Shunt Surgery *Versus* Endoscopic Sclerotherapy for Long-term Treatment of Variceal Bleeding

Early Results of a Randomized Trial

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In September 1982, a prospective randomized trial comparing shunt surgery and endoscopic sclerotherapy for the elective management of variceal hemorrhage in patients with cirrhosis was initiated. Twenty-seven patients have received shunts (distal splenorenal = 23, nonselective = 4) and 30 patients have had chronic sclerotherapy. Eighty-six per cent of patients had alcoholic cirrhosis and 33% were Child's class C. After a mean follow-up of 25 months, 19% of shunt and 57% of sclerotherapy patients have had rebleeding (p = 0.003). Kaplan-Meier survival analysis reveals similar 2-year survival rates for shunt (65%) and sclerotherapy (61%) groups. Only two of 10 sclerotherapy failures have been salvaged by surgery. Post-therapy quantitative hepatic function, frequency of encephalopathy, and cumulative medical costs were similar for both groups. Hepatic portal perfusion and portal pressure at 1 year were better maintained by sclerotherapy than by distal splenorenal shunt. In conclusion, endoscopic sclerotherapy and shunt surgery provide similar results with respect to survival, hepatic function, frequency of encephalopathy, and costs. Sclerotherapy is an acceptable, but not superior, alternative to shunt surgery for treatment of variceal hemorrhage.

THE IDEAL THERAPY for variceal hemorrhage would permanently eliminate this life-threatening complication of portal hypertension and have no adverse effects on hepatic physiology. Unfortunately, no single treatment provides both of these advantages. Surgical portal decompression reliably prevents future bleeding episodes, but alters liver perfusion. Endoscopic sclerotherapy and nonshunting operations minimally influence hemodynamic function, but are generally followed by a higher frequency of recurrent hemorrhage than portal-systemic shunts.

The distal splenorenal shunt (DSRS) is the only commonly used shunting procedure with the capacity of maintaining hepatic portal perfusion. Several controlled trials[1-3] comparing the DSRS to various nonselective shunts have demonstrated a lower frequency of encephalopathy after selective variceal decompression. Based on these studies, as well as other large uncontrolled series,[4,5] the DSRS has emerged as the preferred procedure for most patients when surgical therapy is indicated for variceal hemorrhage. Because some patients, *e.g.*, those with medically intractable ascites, are not candidates for the DSRS, we have evolved a selective operative approach, selecting the type of shunt (DSRS, end-to-side portacaval shunt, or side-to-side portal-systemic shunt) based on each individual's clinical and hemodynamic circumstances.[6]

Because of dissatisfaction with portal decompression and its adverse consequences of encephalopathy and hepatic failure, endoscopic sclerotherapy was reintroduced in the 1970s, first for the emergency management of bleeding varices and subsequently as definitive treatment to prevent recurrent hemorrhage. Several controlled trials[7-10] of sclerotherapy *versus* conventional medical management have shown a beneficial effect of this treatment on frequency of rebleeding, and some trials[7,9] have demonstrated prolonged survival after sclerotherapy.

The current investigation was designed to determine whether shunt surgery (selective approach) or chronic endoscopic sclerotherapy is preferable for patients with cirrhosis who bleed from varices. Only patients who survived their initial hemorrhage are included. Thus,

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elective rather than emergency therapies are compared. Based on previous controlled studies of treatments for variceal hemorrhage in predominantly alcoholic cirrhotic populations, it was anticipated that these two therapies might result in similar survival rates. Therefore, multiple variables were carefully studied to determine the relative impact of these treatment modalities on hepatic functional reserve, hepatic hemodynamic status, psychoneurologic function, and medical costs.

Methods

Patients

The study population comprised 57 patients with cirrhosis and variceal hemorrhage referred between September 1982, and December 1986. During the first 2 years, patients were accrued from the University of Utah Medical Center (N = 18) and Salt Lake Veterans Administration Medical Center (N = 17). After the principal investigator moved to the University of Nebraska Medical Center in August 1984, study patients were derived from that institution (N = 10) and from the Omaha Veterans Administration Medical Center (N = 12). The study population was drawn from a pool of 150 patients who were treated for variceal hemorrhage by surgery or endoscopic sclerotherapy at these four hospitals during these intervals. To be considered for randomization, each patient had to meet the following criteria: (1) historic, clinical, and/or laboratory evidence of cirrhosis (diagnosis confirmed by biopsy in all patients); (2) endoscopic documentation of acute or recent variceal hemorrhage (actively bleeding varix or large nonbleeding varices with no other lesions) requiring at least three units of blood transfusion; (3) residence within 500 miles of Salt Lake City or Omaha; (4) cessation of acute variceal hemorrhage either spontaneously or by use of one or a combination of intravenous vasopressin infusion, balloon tamponade, and emergency endoscopic variceal sclerosis; and (5) patency of the splanchnic venous system demonstrated by visceral angiography. Patients bleeding from gastric varices located more than 2 cm from the esophagogastric junction were excluded. After stabilization from the acute bleeding episode, patients who met the above criteria and who agreed to participation after informed consent were randomized using Efron's biased coin design,[11] based on three liver function strata (modified Child's classification) and type of hospital (University or Veterans Administration). Twenty-eight patients were randomized to shunt surgery and 29 patients were randomized to endoscopic sclerotherapy. One patient refused surgery and was treated with endoscopic variceal sclerosis. In all subsequent analyses, this individual is included in the sclerotherapy group (N = 30; shunt group, N = 27).

