

# Shunt Surgery During the Era of Liver Transplantation

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## Objective

The indications for and the results of portosystemic shunts done in the authors' institution since initiation of a liver transplant program 10 years ago were reviewed.

## Summary Background Data

With the widespread availability of liver transplantation as definitive treatment of chronic liver disease, the role of shunts in the overall management of variceal bleeding needs to be redefined.

## Methods

Seventy-one variceal bleeders with cirrhosis who received a shunt (82% distal splenorenal shunts) because of sclerotherapy failure or because endoscopic treatment was not indicated were reviewed retrospectively. In 44 patients with well-preserved hepatic reserve, the shunt was used as a long-term bridge to transplantation (shunt group 1). The remaining 27 patients with shunts were not transplant candidates mainly because of uncontrolled alcoholism or advanced age (shunt group 2). Survival of both shunt groups was compared to that of 180 adult patients with a history of variceal bleeding who underwent transplantation soon after referral.

## Results

Because of their more advanced liver disease, the liver transplant group had a higher operative mortality rate (19%) than did either of the shunt groups (5% and 7%, respectively) ( $p < 0.02$ ). Kaplan–Meier survival analysis showed better survival in shunt group 1 (seven patients thus far transplanted) than in either the liver transplant group or shunt group 2 during the early years and superior survival of shunt group 1 and the liver transplant group as compared to shunt group 2 during the later years of the analysis. Only two patients from shunt group 1 have died of late postoperative hepatic failure without benefit of liver transplantation.

## Conclusions

A shunt may serve as an excellent long-term bridge to liver transplantation in patients with well-preserved hepatic reserve. Shunt surgery still plays an important role in treatment of selected patients with variceal bleeding who are not present or future transplant candidates.

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From the time of their introduction into clinical practice in the mid-1940s until 15 to 20 years ago, surgically constructed shunts were the only effective options for control of variceal bleeding and prevention of its recurrence. Since then, however, a number of other therapies have become available, resulting in a decreased number of shunts being performed. Endoscopic sclerotherapy and the transjugular intrahepatic portosystemic shunt (TIPS) are less invasive alternatives than shunt surgery, and hepatic transplantation provides definitive treatment not only for bleeding but for end-stage liver disease as well. Has the advent of these newer approaches made shunts obsolete? If not, where in the treatment algorithm do shunts fit in the modern management of portal hypertensive bleeding?

The purpose of the current investigation was to review the results of and to define the evolving role of shunt surgery at the University of Nebraska Medical Center since initiation of our liver transplant program.

## MATERIALS AND METHODS

The liver transplant program at the University of Nebraska Medical Center was initiated in July 1985. All patients with chronic liver disease complicated by variceal bleeding who had either a shunt operation or a liver transplant between July 1985 and February 1995 at our institution were reviewed. During this interval, 77 shunt operations were performed. Excluded from the analysis because they did not have chronic liver disease are six patients who received distal splenorenal shunts for variceal bleeding secondary to portal vein thrombosis (five pediatric patients and one adult in whom portal vein thrombosis developed several months after liver transplantation). The remaining 71 patients with shunts were divided into two groups based on their future transplant candidate status.

Shunt group 1 consisted of 44 patients who were considered potential future transplant candidates but received a shunt for definitive control of variceal bleeding because of well-preserved hepatic functional reserve (Child's class A or B) or, in one case, as an emergency when nonsurgical attempts to control bleeding failed. Shunt group 2 included 27 patients not considered to be future transplant candidates because of age older than 65 ( $N = 11$ ), uncontrolled alcoholism ( $N = 13$ ), cardiopulmonary disease ( $N = 1$ ), mental retardation ( $N = 1$ ), and unwillingness to receive blood transfusions (Jehovah's witness,  $N = 1$ ).

A shunt rather than chronic sclerotherapy was selected for these 71 patients for 1 or more of the following rea-

sons: sclerotherapy failure ( $N = 33$ ), bleeding from gastric varices or portal hypertensive gastropathy ( $N = 7$ ), residence distant from tertiary care facilities ( $N = 50$ ), patient choice ( $N = 5$ ), and no prior variceal bleeding ( $N = 2$ , Budd-Chiari syndrome). Fifty-three patients with shunts (75%) had bled within 1 month of their operation. Preshunt therapy for variceal bleeding included endoscopic variceal sclerosis ( $N = 50$ ) and TIPS ( $N = 2$ ). Nine shunt surgeries (seven in shunt group 1 and two in shunt group 2) were performed urgently within 48 hours of active bleeding.

