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TIPS versus paracentesis for cirrhotic patients with refractory ascites (Review)

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[Intervention Review]

TIPS versus paracentesis for cirrhotic patients with refractory ascites

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ABSTRACT

Background

Refractory ascites (ie, ascites that cannot be mobilized despite sodium restriction and diuretic treatment) occurs in 10 per cent of patients with cirrhosis. It is associated with substantial morbidity and mortality with a one-year survival rate of less than 50 per cent. Few therapeutic options currently exist for the management of refractory ascites.

Objectives

To compare transjugular intrahepatic portosystemic stent-shunts (TIPS) versus paracentesis for the treatment of refractory ascites in patients with cirrhosis.

Search methods

We searched *The Cochrane Hepato-Biliary Group Controlled Trials Register* (January 2006), the *Cochrane Central Register of Controlled Trials* in *The Cochrane Library* (Issue 4, 2005), *MEDLINE* (1950 to January 2006), *EMBASE* (1980 to January 2006), *CINAHL* (1982 to August 2004), and *Science Citation Index Expanded* (1945 to January 2006).

Selection criteria

We included randomised clinical trials comparing TIPS and paracentesis with or without volume expanders for cirrhotic patients with refractory ascites.

Data collection and analysis

We evaluated the methodological quality of the randomised clinical trials by the generation of the allocation section, allocation concealment, and follow-up. Two authors independently extracted data from each trial. We contacted trial authors for additional information. Dichotomous outcomes were reported as odds ratio (OR) with 95% confidence interval (CI).

Main results

Five randomised clinical trials, including 330 patients, met the inclusion criteria. The majority of trials had adequate allocation concealment, but only one employed blinded outcome assessment. Mortality at 30-days (OR 1.00, 95% CI 0.10 to 10.06, P = 1.0) and 24-months (OR 1.29, 95% CI 0.65 to 2.56, P = 0.5) did not differ significantly between TIPS and paracentesis. Transjugular intrahepatic portosystemic stent-shunts significantly reduced the re-accumulation of ascites at 3-months (OR 0.07, 95% CI 0.03 to 0.18, P < 0.01) and 12-months (OR 0.14, 95% CI 0.06 to 0.28, P < 0.01). Hepatic encephalopathy occurred significantly more often in the TIPS group (OR 2.24, 95% CI 1.39 to 3.6, P < 0.01), but gastrointestinal bleeding, infection, and acute renal failure did not differ significantly between the two groups.

Authors' conclusions

The meta-analysis supports that TIPS was more effective at removing ascites as compared with paracentesis without a significant difference in mortality, gastrointestinal bleeding, infection, and acute renal failure. However, TIPS patients develop hepatic encephalopathy significantly more often.

PLAIN LANGUAGE SUMMARY

Patients with refractory ascites may temporarily benefit from transjugular intrahepatic portosystemic stent-shunts

Refractory ascites causes substantial morbidity in patients with cirrhosis. Randomised trials have compared transjugular intrahepatic portosystemic stent-shunts with paracentesis. Mortality, gastrointestinal bleeding, renal failure, or infection did not differ significantly between the two intervention groups. Transjugular intrahepatic portosystemic stent-shunts effectively decreased the risk of ascites fluid re-accumulation, but was associated with an increased risk of hepatic encephalopathy.

BACKGROUND

Ascites refers to the pathologic accumulation of fluid within the peritoneal cavity and develops as a result of elevated portal-vein pressure in 35% to 50% of patients with cirrhosis within 10 years of diagnosis (Gines 1987; D'Amico 1995). Ascites can adversely impact quality of life by causing disabling symptoms such as fatigue, malnutrition, bacterial infections, and dyspnoea (Arroyo 1996a; Such 1998). It also has an effect on mortality with a mean survival of two years after the onset of ascites (Arroyo 1996b).

Initial treatment of ascites consists of dietary sodium restriction and administration of oral diuretics. However, approximately 10% of affected patients develop refractory ascites (Arroyo 1996c), which is defined as an inability to effectively mobilize the fluid despite compliance with the aforementioned treatment regimen or an inability to tolerate aggressive diuresis due to the development of adverse effects (Llach 1988). The development of refractory ascites has a particularly poor prognosis with an associated one-year mortality rate of 50% to 80% (Saunders 1981; Llach 1988; Salerno 1993; Gines 1996a).

Few therapeutic options exist for patients who develop refractory ascites, including direct removal of fluid via large-volume paracentesis, transjugular intrahepatic portosystemic shunts (TIPS), and ultimately liver transplantation (Arroyo 1996b). Paracentesis is a relatively simple and safe procedure (Runyon 1999), and it can be performed in the outpatient setting, providing many patients with immediate relief (Arroyo 1994). However, it does not treat the underlying etiology of ascites development, and thus, does not prevent recurrence. TIPS involves the shunting of portal blood flow past the liver into the systemic circulation, which decompresses the portal system and removes the impetus for ascites formation (Colapinto 1982; Ferral 1993). TIPS has gained popularity because of the ease of insertion without requiring general surgery and the relative effectiveness of the procedure. Complications associated with TIPS include stent occlusion, encephalopathy, infections, and renal failure (Gines 1996a, Freedman 1993, Schiffman 1995, Lebrec 1996). Liver transplantation is another treatment option for patients with refractory ascites. However, with the introduction of the Mathematical End-Stage Liver Disease (MELD) Score, ascites is not often used to estimate severity of liver disease, and patients may have prolonged waiting times for liver transplantation despite suffering from refractory ascites (Wiesner 2001).

This review is an update of a previously published review by us (Saab 2004).

OBJECTIVES

In the present study, we sought to compare the overall mortality rate, treatment efficacy, and complications of TIPS versus paracentesis.

METHODS

Criteria for considering studies for this review

Types of studies

Only randomised clinical trials, published as an article or abstract, were included, and quasi-randomised studies were excluded. Blinding was not required as it would have been difficult to perform on patients undergoing invasive procedures.

Types of participants

Patients with refractory ascites due to cirrhosis and portal hypertension were included. Patients without portal hypertension such as those with malignant ascites were excluded. The diagnosis of liver disease could be made on a combination of biochemical and clinical data.

Types of interventions

The following interventions were compared:

- TIPS versus paracentesis treatment with or without volume expanders.

Any co-interventions (ie, diuretics and sodium restriction) were allowed if used in both arms of the trial.

Surgical portosystemic shunts, peritoneovenous shunts, and orthotopic liver transplantation were not considered in the present systematic review. Surgical portosystemic shunts have fallen out of favour because of significant morbidity and mortality. Peritoneovenous shunts will be addressed in another systematic Cochrane review (see Published notes). There have not been any randomised trials comparing orthotopic liver transplantation versus paracentesis for the treatment of refractory ascites.

Types of outcome measures

(1) Overall mortality, both short-term (30 days) and long-term (24 months).
(2) Re-accumulation of ascites.
(3) Complications such as shunt stenosis, hepatic encephalopathy, renal failure, septicaemia, or gastrointestinal bleeding.

Search methods for identification of studies

We searched *The Cochrane Hepato-Biliary Group Controlled Trials Register* (January 2006), the *Cochrane Central Register of Controlled Trials* in *The Cochrane Library* (Issue 4, 2005), *MEDLINE* (1950 to January 2006), *EMBASE* (1980 to January 2006), *CINAHL* (1982 to August 2004), and *Science Citation Index Expanded* (1945 to January 2006) without language limitations using the search strategies given in Appendix 1 (Royle 2003). We also reviewed citations in relevant primary articles and hand-searched abstracts from national conferences. Abstracts from the American Association for the Study of Liver Diseases (1982 to 2003) and American Gastroenterology Association (1981 to 2004) were searched by reviewing the annual syllabi.

Data collection and analysis

Searches were conducted in duplicate, and data extraction was performed independently by two authors (SS and JMN) and confirmed by consensus.

Application of inclusion criteria

Initially, all identified trials were entered in a trials register. Two authors (SS and JMN) independently applied the inclusion criteria to all identified studies. When a difference of opinion existed on whether to include a particular study or on the data extracted, the third author (BAR) was consulted to reach consensus. When data on

specified outcomes or individual patients were absent, the authors were contacted and asked to supply further details where possible.

Data extraction

The two authors (SS and JMN) extracted the following prespecified characteristics for all included trials independently:

Participants

Age, sex, etiology of the underlying liver disease, severity of the liver disease according the Child-Pugh criteria (Pugh 1973), presence or absence of hepatic encephalopathy, and the degree of renal dysfunction as determined by serum creatinine were recorded.

Patients with refractory ascites due only to cirrhosis and portal hypertension were included. The 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 the following criteria, at least one of which needed to be met: (1) intensive diuretic therapy for at least one week; (2) mean loss of weight less than 200 g/day during the last four days of diuretic treatment and urinary sodium excretion lower than 2 g/day; (3) dietary sodium restriction to 2 g/day; (4) spironolactone 400 mg/day plus furosemide 160 mg/day; (5) recurrence of grade 2 to 3 ascites within four weeks of initial mobilization or within three days after paracentesis; (6) significant adverse effects associated with attempted diuresis (Gines 1996a).

