Liver transplantation in the treatment of bleeding esophageal varices

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From March 1980 to July 1987, 1000 patients with various end-stage liver diseases received orthotopic liver transplants. Of the 1000 patients, three hundred two had definite histories of bleeding from esophageal varices before transplantation. There were 287 patients with nonalcoholic liver diseases and 15 patients with alcoholic cirrhosis. All patients had very poor liver function, which was the main indication for liver transplantation. One- through 5-year actuarial survival rates of the 302 patients were 79%, 74%, 71%, 71%, and 71%, respectively. These survival rates are far better than those obtained with other available modes of treatment for bleeding varices when liver disease is advanced. Long-term sclerotherapy is the treatment of primary choice for bleeding varices. Patients in whom sclerotherapy fails should be considered for liver transplantation unless clear contraindications exist. (SURGERY 1988;104:697-705.)

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MASSIVE HEMORRHAGE FROM esophageal varices is the most devastating complication of portal hypertension in advanced cirrhosis. Several types of portasystemic shunt operations, portoazygous devascularization (nonshunt operation), and endoscopic sclerotherapy have established their own roles, but they all have certain major limitations, particularly when the liver disease is far advanced. Portasystemic shunt is the most effective way to control bleeding from esophageal varices, but it is plagued by a high incidence of hepatic encephalopathy and progressive hepatic failure after the shunt. Although they do not alter hepatic circulation, nonshunt operations and sclerotherapy have high incidences of recurrent bleeding.

Liver transplantation has long been, at least in theory, the most logical treatment for bleeding esophageal varices in patients with far-advanced liver disease. As the results of liver transplantation have significantly improved in recent years, the role of this procedure in the treatment of bleeding esophageal varices should be closely examined.

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PATIENTS AND METHODS

From March 1980 to July 1987, 1000 patients with various liver diseases received orthotopic liver transplants at the University of Colorado Health Sciences Center (in 1980), the University Health Center of Pittsburgh (since 1981), and the Pittsburgh-affiliated Baylor University Medical Center at Dallas (since 1985). Basic immunosuppressive therapy consisted of cyclosporine and corticosteroids, and azathioprine and monoclonal anti-T-lymphocyte antibody (OKT-3) were added to the basic immunosuppression when needed. Of the 1000 consecutive liver recipients, 666 were adults of 18 years or older and 334 were children younger than 18 years. The liver diseases of adult recipients as well as the numbers of patients with each disease are listed in Table I; the same data for pediatric recipients are listed in Table II. The three most common liver diseases among adult recipients were (1) postnecrotic cirrhosis (including chronic active hepatitis and cryptogenic cirrhosis), (2) primary biliary

Table I. Liver diseases of adult recipients

Disease	*No. of patients*
1. Cirrhosis (postnecrotic, cryptogenic, alcoholic)	279
Postnecrotic and cryptogenic	237
(HBsAg positive	36
Alcoholic	41
2. Primary biliary cirrhosis	166
3. Primary sclerosing cholangitis	82
Associated with bile duct cancer	88
4. Liver-based inborn metabolic errors (alpha-1-antitrypsin deficiency, Wilson's, etc)	35
5. Primary hepatic malignancy	33
6. Fulminant hepatic failure	25
7. Secondary biliary cirrhosis	13
8. Budd-Chiari syndrome	13
9. Secondary hepatic malignancy	7
10. Bile duct cancer without sclerosing cholangitis	2
11. Others	11
Total	666

Table II. Liver diseases of pediatric recipients

Disease	*No. of patients*
1. Biliary atresia	179
2. Liver-based inborn metabolic errors (alpha-1-antitrypsin deficiency, Wilson's, etc.).	63
3. Cirrhosis (postnecrotic, cryptogenic)	40
4. Familial cholestatic syndrome	15
5. Fulminant hepatic failure	12
6. Secondary biliary cirrhosis	8
7. Congenital hepatic fibrosis	6
8. Primary hepatic malignancy	3
9. Budd-Chiari syndrome	2
10. Neonatal hepatitis	2
11. Others	4
Total	334

cirrhosis, and (3) primary sclerosing cholangitis. The most common diagnoses in pediatric recipients were (1) biliary atresia (including extrahepatic and intrahepatic type, biliary hypoplasia, and Alagille's syndrome), (2) liver-based inborn metabolic errors (alpha-1-antitrypsin deficiency disease, Wilson's disease, tyrosinemia, and others), and (3) postnecrotic cirrhosis.

