RESEARCH

Trans-jugular intrahepatic porto-systemic shunt placement for refractory ascites: a 'real-world' UK health economic evaluation

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ABSTRACT

Objective To assess the benefit of trans-jugular intrahepatic porto-systemic shunt (TIPS) placement for refractory ascites.

Design A retrospective observational study of all patients undergoing TIPS for refractory ascites in our hospital between 2003 and 2012.

Setting Secondary care.

Patients Cirrhotic patients with refractory ascites.

Main outcome measures We examined direct real-world (National Health Service) health related costs in the year before and after the TIPS procedure took place. Data were collected relating to the need for reintervention and hepatic encephalopathy.

Results Data were available for 24 patients who underwent TIPS for refractory ascites (86% of eligible patients). TIPS was technically successful in all cases. Mean number of bed days in the year prior to TIPS was 30.3 and 14.3 in the year following ($p=0.005$). No patient had ascites at the end of the year after the TIPS with less requirement for paracentesis over the course of the year ($p<0.001$). Mean reduction in cost was £2759 per patient. TIPS was especially cost-effective in patients requiring between 6 and 12 drains per year with a mean saving of £9204 per patient.

Conclusions TIPS is both a clinically effective and economically advantageous therapeutic option for selected patients with refractory ascites.

INTRODUCTION

Ascites is a common complication of cirrhosis and a frequent cause for hospital admission in end stage liver disease.¹ The development of ascites significantly impacts on patients' quality of life, resulting variably in fatigue, bloating, poor nutrition,

dyspnoea and spontaneous bacterial infection. It also heralds a dramatically worse prognosis.^{2,3} Healthcare resource use relating to management of the ascites and other complications of portal hypertension is intensive.

Initially most patients can gain adequate control of their ascites with adherence to a low sodium diet and appropriate diuretic treatment.⁴ As liver disease advances, many patients develop refractory ascites (defined as ascites unresponsive to sodium restriction and dual diuretics at maximum tolerated doses and/or ascites that recur rapidly after paracentesis).⁵ In this situation, the mortality is particularly poor at around 50%–80% at 1 year.^{6–8} In addition, many of these patients will have other complications of portal hypertension, such as variceal bleeding and spontaneous bacterial peritonitis, and are at increased risk of hepatorenal syndrome. Few of these patients are eligible for liver transplantation.

Treatment options for refractory ascites are repeated large-volume paracentesis with albumin replacement and placement of trans-jugular intrahepatic porto-systemic shunt (TIPS). Previous studies have shown no significant difference in the mortality or quality of life with either approach.^{9,10} However, most of these large randomised studies were performed before the use of Polytetrafluoroethane (PTFE) covered stents which have much higher survival rates compared with uncovered stents.^{10,11} Covered TIPS stents combined with increasing experience and understanding of appropriate patient selection (eg, using Model for end stage Liver Disease (MELD)

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scores as predictors of post-TIPS survival) mean it is likely that there will be some survival benefit in addition to the improvement in control of ascites with TIPS over paracentesis.

Although paracentesis is an effective and relatively safe procedure^{12–14} it does not address the underlying portal hypertension. As a result it has to be repeated frequently which has a significant burden on local health resources. A TIPS procedure reduces portal hypertension and is significantly better at keeping patients ascites free.^{9 10 14–18} It also has the theoretical benefits of reduced variceal bleeding and spontaneous bacterial peritonitis (although this has not been borne out in a Cochrane review where there was no significant improvement). The main perceived downsides are cost and limited availability because of necessary expertise required. TIPS has also been associated with increased risk of hepatic encephalopathy.⁹

We were prompted to evaluate our centre's experience with TIPS in this context and were particularly interested in the 'real-world' costs involved. Patients enrolled in trials are usually selected and randomised within a relatively homogenous group not always reflective of all-comers. There is increasing interest in individualising medicine and in day-to-day clinical practice there is much more tailoring of care to the particular nuances of the patient.

METHODS

Patient records were reviewed for all patients receiving TIPS for refractory ascites in our hospital between 1 January 2003 and 1 June 2012.

Information was gathered using a standardised data collection form from the hospital notes and available electronic hospital systems. In patients who were referred from surrounding secondary care institutions we requested any available notes to capture all necessary data. These included demographic data, aetiology of liver disease where clearly established, MELD score at the time of the procedure and data for the 1 year prior to TIPS and 1 year after. We recorded the number and length of hospital stays, ascitic drains, the quantity of Human Albumin Solution, and investigations and procedures for each patient in the study period. The cost of the 'consumables' in each individual TIPS procedure was recorded by interventional radiology. Cases where there was elective coiling of varices were included if the primary indication was refractory ascites (reflecting real-world practice). The portal and hepatic vein pressures preprocedure and postprocedure were recorded as a marker of procedural technical success. Any complications of the TIPS procedure within the study period were identified (specifically encephalopathy as ultimately the only direct complication of the procedure in this study).

