prolong survival [32, 33].

Hepatic Hydrothorax

Hepatic hydrothorax is defined as the presence of a large pleural effusion in a patient with cirrhosis but without primary heart or pulmonary disease [34]. The effusion is usually unilateral on the right side. Ascites is usually detectable but may be absent [34, 35]. Hydrothorax is thought to develop when a congenital defect in the diaphragm exists [34–36]. In the presence of such a defect, ascitic fluid preferentially accumulates in the pleural space because of the negative intrathoracic pressure during inspiration. Hepatic hydrothorax can be large enough to cause life-threatening compromise of respiratory and cardiac function. Various techniques are used to confirm the peritoneal origin of the pleural effusion. Usually, a marker such as air, radiolabeled albumin [36], dye, or ^{99m}Tc–sulfur colloid [34] is injected intraperitoneally, and its appearance is detected in the chest. The initial therapeutic approach is the same as in uncomplicated ascites: salt restriction and diuretics. However, hepatic hydrothorax is frequently refractory to such therapy and tends to reaccumulate rapidly after therapeutic thoracentesis [34, 37]. Frequent thoracentesis results in depletion of albumin stores [35]. Placement of a chest tube for chemical pleurodesis can result in severe loss of fluid, electrolytes, and proteins, as well as in leakage of fluid around the tube when clamped; it is relatively contraindicated [37]. Surgical repair of the diaphragmatic defect has been proposed [38], but major surgery is poorly tolerated by patients with cirrhosis. The TIPS procedure has been reported to resolve this complication [39, 40]. Liver transplantation should be considered in refractory cases.

Umbilical Hernia

Abdominal wall hernias, usually umbilical, are common in patients with ascites [41]. Complications such as incarceration, ulceration of the skin, and frank rupture of the hernia can be serious events in a decompensated patient. Most hernias recur following surgical repair unless ascites is controlled [42].

Treatment

Ascites Not Due to Liver Disease

Treatment of noncirrhotic ascites is directed at the underlying disease whenever possible. Tuberculous ascites is treated with appropriate antibiotics. Chlamydia-associated ascites is cured by antibiotics and carries a good prognosis [43]. Treatment of pancreatic ascites is controversial. Some patients respond to medical treatment such as IV hyperalimentation, salt restriction, and diuretics. Infusion of somatostatin, a hormone that decreases pancreatic exocrine secretion, was reported to stop ascites formation in a patient with alcoholic pancreatitis [44]. Surgical or endoscopic intervention may be needed [44]. Malignant ascites due to peritoneal carcinomatosis does not respond to diuretic therapy [45]; in these patients, whose life expectancy is short, therapeutic paracentesis is appropriate. Because chylous ascites is a manifestation of many diseases, the treatment depends on the underlying disorder. A low-fat diet with medium-chain triglyceride supplemen-

tation is used in congenital lymphangiectasia; chemotherapy is used for lymphoma; and bowel rest and IV hyperalimentation is used for ruptured lymphatic vessels [9].

Ascites Due to Liver Disease

Diet and diuretics.—Sodium restriction and diuretics are the cornerstone of the treatment of cirrhotic ascites. Moderate sodium restriction is an important part of the regimen but is rarely sufficient alone [46]. Fluid restriction is not necessary unless hyponatremia is present. Spironolactone, an aldosterone antagonist that decreases sodium reabsorption in the distal tubule, is the diuretic of choice in treating cirrhotic ascites. Cautious addition of a loop diuretic such as furosemide potentiates the diuretic effect of spironolactone and reduces the risk of developing hyperkalemia. The maximal dose of diuretics recommended is a combination of spironolactone 400 mg/day with furosemide 160 mg/day [47]. Over 90% of patients respond to a combination of salt restriction and diuretics [48].

Large-volume paracentesis.—Large-volume paracentesis is used to relieve tense, symptomatic ascites that is refractory to diuretics. This procedure fell out of favor in the 1950s because of the availability of diuretics and the fear of complications. However, multiple clinical studies in the 1980s demonstrated the safety of large-volume paracentesis for treating cirrhotic ascites [49–51]. Infusion of a plasma expander such as albumin is routinely done in many institutions, though it is controversial whether this is needed with paracentesis of 4–6 l. Although one study reported asymptomatic electrolyte and renal impairment after large-volume paracentesis without colloid infusion [52], other studies have not found such adverse effects [50]. Albumin is given IV in doses of 6–10 g per l of fluid removed. Alternatively, dextran-70 can be given [53]. Usually 4–6 l are removed daily; however, one study reported the safety of total paracentesis (with albumin infusion) removing up to 22 l in one session [51].