Therapy

Selection of shunt was based on each individual's clinical circumstances and hepatic hemodynamic status.[6] Patients with compatible anatomy (splenic vein greater than 7 mm), hepatopetal portal flow on preoperative angiography, and either absent or medically controllable ascites received the DSRS (N = 23). Individuals with ascites intractable to medical management or spontaneous reversal of portal flow on preoperative angiography had a side-to-side portal-systemic shunt (N = 3). Side-to-side shunts used included the side-to-side portacaval shunt (N = 1) and Dacron graft (16–20 mm) interposition shunts (N = 2) in the portacaval or mesorenal positions. A single end-to-side portacaval shunt was done emergently in a patient who massively rebled after randomization. All shunts were constructed by a single surgeon (LFR).

Endoscopic sclerotherapy was performed with a standard upper gastrointestinal flexible endoscope without accessories. During the first 2 years of the investigation, 0.75% sodium tetradecyl sulfate in 50% dextrose was used as sclerosant because 5% sodium morrhuate, which has been used during the last 2 years, was not then available. Intravariceal injections of all columns just above and at 5 cm proximal to the esophagogastric junction were accomplished at the initial session. Approximately 2 mL of sclerosant per injection with a maximum of 20 mL per session was used. Sclerotherapy was repeated at 4- to 6-day intervals until most varices were eradicated. Follow-up endoscopy was scheduled for 4–6 weeks after the last session and then at 6-month intervals unless recurrent hemorrhage intervened. The 30 sclerotherapy patients had 6.7 ± 0.8 SEM sclerosis treatments per patient with a range from 1 to 23 treatments. Eighty per cent of patients were compliant and returned for endoscopy as scheduled. Varices were completely eradicated in 19 patients (63%), but reformed in 12 of these individuals. The only major complication of sclerotherapy was esophageal stricture in three patients, all of whom were successfully dilated. Sclerotherapy was done under the supervision of a single endoscopist at each hospital.

Death of any cause was considered failure of therapy in both groups. Shunt surgery was also considered a failure when shunt thrombosis developed and sclerotherapy was initiated because clinical circumstances or anatomy precluded further surgery. Sclerotherapy failure was defined as change to surgery necessitated by recurrent hemorrhage despite repeated sclerosis sessions. The decision for surgical intervention was made by the individual gastroenterologist and not based on a specific number or degree of severity of recurrent bleeding episodes.

Pretherapy and Post-therapy Evaluations

All patients had an extensive pretherapy evaluation. In addition to routine post-therapy follow-ups at 3–6-month intervals, comprehensive evaluations were completed at 1 year (shunt = 17; sclerotherapy = 17) and 3 years (shunt = 5; sclerotherapy = 7) after shunt surgery or initiation of sclerotherapy. Patients not seen in person were interviewed by telephone. After August 1984, one of the authors (RAC) returned to Salt Lake City to conduct 1- and 3-year evaluations. One sclerotherapy patient has been lost to follow-up.

Routine clinical and laboratory examinations. Physical examination was directed toward detection of ascites and encephalopathy. Episodes of recurrent hemorrhage, employment status, and presence or absence of continuing alcoholism were recorded. Routine laboratory tests included hematocrit, white blood cell count, platelet count, prothrombin time, partial thromboplastin time, serum albumin, total bilirubin, alkaline phosphatase, AST (SGOT), ALT (SGPT), blood urea nitrogen, and creatinine.

Hepatic hemodynamic variables. Hepatic hemodynamic variables were assessed by visceral angiography, measurement of corrected sinusoidal pressure (CSP), and quantitation of effective hepatic blood flow (EHBF) by a low-dose galactose clearance technique. The portal perfusion grade (PPG) was qualitatively determined from the venous phase of the selective superior mesenteric angiogram (grade 1 = good hepatopetal portal flow to grade 4 = absent flow).[12] Preoperative studies (including left renal vein opacification) also provided essential information about splanchnic venous anatomy, and postoperative angiography determined shunt patency status. CSP was measured as hepatic venous wedge pressure minus free hepatic venous pressure. EHBF was estimated as the infusion rate of low-dose galactose (40–66 mg/min) divided by the steady-state plasma concentration of galactose as described by Henderson et al.[13]

Quantitation of hepatic function. Galactose elimination capacity (GEC) was calculated from serial venous blood samples after a bolus intravenous injection of galactose (500 mg/kg body weight).[14] Removal rate of a 5 mg/kg dose of indocyanine green (ICG) was measured from serial plasma concentrations after intravenous injection.[15] A modified Child's score was derived from serum albumin, total bilirubin, and severity of encephalopathy and ascites (Table 1).[16] Each variable was graded from 1 (best) to 3 (worst) to obtain a total score.