Of 652 adult patients who received liver transplants during this same interval, 180 (28%) had bled previously from varices and these patients comprise the transplant group. Thirty-four individuals (19%) had bled within 1 month of the transplant operation. Pretransplant therapy for variceal bleeding included endoscopic variceal sclerosis (140 patients), portosystemic shunt (29 patients), and TIPS (8 patients). Transplantation was selected as the initial therapy after referral to our institution for patients with either limited hepatic functional reserve (Child's class B- and C) or stable liver disease (Child's class A and B+) with symptoms that adversely impacted the quality of life (*e.g.*, fatigue, bone pain, encephalopathy). Transplant patients had either nonalcoholic disease or were abstinent alcoholic patients with cirrhosis and had no other advanced organ system dysfunction (*e.g.*, cardiopulmonary disease) that precluded the transplant operation.

Age, gender, cause of liver disease, and preoperative Child's class were determined for all patients. Child's class was determined by a numeric grading system that was derived from serum albumin, serum bilirubin, neuropsychological status, and ascites status.<sup>1</sup> Child's class was assessed just before surgery.

Operative mortality was defined as death occurring during the same hospitalization as the operation, or within 30 days after surgery for discharged patients. Indicators of postoperative morbidity in the patients who received shunts were recurrent bleeding from portal hypertension, encephalopathy, and ascites. An episode of encephalopathy was defined as an incident of mental confusion related by the patient or a family member or detection of disorientation on interview or asterixis on physical examination by a physician. Encephalopathy was considered mild if it was transient and did not require hospitalization and severe when it required hospitalization and/or prolonged management with lactulose and dietary protein restriction. Neuropsychologic dysfunction developing just before death from hepatic failure was not considered as encephalopathy. Ascites was considered significant if it prolonged hospitalization after a shunt or later required rehospitalization or chronic treatment with diuretics. Shunt patency was assessed in all patients with shunts by either selective

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Accepted for publication April 16, 1996.

**Table 1. PREOPERATIVE CHARACTERISTICS**

	Transplant Group	Shunt Group 1 (future candidate)	Shunt Group 2 (not a candidate)
Number	180	44	27
Age (yr)	49 ± 12	45 ± 14	56 ± 12
Gender (M/F)	103/77	23/21	19/8
Cause of liver disease			
Alcoholic cirrhosis	35*	15*	17*
Posthepatic cirrhosis	51	7	1
Cryptogenic cirrhosis	26	7	7
Primary biliary cirrhosis	28	6	2
Sclerosing cholangitis	21	1	0
Others	19	8	0
Child's class			
A	6	24	6
B	49	18	16
C	125†	2†	5†

\* Transplant group vs. shunt group 1,  $p < 0.05$ ; transplant group vs. shunt group 2,  $p < 0.001$ .

† Transplant group vs. shunt group 1,  $p < 0.001$ ; transplant group vs. shunt group 2,  $p < 0.001$ .

visceral angiography or duplex ultrasonography. As a comparison group rather than a study group for this investigation, only survival and not postoperative morbidity was assessed for the transplant patients.

All results are expressed as mean ± standard deviation of the mean. Variables were compared between groups by the chi square test, t test for unpaired data, or analysis of variance as appropriate. Survival curves were plotted by the Kaplan–Meier method.<sup>2</sup> Differences in survival estimates between groups were determined by the log-rank test.

## RESULTS

### Patient Follow-Up

All patients were observed up to March 1995 or to the time of their death. Mean follow-up for transplant patients, shunt group 1 (transplant candidates), and shunt group 2 was  $37 \pm 29$  months,  $33 \pm 30$  months, and  $33 \pm 31$  months, respectively. No patients have been lost to follow-up.

### Preoperative Comparisons

Table 1 compares the three groups with respect to age, gender, cause of liver disease, and preoperative Child's class. Because decreased hepatic functional reserve was

the primary indication for transplantation, there were significantly more Child's class C patients in the transplant group than in either shunt group. There were higher percentages of patients with alcoholic liver disease in both shunt groups with the greatest percentage (63%) in shunt group 2.

