Improved Quality of Life after Distal Splenorenal Shunt

A Prospective Comparison with Side-to-Side Portacaval Shunt

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The distal splenorenal shunt (DSRS) was compared with the side-to-side portacaval shunt (PCS) in 93 prospectively matched patients with portal hypertension. After 38 months mean follow-up the two shunts had a different incidence of acute encephalopathy (22% in PCS group and 33% in DSRS group) and chronic encephalopathy (35% in PCS group and 17% in DSRS group), but the difference was not statistically significant. However, the only cases of severe and disabling chronic encephalopathy arose after PCS (p = 0.049). Actuarial curves of chronic encephalopathy showed that the maximum rate of encephalopathy (18%) in the DSRS group was reached 27 months after shunt surgery, whereas this value was reached and passed in PCS group only 4 months after shunt. Chronic encephalopathy occurred for a total duration of 20.1 months after PCS and only 11.1 months after DSRS (p = 0.003) and occupied 46.3% of the follow-up of PCS patients, as contrasted to 18.7% of the follow-up of DSRS patients (p = 0.0001). DSRS is associated with a lower global incidence of chronic HE without severe forms and provides a better quality of life than does a nonselective shunt.

PORTAL-SYSTEMIC SHUNTS, removing portal hypertension, represent the only definitive treatment for the prevention of variceal rebleeding.[1] However, suppression of hepatopetal flow could cause the appearance of hepatic encephalopathy (HE) and liver function deterioration.[2]

Distal splenorenal shunt (DSRS), first proposed by Warren et al. in 1967[3] appeared to be an interesting alternative in the treatment of bleeding esophageal varices. The effectiveness of the selective shunt in controlling bleeding has been documented in several reports.[4–6] Moreover, a concomitant significant decrease of HE after DSRS when compared to traditional nonselective shunts was observed.[7–12] The initial enthusiasm has been cooled by recent results of clinical trials, which cast doubts on whether the selective shunt is truly superior in preventing HE.[13–16] In this study results on HE are presented, comparing DSRS with side-to-side portacaval shunt (PCS), a classical nonselective anastomosis.

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Materials and Methods

Between January 1980 and June 1984, 152 adult patients were submitted to portal-systemic shunt for portal hypertension at the First Surgical Clinic of the University of Milan. Ninety-three patients were selected for this study on the basis of the following criteria: (1) biopsy-documented cirrhosis; (2) at least one episode of upper gastrointestinal bleeding caused by esophageal varices and confirmed by endoscopy; (3) proof of hepatopetal portal blood flow during the venous phase of the superior mesenteric angiography; (4) angiographical availability to perform both the shunts; (5) no severe ascites at the time of operation; and (6) surgery on an elective basis only. Patients older than 65 years of age or with hepatic failure (Child's C patients) were also excluded. Table 1 shows the reasons for the exclusion of 59 patients. Informed written consent was obtained from all patients prior to their inclusion in the study. A group of 47 patients submitted to a PCS was matched by a group of 46 patients who had received a DSRS. Patients were matched for age, sex, number of preoperative bleeds, type of cirrhosis, degree of portal perfusion, and preoperative functional hepatic reserve as determined by the Child's classification and by a global score, already described by the authors.[6]

Patients were submitted to one of the shunts according to an alternative method of assignment in the morn-

TABLE 1. *Reasons for the Exclusion of the Patients from the Study*

	No. of Patients
Prophylactic shunts	12
Emergency shunts	15
Budd-Chiari syndrome	4
Other PCS	8
Central splenorenal shunts	13
Other shunts	6
Nonselected patient	1
Total	59

ing before shunt surgery. However, when the selected shunt was intraoperatively judged unsuitable for anatomic reasons and the other shunt could be performed, the patient still included in the study because all the criteria for inclusion were met. This method was chosen because randomization was not feasible in this department.[6] The sample requirements to demonstrate an increase in survival at 5 years of the 10% are about 500 patients for each group, applying standard power (80%), Type I error ($p < 0.05$), and a two-tailed t-test.[17] This would mean that a long recruitment period and/or multicenter study can be expected to provide meaningful results. However, HE is the most important complication of shunt surgery. Therefore, the value of DSRS in preventing HE was studied. The sample requirements to demonstrate a decrease in HE from 40% to 15% are about 46 patients for each group, applying standard power (80%), Type I error ($p < 0.05$) and a two-tailed t-test.[17] The choice of this method of assignment and this specific objective has limited the recruitment period to 54 months.