Psychoneurologic evaluation. An episode of clinical encephalopathy was defined as an incident of mental confusion related by the patient or a family member, or detection of disorientation by a physician. When no precipitating factors were identified, the episode of encephalopathy was considered spontaneous. Induced encephalopathy was defined as mental confusion occurring during gastrointestinal hemorrhage. Disorientation or coma appearing just before death from hepatic failure was excluded. Electroencephalograms (EEG) were graded as normal or abnormal by the criteria of Parsons-Smith.[17] The single psychometric test used was the numbers connection test.[18] Venous blood ammonia was obtained in the fasting state.

TABLE 1. *Determination of Child's Score*

Points	Albumin (g %)	Bilirubin (mg %)	Encephalopathy	Ascites
1	≥3.5	≤1.5	None	None
2	3.0–3.4	1.6–2.5	Mild	Present
3	<3.0	>2.5	Moderate to severe	Tense

A = 4–5 points, B = 6–7 points, C = 8–12 points.

Cost analysis. Both initial and total medical costs for each therapy were calculated and compared. Initial medical costs were defined as those incurred during the hospitalization in which shunt surgery was performed or sclerotherapy initiated. Total costs included the initial hospitalization, all subsequent hospitalizations required for treatment of recurrent hemorrhage and complications of therapy or chronic liver disease, and outpatient endoscopic evaluation with or without variceal sclerosis. Only patients from the University of Utah (N = 18) and University of Nebraska (N = 10) were included in the cost analysis; all patients from the Veterans Administration Hospital were excluded.

Statistical analysis. The Kaplan-Meier method was used to plot survival and failure of therapy curves, which were compared by the log rank test.[19] Groups were compared before therapy and at 1 year and 3 years after therapy by chi-square analysis (qualitative variables) and the unpaired t-test (quantitative variables). Serial variables within a group were analyzed by the paired t-test.

Results

Pretherapy Comparison of Shunt and Sclerotherapy Groups

The shunt and sclerotherapy groups were comparable at randomization with respect to cause of cirrhosis, Child's score, quantitative hepatic function and hemodynamic variables, and measurements of neuropsychologic function (Table 2). In addition, all routine blood chemistries, coagulation variables, and hematologic indices were not significantly different between the two

TABLE 2. *Pretherapy Comparison of Shunt and Sclerotherapy Groups*

	Shunt (N = 27)	Sclerotherapy (N = 30)
Alcoholic cirrhosis (%)	81	90
VA patients (%)	48	53
Child's score	6.4 ± 0.4*	6.5 ± 0.3
Bilirubin (mg/dL)	1.9 ± 0.2	1.6 ± 0.2
Albumin (g/dL)	3.3 ± 0.1	3.2 ± 0.1
Encephalopathy (%)	26	30
Ascites (%)	33	47
GEC (mg/min)	271 ± 20	265 ± 16
ICG removal rate (mg/kg/min)	0.21 ± 0.04	0.19 ± 0.03
Hepatic blood flow (mL/min)	1405 ± 79	1314 ± 92
Hepatopetal portal flow (grades 1–3; %)	96	93
Corrected sinusoidal pressure (mmHg)	16.0 ± 1.0	16.6 ± 1.2
Abnormal EEG (%)	33	17
Numbers connection test (sec)	50 ± 4	46 ± 3
Fasting ammonia (μmol/L)	44 ± 5	51 ± 7

* Values expressed as mean ± SEM.

groups. Based on the Child's grading system used, nine shunt (33%) and 10 sclerotherapy patients (33%) were Child's grade C.

Survival

Early mortality (within 1 month of surgery or initiation of sclerotherapy) occurred in one patient in each group. The early postoperative shunt death occurred after an emergency portacaval shunt in a patient who massively rebled after randomization but before elective surgery could be performed. The single early sclerotherapy fatality was secondary to uncontrolled hemorrhage after the first sclerosis session.

Surviving shunt and sclerotherapy patients have been followed up for a mean of 24.4 ± 3.3 and 25.2 ± 3.3 months, respectively. Figure 1 shows Kaplan-Meier survival plots for the two groups as of March 1, 1987. These two curves as well as 2-year survival rates for shunt (65%) and sclerotherapy (61%) groups are not significantly different. Two of four patients in whom sclerotherapy failed who had surgery (splenectomy plus devascularization = 1, interposition mesocaval shunt = 1, end-to-side portacaval shunt = 2) for uncontrolled hemorrhage are still surviving.

