The Emory Prospective Randomized Trial: Selective Versus *Nonselective Shunt to Control Variceal Bleeding*

Ten-year Follow-up

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From 1971 to 1975, 55 patients with variceal bleeding secondary to cirrhosis were entered into a prospective randomized trial comparing distal splenorenal (selective) and H-graft interposition (nonselective) shunt. This 10-year follow-up documents that selective shunt is better ($p < 0.05$) in four of the five variables monitored. (1) Control of bleeding: selective shunt prevented variceal bleeding better than interposition shunt due to the higher ($0.05 < p < 0.1$) occlusion rate (30%) of interposition shunt. (2) Selective shunt maintained postoperative portal perfusion better ($p < 0.01$) than patent interposition shunt. Seventy-five per cent of selective shunt survivors have portal perfusion at 10 years: no patient with a patent nonselective shunt perfuses the liver. (3) Quantitative liver function was better preserved ($p < 0.01$) 10 years after selective shunt than nonselective shunt. (4) Postoperative encephalopathy occurred in fewer ($p < 0.01$) selective (27%) than nonselective (75%) shunt patients over the 10 years. (5) Survival: in the randomized population, the improved survival in the selective shunt subgroup did not reach statistical significance. However, improved survival was confirmed in nonalcoholics. Five of eight nonalcoholics operated with selective shunt are alive at 10 years with patent shunts. No nonalcoholic, of seven total, operated with nonselective shunt survived 10 years with a patent shunt. These data show that selective shunt was superior to nonselective shunt. There was less rebleeding and encephalopathy after distal splenorenal shunt; postoperative portal perfusion and hepatic function were maintained.

DEATH FROM VARICEAL HEMORRHAGE is the most devastating complication of portal hypertension. Surgeons have sought the optimum treatment for 80 years, and yet debate persists. This reflects the wide spectrum of available therapy options, plus the diversity of disorders that have portal hypertensive bleeding as a symptom.[1,2]

The first successful therapy for variceal bleeding was achieved in 1903 when Vidal performed a portacaval anastomosis in a cirrhotic patient with bleeding varices.[3] Prior to Vidal's operation, Pavlov's research had shown that Eck fistula produced liver atrophy and hepatic encephalopathy in experimental animals.[4,5] Vidal's patient experienced hepatic encephalopathy before dying of generalized sepsis,[6] thus fulfilling Pavlov's prediction of the likely course following portal diversion. For the next 40 years, few portacaval anastomoses were performed because of technical difficulties and the fear that total diversion of portal blood from the diseased liver would cause the portaprival syndrome.

In the 1930s, Dr. Allen O. Whipple and colleagues studied the natural history of portal hypertensive bleeding in patients with cirrhosis. Faced with the lack of effective treatment, Whipple courageously reassessed portacaval shunt. Although Whipple was aware of Pavlov's experiments,[7] newer work by Dr. George Whipple appeared to refute the causative role of portal venous diversion in the portaprival syndrome.[8] Whipple's remarkable initial success, published in 1945,[9] triggered an explosion of enthusiasm for portacaval shunt and its variations. However, over the next 15 years, clinical experience reaffirmed Pavlov's original observations on portal venous deprivation. The controlled trials with prophylactic and therapeutic portacaval shunt confirmed that shunted patients lived no longer than unoperated controls. Only the mode of death was changed. Unshunted patients

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died of recurrent bleeding; shunted subjects succumbed to hepatic encephalopathy and liver failure.[10-16]

Three alternative modes of therapy which acknowledged the importance of continued portal perfusion appeared: endoscopic sclerosis,[17-25] nonshunt procedures,[26-33] and selective shunt.[34] The first two options play an important role in acute control of bleeding, and may represent definitive management in patients who are not shunt candidates. Unfortunately, both have significant rates of rebleeding. The specific goals of selective shunt are trans-splenic decompression of gastroesophageal varices and maintenance of postoperative portal perfusion and intestinal venous hypertension. Initial experience with selective shunt documented that these aims could be achieved and led to this and five other controlled trials comparing distal splenorenal (DSRS) and nonselective shunt.[35-40] An additional prospective randomized study comparing selective and nonselective shunts in patients with schistosomiasis has recently appeared.[41]

Previous publications have followed this trial at progressive time intervals.[42-45] This report presents the 10-year follow-up data and echoes the findings at the earlier time periods. Combined with results of other controlled and uncontrolled experience, these data show the superiority of selective shunt in the management of variceal bleeding in cirrhotic patients.