A total of 302 liver recipients had definite histories of hemorrhage from esophageal varices before liver transplantation; 217 were adults and 85 were children. The types of liver disease in these adult and pediatric variceal bleeders and the number of patients affected are listed in Tables III and IV. The liver function and the general condition of these 302 patients were all very poor and were classified in Child's class C category. Furthermore, 22 patients had undergone nonselective shunt, 15 patients had undergone selective shunt, and 5 patients had undergone nonshunt operations for treatment of bleeding esophageal varices before liver transplantation. Two hundred nineteen patients had undergone endoscopic sclerotherapy for esophageal varices.

The survival data were analyzed as of Feb. 1, 1988, by the method of Kaplan-Meier. The follow-up period ranged from 6 months to 6 years 11 months, with a median follow-up of 2 years 3 months. None of the patients was lost from the follow-up. The statistical comparisons were made by the methods of Breslow and of Mantel-Cox. The difference was considered as significant when p value was less than 0.05.

RESULTS

The overall survival rates of the 1000 consecutive patients after liver transplantation were 72% at 1 year, 67% at 2 years, 65% at 3 years, 64% at 4 years, and 63% at 5 years with cyclosporine-steroid therapy. These survivals were three times higher than those obtained with azathioprine-steroid therapy before 1980 (Fig. 1). The survival rates of 666 adult recipients were nearly identical to those of 334 pediatric recipients.

The survival rates of 302 patients who had bled from esophageal varices before transplantation (esophageal bleeders) were 79% at 1 year, 74% at 2 years, and 71% at 3, 4, and 5 years after transplantation. Survival of 698 patients who had no history of variceal bleeding (variceal nonbleeders) was 69% at 1 year, 64% at 2 years, 62% at 3 years, 60% at 4 years, and 59% at 5 years. The survival rates of variceal bleeders were significantly higher than those of nonbleeders ($p < 0.01$), as shown in Fig. 2. The survival rates of 217 adult esophageal bleeders were 78% at 1 year, 73% at 2 years, and 68% at 3, 4, and 5 years after transplantation, and those of 85 pediatric esophageal bleeders were 80% at 1 year and 77% at 2, 3, 4, and 5 years. There was no statistically significant difference in survival rates between adult and pediatric esophageal bleeders.

The survival rates after liver transplantation were compared among the esophageal bleeders with the three most common adult liver diseases (Fig. 3) and also among those with the three most common pediatric

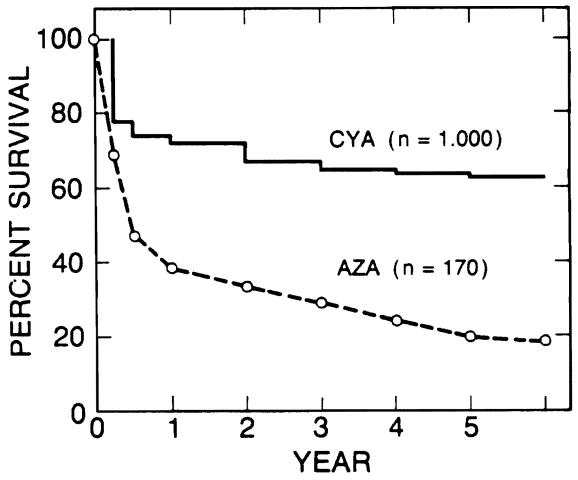

Fig. 1. Survival rates after liver transplantation have improved significantly since the introduction of cyclosporine in 1980. *CyA,* cyclosporine group, 1,000 patients; *AZA,* azathioprine group, 170 patients.