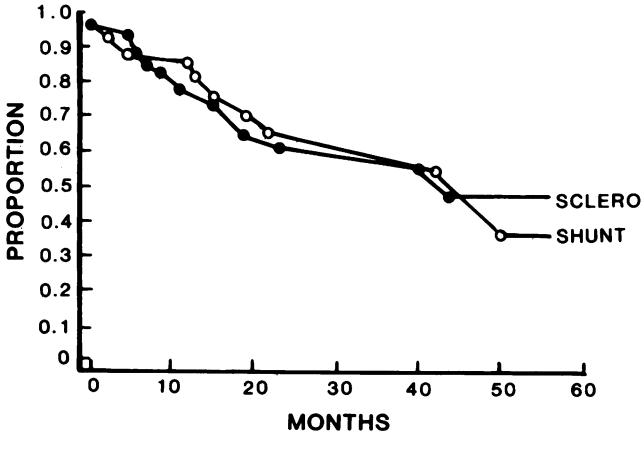

FIG. 1. Kaplan-Meier survival curves for shunt surgery (O) and endoscopic sclerotherapy (●). The curves are not different at any time interval.

The predominant cause of death was different in the sclerotherapy and shunt groups. Eight of the 12 sclerotherapy deaths (67%) resulted from recurrent hemorrhage. Of these eight patients, one died of continuing hemorrhage 5 days after randomization, two died after surgery (2 weeks after mesocaval shunt and 2 years after splenectomy plus devascularization), three died in outlying hospitals more than 300 miles from the tertiary care center, and two died of hepatic failure induced by hemorrhage and were unacceptable candidates for surgery. Six of the eight patients had had endoscopy within the previous month, five bled from gastric varices or portal hypertensive gastropathy rather than from the esophagus, and only one patient was noncompliant. The remaining four sclerotherapy fatalities were secondary to hepatic failure (N = 1), esophageal carcinoma (N = 1), and pneumonia (N = 2). The mean pretherapy Child's score of nonsurviving patients (6.6 ± 0.6) was identical to that of survivors (6.6 ± 0.4).

Six of the 10 shunt deaths (60%) were secondary to hepatic failure. Four of these individuals had resumed heavy alcohol consumption, and the other two had nonalcoholic cirrhosis. Two shunt patients died of recurrent variceal hemorrhage (one after thrombosis of DSRS and one after emergency portacaval shunt for recurrent hemorrhage before elective surgery). The remaining shunt deaths were due to myocardial infarction (N = 1) and ruptured abdominal aortic aneurysm (N = 1). Six of 23 (26%) patients who received the DSRS and three of four (75%) patients with nonselective shunts have died. The mean preoperative Child's score for nonsurviving shunt patients (7.2 ± 0.6) was not significantly higher than for survivors (6.0 ± 0.5).

Failure of Therapy

Failure of therapy (death or change in therapy) curves for the two groups are shown in Figure 2. At no point are the two curves significantly different. Fourteen patients (12 deaths and two survivors of shunt surgery) failed sclerotherapy. Two sclerotherapy patients had surgery and subsequently died. Failure was caused by recurrent hemorrhage in 10 patients (71%). These patients had 8.4

± 1.2 sclerosis sessions and experienced 3.3 ± 0.6 recurrent hemorrhages requiring 5.8 ± 0.7 units of blood per episode. No pretherapy variables significantly separated sclerotherapy successes from failures.

All 10 therapy failures in the shunt group were due to death rather than change of therapy. The single patient who was treated with chronic sclerotherapy after DSRS thrombosis eventually died of recurrent hemorrhage. Early postoperative shunt thrombosis developed in two patients (one DSRS and one interposition portacaval shunt), but both patients were successfully reshunted (one end-to-side portacaval shunt and one interposition portacaval shunt). The overall shunt thrombosis rate was 11%. The only preoperative variable that significantly separated success (survival) from failure (death) in the shunt group was GEC (survivors = 298 ± 26 mg/min, nonsurvivors = 217 ± 20 mg/min; p = 0.05).

Recurrent Hemorrhage

The percentage of patients who rebled, number of rebleeding episodes, and number of units of blood transfusion were all significantly higher in the sclerotherapy group (Table 3). Of the 17 sclerotherapy patients who rebled, 10 (59%) were therapy failures and are discussed above. The remaining seven patients have had either one or two recurrent hemorrhages that have been successfully controlled with sclerotherapy. Most hemorrhages have been documented to be from varices or hypertensive gastropathy by endoscopy; no other lesions have been identified. Pretherapy prothrombin time and partial thromboplastin time were significantly longer (p = 0.05 and p = 0.004, respectively) in sclerotherapy patients who rebled. All other pretherapy variables were similar in patients with and without recurrent hemorrhage.

Three of the five shunt patients who rebled had shunt thrombosis. The remaining two patients had mild recurrent hemorrhage in the early postoperative interval and had patent DSRS by angiography.

