H.8 Transjugular intrahepatic portosystemic shunt (TIPS) versus large volume paracentesis (LVP) for ascites

Study	Narahara 2011[91]
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	1 (n=60)
Countries and setting	Conducted in Japan; setting: enrolled from author's department
Line of therapy	Second line
Duration of study	Follow-up (post-intervention): reported up to 24 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: diagnosis of cirrhosis made on basis of laboratory and ultrasonographic findings or transjugular liver biopsy

Study	Narahara 2011[91]
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients with cirrhosis and refractory ascites who presented with a Child-Pugh score of <11, serum bilirubin of <3 mg/dl and creatinine of <1.9 mg/dl were admitted to the department and considered for inclusion in this study
Exclusion criteria	Age greater than 70 years, episodes of chronic hepatic encephalopathy, hepatocellular carcinoma or other malignancy, complete portal vein thrombosis with cavernomatous transformation, active infection, severe cardiac or pulmonary disease, and organic renal disease (urine protein level >500 mg/24 hours, active sediment, or small kidneys on ultrasonography)
Recruitment/selection of patients	Between September 2000 and December 2007 consecutive Japanese patients with cirrhosis and refractory ascites were enrolled
Age, gender and ethnicity	Age – mean (SD): TIPS: 57.9 (8.6) and LVP: 61.1 (8.1) years. Gender (M:F): 44/16. Ethnicity: Japanese.
Further population details	1. Age of patient: mean under 65 years. 2. Current or past encephalopathy: excluded patients with episodes of chronic 3. Severity of underlying liver disease at the time of intervention (measured by MELD): mean score below 15.
Extra comments	The aim of this study was to include cirrhotic patients with good hepatic and renal function. The model for end stage liver disease (MELD) score was not used as an inclusion criterion because the cut-off value for predicting good survival of patients undergoing TIPS was not clearly indicated when this study was initiated.
Indirectness of population	No indirectness
Interventions	(n=30) Intervention 1: TIPS. After the TIPS tract was created, an expandable stent was placed and dilated to obtain a portosystemic pressure gradient of below 12 mmHg. The stent was initially dilated to 6 or 8 mm in diameter. If the portosystemic pressure gradient remained above 12 mmHg, the stent was further dilated to 8 or 10 mm. Did not use a covered stent as not available in Japan. Patients received lactulose to ensure a few soft bowel movements per day in order to prevent hepatic encephalopathy. Duration: median follow-up of 598 days. Concurrent medication/care: diuretics were given before and after randomisation in both groups, but the doses were adjusted according to clinical need. Patients were discharged when their hepatic and renal functions were stable or improved. All patients were followed up monthly at the outpatient clinic after discharge. All patients were instructed not to drink alcohol. Further details: 1. Type of TIPS stent: uncovered Comments: none (n=30) Intervention 2: LVP – LVP with albumin infusion. Patients received sodium restriction (85 mEq/day) and treatment with diuretics. Large volume paracentesis (4 or more litres) was performed along with intravenous infusion of albumin (6 g/l ascites removed). Recurrent ascites was treated with repeated paracentesis plus albumin if necessary. Duration: median follow-up 227 days. Concurrent medication/care: diuretics were given before and after

Study	Narahara 2011[91]
	randomisation in both groups, but the doses were adjusted according to clinical need. Patients were discharged when their hepatic and renal functions were stable or improved. All patients were followed up monthly at the outpatient clinic after discharge. All patients were instructed not to drink alcohol. Further details: 1. Type of TIPS stent: N/A Comments: none
Funding	Funding not stated (not stated)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TIPS versus LVP WITH ALBUMIN INFUSION Protocol outcome 1: Re-accumulation of ascites at end of study - Actual outcome: re-accumulation of ascites at 24 months; group 1: 22/30, group 2: 27/30; risk of bias: low; indirectness of outcome: no indirectness Protocol outcome 2: Transplant-free survival at 12 months - Actual outcome: survival at 24 months; HR 0.35 (95% CI 0.17 to 0.7) reported; risk of bias: low; indirectness of outcome: no indirectness Protocol outcome 3: Hepatic encephalopathy at end of study - Actual outcome: hepatic encephalopathy at end of study; group 1: 20/30, group 2: 5/30; risk of bias: low; indirectness of outcome: no indirectness	
Protocol outcomes not reported by the study	Health-related quality of life at end of study; spontaneous bacterial peritonitis at end of study; renal failure at end of study; length of stay at end of study; readmission rate at end of study

Study (subsidiary papers)	Saab 2006[113] (Gines 2002[54], Rossle 2000[112], Salerno 2004[116], Sanyal 2003[119])
Study type	Systematic review
Number of studies (number of participants)	5 (n=330)
Countries and setting	Conducted in Canada, France, Germany, Italy, Spain, USA; setting: not reported in systematic review
Line of therapy	Second line
Duration of study	Intervention + follow up: 12–60 months after inclusion
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: diagnosis of liver disease could be made via a combination of biochemical and clinical data. The definition of refractory ascites in the individual trial was assessed by set criteria.

Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients with refractory ascites due to cirrhosis and portal hypertension
Exclusion criteria	Patients without portal hypertension such as those with malignant ascites were excluded
Recruitment/selection of patients	Consecutive patients with cirrhosis and refractory ascites
Age, gender and ethnicity	Age – range: not reported. Gender (M:F): 69% /31%. Ethnicity: systematic review – not reported.
Further population details	1. Age of patient: mean under 65 years for all studies. 2. Current or past encephalopathy: Sanyal: excluded patients with active hepatic encephalopathy (grade 2 or higher); Rossle: excluded patients with hepatic encephalopathy grade 2 or higher; Gines: excluded patients with chronic hepatic encephalopathy; Salerno: excluded patients who had a history of recurrent episodes of hepatic encephalopathy. 3. Severity of underlying liver disease at the time of intervention (measured by MELD): Salerno: mean score below 15; all other studies not reported.
Extra comments	None
Indirectness of population	No indirectness
Interventions	(n=162) Intervention 1: TIPS. Prescribed diuretics and sodium intake restriction, and underwent an initial paracentesis before the TIPS procedure with repeat paracentesis as needed. Duration: not reported. Concurrent medication/care: medical management (diuretics and sodium restriction) and any co-interventions were allowed if used in both groups of the study. Further details: 1. Type of TIPS stent: Sanyal: not reported; Gines: not reported; Rossle: not reported; Salerno: not reported. Comments: none (n=168) Intervention 2: LVP – LVP with albumin infusion. Treated with diuretics, dietary sodium restriction, and large volume paracentesis as indicated. Paracentesis with infusion of 8 g of albumin per litre of ascitic fluid removed was performed in 4 of the studies. Duration: outpatient procedure. Concurrent medication/care: medical management (diuretics and sodium restriction) and co-interventions were allowed if used in both groups of the study. Further details: 1. Type of TIPS stent: N/A Comments: none
Funding	Academic or government funding (Cochrane Review – external funding from (1) The Danish Medical Research Council's Grant on Getting Research into Practice, Denmark and (2) the Copenhagen Hospital Corporation Medical Research Council's Grant on Getting Research in to Practice [GRIP], Denmark).

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TIPS versus LVP WITH ALBUMIN INFUSION Protocol outcome 1: Re-accumulation of ascites at end of study - Actual outcome: re-accumulation of ascites at 12 months; group 1: 60/133, group 2: 111/137; risk of bias: low; indirectness of outcome: no indirectness Protocol outcome 2: Health-related quality of life at end of study - Actual outcome for Sanyal 2003[119]: quality of life – physical score (SF-36 score used to calculate physical component scale) at 12 months; group 1: mean 2.33 (SD 12); n=52, group 2: mean 5.69 (SD 10); n=57; SF-36 physical component scale not reported. High score=poor outcome; risk of bias: high; indirectness of outcome: no indirectness - Actual outcome for Sanyal 2003[119]: quality of life – mental score (SF-36 score used to calculate physical component scale) at 12 months; group 1: mean 1.83 (SD 7.6); n=52, group 2: mean 3.96 (SD 10); n=57; SF-36 mental component scale not reported. High score=poor outcome; risk of bias: very high; indirectness of outcome: no indirectness Protocol outcome 3: Transplant-free survival at 12 months - Actual outcome for Rossle 2000[112]: survival without the need for transplantation at end of study; HR 0.44 (95% CI 0.22 to 0.87) reported; risk of bias: high; indirectness of outcome: no indirectness - Actual outcome for Sanyal 2003[119]: transplant-free survival at end of study; HR 0.91 (95% CI 0.48 to 1.73) calculated – from logrank P-value; risk of bias: low; indirectness of outcome: no indirectness - Actual outcome for Gines 2002[54]: survival without liver transplantation at end of study; HR 1.12 (95% CI 0.65 to 1.93) calculated – from curve + numbers at risk; risk of bias: low; indirectness of outcome: no indirectness - Actual outcome for Salerno 2004[116]: survival without liver transplantation at end of study; HR 0.34 (95% CI 0.15 to 0.78) reported; risk of bias: low; indirectness of outcome: no indirectness Protocol outcome 4: Spontaneous bacterial peritonitis at end of study - Actual outcome for Gines 2002[54]: SBP at end of study; group 1: 2/35, group 2: 4/35; risk of bias: low; indirectness of outcome: no indirectness - Actual outcome for Sanyal 2003[119]: SBP at end of study; group 1: 4/52, group 2: 2/57; risk of bias: low; indirectness of outcome: no indirectness Protocol outcome 5: Renal failure at end of study - Actual outcome: acute renal failure at end of study; group 1: 12/87, group 2: 19/92; risk of bias: low; indirectness of outcome: no indirectness Protocol outcome 6: Hepatic encephalopathy at end of study - Actual outcome: hepatic encephalopathy at end of study; group 1: 87/162, group 2: 60/168; risk of bias: low; indirectness of outcome: no indirectness	
Protocol outcomes not reported by the study	Length of stay at end of study; readmission rate at end of study