### Shunts Performed

In both shunt groups, 68 (82%) of patients received a distal splenorenal shunt. The eight nonselective shunts in shunt group 1 (five side-to-side portacaval or interposition shunts and three end-to-side portacaval shunts) were done for Budd–Chiari syndrome ( $N = 3$ ), ileal stomal varices ( $N = 1$ ), absent spleen ( $N = 1$ ), emergency ( $N = 1$ ), and ascites ( $N = 2$ ). The five nonselective shunts in shunt group 2 (four side-to-side portacaval or interposition shunts and one end-to-side portacaval shunt) were done for ascites ( $N = 4$ ) and as an emergency ( $N = 1$ ).

### Conversion to Transplantation

Seven patients in shunt group 1 have been transplanted (Table 2). Six (86%) of these individuals survived the transplant procedure and still are living. Another two patients presently are listed for transplantation.

### Survival

The operative mortality rate was significantly greater in the higher risk transplant group (19%,  $p < 0.02$ ). There were two operative deaths in each of the shunt groups. The two early deaths in shunt group 1 were a Child's class A alcoholic patient with cirrhosis in whom severe pancreatitis developed after a distal splenorenal shunt and a Child's class C patient with primary biliary cirrhosis who underwent an emergency nonselective shunt when all nonoperative means to control bleeding had failed. Operative deaths in shunt group 2 were caused by hepatic and renal failure in a Child's class C alcoholic patient with cirrhosis and recurrent hemorrhage in an elderly patient with primary biliary cirrhosis in whom early thrombosis of her distal splenorenal shunt developed.

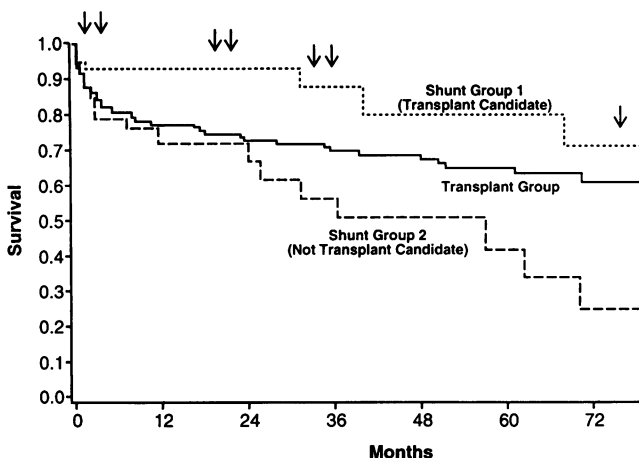
In the analysis of the survival curves at year 1, shunt group 1 (future transplant candidates) had better survival than either the transplanted patients or those of shunt group 2 ( $p < 0.02$ ) (Fig. 1). However, by 5 years, shunt group 2 patients fared significantly worse ( $p < 0.03$ ) than did the other two groups of patients that were no longer significantly different. Survival of shunt group 1 patients was enhanced by salvaging six patients with hepatic transplantation when progressive disease developed (Table 2). The shunt group 1 survival curve is no longer significantly different from the other two survival curves during the

**Table 2. SHUNT GROUP 1 PATIENTS TRANSPLANTED**

Patient Number	Age	Sex	Child's Class (at time of shunt)	Cause of Liver Disease	Date of Shunt	Type of Shunt	Interval Between Shunt and Transplant	Reason for Transplant	Present Status (months after transplant)
1	44	M	A	Sclerosing cholangitis	4/88	DSRS	76 mo	Recurrent cholangitis	Alive (7)
2	37	M	A	Hepatitis B	11/88	DSRS	1 mo	Postshunt hepatic failure	Operative mortality (primary nonfunction of graft)
3	8	F	A	Biliary atresia	1/91	DSRS	23 mo	Fatigue	Alive (28)
4	50	F	B	Budd–Chiari syndrome	12/91	S-S PCS	37 mo	Occluded shunt	Alive (3)
5	54	M	B	Cryptogenic cirrhosis	3/92	DSRS	12 mo	Progressive disease (hepatoma)	Alive (24)
6	31	F	B	Budd–Chiari syndrome	7/92	S-S PCS	10 days	Occluded shunt	Alive (32)
7	52	M	A	Cryptogenic cirrhosis	3/93	DSRS	19 mo	Progressive disease	Alive (5)

DSRS = distal splenorenal shunt; S-S PCS = side-to-side portacaval shunt.

early years of the analysis if the patients salvaged by transplantation are considered mortalities, which would have been the result if transplantation were not available. Including the two operative deaths, eight patients (18%) in shunt group 1 have died (Table 3). Hepatic failure has been the cause of late death in only three individuals. One patient died after liver transplantation and two were no longer transplant candidates when hepatic failure developed, one because of severe aortic stenosis 6.5 years after a distal splenorenal shunt and one because of sudden onset of sepsis 3.5 years after a distal splenorenal shunt.