Interventions

In the TIPS group, the type and number of shunts, shunt diameter, any co-administered anticoagulation, success of shunt placement, and reduction in portal pressure were registered. The alternative treatment was paracentesis, for which the number of paracenteses performed, the ascitic volume removed, and volume expander (use, type, and dose) were registered. Medical management (sodium restriction and diuretic use) and co-interventions were allowed if used in both arms of the trial.

Outcome measures

The mortality rate, efficacy as measured by re-accumulation of ascites, and occurrence of complications were recorded. The associated complications that were included in the analysis were: hepatic encephalopathy, gastrointestinal bleeding, and infection/septicaemia. The definition of ascites improvement could be subjective or objective, or both through evaluation of abdominal distention, edema, body weight, or ultrasound, or not defined.

Assessment of methodological quality

The methodological quality, defined as the confidence that the design and report will restrict bias in the intervention comparison (Moher 1998), was evaluated independently by the authors. According to empirical evidence (Schulz 1995; Jadad 1996; Moher 1998; Jüni 2001; Kjaergard 2001) we assessed the methodological quality by the generation of the allocation sequence, allocation concealment, double blinding, and follow-up.

Generation of the allocation sequence

- Adequate, if the allocation sequence was generated by a computer or random number table. Drawing of lots, tossing of a coin, shuffling of cards, or throwing dice will be considered as adequate if a person who was not otherwise involved in the recruitment of participants performed the procedure.
- Unclear, if the trial was described as randomised, but the method used for the allocation sequence generation was not described.
- Inadequate, if a system involving dates, names, or admittance numbers were used for the allocation of patients. These studies are known as quasi-randomised and were excluded from the present review when assessing beneficial effects.

Allocation concealment

- Adequate, if the allocation of patients involved a central independent unit, on-site locked computer, identically appearing numbered drug bottles or containers prepared by an independent pharmacist or investigator, or sealed envelopes.
- Unclear, if the trial was described as randomised, but the method used to conceal the allocation was not described.
- Inadequate, if the allocation sequence was known to the investigators who assigned participants or if the study was quasi-randomised.

Blinding (or masking)

- Adequate, if the trial was described as double blind and the method of blinding involved identical placebo or active drugs.
- Unclear, if the trial was described as double blind, but the method of blinding was not described.
- Not performed, if the trial was not double blind.

Follow-up

- Adequate, if the numbers and reasons for dropouts and withdrawals in all intervention groups were described or if it was specified that there were no dropouts or withdrawals.
- Unclear, if the report gave the impression that there had been no dropouts or withdrawals, but this was not specifically stated.
- Inadequate, if the number or reasons for dropouts and withdrawals were not described.

Furthermore, we registered whether the randomised clinical trial used an intention-to-treat analysis.

Statistical methods

All analyses were performed according to the intention-to-treat method, ie, all randomised patients were included, and patients that did not meet the outcome measure were considered failures. We used the statistical package RevMan 4.2.8 (RevMan 2003) provided by The Cochrane Collaboration. A random-effects model was employed due to the anticipated variability between trials in terms of patient populations, interventions, and concomitant interventions (DerSimonian 1986; Schulz 1995; Jadad 1996; Moher 1998; Jüni 2001; Kjaergard 2001). Sensitivity analyses were performed on clinically important outcomes and to determine the cause of heterogeneity, if it existed (Egger 1997). Levels of clinical significance were set at $P < 0.05$, and significant heterogeneity was set at $P < 0.10$.

Sensitivity analyses according to allocation concealment, dose of diuretic used, and degree of sodium restriction diet used were to be performed if sufficient number of trials were identified.

RESULTS

Description of studies

Search Results

Among the 96 references that were identified, we excluded 28 duplicates and 41 irrelevant references by reading the abstracts. Of the remaining 27 references, we excluded 19 for the following reasons: the studies were not randomised (n = 7), TIPS was not compared to medical therapy (n = 8), surgical therapy as opposed to TIPS was compared (n = 2), or the criteria for refractory ascites were not met (n = 2). Of the remaining eight references, three were abstracts of preliminary data of two of the randomised clinical trials used in this study.

Trial characteristics

The five included randomised trials (Lebrec 1996; Rössle 2000; Gines 2002; Sanyal 2003; Salerno 2004) were published as peer-reviewed, original articles (Appendix 1). They included a total of 330 patients, of whom 162 underwent TIPS and 168 underwent paracentesis. The group undergoing medical therapy was treated with diuretics, dietary sodium restriction, and large-volume paracentesis as indicated. The TIPS arm was prescribed diuretics and sodium intake restriction, and underwent an initial paracentesis before the TIPS procedure with repeat paracentesis as needed. Paracentesis with infusion of 8 g of albumin per litre of ascitic fluid removed was performed in four of the randomised trials (Rössle 2000; Gines 2002; Sanyal 2003; Salerno 2004). One trial did not report the amount of albumin used with paracentesis (Lebrec 1996).

The number of people in each trial ranged from 25 to 109 (Lebrec 1996; Rössle 2000; Gines 2002; Sanyal 2003; Salerno 2004). Men composed 69% of the patients. The cause of underlying disease was described in all of the patients, and 65% had alcoholic cirrhosis. The mean Child-Pugh score ranged from 8.7 to 9.3. The mean success rate of TIPS placement was 84% (range 45% to 97%). Portal pressure gradient was reduced from 20 ± 1 mmHg to 13 ± 1 mmHg (Lebrec 1996), from 19.1 ± 0.8 mmHg to 8.7 ± 0.4 mmHg (Gines 2002), 24 ± 6 mmHg to 10 ± 4 mmHg (Rössle 2000), 19.8 ± 4.8 mmHg to 8.3 ± 3.6 mmHg (Sanyal 2003), and 22.5 ± 1.1 mmHg to 8.7 ± 0.6 mmHg (Salerno 2004). In the paracentesis group from each study, a single large volume paracentesis was performed to completely remove ascites at the start of therapy (Lebrec 1996; Rössle 2000; Gines 2002; Sanyal 2003; Salerno 2004). In three of the trials, there was no record of the volumes of initial ascitic fluid removed (Lebrec 1996; Rössle 2000; Salerno 2004). Gines et al noted that the initial paracentesis had a mean volume of 7.4 L (Gines 2002), and Sanyal et al noted that the mean volume removed from the two months prior was 17 L for the TIPS group and 19 L for patients undergoing paracentesis (Sanyal 2003).

Recurrent ascites was defined clinically in all trials (Lebrec 1996; Rössle 2000; Gines 2002; Sanyal 2003; Salerno 2004). The development of moderate or tense ascites and the need for large volume paracenteses was perceived as treatment failure (Gines 2002; Lebrec 1996; Rössle 2000; Salerno 2004; Sanyal 2003). The five included trials described follow-up and withdrawals/drop-outs (Lebrec 1996; Rössle 2000; Gines 2002; Sanyal 2003; Salerno 2004), and all of the trials used an intention-to-treat analysis to analyze their data.

Risk of bias in included studies

Generation of the allocation sequence was unclear in all the five trials. Allocation concealment was adequate in four trials (Lebrec 1996; Gines 2002; Sanyal 2003; Salerno 2004) and unclear in the fifth trial (Rössle 2000). None of the trials used double blinding as anticipated, and none of them employed blinded outcome assessment.

In the five trials, there was a description of follow-up and withdrawals or drop-outs (Lebrec 1996; Rössle 2000; Gines 2002; Sanyal 2003; Salerno 2004). All five trials used an intention-to-treat analyses to analyse their data.

Effects of interventions

Thirty-day mortality

The incidence of mortality at 30-days did not differ significantly between the TIPS and paracentesis groups (OR 1.00, 95% CI 0.10 to 10.06, P = 1.00; 2 trials) (Comparison 1.01). No statistically significant heterogeneity was identified (P = 0.36). At 30-days, the mortality rate in the TIPS group was 2.3% and 2.3% in the paracentesis group.

Twenty-four-month mortality

There was no significant difference in 24-month mortality between the TIPS and paracentesis groups (OR 1.29, 95% CI 0.65 to 2.56, P = 0.5; 5 trials) (Comparison 2.01), and no significant difference between TIPS versus paracentesis in patients receiving the maximum furosemide dose of 160 mg per day (OR 1.47, 95% CI 0.85-2.56, P = 0.17; 3 trials) (Comparison 2.02) or in patients receiving the maximum spironolactone dose of 400 mg per day (OR 0.93, 95% CI 0.42 to 2.02, P = 0.8; 3 trials) (Comparison 2.03). There was statistically significant heterogeneity between the TIPS- and paracentesis-treated groups in terms of 24-month mortality (P = 0.1).

Three-month ascitic fluid re-accumulation

Patients who underwent TIPS were significantly less likely to have ascitic fluid re-accumulation than those treated with medical therapy at three months (OR 0.07, 95% CI 0.03 to 0.18, P < 0.01; 3 trials) (Comparison 3.01). There was no significant heterogeneity (P = 0.99).