Management of Refractory Ascites

Refractory ascites is defined as either persistence of ascites in spite of maximal diuretic therapy and adherence to salt restriction or development of renal insufficiency, electrolyte abnormalities, or other complications of diuretics [54]. After maximal doses of diuretics, further increase in dose or addition of a third diuretic is seldom helpful [54]. The development of refractory ascites usually indicates advanced underlying disease; the 1-year survival rate is only 25% [55]. Therapeutic options for this group of patients are few. Because most patients with refractory ascites will die within a year, suitable candidates should be considered for orthotopic liver transplantation if no contraindications exist.

Most patients with refractory ascites require large-volume paracentesis at intervals of 2–3 weeks depending on the severity of sodium retention and the amount of fluid removed at each session. Many centers routinely perform total paracentesis on such patients [54]. This procedure can be performed on an outpatient basis. It is the ideal approach for patients awaiting liver transplantation and for palliation of patients with short estimated survival, but its applicability depends on compliance and whether the patient lives close to a center where paracentesis can be performed.

Peritoneovenous Shunt

The LeVeen shunt was introduced in 1974 for management of ascites [56]. One limb of the shunt lies in the peritoneal cavity and the other in the superior vena cava close to the entrance of the right atrium. A valve at the venous end prevents backflow of blood into the tubing; flow is maintained by peritoneovenous pressure gradient. Other shunts, such as the Denver, were subsequently introduced but have not been proved superior [56]. Peritoneovenous shunts result in rapid resolution of ascites in most patients but are associated with a large number of complications such as disseminated intravascular coagulation, high-output heart failure, and sepsis [55, 58]. Shunt occlusion with reaccumulation of ascites occurs in 50% of patients within a year [57]. Studies comparing peritoneovenous shunting to intensive medical therapy including large volume paracentesis [48, 59] showed no difference in survival.

Surgical Portosystemic Shunts

Surgical portosystemic shunts where the portal vein is used as an outflow tract (such as the side-to-side portacaval shunt and the mesocaval shunt) relieve portal hypertension and are effective in clearing ascites. However, because of the high incidence of hepatic encephalopathy (50% in one study [60]) and of the high surgical mortality in patients with advanced liver disease, this approach is seldom used. Removal of portal flow can be deleterious in a failing liver, and hepatic insufficiency can be precipitated.

Transjugular Intrahepatic Portosystemic Shunt Procedure

The recently introduced TIPS procedure has gained popularity as a treatment for the complications of portal hypertension. In this procedure, a tract is created between branches of the hepatic and portal veins, resulting in an intrahepatic portosystemic shunt with a concomitant reduction in portal pressure. The procedure is most commonly used in the treatment of recurrent esophageal variceal bleeding, especially in patients awaiting liver transplantation [38].

Experience with the TIPS procedure in treating ascites is still limited; published reports are preliminary, and most include few patients. Ferral et al. [61] performed the procedure on 14 patients with refractory ascites, of whom seven had complete resolution of their ascites. In a study done in France, some patients had their ascites relieved; others died of liver failure [62]. In a recent pilot study, 15 of 19 patients with refractory ascites, mostly cirrhotic, became responsive to diuretics after TIPS placement [63]. In a large series [64] in which TIPS was performed mainly for variceal bleeding, 49 of 59 patients with ascites had improved control of this complication. TIPS was also reported to relieve ascites in patients with Budd-Chiari syndrome [65]. The preliminary results of a

controlled trial have indicated a worse course in patients with Child's class C (advanced liver disease) treated with TIPS for intractable ascites [66]. In some cases of hepatic hydrothorax, resolution of fluid accumulation was obtained [39, 40]. Three series published this year have also documented hemodynamic and hormonal changes after placement of TIPS for refractory ascites [67–69].