**Figure 1.** Kaplan–Meier survival analysis of shunt group 1 (···), transplant group (—), and shunt group 2 (---). The vertical lines on the shunt group 1 curve indicate when patients from that group underwent liver transplantation. Survival of shunt group 1 is significantly different from that of the transplant group ( $p = 0.003$ ) and shunt group 2 ( $p = 0.018$ ) at 1 year (log–rank test). At 5 years, the shunt group 1 and transplant group curves are no longer different, but both are significantly different from the shunt group 2 curve ( $p = 0.006$  and  $p = 0.029$ , respectively).

Sixteen shunt group 2 patients (63%) have died with hepatic failure being the predominant cause of death (9 patients) (Table 3).

### Postshunt Morbidity

The number of patients in each shunt group in whom shunt occlusion, rebleeding, encephalopathy, and ascites developed either in the perioperative period or during long-term follow-up is listed in Table 4. The two patients with shunt thrombosis (one interposition portacaval shunt and one side-to-side portacaval shunt) in shunt group 1 had the Budd–Chiari syndrome and both subsequently were transplanted. The single episode of recurrent bleeding in shunt group 1, presumably secondary to transient renal venous hypertension, was in a patient with a patent distal splenorenal shunt. The only perioperative shunt occlusion (distal splenorenal shunt) in shunt group 2 was followed by massive rebleeding, which ultimately was treated by splenectomy and esophagogastric devascularization. Hepatic failure de-

**Table 3. CAUSES OF DEATH IN SHUNT PATIENTS**

Cause of Death	Shunt Group 1	Shunt Group 2
Operative mortality	2	2
Hepatic failure	3	9
Nonhepatic malignancy	2	2
Ruptured aneurysm	1	0
Suicide	0	1
Gastrointestinal hemorrhage	0	1
Sepsis	0	1
Total	8	16

**Table 4. POSTSHUNT MORBIDITY**

Complication	Shunt Group 1	Shunt Group 2
Early postoperative		
Shunt occlusion	1	1
Rebleeding	1	1
Mild encephalopathy	4	2
Moderate-severe encephalopathy	0	2
Ascites	7	7
Late postoperative		
Shunt occlusion	1	1
Rebleeding	0	2
Mild encephalopathy	1	1
Moderate-severe encephalopathy	2	0
Ascites	1	1

veloped in this elderly patient, who initially was Child's class A, after the second operation and the patient died. The late postoperative shunt thrombosis in shunt group 2 was presumed rather than proved. Massive upper gastrointestinal bleeding developed in this individual, who died in another hospital 7 months after a distal splenorenal shunt. Although early postoperative duplex ultrasonography showed a patent shunt, neither late postoperative studies of shunt patency nor an autopsy was performed. The other shunt group 2 patient who rebled did so on multiple occasions. Several upper gastrointestinal endoscopies showed esophagitis, esophageal ulcers, and gastritis, but no varices; repeat duplex ultrasonograms showed a patent distal splenorenal shunt.

The two individuals in shunt group 2 in whom persistent and severe encephalopathy developed soon after a distal splenorenal shunt were elderly alcoholic patients with cirrhosis. They both died of hepatic failure approximately 3 months after surgery. All other episodes of perioperative encephalopathy were transient, promptly responded to protein restriction and administration of lactulose, and did not recur. Moderate-to-severe encephalopathy developed in only two patients with shunts, both of whom were in shunt group 1, at 3 and 6 years after a distal splenorenal shunt. Both of these patients died approximately 6 months after the onset of encephalopathy and were not transplanted because of ongoing sepsis and severe aortic stenosis, respectively.

Ascites severe enough to prolong hospitalization developed in the early postoperative interval in seven patients in each shunt group; all of these patients had received a distal splenorenal shunt. Except for one patient in each group, ascites was not a chronic problem.

