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Disability index in a randomized controlled trial of emergency sclerotherapy versus portacaval shunt for bleeding varices in cirrhosis

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Abstract

BACKGROUND: Disability has not been studied after emergency treatment of bleeding esophageal varices (BEV). We created a disability index (DI) in a randomized controlled trial comparing emergency endoscopic therapy (EST) versus emergency portacaval shunt (EPCS).

METHODS: There were 211 unselected, consecutive patients with cirrhosis and acute BEV who were randomized to EST (n = 106) or EPCS (n = 105). Diagnostic work-up and treatment were performed within 8 hours. Ninety-six percent underwent more than 10 years follow-up evaluation. Disability was measured by assessing 9 factors to create a DI.

RESULTS: Ten-year survival was 8% after EST versus 51% after EPCS ($P < .001$). EPCS had a significantly better DI. The EST and EPCS values were as follows: liver function improvement: not applicable and ++; worsening liver function, ++ and not applicable; portal-systemic encephalopathy (PSE) incidence, 36 and 15; PSE episodes, 179 and 94; packed red blood cell

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units, 1,005 and 320; hospital readmissions, 387 and 292; and number of readmission days, 9.6 and 4.7. All of the *P* values were less than .001.

CONCLUSIONS: EPCS resulted in a markedly better DI than EST, a significantly higher survival rate, better control of bleeding, and a lower incidence of PSE. EPCS is an effective first-line emergency treatment of BEV.

Keywords

Quality of life; Bleeding varices; Endoscopic sclerotherapy; Portacaval shunt

Emergency treatment of bleeding esophageal varices (BEV) in patients with cirrhosis is of paramount importance because of the high mortality rate surrounding the episode of acute bleeding.^{1,2} Nevertheless, there is a paucity of randomized controlled trials (RCTs) of emergency surgical therapy and an overall lack of data showing the superiority of any of the several widely used emergency measures. Moreover, there are no reports that contain specific information on the disability after emergency treatment of survivors of any of the several widely used forms of emergency therapy.

From April 8, 1988, to December 31, 2005, we conducted an RCT in 211 unselected, consecutive patients ("all comers") with cirrhosis and acute BEV in whom emergency and long-term repetitive endoscopic sclerotherapy (EST) was compared with emergency direct portacaval shunt (EPCS). The trial was a community-wide endeavor and was known as the San Diego Bleeding Esophageal Varices Study. By prior agreement, board-certified gastroenterologists, surgeons, and emergency physicians in 4 adjacent counties with a population of 8.5 million referred patients with acute BEV to the University of California, San Diego (UCSD) Medical Center for entry in the RCT. In several recent publications, we described the study in detail and reported the outcomes with regard to control of bleeding, survival, development of portal-systemic encephalopathy (PSE), costs of care, results of rescue portacaval shunt (PCS) for failed EST, and detection and treatment of hepatocellular carcinoma.³⁻⁷ This report focuses on objective measures of long-term disability after discharge from the index hospital admission.

Patients and Methods

Our recent publications³⁻⁶ provided detailed descriptions of our RCT and included full information on the methods, definitions, and protocols in the following categories: (1) design of study; (2) patient eligibility; (3) key definitions (bleeding esophageal varices, unselected patients [all comers], EST, long-term EST, EPCS, failure of emergency primary therapy, failure of long-term therapy, rescue therapy, informed consent); (4) randomization; (5) emergency diagnostic work-up; (6) quantitative Child classification; (7) initial emergency therapy during work-up; (8) post-treatment therapy; (9) lifelong follow-up evaluation; (10) quantitation of PSE; and (11) data collection.

Patients randomized to EPCS underwent a direct portacaval shunt: side-to-side in 99 patients and end-to-side in 6 patients. The study protocol and consent forms were approved before the start of the study and at regular intervals thereafter by the UCSD Human Subjects

Committee (Institutional Review Board). Figure 1 is a consort flow diagram that shows the overall design and conduct of the RCT.^{8,9}

All patients, without selection, who met the criteria for the diagnosis of acute BEV resulting from cirrhosis and whose bleeding required transfusion of 2 or more units of blood were eligible for inclusion in the study. Patients whose history included more than one session of EST were not eligible for the study. For patients transferred from area hospitals, a requirement was observation of upper gastrointestinal (UGI) bleeding within 48 hours of transfer.