Preoperative Evaluation

History of cirrhosis was collected in each patient with particular attention to previous episodes of gastrointestinal bleeding and evidence of either primary or posthemorrhagic hepatic failure (jaundice, ascites, or edema) (Table 2). Physical examination was specifically directed to the assessment of nutritional state, hepatosplenomegaly, jaundice, ascites, and edema. Routine laboratory tests were employed to evaluate the functional state of the liver. An overall assessment of the severity of liver disease was made. The mean index of PCS cases (0.58 ± 0.08) was similar to that of DSRS (0.60 ± 0.06; NS). Serum α-fetoprotein was routinely determined in order to screen the presence of hepatic neoplasm. The etiology of cirrhosis was determined on the basis of clinical history, serum markers of viral hepatitis, and liver biopsy (Table 3). The presence of esophageal varices was assessed by endoscopic examination. Criteria used for classifying the endoscopic findings were based on the General Rules for Recording Endoscopic Findings on Esophageal Varices compiled by the Japanese Research Society for Portal Hypertension.[18]

TABLE 2. *Preoperative Characteristics of the Two Study Groups*

	PCS (N = 47)	DSRS (N = 46)	p Value
Age (mean)	50.2 ± 9.5	54.0 ± 7.0	0.05
Sex (M/F)	38/9	31/15	NS
Bleeding episodes from esophageal varices (mean)	1.57	1.82	NS
Primitive hepatic falure (none/one or more)	17/30	19/27	NS
Child's classification			
A	0	0	NS
B	46	46	
C	1	0	
Portal perfusion			
1	30%	35%	NS
2	48%	42%	
3	22%	23%	

TABLE 3. *Etiology of Liver Cirrhosis*

	PCS	DSRS
Posthepatitic	16	19
Alcoholic	23	18
Cryptogenetic	7	8
Other	1	1

Cerebral function was assessed by a complete neurologic examination, taking into account the mental state, asterixis, electroencephalographic findings (EEG) and the trail making test.[19,20] All were assessed using the 0–4 rating system proposed by Conn.[21] The Cancelling As test was also used[22] and rated by the same method. This test assesses preattentive visual processing. The subject is asked to cancel out words containing As from long list of words in a specified time period. Each parameter was arbitrarily weighed in proportion to its importance. An overall score for HE was calculated from the sum of the values for each of the five parameters (Table 4). HE was considered acute if it was precipitated by gastrointestinal bleeding, acute binge drinking, or pharmacologic or dietary imbalances, of brief duration and easily controlled with elimination of the precipitating cause. HE was con-

TABLE 4. *Assessment of HE*

	Degree				
	0	1	2	3	4
Mental state	0	4	8	12	16
Asterixis	0	1	2	3	4
Cancelling A's test	0	0.5	1	1.5	2
TMT.	0	0.5	1	1.5	2
EEG.	0	1	2	3	4

No HE = 0–4.
Mild HE = 5–10.
Moderate HE = 11–20.
Severe HE = 20.

sidered chronic if it was spontaneous, of long duration, and more difficult to manage. Preoperative HE was excluded in all patients.

A visceral angiography was obtained by selective catheterization of celiac axis and superior mesenteric artery. The venous phase of angiography showed patency of the portal venous system and hepatopetal portal flow in all patients. The degree of hepatic perfusion was evaluated according to the criteria of Nordlinger et al.[23]

Operative Management

All patients were operated by the same surgical team and in the same time period. Side-to-side PCS was performed following standard technique. DSRS was constructed according to a previously described technique (37 cases)[3,4] or by a modification (nine cases).[24] A complete portal-azygous disconnection, with interruption of the left gastric, right gastroepiploic, and pyloric veins was always added.

Mesenteric venous pressure before and after the construction of the anastomosis was intraoperatively recorded by direct catheterization of an ileal vein, the plane of the caval vein was used as 0 baseline. Furthermore, direct measurement of splenic pressure was obtained in all DSRS patients.

Postoperative Evaluation

After surgery all vital parameters were continuously monitored and serial laboratory tests of hepatic function were obtained. An esophageal endoscopy was performed in each patient. A visceral angiography was performed on the tenth average postoperative day only in patients submitted to DSRS. Shunt patency was directly verified on the venous phase of angiography in the DSRS group and indirectly by endoscopic variceal examination in the PCS group. Three DSRS patients and one PCS patient were excluded from the analysis of the later results because two patients died in the early postoperative period (one for each group). One DSRS patient had shunt thrombosis and one with Britton's operation had lack of splenic ligation resulting in a side-to-side splenorenal shunt. The former was given beta-blockade therapy. Both patients were still alive without complications with a follow-up of 36 and 42 months, respectively.