Methods

Patient Population

Patients were entered from three hospitals of the Emory University Affiliated Hospitals System: Emory University Hospital, Grady Memorial Hospital, and the Atlanta Veterans' Administration Hospital (Table 1). Randomization criteria were: (1) biopsy proven cirrhosis; (2) at least one episode of documented variceal bleeding requiring three or more units of blood; (3) absence of ascites (transient ascites with a bleeding episode did not preclude randomization); (4) vascular anatomy amenable to either shunt; and (5) presence of hepatopedal flow, as graded in the venous phase of the splenic or superior mesenteric arteriogram.[46] The two groups were comparable by all variables monitored.

Randomization Process

Patients were randomized to DSRS or nonselective shunt just prior to surgery. Twenty-eight patients were randomized for nonselective shunt; 27 for DSRS. Two patients randomized for selective shunt received nonselective shunt because of intraoperative technical considerations, and a third refused nonselective shunt because of personal conviction. Data are presented on the 29 nonselective and 26 selective shunts actually performed. Randomization was terminated after 55 patients because selective shunt was shown to be superior to nonselective shunt with regard to encephalopathy.

TABLE 1. *Prerandomization Clinical and Laboratory Data of the Two Study Groups*

	Selective (N = 26)	Nonselective (N = 29)	p Value
Age (mean, years)	49	51	>0.1
Sex (male)	16 (62%)	19 (66%)	>0.1
Alcoholic cirrhosis	18 (69%)	22 (76%)	>0.1
Private patients	14 (54%)	20 (69%)	>0.1
GMH and AVAH patients	12 (46%)	9 (31%)	>0.1
Hct (%)	36 ± 6.0	35 ± 4.0	>0.1
Prothrombin time (sec prolonged)	1.6 ± 1.4	1.8 ± 1.0	>0.1
Albumin (g/100 ml)	3.7 ± 0.7	3.7 ± 0.6	>0.1
Total bilirubin	1.5 ± 1.3	1.5 ± 0.7	>0.1
Child's score	6.7 ± 1.6	7.1 ± 1.6	>0.1
Maximal rate of urea synthesis (PO) mg N/hr/kgm $BW^{0.75}$	46.4 ± 9.9	42.4 ± 10.6	>0.1

Surgery Performed

Distal splenorenal shunt has three components (Fig. 1): (1) division of the splenic vein as it joins the superior mesenteric vein and anastomosis to the superior aspect of the left renal vein; (2) gastric devascularization; and

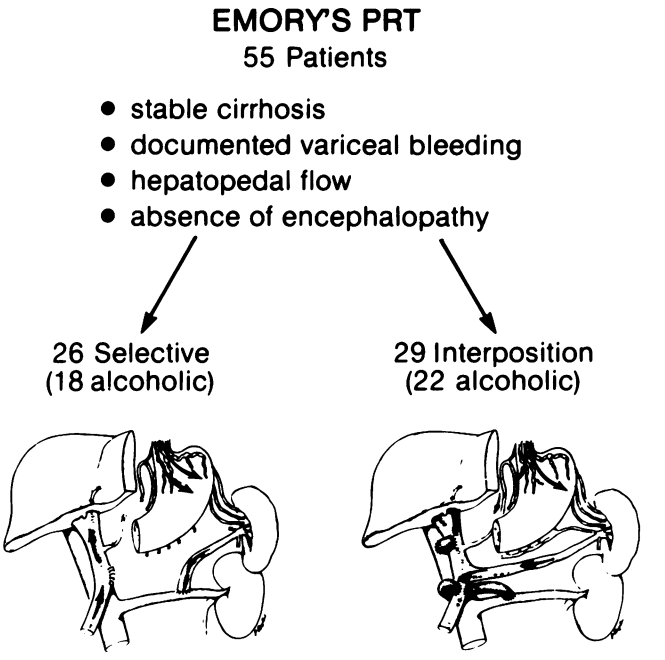


FIG. 1. Selective shunt (distal splenorenal shunt) has three components. Interposition nonselective shunt is functionally a side-to-side portacaval shunt.

(3) coronary azygous disconnection. The aims of distal splenorenal shunt are achieved only if gastric devascularization and coronary azygous disconnection are performed.[34]

Nonselective shunt is any shunt that allows total decompression of the portal venous hypertension into the systemic circulation (Fig. 1). Dacron® H-graft interposition shunts, which physiologically are identical to side-to-side portacaval shunts, were performed in the majority of patients.[47] Eighteen patients received mesorenal, six mesocaval, three side-to-side splenorenal, one splenocaval, and one, end-to-side portacaval shunt.

Evaluation

All 55 patients were evaluated prior to surgery with standard laboratory studies, liver biopsy, and visceral angiography. Forty-one patients were hospitalized in the Clinical Research Facility and studied under standardized conditions. Forty-seven of 49 patients who survived surgery were readmitted to the Clinical Research Facility on one or more occasions in the 10-year postoperative period.

