Received: 24 July 2023 | Accepted: 5 December 2023

DOI: 10.1002/ueg2.12539

REVIEW ARTICLE

ueg journal WILEY

Recent developments in the management of ascites in cirrhosis

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Abstract

In recent years, advances have been made for treating ascites in patients with cirrhosis. Recent studies have indicated that several treatments that have been used for a long time in the management of portal hypertension may have beneficial effects that were not previously identified. Long-term albumin infusion may improve survival in patients with cirrhosis and ascites while beta-blockers may reduce ascites occurrence. Transjugular intrahepatic porto-systemic shunt (TIPS) placement may also improve survival in selected patients in addition to the control with ascites. Low-flow ascites pump insertion can be another option for some patients with intractable ascites. In this review, we summarize the latest data related to the management of ascites occurring in cirrhosis. There are still unanswered questions, such as the optimal use of albumin as a long-term therapy, the place of beta-blockers, and the best timing for TIPS placement to improve the natural history of ascites, as well as the optimal stent diameter to reduce the risk of shunt-related side-effects. These issued should be addressed in future studies.

KEYWORDS

albumin, ascites, ascites pump, liver cirrhosis, transjugular intrahepatic porto-systemic shunt

INTRODUCTION

Liver cirrhosis is the late stage of chronic liver disease and is responsible for a considerable global healthcare burden.[1] Cirrhosis can progress from a compensated phase, which is often asymptomatic, to a decompensated phase in which liver function is severely compromised or clinical portal hypertension (PHT) or other complications occur. Ascites is a clinical sign, and the most common complication, of decompensated liver cirrhosis and indicates worse prognosis and higher mortality.[2] In the setting of cirrhosis, the pathogenesis of cirrhotic ascites is attributed to several distinct pathways, which makes the mechanism of ascites formation more intriguing and treatment of ascites more challenging. In this review, we summarize current knowledge regarding the pathogenesis of cirrhotic ascites and discuss the therapeutic options for ascites treatment while highlighting areas of current discussion and debate in the field.

THE PHYSIOPATHOLOGY OF ASCITES FORMATION IN CIRRHOSIS

Hepatic ascites in cirrhosis arises from a complex interplay of factors, primarily driven by impaired liver function, PHT, vascular dysfunction, and systemic inflammation (Figure 1). Understanding these

Tian Lan and Ming Chen contributed equally to this manuscript.

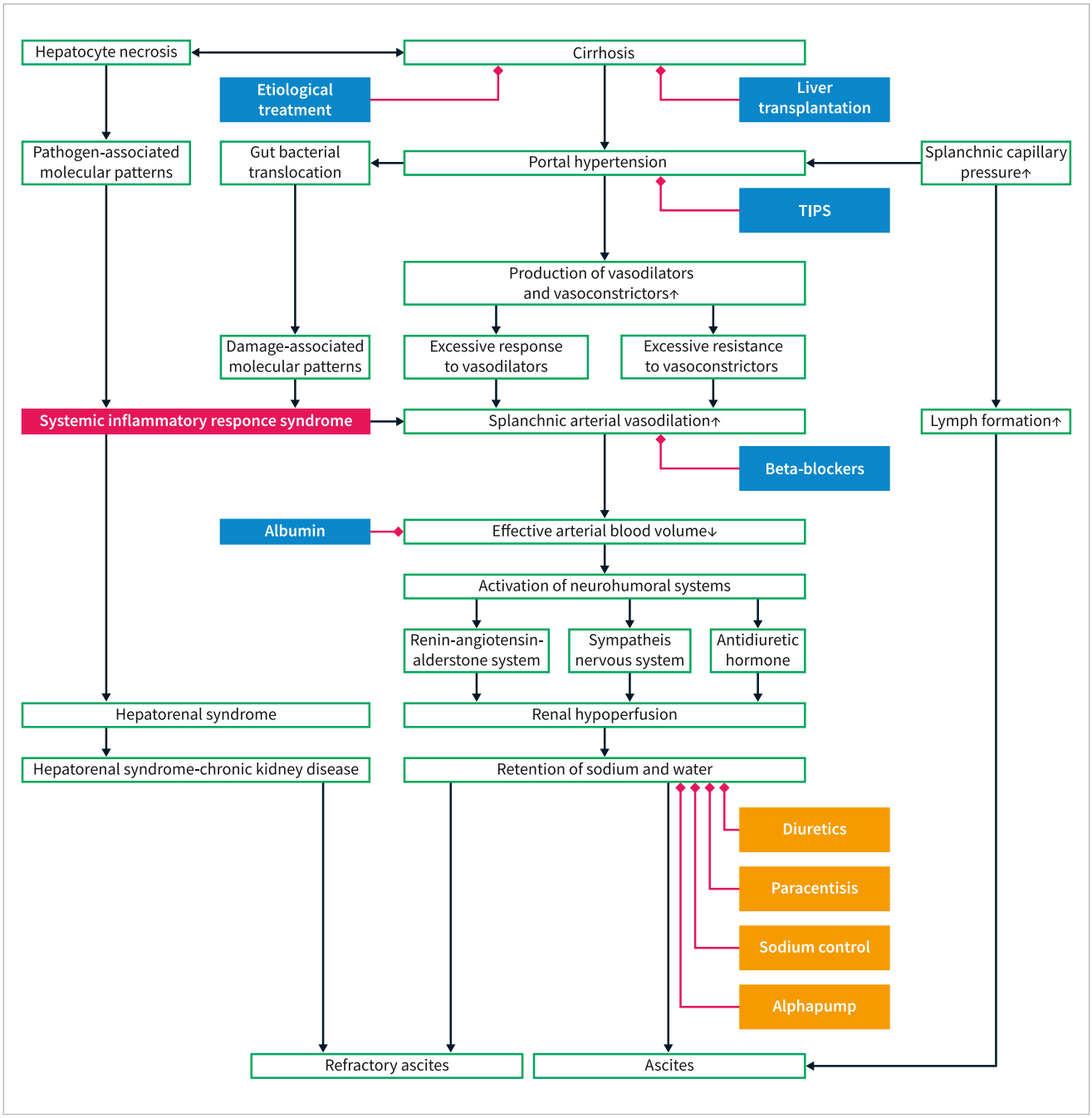

FIGURE 1 The pathogenesis and therapeutic targets of ascites in cirrhosis. The pathophysiological mechanisms of ascites formation involve impaired liver function, portal hypertension, vascular dysfunction, and systemic inflammation. Therapeutic options include etiological treatment, sodium control, diuretics, beta-blockers, albumin infusion, paracentesis, transjugular intrahepatic portosystemic shunt (TIPS), Alphapump, and liver transplantation. Therapeutic interventions that are capable of modifying the course of the disease are indicated in green and those that are not are indicated in orange.

intricate processes is crucial for the management and treatment of hepatic ascites in patients with cirrhosis.

