A meta-analysis of transjugular intrahepatic portosystemic shunt versus paracentesis for refractory ascites
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CRD summary
This review assessed the use of transjugular intrahepatic portosystemic shunt (TIPS) versus paracentesis in the treatment of cirrhotic patients with refractory ascites. The authors concluded that the improved ability of TIPS to control ascites does not result in improved survival, but in an increased incidence of encephalopathy. The conclusions of this generally good quality systematic review are likely to be reliable.

Authors' objectives
To assess the use of transjugular intrahepatic portosystemic shunt (TIPS) versus paracentesis in the treatment of cirrhotic patients with refractory ascites, in terms of mortality and risk of encephalopathy.

Searching
MEDLINE and EMBASE (from 1989 to 2005) and the Cochrane CENTRAL Register were searched for studies published in the English language; the search terms were reported. The authors also searched abstracts from meetings of the American Gastroenterological Association, the American Association for the Study of Liver Disease, the European Association for the Study of the Liver and the British Society of Gastroenterology.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion. Most of the included RCTs were multicentre RCTs.

Specific interventions included in the review
Studies that compared TIPS with repeated large-volume paracentesis were eligible for inclusion. In the included studies, patients allocated to TIPS received a non-covered stent (where stated, most received a balloon expandable stent); patients allocated to paracentesis also received albumin infusion as standard, or when clinically indicated.

Participants included in the review
Studies of cirrhotic patients with refractory ascites were eligible for inclusion. The included studies were of cirrhotic patients with ascites of difficult control, either refractory or recidivant. All studies excluded patients with encephalopathy over grade 2, portal vein thrombosis, hepatocellular carcinoma or parenchymal renal disease. Most of the studies excluded patients with terminal liver disease. The average age of the patients ranged from 50 to 61 years; all patients were younger than 77 years. The proportion of patients with alcoholic cirrhosis ranged from 39 to 83%. The proportion of patients classed as Child C ranged from 22 to 79%, where reported, and the mean Child-Pugh score ranged from 8.7 to 9.4 points.

Outcomes assessed in the review
Studies that reported at least one of the following outcome measures were eligible for inclusion: recurrence of ascites, encephalopathy or mortality. Recurrence of ascites was defined as ascites requiring paracentesis, encephalopathy was defined as any episode of clinically overt encephalopathy, and mortality was defined as any death occurring during follow-up or the need for liver transplantation.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The authors assessed the quality of the included trials on the basis of the following criteria: allocation sequence generated by computer random numbers; allocation concealment; similarity of the groups at baseline (less than 25% difference in any variable); intention-to-treat analysis; and adequate potency of the treatments to detect a difference in mortality. Each criterion was rated as present (1 point) or absent (0 points); the exception was the second criterion, which was worth 3 points if randomisation was central and 1 point if sealed, opaque envelopes were used. Any trial that satisfied at least four of the five criteria was judged to be of a high quality. The authors did not state how many reviewers performed the validity assessment.

**Data extraction**

Two reviewers independently extracted the data from the included studies, and any disagreements were resolved by consensus amongst the review team. Relative risks (RRs) with 95% confidence intervals (CIs) were calculated for each study.

**Methods of synthesis**

How were the studies combined?
The pooled RR and 95% CI were calculated using a fixed-effect meta-analysis unless statistical heterogeneity was observed, in which case a random-effects model (DerSimonian and Laird) was used. For survival analysis, an indirect log hazard ratio and variance estimation were calculated using the log rank test result and the total number of events observed in the two groups; this was expressed as a pooled hazard ratio (HR). The numbers-needed-to-treat (NNT) or -harm (NNH) were calculated as the inverse of the absolute risk difference between the treatment groups.

How were differences between studies investigated?
The chi-squared and I-squared tests were used to assess statistical heterogeneity. Subgroup analyses were performed to assess the effects on the results of study quality, etiology of liver disease, albumin infusion after paracentesis, and the inclusion of patients with recidivant ascites.

**Results of the review**

Five RCTs (n=330) were included in the review.

Three trials were rated high quality, achieving a score of 6 out of a possible 7 points; the other two scored 3 and 4 points.

Recurrence of ascites was statistically significantly lower in the TIPS group than in the paracentesis group (RR 0.56, 95% CI: 0.47, 0.66; NNT 3; 5 RCTs). There was no significant heterogeneity.

Encephalopathy was statistically significantly more common in the TIPS group than in the paracentesis group (RR 1.36, 95% CI: 1.1, 1.68; NNH 6; 5 RCTs). Severe encephalopathy was statistically significantly more common in the TIPS group than in the paracentesis group (RR 1.72, 95% CI: 1.14, 2.58; 4 RCTs). There was no significant heterogeneity for either outcome.

There was no statistically significant difference in mortality between the TIPS group and the paracentesis group (RR 0.93, 95% CI: 0.67, 1.28; 5 RCTs). There was statistically significant heterogeneity for this outcome (p=0.09; I-squared 48%). The pooled HR was 1.09 (95% CI: 0.84, 1.88).

There was no statistically significant difference in liver-related mortality between the TIPS group and the paracentesis group (RR 0.75, 95% CI: 0.53, 1.04; 4 RCTs). There was no significant heterogeneity.

The only subgroup analysis to affect the results was that of the 2 RCTs that included patients with recidivant ascites as well as patients with refractory ascites, which showed statistically significantly lower mortality in the TIPS group (RR 0.68, 95% CI: 0.49, 0.93). There was no statistically significant difference in mortality in the 3 RCTs that only included patients with refractory ascites (RR 1.17, 95% CI: 0.86, 1.6).
Authors' conclusions
In patients with refractory ascites, the improved ability of TIPS to control ascites did not result in improved survival, but in an increased incidence of encephalopathy.

CRD commentary
The review question was clear in terms of the study design, participants, interventions and outcomes of interest. The authors searched relevant electronic databases and conference abstracts to identify studies, thereby reducing the potential for publication bias. However, only studies reported in English were sought, which increases the potential for language bias. Two independent reviewers extracted the data, thus reducing the potential for reviewer bias and errors. However, since the authors did not state how the studies were selected for the review or how many reviewers performed the validity assessment, reviewer bias and error cannot be ruled out. The criteria for assessing the validity of the included studies were appropriate, and the impact of study quality on the results was investigated. Most of the included studies were high quality, which strengthens the results of the review. Adequate details of the included studies were reported. The statistical synthesis appears appropriate. The authors assessed statistical heterogeneity, conducted various subgroup analyses, and potential sources of heterogeneity were discussed.

This was generally a good-quality systematic review and the conclusions are likely to be reliable. The authors' recommendations for future research also appear appropriate.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors stated that the impact of TIPS in patients with recidivant ascites should be evaluated; that future studies should consider variables with an impact on the outcome of patients with refractory ascites, for example, spontaneous improvement in sodium retention; and that future studies should assess health-related quality of life and care costs.

Funding
Ministerio de Ciencia y Tecnologia, grant number BFI 2003-03858; Ministerio de Sanidad y Consumo, Instituto de Salud Carlos III, grant number C03/02.

Bibliographic details

PubMedID
16139922

DOI
10.1016/j.jhep.2005.06.005

Indexing Status
Subject indexing assigned by NLM

MeSH
Ascites /etiography /therapy; Hepatic Encephalopathy /etiography; Humans; Liver Cirrhosis /complications; Paracentesis; Portasystemic Shunt, Transjugular Intrahepatic /adverse effects

AccessionNumber
12005002211
Date bibliographic record published
31/05/2007

Date abstract record published
31/05/2007

Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.