The prices of 2012 were used. The cost of one hospital day was standardised at £350 which was a figure provided by the hospital finance department for an

elective admission in the hospital day unit. We use the Bonano catheter system for ascitic drains which costs £35 per unit. One unit (100 ml) of Human Albumin Solution (20%) costs £50 at the time of result analysis (information from hospital pharmacy). One patient had a recurrent hepatic hydrothorax which required draining on multiple occasions.

Admissions were classified as secondary to chronic liver disease if they were complications of portal hypertension, encephalopathy or otherwise felt to be clearly related—in one patient an admission for a strangulated umbilical hernia was included as it was felt secondary to the presence of ascites. Paired t tests were used in statistical analyses.

RESULTS

There were a total of 150 TIPS procedures performed in the study period. Of these, 28 (19%) were primarily for the treatment of refractory ascites (including one patient who had a recurrent hepato-hydrothorax: the cost for this procedure was considered equivalent to an ascitic drain). Nine of these were performed in patients referred from surrounding secondary care institutions and of these four did not have sufficient notes available for a full data set and are subsequently excluded in the study. The remaining 24 cases are subsequently described (86% of potentially eligible patients within study period) with full data on hospital length of stay and resource use.

Patient characteristics: 62.5% of patients were male. Mean age at TIPS procedure was 57.1 (33.3–78.6). The mean MELD score at this time was 13.1 (6–26). Alcoholic cirrhosis was the most common aetiology. There was a mean of 8.5 (1–26) ascitic drains per patient performed in the year preceding TIPS, 30 units of Human Albumin Solution (HAS) used (1–104) and 30.3 inpatient hospital days (6–78) per patient.

In addition to admissions and hospital days for paracentesis (ie, independent of number of drains performed), on average patients had two admissions before TIPS and a mean length of stay of 19.8 hospital days relating to chronic liver disease (21.5 for all admissions). After TIPS the mean number of admissions was 1.3 with a mean number of 10.8 hospital days secondary to chronic liver disease (13.8 days spent in hospital for any cause). The difference in the number of hospital days excluding those for paracentesis was not significant ($p=0.19$). However, when including hospital days for paracentesis, the difference was highly significant ($p=0.01$), mostly reflecting the success in reducing ascites after TIPS (number of ascitic drains 8.5 vs 1.0; $p=0.00$).

The number of days spent in hospital where the primary indication for admission was encephalopathy increased after procedure from a mean of 2.0 (0–27) to a mean of 7.0 (0–117). Five patients had admissions for encephalopathy prior to TIPS which increased to nine after (38%). Seven patients

developed new encephalopathy after TIPS and interestingly three patients who had admissions for encephalopathy preprocedure did not have any post-TIPS.

All TIPS procedures were technically successful at the time of the index procedure with reductions in the porto-systemic gradient for all (mean reduction 15.0 mm Hg). There were no immediate complications. All patients received covered stents. One patient required their TIPS narrowing for refractory encephalopathy but otherwise no reintervention was required. There were no episodes of TIPS blockage during the follow-up period.

The mean TIPS survival to the end of study period was 25.9 months but there was a wide distribution (5 days to 5 years; SD 18.7). In all, 65% survived at least 1 year. One patient only survived for 5 days due to her liver disease being more severe than initially appreciated.

The majority of patients had no clinical or radiological evidence of ascites after their procedures (77% at 28 days). This progressively improved throughout the study period. At 6 months, only 12% of patients required ascitic drainage and at 1 year no patients who survived this long had detectable ascites. The incidence of clinically evident encephalopathy was 15% at 1 month, 20% at 6 months and 12% at 1 year.

The compound cost of their care is illustrated in table 1. The average net saving was £2759 for an individual patient as compared with the costs involved in their care in the year preceding TIPS. This number includes the cost of the procedure itself and the management of any complications requiring hospital admission.

In patients who required six or less drains in the year preceding TIPS (n=13), the net average saving was £995 per patient. In patients requiring 6–12 drains in the year preceding TIPS (n=6), the average saving was £9203.68 per patient. In patients requiring more than 12 drains (n=5) in the year preceding, there was a net cost of £1409.83 but this figure was heavily influenced by one patient who had a 106-day hospital admission (total net cost £24 258.85) after the procedure mainly due to a considerable delay in discharge while suitable accommodation was found, and unrelated to the TIPS procedure or liver disease directly. With this patient excluded as an outlier, the average net saving was £4569.86.