The peripheral arterial vasodilation hypothesis

Currently, the most accepted theory of ascites formation is the so-called peripheral arterial vasodilation hypothesis.[3] According to this theory, PHT is the main driving factor for the development of hepatic ascites. PHT promotes the production and reduces the degradation of endogenous vasodilators involved in the modulation of systemic vascular resistance, including nitric oxide (NO), vasoactive intestinal peptide, substance P, carbon monoxide, platelet activating factor, prostacyclin, and endocannabinoids, leading to visceral arterial vasodilation, pooling of blood in the visceral circulation, and inadequate arterial filling.[4–6] The combination of these factors leads to a decrease in effective blood volume.[7] Effective hypovolemia is a key event in the formation of ascites as it

activates neurohumoral systems capable of promoting vasoconstriction and renal sodium-water retention, such as the renin-angiotensin-aldosterone system, the sympathetic nervous system, and antidiuretic hormone.[8,9] The kidneys are susceptible to the vasoconstrictive effects of these various systems, resulting in renal vasoconstriction, renal hypoperfusion and subsequent renal sodium and water retention, leading to the development of hepatorenal syndrome-chronic kidney disease (HRS-CKD) and refractory ascites (RA).[10] Development of RA, defined as ascites that cannot be managed or the early recurrence of which cannot be satisfactorily prevented by medical therapy, is associated with a significant reduction in survival to 50% at 6 months. RA is associated with elevated ascites formation that exceeds peritoneal resorption,[11] and is related to the development of many complications, including hyponatremia and HRS-CKD. Moreover, extrahepatic hyporeactivity to vasoconstrictors is another characteristic of advanced cirrhosis, contributing to visceral vasodilation.[4] In addition, left ventricular dysfunction and the development of cirrhotic cardiomyopathy may impair cardiac output and further decrease effective blood volume, resulting in increased sodium and water retention and the formation of ascites.[9]

The systemic inflammation hypothesis

Emerging evidence has shown that systemic inflammation and immune system activation play a crucial role in the development of ascites in cirrhosis.[12,13] First, PHT increases intestinal mucosal permeability and facilitates the translocation of pathogen-associated molecular patterns from the gut lumen into the systemic circulation through the mesenteric lymphatics, leading to systemic infection and endotoxemia.[9,10,14] Nevertheless, a recent study indicated that bacterial translocation might occur at an earlier stage of cirrhosis and trigger systemic inflammation, independent of the progression of PHT, in patients with advanced chronic liver disease.[15] More evidence is needed to identify the role of bacterial translocation in the pathophysiology of PHT and cirrhotic ascites. Second, chronic liver injury with hepatocellular necrosis releases circulating damage-associated molecular patterns, which are intracellular components released by dying or damaged host cells.[9,16] The resulting increase in pro-inflammatory molecules and vasodilators exacerbates existing visceral vasodilation and subsequent inadequate arterial filling, further disrupting systemic hemodynamics and leading to the progression of ascites.[10] Moreover, visceral and systemic inflammation may impair renal prostaglandin synthesis and promote visceral thrombosis, exacerbating renal sodium-water retention and PHT, ultimately leading to the continuous formation of ascites.[17–19]

CURRENT DATA ON THE USE OF MEDICAL TREATMENTS IN PATIENTS WITH ASCITES AND CIRRHOSIS

The treatment strategy for cirrhotic ascites is based on the etiology of cirrhosis and the grading of ascites. Suppressing etiological factors (such as antiviral agents for viral hepatitis, alcohol abstinence for alcohol-related liver disease) of liver cirrhosis remain the fundamental therapy for halting the progression of decompensation and improving survival rates for patients with ascites.[7] For grade I/mild ascites, which is detectable only by ultrasound, no specific therapy targeting ascites is recommended. For grade I/mild ascites, which is only detectable by ultrasound, no specific therapy targeting ascites is recommended. For grade II/moderate ascites, which is characterized by moderate symmetrical abdominal distension, moderate sodium control (defined as 80–120 mmol salt per day) and diuretics are suggested to limit the intake of sodium and decrease the volume of accumulating fluid in the abdominal cavity.[20,21] It is worth noting that patients can demonstrate low compliance or inappropriate implementation of moderate sodium control, leading to a 20% decrease in daily caloric intake, highlighting the importance of appropriate nutritional support and patient education on this issue.[22] As for grade III/large or gross ascites with marked abdominal distension, in addition to diuretics, large volume paracentesis (LVP), albumin infusion, and transjugular intrahepatic porto-systemic shunt (TIPS) should also be taken into consideration.

Diuretics

For the treatment of ascites occurring in cirrhosis, sodium intake control alone can only improve ascites in 10% of patients and is thus often accompanied by diuretics.[22] Although the use of diuretics does not improve patient survival, they are still the first-line therapy targeting ascites.[20] Generally, current guidelines recommend spironolactone with a starting dosage of 100 mg/day for first onset of moderate ascites, as it requires less dosage modification and is preferable for outpatients.[20,21,23] On the other hand, daily combination therapy with spironolactone (100 mg) and furosemide (40 mg) is suggested for chronic or recurrent ascites because faster resolution can be achieved. A stepwise dosage increase every 72 h up to 400 mg/day of spironolactone and 120 mg/day of furosemide can be considered according to patient response.[20,21,23] Surveillance of diuretic therapy, such as monitoring body weight loss and edema, is critical to optimize the benefit of diuretic treatment.[20,21,23] For RA that responds poorly to diuretics or hinders the use of maximum dosage of diuretics because of significant side effects, other treatment options should be instituted as continued diuretic use is often futile while escalating the risk of complications.[21]

Paracentesis and albumin infusion

Paracentesis is an important method for the diagnosis and treatment of cirrhotic ascites. Ascitic fluid protein and serum ascites albumin gradient (SAAG, SAAG = serum albumin−ascitic fluid albumin) are important tools for determining the etiology of ascites. Usually, low ascitic fluid protein (<2.5 g/dL) with elevated SAAG (>1.1 g/dL) indicates cirrhotic ascites, and low ascitic fluid protein (<1.5 g/dL) predicts a higher risk for the development of spontaneous bacterial peritonitis.[24] Of note, a meta-analysis demonstrated that long-term norfloxacin prophylaxis reduces the risk of spontaneous bacterial peritonitis in patients with low ascites protein concentration[25]. For gross ascites or RA, LVP is the first-line therapy to reduce the volume of ascites and alleviate symptoms. Ginés et al. found that, compared to diuretics, LVP was more effective for elimination of tense ascites and less likely to induce complications, while the survival rate was comparable between the two groups.[26] For patients who require frequent LVP and who are not candidates for TIPS or liver transplant, implantation of indwelling peritoneal catheters may be a practical option. Plasma volume expansion after LVP is recommended to reduce the risk of post-paracentesis circulatory dysfunction (PPCD).[26] When more than 5 L of ascites is removed by LVP, albumin infusion (8 g/L of ascites removed) is recommended to expand plasma volume. Albumin surpasses other artificial plasma expanders concerning its effects on reduction of the occurrence of PPCD and other complications as well as mortality, showed by a meta-analysis of randomized trials.[27] Nevertheless, a recent multicenter randomized controlled trial (RCT) failed to observe significant benefit of short-term albumin infusion (up to 14 days) on survival and cirrhosis complications.[23]

In addition to a role as a plasma expander, albumin has multifaceted functions as a potent antioxidant and immunomodulator. Albumin also improves cardiocirculatory function and prevents systemic inflammation in patients with decompensated cirrhosis.[12] During the past few years, several studies that have focused on the long-term use of albumin for ascites occurring in cirrhosis have arrived at contradictory conclusions. In the human Albumin for the treatmeNt of aScites in patients With hEpatic ciRrhosis (ANSWER) study, Caraceni et al. found that long-term human albumin administration significantly improved overall survival in patients with cirrhosis and uncomplicated ascites compared to standard medical treatment alone.[28] Furthermore, the need for paracentesis and the incidence of complications were decreased in the standard treatment plus long-term albumin group. Another prospective, non-randomized study included patients with RA and applied different dosages of long-term albumin administration. In line with the former study, long-term albumin infusion prolonged survival and reduced the incidence of complications.[29] In contrast, in the MACHT (Midodrine and Albumin for CirrHotic patients in the waiting list for liver Transplantation) study, midodrine plus albumin failed to either improve 1-year mortality or prevent complications in patients with cirrhosis and ascites awaiting liver transplantation, despite the fact that plasma renin activity and plasma norepinephrine were slightly suppressed.[29] The major features of and differences between the ANSWER and the MACHT studies are listed in Table 1. The discrepant results of these studies might be explained by heterogeneity in the dosages of albumin infusion, grading of ascites, and liver function. Therefore, further clinical research is warranted to establish a consensus on the effectiveness of long-term albumin infusion for cirrhotic ascites treatment.

