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Percutaneous implant of Denver peritoneovenous shunt for treatment of refractory ascites: a single center retrospective study

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Abstract. – OBJECTIVE: Refractory ascites is defined as a lack of response to high doses of diuretics or the development of diuretic related side effects, which compel the patient to discontinue the diuretic treatment. Current therapeutic strategies include repeated large-volume paracentesis and transjugular intrahepatic portosystemic shunts (TIPS). Peritoneovenous shunt (Denver shunt) should be considered for patients with refractory ascites who are not candidates for paracentesis or TIPS. This study presents our case series in the implant of Denver peritoneovenous shunt.

PATIENTS AND METHODS: Sixty-two patients underwent percutaneous placement of Denver shunt between November 2003 and July 2014. There were 36 men and 26 women. Ascites was secondary to alcoholic cirrhosis in six patients, cryptogenic cirrhosis in six, and virus-related cirrhosis in fifty of them. Liver cirrhosis was classified as Child B in 22 patients and Child C in 40 (no patient was Child A).

RESULTS: All implants were successfully performed. There were no intraoperative problems or lethal complications; our patients were hospitalized for 2 or 3 days. Postoperative complications included: infection of the shunt in 3 patients (4.8%), shunt obstruction in 4 (6.4%) and transient abdominal pain in 4 (6.4%). Significant symptomatic relief was obtained in all patients.

CONCLUSIONS: The percutaneous placement of a Denver shunt is a technically feasible and effective method for symptomatic relief of refractory ascites.

Key Words:
Refractory ascites, Cirrhosis, PVS, TIPS, Paracentesis.

List of Abbreviations

TIPS: Transjugular intrahepatic portosystemic shunts; PVS: Peritoneovenous shunt; OS: Overall survival; HR: Hazard Ratio; DIC: Disseminated intravascular coagulopathy.

Introduction

Ascites is the most frequent complication of cirrhosis and it is related to splanchnic vasodilatation leading to the development of hyperdynamic circulation, ineffective volemia and activation of the vasoconstrictor system[1]. Ascites is an adverse consequence of hemodynamic dysfunctions that increase nitric oxide production[2]. Refractory ascites is characterized by a failure of response to common treatments like a low sodium diet and diuretics[3]. It can be an expression of hepatic cirrhosis or of a malignancy in some cases[4]. The therapeutic options that are usually considered in patients with refractory ascites are repeated paracenteses or the positioning of Transjugular Intrahepatic Portosystemic Shunts (TIPS). Both techniques, however, may induce several side effects. The peritoneovenous shunt (PVS) has been reported as an appropriate alternative treatment for managing refractory ascites[5]; it's an implantable device that carries the ascites into the systemic circulation through a surgically placed subcutaneous plastic cannula with a one-way pressure valve[6,7]. The aim of this retrospective study was to evaluate the long-term outcomes of

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PVS (Denver shunt, Denver Biomaterials, Golden, CO, USA) in cirrhotic patients with refractory ascites treated at our institute.

Patients and Methods

Patients

Retrospectively, we analyzed sixty-two patients who underwent placement of a Denver shunt for the treatment of refractory ascites at our institute from November 2003 to July 2014. The trial was approved by the "Foundation G. Pascale" Institutional Review Board, Naples, Italy. Patients with hepatocellular carcinoma or other malignancies were excluded from our study. Before surgery, all patients had received various medical treatments, including the execution of paracentesis and administration of diuretics. According to the criteria of the International Ascites Club (8), the refractory ascites is defined when: (1) the patient did not respond to sodium chloride restriction (5 g/24 hours) and to the administration of the maximum doses of diuretics (up to 400 mg/day of spironolactone and up to 160 mg/day of furosemide); (2) the patient developed side effects which in turn precluded the administration of effective doses of diuretics; (3) over the last twelve months, he was hospitalized at least 3 times for having high ascitic fluid. The presence of hepato-renal syndrome, a bilirubin value more than 7 mg/dl or value of PT-INR greater than 2.2 were considered as contraindications to the procedure.