No patient was lost to follow-up; two patients have refused inpatient re-evaluation.

A complete evaluation consisted of: history, physical examination, and standard and quantitative tests. Records of hospitalization elsewhere were pursued. Clinical and laboratory evaluations were combined to give a Child's class.[48] In later reports,[44] a modified Child's score emphasizing serum albumin, total bilirubin, and three clinical parameters (nutrition, ascites, and encephalopathy) was employed.[49]

Quantitative Studies

Maximal rate of urea synthesis (MRUS)[50,51] and ammonium chloride tolerance[52] were used to measure liver function for the first 6 years of the study. Galactose elimination capacity (GEC) was used as our quantitative function test for the latter 7 years.[53] Liver volume was measured by computed tomography (CT) scan.[54]

Hepatic encephalopathy was evaluated by history, clinical examination, psychometrics, and electroencephalogram (EEG). Electroencephalograms were graded by the Parsons-Smith classification.[55] Work published in conjunction with this trial[43,56] showed that psychometric tests, physical examination, and electroencephalogram could define subclinical hepatic encephalopathy.

Portal perfusion was graded on the venous phase of the superior mesenteric arteriogram (I: normal; IV: absent or reversal of flow).[46] Shunt patency was documented by arteriovenography. Initially, the venous phase of the splenic and superior mesenteric arteriogram was used to assess selective and nonselective shunt patency. In recent years, direct catheterization of shunts has been used because of the added advantage of measuring pressure gradients across anastomoses. Nutritive liver blood flow has been measured by low-dose galactose clearance.[57]

Definitions

Hepatic encephalopathy. Clinical encephalopathy was defined as an episode of mental confusion clearly related by the patient of family member, or detection of disorientation by a physician. Confusion or coma prior to death from hepatic failure were excluded, as was acute encephalopathy associated with electrolyte imbalance, recurrent bleeding, or drugs. Subclinical encephalopathy is the triad of hyperammonemia, abnormal EEG, and deranged psychometric tests. For this report, we define the functional spectrum of encephalopathy as in Table 6.

Portal perfusion. This was defined as present if the portal vein or any of its tributaries visualized on the venous phase of the superior mesenteric arteriogram (grades I through III). In the third report of this trial,[44] grades III and IV were combined and defined as portal flow absent. We have now reverted to the original definition, as we believe *some* prograde flow is present if the portal vein is visualized in venous phase superior mesenteric angiography.

Shunt-related morbidity. Morbidity after shunt surgery can be separated from liver failure which may represent progressive disease. Shunt-related morbidity was defined as shunt occlusion, recurrent variceal bleeding, or serious encephalopathy (grades II, III, and IV).

Statistics

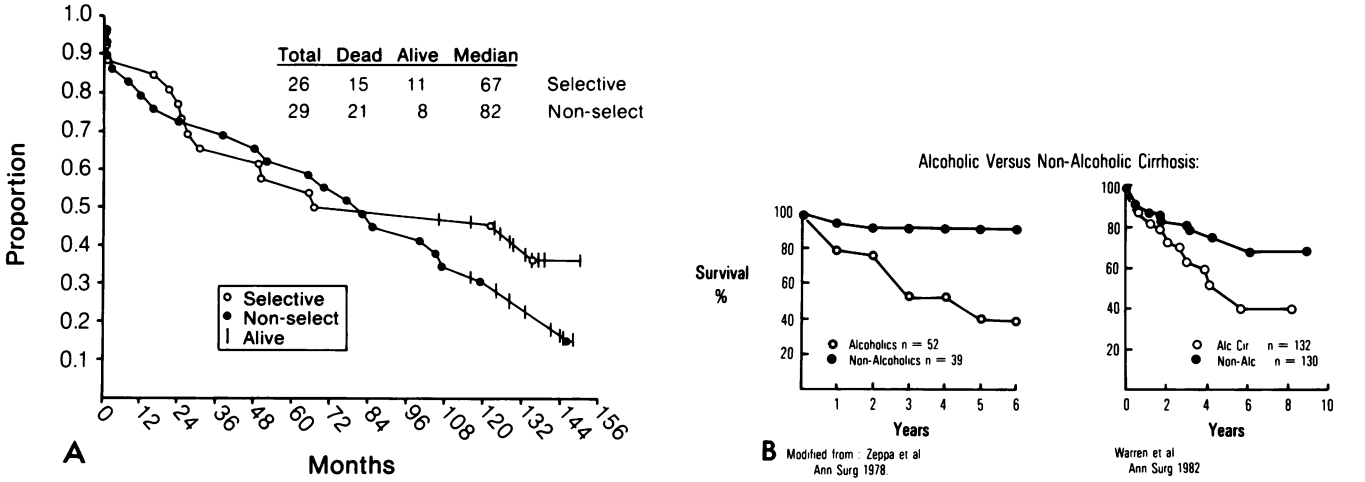
The data generated from the evaluations conducted before and after surgery were analyzed using multiple methods including Fisher's exact test, paired and unpaired t-test, and analysis of variance with multiple pairwise comparisons.