Patients were checked at the first, third, and sixth month after discharge; follow-up was then extended to at least twice yearly on an outpatient basis. At each visit liver function was assessed by a complete clinical and biologic examination. A longitudinal assessment of liver function was made by calculating an index based on a battery of laboratory tests (albumin, total bilirubin, prothrombin time, SGOT, alkaline phosphatase) using the same method as for the assessment of the global score of functional hepatic reserve.[6] This index was obtained at 6 months and then yearly after surgery and compared each time with preoperative values. The assessment of neurologic status was performed using the afore-mentioned criteria. An EEG was obtained at least once a year. Any period of chronic HE in any month was counted as 1 month in that functional category.[11] An assessment of quality of life was calculated by dividing the number of months with chronic HE by the follow-up of each patient, giving a percentage.[11] Evidence of HE between two subsequent controls was determined based on history of neuropsychiatric aberrations described by the patients and/or reliable witnesses that were not explained by stroke, intoxication, or other disorder. A return to drinking was based on patient's statements, the authors' assessment, and informations from relatives. Continued drinking was defined as daily consumption in excess of 1 L of wine and/or hard liquors. All the patients were on a protein-balanced diet (1 g protein/kg body weight) and administered lactulose prophylactic treatment; the dosage was started at 60 g/day in three divided doses and adjusted thereafter to induce at least one bowel movements per day.

Data Management and Statistical Analysis

Initial evaluation and subsequent follow-up data were collected on 1-2-3 databases (Lotus Development Corp.) for computer input (Epson PC AX, Seiko Epson Corp.) and subsequent analysis (Microstat Ecosoft, Inc., Indianapolis, IN). Cumulative curves of chronic HE were analyzed by the Kaplan-Meier method and were compared by the log-rank test.[25] Comparison between groups was made by the chi square test for proportions and Mann-Whitney U-test for the means.

Results

Prior to inclusion in the study, acute HE had occurred in eight of the 47 patients in the PCS group (17%) and in ten of the 46 patients in the DSRS group (21%) (NS). In most patients HE was associated with gastrointestinal bleeding, was transient, and cleared with minimal therapeutic steps including lactulose and sometimes amino acid infusion. Postoperatively, acute HE occurred in four of the 46 patients in the PCS group (9%) and in six of the 43 patients in the DSRS group (14%) (NS). Long-term follow-up was complete in 100% of patients. Mean follow-up time from operation to last data analysis (both alive and dead patients) was 39 months in the DSRS group and 41 months in the PCS group (range: 24–79 months; NS). Acute HE was observed in ten of 46 patients in the PCS group (22%) compared to 14 of 43 patients in the DSRS group (33%) (NS). Chronic HE was evaluated by its incidence, seriousness, onset, and duration. Chronic HE was observed in 16 patients in the PCS group (35%) and in seven patients in the DSRS group (17%) (NS). Chronic HE was mild in eight PCS

patients (17%), moderate in four (9%), and severe in four others (9%). After DSRS no severe HE was found, but five patients (12%) suffered a mild form and two (5%) a moderate form. The difference in the incidence of severe HE between PCS and DSRS groups was slightly significant ($p = 0.049$). The cumulative curve of patients free of chronic HE (Fig. 1) showed that the maximum rate of HE in DSRS group (18%) was reached 27 months after shunt surgery, whereas this value was reached and passed only 4 months after PCS. The 16 patients in the PCS group experienced a mean of 20.1 months (±14.9) with chronic HE, whereas the mean for the seven patients in the DSRS group was only 11.1 months (±8.1) ($p = 0.003$). These 16 PCS patients had 46.3% (±30%) of their follow-up period with chronic HE, whereas the seven DSRS patients had only 18.7% (±14.6%). This difference is highly significant ($p = 0.0001$).

Figure 2 demonstrates the mean indices of liver function calculated for the two surgical groups during the follow-up period. The DSRS did not cause any significant worsening of hepatic function, whereas PCS did.

