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Use of Peritoneovenous Shunts in Patients with Intractable Ascites in the Era of Liver Transplantation

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Abstract

Background: Intractable ascites is a debilitating complication of decompensated liver disease. Peritoneovenous shunts are an option when medical treatment or radiological shunts have failed or are contraindicated. The aim of this study was to see if in those patients with intractable ascites awaiting or considered unsuitable for liver transplantation, the insertion of a peritoneovenous shunt improved the clinical outcome of the patient.

Materials and Methods: Patients who had insertion of a peritoneovenous shunt for intractable ascites between January 2012 and October 2017 were studied. Clinical and biochemical data was compared before and after shunt insertion and outcomes reviewed.

Results: Fourteen patients who had a peritoneovenous shunt inserted were recruited into the study. The main indication was ascites arising from cirrhosis due to alcohol (43%). Of nine patients discharged from hospital, 8 (89%) decreased their ascites, with 4 of them (44%) not requiring further paracentesis. All 6 patients with renal impairment who were discharged improved their renal function after shunt insertion.

Discussion and Conclusion: Insertion of a peritoneovenous shunt is an option for patients with refractory ascites not responding to medical treatment, when other therapies are contraindicated. In addition to palliation of symptoms, it also improves clinical outcomes and can serve as a bridge to liver transplantation.

Keywords: Ascites; Drainage; Liver Failure; Peritoneovenous

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Introduction

Formation of ascites is the first sign of decompensation of liver disease in approximately half of cirrhotic patients [1]. The etiology of ascites is multifactorial but revolves around sinusoidal hypertension producing outflow obstruction and increased retention of sodium and water in the kidneys [2]. The progression from compensated to decompensated disease, and refractory ascites not responding to diuretics results in a debilitating condition severely limiting the quality and length of life of the patient. Leveen et al. [3] first described the use of a surgically inserted single valve unidirectional shunt to return the ascitic fluid to the circulation in 1974. Since then several modifications have been made to make it more efficient and compact. We report our experience of using Peritoneovenous Shunts (PVS) in a single institution where liver transplantation is readily available. Our aim was to see if in those patients with intractable ascites awaiting or considered unsuitable for liver transplantation, the insertion of a peritoneovenous shunt improved the clinical outcome of the patient.

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Methods

Patients who had insertion of a peritoneovenous shunt for intractable ascites from January 2012 till October 2017 were studied. Case notes were reviewed retrospectively for each patient. Patient demographics were collected. Clinical and biochemical data was compared before insertion of shunt and post-operatively. Patients were usually considered for PVS if Transjugular Intrahepatic Portosystemic Shunting (TIPS) was contraindicated due to portal vein thrombosis, synthetic dysfunction, and malignancy, history of encephalopathy or short life expectancy. Patients whose peritoneovenous shunt was inserted for conditions unrelated to liver disease were excluded (Figure 1).

Denver® shunts (Denver Biomaterials, Golden, CO, USA) were used for this purpose and were

inserted surgically. A Denver shunt is a device consisting of two catheters connected to a flexible pump chamber containing one or two valves. A small transverse subcostal incision is made. The rectus sheath is opened, muscle split, peritoneal cavity entered and ascites drained. In our institution enough ascites is drained as to make the patient comfortable. Depending on the amount drained, albumin may or may not be given. The fenestrated peritoneal limb is inserted through this opening into the peritoneal cavity and secured using purse string sutures. The muscles are approximated. Another incision is made at the level of the sternocleidomastoid in the neck. The venous catheter of the device is then tunneled subcutaneously and inserted through a venotomy made in the internal jugular vein, with the distal tip positioned into the superior vena cava/right atrial junction, and is also secured with sutures. The pump chamber is positioned in the lower chest and it is pumped to prime the device and the wounds are both closed. Prophylactic antibiotics are given for 24 h and the patient is instructed to press the chamber five times on four occasions each day in order to maintain patency of the shunt and prevent thrombosis at the tip of the venous catheter.

When the intra-abdominal pressure is 3 mmHg above the central venous pressure, ascitic fluid moves into the shunt and back into the circulation. The valves in the pump chamber prevent reflux of blood into the chamber. We use shunts with double valves. If a shunt with a single valve is used, as is ideal with thick viscous fluid like chylous ascites, the patient has to manually compress the venous catheter after pumping to prevent reflux. When diuretics have been stopped pre-operatively because of intolerance, they can be reintroduced gradually until the fluid overload is resolved. The patients were followed up till their death or July 2018. An interactive online software was used for statistical analysis and can be found at http://www.quantpsy.org/chisq/chisq.htm. A p-value of <0.05 was considered statistically significant.