Results

Survival/Mortality

All surviving patients have been followed a minimum of 110 months (9.2 years). Mean follow-up for selective shunt survivors is 129 ± 12 months (10.8 years) and not significantly different that that for nonselective shunt (135 ± 11 months: 11.3 years). No patient has been lost to follow-up.

Hospital mortality was defined as death within 30 days of surgery, or death occurring in the same hospitalization as surgery. There were three such deaths in each group.



FIGS. 2A and B. *A, left,* Kaplan-Meier Survival Plot: there was no significant difference in the selective or nonselective shunt curve at any point during the 10-year follow-up period. *B, right,* Survival after selective shunt is better ($p < 0.05$) in nonalcoholics than alcoholics.

Figure 2 shows the Kaplan-Meier survival curves for the two groups. The two survival curves are not significantly different. Eight selective and eight nonselective shunt patients died during the first 5 years after surgery. From the fifth to the tenth year following surgery, four selective and 10 nonselective shunt patients expired. Individual patient mortalities are summarized in Table 2. Selective shunt survival at 10 years (41%) is not significantly different from nonselective shunt (28%). Mean (129 *vs.* 135 months) and median (67 *vs.* 82 months) survival are not significantly different. Patients with nonalcoholic liver disease have a different survival pattern from those with alcoholic liver disease. Eight nonalcoholic patients had selective shunt: five (63%) survive at 10 years with patent shunts. Seven nonalcoholic patients had nonselective shunt: two (29%) survive at 10 years; neither has a patent shunt.

Shunt Patency and Bleeding Control

Forty-nine of 55 patients had shunt status determined by angiograph or by autopsy in the follow-up period.

TABLE 2. *Mortalities*

Selective Shunts			Nonselective Shunts		
Patient	Time Until Death (Months)	Cause	Patient	Time Until Death (Months)	Cause
1	1*	Hepatic failure	16	1*	Hepatic failure
2	1*	Hepatic failure	17	1*	Hepatic failure
3	1*	Sepsis	18	1*	Hepatic failure
4	16	Hepatic failure	19	3	Hepatic failure
5	21	Hepatic failure; alcoholism	20	8	Hepatic failure
6	24	DIC, Renal failure	21	12	Hepatic failure
7	25	Hepatic failure; alcoholism	22	16	Gastric cancer
8	27	Hepatic failure; alcoholism	23	24	Suicide
9	31	GI hemorrhage	24	38	Hepatic failure
10	49	Hepatic failure; alcoholism	25	48	Hepatic failure
11	50	Alcoholic hepatitis	26	52	Hepatic failure
12	65	Sepsis	27	65	Cancer
13	67	Bronchopneumonia	28	70	Mandibular cancer
14	122	Brain hemorrhage	29	77	Cancer, floor of mouth
15	135	Renal failure	30	82	MI
			31	85	Hepatic failure
			32	100	Hepatic failure
			33	105	Hepatic failure
			34	107	Hepatoma
			35	119	GI hemorrhage
			36	151	GI hemorrhage

* Hospital mortality.

TABLE 3. *Postoperative Portal Perfusion*

	Preoperative		1 to 2 Years		3 to 4 Years		7 Years		10 years	
	S*	N*	S	N	S	N	S	N	S	N
Portal perfusion	26	29	14	1	9	2	9	4	6	2
No perfusion	0	0	2	23	3	13	2	9	2	6
p			<0.001		<0.002		<0.02		<0.07	
Patent	NA	NA								
Portal perfusion			14	0	9	0	9	0	6	0
No perfusion			2	23	3	12	2	7	2	4
p			<0.001		<0.001		<0.002		<0.03	
Occluded	NA	NA								
Portal perfusion			0	0	0	2	0	4	0	2
No perfusion			0	1	0	1	0	2	0	2

* S = Selective; N = Nonselective.