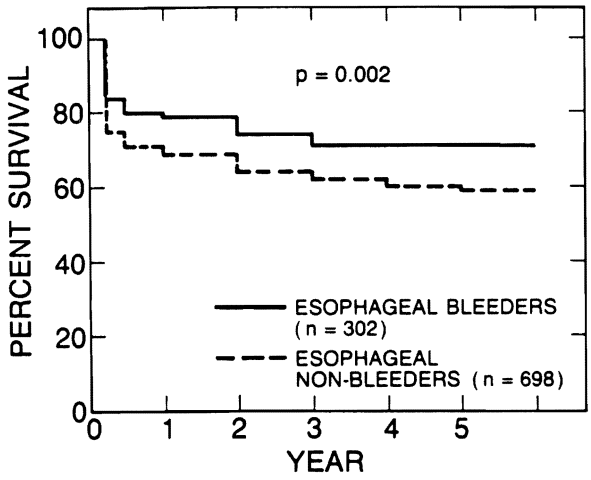

Fig. 2. Survival rates of 302 patients who had bled from esophageal varices before transplantation *(esophageal bleeders)* were better than those of 698 patients who had not bled *(esophageal nonbleeders)*. The difference was statistically significant ($p = 0.002$).

Table III. Liver diseases of adult recipients who had a definite history of bleeding from esophageal varices

Disease	*No. of patients*
1. Postnecrotic and cryptogenic cirrhosis	85
2. Primary biliary cirrhosis	63
3. Primary sclerosing cholangitis	31
4. Liver-based inborn metabolic errors (alpha-1-antitrypsin deficiency, Wilson's, etc.)	16
5. Alcoholic cirrhosis	15
6. Secondary biliary cirrhosis	4
7. Budd-Chiari syndrome	2
8. Biliary atresia	1
Total	217

Table IV. Liver disease of pediatric recipients who had a definite history of bleeding from esophageal varices

Disease	*No. of patients*
1. Biliary atresia	37
2. Liver-based inborn metabolic errors (alpha-1-antitrypsin deficiency, Wilson's etc.)	19
3. Postnecrotic and cryptogenic cirrhosis	15
4. Congenital hepatic fibrosis	5
5. Familial cholestatic syndrome	4
6. Secondary biliary cirrhosis	4
7. Primary sclerosing cholangitis	1
Total	85

liver diseases (Fig. 4). There was no statistically significant difference in survival rates among the liver diseases in either the adult or the pediatric esophageal bleeders. The survival rates of 15 variceal bleeders with alcoholic cirrhosis were 93% at 1 year and 76% at 2 years after transplantation; these rates were similar to those of patients with nonalcoholic liver disease.

There were 42 patients who had had some kind of operation for bleeding esophageal varices (22 nonselective shunts, 15 selective shunts, and 5 nonshunt operations). The survival rates of these 42 patients were 71% at 1 and 2 years and 65% at 3, 4, and 5 years after transplantation. Survival rates of the 260 patients who had not had an operation for bleeding varices were 80% at 1 year, 75% at 2 years, and 73% at 3, 4, and 5 years after transplantation (Fig. 5). Seven (17%) of 42 patients of the former group died within a month after transplantation, in contrast with 21 (8%) of the 260 patients of the latter group. However, the differences in short- and long-term survival rates of the two groups have not reached statistical significance.

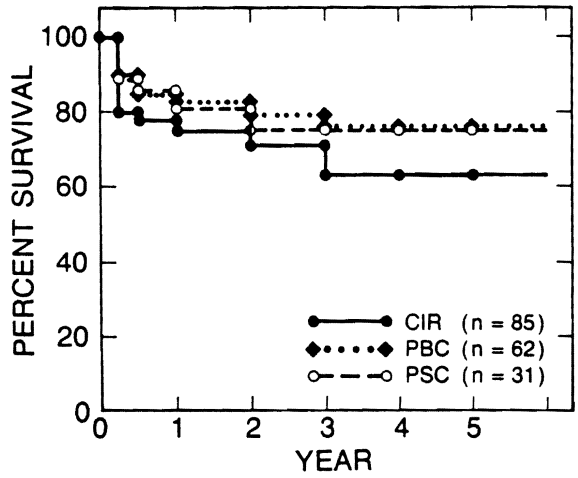

Fig. 3. Survival rates of esophageal bleeders were similar among the three most common adult liver diseases. *CIR*, postnecrotic or cryptogenic cirrhosis; *PBC*, primary biliary cirrhosis; *PSC*, primary sclerosing cholangitis.