Hepatic Function

Neither the quantitative hepatic function tests nor the conventional measures of liver function were significantly different between groups at 1 or 3 years. Likewise, serial GEC, ICG, and Child's score determinations showed no significant changes at 1 year in either group (Table 4). Too few serial measurements have been completed at 3 years for statistical analysis.

Hepatic Hemodynamic Data

Early postoperative angiography showed preservation of hepatic portal perfusion after 20 of 23 DSRSs and

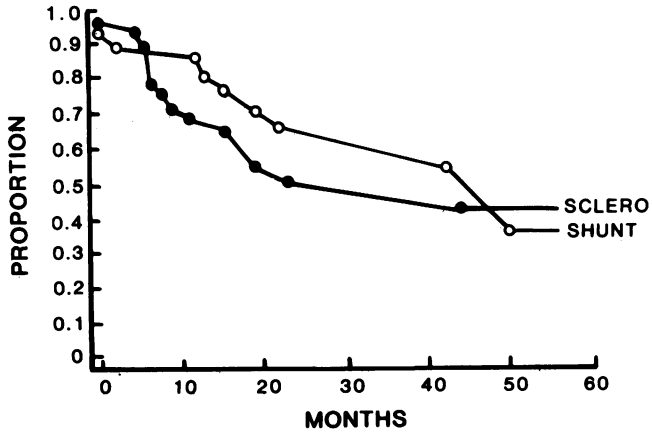

FIG. 2. Kaplan-Meier plots of therapy failure for shunt surgery (O) and endoscopic sclerotherapy (●). The curves are not significantly different at any time interval.

after none of the nonselective shunts. Likewise, corrected sinusoidal pressure (CSP) was maintained in the early postoperative interval after DSRS (preoperative = 15.7 ± 0.9 mmHg, postoperative = 18.0 ± 1.6 mmHg). Analysis of unpaired data at 1 and 3 years showed a significant difference between groups in only CSP at 1 year (shunt = 9.9 ± 1.1 mmHg, sclerotherapy = 16.4 ± 1.8 mmHg; p = 0.01). Serial measurements of EHBF, PPG, and CSP showed a significant change in PPG and CSP in the shunt group at 1 year (Table 5). Four of seven patients who had DSRS and one of eight patients who had sclerotherapy had a worse PPG at 1 year than before therapy (Fig. 3). Since all nonselective shunt patients had lost portal flow immediately after surgery, late postoperative angiograms were not done in these individuals. When nonselective shunt patients surviving at 1 year (shunt group = 3, sclerotherapy group = 2) are considered with DSRS and sclerotherapy patients who had late postoperative angiography, five of 10 shunt patients (50%) and seven of 10 sclerotherapy patients (70%) had evidence of continuing hepatic portal perfusion at 1 year. Two of three angiograms performed at 3 years after DSRS showed hepatopetal portal flow; the single 3-year study in the sclerotherapy group also revealed preservation of portal flow.

Psychoneurologic Function

Four (16%) at-risk shunt patients and two (7%) sclerotherapy patients had at least one episode of spon-

TABLE 3. *Recurrent Hemorrhage*

	Shunt	Sclerotherapy	p
Patients	5 (19%)	17 (57%)	0.003
Episodes	5	48	<0.001
Units of transfusion	28	280	<0.001

TABLE 4. *Serial Hepatic Function and Child's Score*

	Shunt			Sclerotherapy		
	N	Preoperative	1 Year	N	Preoperative	1 Year
Child's score	17	6.5 ± 0.5	5.9 ± 0.5	17	6.7 ± 0.4	5.7 ± 0.4
GEC (mg/min)	11	284 ± 30	279 ± 34	15	261 ± 20	254 ± 19
ICG (mg/kg/min)	10	0.17 ± 0.04	0.17 ± 0.04	15	0.19 ± 0.04	0.20 ± 0.04

taneous encephalopathy during the follow-up interval (Table 6). This complication required hospitalization on four occasions (two patients) in the shunt group and a single hospitalization in the sclerotherapy group. An additional four (14%) sclerotherapy patients had encephalopathy in association with recurrent hemorrhage. Nine shunt (43%) and six sclerotherapy (26%) patients had an abnormal EEG on at least one occasion after initiation of therapy. Overall, there were no differences between groups with respect to clinical, EEG, or psychometric manifestations of post-therapy encephalopathy (Table 6).

Medical Costs

Initial medical costs were significantly higher for shunt patients ($22,473 ± 3521, N = 14) than for sclerotherapy patients ($10,410 ± 1893, N = 14) ($p = 0.007$). However, total medical costs were similar in the two groups (shunt = $34,474 ± 5499; sclerotherapy = $37,648 ± 6392) during a mean follow-up interval of 20 ± 5 and 24 ± 6 months for shunt and sclerotherapy patients, respectively. The higher follow-up costs in the sclerotherapy group were due to the need for serial endoscopies and more frequent hospitalizations (shunt = 16, sclerotherapy = 34) in that group.