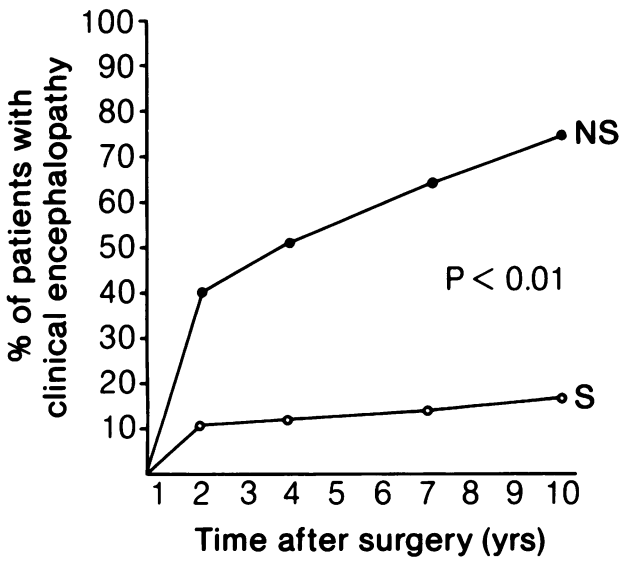


FIG. 3. Encephalopathy after nonselective shunt (NS) increases over time and develops before hepatic failure. Encephalopathy after selective shunt (S) evolves as liver function decreases.

Nonselective shunts. Nine shunts in eight patients occluded: four rebled from varices; two died of rebleeding; and two have been controlled to date with sclerotherapy. One additional patient whose shunt patency was unproven bled massively and died in liver failure. Eight additional patients with patent shunts had upper gastrointestinal bleeding during the 10 years after surgery. Two bled from duodenal ulcer; two from gastritis; one from gastric cancer; and the source was undetermined in the remaining three.

Selective shunts. Three of 21 patients with selective shunts studied had occluded shunts; two rebled from varices. Three additional patients with documented patent shunts rebled; one from an ulcer; two from gastritis. Upper gastrointestinal bleeding occurred in three other patients whose shunt status was not documented: in two, this was associated with terminal liver failure; the third bled massively in an outlying hospital and died. All 10-year survivors have patent shunts and have not rebled.

The time of shunt occlusion is different for selective and nonselective shunts. Selective shunt occlusions occurred soon after surgery. In contrast, nonselective interposition shunt occlusions continued to occur late; six of the nine occurred 4 to 7 years after surgery. The single nonselective shunt occluding in the first postoperative month led to rebleeding. A second interposition shunt was constructed which occluded 7 years later, leading to further variceal bleeding.

Portal Perfusion

All patients had prograde portal perfusion as a criterion for study entry (Table 3). Portal perfusion was maintained after selective shunt in 14 of 16 patients studied at 1 to 2 years; nine of 12 patients at 4 years; nine of 11 patients at 7 years; and six of eight patients having angiography at ten years.

Patients with nonselective shunts lost portal perfusion immediately unless they had shunt thrombosis. Four of the nine shunt occlusions resulted in restoration of portal perfusion.

Encephalopathy

Absence of encephalopathy was an entry criteria for this trial. Postoperative encephalopathy was more common after nonselective shunt ($p < 0.01$). When *all* patients in the study are considered, 22 of the 29 (75%) nonselective shunt patients suffered clinical encephalopathy at some time during the study. Seven of 26 (27%) selective shunt patients exhibited clinical encephalopathy at some point in the postoperative period. Nonselective shunt patients developed clinical encephalopathy before they evolved liver failure (Table 2). Selective shunt patients usually developed encephalopathy as liver function deteriorated over time.

Figure 3 summarizes the evolution of clinical encephalopathy in survivors with patent shunts at each evalu-

TABLE 4A. *Quantitative Liver Function**

	Preoperative			0 to 12 months			3 to 4 years			7 Years			10 Years		
	S†	N†	p	S	N	p	S	N	p	S	N	p	S	N	p
MRUS (mg/hr/ kgm BW)	47 ± 10	44 ± 10	NS	46 ± 9	31 ± 15	<0.01	45 ± 15	42 ± 7	>0.1						
NH_4Cl tolerance (ug min/ 100 ml)	0.16 ± 0.02†	0.14 ± 0.02‡	NS	0.14 ± 0.03‡	0.06 ± 0.01‡	<0.01	5689 ± 3536	8046 ± 3542	>0.1						
Antipyrine Clearance (mls/min)							39 ± 19	24 ± 12	>0.1						
GEC (mg/min)							321 ± 86	293 ± 85	>0.1	345 ± 87	310 ± 119	NS	316 ± 91	285 ± 61	NS

* All patients: patent and occluded shunts.
† S = Selective; N = Nonselective.
‡ Grams per kilogram BW.[42,43]

ation time. The incidence of clinical encephalopathy at each reporting period follows: (1) nonselective shunt; 1 year, 44%; 3 years; 52%; 7 years, 66%, 10 years, 75%; (2) selective shunt: 1 year, 12%; 3 years 12%; 7 years, 15%; 10 years, 18%.