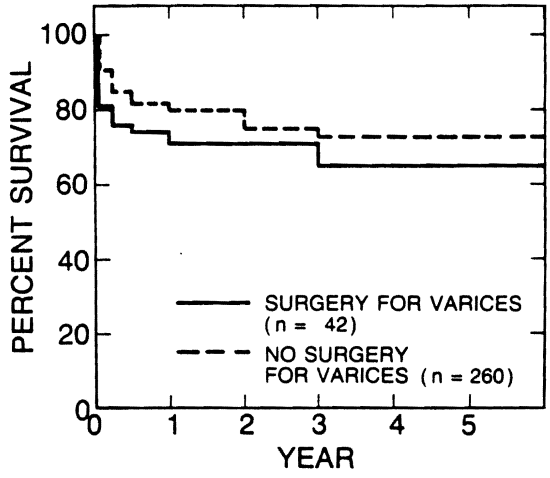

Fig. 5. Survival rates of 42 patients who had had some kind of operation for bleeding varices before liver transplantation were lower than those of 260 patients who had not had any such operation before transplantation. The difference, however, was not statistically significant.

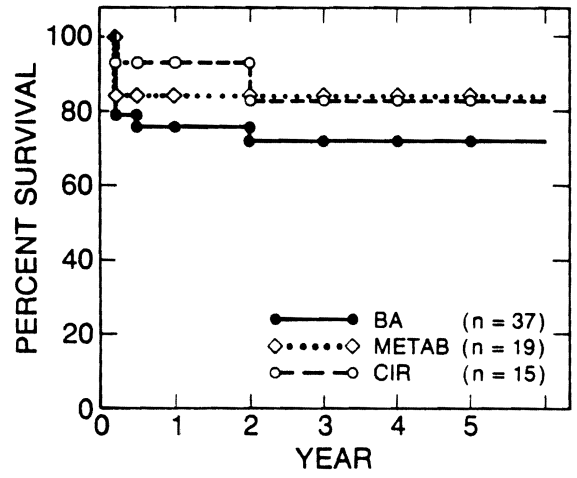

Fig. 4. Survival rates of esophageal bleeders were similar among the three most common pediatric liver diseases. *BA*, biliary atresia; *METAB*, liver-based inborn metabolic errors; *CIR*, postnecrotic or cryptogenic cirrhosis.

DISCUSSION

For more than four decades, portal-systemic shunts were readily accepted as the most effective treatment of bleeding from esophageal varices. Enthusiasm, however, started to wane more than two decades ago, when it became apparent that the price of preventing hemorrhage from esophageal varices by portal-systemic shunts was dehumanizing encephalopathy and progressive hepatic dysfunction.

Three controlled studies of prophylactic portal-systemic shunts concluded more than 15 years ago that, in spite of excellent protection from variceal hemorrhage, patients who had such shunts had poorer survival rates than patients who were treated with medical supportive measures alone, apparently because of increased frequency of death from hepatic failure among patients with shunts.[1-3] Three controlled studies of therapeutic shunts also failed to show a statistically significant difference in the long-term survival rates between the patients with shunts and the medically treated patients after more than 10 years of follow-up.[4-6]