Results

Baseline characteristics

Between January 2012 and October 2017, 16 patients with medically intractable ascites had insertion of a Denver shunt. Two patients with ascites secondary to chronic pancreatitis and chronic lymphocytic leukemia were excluded. Patient demographics are shown in Table 1. The cause of ascites is shown in Table 2. The main indication was ascites arising from cirrhosis due to alcohol related liver disease (43%) followed by hepatitis C (22%). 57% of patients had renal impairment with a median estimated Glomerular Filtration Rate (eGFR) of 54 mL/min/1.73 m^2 (IQR 42 to 90), 64% had a history of variceal bleeding, 50% had previous episodes of hepatic encephalopathy and 36% had had spontaneous bacterial peritonitis. Only one patient was listed for liver transplantation due to medical contraindications in the other patients, including persistent drinking, high cardiac risk for surgery, malnutrition, and sarcopenia.

Complications

Of 14 patients, 3 died within thirty days of valve insertion, with a 30-day mortality rate of 21%. A patient with Non-Alcoholic Steatohepatitis (NASH) cirrhosis died within 9 days whilst another one with cystic fibrosis related liver disease died 13 days after insertion, both due to continued liver decompensation, rather than related to shunt insertion. Another patient with HCV recurrence in a liver graft (transplanted 8 years previously), died 30 days after insertion due to sepsis and gastrointestinal bleeding. Another patient with alcohol related Chronic Liver Disease (ALD) and Hepatocellular Carcinoma (HCC), had initial improvement of ascites but developed gastrointestinal bleeding and died 33 days after insertion.

There was one problematic access in the patient with cystic fibrosis where the venous limb of the shunt was inserted into the subclavian vein, which was the only patent vessel due to bilateral internal jugular thrombosis from previous central line insertions.

A patient with Hepatitis C Virus (HCV) developed infection related to the shunt. This responded to antibiotics but was too unwell to have it removed. This patient had gastrointestinal bleeding and died two months postshunt insertion. One patient had pulmonary edema and one patient had an episode of encephalopathy, all of which resolved spontaneously. This gives a morbidity of 43%. A patient with ALD had late infection of the shunt; 18 months post insertion and requires re-insertion.

Table 1: Patient Demographics (n=14) and baseline values preshunt and at follow up.

Male: Female	07:07	
Median (IQR) Age/yrs	56 (49-64)	
Renal Impairment	8 (57%)	
Gastrointestinal bleeding	9 (64%)	
Encephalopathy	7 (50%)	
Spontaneous bacterial Peritonitis	5 (36%)	
Diuretic Intolerant	10 (71%)	
	Pre-shunt	Post-shunt
Median (IQR) eGFR ml/min/1.73 m^2	54 (42-90)	78 (52.5-90)
Median (IQR) Bilirubin µmol/l	31.5 (18-63)	31 (9-85)
Median (IQR) Albumin g/l	35.5 (29-39)	33 (29-39)
Median (IQR) weight kg	69 (53-85)	64 (49.5-87)

Table 2: Underlying liver disease causing ascites.

Alcoholic Liver Disease	6 (43%)
Viral Hepatitis	3 (22%)
Non-Alcoholic Steatohepatitis	2 (14%)
Primary Biliary Cirrhosis	1 (7%)
Cystic Fibrosis related liver disease	1 (7%)
Primary Hepatocellular Carcinoma	1 (7%)

Table 3: Variables in relation to clinical situation (values are median, IQR).

	Improved	Not improved	P values
eGFR pre-shunt	54 (36.5-80)	54 (49-90)	
Post-shunt ml/min/1.73 m^2	84 (62-90)	76 (31.5-90)	**p=0.69**
Bilirubin pre-shunt	20 (11 - 33)	52 (32-83)	
Post-shunt	11.5 (5-27.5)	108.5 (54-455)	**p=0.001**
Albumin pre-shunt	34 (29-38.5)	36.5 (31-39)	
Post-shunt	32 (30-39.5)	33.5 (27-36)	**p=0.94**
Weight pre-shunt	66 (55-86)	61 (53-73)	
Post-shunt	65.5 (55-96)	56 (40-77)	**p=0.76**
UKELD score	53.5 (52-56)	61.5 (59-67)	
≤ 50	1	-	
51–60	7	3	
≥ 61	-	3	**p=0.07**
MELD score	15 (11-20)	24 (20-32)	