Twelve-month ascites fluid re-accumulation

Ascites re-accumulation was significantly less in the TIPS group as compared to the group treated with paracentesis at 12 months (OR 0.15, 95% CI 0.08 to 0.28, P < 0.01; 4 trials) (Comparison 4.01), and there was no significant heterogeneity (P = 0.80).

Patients in the TIPS group were significantly less likely to have re-accumulation of ascitic fluid when treated with the maximum furosemide dose of 160 mg per day (OR 0.12, 95% CI 0.06 to 0.27, P < 0.01; 2 trials) (Comparison 4.02) and when treated with the maximum spironolactone dose of 400 mg per day (OR 0.12, 95% CI 0.06 to 0.27, P < 0.01; 2 trials) (Comparison 4.03). Twelve-month efficacy was better in the TIPS groups than the paracentesis group despite sodium restriction of less than 2 grams per day (OR 0.15, 95% CI 0.08 to 0.28, P < 0.01; 4 trials) (Comparison 4.04). Only one trial reported 24-month efficacy, which revealed that 33 of 35 patients from both groups developed ascites requiring more than one paracentesis per month (Gines 2002).

Complications

Thirty-one per cent of patients in the TIPS group experienced gastrointestinal bleeding, infection/septicemia, acute renal failure and/or hepatic encephalopathy compared with 24% in the paracentesis group.

There was no statistical difference between the TIPS and paracentesis groups regarding frequency of gastrointestinal bleeding (OR 0.75, 95% CI 0.37 to 1.54, P = 0.4; 3 trials) (Comparison 5.01), infection/septicemia (OR 1.05, 95% CI 0. 22 to 4.94, P = 1; 2 trials) (Comparison 5.02), and acute renal failure (OR 0.64, 95% CI 0.15 to 2.72, P = 0.5; 2 trials) (Comparison 5.03). However, the incidence of hepatic encephalopathy was significantly increased in the TIPS treated group as compared to patients treated with medical therapy (OR 2.24, 95% CI 1.39 to 3.6, P < 0.01; 5 trials) (Comparison 5.04).

Shunt occlusion was reported in 4 trials and occurred in 43 out of 129 patients (33%) undergoing TIPS within a year. In two trials, hospitalization rates of patients undergoing TIPS versus paracentesis were 2.8 days and 2.9 days, respectively.

Quality of life

One trial assessed quality of life using a general quality of life questionnaire (Short Form-36 [SF-36]) (Sanyal 2003). Both groups reported a general improvement in both the physical and mental components of the SF-36. According to Sanyal et al, there did not appear to be a significant difference in quality of life between the TIPS and paracentesis groups, but the statistical results for their comparisons were not stated.

Funnel plots

Due to the paucity of trials we did not perform funnel plot analyses.

DISCUSSION

According to the results of this study, which compared the role of TIPS versus paracentesis for the treatment of refractory ascites due to cirrhosis, TIPS is more efficacious in clearly ascites at 3- and 12-month intervals, despite no difference in short- or long-term mortality between the two treatments options. Although there was no significant increase in the frequency of gastrointestinal bleeding, infection/septicemia, and acute renal failure, there was a greater incidence of hepatic encephalopathy in the TIPS group.

There was no overall difference in survival between patients treated with TIPS compared with those who underwent management with paracentesis, even in patients with Child-Pugh class C (Rössle 2000; Gines 2002; Sanyal 2003; Salerno 2004). One trial did identify a higher mortality in patients who underwent TIPS with Child-Pugh class C (P = 0.027) (Lebrec 1996), but this was not confirmed in the other trials. More studies are needed to assess the impact of liver disease severity on survival after TIPS (Russo 2003). In addition, other measures of disease severity, such as the MELD score, should be incorporated in future analyses (Malinchoc 2000).

Our study demonstrated an increase risk of hepatic encephalopathy in patients treated with TIPS, as was reported in several studies in terms of both frequency and severity (Lebrec 1996; Rössle 2000; Gines 2002; Sanyal 2003; Salerno 2004). A previous history of encephalopathy is a predictor of post-TIPS hepatic encephalopathy, so this finding is somewhat surprising given the exclusion criteria of grade 2 hepatic encephalopathy in three trials (Rössle 2000; Sanyal 2003; Salerno 2004) and history of chronic encephalopathy in one study (Gines 2002) at the time of enrollment. As a potential explanation for this finding, patients with a history of severe hepatic encephalopathy may not have been excluded if their encephalopathy was aggressively controlled at the time of screening, or patients may have had mild, or subclinical, encephalopathy that did not meet criteria for exclusion.

Our study focused on two treatments of refractory ascites: TIPS and medical management. Another treatment option includes peritoneovenous shunts, which work by an alternative mechanism and rely on the difference between intrathoracic and peritoneal pressure to return ascitic fluid to the vasculature. Although several studies have reported on the efficacy of peritoneovenous shunts in the treatment of refractory ascites (Gines 1996), we did not include this treatment modality in the study because these shunts have fallen out of favor in clinical practice due to the frequency of complications, including occlusion and associated infections (Zervos 1997). In one study of 48 patients, 13 patients underwent shunt revisions because of occlusion or infection (Moore 2003).

There are several limitations in the trials comparing TIPS and paracentesis that should be addressed. First, blinding of outcome analysis was not discussed in the published trials, and thus, the efficacy and safety of invasive treatments may have been over-estimated (Kjaergard 2001). Also, quality of life assessment was not incorporated in most trials. Patient-oriented measures need to be assessed. For instance, does the risk of hepatic encephalopathy outweigh the relief from refractory ascites?

Quality of life was only assessed in one trial (Sanyal 2003), despite its importance as an outcome measure when comparing invasive treatments. Both the physical and mental components of the questionnaire (SF-36) improved after treatment in the two groups, although there was no statistical difference between the groups. Improvement in ascites control with any therapeutic measure may have overshadowed differences in quality of life between interventions. Future studies should consider disease specific quality-of-life instruments that may be more sensitive to changes in the quality of life in patients with liver disease.

The published trials were initiated prior to standard use of the MELD score to predict TIPS mortality and prior to development of the covered stent (Malinchoc 2000; Bureau 2004). Covered stents appear to remain patent significantly longer than uncovered stents, and in one nonrandomised trial, there was a survival advantage associated with the covered stent (Angermayr 2003; Bureau 2004). Other studies incorporating MELD score and covered stents should now be considered.

Data on rehospitalization were not complete, limiting the analysis of the impact of either treatment modality on the need for repeat hospitalizations. In three of the five trials, rehospitalization rates were not discussed, and in the remaining two trials, the rehospitalization rate was given in terms of unscheduled hospital visits and not rehospitalization due to recurrence of ascites (Rössle 2000; Sanyal 2003). Only one study made a statistical comparison, which showed that rehospitalization rates due to unscheduled visits were similar in both the TIPS and paracentesis group (Rössle 2000).

In conclusion, our results indicate that TIPS effectively decreases the re-accumulation of ascitic fluid for up to 12 months without concomitant increase risk of mortality in properly selected patients

with refractory ascites. However, this comes at the risk of hepatic encephalopathy, which was significantly more common in patients treated with TIPS. Future studies need to employ quality of life outcomes to determine if the risks of encephalopathy from TIPS are outweighed by alleviation of refractory ascites.

AUTHORS' CONCLUSIONS

Implications for practice

Patients with refractory ascites benefit from improved control of their ascites without an associated increase in mortality. However, patients should be advised regarding the risk of hepatic encephalopathy.

Implications for research

Further trials should report long-term follow-up of patients undergoing TIPS for refractory ascites. Quality of life measures and costs should be incorporated in further trials, which should use adequate methods for conduct and report (http://www.consort-statement.org).