With increasing disenchantment with portal-systemic shunting, considerable efforts were expended in developing new operations or modifying old ones that prevent variceal hemorrhage efficiently without significantly altering hepatic circulation. The distal splenorenal shunt was introduced in 1967 by Warren, Zeppa, and Fomon[7] as a selective shunt. In the last decade, the effectiveness of this selective shunt has been assessed in five different randomized controlled studies.[8-12] All of these well-designed studies failed to show the survival superiority of selective shunt over nonselective shunt despite initial claims. Meanwhile, nonshunt operations (portal azygos disconnection) improved the old techniques and achieved survival rates similar to those achieved with shunt operations, although the incidence of rebleeding was higher than with the shunts.[13-15] Since endoscopic sclerotherapy was reintroduced by Johnston and Rogers,[16] the long-term management of

Table V. Survival comparison among various treatments for bleeding esophageal varices (Child's classes A, B, and C)

Treatment	*No. of patients*	*Survival rates (%)*				
		1 yr	*2 yr*	*3 yr*	*4 yr*	*5 yr*
Jackson et al. (1971)						
Nonselective shunt	67	80*	73*	62*	58*	55*
Medical	77	80	66*	43*	35*	32*
Resnick et al. (1974),						
Nonselective shunt	54	70*	58*	50*	48*	48*
Medical	25	67*	52*	40*	40*	40*
Reynolds et al. (1981)						
Nonselective shunt	41	—	72*	64*	52*	44
Medical	37	—	60*	44*	36*	22
Conn et al. (1981)						
Selective shunt	24	76*	70*	—	—	—
Nonselective shunt	29	70*	67*	—	—	—
Langer et al. (1985)						
Selective shunt	38	80*	76*	63*	54*	51*
Nonselective shunt	40	90*	85*	70*	56*	56*
Millikan et al. (1985)						
Selective shunt	26	85*	77*	65*	60*	55*
Nonselective shunt	29	80*	72*	70*	65*	60*
Warren et al. (1986)						
Sclerotherapy†	36	90*	84	82*	82*	—
Selective shunt	35	70*	59	45*	45*	—
Rikkers et al. (1987)						
Sclerotherapy	30	77*	61	60*	50*	—
Selective shunt‡	27	75*	65	60*	39*	—
Yamamoto et al. (1976)						
Nonshunt operation	64	81	75	70	70	65
Sugiura et al. (1984)						
Nonshunt operation	256	87	84	81	78	78
Spence et al. (1985)						
Nonshunt operation	100	73	65	54	51	47
Present study (1988)						
Liver transplantation	302	79	74	71	71	71

*Value estimated from survival curve.
†Sclerotherapy failures were rescued by surgical therapy.
‡Twenty-three selective shunts and four nonselective shunts.

bleeding varices by this endoscopic procedure has spread worldwide.

Having failed to improve the survival rates, selective shunt was critically examined against long-term sclerotherapy by two randomized trials.[17, 18] In their preliminary report Warren and his associates[17] concluded that sclerotherapy gave significantly better survival than the selective shunt when the sclerotherapy failures were rescued with surgical therapy, including selective and nonselective shunts and nonshunt operations. Rikkers and his associates[18] reported that endoscopic sclerotherapy and shunt surgery (23 selective shunts and 3 nonselective shunts) provided similar results with respect to survival, hepatic function, and frequency of encephalopathy.

Table V compares the survival rates of 302 liver recipients who had a definite history of variceal hemorrhage with those reported in eight well-studied control trials of therapeutic shunt operations[4-6, 10-12, 17, 18] and three uncontrolled series of nonshunt operations.[13-15] As the outcomes of shunt and nonshunt operations are highly influenced by the hepatic functional reserve of the patients at the time of operation,[19] the results of one study cannot be simply compared with those of another. More than 75% of the patients in each report listed in Table V had good hepatic function

Table VI. Survival comparison among various treatments for bleeding esophageal varices (Child's class C, poor liver function)

Treatment	*No. of patients*	*Survival rates (%)*				
		1 yr	*2 yr*	*3 yr*	*4 yr*	*5 yr*
Turcotte et al. (1973)						
Nonselective shunt	50	36	32	22	20	17
Yamamoto et al. (1976)						
Nonshunt operation	13	39	30	22	22	18
Warren et al. (1982)						
Selective shunt	?	60*	53*	45*	40*	35*
Nonselective shunt	?	50*	40*	37*	20*	15*
Rikkers et al. (1984)						
Shunt and nonshunt operation†	24	45	35*	30*	20*	17*
Chandler et al. (1985)						
Shunt‡	30	36	30	25	20	13
Spence et al. (1985)						
Nonshunt operation	25	70	53	38	38	35
Present study (1988)						
Liver transplantation	302	79	74	71	71	71