Beta-blockers

Non-selective beta-blockers (propranolol or carvedilol) counteract the splanchnic vasodilation observed in cirrhosis. Due to its intrinsic anti-alfa-1 adrenergic effects, carvedilol is a more potent portal pressure lowering drug. In addition to their usefulness as a prophylactic treatment for variceal bleeding, recent studies have revealed previously unknown positive effects of these drugs in the management of ascites. The PREDESCI trial observed a reduced incidence of ascites formation in patients with compensated cirrhosis treated with beta-blockers during a median follow-up of 37 months compared to placebo (9% vs. 20%, respectively, $p = 0.03$).[30] These results were recently confirmed in a meta-analysis of individual participant data from four RCTs in which the incidence of decompensation of cirrhosis was reduced when the hepatic pressure gradient decreased by at

TABLE 1 Differences between the ANSWER and MACHT studies.

	MACHT study[29]	ANSWER study[28]
Design	Randomized placebo-controlled trial	Open-label randomized trial
Number of patients (intervention/control)	173 (87/86)	431 (218/213)
Baseline MELD score (intervention/control)	17/18	12/13
Treatment	Albumin 40 g every 15 days plus midodrine per day.	Albumin 40 g twice a week for 2 weeks, then 40 g every week.
Duration of albumin treatment (median)	63 days	17.6 months
Impact on cirrhosis complications and survival	No significant effect	Improved survival and complication rates

Abbreviation: MELD, model for end-stage liver disease.

least 10% or under 10 mmHg.[31] **In addition, this study also observed a survival benefit in patients treated with carvedilol, an effect likely related to non-hemodynamic effects of beta-blockers, such as the reduction of bacterial translocation and related systemic inflammation, which leads to a further increase in portal pressure (see "Physiopathology of ascites formation in cirrhosis" for more details). According to these results, the Baveno VII conference recommended the use of carvedilol in patients with clinically significant PHT defined by a porto-systemic gradient ≥10 mmHg or by the combined use of liver stiffness and platelet count. Carvedilol can be used without screening for esophageal or gastric varices by upper gastrointestinal endoscopy when liver stiffness is > 25 kPa, or when liver stiffness is between 20 and 25 kPa and platelet count is < 150 g/L, or when liver stiffness is between 15 and 20 kPa and platelet count is < 110 g/L.**[32] However, modalities for using beta-blockers to prevent ascites formation or to improve survival in the context of ascites occurring in cirrhosis as well as precise criteria for patient selection still have to be defined. Finally, one should keep in mind that beta-blockers should not be used in cases of spontaneous bacterial peritonitis or in cases of RA. In these situations, the detrimental effects of these medications outweigh their potential benefit.

ADVANCES IN THE USE OF TRANSJUGULAR INTRAHEPATIC PORTO-SYSTEMIC SHUNT IN PATIENTS WITH ASCITES AND CIRRHOSIS

The aim of TIPS placement in cirrhosis is to reduce portal pressure and related complications. The hemodynamic consequences of TIPS insertion in patients with cirrhosis and ascites have been reviewed in detail elsewhere.[33,34] While a large amount of data indicates that TIPS improves the control with ascites, recent data have also indicated that it may reduce mortality. However, the efficacy of TIPS is difficult to predict at an individual level and this is likely to be related to several patient characteristics that may influence outcomes.

The characteristics that should be considered in a TIPS candidate are as follows.

Stage of ascites at which TIPS is placed: refractory versus recurrent

An initial important issue is the timing at which TIPS placement is performed in the treatment of ascites. For decades, TIPS has been considered for the treatment of RA, which refers to "ascites that cannot be resolved or that recurs early after LVPs and cannot be prevented by medication".[20] Most available data on the usefulness of TIPS in this setting concern patients treated with baer stents. Four RCTs have evaluated the usefulness of TIPS in patients with RA[35–38] and two have evaluated patients treated with both recurrent and RA[39,40] (Table 2). These results were synthesized in six meta-analyses. Overall, TIPS is effective for preventing ascites recurrence in approximately half of the patients and this effect was obtained without increasing the risk of hepatic encephalopathy (HE).[42–47] Regarding survival, the individual patient meta-analysis by Salerno et al. (which did not include one RCT in which survival was significantly lower in patients receiving TIPS[36]) identified a transplant-free survival benefit in the TIPS group.[47] This result was confirmed in a recent RCT that demonstrated a significant improvement in survival in patients receiving baer stent TIPS (80% overall survival at 1 year) compared to patients receiving standard medical treatment (49% overall survival at 1 year).[37] Of note, this study included patients with well-preserved liver and kidney function, and this may, at least in part, explain why a survival benefit was observed.

More recently, data have accumulated for the use of TIPS at earlier stages, that is, for the treatment of recurrent/recidivant ascites. Although the definition of recurrent/recidivant ascites differs across studies, this refers to an earlier stage of the disease in which several LVPs are required.[20,32,48,49] In a RCT that assessed the usefulness of PTFE-covered TIPS in patients with recurrent ascites, the 1-year transplant-free survival rate of patients in the TIPS group was significantly higher than that of control patients treated with standard-of-care (93% vs. 52%) and HE did not occur more frequently in the TIPS group.[49] Three features may explain why TIPS was able to improve survival in this study: first, TIPS was used at earlier stages of the disease, that is, in patients with recurrent/recidivant ascites rather than for RA; second, patients had relatively well-preserved liver and kidney function, as was the case in the study from Narahara et al. in RA[37]; third, the study from Bureau et al. used PTFE-covered stent-grafts.[50] Even if these results need confirmation, these findings may help to select patients in which TIPS is more likely to improve survival in addition to the control of ascites. Figure 2 summarizes the indications of TIPS in ascites.

Liver function and risk of hepatic encephalopathy following TIPS

Liver failure and HE are the two complications most feared after TIPS placement. Several predictive models for assessing the risk of HE and the risk of death following TIPS insertion exist.[51,52] In a recent study that included patients who received TIPS for RA (25% of the study population) and secondary prophylaxis for variceal bleeding (75% of the study population), Bettinger et al. proposed the Freiburg index of post-TIPS survival (FIPS) score to identify high-risk patients with a poor prognosis after TIPS.[53] This score includes bilirubin, creatinine, albumin, and age as predictors of survival. The FIPS score has higher discriminative ability than all other prognostic models with a c-index of 0.741 and 0.716 for 3- and 6-month survival, respectively. In the subanalysis including only patients with RA, the c-index of the FIPS score was 0.961 and 0.705 for 3- and 6-month survival, respectively. Overall, these studies faced similar limitations including their retrospective nature, inclusion of a heterogeneous population of patients, and lack of strong validation.[33] Testing for minimal HE before TIPS insertion does

TABLE 2 Randomized controlled trials of TIPS versus LVPs and albumin infusion for recurrent/recidivant or refractory ascites.