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CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Gines 2002

Methods	Generation of allocation sequence: Unclear, no information, apart from the facts that the schedule was centre-based and patients were stratified according to renal failure (serum creatinine > 133 µmol/L). Allocation concealment: Adequate (central randomisation with sealed opaque envelopes). Blinding: No blinding. Follow-up: Adequate. More than 26 months after inclusion. Lost to follow-up: One patient in the paracentesis group. Intention-to-treat analysis: Yes.
Participants	Country: Spain and USA. Patients evaluated for inclusion: 119 consecutive patients with cirrhosis and refractory ascites. All of them lacked response to low dose sodium diet and spironolactone 400 mg/day plus furosemide 160 mg/day. Inclusion criteria: cirrhotic patients with refractory ascites. Exclusion criteria: age < 18 or > 75 years, bilirubin > 10 mg/dL (171 micromol/L), INR < 2.5, platelets < 40,000, creatine > 3 mg/dL (265 micromol/dL), hepatocellular carcinoma, complete portal vein thrombosis, sepsis, multiorgan failure, hepatorenal syndrome type 1, and chronic encephalopathy. Etiology: 56% alcoholic cirrhosis. Randomised participants: 70; 50 males and 20 females: aged 59+/- 2 years in the TIPS group and 56 +/- in the paracentesis plus albumin group.
Interventions	Seventy patients assigned to one of the two treatment groups. Invasive: 35 patients to TIPS procedure. Medical: 35 patients to repeated large-volume paracentesis plus intravenous albumin (8 g/L removed). Diuretics were given during follow-up only if urine sodium under diuretic therapy was < 20 mEq/day. Furosemide and spironolactone were given during follow-up (TIPS:49+/- 7 mg/day and 129 +/- 17 mg/day; paracentesis 53 +/- 8 mg/day and 135 +/- 22 mg/day). Patients in the paracentesis group with past history of variceal bleeding and/or moderate or large oesophageal varices were treated with beta-blockers. Prophylactic antibiotic therapy was given throughout the study period to patients with past history of bacterial peritonitis or for seven days to patients developing gastrointestinal bleeding.
Outcomes	Primary outcome: survival without liver transplantation. Secondary outcomes: recurrence of ascites, hepatorenal syndrome, hyponatraemia, gastrointestinal bleeding, infection, spontaneous bacterial peritonitis, hepatic encephalopathy, and cost.

Gines 2002 *(Continued)*

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - Adequate

Lebrec 1996

Methods	Generation of allocation sequence: Unclear, no information. Allocation concealment: Adequate (opaque envelopes). Blinding: No blinding. Follow-up: Adequate. Patients were followed up to 34 months after inclusion. Lost to follow-up: No patients were lost to follow up. Intention-to-treat analysis: Yes.
Participants	Country: France. Patients evaluated for inclusion: 25 patients with histologically proven cirrhosis and refractory ascites. Refractory ascites was defined by no response, defined as a loss of body weight of less than 200 g/day following sodium restriction and maximal diuretic therapy (furosemide 120 mg/day and spironolactone 300 mg/day) for 5 days. Inclusion criteria: cirrhotic patients with refractory ascites to medical treatment. Exclusion criteria: hepatic encephalopathy, > 70 years of age, severe disease other than liver disease, pulmonary hypertension, hepatocellular carcinoma, spontaneous bacterial peritonitis or sepsis, severe alcoholic hepatitis, portal or hepatic vein obstruction or thrombosis, obstruction of biliary tract, obstruction of the hepatic artery, creatinine > 1.7 mg/dL.
Interventions	Twenty-five patients assigned to one the two following treatment groups. Invasive: 13 patients to TIPS procedure. Medical: 12 patients to large-volume paracentesis with albumin infusion if Cr clearance > 60 mL/min. During follow-up both groups were treated with a low sodium diet and fluid restriction . The medical group was treated with paracentesis with albumin if Cr clearance > 60 mL/min, and diuretics (doses not mentioned). Patient who underwent TIPS were treated with one large volume paracentesis. Patients that underwent TIPS procedure and were anticoagulated for four days with IV heparin and ofloxacin 400 mg/day x 3 days. Beta antagonists were discontinued in all patients.
Outcomes	Primary outcome: survival and efficacy of treatment measured. Secondary outcome: hepatic encephalopathy, hemodynamic measurements. Hemodynamic values: wedged hepatic pressure, free hepatic venous pressure, portal blood vein velocity, portal blood flow, hepatic artery blood flow, CI, MAP SVR, RA pressure, pulmonary wedge pressure, PA pressure. Renal: GFR, serum Na, Cr, renal blood flow. Liver: AST, ALT, total bilirubin lactate, PT. Neurohormonal factors: vasopressin, norepinephrine, aldosterone, renin were measured up to four months.

Lebrec 1996 *(Continued)*

Notes	Medical therapy was not clearly described.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - Adequate

Rössle 2000

Methods	Generation of allocation sequence: Unclear, no information, apart from the fact that it was performed in blocks. Patients were stratified at randomisation according to sex and age (older than 60 years, or 60 years and younger than 60 years). Allocation concealment: Unclear. No information. Blinding: No blinding. Follow-up: Adequate. Patients were followed up to 60 months after inclusion. Lost to follow-up: No patients were lost to follow-up. Intention-to-treat analysis: Yes
Participants	Country: Germany. Patients evaluated for inclusion: 155 consecutive patients with cirrhosis and refractory ascites. Patients were considered to be refractory if they did not have a response after 4 weeks of treatment with spironolactone 400 mg/day plus furosemide 120 mg/day or were intolerant to treatment. Inclusion criteria: cirrhotic patients with refractory ascites or recurrent ascites. Exclusion criteria: hepatic encephalopathy grade 2 or greater, total bilirubin > 5 mg/dL, serum creatine > 3 mg/dL, portal vein thrombosis, hepatic hydrothorax, malignant ascites, failure of paracentesis. Randomised participants: 60; 42 males and 18 females: aged 58 +/- 11 years in the TIPS group and 61 +/- 8 years in the paracentesis and albumin group.
Interventions	Sixty patients assigned to one the two following treatment groups. Invasive: 29 patients to TIPS procedure Medical: 31 patients to large-volume paracentesis with albumin infusion (8 g/L removed). During follow-up patients assigned to paracentesis received dietary treatment and treatment with diuretics given at tolerable doses. After the creation of a shunt, the doses of diuretic agents were adjusted according to clinical need (assessed in terms of urine production, body weight, and the presence or absence of edema).
Outcomes	Primary outcome: survival without transplantation. Secondary outcome: response to treatment and the occurrence of procedure-related complications.
Notes	Patients with poor renal function and unsuccessful paracentesis were excluded.

Risk of bias

Bias	Authors' judgement	Support for judgement

Rössle 2000 *(Continued)*

Allocation concealment?	Unclear risk	B - Unclear

Salerno 2004

Methods	Generation of allocation sequence: Unclear, no information. Allocation concealment: Unclear. Blinding: No blinding. Follow-up: Adequate. Patients were followed up to on average 18.2 +/- 2.3 months after inclusion. Lost to follow-up: 2 patients were lost to follow-up in the TIPS group. Intention-to-treat analysis: Yes.
Participants	Country: Italy. Patients evaluated for inclusion: 137 consecutive patients with cirrhosis and refractory or recidivant ascites. Patients were considered to be refractory if there was a lack of response to a low sodium diet and spironolactone 400 mg/day plus furosemide 160 mg/day. Patients were considered recidivant by the recurrence of at least 3 episodes of tense ascites within a 12-month period despite low sodium diet and adequate diuretic doses. Inclusion criteria: Cirrhotic patients with refractory or recidivant ascites. Exclusion criteria: age above 72 years, recurrent hepatic encephalopathy of grade 2 or more, a serum bilirubin level greater than 6 mg/dL, a serum creatinine level greater than 3 mg/dL, a Child-Turcotte-Pugh Score higher than 11, complete portal vein thrombosis, hepatocellular cancer, recent gastrointestinal bleeding (< 15 days), serious cardiac or pulmonary dysfunctions, ongoing bacterial infection and a serum ascites albumin gradient lower than 11g/L. Randomised patients: 66; 49 males and 11 females ages 58 +/- 1.3 years in the TIPS group and 60 +/- 1.3 years in the paracentesis group.
Interventions	Sixty six patients assigned to one of the two following treatment groups. TIPS: 33 patients to this procedure. Paracentesis with albumin infusion (8 g/L removed): 33 patients to this procedure. During follow-up patients were prescribed diuretic drugs (doses adjusted to clinical needs and tolerability of each patient) and a low sodium diet (80 mEq/day).
Outcomes	Primary outcome: survival without liver transplantation. Secondary outcome: the failure of treatment, occurrence of complications and need for rehospitalization.
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Unclear risk	B - Unclear

Sanyal 2003

Methods	Generation of allocation sequence: Unclear, no information. Allocation concealment: Adequate (centralized). Blinding: No blinding. Follow-up: Adequate. Patients were followed up to 12 months after inclusion. Lost to follow-up: No patients were lost to follow-up. Intention-to-treat analysis: Yes.
Participants	Country: USA, Canada. Patients evaluated for inclusion: 525 consecutive patients with cirrhosis and refractory ascites. Refractory ascites was defined according to the International Ascites Club criteria. Inclusion criteria: cirrhotic patients with refractory ascites with stable renal function (serum creatinine level < 1.5 mg/dL for at least 7 days). Exclusion criteria: failure to obtain consent, pregnancy, causes of ascites other than cirrhosis, incurable cancers or non-hepatic systemic diseases that were likely to limit life expectancy to <1 year, advanced liver failure (bilirubin level > 5 mg/dL, international normalized ratio > 2 despite administration of vitamin K, congestive heart failure (defined clinically by chest x-ray and echocardiography), acute renal failure, parenchymal renal disease (urine protein level > 500 mg/24 h, active sediment, or small kidneys on sonography), portal vein thrombosis, active sepsis, active encephalopathy (grade II or higher), florid alcoholic hepatitis, hepatocellular carcinoma (based on ultrasonography and -fetoprotein levels), and gastrointestinal hemorrhage within 6 weeks of randomisation. Randomised participants: 109; 72 males and 37 females: aged 56 +/- 9 years in the TIPS group and 52 +/- 9 years in the paracentesis and albumin group.
Interventions	One hundred and nine patients assigned to one the two following treatment groups. Invasive: 52 patients to TIPS procedure and paracentesis with albumin infusion (8 g/L removed). Medical: 57 patients to large-volume paracentesis with albumin infusion (8 g/L removed). During the follow-up all patients remained on a sodium-restricted diet, and treatment with diuretics was restarted. Doses of diuretics were increased based on the stepped-care approach previously described. Repeat total paracenthesis with infusion of albumin was performed in both arms for tense, symptomatic ascites with weight gain >10 lb from immediately previous nadir weight despite maximal diuretic therapy or inability to use an effective dose of diuretics due to diuretic-related side effects.
Outcomes	Primary outcome: recurrence of ascites requiring therapeutic paracentesis and mortality. Secondary outcome: worsening encephalopathy, liver and renal function, frequency of hepatorenal syndrome, and variceal bleed.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Cr clearance = creatinine clearance
mEq = milliequivalents