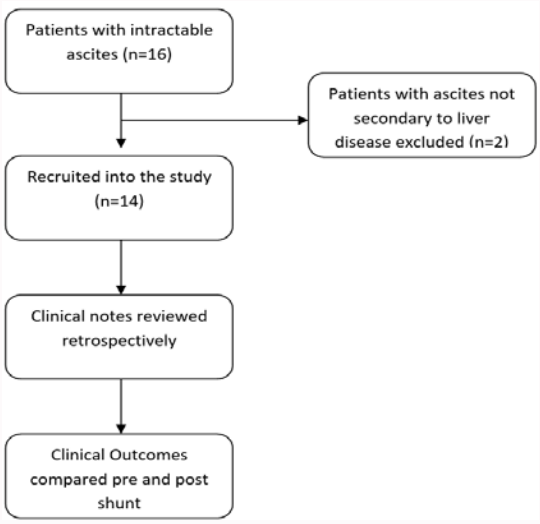

Figure 1: Flowchart showing study design.

Efficacy of peritoneovenous shunts

Median variables before and after shunt insertion are shown in Table 1. Best values postshunt insertions were taken. Of note is that renal function (eGFR) was better after shunt insertion (78 *vs.* 54 ml/min/1.73 m^2), especially in those who improved clinically (84 *vs.* 54 ml/min/1.73 m^2, Table 3). Serum bilirubin was lower post shunt in those who were relieved of their ascites. This reached statistical significance (p=0.001). Table 3 compares median variables pre- and post-shunt insertion in relation to clinical progress, i.e. whether they improved or not.

Of 9 patients who survived longer term follow up, 4 (44%) were permanently relieved of ascites and did not require further paracentesis. Four patients were improved but 3 patients required one paracentesis and one patient two paracentesis post-procedure. Pre-operatively the majority of these patients required weekly large volume paracentesis, giving a success rate in those patients who make it out of hospital of 89%. One patient (11%) was not helped by the shunt. Hepatic hydrothorax resolved in two patients post shunt.

Of 8 patients with pre-insertion renal impairment, 6 improved, all of whom were discharged from hospital. 3 patients maintained their renal function over the period of follow up. One patient on dialysis for 4 months managed to come off dialysis for two years before requiring further renal support. Patients with UKELD score above 60 did not improve (p=0.07, Table 3). In this cohort lower scores did not confer a survival benefit.

Survival

Four patients are alive with a median follow up of 365 days (range 9 to 1030 days). Kaplan-Meier survival analysis is presented in Figure 2. A patient with ALD is alive 34 months after insertion. This patient had hepatorenal syndrome and managed to come off dialysis. He recompensated and his liver function tests remained well, obviating the need for a liver transplant. One patient with Primary Bilary Cirrhosis was successfully transplanted 8 months after insertion and is clinically well 19 months post insertion. Two other patients with ALD are doing well 19 and 24 months after the insertion of the shunt.

A patient with poorly differentiated hepatocellular carcinoma died six months after insertion although her ascites was relieved

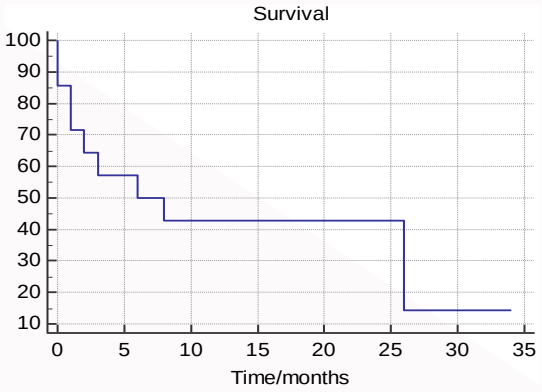

Figure 2: Kaplan-Meier curve showing long term survival.

by the shunt. Two patients with ALD and HCV cirrhosis died 26 months after the PVS. In both cases the ascites was relieved although the patient with ALD required two further paracentesis. A patient with NASH was relieved of ascites but died 3 months post insertion. Another patient with ALD died at 8 months post insertion. The PVS did not relieve the ascites in this case.