Technical complications and complications related to portosystemic shunting are common after this procedure. Technical complications include hemobilia and biliary vascular fistula, liver hematoma, stent migration, and intraabdominal bleeding [70]. Shunt occlusion or stenosis is a major problem, occurring in close to 50% of patients within a year [71]. Following the pro-cedure, Doppler sonography should be performed at regular intervals to identify patients needing shunt revision [72]. Complications related to portosystemic shunting include hepatic encephalopathy, worsening of the hyperdynamic circulatory state, and precipitation of liver failure. Hepatic encephalopathy develops in 20% of patients; at highest risk are the elderly and those who have shunts with a large diameter [73, 74]. In most cases, however, the encephalopathy responds to medical therapy. The hemodynamic effects of TIPS can be detrimental. Patients with cirrhosis and portal hypertension are usually in a hyperdynamic circulatory state, that is, they have high cardiac output and low systemic vascular resistance. Placement of TIPS, at least initially, leads to worsening of this hyperdynamic state [75]. Following the procedure, cardiac preload immediately increases [75]; in patients with decreased cardiac reserve, this can lead to pulmonary edema from high-output failure. In patients with advanced liver disease, the 1-year survival rate following TIPS placement is poor [76, 77]. TIPS can precipitate progressive liver failure [78] that requires urgent liver transplantation, if possible.

How could the efficiency of TIPS in cases of refractory ascites be maximized? Measurement of the portacaval gradient before and after placement of TIPS provides an assessment of the degree of decompression attained with the procedure. Although a gradient of 12 mm Hg is important in the pathogenesis of both esophageal varices and variceal bleeding [79], the level of portal hypertension associated with ascites is more variable. Thus, it is preferable initially to place a stent of a lower diameter and observe the evolution rather than to attempt a large decompression. If unresponsive to diuretics, patients can be progressively dilated so that a threshold point may be reached where responsiveness occurs.

Summary

Cirrhotic patients with ascites that is not controlled by medical therapy present a serious management problem. History, physical examination, and analysis of the ascitic fluid exclude other causes of ascites. Systemic hemodynamic factors and intrarenal abnormalities contribute to the pathogenesis of intractable ascites. Once a patient has been deemed a failure of medical therapy, the decision to place a TIPS for intractable ascites should weigh the patient's functional status as well as the management of post-shunt liver failure. The results of controlled trials now in progress are eagerly awaited.