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Acharya 1992	Randomised trial comparing dextran and large volume paracentesis versus diuretic treatment. There was no comparison with TIPS.
Altman 1998	Randomised trial comparing hydroxyethyl starch versus albumin as a plasma expander in patients treated with large volume paracentesis. There was no comparison with TIPS.
Antillon 1993	Randomised trial comparing extracorporeal ultrafiltration and intravenous reinfusion of ascitic fluid versus large-volume paracentesis. There was no comparison with TIPS.
Bernardi 1993	Randomised trial comparing two different diets in the treatment of refractory ascites. Did not include the type of medical or surgical treatment that patients in the study underwent.
Bruno 1992	Randomised trial comparing spontaneous ascites filtration and reinfusion with total paracentesis with intravenous albumin infusion in cirrhotic patients with tense ascites. Did not compare with TIPS.
Funlenwider 1986	Randomised trial comparing LeVeen versus Denver peritoneovenous shunts for refractory ascites secondary to cirrhosis. Did not compare with TIPS.
Garcia-Compean 1993	Randomised trial comparing large volume paracentesis with/without albumin infusion versus medical treatment. Did not compare with TIPS.
Gines 1987	Randomised trial comparing paracentesis versus diuretic treatment in patients with refractory ascites. Did not compare with TIPS.
Gines 1996	Randomised controlled trial which compared large volume paracentesis with different volume expanders. Did not compare with TIPS.
Graziotto 1997	Paracentesis versus ascitic fluid reinfusion. There was no comparison with TIPS. Was not performed in patients with refractory ascites.
Langer 1995	Randomised trial comparing distal splenorenal shunt with end-to-side portacaval shunt. No comparison to standard medical therapy.
Quintero 1985	Randomised trial comparing large volume paracentesis versus diuretic treatment in refractory ascites. There was no comparison with TIPS.
Rikkers 1978	Randomised trial comparing selective versus non-selective splenorenal shunt. Did not compare shunt procedure with medical therapy. Was not performed on patients with refractory ascites.
Salerno 1987	Randomised trial comparing paracentesis with/without albumin infusion versus diuretic treatment. There was no comparison with TIPS.
Salerno 2002	Randomised trial comparing TIPS and medical therapy. It is unclear if the patients had refractory ascites. Abstract, intermediate results, no long-term follow up.
Smart 1990	Randomised trial comparing large volume paracentesis with albumin versus medical therapy. There was no comparison with TIPS.
Sola 1994	Randomised trial comparing paracentesis versus diuretic treatment. There was no comparison with TIPS.

Study	Reason for exclusion
Wapnick 1979	Randomised trial comparing peritoneovenous shunt and medical therapy. Did not define refractory ascites, not blinded. Medical therapy consisted of diuretic treatment only, no large volume paracentesis.
Zervos 1996	Randomised trial comparing TIPS versus peritoneovenous shunt in the treatment of refractory ascites. There was no comparison to medical treatment.

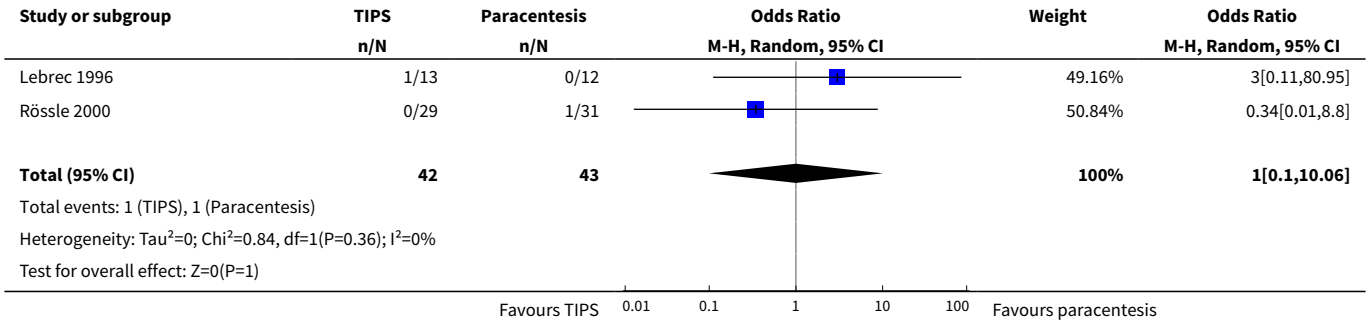
TIPS = transjugular intrahepatic portosystemic stent-shunt

DATA AND ANALYSES

Comparison 1. TIPS versus paracentesis - mortality

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 30-day mortality	2	85	Odds Ratio (M-H, Random, 95% CI)	1.00 [0.10, 10.06]

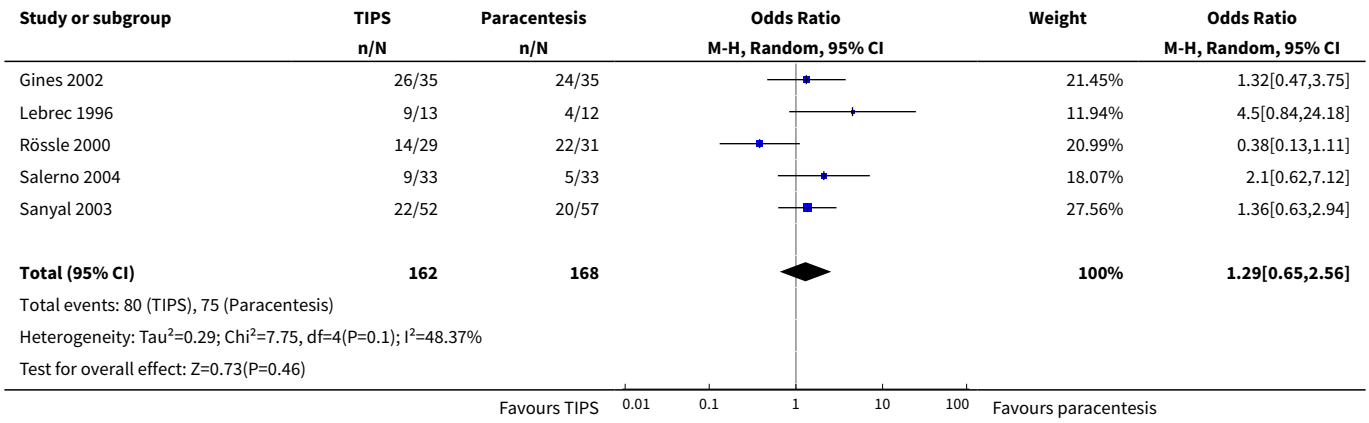
Analysis 1.1. Comparison 1 TIPS versus paracentesis - mortality, Outcome 1 30-day mortality.