Methods

The procedure is performed under local anesthesia. The Denver shunt consists of fenestrated peritoneal catheter, venous catheter, and flexible pump chamber containing a one-way valve. The pump chamber site was made over the lower rib cage to facilitate manual compression of the pump. The peritoneal end of the shunt was placed at the most caudal part of the pelvis, the internal jugular vein detected by the ultrasound was chosen as a venous access, while the final location of the tip of the venous limb of the shunt was evaluated by fluoroscopy. Before surgery, most of the ascites fluid was removed and the patient received antibiotic prophylaxis. All procedures were successful and patients were discharged 1-2 days later, without any complications. After the procedure, patients were followed on an outpatients' basis. The measurement of abdominal circumference was performed before the procedure and every 3 days for 30 days.

Statistical Analysis

The univariate risk of death was examined: overall survival (OS) curves were estimated by the Kaplan-Meier and selected variables were compared using a two-sided log-rank test. The Cox proportional hazards model was fitted to assess the association between the appearance, or lack thereof, of complications to the procedure and the risk of death; hazard ratio (HR) and 95% CI was estimated, and adjusted for age, gender and Child-Pugh Score. SPSS statistical package version 23.0 (SPSS Inc., Chicago, IL, USA) was used for all statistical analysis.

Results

The cohort consisted of 36 men and 26 women. The etiology of cirrhosis was alcoholic in 6 patients, viral in 50 and cryptogenic in 6; 22 patients were Child B and 40 were Child C (no patient was Child A) (Table I). The shunt placement was successfully performed in all patients with no perioperative complications (e.g. hematoma or bad positioning of the catheter). Using the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE version 4.0), we identified major and minor complications: 7 of the 62 patients (11%) had major complications, 3 patients developed a shunt infection and 4 patients had an obstruction of the shunt (occlusion of the lumen of the catheter caused by fibrin). 4 of the 62 patients (6%) with minor complica-

Table I. Patient Characteristics.

	N 62	(%) 100
Gender		
Male	36	58.1
Female	26	41.9
Age		
≤ 69	33	53.2
≥ 70	29	46.8
Etiology		
HCV	38	61.3
HBV	12	19.4
HETOC	6	9.7
CRPTO	6	9.7
Child		
Child B (moderate)	22	35.5
Child C (heavy)	40	64.5
Complications		
No complication	51	82.3
Abdominal pain	4	6.5
Obstructed/shunt infection	7	11.3

Table II. Univariate analysis OS.

	Median survival (months)	(95% CI)	p*
Gender			< 0.0001
Male	5	(3.2-6.8)	
Female	13	(11.3-14.6)	
Age			0.001
≤ 69	13	(11.6-14.4)	
≥ 70	7	(5.3-8.7)	
Etiology			0.7
HCV	8	(1.9-14.0)	
HBV	13	(11.9-14.1)	
HETOC	8	(1.9-14.0)	
CRPTO	14	(7.2-20.8)	
Child			< 0.0001
Child B (moder)	14	(13.1-14.9)	
Child C (grave)	7	(5.2-8.8)	
Complications			< 0.0001
No complication	13	(11.9-14.1)	
Abdominal pain	8	(0.1-18.7)	
Obstructed/shunt infection	3	(2.4-3.6)	

*Log-rank test.