Discussion

The major finding of this study is that elective shunt surgery and chronic endoscopic sclerotherapy provide similar long-term survival rates and quality of life for cirrhotic patients who bleed from esophageal varices. The most common causes of death in shunt and sclerotherapy patients were hepatic failure and recurrent hemorrhage, respectively. Despite a comprehensive pretherapy evaluation that included multiple hemodynamic variables and quantitative measures of hepatic function, no test accurately predicted survival in the sclerotherapy group. Although functional hepatic reserve, usually assessed by Child's class, has been a useful prognosticator in some sclerotherapy series,[7,20] pretherapy Child's score was identical in patients who survived and in those who died after endoscopic sclerosis in the current investigation. In contrast, quantitative hepatic function as estimated by GEC predicted survival after shunt surgery. After a 2-year minimum follow-up, five of seven shunt patients with a preoperative GEC less than 250 mg/min have died. Only one patient with a GEC greater than 250 mg/min has died. Although preoperative Child's score was higher (worse hepatic function) in nonsurvivors than in survivors in the shunt group, this difference did not reach statistical significance. These results suggest that chronic sclerotherapy may be preferable to shunt surgery for patients with marginal hepatic reserve.

The 57% of sclerotherapy patients in whom recurrent hemorrhage developed is in the range reported by others.[7,8,20] Ten of the 17 patients with recurrent bleeding had catastrophic hemorrhage, which resulted in death in eight patients. Four of the ten patients had surgery, and two are currently alive. Thus, only two sclerotherapy failures have been salvaged by surgery. Several factors account for this low salvage rate. Recurrent hemorrhage was severe in all of these patients and the location of bleeding in the stomach rather than the esophagus in several individuals prevented temporary

TABLE 5. *Serial Hepatic Hemodynamic Data*

	Shunt			Sclerotherapy		
	N	Preoperative	1 Year	N	Preoperative	1 Year
EHBF (mL/min)	11	1418 ± 109	1191 ± 93	14	1294 ± 112	1155 ± 49
PPG	7	2.0 ± 0.3*	2.6 ± 0.5*	8	1.8 ± 0.4	1.9 ± 0.4
CSP (mmHg)	6	15.3 ± 2.6†	9.7 ± 1.3†	8	13.6 ± 1.8	16.4 ± 1.8

* $p = 0.03$. † $p = 0.04$.

TABLE 6. *Psychoneurologic Data*

	Shunt		Sclerotherapy	
	Preoperative	Postoperative	Preoperative	Postoperative
Spontaneous encephalopathy (%)	4	16	7	7
Induced encephalopathy (%)	22	0	23	14
Abnormal EEG (%)	33	43	17	26
Numbers connection test (sec)	45 ± 3 (15)	41 ± 2 (15)	47 ± 5 (17)	44 ± 6 (17)
Fasting ammonia (μmol/L)	39 ± 6 (10)	48 ± 7 (10)	50 ± 6 (15)	62 ± 11 (15)

( ) denotes number of patients; paired data before operation to 1 year after operation.

control by balloon tamponade or endoscopic sclerotherapy. In addition, three patients who failed sclerotherapy lived more than 300 miles from the tertiary hospital and bled to death before they could be transported. The three patients who died in our hospitals without surgical intervention had severe hepatic functional decompensation and coma develop secondary to recurrent hemorrhage. These patients were believed to be nonsalvageable, therefore surgery was not performed.

Although a majority of recurrent bleeding episodes (69%) occurred during the first year before variceal eradication was complete in many patients, five of eight fatal hemorrhages occurred in years 2–4, and three of these patients had had prior eradication of esophageal varices. Others[7,8] have also reported recurrent hemorrhage after variceal eradication, confirming the necessity of serial endoscopies in such patients. However, even careful follow-up is no guarantee against fatal hemorrhage as six of the eight patients who bled to death in this series had had endoscopy within 1 month of the fatal episode. Four of these patients had received variceal injections during endoscopy. Because of the frequency and severity of recurrent hemorrhage, pretherapy variables were analyzed to determine if any were predictors of this complication. Only prothrombin time and partial thromboplastin time separated the subgroup that rebled from the subgroup that did not, but the large overlap between subgroups limited the usefulness of these tests for prediction of recurrent hemorrhage.