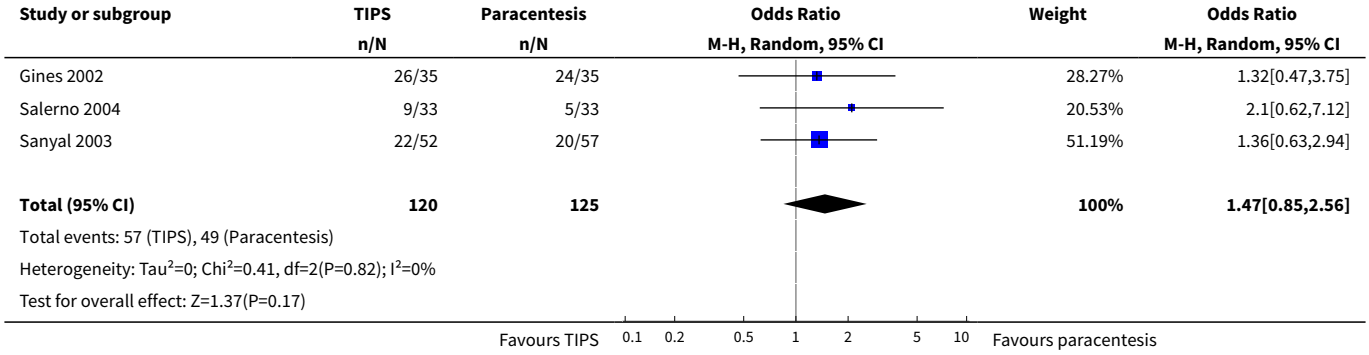
Comparison 2. TIPS versus paracentesis - mortality

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 24-month mortality	5	330	Odds Ratio (M-H, Random, 95% CI)	1.29 [0.65, 2.56]
2 24 months mortality - furosemide 160 mg/d	3	245	Odds Ratio (M-H, Random, 95% CI)	1.47 [0.85, 2.56]
3 24 month mortality - spironolactone 400mg/d	3	239	Odds Ratio (M-H, Random, 95% CI)	0.93 [0.42, 2.02]

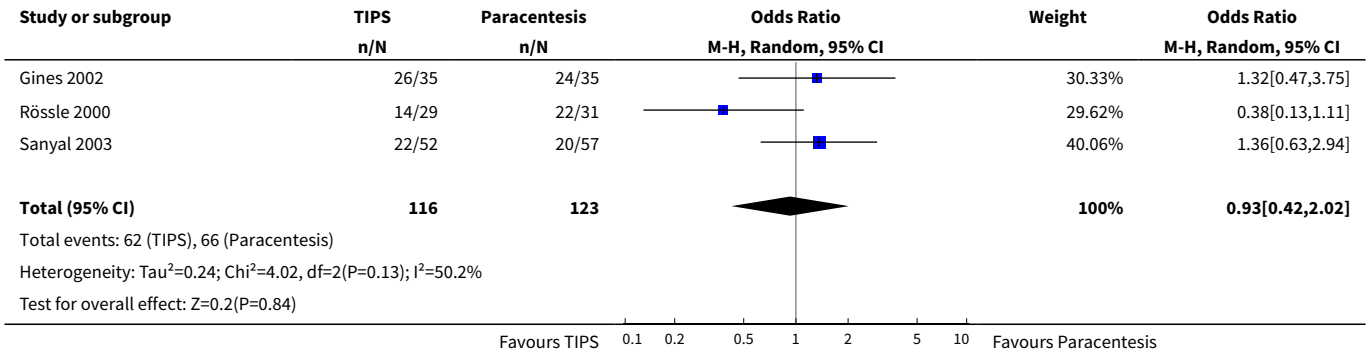
Analysis 2.1. Comparison 2 TIPS versus paracentesis - mortality, Outcome 1 24-month mortality.



Analysis 2.2. Comparison 2 TIPS versus paracentesis - mortality, Outcome 2 24 months mortality - furosemide 160 mg/d.



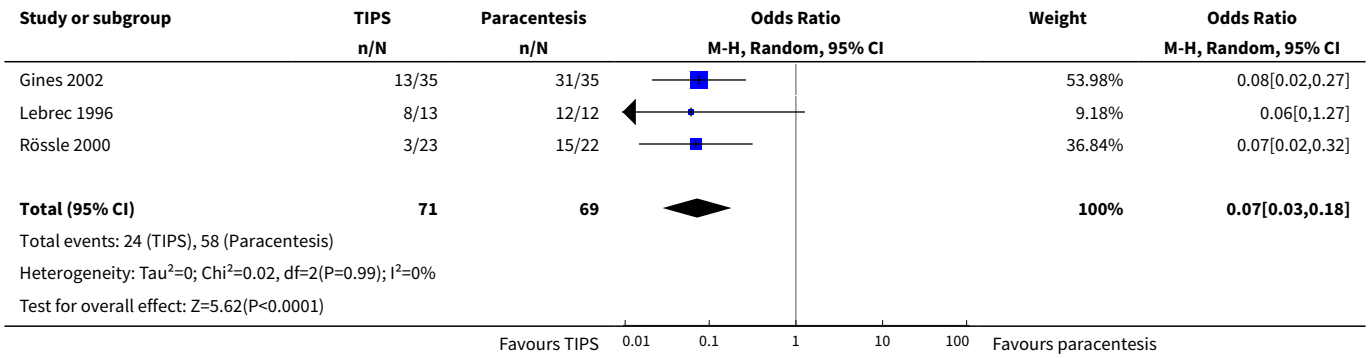
Analysis 2.3. Comparison 2 TIPS versus paracentesis - mortality, Outcome 3 24 month mortality - spironolactone 400mg/d.



Comparison 3. TIPS versus paracentesis - ascites re-accumulation

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 3-months ascites re-accumulation	3	140	Odds Ratio (M-H, Random, 95% CI)	0.07 [0.03, 0.18]

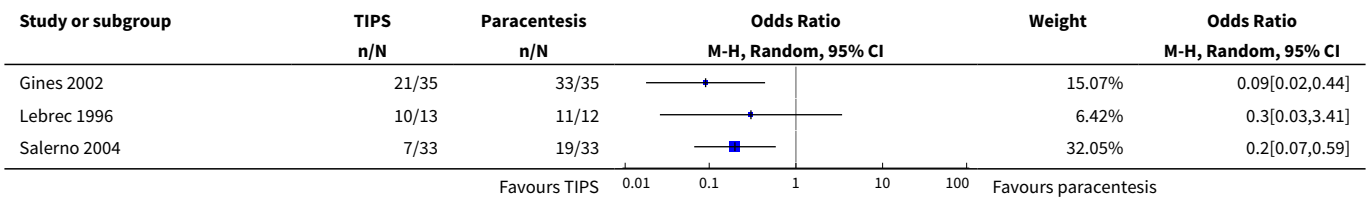
Analysis 3.1. Comparison 3 TIPS versus paracentesis - ascites re-accumulation, Outcome 1 3-months ascites re-accumulation.

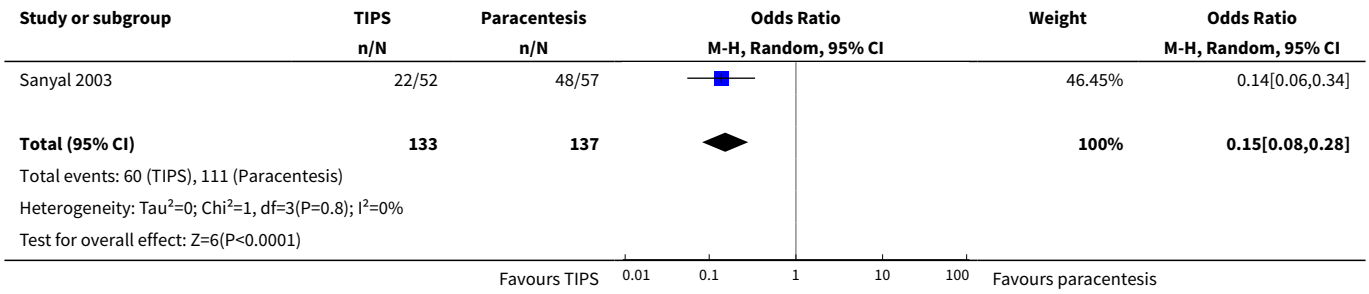


Comparison 4. TIPS versus paracentesis - ascites re-accumulation

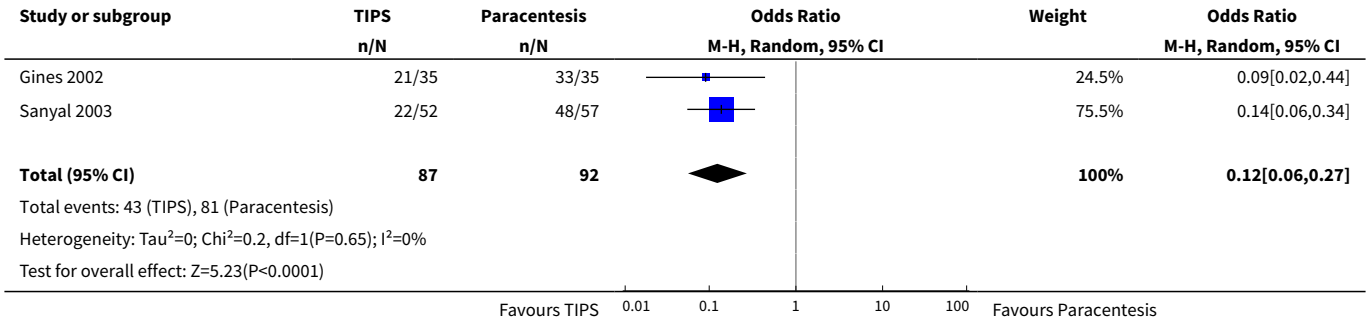
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 12-month ascites re-accumulation	4	270	Odds Ratio (M-H, Random, 95% CI)	0.15 [0.08, 0.28]
2 12 month ascites re-accumulation - furosemide 160mg/d	2	179	Odds Ratio (M-H, Random, 95% CI)	0.12 [0.06, 0.27]
3 12 month ascites re-accumulation - spironolactone 400mg/d	2	179	Odds Ratio (M-H, Random, 95% CI)	0.12 [0.06, 0.27]
4 12 month re-accumulation - sodium < 2g/d	4	270	Odds Ratio (M-H, Random, 95% CI)	0.15 [0.08, 0.28]

Analysis 4.1. Comparison 4 TIPS versus paracentesis - ascites re-accumulation, Outcome 1 12-month ascites re-accumulation.