## DISCUSSION

As more treatment options have become available, the management of patients with bleeding secondary to portal

hypertension has become more complex. The challenge to the treating physician or surgeon is to determine which therapy or sequence of treatments is likely to provide the optimal result for an individual patient. Because transplantation is the only treatment that addresses the underlying liver disease as well as its hemorrhagic complications, a major consideration in the decision-making process is to determine which variceal bleeders are transplant candidates and when in the course of their disease should they be transplanted. Since initiation of our liver transplant program at the University of Nebraska Medical Center in 1985, all potential transplant candidates (generally all nonalcoholic patients with cirrhosis and abstinent alcoholic patients with cirrhosis with no other major organ system dysfunction that would preclude successful transplantation) with a history of variceal bleeding have been placed on the transplant list soon after referral if they had hepatic functional decompensation (Child's class B- or C) and/or nonbleeding complications of their disease (*e.g.*, advanced fatigue, troublesome ascites, encephalopathy, or bone pain) that adversely impacted the quality of their lives. With few exceptions, bleeding could be controlled successfully in these patients by endoscopic sclerotherapy or more recently by TIPS insertion until a donor liver became available. This subset of 180 transplant patients with a history of bleeding generally has fared well with an early mortality rate of 19% and a 5-year survival rate of nearly 70%. These survival results are superior to those of any other reported series of predominantly Child's class C patients in whom nontransplant therapies were used for long-term prevention of recurrent bleeding.<sup>3,4</sup> Liver transplantation has become the standard of care for such patients.

A more controversial group are potential transplant candidates who present with portal hypertensive bleeding, well-preserved hepatic functional reserve (Child's class A and B+), and no other significant complications of their liver disease. Depending on individual physician preference, these patients may undergo any one of the following therapies: early transplantation, chronic sclerotherapy, TIPS, or shunt, the latter three being used as long-term bridges to transplantation for patients in whom hepatic failure eventually develops.

The recently developed TIPS procedure, because it does not require a major operation, might appear to be the ideal approach for this subset of patients. When done by experienced personnel, TIPS insertion is successful in >95% of patients, it effectively decompresses the portal venous circulation, and major early complications are infrequent.<sup>5,6</sup> However, with presently available technology, late TIPS failure rates are high, with stenosis or occlusion developing in approximately 50% of patients by 2 years in some series.<sup>5,7</sup> Transjugular intrahepatic portosystemic shunt stenosis or thrombosis frequently is followed by

recurrent bleeding.<sup>5</sup> Additionally, a widely patent TIPS serves as a completely decompressing nonselective shunt with encephalopathy rates in several series similar to those seen after a portacaval shunt.<sup>6-8</sup> Conversely, TIPS is an excellent option for variceal bleeders who will require transplantation in the near future and for nontransplant candidates with hepatic functional decompensation who are not likely to survive for long because of their advanced liver disease.<sup>8,9</sup> These are the settings in which TIPS presently is used in our institution.

Since its reintroduction during the 1970s, endoscopic sclerotherapy has become the most frequently used treatment for patients with bleeding varices. Variceal sclerosis, more than any other method, has been responsible for the marked decline in shunt surgery that has been observed in most hospitals during the past 15 years. Before the advent of TIPS, one major liver transplant group stated that sclerotherapy is an acceptable bridge to transplantation for nearly all patients.<sup>4</sup> These authors believe that when sclerotherapy fails, transplantation should be done promptly. In the view of these authors, portosystemic shunts no longer have a role in the treatment of variceal bleeding.

Controlled trials of chronic sclerotherapy *versus* shunt as definitive treatment for patients with bleeding varices have given conflicting results. In all investigations, shunt has prevented recurrent bleeding more effectively, but survival results have varied.<sup>10</sup> Two studies in this country, both with mean follow-ups in excess of 7 years, have compared the distal splenorenal shunt to chronic sclerotherapy.<sup>11,12</sup> One trial in which the patients were accrued from a large metropolitan area showed superior survival for the sclerotherapy group, one third of whom underwent salvage shunt surgery when they did not respond to sclerotherapy.<sup>12</sup> The other investigation from our institution accrued patients from a wide, sparsely populated geographic area. In this controlled study, long-term survival was superior in the distal splenorenal shunt group.<sup>11</sup> The sclerotherapy failure rate was similar to that in the other investigation (approximately one third of patients), but few sclerotherapy failures were salvaged by subsequent shunt surgery, mainly because they resided a long distance from tertiary care facilities. Encephalopathy rates in both of these studies were similar in sclerotherapy and selective shunt groups. Based on the results of our trial, we have preferred a shunt to endoscopic treatment for rural patients when long-term control of bleeding is the objective, whether the patient is or is not a future transplant candidate. Other indications for shunt surgery in the current report were gastric bleeding either from varices or portal hypertensive gastropathy, neither of which is treated effectively by endoscopic means, and patient non-compliance, which often leads to inability to follow a chronic sclerotherapy regimen.