Encephalopathy represents a spectrum as defined in Methods. We have applied this classification to the survivors. The single encephalopathic selective shunt patient has episodic clinical encephalopathy. She was graded Functional Class III because she is functional in her family unit. The six nonselective shunt survivors who have clinical encephalopathy also represent a spectrum. One patient is Class IV. In spite of severe (20 g) protein restriction and neomycin therapy, he is continually confused. Four patients are Functional Class III. All have persistent hyperammonemia and episodic confusion on protein restriction and lactulose therapy. They are functional in their home/social unit, but none work. The last patient is Class II. She is functional in her home situation and works part-time.

Quantitative Liver Function

Serial changes are summarized in Tables 4A and B. One year after surgery, MRUS and ammonium chloride tolerance deteriorated ($p < 0.01$) in nonselective shunt patients, but did not change in selective shunt subjects. Four years after surgery, MRUS was not significantly different between selective and nonselective shunt survivors. This analysis included nonselective shunt survivors with occluded shunts and portal perfusion. When survivors with portal perfusion were compared to survivors who had lost portal perfusion, MRUS, ammonium chloride tolerance, and galactose elimination capacity were significantly better in those with portal perfusion.

The 7-year postoperative evaluation studied 13 survivors in both the selective and nonselective shunt groups. Six of the 13 nonselective shunts had occluded. All selective shunts studied (N = 11) were patent. Galactose elimination capacity was better ($p < 0.05$) in selective shunt survivors than nonselective shunt survivors with patent shunts. This same finding was confirmed at the 10-year follow-up.

Shunt Related Morbidity

Ten (38%) selective shunt patients suffered shunt-related morbidity over 10 years. Seven patients had clinical encephalopathy and three occluded shunts. Two re-bled from varices.

Twenty-seven (93%) nonselective shunt patients had shunt-related morbidity over 10 years; 19 had clinical encephalopathy and eight occluded shunts. Four rebled from varices.

When the 10-year survivors are considered, one of 11 (9%) selective shunt patients and seven of eight (88%) nonselective shunt subjects have shunt related morbidity. The selective shunt patient is a Functional Class III encephalopathic. Four (50%) of nonselective shunt survivors have occluded shunts and three have rebled from varices. Three of the remaining four have clinical encephalopathy.

Discussion

These data generated from the 10-year follow-up evaluation echo the findings at earlier study points and

TABLE 4B. *Patent Shunts*

	GEC (mg/min)		
	3 to 4 Years	7 Years	10 Years
1. Selective (patent)	321 ± 86 (12)*	345 ± 87 (10)	316 ± 91 (8)
2. Nonselective (patent)	256 ± 68 (12)	253 ± 64 (4)	259 ± 50 (4)
3. Nonselective (occluded)	315 ± 82 (2)	367 ± 143 (4)	312 ± 67 (4)
1 *vs.* 2	<0.05	<0.05	<0.05
1 *vs.* 3	>0.1	>0.1	>0.1
2 *vs.* 3	>0.1	>0.1	>0.1

* (N) = Patients studied.

TABLE 5. *Other Prospective Randomized Trials Comparing Selective with Nonselective Shunt*

Selective Shunt*	Population		Operative Mortality†	Late Mortality	Encephalopathy	Shunt Occlusion
	Alcoholic	Nonalcoholic				
1[36]	13	0	1/13	5/13	—	0/12
2[37]	21	6	5/27	8/27	3/22	2/18
3[38]	21	3	2/24	6/24	6/19	3/19
4[39]	22	1	1/23	4/23	1/22	1/22
5[40]	19	0	2/19	5/19	2/17	—
Nonselective Shunt						
1	14	0	1/14	4/14	—	2/14
2	16	12	0/28	9/28	14/28	0/28
3	26	3	6/29	12/29	5/22	2/23
4	14	5	0/19	0/19	2/19	1/19
5	16	0	4/16	6/16	3/12	—

* References.

† In-hospital or 30-day mortality.

support the conclusion that selective shunt is superior to nonselective shunt as therapy for cirrhotics with variceal bleeding.

Selective shunt controls bleeding better than H-graft interposition nonselective shunt because the latter occludes over time. The vein-to-vein anastomosis of distal splenorenal shunt will remain patent just as vein-to-vein end-to-side portacaval shunts remain patent. If shunt occlusion occurs after selective shunt, it is usually due to the technical aspects of splenic vein dissection[58] or to a poor-quality splenic or renal vein. Selective shunts at risk to occlude usually can be identified at surgery, and will obstruct during the first week following surgery. This defines the necessity of postoperative angiography during the first 10 days after surgery. If selective shunt revision is required, it is technically easier in the 2 weeks after original procedure.

The progressive occlusion of H-graft interposition shunts observed in this trial has also been reported by Smith[59] and Stipa.[60] H-graft interposition shunt is not as effective in controlling bleeding as end-to-side or side-to-side portacaval shunt.[61–65] Selective shunt is.