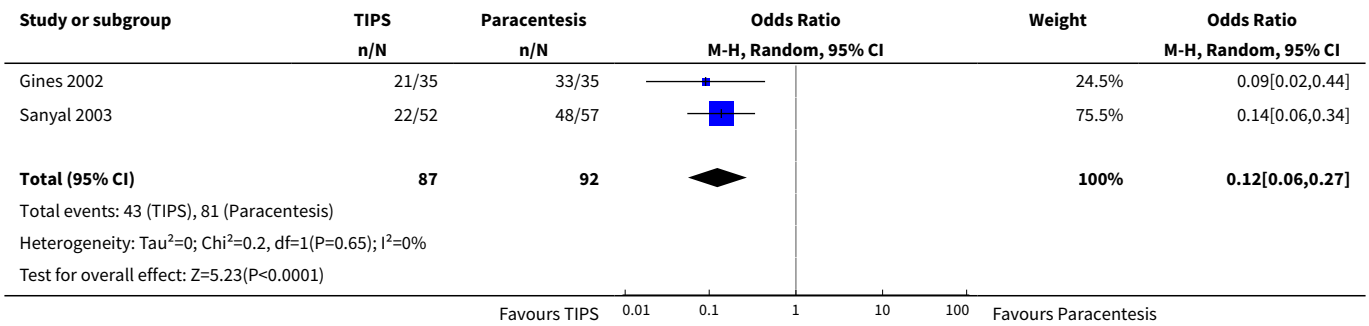




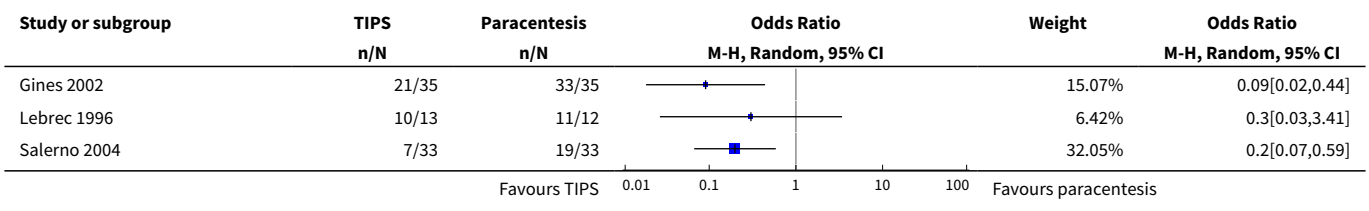
Analysis 4.2. Comparison 4 TIPS versus paracentesis - ascites re-accumulation, Outcome 2 12 month ascites re-accumulation - furosemide 160mg/d.

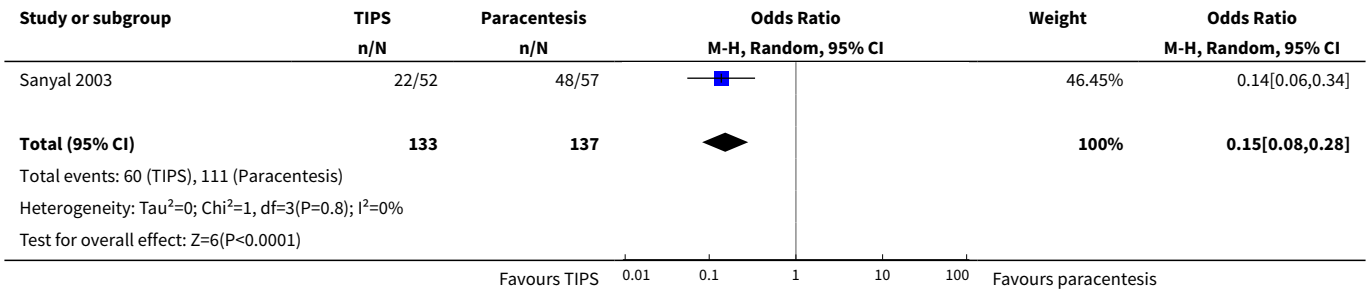


Analysis 4.3. Comparison 4 TIPS versus paracentesis - ascites re-accumulation, Outcome 3 12 month ascites re-accumulation - spironolactone 400mg/d.



Analysis 4.4. Comparison 4 TIPS versus paracentesis - ascites re-accumulation, Outcome 4 12 month re-accumulation - sodium < 2g/d.

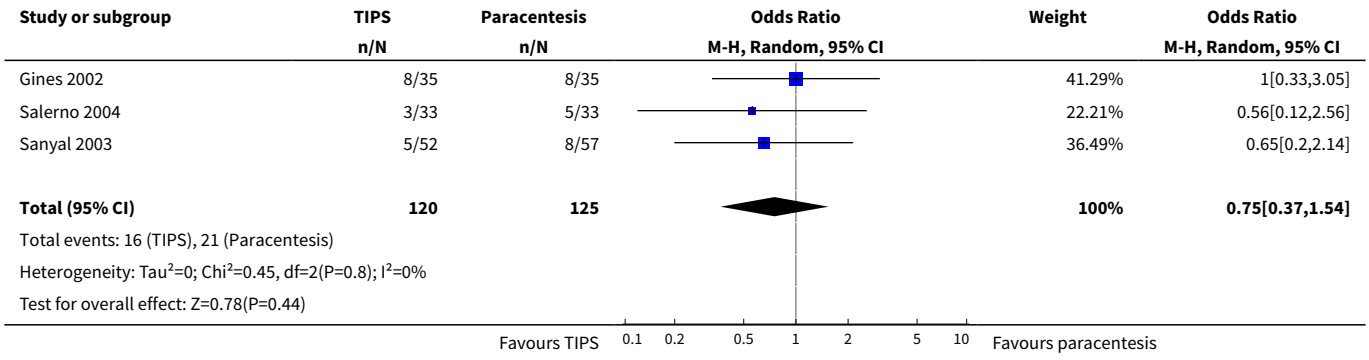




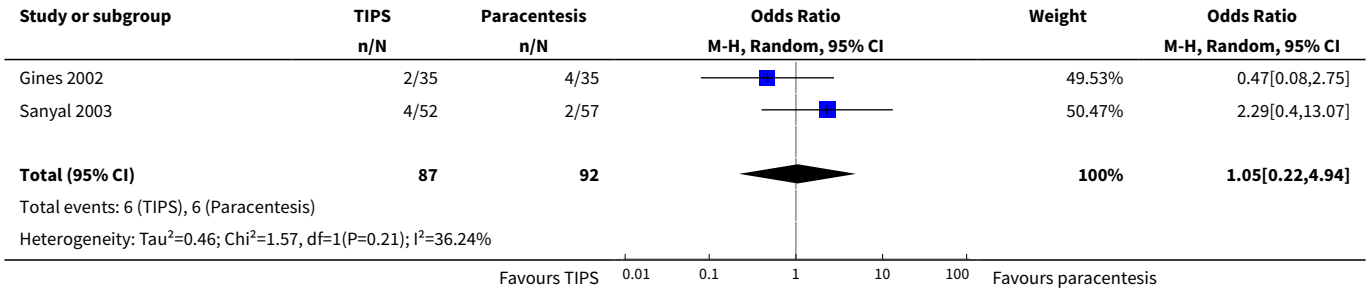
Comparison 5. TIPS versus paracentesis - complications

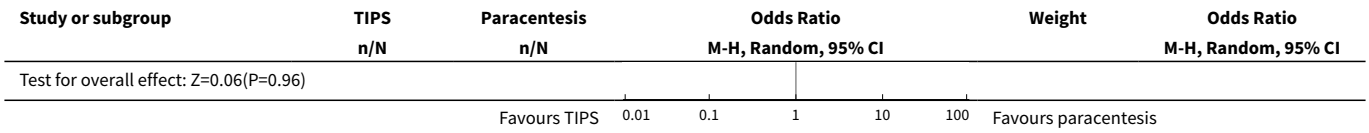
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Gastrointestinal bleeding	3	245	Odds Ratio (M-H, Random, 95% CI)	0.75 [0.37, 1.54]
2 Septecemia/infection	2	179	Odds Ratio (M-H, Random, 95% CI)	1.05 [0.22, 4.94]
3 Acute renal failure	2	179	Odds Ratio (M-H, Random, 95% CI)	0.64 [0.15, 2.72]
4 Hepatic encephalopathy	5	330	Odds Ratio (M-H, Random, 95% CI)	2.24 [1.39, 3.60]

Analysis 5.1. Comparison 5 TIPS versus paracentesis - complications, Outcome 1 Gastrointestinal bleeding.