DISCUSSION

In this study we have found that, in the majority, TIPS is a cost-effective and clinically useful procedure for patients with refractory ascites who would have otherwise been attending for frequent paracentesis. It becomes cost-effective within 1 year of intervention and therefore in patients who survive longer than this period it becomes increasingly cost-effective. The

biggest contributor to the overall cost of care is the number of inpatient hospital days for each patient and there is a significantly reduced attendance to hospital after TIPS procedure. There is a suggestion that TIPS reduces hospital days independently from its contribution in reducing attendance for paracentesis but this was not significant in this small study. As well as absolute cost savings this will also free up resources for use elsewhere. The PTFE stent is the single largest contributing cost to the procedural costs.

Careful patient selection improves results and cost-effectiveness of TIPS. In general, the best patients are those who have a fast rate of ascites accumulation, stable and less advanced liver disease, no previous encephalopathy and who are likely to survive longer. The most cost-effective group in this series are those patients who were having paracentesis every 1–2 months. There are other considerations (eg, severe symptoms) which are more difficult to quantify and ultimately each case should be assessed individually by experienced clinicians.

We have not been able to capture out of hospital costs in this study. However, patients spent significantly less time in hospital postprocedure which we take to be a marker of improved health and quality of life. At least some of the patients are known to have returned to work after the procedure which if anything may have enhanced the economic and societal benefits further.

Of particular note in this series is a very high rate of technical procedural success. Some may see the reduction in porto-systemic gradients as quite aggressive. Despite this reduction, there was an incidence of encephalopathy which is largely in keeping with other studies reported rates.^{10 14 18} All of the inserted stents were PTFE covered and there was also no incidence of stent stenosis, thereby avoiding the cost of reintervention.

This is a small retrospective study from a single centre which limits extrapolation to other centres, particularly those outside the UK. The costs involved are estimated and therefore need to be interpreted with appropriate scepticism; for example, there are significant differences in the cost of a hospital day depending on the ward and level of care provided. However, the study aims to present what actually happens in our hospital, which is likely to be similar to other similar centres providing TIPS insertion. As a retrospective study we could not include any quality of life assessments which would help in a more thorough evaluation.

CONCLUSIONS

In our selected patients, TIPS for refractory ascites has a very high technical and clinical success rate, particularly in patients requiring paracentesis at a frequency of more than once every 2 months. Bed occupancy is reduced compared with care pre-TIPS. Cost-effectiveness is achieved by 1 year and as a result resources are released

Table 1 Breakdown of costs by individual patient

Patient number	Real-world cost in the year preprocedure (£)	Cost of TIPS procedure* (£)	Real-world cost in the year postprocedure (£)	Net saving at 1 year postprocedure† (£)
1	21 710	2575.27	15 375	3759.73
2	11 910	5560.71	2500	3849.29
3	9425	2829.36	11 425	−4829.36
4	5960	3235.55	2535	189.45
5	16 040	2699.96	7000	6340.04
6	15 430	2330.66	135	12 964.34
7	3350	2553.89	1400	−603.89
8	2650	3428.45	1050	−1828.45
9	24 200	2464.76	7240	14 495.24
10	16 940	4655.51	9885	2399.49
11	6735	2464.98	14 355	−10 084.98
12	8030	2478.18	3150	2401.82
13	2910	2868.81	1860	−1818.81
14	14 155	2357.89	700	11 097.11
15	22 510	2430.84	1750	18 329.16
16	5980	3404.77	8400	−5824.77
17	9670	2484.01	1750	5435.99
18	14 025	3179.34	5255	5590.66
19	5345	2468.85	700	2176.15
20	16 200	2658.85	37 800	−24 258.85
21	10 050	3098.13	700	6251.87
22	17 405	2487.39	1750	13 167.61
23	11 110	2487.39	700	7922.61
24	2975	2487.39	1400	−912.39
Total net saving:				£66 209.06

*Variable cost due to use of different stent types and coils plus different volumes of contrast.

†Net saving calculated by subtracting procedure cost and cost after TIPS from cost in year prior.

TIPS, trans-jugular intrahepatic porto-systemic shunt.

for use elsewhere. The main downside was of encephalopathy which could usually be managed out of hospital.

What this study adds

In appropriately selected patients TIPS is also a cost effective way of treating refractory ascites.

How might it impact on clinical practice in the foreseeable future

Early referral for TIPS should be considered in patients who attend frequently for therapeutic paracentesis.

Contributors MW confirms that all authors contributed to the design and execution of this study and were all involved in the analysis of results and the production and reviewing of the manuscript. MJP, MW and NG collected and analysed the clinical data. MJP and MW wrote the manuscript. BS and NH inserted the TIPS and collated and analysed the radiology data. MW, BS and NH conceived the idea for the study. All authors

reviewed and amended the final draft of the paper and the resubmitted version. MW is responsible for the overall content and is the guarantor for the data presented. The authors acknowledge the contribution of Dr Charlotte Pither who helped collect some of the source data.

Competing interests None.

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