Failure of emergency primary therapy occurred when, after replacement of blood loss before and during primary treatment, continued or recurrent bleeding after EST or EPCS required transfusion of 6 U or more of packed red blood cells (PRBCs) during the first 7 days after entry into the study, with active bleeding occurring during or after administration of the sixth unit. Failure of long-term therapy occurred when, after 7 days in the study, recurrent UGI bleeding, shown by endoscopy to be coming from esophagogastric varices, required treatment with a total of 8 U or more of blood transfusion during any 12-month period or, in addition, required blood transfusions after the attending faculty endoscopist had declared the esophageal varices obliterated or gone. Rescue therapy was cross-over treatment applied, whenever possible, to patients in either group in whom failure of primary therapy was declared (ie, rescue PCS for EST failure, and rescue EST for PCS failure).

Informed consent to participate in the RCT was obtained from every patient by a physician co-investigator before randomization to the treatment groups, and witnessed by a third party who was not a participant in the study. Before obtaining consent, patients were given a thorough explanation of the risks and benefits of all treatment options, including those not involved in the RCT. When it was not possible to obtain informed consent because of an altered sensorium, 2 patient advocates were assigned to the patient by a panel of faculty physicians who were not involved in the study to determine if consent should be given.

Disability index

The disability index (DI) was measured regularly by assessing the following factors: (1) liver function as determined by quantitative Child risk class; (2) development of recurrent PSE; (3) number of PSE episodes; (4) units of PRBC transfusion for gastrointestinal bleeding; (5) number of hospital readmissions; (6) days of hospitalization during readmission; (7) return to work, including housekeeping; (8) abstinence from alcoholism; and (9) portacaval shunt patency. These 9 objective factors were weighted numerically to produce a composite DI in which the lower the score, the better the DI.

Statistical analysis

The comparison between the EST and EPCS groups used the Fisher exact test for binary outcomes (eg, control of bleeding, incidence of recurrent PSE), and the Wilcoxon rank-sum test for continuous outcomes (eg, units of PRBC transfusion, number of recurrent PSE episodes, number of hospital readmissions). The length of survival was compared using the Gehan–Wilcoxon rank test. The change in Child class was compared for each time interval

using the exact Wilcoxon rank-sum test, adjusted for ties. The average change in Child class during the first 5 years was computed by averaging the duration of time in years spent by the patients at risk (alive) in each category (improved, unchanged, or worse). The comparison of the number of hospital readmissions and number of readmission days by year used the Wald test of the Poisson model. The overall DI was computed for each group and each year by adding up the scores of the 9 components. The DI was compared between the 2 groups assuming a Poisson (log-linear) model, with different means for the different categories, and a constant group effect. At the beginning of the study, on advice of the External Advisory, Data Safety, and Monitoring Committee, it was decided in advance not to perform an interim analysis of the data so as not to diminish the power of the final analysis.

Results

EST versus EPCS: overall outcome data

Our recent publications provided detailed data on the clinical characteristics of the 211 patients including diagnostic findings, data on survival, data on control of bleeding, and data on PSE.³⁻⁷

There were no significant differences in the clinical characteristics of the 2 groups on entry in the RCT. Cirrhosis ultimately was shown by liver biopsy obtained percutaneously or during surgery in all patients. Definitive treatment was initiated in fewer than 24 hours after onset of bleeding in all patients. EPCS controlled bleeding permanently in all patients, whereas EST achieved permanent control of bleeding in only 20% of patients. Survival rates were significantly higher after EPCS than after EST at all time intervals and in all Child classes ($P < .001$). Patients with the most severe liver disease in Child risk class C realized substantial long-term survival after EPCS.