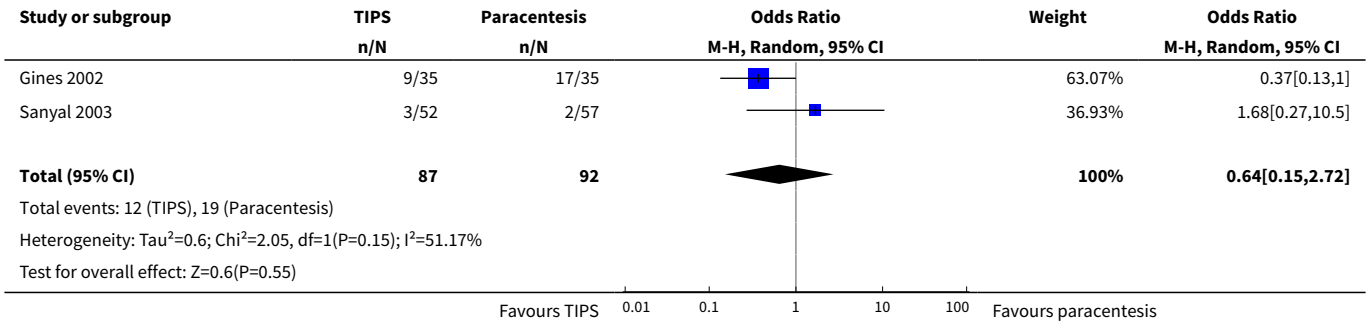


Analysis 5.2. Comparison 5 TIPS versus paracentesis - complications, Outcome 2 Septecemia/infection.

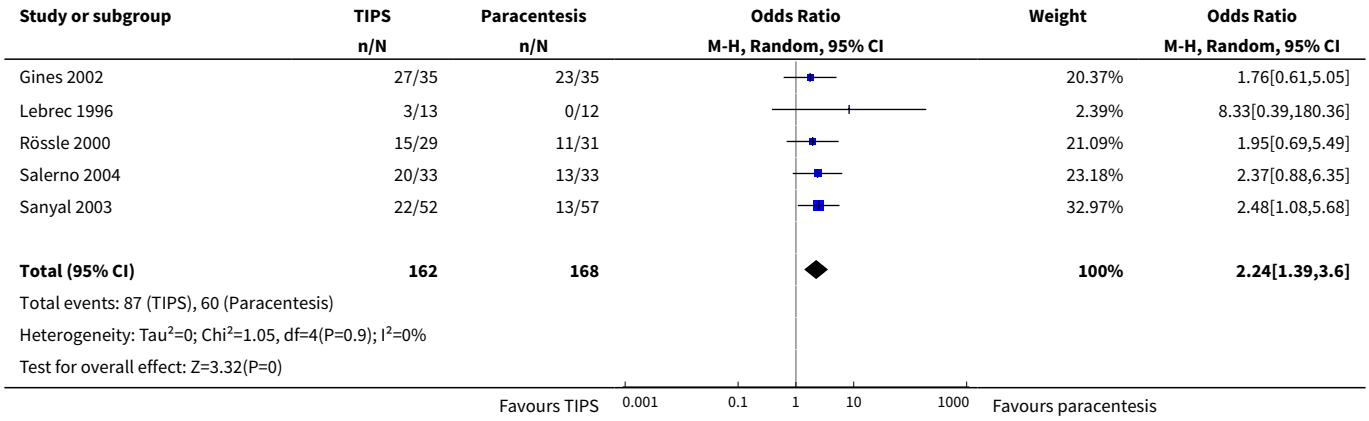




Analysis 5.3. Comparison 5 TIPS versus paracentesis - complications, Outcome 3 Acute renal failure.



Analysis 5.4. Comparison 5 TIPS versus paracentesis - complications, Outcome 4 Hepatic encephalopathy.



APPENDICES

Appendix 1. Search Strategies

Database	Timespan	Search strategy
The Cochrane Hepato-Biliary Group Controlled Trials Register	January 2006.	transjugular intrahepatic port*systemic shunt*' OR TIPS* OR 'peritoneovenous shunt*' OR 'port*systemic anastomosis' OR 'peritoneum vein shunt*') AND ascites

(Continued)

Cochrane Central Register of Controlled Trials in The Cochrane Library	Issue 4, 2005.	#1 PORTASYSTEMIC SHUNT TRANSJUGULAR INTRAHEPATIC explode all trees (MeSH) #2 PERITONEOVENOUS SHUNT explode all trees (MeSH) #3 ((transjugular next intrahepatic next portasystemic next stent-shunt*) or tips* or (peritoneovenous next shunt*) or (portasystemic next anastomosis) or (peritoneum next vein next shunt*)) #4 (#1 or #2 or #3) #5 ASCITES explode all trees (MeSH) #6 (refractory next ascites) #7 (#5 or #6) #8 (#4 and #7)
MEDLINE (WinSPIRS 5.0)	1950 to January 2006.	#1 explode "portosystemic-anastomosis"/ all subheadings #2 explode "peritoneum-vein-shunt"/ all subheadings #3 (transjugular intrahepatic port?systemic stent-shunt*) or TIPS* or (peritoneovenous shunt*) or (port?systemic anastomosis) or (peritoneum vein shunt*) #4 #1 or #2 or #3 #5 explode "ascites"/all subheadings #6 refractory ascites #7 #5 or #6 #8 #4 and #7 #9 random* or blind* or placebo* or meta-analysis #10 #8 and #9
EMBASE (WinSPIRS 5.0)	1980 to January 2006.	#1 explode "Portasystemic-Shunt-Transjugular-Intrahepatic"/ all subheadings #2 explode "Peritoneovenous-Shunt"/ all subheadings #3 (transjugular intrahepatic port?systemic stent-shunt*) or TIPS* or (peritoneovenous shunt*) or (port?systemic anastomosis) or (peritoneum vein shunt*) #4 #1 or #2 or #3 #5 explode "Ascites"/ all subheadings #6 refractory ascites #7 #5 or #6 #8 #4 and #7 #9 random* or blind* or placebo* or meta-analysis #10 #8 and #9
CINAHL (WinSPIRS 5.0)	1982 to August 2004.	#1 explode "Portasystemic-Shunt-Surgical"/ all topical subheadings / all age subheadings #2 (transjugular intrahepatic port?systemic stent-shunt*) or TIPS* or (peritoneovenous shunt*) or (port?systemic anastomosis) or (peritoneum vein shunt*) #3 #1 or #2 #4 explode "Ascites"/ all topical subheadings / all age subheadings #5 refractory ascites #6 #4 or #5 #7 #3 and #6 #8 random* or blind* or placebo* or meta-analysis; #9 #7 and #8 #9 #7 and #8
Science Citation Index Expanded (http://portal.isiknowledge.com/portal.cgi?DestApp=WOS&Func=Frame)	1945 to January 2006.	transjugular intrahepatic port*systemic shunt*' OR TIPS* OR 'peritoneovenous shunt*' OR 'port*systemic anastomosis' OR 'peritoneum vein shunt*') AND ascites

WHAT'S NEW

Date	Event	Description
17 October 2008	Amended	Converted to new review format.

HISTORY

Protocol first published: Issue 2, 2002
Review first published: Issue 3, 2004

Date	Event	Description
23 August 2006	New search has been performed	Conclusions changed.

CONTRIBUTIONS OF AUTHORS

Sammy Saab - conception and design, interpretation of the data, drafting, critical revision, and final approval of the review.

Jose Nieto - design of the study, the analysis and interpretation of the data, drafting, critical revision, and final approval of the review.

David Ly - analysis and interpretation of the data, critical revision and final approval of the review.

Bruce Runyon - critical revision of the review for intellectual content and final approval.

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- No sources of support supplied

External sources

- The Danish Medical Research Coucil's Grant on Getting Research into Practice, Denmark.
- The Copenhagen Hospital Corporation Medical Research Council's Grant on Getting Research into Practice (GRIP), Denmark.

NOTES

Changes performed in the protocol section of this systematic review:

In the published version of the protocol 'Surgical versus medical treatment of refractory ascites' Saab et al, Issue 2, 2002, we intended to let the decision, between using a fixed-effect model or a random-effects model to analyze the data, depend on homogeneity or heterogeneity among the included trials. However, this approach is no longer endorsed by The Cochrane Collaboration and we followed their recommendations.

Further, for clarity we decided to divide the protocol into two parts. Thus, this first review on TIPS versus paracentesis is prepared and is updated for issue 4 2006 of The Cochrane Library. The second review is not prepared yet, but it will compare peritoneovenous shunts and medical treatment.

INDEX TERMS

Medical Subject Headings (MeSH)

*Paracentesis [mortality]; *Portasystemic Shunt, Transjugular Intrahepatic [mortality]; Ascites [etiology] [mortality] [*therapy]; Liver Cirrhosis [*complications]; Randomized Controlled Trials as Topic

MeSH check words

Humans