In addition to prevention of variceal hemorrhage, two objectives of the DSRS are preservation of hepatic portal perfusion and maintenance of portal hypertension. Portal blood contains hepatotrophic hormones essential for maintaining liver size and function and unidentified substances believed to cause encephalopathy when they bypass the liver. Splanchnic venous hypertension may inhibit intestinal absorption of these cerebral toxins.[21] One aim of the current investigation was to determine whether portal flow is more rapidly collateralized after selective variceal decompression (DSRS) than occurs in the natural history of cirrhotic portal hypertension (sclerotherapy group). Both portal flow and CSP were well maintained in the early postoperative studies after DSRS. However, PPG was significantly increased (worsened) 1 year after DSRS, but was unchanged in the sclerotherapy group. Others[22,23] have also reported gradual loss of hepatic portal perfusion during the late postoperative interval after the DSRS, especially in patients with alcoholic cirrhosis. CSP, which reflects portal venous pressure in patients with cirrhosis,[24] was also significantly decreased 1 year after DSRS. Thus far, these late postoperative hemodynamic effects of the DSRS have not translated into major alterations in hepatic or psychoneurologic function. Although a higher percentage of shunt patients have developed spontaneous encephalopathy and abnormal EEGs, the differences between groups are not statistically significant. It is possible that differences in these variables as well as in the quantitative tests of hepatic function may become apparent as the interval of follow-up lengthens.

The results of this study differ from the recently published Emory University trial by Warren and coworkers[20] who reported significantly longer survival and better hepatic function in cirrhotic patients treated by sclerotherapy than for those undergoing elective DSRS.

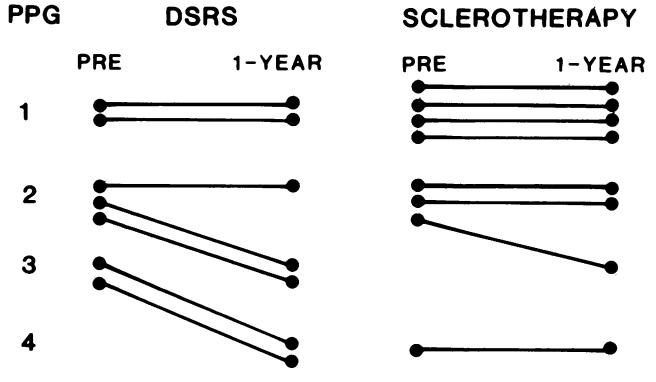

FIG. 3. Angiographic portal perfusion grades (PPG) before and 1 year after DSRS and endoscopic sclerotherapy. The change in PPG is significant after DSRS ($p = 0.03$) but not after sclerotherapy.

Two-year survival rates for the shunt groups in the two trials are similar (current study, 65%; Emory trial, 59%). In contrast, survival at 2 years after initiation of sclerotherapy in the Emory trial (84%) was greater than for our sclerotherapy group (61%). The major difference between the two investigations is the greater success of the Emory group in salvaging sclerotherapy failures by shunt surgery. At the time of their report, 11 sclerotherapy patients (31%) had undergone surgery and eight (22%) were still surviving. Only four patients (13%) in our sclerotherapy group received surgery and two (7%) are currently alive. Our inability to salvage more sclerotherapy failures was due to generally catastrophic recurrent hemorrhage, often during the first episode, which led to rapid deterioration of hepatic function.

Although the designs of these two trials are similar, several subtle differences may account for the conflicting results observed. First, the patient populations are different. The current investigation contains higher percentages of alcoholic cirrhotics (86% *vs.* 61%) and Veterans Administration Hospital patients (51% *vs.* 0). Although Warren and co-workers[20] reported a higher percentage of Child's C patients than in the current study (44% *vs.* 33%), the methods of classifying patients differ. Analysis of pretherapy data from the two investigations shows higher mean bilirubin and lower mean albumin and GEC in our trial, suggesting inclusion of patients with more advanced hepatic dysfunction. Only patients acceptable for the DSRS (hepatopetal portal flow and manageable ascites) were entered into the Emory trial. We accepted all patients who could undergo any type of shunt, although only three patients had spontaneous reversal of portal flow on pretherapy angiography and 85% of patients in the shunt group received the DSRS. Finally, in the current study, a significant percentage of patients (including three sclerotherapy failures) had to travel over 300 miles to return to the tertiary hospital because of the relatively sparse population and large geographic area of the Intermountain West and Plains compared with the Southeast. Thus, shunt surgery may be preferable to chronic sclerotherapy for patients living in such remote areas. Although it cannot be determined whether these factors account for the differences in results, they should be considered when interpreting the data from the two trials.

The only other study[25] that has compared shunt surgery and sclerotherapy comprised exclusively Child's C cirrhotic patients who were receiving emergency therapy for acutely bleeding varices. Therefore, it is not directly comparable to either the current investigation or the Emory trial.[20] This report by Cello and co-workers[25] showed similar short- and long-term survival rates for portacaval shunt and sclerotherapy patients. As in the current trial, recurrent hemorrhage was significantly more common in the sclerotherapy group and total medical costs were similar for both therapies, even though shunt surgery was significantly more expensive during the initial hospitalization.