Discussion

Leveen et al. [3], in their original paper, described their experience of 45 patients with intractable ascites treated with a LeVeen shunt. As in our series, some of these patients (n=9) were in the terminal phase of their disease. Two required shunt removal following infection. Of 34 patients, 26 (76%) cleared their ascites at a follow up of six to eighteen months. The authors confirmed this finding in a later paper [4] reporting their further experience with PVS. Of 9 patients with hepatorenal syndrome, 5 improved after PVS. These two papers showed that resolution of ascites led to better nutrition and increased muscle mass, as patients are able to eat more.

Subsequently, there have been conflicting reports as to the efficacy or otherwise of PVS. A comparison with TIPS by Rosemurgy et al. [5] randomized 32 patients with medically intractable ascites to either TIPS or PVS. Median duration of shunt patency was similar between the two groups but assisted shunt patency (i.e. after intervention to unblock or replace the shunt) was longer after TIPS (31.1 months *vs.* 13.1 months, p<0.01). Survival after TIPS was 28.7 months *vs.* 16.1 months after PVS. Control of ascites was achieved more rapidly after PVS then TIPS (73% *vs.* 46% at 1 month) but longer-term efficacy favored TIPS (85% *vs.* 40% at 3 years). The authors of this paper therefore concluded that TIPS should be preferentially used if the patient with intractable ascites had prospects of long-term survival and concluded that their paper was "A requiem for peritoneovenous shunt."

Dumortier et al. [6] compared 36 patients who had PVS insertion after being listed for liver transplantation with a historical cohort of 18 patients listed for transplantation without PVS insertion. The authors found that PVS provided effective palliation in 30 patients (83%) and median glomerular filtration rate improved significantly from 0.642 to 0.987 ml/s (p<0.05). Of 36 patients listed, 18 were transplanted. When compared to the historical cohort, they found that the incidence of post liver transplantation renal failure was significantly lower in the PVS cohort (3/18 *vs.* 13/18, p<0.05). During liver transplant, red blood cell transfusion requirements were significantly lower in the PVS groups (4 units *vs.* 7 units, p<0.05) and

concluded that PVS could be effective bridging therapy for listed transplantation candidates with refractory ascites, when the waiting time to transplant is not long.

More recently, Piccirrillo et al. [7] reported on 62 patients with intractable ascites who were not suitable for TIPS or regular paracentensis and underwent insertion of PVS. Median survival was 13 months in patients with no complications, 8 months in those with transient pain, and 3 months in those with blockage or infection. After shunt surgery, 35 patients (56%) did not require paracentesis, 20 (32%) required a single paracentesis, while 7 (12%) needed two paracentesis. Won et al. [8] also reported their experience of percutaneous placement of Denver shunt in 55 patients with refractory ascites. 17 of these patients had ascites secondary to carcinomatosis. Symptomatic improvement was achieved in all but one patient. The overall survival rate was 70.3% at 30 days, 44.6% at 180 days, and 30.9% at 1 year, with a mean shunt patency of 77.5%. From the studies mentioned above only the latter one included malignant ascites. The other studies were concerned mainly with hepatic ascites arising mostly from either alcohol or viral related cirrhosis. Only the study by Rosemurgy et al. [5] included patients being considered for liver transplantation.

Our group of patients was a heterogeneous group and included patients with end-stage liver disease and malignant hepatobiliary disease. Our overall mortality rate of 21% at 30 days has to be taken in context of some patients being very sick with disease at time of insertion. In several studies mentioned above, patients who were at the terminal stage of their disease were excluded. Our morbidity rate of 43% also compares well, with rates in the above studies varying from 18% to 50% [6-8]. Our out of hospital efficacy rate of 89% is similar to figures mentioned above. Even in the palliative setting the PVS helped. In one patient the PVS served as a bridge to liver transplantation. Another patient who was declined for liver transplant because of co-morbidities, improved to the point of recompensation postshunt insertion and not requiring transplantation. In those patients who were relieved of ascites, bilirubin and renal function improved, although the latter didn't reach statistical significance.

An automated subcutaneous pump which moves ascites from the peritoneal cavity into the bladder has also been described [9]. In a recent randomized trial, this pump significantly decreases the requirements for paracentesis compared with standard large volume paracentesis. There was also a significant higher rate of adverse events in the automated pump group (mainly acute kidney injury and pump related issues) [10].

Our study is a retrospective study with small numbers. However, peritoneovenous shunts continue to have a definite role in the management of selected patients with intractable ascites in the era of liver transplantation. They are of value if TIPS is contraindicated, and may improve renal function, even in patients with established hepatorenal syndrome. PVS can also be used effectively as a palliative measure and as a bridge to liver transplantation.

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