Selective shunt preserves postoperative portal perfusion; patent H-graft interposition shunts cannot and do not. Critics of selective shunt[66–69] have suggested that portal perfusion is rapidly lost after surgery. The fact that 75% of the 10-year selective shunt survivors have portal perfusion refutes this claim. Some patients do lose portal perfusion after selective shunt. At least three factors are involved. Failure to perform adequate coronary azygous disconnection will result in early loss of portal perfusion. Over time, transpancreatic collaterals evolve after selective shunt. In alcoholics, this pancreatic sump[70] facilitates loss of portal perfusion. As Figure 4 shows, however, collateralization *per se* does not equate with loss of portal perfusion. In spite of massive transpancreatic collateralization, excellent portal perfusion (and quantitative liver function) are maintained 11 years after selective shunt. Alcoholics lose portal perfusion more frequently and rapidly than nonalcoholics, which

TABLE 6. *Functional Classification of Encephalopathy*

	Functional Limitation	Dietary Protein Restriction	Lactulose/ Neomycin Therapy	EEG	Fasting Hyperammonia	Fasting Abnormal Amino Acid Profile
I	None	None	None	Normal	None/mild	Rare
II	Minimal; functional in home; usually can work	Mild (60 g)	±	Normal 0–A	Common	±
III	Moderate; usually functional in family unit; rarely works	Moderate (40 g)	Required	Abnormal B–C	Usual	Usual
IV	Functionally disabled; near total care in home or institution	Severe (20–30 g)	Required	Abnormal C	Unusual if absent	Unusual if absent

coincides with the evolution of the hyperdynamic state.[71] We propose that the lowered peripheral resistance of the hyperdynamic state and collateralization are additive and are responsible for the accelerated loss of portal perfusion in the alcoholic cirrhotic. Splenopancreatic disconnection, which is an extension of selective shunt,[70] may prevent loss of portal perfusion in alcoholics.

Selective shunt maintained quantitative liver function better than nonselective shunt. This was observed at every time period after surgery including the 10-year follow-up evaluation.

The same observation was true for encephalopathy. Selective shunt had a lower incidence of postoperative encephalopathy at every time period after surgery. Except for Conn's report,[38] selective shunt was superior to nonselective shunt in the other controlled trials. As pointed out by Zeppa,[74] this may reflect inexperience of the surgeon rather than failure of the procedure. The 18% of encephalopathy in the 10-year selective shunt survivors compares favorably with the 20% 5- and 8-year incidence in unoperated subjects reported by Jackson and Resnick.[11-14]

Survival was the final variable monitored during this trial. Eleven selective (42%) and four (14%) nonselective shunt patients have survived 10 years after surgery with patent shunts. Four additional nonselective shunt patients were alive at 10 years with occluded shunts. The patients prevent the increased survival after selective shunt from achieving statistical significance. The same problem of shunt occlusion confounds analysis of survival in the nonalcoholic subpopulation. As shown by Zeppa[75] and the Emory 10-year experience,[76] selective shunt prolongs survival ($p < 0.05$) in nonalcoholics. In this controlled trial, eight nonalcoholics were operated with selective shunt. Five (63%) survive at 10 years with patent shunts. Seven patients received nonselective shunt. None survived 10 years with a patent shunt; two (29%) survived with occluded shunts.

Randomized and nonrandomized studies suggest that selective shunt does not prolong survival when compared to nonselective shunt in alcoholics (Table 5). This may in part be due to the more rapid loss of portal perfusion and the evolution of the hyperdynamic state that characterizes the alcoholic. Quantitative data have shown that alcoholics who lose portal perfusion can maintain good hepatocyte function 1 year after surgery, but this is associated with a significant increase in cardiac output and nutritive hepatic blood flow.[70] It is of note in Figure 2 that the alcoholic/nonalcoholic survival curves begin to separate at 2 years. It is logical to infer from Pavlov's principles and the hepatotrophic factor concept advanced by Starzl[77] that, in hyperdynamic selective shunt patients who lose portal perfusion, function and survival will decline.

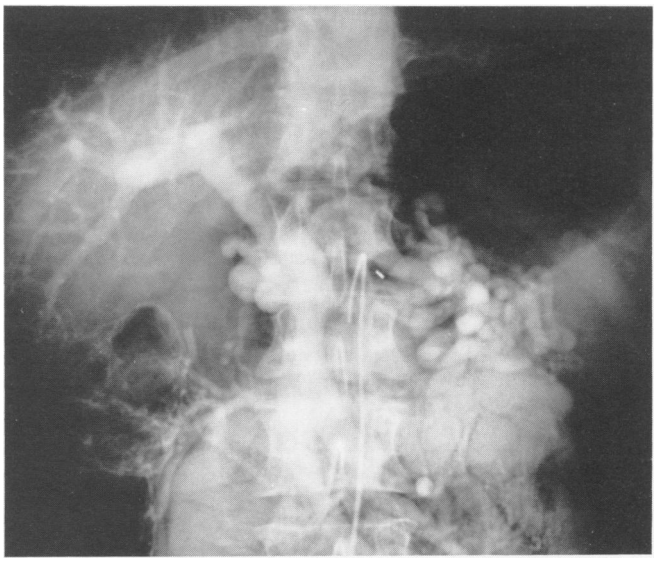


FIG. 4. Venous phase of superior mesenteric arteriogram 11 years after surgery in a nonalcoholic posthepatitic cirrhotic with a patent selective shunt.