REFERENCES

1. Runyon BA, Hoefs JC, Morgan TR. Ascitic fluid analysis in malignancy-related ascites. *Hepatology* **1988**; 8 1104–1109
2. Witte MH, Witte CL, Dumont AE. Progress in liver disease: physiological factors involved in the causation of cirrhotic ascites. *Gastroenterology* **1971**;61:742–750
3. Lieberman FL, Denison EK, Reynolds TB. The relationship of plasma volume, portal hypertension, ascites, and renal sodium retention in cirrhosis: the overflow theory of ascites formation. *Ann N Y Acad Sci* **1970**;70:202–206
4. Levy M, Wexler MJ. Hepatic denervation alters first-phase urinary sodium excretion in dogs with cirrhosis. *Am J Physiol* **1987**;253:F664–F671
5. Rector WG Jr, Robertson AD, Lewis FW, Adair OV. Arterial underfilling does not cause sodium retention in cirrhosis. *Am J Med* **1993**;95:286–295
6. Schrier RW, Arroyo V, Bernardi M, Epstein M, Henriksen JH, Rodes J. Peripheral arterial vasodilation hypothesis: A proposal for the initiation of renal sodium and water retention in cirrhosis. *Hepatology* **1988**;8:1151–1157
7. Albillos A, Colombato LA, Groszmann RJ. Vasodilatation and sodium retention in prehepatic portal hypertension. *Gastroenterology* **1992**;102:931–935
8. Schrier RW. Pathogenesis of sodium and water retention in high-output and low-output cardiac failure, nephrotic syndrome, cirrhosis, and pregnancy. *N Engl J Med* **1988**;319:1065–1072
9. Press OW, Press NO, Kaufman SD. Evaluation and management of chylous ascites. *Ann Intern Med* **1982**;96:358–364
10. Wolfe JHN, Behn AR, Jackson BT. Tuberculous peritonitis and role of diagnostic laparoscopy. *Lancet* **1979**;4/21:852–853
11. Cattau EL, Benjamin SB, Knuff TE, Castell DO. The accuracy of the physical examination in the diagnosis of suspected ascites. *JAMA* **1982**; 247:1164–1166
12. Goldberg BB, Goodman GA, Clearfield HR. Evaluation of ascites by ultrasound. *Radiology* **1970**;96:15–22
13. Mallory A, Schaefer JW. Complications of diagnostic paracentesis in patients with liver disease. *JAMA* **1978**;239:628–630
14. Runyon BA. Paracentesis of ascitic fluid: a safe procedure. *Arch Intern Med* **1986**;146:2259–2261
15. Runyon BA, Montano AA, Akriviadis EA, Antillon MR, Irving MA, McHutchison JG. The serum-ascites albumen gradient is superior to the exudate-transudate concept in the differential diagnosis of ascites. *Ann Intern Med* **1992**;117:215–220
16. Rector WG, Reynolds TB. Superiority of the serum-ascites albumin difference over the ascites total protein concentration in separation of "transudative" and "exudative" ascites. *Am J Med* **1984**;77:83–85
17. Runyon BA, Antillon MR, Akriviadis A, McHutchison JG. Bedside inoculation of blood culture bottles with ascitic fluid is superior to delayed inoculation in the detection of spontaneous bacterial peritonitis. *J Clin Microbiol* **1990**;28:2811–2812
18. Karney WW, O'Donoghue JM, Ostrow JH, Holmes KK, Beaty HN. The spectrum of tuberculous peritonitis. *Chest* **1977**;72:310–315
19. Runyon BA, Hoefs JC. Ascitic fluid analysis in the differentiation of spontaneous bacterial peritonitis from gastrointestinal tract perforation into ascitic fluid. *Hepatology* **1984**;3:447–450
20. De Groen PC, Rakela J, Moore SC, et al. Diagnostic laparoscopy in gastroenterology. A 14-year experience. *Dig Dis Sci* **1987**;32:677–681
21. Manohar A, Simjee AE, Haffejee AA, Pettengell KE. Symptoms and investigative findings in 145 patients with tuberculous peritonitis diagnosed by peritoneoscopy and biopsy over a five year period. *Gut* **1990**; 31:1130–1132
22. Almdal TP, Skinhoj P. Spontaneous bacterial peritonitis in cirrhosis. Incidence, diagnosis and prognosis. *Scand J Gastroenterol* **1987**;22:295–300
23. Runyon BA. Low-protein-concentration ascitic fluid is predisposed to spontaneous bacterial peritonitis. *Gastroenterology* **1986**;91:1343–1346
24. Runyon BA. Patients with deficient ascitic fluid opsonic activity are predisposed to spontaneous bacterial peritonitis. *Hepatology* **1988**;8:632–635
25. Runyon BA. Gastrointestinal hemorrhage markedly increases the risk of development of spontaneous bacterial peritonitis. *Gastroenterology* **1986**;90:1763
26. Rimola A, Soto R, Bory F, Arroyo V, Piera C, Rodes J. Reticuloendothelial system phagocytic activity in cirrhosis and its relation to bacterial infections and prognosis. *Hepatology* **1984**;4:53–58
27. Runyon BA, Hoefs JC. Culture-negative neutrocytic ascites: a variant of spontaneous bacterial peritonitis. *Hepatology* **1984**;4:1209–1211
28. Pinzello G, Simonetti RG, Craxi A, Di Piazza S, Spano C, Pagliaro L. Spontaneous bacterial peritonitis: A prospective investigation in predominantly nonalcoholic cirrhotic patients. *Hepatology* **1983**;3:545–549