tions had transient abdominal pain (which was resolved spontaneously) (Table I). All patients showed a reduction in abdominal circumference and body weight. During follow-up, a reduction in dosage of diuretics and in the need to carry out evacuative paracentesis could be seen; in this case, the potassium-sparing dose (spironolactone or potassium canrenoate) needed was 200 mg/day, while that of loop diuretics (furosemide) was 50 mg/day. In reference to the number of paracenteses per month, after positioning the shunt, 35 patients (56%) did not carry out paracentesis, 20 (32%) required a single paracentesis, while 7 (12%) needed two paracenteses (before the procedure, all patients underwent at least one paracentesis per month). Table II shows the univariate survival analysis for selected variables; there is a statistically significant difference for gender: men reported a median survival time of 5 months (95% CI 3.2-6.8) while the median survival time for women was of 13 months (95% CI 11.3-14.6) ($p < 0.001$). For those with Child, the median survival time was 14 months (95% CI 13.1-14.9) in patients with Child B and 7 months (95% CI 5.2-8.8) in patients with Child C ($p < 0.001$). Based on the presence or absence of complications following the procedure, the median survival time was 13 months (95% CI 11.9 to 14.1) in patients who had no complications, 8 months (95% CI 0.1-18.7) in those who had transient pain, and 3 months (95% CI 2.4 to 3.6) in those who had blockage or infection from the device ($p < 0.0001$). No significant difference was observed for the etiology ($p = 0.7$). Prognostic associations of "appearance, or lack thereof, of complications related to the procedure" was assessed through Cox regression model, a highly significant risk was found for obstructed/infected shunt, HR = 8.18 95% CI (2.63-25.37), while no association was found for abdominal pain ($p = 0.2$) (Table III). Figure 1 shows the significant OS related to the onset, or lack thereof, of complications associated to the procedure; the black line indicates the absence of complications, the dotted line indicates the occurrence of transient abdominal pain and the gray one indicates obstruction/infection of the device ($p < 0.0001$).

Table III. Adjusted multivariate Cox model.

	Overall survival		
	HR*	(95% CI)	p-value
No complication	1†		
Abdominal pain	1.95	(0.65-5.87)	0.2
Obstructed/shunt infection	8.18	(2.63-25.37)	< 0.0001

*Cox model adjusted for terms of age, gender and child. †Reference category

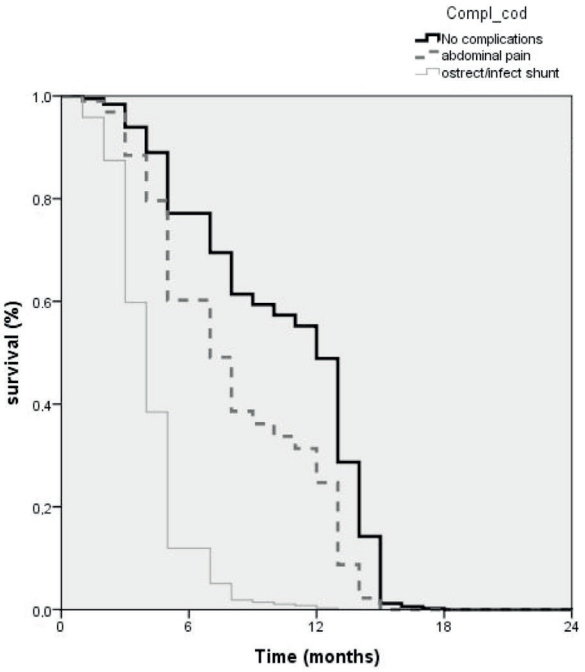

Figure 1. Overall survival associated to the procedure based on complications. The black line indicates the absence of complications; the dotted line indicated the occurrence of transient abdominal pain; the grey line indicates the obstruction/infection of the device.