*Value estimated from survival curve.
†Fifteen nonselective shunt, seven selective shunts, and two nonshunt operations.
‡Both selective and nonselective operations.

or moderately impaired hepatic function (Child's class A and B), and fewer than 25% of them had advanced hepatic dysfunction (Child's class C). On the other hand, all the patients who received liver transplants had advanced hepatic dysfunction or far-advanced hepatic dysfunction. Despite this severe disadvantage of preoperative condition, the survival rates of liver transplant recipients who had had variceal hemorrhage were better than or similar to those of patients who had had other kinds of conventional therapy (Table V).

Because the surgical therapy for esophageal varices is usually withheld from the patients with advanced hepatic dysfunction (Child's class C), the literature contains few survival data for these patients.[13, 15, 19-22] In Table VI the results obtained with liver transplantation are compared with those achieved in patients with advanced hepatic dysfunction after conventional surgical therapy. It is obvious that the survival rates of liver transplant recipients are far better than those achieved with conventional types of surgical therapy when the liver disease is advanced.

As each disease has its own natural history, the results of various kinds of therapy for variceal hemorrhage should ideally be compared among patients with portal hypertension of similar etiology. In the literature, however, whether the etiology of cirrhosis will influence long-term survival after shunt operation is a matter of considerable controversy. Some investigators found that after shunt operations patients with nonalcoholic cirrhosis had significantly better long-term survival rates than those with alcoholic cirrhosis,[21, 22] but others could not find a difference between the two groups.[11, 24, 25] Our recent review of 1000 liver transplantations under cyclosporine-steroid immunosuppressive therapy[26] has shown that the survival rates were similar among the three most common adult liver diseases (postnecrotic cirrhosis, primary biliary cirrhosis, and sclerosing cholangitis) and among the three most common pediatric liver diseases (biliary atresia, liver-based inborn metabolic errors, and postnecrotic cirrhosis). The survival rates of alcoholic cirrhosis were also similar to overall survival rates, although the numbers were small. In this study of the subgroup of 302 patients who had bled from esophageal varices, the original liver diseases did not influence the survival rates after liver transplantation.

The survival rates of the 42 patients who had had shunt or nonshunt operations for treatment of bleeding esophageal varices before liver transplantation were lower than those of patients in whom variceal hemorrhage was treated medically and/or with long-term endoscopic sclerotherapy, but the difference was not statistically significant. It is obvious, however, that a previous shunt or nonshunt operation made the trans-

plant operation more difficult and thereby increased early mortality, as shown in Fig. 5.

Recently two randomized control trials[17,18] have shown that long-term sclerotherapy can provide the same (or better) survival rates as the distal splenorenal shunt, which is generally considered the best among shunt operations. Although the data are not available for nonshunt operations, the results can be expected to be similar to those of shunt operations. The survival rates after liver transplantation for patients with advanced liver disease who had bled from varices are quite satisfactory as presented here. There are ample data in the literature, as discussed, that support long-term sclerotherapy as the treatment of first choice for bleeding esophageal varices. The patients in whom long-term sclerotherapy failed should be considered for liver transplantation, unless some clear contraindications for transplantation exist. We believe that shunt or nonshunt opertions should not be performed for treatment of variceal hemorrhage, except under the most unusual circumstances. Liver transplantation is the treatment of choice for many patients with advanced liver disease after failure of sclerotherapy.

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DISCUSSION

Dr. Marvin J. Wexler (Montreal, Canada). One can't help but stand in awe of the tremendous experience and

excellent results of the Pittsburgh group and their perseverance and tenacity over the years in the face of all opposition. The medical community and, indeed, the entire population of patients with liver disease owe a tremendous debt of gratitude.