Author	Sample size	TIPS	Main inclusion criteria	Main exclusion criteria	Safety	Efficacy (TIPS vs. LVP)
Lebrec[36]	25 patients randomized 1:1	Uncovered	Cirrhosis and RA	Age >70 years; HE ≥ grade 2; PVT; biliary obstruction; serum creatinine >1.7 mg/dL; HCC; active bacterial infection; severe non-hepatic disease; pulmonary hypertension	Increased incidence of HE in the TIPS group	2-year OS: 29% versus 56%
Rossle[39]	60 patients randomized 1:1	Uncovered	Cirrhosis and RA (55%) or patients with recurrentascites (45%)	HE ≥ grade 2; PVT; bilirubin >5 mg/dL; serum creatinine >3 mg/dL; advanced HCC; hepatic hydrothorax; technical failure of paracentesis	No difference in the incidence of HE	1- and 2-year TFS: 69% and 58% versus 52% and 32% (n.s.); 61% versus 18% of patients had no ascites at 3 months
Gines[35]	70 patients randomized 1:1	Uncovered	Cirrhosis and RA	Age <18 or >75 years; HE ≥ grade 2; PVT; bilirubin >10 mg/dL; serum creatinine >3 mg/dL; prothrombin index <40%, platelet count <40 G/L; chronic heart failure; HCC; parenchymal kidney disease	No difference in HE incidence but more episodes of severe HE in the TIPS group	1- and 2-year TFS: 41% and 26% versus 35% and 30% (n.s.); median time to recurrence of ascites of 171 versus 20 days
Sanyal[38]	109 patients randomized 1:1	Uncovered	Cirrhosis and RA; serum creatinine <1.5 mg/dL	HE ≥ grade 2, PVT; bilirubin >5 mg/dL; INR >2; HCC; bacterial infection; alcoholic hepatitis; cardiopulmonary failure; pulmonary hypertension; parenchymal kidney disease; recent gastrointestinal bleeding; life-limiting non-hepatic disease	Increased incidence of moderate to severe HE in the TIPS group (38% vs. 21%)	TFS: 19.6 versus 12.4 months; lower rate of recurrent ascites in the TIPS group
Salerno[40]	66 patients randomized 1:1	Uncovered	Cirrhosis and RA (68%) or patients with recurrent ascites (32%)	Age >72 years; HE ≥ grade 2; PVT; Child-Pugh >11 points; bilirubin >6 mg/dL; serum creatinine >3 mg/dL; advanced HCC; bacterial infection; cardiopulmonary failure; recent GI bleeding	Incidence of HE: 61% (TIPS group) versus 39% (LVPs group) (n.s.); greater number of severe episodes of HE per patient in the TIPS group	1- and 2-year TFS: 77% and 59% versus 52% and 29%; lower rate of treatment failure in the TIPS group
Narahara[37]	60 patients randomized 1:1	Uncovered	Cirrhosis and RA Child-Pugh <11 points; bilirubin <3 mg/dl; serum	Age >70 years; previous episodes of HE; PV cavernoma; HCC or other malignancy; active infection;	Increased incidence of HE and severe HE in the TIPS group	1- and 2-year OS: 80% and 64% versus 49% and 35%; improved control of ascites and less

TABLE 2 (Continued)

Author	Sample size	TIPS	Main inclusion criteria	Main exclusion criteria	Safety	Efficacy (TIPS vs. LVP)
			creatinine <1.9 mg/dL	active severe cardiac or pulmonary disease; organic kidney disease		treatment failure, in the TIPS group
Bureau[41]	62 patients randomized 1:1	PFTE-covered	Cirrhosis; age >18/<70 years; recurrent tense ascites requiring at least 2 LVP within the prior 3 weeks	>6 LVPs within the previous 3 months; expected to receive transplant within the next 6 months or on waiting list; recurrent overt HE; PVT, Child-Pugh >12 points; bilirubin >5.8 mg/dL; serum creatinine >2.8 mg/dL; HCC; chronic heart failure; pulmonary hypertension	No difference in rates of overt HE	1-year TFS: 93% versus 52%; 89% versus 29% of patients free of treatment failure

Abbreviations: HCC, hepatocellular carcinoma; HE, hepatic encephalopathy; INR, international normalized ratio; LVP + A, large volume paracentesis with albumin infusion; n.s., not significant; OS, overall survival; PFTE, polytetrafluoroethylene; PVT, portal vein thrombosis; RA, refractory ascites; TFS, transplant-free survival; TIPS, transjugular intrahepatic porto-systemic shunt.
Adapted from ref.[34]

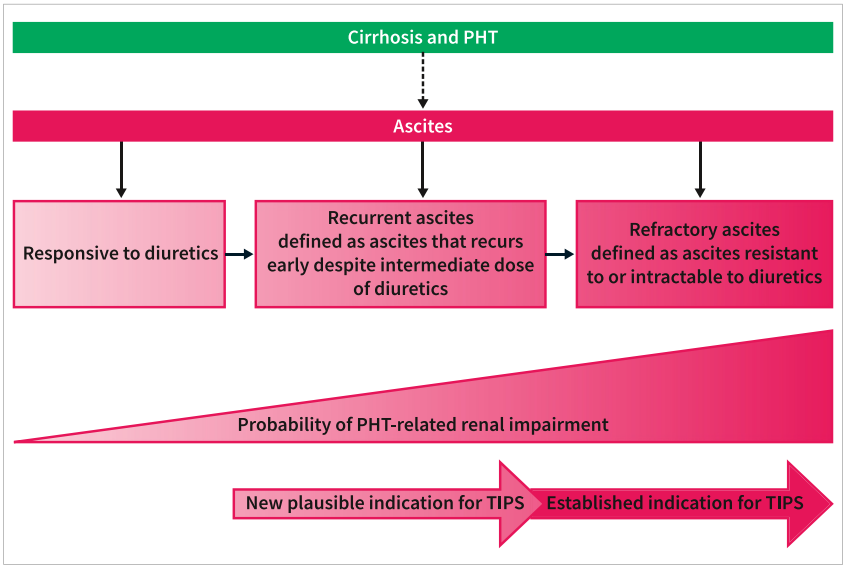

FIGURE 2 Indications of TIPS in ascites. PHT, portal hypertension; TIPS, transjugular intrahepatic porto-systemic shunt. Adapted from ref.[33]

not guarantee that overt HE will not appear after TIPS.[54] In the end, the decision to place a TIPS is often made on an individual basis. Experts usually advocate that TIPS is contraindicated in patients with a history of recurrent or persistent overt HE or in those with advanced liver dysfunction defined by a Child–Pugh score >13 or a Model for End-Stage Liver Disease (MELD) score >19.[55,56] However, there is insufficient evidence to recommend a cut-off value of bilirubin, MELD score, or Child–Pugh score above which TIPS should be contraindicated as a treatment for ascites.[57] Of note, rifaximin has been proven to be effective for reducing the risk of HE following TIPS insertion.[58] Another way to reduce post-TIPS HE is to use a stent-graft under-dilated to <8 mm.[59]

Cardiac function

TIPS may induce cardiac decompensation as it causes a sudden increase in cardiac preload. Available data indicate that cardiac decompensation occurs in 10%–20% of patients receiving TIPS. The most robust data on the risk of cardiac failure following TIPS came from a recent prospective study, which showed that the presence of aortic stenosis was associated with a high risk of cardiac decompensation.[51] Conversely, the absence of diastolic dysfunction criteria at echocardiography, a level of brain natriuretic peptide (BNP) < 40 pg/mL, and a NT-proBNP <125 pg/mL allowed the identification of patients at low risk of cardiac decompensation. Thus, the identification of patients with cardiomyopathy is mandatory in TIPS candidates. In patients in which pre-existing alterations of cardiac reserve may exist, a stent-graft under-dilated to <8 mm may be a pragmatic way to reduce the risk of post-TIPS cardiac failure. In case of good tolerance, the stent-graft can be progressively dilated according to clinical response.[33,60]

Kidney function

The importance of kidney injury in the setting of ascites treated with TIPS is related to two issues: (a) chronic kidney injury as a potential contraindication for TIPS, and (b) HRS as a potential indication for TIPS.