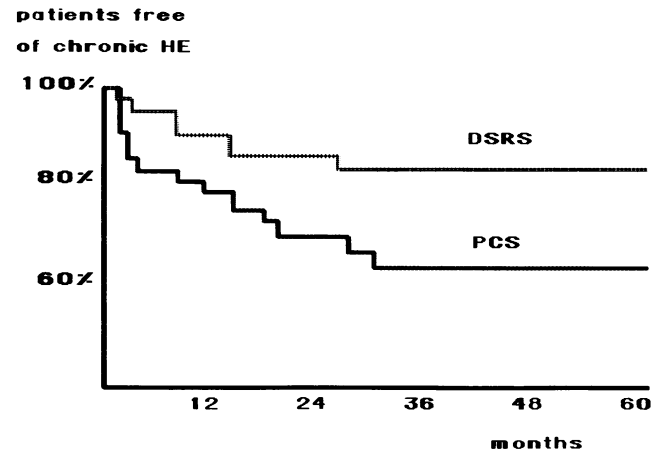

FIG. 1. Actuarial curves of patients free of chronic HE.

Discussion

The aim of this study was to compare the incidence of HE after DSRS and PCS in two homogeneous groups of cirrhotic patients, matched for clearly established criteria of inclusion. The two groups of patients were homogeneous with regard to liver function, type of cirrhosis, preoperative portal hemodynamics, and indications for surgery. Some advantages of this study were that DSRS was compared only with PCS as a nonselective shunt, surgery was performed by the same team that had acquired experience with 590 nonselective and 60 selective shunts,[1] ensuring fairly good standardization of the surgical approach, and serial follow-up checks were made for virtually the same period for both groups. Finally, no patient was lost during follow-up period.

Assessment of HE and quantification of its symptoms remain a much debated point with no immediate solution in sight.[26] Severe forms are easy enough to identify, but subclinical signs are easy to overlook on superficial examination. We attempted to standardize our assessment of these disturbances using a score of HE amply inspired by the criteria set out by Conn et al.[21] Using an empirical rating scale, the absence of HE, and mild, moderate, and severe forms were defined. A clear-cut definition was used for acute and chronic HE because of the widely differing impact of these two forms on social life and habits. Isolated and recurrent episodes of acute HE occurred more often after DSRS than PCS; this difference, however, was not statistically significant and also not clinically relevant. Other studies showed that acute HE, as it was induced by comagenic events, occurred in equally large fractions of both shunted and nonshunted patients.[27-30] These data indicate that acute HE is a common phenomenon in cirrhotic patients with portal hypertension. On the other hand, chronic HE was usually associated with portal-systemic shunts.[27] Six prospective studies compared DSRS and nonselective shunts; results have shown a significantly lower frequency of HE following DSRS.[7-16]

The results of the current study showed that the quality of life after DSRS is superior to that after PCS. This finding is based on the different behavior of chronic HE in the two groups regarding to incidence, seriousness, onset, and duration. First, after a follow-up of at least 2 years only 17% of DSRS patients have experienced chronic HE, as contrasted to 35% of PCS patients. This difference, however, was not statistically significant, but it seems to be clinically important. The size of the study may have prevented the observation of a significant effect. Second, the only cases of severe and disabling chronic HE arose after PCS, and this was slightly statistically significant. One cause for severe forms of chronic HE could be continued alcoholism. A direct relationship between active drinking and spontaneous HE was seen

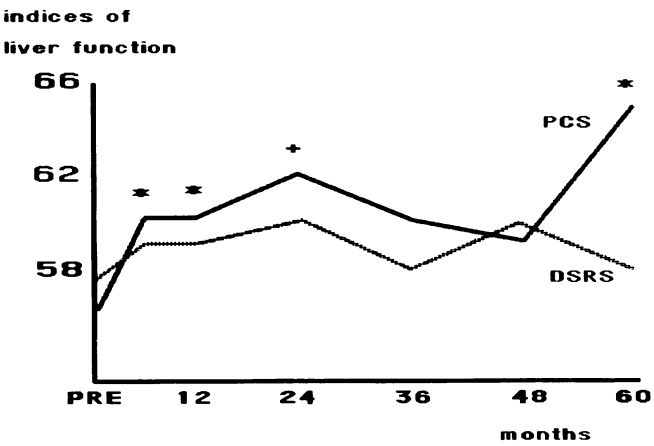

FIG. 2. Longitudinal trend of indices of liver function in PCS group. *$p < 0.05$ and +$p < 0.02$ compared to preoperative values.