In summary, at a mean follow-up interval of 2 years, this randomized trial has shown similar survival rates, levels of hepatic and neuropsychologic function, and total medical costs after shunt surgery (85% DSRS) and chronic endoscopic sclerotherapy. Hepatic portal perfusion and portal pressure were better maintained after sclerotherapy, but this hemodynamic advantage has not yet resulted in a differential in hepatic function between groups. Recurrent hemorrhage was more frequent after sclerotherapy (57%) and was the most common cause of therapy failure. Because of the severity of recurrent bleeding and geographic distribution of patients, only two of 10 sclerotherapy failures have been salvaged by surgery. Although none of the pretherapy variables predicted failure of sclerotherapy, preoperative GEC was significantly higher in shunt survivors than in nonsurvivors, suggesting that patients with limited hepatic functional reserve might be better served by sclerotherapy than by shunt.

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Discussion

DR. LOUIS R. M. DEL GUERCIO (New York, New York): I am filled with admiration for the authors' ability to perform this difficult piece of work in such a fine fashion. Those who deal with these types of patients know how difficult it is to maintain such controls.

I rise simply to speak about the patients who fail sclerotherapy. Sclerotherapy can be compared with the little girl with the curl in the middle of her forehead. When it's good, it's very, very good, and when it's bad, it's terrible. The question is what to do with the sclerotherapy failures.

The authors point out that they could salvage only 20% of these sclerotherapy failures, that is, those who continue to bleed despite attempts at sclerotherapy.

(Slide) We have been very concerned with this because at our institution, the Westchester County Medical Center, most bleeding cirrhotics who are referred to us are sclerotherapy failures.

What we do is a combination of splenic artery embolization through the standard Seldinger approach, putting Gianturco coils in the splenic artery to reduce the splenic contribution to portal flow and to reduce the degree of secondary hypersplenism with improvement in platelet counts.

The second part of the procedure is performed through a minilaparotomy in the x-ray suite under local anesthesia. We cannulate a branch of the mesenteric vein, go up into the portal system, and internally sclerose the coronary collaterals to the varices with absolute alcohol and use Gianturco coils to plug off the collaterals. In other words, this is a nonoperative Sugiura operation.

(Slide) In 36 consecutive patients (no one excluded) who were sclerotherapy failures, all of the Class B patients survived for at least 1 year. The red shows the survival of the Class C cirrhotics where 60% survived for at least 1 year, and the combination of Bs and Cs had an even better survival.

This is a satisfactory alternative to shunt surgery and can be done expeditiously in the x-ray department.

My question to the authors is: what are their plans in terms of better management of the sclerotherapy failures?

DR. JOHN PHILIP SANDBLOM (Sweden): I first express great happiness in having survived to be able to attend once more the summit of the surgical year, the meeting of the American Surgical Association! This gives me the opportunity to discuss one of the great interests in my surgical life with this excellent presentation of comparing shunt and sclerotherapy in portal hypertension.

My experience is long; it started 40 years ago and we once had one of the largest series of shunt operations in the world. I have always advocated the shunts for portal hypertension, although during recent years less successfully, as these have been in less favor. I am therefore very pleased to have this judged objectively with a prospective study, to see that the two methods are equal in many respects, and that we shall be able to continue doing the shunts with good prospects.

There are two more benefits from normalization of the portal pressure. Firstly, it corrects the stasis in the splanchnic tissues, for example in the gastric mucosa where erosive gastritis often ensues. Secondly, it relieves the patients of the great danger of severe hemorrhage after abdominal trauma or abdominal operations. I have once seen a patient with portal hypertension die of hemorrhage during a simple cholecystectomy.

In our series we had several cases of biliary cirrhosis due to ascending cholangitis from biliodigestive shunts. These patients often need reoperations for correction of anastomotic strictures.

In the first case we had great difficulties with hemorrhage. In the three remaining cases, we performed the operation in two stages: first the shunt operation and then when the portal pressure had been reduced to normal, with hemostasis.

I ask the authors if they have any experience with the advantage of normalizing the portal pressure in these cases.

DR. J. MICHAEL HENDERSON (Atlanta, Georgia): I congratulate Dr. Rikkers for putting surgical decompression and endoscopic sclerosis of varices to the true test of a prospective randomized clinical trial. In a similar trial at Emory our data look different.

My main area of discussion will focus on failures of sclerotherapy. In our study, 16 of 37 patients randomized to sclerotherapy either died or failed that therapy: four patients had their bleeding controlled, but have died of hepatic failure, one patient in this group has died of bleeding, which is in marked contrast to Dr. Rikkers' study, the other 11 patients had recurrent bleeding severe enough to be considered sclerotherapy failures and crossed over to shunt surgery. There was no operative mortality in these 11 cross-over patients, but four have subsequently died of hepatic failure at 3–47 months after cross-over.

The second major difference in the results of our two studies lies in the effect of therapy on liver function. At randomization, the severity of liver disease appears similar in the two studies. Our study, in contrast to Dr. Rikkers', showed significant improvement in hepatocyte function in the sclerotherapy group over time. Improvement in the galactose elimination capacity occurred predominantly in alcoholic