Chronic kidney injury as a potential contraindication for TIPS

A large amount of data indicates that renal dysfunction aggravates the risk of post-TIPS HE and is the most common predictive factor of unfavorable response to TIPS.[33] Indeed, prospective studies investigating the role of TIPS in RA have observed that the most common predictive factors of unfavorable response to TIPS are creatinine level or clearance.[61–64] However, the degree of renal dysfunction above which TIPS should be contraindicated is unknown. This is likely due to the multifactorial nature of kidney dysfunction in patients with cirrhosis and ascites.

HRS as a potential indication for TIPS

On the other hand, TIPS improves kidney function in most patients, mainly in those with moderate kidney dysfunction. Renal improvement has also been observed in studies that included a limited number of patients with type 1 HRS.[65,66] In a meta-analysis including nine studies, improvement of renal function was also observed in patients with RA further complicated by type 1 or type 2 HRS and treated with TIPS. One-year survival was 47% in those with type 1 HRS and 64% in patients with type 2 HRS.[67] In this setting, TIPS may be considered to be a bridge to liver transplantation in selected patients. However, evidence supporting the use of TIPS in patients with severely impaired kidney function is limited, and the applicability of TIPS for patients with type 1 HRS is very limited because, in most patients, TIPS is contraindicated because of severe liver failure.[65,66,68] For these patients, the best therapeutic option is liver transplantation.

In addition to the severity of kidney dysfunction, the decision to place TIPS in these patients is often made considering other predictors of outcome.

Age and sarcopenia

Older age is associated with poor prognosis after TIPS insertion and is an independent predictor of HE[60] as well as survival.[47,53] There are few data on the use of TIPS in elderly patients (>60 years)[69,70] which makes it difficult to define a cut-off above which TIPS should not be performed. A recent article assessed the efficacy and tolerance of TIPS in older patients. While mortality was increased in older patients, TIPS placement was feasible and should not be precluded in patients older than 70 years.[71] In these patients, creatinine and sodium levels were predictors of outcome. At the end, the decision to place a TIPS in "old" patients is often made on a case-by-case basis.

Regarding sarcopenia, pre-TIPS sarcopenia is an independent predictor of post-TIPS HE.[72] Conversely, TIPS has been associated with skeletal muscle gain and with a reduced risk of HE,[73–75] which may translate into increased survival.[76] Here again, the decision to place a TIPS in sarcopenic patients should be made on a case-by-case basis.

Summary

The perfect candidate for TIPS insertion in the setting of ascites occurring in cirrhosis is a patient with recurrent/recidivant ascites or RA, below 65 years old, without a history of recurrent or persistent overt HE, without advanced liver dysfunction defined by a Child–Pugh score >13 or a MELD score >19, without aortic stenosis or diastolic dysfunction, and without severe kidney impairment.[33] In clinical practice, most patients do not fulfill all criteria and the decision to place TIPS is made considering positive and negative predictors of outcome on an individual basis. If it is feared that TIPS may be poorly tolerated, a stent-graft under-dilated to <8 mm may help to limit the risk of HE. Considering the negative impact of ascites occurrence in patients with cirrhosis, liver transplantation should always be discussed in patients without clear contraindication.

RECENT DATA ON LOW-FLOW ASCITES PUMPS FOR THE TREATMENT OF ASCITES IN CIRRHOSIS

Automated low-flow ascites pump systems (Alfapump system®) use an automated pump that allows the removal of ascites from the peritoneal cavity and elimination into the urinary bladder. According to recent studies and a meta-analysis, 62% of patients did not require

LVP after automated low-flow ascites pump insertion and the number of LVPs decreased by a mean of 2.1 per month.[77,78] Interestingly, automated low-flow ascites pumps also improve patient health-related quality of life early on after treatment initiation, while the low-flow ascites pump remains functional.[49,79] However, several safety issues limit the use of this device in clinical practice. Of note, no compensatory albumin infusion is made in this setting and acute kidney injury occurred in 30% of patients, while serum creatinine increased by a mean of 23 μmol/L after low-flow ascites pump insertion. Other severe side effects, such as urinary tract infection and bacterial peritonitis, occurred in 20%–27% of the patients. Long-term antibiotic therapy seems to be sufficient for the prevention of septic complications.[59] With these data in mind, it does not seem advisable to consider low-flow ascites pump insertion in patients with preexisting renal dysfunction or in those who have just recovered from a urinary tract infection or from bacterial peritonitis. One unsettled issue is whether albumin infusions could prevent kidney injury. In line with this issue, a recent study indicated that clinical complications in patients with RA related to performing low-volume drainage without albumin infusion were associated with the daily volume drained, a complication occurring more frequently when more than 1.5 L of ascites was drained per day.[80] Criteria allowing the appropriate selection of patients who are candidates for Alfa-pump are also warranted. These issues should be addressed in future studies.

CONCLUSIONS AND FUTURE PERSPECTIVES

Although ascites occurring in cirrhosis has long been known to be a major complication of decompensated cirrhosis and its standard-of-care has been well defined for a long time, recent studies have identified positive effects of several therapies already used for treating PHT that were not previously identified. Long-term use of albumin, use of beta-blockers, and TIPS insertion have shown promising results for either improving survival in selected patients or reducing ascites occurrence. Current therapeutic interventions that are capable of modifying the course of the disease are indicated in green and those that are not are indicated in orange in Figure 1. Unanswered questions remain in the field of ascites management, underlining the need for high-quality clinical trials to identify the best strategies for patient care.

AUTHOR CONTRIBUTIONS

Review concept: Pierre Deltenre and Chengwei Tang. Drafting the manuscript: Abstract: Pierre Deltenre. Physiopathology of ascites formation in cirrhosis: Tian Lan, Ming Chen, and Chengwei Tang. Current data on the use of medical treatments in patients with ascites and cirrhosis: diuretics: Tian Lan, Ming Chen, and Chengwei Tang; paracentesis and albumin infusion: Tian Lan, Ming Chen, and Chengwei Tang; beta-blockers: Pierre Deltenre. Advances in the use of transjugular intrahepatic porto-systemic shunt in patients with ascites and cirrhosis: Pierre Deltenre. Recent data on low-flow ascites pump for the treatment of ascites in cirrhosis: Pierre Deltenre. Conclusions: Pierre Deltenre, Tian Lan, Ming Chen, and Chengwei Tang. Revision: Pierre Deltenre and Chengwei Tang. Approval of final version: Pierre Deltenre and Chengwei Tang.