A shunt with subsequent transplantation as necessary served the patients in shunt group 1 (potential future transplant candidates) well. The initial risk was low with an operative mortality rate of only 5%, long-term complications such as encephalopathy and ascites were infrequent, and after a mean follow-up of nearly 3 years, only seven patients (16%) have required transplantation. Many of these patients with shunts continue to do well for as long as 9 years after surgery and may never need transplantation. Thus, the shunt will serve as a long-term bridge to transplantation for only a fraction of this group; for the remainder, the shunt will be their definitive treatment. In another comparison of patients undergoing either the distal splenorenal shunt (good hepatic reserve) or liver transplantation (poor hepatic reserve) by Henderson et al.,<sup>13</sup> a similar excellent long-term survival of the good risk patients with shunts was observed even though salvage transplant operations were not done. However, 8% of the patients with shunts in this study did not have liver disease.

Survival of the shunted transplant candidates (82% with distal splenorenal shunts), bolstered by salvage transplant operations in seven patients, was significantly better than that of the transplant group itself during the first few years of follow-up. This does not show superiority of shunt over transplant as the hepatic functional reserve of the two groups was considerably different, but rather that an initial shunt followed by future transplantation when necessary is the preferred sequence in this group of patients. The survival curves of these two groups are not significantly different if the patients salvaged by transplantation are considered mortalities, which would have been the case if transplantation were not available. One of the two operative mortalities in this shunt group was a desperate attempt at salvaging an actively bleeding patient in Child's class C with a shunt operation after all nonoperative treatments had failed. Transjugular intrahepatic portosystemic shunt, which then was not available, would now be the preferred therapy as a short-term bridge to transplantation for this patient. Except for the two early deaths, only three patients in this shunt group have died of hepatic failure. Two of these patients were assessed carefully for possible transplantation when hepatic function deteriorated and were deemed to no longer be transplant candidates because of advanced cardiac disease in one and uncontrolled sepsis in the other; the third patient died in the early postoperative interval after transplantation. All other deaths in this shunt group were from non-hepatic causes and would likely have occurred even if the patients initially had undergone transplantation.

Several studies have shown that a prior portosystemic shunt is not a barrier to subsequent liver transplantation.<sup>14,15</sup> Although the operation may be more technically challenging and require more blood replacement, in most

series survival has not been compromised. Of the seven patients who underwent transplantation after an initial shunt operation in this study, six still are surviving. Hepatic functional decompensation developed in the seventh patient during the early postoperative interval after a distal splenorenal shunt. His first donor liver failed to function, and he then died of multiple complications after a second liver transplant.

Shunts also remain a reasonable option for selected patients with variceal bleeding who are not present or future transplant candidates because of advanced age, unresolved alcoholism, or other reasons. Although chronic endoscopic treatment is the preferred therapy for many such patients, a shunt should be done when sclerotherapy failure becomes evident, for patients in whom gastric bleeding develops, and for those individuals who do not have easy access to tertiary medical and surgical care.<sup>11</sup> Transjugular intrahepatic portosystemic shunt should be reserved for patients who are unacceptable surgical risks and who have limited life expectancy because of decreased hepatic functional reserve. Nontransplant candidates who underwent a shunt in the current investigation had 1-year and 5-year survival rates of 72% and 42%, respectively. As would be expected considering the criteria for inclusion in this group and the nonavailability of transplantation, most deaths were caused by hepatic failure. Just like the better risk patients with shunts who were future transplant candidates, quality of life also was quite good with infrequent episodes of encephalopathy or ascites. As in most other selective and nonselective shunt series, shunt occlusion and recurrent variceal bleeding were uncommon.

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