29. Cabrera J, Arroyo V, Ballesta AM, et al. Aminoglycoside nephrotoxicity in cirrhosis. *Gastroenterology* **1982**;82:97–105
30. Felisart J, Rimola A, Arroyo V, et al Cefotaxim is more effective than ampicillin-tobramycin in cirrhotics with severe infections. *Hepatology* **1985**;5:457–462
31. Tito L, Rimola A, Gines P, Lach J, Arroyo V, Rodes J. Recurrence of spontaneous bacterial peritonitis in cirrhosis: frequency and predictive factors. *Hepatology* **1988**;8:27–31
32. Gines P, Rimola A, Planas R et al. Norfloxacin prevents spontaneous bacterial peritonitis recurrence in cirrhosis: results of a double-blind, placebo-controlled trial. *Hepatology* **1990**;12:716–724
33. Soriano G, Guarner C, Teixido M, Such J, Barrios J, Enriques J, Vilardell F. Selective intestinal decontamination prevents spontaneous bacterial peritonitis. *Gastroenterology* **1991**;100:477–481
34. Rubinstein D, McInnes IE, Dudley FJ. Hepatic hydrothorax in the absence of clinical ascites: diagnosis and management. *Gastroenterology* **1985**; 88:188–191
35. Llaneza PP, Salt II WB. Unilateral pleural effusion without clinical ascites in Laennec's cirrhosis. *Dig Dis Sci* **1985**;30:88–91
36. Lieberman FL, Hidemura R, Peters RL, Reynolds TB. Pathogenesis and treatment of hydrothorax complicating cirrhosis with ascites. *Ann Intern Med* **1966**;64:341–351
37. Runyon BA, Greenblatt M, Ming RHC. Hepatic hydrothorax is a relative contraindication to chest tube insertion. *Am J Gastroenterol* **1986**; 81:566–567
38. Conn HO. Transjugular intrahepatic portal-systemic shunts: the state of the art. *Hepatology* **1993**;17:148–158
39. Strauss RM, Martin LG, Kaufman SL, Galloway JR, Waring JP, Boyer TD. Role of transjugular intrahepatic portosystemic shunt (TIPS) in the primary management of refractory cirrhotic hydrothorax. (abstr) *Hepatology* **1992**;16:85
40. Gordon FD, Stokes KR, Anastopoulos H, Perry LJ, et al. The successful use of transjugular intrahepatic portosystemic shunt (TIPS) in the treatment of symptomatic hepatic hydrothorax (abstr). *Gastroenterology* **1994**;106:899
41. Belghiti J, Rueff B, F Fekete. Umbilical hernia in cirrhotic patients with ascites. Prevalence, course and management (abstr). *Gastroenterology* **1983**;84:1363
42. Runyon BA, Juler GL. Natural history of repaired umbilical hernias in patients with and without ascites. *Am J Gastroenterol* **1985**;80:38–39
43. Muller-Schoop JW, Wang SP, Munzinger J, Schlapfer HU, Knoblauch M, Ammann RW. Chlamydia trachomatis as possible cause of peritonitis and perihepatitis in young women. *Br Med J* **1978**;1:1022–1024
44. Oktedalen O, Nygaard K, Osnes M. Somatostatin in the treatment of pancreatic ascites. *Gastroenterology* **1990**;99:1520–1523
45. Pockros PJ, Woods S. Malignant ascites from peritoneal carcinomatosis is immobile in comparison to cirrhotic ascites. *Hepatology* **1988**;8:1450
46. Gerbes AL. Medical treatment of ascites in cirrhosis. *J Hepatol* **1993**; 17(suppl 2):S4–S9
47. Runyon BA. Care of patients with ascites. *N Engl J Med* **1994**;330:337–342
48. Stanley MM, Ochi S, Lee KK, et al. Peritoneovenous shunting as compared with medical treatment in patients with alcoholic cirrhosis and massive ascites. *N Engl J Med* **1989**;321:1632–1638
49. Simon DM, McCain JR, Bonkovsky HL, Wells JO, Hartle DK, Galambos J. Effects of therapeutic paracentesis on systemic and hepatic hemodynamics and on renal and hormonal function. *Hepatology* **1987**;7:423–429
50. Pinto PC, Amerian J, Reynolds TB. Large-volume paracentesis in non-edematous patients with tense ascites: its effect on intravascular volume. *Hepatology* **1988**;8:297–210
51. Tito L, Gines P, Arroyo V,et al. Total paracentesis associated with intravenous albumin management of patients with cirrhosis and ascites. *Gastroenterology* **1990**;98:146–151
52. Gines P, Tito L, Arroyo V, et al. Randomized comparative study of therapeutic paracentesis with and without intravenous albumin in cirrhosis. *Gastroenterology* **1988**;94:1493–1502
53. Planas R, Gines P, Arroyo V, et al. Dextran-70 versus albumin as plasma expanders in cirrhotic patients with tense ascites treated with total paracentesis. *Gastroenterology* **1990**;99:1736–1744
54. Runyon BA. Refractory ascites. *Semin Liver Dis* **1993**;13:343–351
55. Bories P, Compean DG, Michel H, et al. The treatment of refractory ascites by the LeVeen shunt. A multi-centre controlled trial (57 patients). *J Hepatol* **1986**;3:212–218
56. Leveen HH, Christoudias G, Ip M, Luft R, Falk G, Grosberg S. Peritoneovenous shunting for ascites. *Ann Surg* **1974**;180:580–591