ACKNOWLEDGMENTS

The authors acknowledge the contribution of a medical writer, Sandy Field, Ph.D., for her assistance concerning English-language editing. The authors did not receive any funding for this article.

CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to declare.

DATA AVAILABILITY STATEMENT

Data sharing not applicable.

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REFERENCES

1. Devarbhavi H, Asrani SK, Arab JP, Nartey YA, Pose E, Kamath PS. Global burden of liver disease: 2023 update. J Hepatol. 2023;79(2):516–37. https://doi.org/10.1016/j.jhep.2023.03.017
2. D'Amico G, Garcia-Tsao G, Pagliaro L. Natural history and prognostic indicators of survival in cirrhosis: a systematic review of 118 studies. J Hepatol. 2006;44(1):217–31. https://doi.org/10.1016/j.jhep.2005.10.013
3. 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(5):1151–7. https://doi.org/10.1002/hep.1840080532
4. Alukal JJ, John S, Thuluvath PJ. Hyponatremia in cirrhosis: an update. Am J Gastroenterol. 2020;115(11):1775–85. https://doi.org/10.14309/ajg.0000000000000786
5. Iwakiri Y Pathophysiology of portal hypertension. Clin Liver Dis. 2014;18(2):281–91. https://doi.org/10.1016/j.cld.2013.12.001
6. Martell M, Coll M, Ezkurdia N, Raurell I, Genescà J. Physiopathology of splanchnic vasodilation in portal hypertension. World J Hepatol. 2010;2(6):208–20. https://doi.org/10.4254/wjh.v2.i6.208
7. Tonon M, Piano S. Cirrhosis and portal hypertension: how do we deal with ascites and its consequences. Med Clin North Am. 2023;107(3):505–16. https://doi.org/10.1016/j.mcna.2022.12.004
8. Madoff DC, Cornman-Homonoff J, Fortune BE, Gaba RC, Lipnik AJ, Yarmohammadi H, et al. Management of refractory ascites due to portal hypertension: current status. Radiology. 2021;298(3):493–504. https://doi.org/10.1148/radiol.2021201960
9. Zaccherini G, Tufoni M, Iannone G, Caraceni P. Management of ascites in patients with cirrhosis: an update. J Clin Med. 2021;10(22):5226. https://doi.org/10.3390/jcm10225226
10. Adebayo D, Neong SF, Wong F. Ascites and hepatorenal syndrome. Clin Liver Dis. 2019;23(4):659–82. https://doi.org/10.1016/j.cld.2019.06.002
11. Henriksen JH, Siemssen O, Krintel JJ, Malchow-Moller A, Bendtsen F, Ring-Larsen H. Dynamics of albumin in plasma and ascitic fluid in patients with cirrhosis. J Hepatol. 2001;34(1):53–60. https://doi.org/10.1016/s0168-8278(00)00009-x
12. Arroyo V, Angeli P, Moreau R, Jalan R, Clària J, Trebicka J, et al. The systemic inflammation hypothesis: towards a new paradigm of acute decompensation and multiorgan failure in cirrhosis. J Hepatol. 2021;74(3):670–85. https://doi.org/10.1016/j.jhep.2020.11.048