However, I think the problem being discussed—"Liver Transplantation in the Treatment of Bleeding Varices"—must be put into perspective. The authors have taken a population of 1000 patients who underwent liver transplantation—for accepted indications of progressive end-stage liver failure—and retrospectively found 300 who, in their history, had also had hemorrhages from esophageal varices. Because the results of liver transplantation have been so good in this group, they suggest that this is the best treatment for varices, a logic that is faulty and unacceptable, not even a "true—true and unrelated" in the multiple-choice jargon.

Let's look more closely at the 302 patients:

1. Almost 30% were children.
2. Fifteen percent had already had a shunt or nonshunt operation for varices (and, I might add, "survived"), and 72% had undergone successful chronic sclerotherapy.
3. Only 15 patients had alcoholic cirrhosis; indeed, of their 1000 patients, only 42 had alcoholic cirrhosis, believed by many to be the worst-risk group for transplantation.
4. None were reported to be actively bleeding, and indeed none was even described as having previous unsuccessful variceal therapy. Having survived such treatment, they were therefore an excellent preselected good-risk group from the standpoint of their varices, despite their advanced liver disease.

On the other hand, it must be pointed out that:

1. Patients with nonalcoholic liver disease do very well with selective shunts, as Drs. Warren and Zeppa have shown.
2. As Dr. Chung, as well as ourselves and Dr. Rikkers and the Emory group, has just shown, 70% to 75% of the patients require no treatment modality for control of their varices other than sclerotherapy.

To suggest that patients in whom conventional sclerosis has failed will do well as the patients presented today is pure conjecture, and it demands an analysis of the reasons for (and the mechanism of) failure of sclerosis. Are these patients bleeding from esophageal necrosis or ulcer? Is there portal or splenic thrombosis? What are their portal hemodynamics and collaterals so that they fail?

Finally, what about the conditions under which such therapy may be required, that is, actively bleeding or less than optimum conditions, both operative and nonoperative, not to mention cost, organ procurement, shortage, etc.

I fear that what we may be seeing here in their enthusiasm may lead to the problem often seen when new treatment modalities succeed, which is misuse and abuse, and I would urge a note of caution. The ability to carry out an operation is not an indication to do it.

Dr. William Millikan (Atlanta, Ga.). I would like to thank Dr. Wexler for speaking first, for two reasons. First, his critical analysis of the study summarizes those things that needed to be said. Second, just as he reinforced the value of Dr. Chung's uncontrolled trial, he reiterated the need for controlled trials in the future, comparing other types of modalities for treatment of variceal bleeding with liver transplantation.

This is taken from Dr. Iwatsuki's paper, and the comments I am about to make represent not only my own but those of Drs. Warren, Henderson, Galloway, Jennings, and Stewart, who perform not only the shunt surgery but the liver transplantations at Emory.

This statement is made and is a result of his survival analysis in 302 patients. We agree 100% that liver transplantation is the treatment of choice for patients with end-stage liver disease, whether they have or have not bled from varices.

The approach that has evolved for evaluation of sclerotherapy failures at Emory over the last several years is a continuation of the work that has been done since 1971. All patients who are referred are evaluated with quantitative studies of the hepatic data base, which includes studies to quantitate liver function, heaptic hemodynamics, liver volume, and liver biopsy. These define the hepatic reserve, which dictates therapy. We believe that no single therapy is the best therapy for all patients.

Two examples explain the use of this system.

First, a 50-year-old man with posthepatic cirrhosis experienced rebleeding in gastric varices after 10 sclerotherapy sessions. This patient had been classified in Child's class C, but further evaluation with the quantitative studies showed that he had excellent hepatic function by galactose elimination capacity and also by the results of the amino acid tolerance test generated after protein load.

Liver blood flow was elevated. Portal blood flow was prograde. He had maintenance of liver volume. His biopsy showed stable cirrhosis without marked activity.