57. Fulenwider JT, Galambos JD, Smith RB, Henderson MJ, Warren WD. LeVeen vs Denver peritoneovenous shunts for intractable ascites of cirrhosis. A randomized, prospective trial. *Arch Surg* **1986**;121:351–355
58. Greig PD, Langer B, Blendis LM, Taylor BR, Glynn MFX. Complications after peritoneovenous shunting for ascites. *Am J Surg* **1980**;139:125–131
59. Gines P, Arroyo V, Vargas V, et al. Paracentesis with intravenous infusion of albumin as compared with peritoneovenous shunting in cirrhosis with refractory ascites. *N Engl J Med* **1991**;325;829–835
60. Franco D, Vons C, Traynor O, de Smadja C. Should portosystemic shunt be reconsidered in the treatment of intractable ascites. *Arch Surg* **1988**; 123:987–991
61. Ferral H, Bjarnason H, Wegryn SA, et al. Refractory ascites: Early experience in treatment with transjugular intrahepatic portosystemic shunt. *Radiology* **1993**;189:795–801
62. Grange JD, Boudghene F, Dussaule JC, et al. Transjugular intrahepatic portosystemic shunts (TIPS) in cirrhotic patients with refractory ascites. Clinical efficacy and acute effects on aldosterone and atrial natriuretic factor (abstr). *Gastroenterology* **1993**;104:909
63. Pomier-Layrargues G, Legault L, Roy L, Dufresne PM, Lafortune M, Fenyves D. TIPS for treatment of refractory ascites: a pilot study (abstr). *Hepatology* **1993**;18:103
64. LaBerge JM, Ring EJ, Gordon RL, et al. Creation of transjugular intrahepatic portosystemic shunts with the Wallstent endoprosthesis: results in 100 patients. *Radiology* **1993**;187:413–420
65. Ochs A, Sellinger M, Haag K, et al. Transjugular intrahepatic portosystemic stent-shunt (TIPS) in the treatment of Budd-Chiari syndrome. *J Hepatol* **1993**;18:217–225
66. Lebree D, Giuilly N, Hadengue A, Vilgrain V, Lassen C, Poynard T. Transjugular intrahepatic portosystemic shunt vs paracentesis for refractory ascites: results of a randomized trial (abstr). *Hepatology* **1994**;20:201A
67. Ochs A, Rossle M, Haag K, et al. The transjugular intrahepatic portosystemic stent–shunt procedure for refractory ascites. *N Engl J Med* **1995**;332: 1192–1197
68. Somberg KA, Lake JR, Tomlanovich ST, LaBerge JM, Feldstein V, Bass NM. Transjugular intrahepatic portosystemic shunts for refractory ascites: assessment of hormonal response and renal function. *Hepatology* **1995**;21:709–716
69. Quiroga J, Sangro B, Nuñez M, et al. Transjugular intrahepatic portal-systemic shunt in the treatment of refractory ascites: effect on clinical, renal, humoral and hemodynamic parameters. *Hepatology* **1995**;21:986–994
70. Rossle M, Haag K, Blum U, Ochs A, Sellinger M , Langer M. TIPS: Technical and early clinical complications (abstr). *Hepatology* **1993**;18:103
71. Peron JM, Rousseau H, Vinel JP, et al. Long term follow up study of transjugular intrahepatic portosystemic shunts (TIPS) (abstr). *Hepatology* **1993**;18:102
72. Martinet JP, Colombato LA, Lafortune M, et al. Usefulness of doppler-US in the evaluation of TIPS function (abstr). *Gastroenterology* **1994**;106:938
73. Sellinger M, Haag K, Ochs A, Noeldge G, Gerok W, Roessle M. Factors influencing the incidence of hepatic encephalopathy in patients with transjugular intrahepatic portosystemic stent-shunt (TIPS). *Hepatology* **1992**; 16 (suppl):122A
74. Blei AT. Hepatic encephalopathy in the age of TIPS. *Hepatology* **1994**;20: 249–252
75. Azoulay D, Castaing D, Dennison A, Martino W, Eyraud D, Bismuth H. Transjugular intrahepatic portosystemic shunt worsens the hyperdynamic circulatory state of the cirrhotic patient: preliminary report of a prospective study. *Hepatology* **1994**;19:129–132
76. Kamath PS, Malinchoc M, Peine CJ, Rank JM, Herman ME. Risk factors associated with the survival following the TIPS procedure (abstr). *Gastroenterology* **1994**;106:914
77. Somberg KA, Doherty CA, Simor M, Lake JR, LaBerge JM. Long-term outcome after transjugular intrahepatic portosystemic shunts (TIPS) (abstr). *Gastroenterology* **1994**;106:988
78. Somberg KA, Lake JL, Doherty MM, et al. The clinical course following transjugular intrahepatic portosystemic shunts (TIPS) in liver transplant candidates (abstr). *Hepatology* **1993**;18:103
79. Garcia-Tsao G. Groszman RJ, Fidsher RL, Conn HO, Atterbury CE, Glickman M. Portal pressure, pressure of gastroesophageal varices and variceal bleeding. *Hepatology* **1985**;5:419–424

The reader's attention is directed to the commentary on this article, which appears on the following pages.