13. Bernardi M, Moreau R, Angeli P, Schnabl B, Arroyo V. Mechanisms of decompensation and organ failure in cirrhosis: from peripheral arterial vasodilation to systemic inflammation hypothesis. J Hepatol. 2015;63(5):1272–84. https://doi.org/10.1016/j.jhep.2015.07.004
14. Wiest R, Lawson M, Geuking M. Pathological bacterial translocation in liver cirrhosis. J Hepatol. 2014;60(1):197–209. https://doi.org/10.1016/j.jhep.2013.07.044
15. Simbrunner B, Caparros E, Neuwirth T, Schwabl P, Königshofer P, Bauer D, et al. Bacterial translocation occurs early in cirrhosis and triggers a selective inflammatory response. Hepatol Int. 2023;17(4):1045–56. https://doi.org/10.1007/s12072-023-10496-y
16. Kubes P, Mehal WZ. Sterile inflammation in the liver. Gastroenterology. 2012;143(5):1158–72. https://doi.org/10.1053/j.gastro.2012.09.008
17. Engelmann C, Claria J, Szabo G, Bosch J, Bernardi M. Pathophysiology of decompensated cirrhosis: portal hypertension, circulatory dysfunction, inflammation, metabolism and mitochondrial dysfunction. J Hepatol. 2021;75(Suppl 1):S49–66. https://doi.org/10.1016/j.jhep.2021.01.002
18. Iwakiri Y, Trebicka J. Portal hypertension in cirrhosis: pathophysiological mechanisms and therapy. JHEP Rep. 2021;3(4):100316. https://doi.org/10.1016/j.jhepr.2021.100316
19. Wong F. Management of refractory ascites. Clin Mol Hepatol. 2023;29(1):16–32. https://doi.org/10.3350/cmh.2022.0104
20. European Association for the Study of the Liver. Electronic address eee, European Association for the Study of the L. EASL Clinical Practice Guidelines for the management of patients with decompensated cirrhosis. J Hepatol. 2018;69(2):406–60.
21. Biggins SW, Angeli P, Garcia-Tsao G, Ginès P, Ling SC, Nadim MK, et al. Diagnosis, evaluation, and management of ascites, spontaneous bacterial peritonitis and hepatorenal syndrome: 2021 practice guidance by the American association for the study of liver diseases. Hepatology. 2021;74(2):1014–48. https://doi.org/10.1002/hep.31884
22. Morando F, Rosi S, Gola E, Nardi M, Piano S, Fasolato S, et al. Adherence to a moderate sodium restriction diet in outpatients with cirrhosis and ascites: a real-life cross-sectional study. Liver Int. 2015;35(5):1508–15. https://doi.org/10.1111/liv.12583
23. Aithal GP, Palaniyappan N, China L, Härmälä S, Macken L, Ryan JM, et al. Guidelines on the management of ascites in cirrhosis. Gut. 2021;70(1):9–29. https://doi.org/10.1136/gutjnl-2020-321790
24. Singh V, De A, Mehtani R, Angeli P, Maiwall R, Satapathy S, et al. Asia-Pacific association for study of liver guidelines on management of ascites in liver disease. Hepatol Int. 2023;17(4):792–826. https://doi.org/10.1007/s12072-023-10536-7
25. Loomba R, Wesley R, Bain A, Csako G, Pucino F. Role of fluoroquinolones in the primary prophylaxis of spontaneous bacterial peritonitis: meta-analysis. Clin Gastroenterol Hepatol. 2009;7(4):487–93. https://doi.org/10.1016/j.cgh.2008.12.018
26. Ginés P, Arroyo V, Quintero E, Planas R, Bory F, Cabrera J, et al. Comparison of paracentesis and diuretics in the treatment of cirrhotics with tense ascites. Results of a randomized study. Gastroenterology. 1987;93(2):234–41. https://doi.org/10.1016/0016-5085(87)91007-9
27. Bernardi M, Caraceni P, Navickis RJ, Wilkes MM. Albumin infusion in patients undergoing large-volume paracentesis: a meta-analysis of randomized trials. Hepatology. 2012;55(4):1172–81. https://doi.org/10.1002/hep.24786
28. Caraceni P, Riggio O, Angeli P, Alessandria C, Neri S, Foschi FG, et al. Long-term albumin administration in decompensated cirrhosis (ANSWER): an open-label randomised trial. Lancet. 2018;391(10138):2417–29. https://doi.org/10.1016/s0140-6736(18)30840-7
29. Di Pascoli M, Fasolato S, Piano S, Bolognesi M, Angeli P. Long-term administration of human albumin improves survival in patients with cirrhosis and refractory ascites. Liver Int. 2019;39(1):98–105. https://doi.org/10.1111/liv.13968
30. Villanueva C, Albillos A, Genesca J, Garcia-Pagan JC, Calleja JL, Aracil C, et al. Beta blockers to prevent decompensation of cirrhosis in patients with clinically significant portal hypertension (PREDESCI): a randomised, double-blind, placebo-controlled, multicentre trial. Lancet. 2019;393(10181):1597–608. https://doi.org/10.1016/s0140-6736(18)31875-0
31. Villanueva C, Torres F, Sarin SK, Shah HA, Tripathi D, Brujats A, et al. Carvedilol reduces the risk of decompensation and mortality in patients with compensated cirrhosis in a competing-risk meta-analysis. J Hepatol. 2022;77(4):1014–25. https://doi.org/10.1016/j.jhep.2022.05.021
32. de Franchis R, Bosch J, Garcia-Tsao G, Reiberger T, Ripoll C, Baveno VIIF, et al. Baveno VII - renewing consensus in portal hypertension. J Hepatol. 2022;76(4):959–74. https://doi.org/10.1016/j.jhep.2021.12.022
33. Deltenre P, Zanetto A, Saltini D, Moreno C, Schepis F. The role of transjugular intrahepatic portosystemic shunt in patients with cirrhosis and ascites: recent evolution and open questions. Hepatology. 2023;77(2):640–58. https://doi.org/10.1002/hep.32596
34. Garcia-Pagan JC, Saffo S, Mandorfer M, Garcia-Tsao G. Where does TIPS fit in the management of patients with cirrhosis? JHEP Rep. 2020;2(4):100122. https://doi.org/10.1016/j.jhepr.2020.100122
35. Gines P, Uriz J, Calahorra B, Garcia–Tsao G, Kamath PS, Del Arbol LR, et al. Transjugular intrahepatic portosystemic shunting versus paracentesis plus albumin for refractory ascites in cirrhosis. Gastroenterology. 2002;123(6):1839–47. https://doi.org/10.1053/gast.2002.37073
36. Lebrec D, Giuily N, Hadengue A, Vilgrain V, Moreau R, Poynard T, et al. Transjugular intrahepatic portosystemic shunts: comparison with paracentesis in patients with cirrhosis and refractory ascites: a randomized trial. French Group of Clinicians and a Group of Biologists. J Hepatol. 1996;25(2):135–44. https://doi.org/10.1016/s0168-8278(96)80065-1
37. Narahara Y, Kanazawa H, Fukuda T, Matsushita Y, Harimoto H, Kidokoro H, et al. Transjugular intrahepatic portosystemic shunt versus paracentesis plus albumin in patients with refractory ascites who have good hepatic and renal function: a prospective randomized trial. J Gastroenterol. 2011;46(1):78–85. https://doi.org/10.1007/s00535-010-0282-9
38. Sanyal AJ, Genning C, Reddy KR, Wong F, Kowdley KV, Benner K, et al. The North American study for the treatment of refractory ascites. Gastroenterology. 2003;124(3):634–41. https://doi.org/10.1053/gast.2003.50088
39. Rossle M, Ochs A, Gulberg V, Siegerstetter V, Holl J, Deibert P, et al. A comparison of paracentesis and transjugular intrahepatic portosystemic shunting in patients with ascites. N Engl J Med. 2000;342(23):1701–7. https://doi.org/10.1056/nejm200006083422303
40. Salerno F, Merli M, Riggio O, Cazzaniga M, Valeriano V, Pozzi M, et al. Randomized controlled study of TIPS versus paracentesis plus albumin in cirrhosis with severe ascites. Hepatology. 2004;40(3):629–35. https://doi.org/10.1002/hep.20364
41. Bureau C, Thabut D, Oberti F, Dharancy S, Carbonell, N, Bouvier A, BouvierTransjugular intrahepatic portosystemic shunts with covered stents increase transplant-free survival of patients with cirrhosis and recurrent ascites. Gastroenterology. 2017;152(1):157–63.
42. Albillos A, Banares R, Gonzalez M, Catalina MV, Molinero LM. A meta-analysis of transjugular intrahepatic portosystemic shunt versus paracentesis for refractory ascites. J Hepatol. 2005;43(6):990–6.
43. Bai M, Qi XS, Yang ZP, Yang M, Fan DM, Han GH. TIPS improves liver transplantation-free survival in cirrhotic patients with refractory ascites: an updated meta-analysis. World J Gastroenterol. 2014;20(10):2704–14.