Our assessment of the situation was that the patient had excellent heptic reserve. He underwent a distal splenorenal shunt with splenopancreatic disconnection. He has recently completed his 1-year evaluation in our Clinical Research Center and is doing well. He is back at work.

Retrograde comparison of this patient's quantitative studies and the results of the 12-year follow-up of Emory's controlled trial lead us to believe that this man has an excellent chance of having a 10-year or 15-year survival.

The second patient was a 32-year-old woman with chronic active cirrhosis. She bled from gastric and duodenal varices. She was classified as belonging to Child's class B. Evaluation of her quantitative studies showed a marked deterioration in quantitative function and a small liver. She had reversal of portal flow. Our feeling was that this patient had very limited hepatic reserve.

She underwent a liver transplant. She was our second patient, and she has just completed a 1-year follow-up and is doing well.

Again, we believe that no single therapy represents the best

treatment for all patients, and we think that the therapy for sclerosis failures should be based on analysis of functional hepatocyte reserve.

Again, the Emory group appreciates the opportunity to review this manuscript. We think it is a very significant contribution and congratulate Dr. Iwatsuki on his presentation.

Dr. L. Rikkers (Omaha, Neb.). I would agree with the two previous discussants that Dr. Iwatsuki's conclusions may go a bit too far.

I agree that many nonalcoholic cirrhosis patients with end-stage liver disease who bleed from varices are better served by liver transplantation than by shunt surgery or sclerotherapy. In our institution, liver transplantation has been more responsible for the marked decline in the number of shunts performed than has sclerotherapy.

However, many alcoholic cirrhosis patients in whom sclerotherapy fails are not candidates for liver transplantation, and we believe that shunt surgery still plays a major role in the management of these patients.

If one is forced to resort to shunt surgery for whatever reason in a patient who is a future candidate for liver transplantation, which shunt would you prefer be done? Sedond, if you are doing a liver transplant in a patient who has had a previous distal splenorenal shunt, do you think that the shunt should be dismantled? We recently transplanted a liver into a patient with a distal splenorenal shunt, and a postoperative portal vein thrombosis developed. Our two transplant surgeons, Dr. Wood and Dr. Shaw, also performed a splenectomy, but the shunt remained functional and stole blood from the portal vein, which then thrombosed. I would be interested to know how you approach this problem.

Dr. Iwatsuki (closing). First, I would like to answer the questions of Dr. Wexler. The main indication for liver transplantation in all our patients is liver failure, not variceal hemorrhage. I have not said that all esophageal bleeders should undergo liver transplantation. I said that we should try long-term sclerotherapy first. If we try enough sclerotherapy, we can avoid shunt operations. As the control studies at Emory University and the University of Nebraska indicate, there are actually more survivors among patients with long-term sclerotherapy than among those with shunts. We are doing probably too many shunt operations for no good reasons.

It is still not certain whether the prognosis for alcoholic cirrhosis is worse than that for nonalcoholic cirrhosis after shunt operation; at least it is not clear in the literature.

Although not included in the text, there were approximately 10 patients who went into the operating room with active variceal bleeding. All the variceal bleeding stopped immediately after the liver transplantation.

Dr. Millikan, I agree with you that the measurement of hepatic reserve is very important. Child's classification was based on clinical observation of alcoholic cirrhosis. It is still a very useful classification, but it may not be applied to the patients who have primary biliary cirrhosis, sclerosing cholangitis, or biliary atresia. Their bilirubin levels are usually too high for Child's classification.

Dr. Rikkers asked me what kind of shunt operation I would do if I had to do one. For more than 7 years in Pittsburgh we have done fewer than 10 shunt operations for bleeding varices. From the transplant point of view, I prefer to stay away from the hepatic hilum if I have to do a shunt operation. I probably prefer an H-graft mesocaval shunt. It is a simple operation, and the shunt can be taken down easily. Distal splenorenal shunt may be my second choice. This operation has been modified twice. More and more devascularization has been added, which may create some difficulty during transplant hepatectomy. The distal splenorenal shunt should be taken down when the portal flow is not adequate. In many cases the portal flow increased after removal of the shunt, namely, splenectomy.