only in the DSRS group.[16] This suggests that the natural history of chronic HE in this population depends on the direct effect of continued drinking, whereas the development of HE after PCS is hemodynamic above all.[16] Five PCS patients (11%) and four DSRS patients (9%) had returned to drinking. However, none of these patients had severe HE and only one DSRS patient had a moderate form. Moreover, we analyzed if the difference in the incidence of severe form could be caused by a dietary imbalance, constipation, and/or additional therapies. HE in PCS group was not caused by other disorders. Two PCS patients and four DSRS patients were on a free diet, whereas five PCS patients had to interrupt the protein intake to prevent the development of chronic HE (NS). Lactulose prophylactic treatment was interrupted in three PCS and in five DSRS patients of their own free will (NS). Oral BCAA dietary supplementation (Friliver, Bracco) was necessary in nine PCS patients and in four DSRS patients (NS). Third, in those patients in whom chronic HE developed after DSRS, it did so later in their postoperative course. Chronic HE developed so soon after PCS that its incidence surpassed the maximum incidence of HE in DSRS group (18%) just 4 months after hospital discharge. Fourth, chronic HE lasted longer after PCS than after DSRS. This influenced the lifestyle of PCS patients including modifications of their work performance or partial limitations of household ability. Some patients required assistance for the basic activities of daily living. In contrast, HE caused 38 late admissions in 19 PCS patients but only 18 late admissions in 11 DSRS patients. Thus, the risk of admission for HE was almost twofold higher in the PCS group (0.83 *vs.* 0.42 admissions per patient; $p = 0.037$). Furthermore, these admissions were caused by acute HE in all but three PCS patients who were admitted for chronic HE. The reasons for this better quality of life in DSRS group are still discussed.

Chronic HE is related to three physiologic factors: hepatic portal perfusion, portal–systemic collaterals, and intestinal venous hypertension that affects intestinal absorption.[31,32] Altered portal hemodynamics impairs liver function in cirrhotics, which may be responsible for the development of chronic HE.[30,33] However, much controversy exists regarding HE following shunt surgery, namely, whether it is due to the shunt itself or to the hepatic damage.

Suppression of portal diversion led to complete reversal of severe, disabling postshunt encephalopathy.[34,35] It has reported a low frequency of HE in portal hypertension with good preservation of hepatic function such as schistosomiasis[36] or Budd-Chiari syndrome.[37] In contrast, the incidence of HE in patients with an impaired liver function (Child's C risk) submitted to endoscopic sclerotherapy was similar to that of shunted patients.[38] However, these can be considered borderline cases in whom it is possible (at least theoretically) to separate the altered portal hemodynamic effect from the impaired liver function. In the majority of cases, this is very difficult. In this study the cumulative curve of patients free of chronic HE (Fig. 1) after PCS seems to have two components: a rapid initial slope for 12 months after discharge followed by a more gentle slope thereafter, whereas the curve after DSRS showed a more progressive slope from beginning to end. The rapid development of chronic HE after PCS could be due to the improvised loss of portal perfusion contributing to hepatocellular damage (Fig. 2). However, the progressive development of chronic HE after DSRS could be due to the evolutive chronic disease. It is known that loss of liver volume occurs in unoperated patients and probably represents the natural history of disease.[39]

Portacaval shunt diverts portal venous flow away from the liver, contributing to liver failure. Furthermore, a toxic substance or substances from the gastrointestinal tract bypass their normal metabolic site in the liver and reach the brain in high concentrations, where they produce cerebral dysfunction. Finally, total portal-systemic shunt causes increased ammonia absorption from the small and large bowel due to decompression of the splanchnic circulation.

DSRS should represent optimal surgical therapy because postoperative portal perfusion and superior mesenteric–portal venous hypertension are maintained; these aim to preserve liver cell function in the already impaired liver of cirrhotics.[12] However, six randomized controlled trials have demonstrated conflicting results regarding subsequent incidence of HE.[9,11–14,16]

The lack of a clearly positive effect on HE after DSRS may be due to (besides afore-mentioned natural history of liver disease) the progressive loss of shunt selectivity.[40–43] In our experience of 118 DSRS performed, preoperative and postoperative splanchnic angiography were evaluated in 80 cases. Patients with loss of portal perfusion had higher incidence of chronic HE (25%) than patients with other degrees of perfusion (6%, ($p = 0.02$) (unpublished observation). The rate of loss of perfusion may be accelerated by inadequate portal-azygous disconnection.[44,45] High rates of HE after modified DSRS (without portal-azygous disconnection) seem to confirm these data.[46,47] Warren et al.[48] projected that if the splenic vein were completely separated from the pancreas during selective shunt, (splenopancreatic disconnection) the so-called pancreatic siphon would not develop and postoperative portal perfusion and shunt selectivity could be preserved.

In conclusion, DSRS is associated with less global incidence of chronic HE, absence of severe forms, less rapid development during follow-up, and less duration of episodes providing a better quality of life than does a nonselective shunt.

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