44. D'Amico G, Luca A, Morabito A, Miraglia R, D'Amico M. Uncovered transjugular intrahepatic portosystemic shunt for refractory ascites: a meta-analysis. Gastroenterology. 2005;129(4):1282–93.
45. Deltenre P, Mathurin P, Dharancy S, Moreau R, Bulois P, Henrion J, et al. Transjugular intrahepatic portosystemic shunt in refractory ascites: a meta-analysis. Liver Int. 2005;25(2):349–56.
46. Saab S, Nieto JM, Lewis SK, Runyon BA. TIPS versus paracentesis for cirrhotic patients with refractory ascites. Cochrane Database Syst Rev. 2006;4:CD004889.
47. Salerno F, Camma C, Enea M, Rossle M, Wong F. Transjugular intrahepatic portosystemic shunt for refractory ascites: a meta-analysis of individual patient data. Gastroenterology. 2007;133(3):825–34.
48. Arroyo V, Gines P, Gerbes AL, Dudley FJ, Gentilini P, Laffi G, et al. Definition and diagnostic criteria of refractory ascites and hepatorenal syndrome in cirrhosis. International Ascites Club. Hepatology. 1996;23(1):164–76.
49. Bureau C, Adebayo D, Chalret de Rieu M, Elkrief L, Valla D, Peck-Radosavljevic M, et al. Alfapump(R) system vs. large volume paracentesis for refractory ascites: a multicenter randomized controlled study. J Hepatol. 2017;67(5):940–9.
50. Bureau C, Garcia Pagan JC, Layrargues GP, Metivier S, Bellot P, Perreault P, et al. Patency of stents covered with polytetrafluoroethylene in patients treated by transjugular intrahepatic portosystemic shunts: long-term results of a randomized multicentre study. Liver Int. 2007;27(6):742–7.
51. Billey C, Billet S, Robic MA, Cognet T, Guillaume M, Vinel JP, et al. A prospective study identifying predictive factors of cardiac decompensation after transjugular intrahepatic portosystemic shunt: the Toulouse Algorithm. Hepatology. 2019;70(6):1928–41.
52. Nardelli S, Gioia S, Pasquale C, Pentassuglio I, Farcomeni A, Merli M, et al. Cognitive impairment predicts the occurrence of hepatic encephalopathy after transjugular intrahepatic portosystemic shunt. Am J Gastroenterol. 2016;111(4):523–8.
53. Bettinger D, Sturm L, Pfaff L, Hahn F, Kloeckner R, Volkwein L, et al. Refining prediction of survival after TIPS with the novel Freiburg index of post-TIPS survival. J Hepatol. 2021;74(6):1362–72.
54. Ehrenbauer AF, Schneider H, Stockhoff L, Tiede A, Lorenz C, Dirks M, et al. Predicting overt hepatic encephalopathy after TIPS: value of three minimal hepatic encephalopathy tests. JHEP Rep. 2023;5(9):100829.
55. Fagiuoli S, Bruno R, Debernardi Venon W, Schepis F, Vizzutti F, Toniutto P, et al. Consensus conference on TIPS management: techniques, indications, contraindications. Dig Liver Dis. 2017;49(2):121–37.
56. Horhat A, Bureau C, Thabut D, Rudler M. Transjugular intrahepatic portosystemic shunt in patients with cirrhosis: indications and posttransjugular intrahepatic portosystemic shunt complications in 2020. United Eur Gastroenterol J. 2021;9(2):203–8.
57. Boike JR, Thornburg BG, Asrani SK, Fallon MB, Fortune BE, Izzy MJ, et al. North American practice-based recommendations for transjugular intrahepatic portosystemic shunts in portal hypertension. Clin Gastroenterol Hepatol. 2022;20(8):1636–62.e36.
58. Bureau C, Thabut D, Jezequel C, Archambeaud I, D'Alteroche L, Dharancy S, et al. The use of rifaximin in the prevention of overt hepatic encephalopathy after transjugular intrahepatic portosystemic shunt: a randomized controlled trial. Ann Intern Med. 2021;174(5):633–40.
59. Wong F. Innovative approaches to the management of ascites in cirrhosis. JHEP Rep. 2023;5(7):100749.
60. Schepis F, Vizzutti F, Garcia-Tsao G, Marzocchi G, Rega L, De Maria N, et al. Under-dilated TIPS associate with efficacy and reduced encephalopathy in a prospective, non-randomized study of patients with cirrhosis. Clin Gastroenterol Hepatol. 2018;16(7):1153–1162e7.
61. Crenshaw WB, Gordon FD, McEniff NJ, Perry LJ, Hartnell G, Anastopoulos H, et al. Severe ascites: efficacy of the transjugular intrahepatic portosystemic shunt in treatment. Radiology. 1996;200(1):185–92.
62. Dechene A, El Fouly AH, Bechmann LP, Jochum C, Saner FH, Gerken G, et al. Acute management of refractory variceal bleeding in liver cirrhosis by self-expanding metal stents. Digestion. 2012;85(3):185–91.
63. Nazarian GK, Bjarnason H, Dietz CA, Jr., Bernadas CA, Foshager MC, Ferral H, et al. Refractory ascites: midterm results of treatment with a transjugular intrahepatic portosystemic shunt. Radiology. 1997;205(1):173–80.
64. Somberg KA, Lake JR, Tomlanovich SJ, LaBerge JM, Feldstein V, Bass NM. Transjugular intrahepatic portosystemic shunts for refractory ascites: assessment of clinical and hormonal response and renal function. Hepatology. 1995;21(3):709–16.
65. Guevara M, Gines P, Bandi JC, Gilabert R, Sort P, Jiménez W, et al. Transjugular intrahepatic portosystemic shunt in hepatorenal syndrome: effects on renal function and vasoactive systems. Hepatology. 1998;28(2):416–22.
66. Wong F, Pantea L, Sniderman K. Midodrine, octreotide, albumin, and TIPS in selected patients with cirrhosis and type 1 hepatorenal syndrome. Hepatology. 2004;40(1):55–64.
67. Song T, Rossle M, He F, Liu F, Guo X, Qi X. Transjugular intrahepatic portosystemic shunt for hepatorenal syndrome: a systematic review and meta-analysis. Dig Liver Dis. 2018;50(4):323–30.
68. Ponzo P, Campion D, Rizzo M, Roma M, Caviglia GP, Giovo I, et al. Transjugular intrahepatic porto-systemic shunt in cirrhotic patients with hepatorenal syndrome - chronic kidney disease: impact on renal function. Dig Liver Dis. 2022;54(8):101–11081.
69. Li Y, Wang F, Chen X, Li B, Meng W, Qin C. Short outcome comparison of elderly patients versus nonelderly patients treated with transjugular intrahepatic portosystemic stent shunt: a propensity score matched cohort study. Medicine (Baltim). 2017;96(29):e7551.
70. Stockhoff L, Schultalbers M, Tergast TL, Hinrichs JB, Gerbel S, Meine TC, et al. Safety and feasibility of transjugular intrahepatic portosystemic shunt in elderly patients with liver cirrhosis and refractory ascites. PLoS One. 2020;15(6):e0235199.
71. Vizzutti F, Celsa C, Calvaruso V, Enea M, Battaglia S, Turco L, et al. Mortality after transjugular intrahepatic portosystemic shunt in older adult patients with cirrhosis: a validated prediction model. Hepatology. 2023;77(2):476–88.
72. Benmassaoud A, Roccarina D, Arico F, Leandro G, Yu B, Cheng F, et al. Sarcopenia does not worsen survival in patients with cirrhosis undergoing transjugular intrahepatic portosystemic shunt for refractory ascites. Am J Gastroenterol. 2020;115(11):1911–4.
73. Montomoli J, Holland-Fischer P, Bianchi G, Grønbaek H, Vilstrup H, Marchesini G, et al. Body composition changes after transjugular intrahepatic portosystemic shunt in patients with cirrhosis. World J Gastroenterol. 2010;16(3):348–53.
74. Plauth M, Schutz T, Buckendahl DP, Kreymann G, Pirlich M, Grüngreiff S, et al. Weight gain after transjugular intrahepatic portosystemic shunt is associated with improvement in body composition in malnourished patients with cirrhosis and hypermetabolism. J Hepatol. 2004;40(2):228–33.
75. Tsien C, Shah SN, McCullough AJ, Dasarathy S. Reversal of sarcopenia predicts survival after a transjugular intrahepatic portosystemic stent. Eur J Gastroenterol Hepatol. 2013;25(1):85–93.
76. Dasarathy J, Alkhouri N, Dasarathy S. Changes in body composition after transjugular intrahepatic portosystemic stent in cirrhosis: a critical review of literature. Liver Int. 2011;31(9):1250–8.
77. Lepida A, Marot A, Trepo E, Degre D, Moreno C, Deltenre P. Systematic review with meta-analysis: automated low-flow ascites pump therapy for refractory ascites. Aliment Pharmacol Ther. 2019;50(9):978–87.

78. Stirnimann G, Berg T, Spahr L, Zeuzem S, McPherson S, Lammert F, et al. Final safety and efficacy results from a 106 real-world patients registry with an ascites-mobilizing pump. Liver Int. 2022;42(10):2247–59.
79. Stepanova M, Nader F, Bureau C, Adebayo D, Elkrief L, Valla D, et al. Patients with refractory ascites treated with alfapump® system have better health-related quality of life as compared to those treated with large volume paracentesis: the results of a multicenter randomized controlled study. Qual Life Res. 2018;27(6):1513–20.
80. Tergast TL, Griemsmann M, Stockhoff L, Port K, Heidrich B, Cornberg M, et al. Daily low-volume paracentesis and clinical complications in patients with refractory ascites. JAMA Netw Open. 2023;6(7):e2322048.

How to cite this article: Lan T, Chen M, Tang C, Deltenre P. Recent developments in the management of ascites in cirrhosis. United European Gastroenterol J. 2024;1–12. https://doi.org/10.1002/ueg2.12539