Discussion

For 11 years, we collected 62 cases of patients with refractory ascites, who underwent placement of a Denver shunt. Refractory ascites has a significant impact on survival and on the patients' quality of life[9]. Therapeutic options usually considered are the evacuative paracentesis and transjugular intrahepatic portosystemic shunt (TIPS)[10]. Evacuative paracentesis is the treatment of choice; it is not, however, conclusive, since the peritoneal effusion tends to recur with variable speeds from patient to patient. If the relapse occurs quickly, the need to perform repeated paracentesis, in a relatively short period of time, compromises the quality of life of patients and implicates high costs[11]. Repeated paracentesis, also exposes patients to the risk of hypovolemia, hypotension or hypoproteinemia, sepsis, and rare, but possible, intestine perforation[12]. TIPS is an alternative to evacuative paracentesis[13]; by reducing portal hypertension, it improves renal perfusion and renal excretion of sodium, and therefore the response to diuretics causes a slowdown until depletion in the production of ascites. This method is not however free of complications. Among the most frequent are stenosis or complete occlusion for thrombosis of the stent, as well as the appearance or worsening of hepatic encephalopathy. Therefore, it cannot be used routinely in patients with refractory ascites because of its major contraindications which are: pre-existing hepatic encephalopathy, aging, cardio-respiratory disease, Child score > 11, infected ascites. The peritoneum-venous shunt was introduced in 1974 by LeVeen et al[14] al for the treatment of refractory ascites. LeVeen's shunt consists of a fenestrated catheter placed in the abdominal cavity, connected, through a one-way valve, to another catheter that reaches up to the neck in the subcutaneous layer of the skin, where it enters in the subclavian or jugular vein with the tip positioned at 2 cm from the atriocaval junction; when the abdominal pressure exceeds at least 3 cm of H_2O in the vein, the valve opens and allows the passage of ascites in the vascular system. The Denver shunt is a variant; in fact, thanks to a manual pump that is placed in the subcutaneous layer of the skin, the patient can directly adjust and control the transfer of the ascites to the blood stream, reducing the possibility of occlusion of the device. Its positioning is performed in the operating room under local anesthesia. Our patients were hospitalized for 2 or 3 days. All procedures were carried out successfully, no one needed bed rest and all patients started to ambulate immediately after the procedure. The peri-operative complications, described in the literature, may be secondary to systemic overload (acute pulmonary edema, gastrointestinal hemorrhage from ruptured esophageal varices), to the infusion of ascites into the circulation, which dilutes the clotting elements and activates coagulation (disseminated intravascular coagulopathy [DIC]) or infectious[15]. To reduce their impact, as indicated in the methods section, we performed the removal of most of the ascites fluid before the operation and administration of antibiotic prophylaxis. Among the complications that appear over time, the most frequent are the obstruction of the device, usually due to the deposition of fibrin within the valve or around the vein, and infections, often supported by the valve colonization[16]. Among our patients, 4 reported transient abdominal pain, which was resolved spontaneously within a few hours; 3 developed a shunt infection, after a long period of time after the procedure; and 4 showed an obstruction of the shunt. The two groups of patients who suffered infection and occlusion, had the device removed and no longer repositioned. In these patients, the

overall survival rate was significantly lower ($p < 0.0001$). In patients undergoing the procedure, the majority (56%) did not need to have an evacuative paracentesis done during the follow-up, and the dose of diuretics necessary to control the ascites was reduced (mean of 200 mg/day of spironolactone and 50 mg/day of furosemide). Hence, patients, followed on an outpatient basis, reported an improvement in quality of life, above all the reduction of re-admissions to hospital. In RCTs, PVS has been shown to be as effective as paracentesis + albumin and to have a similar rate of complications and a comparable survival rate[17]. From our study, it is also clear that patient survival rate was significantly influenced by the degree of hepatic impairment (14 months in Child B patients and 7 months in those Child C). In 1985, Deans et al[18] emphasized that the seriousness of the underlying disease influenced the mortality rate after the shunt positioning. Therefore, an accurate selection of patients is necessary before the procedure, eliminating patients who are prone to have a severe hepatic impairment that seems to be associated with the appearance of postoperative complications. In a recent paper, Kim et al[19] propose an algorithm for management after TIPS, which is based on the surveillance Doppler ultrasound for asymptomatic patients, followed by advanced imaging techniques to treat any stenosis and occlusions. For patients whose clinical response was initially poor, they suggest a TIPS venogram with pressure measurements. Abbas et al[20], in a 2007 paper, also concluded that the Denver shunt offered a good palliation, but that its use should be set-aside in selected cases. However, it is difficult to compare clinical records since there isn't much literature on the use of the Denver shunt in patients with refractory ascites not complicated by tumors. In fact, today, this procedure is mostly used for the treatment of patients with malignant ascites.

Conclusions

The positioning of the Denver shunt is safe and effective in the treatment of refractory ascites, representing an alternative to repeated paracentesis and TIPS for patients who cannot be managed or are not candidates for these procedures. Since not all the patients are equal, it would be useful to develop an algorithm for the treatment of refractory ascites, which would take into consideration the positioning of the Denver Shunt as well.

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Conflict of Interest

The Authors declare that they have no conflict of interests.

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