Key questions remain. The pathophysiology of the hyperdynamic state must be carefully studied because its development coincides with a decreased trend in survival. A major step toward better understanding of the problem has been made with the ability to accurately monitor liver blood flow. Quantitative measurement of portal flow (milliliters per minute) should be available in the near future using Doppler ultrasound. Careful experimental work must be done to substantiate this method. These data support Pavlov's conclusions and define the need for continued metabolic studies of hepatotrophic factors (insulin) and the altered nitrogen metabolism of cirrhosis.

This trial, which has spanned 13 years, has shown that the original three tenets of selective shunt are clinically and physiologically valid. Selective shunt ameliorates the metabolic sequellae of the portaprival syndrome. "Long-term control of bleeding, survival with clinical well-being has been achieved."[78] We conclude:

1. Selective shunt prevents rebleeding from gastroesophageal varices.
2. Selective shunt maintains postoperative portal perfusion and liver function better ($p < 0.05$) than nonselective shunt.
3. Hepatic encephalopathy is significantly less ($p < 0.01$) frequent after selective shunt than nonselective shunt.
4. Survival in nonalcoholics is better after selective shunt than nonselective shunt.
5. Selective shunt is the surgical procedure of choice in patients with recurrent variceal bleeding.

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Discussion

Dr. Robert Zeppa (Miami, Florida): We are indebted to Dr. Millikan and his colleagues for this elegant work. In fact, when you have an opportunity to review the manuscript in the *Annals of Surgery*, you will find that it is more than elegant and extraordinarily informative.

This is a trial that has been carried out longer than any other prospective randomized trial concerning efficacy of shunts, short of the first one that was done in Boston. None of the others have been carried out this far, and that one in Boston stopped at 7 years.

This well-written paper carries the meat of the argument, summarized by Dr. Millikan, clearly showing the therapeutic advantage of distal splenorenal shunt.

I would like to corroborate Dr. Millikan's findings (slide) concerning survival of nonalcoholics. My colleagues and I, Drs. Hutson, Livingston, and Levi, updated this information as of July 1983. The middle bar is an actuarial analysis of survival of our entire group at that time, with the numbers listed on the slide. The upper graph depicts the survival of nonalcoholics out to 8 years. The standard errors are still too large at this point. It will be 15 years from the time we started this until we will be able to tell you about the 10-year survival with a degree of confidence.

Note the standard errors. We begin to see, as Dr. Millikan point out, a separation in survival in those groups at about 2 years. The lower curve depicts the survival of the alcoholics, but within this cohort of nonalcoholic patients, uniformity is not the order of the day.

(Slide) Examine this particular curve, actuarial analyses. This depicts the survival of our patients who were on steroids, 20% of the population of nonalcoholics. Note the improved survival of those not on steroids when you pull these patients out.

I would like to ask Dr. Millikan three questions. Does age play a role in the encephalopathy after distal splenorenal shunt in your series? In ours it has not—which in entirely different from the experience reported for total portal diversion.

Second, are there later measurements of the maximum rate of urea synthesis? From the manuscript, it seemed to have improved in 4 years, and I wonder if that is just a reflection of those patients with rags in the venous system, where clots develop.

Third, do you have any data at all concerning survival in the alcoholic cohort where continued alcohol abuse is a problem? Dr. Hutson, your Local Arrangements Chairman, has been looking at our population of patients who have, we think, stopped drinking, and we have gone through a long rigamarole. We have no statistically significant information now, but the trend seems to be that these people will have, following distal splenorenal shunt, an equal survival to the nonalcoholics.

It was a pleasure to listen to this very important, scholarly work. I believe that this presentation represents the final effective nail in the coffin of the Philistines, who have doubted the efficacy of distal splenorenal shunt in the therapy of variceal hemorrhage.

Dr. Jere W. Lord, Jr. (New York, New York): I did not realize I would be among the Philistines. In fact, I agree with Dr. Zeppa that this excellent paper by Dr. Millikan and his associates has relegated central venous shunts, such as splenorenal and interposition mesocaval,