The incidence of recurrent PSE after EPCS (15%) was less than half the frequency after EST (35%) ($P < .001$). EST patients had a total of 179 episodes of PSE and 146 PSE-related hospital admissions, compared with EPCS patients who had 94 episodes of PSE and 87 hospital admissions ($P = .003$). Recurrent UGI bleeding, which was rare in the EPCS group, was a major causative factor of PSE in almost half of the EST patients.

DI

Liver function (Child risk class).

An important objective measure of disability in patients with cirrhosis is long-term liver function as reflected in the Child risk class. Quantitative Child risk class was determined monthly during the first year after study entry and every 3 months thereafter. A decrease of 2 or more points compared with the score on study entry reflected an improvement in liver function; conversely, an increase of 2 or more points represented a worsening of liver function. Table 1 shows the serial changes in Child risk classes separately for patients who were in Child classes A and B, or C, on entry in the study, and overall for the entire EST group and the entire EPCS group.

Overall, improvement in liver function occurred for 59% of the follow-up period in the EPCS group, but for only 33% of the follow-up period in the EST group. This difference was highly significant ($P < .001$). Overall worsening of liver function was observed in 31% of the measurements obtained in the EST group, compared with 10% in the EPCS group. Again, the difference was significant ($P < .001$). During the 10 years after entry in the study, only 7 of the 91 patients in the EST group who were discharged from the index hospitalization (8%) survived. In contrast, 45 of the 88 EPCS patients (51%) remained alive beyond 10 years. In general, liver function stabilized or improved in a substantial majority of the patients treated by EPCS. The differences in liver function between the EST and EPCS groups were most striking in Child class C, in which improvement in liver function was most important. One year after entry in the study, liver function had improved in 8 of 19 surviving class C patients (42%) in the EST group compared with 17 of 19 surviving class C patients (89%) in the EPCS groups ($P = .005$). After 2 years the results in regard to improved liver function were 6 of 12 patients (50%) in the EST group compared with 15 of 16 surviving patients (94%) in the EPCS group ($P = .006$). By the third year after study entry, 13 of 18 (72%) entering class C patients who received EST had died, whereas only 2 of the 19 (10%) entering class C patients who underwent EPCS had died.

PSE.

A second important objective measure of disability is the presence or absence of PSE, which was determined according to clearly defined criteria described in our recent publication⁴ in patients who were discharged from the initial hospitalization and survived more than 30 days after study entry. This population numbered 91 in the EST group and 88 in the EPCS group. Table 2 summarizes the data on PSE. Thirty-three patients (36%) who underwent EST and 13 patients (15%) who were treated by EPCS developed recurrent PSE, which was a highly significant difference ($P = .001$). The total number of identified PSE episodes was 179 in the EST group, compared with 94 in the EPCS group ($P = .003$). Hospital readmissions for treatment of PSE were 146 in EST patients, compared with 87 in EPCS patients ($P = .003$). The calculated yearly frequency of PSE was .49/y in the EST group and .13/y in the EPCS group ($P = .003$).

UGI bleeding related to portal hypertension, usually from BEV, was the main cause of recurrent PSE or a contributing cause in 50% of the PSE episodes in patients treated by EST. In contrast, UGI bleeding played a role in only 8 episodes (8%) of PSE in the EPCS group. This difference was highly significant ($P < .001$).

It is clear that recurrent PSE had a negative influence on the DI in patients randomized to EST, in large part because of failure to permanently control variceal bleeding.

Blood transfusions for UGI bleeding.

The requirement for blood transfusions because of UGI bleeding almost always was related to readmission to the hospital and together these factors impacted the DI negatively. After discharge from the initial hospitalization, surviving patients treated by EST required a total of 1,005 PRBC transfusions for UGI bleeding, an average of 10.81 PRBC units per patient. In contrast, patients who underwent EPCS required 320 U of PRBC after discharge from the

index hospital admission, or about a third as many blood transfusions as in the EST group. The difference was highly significant ($P < .001$). The requirement for PRBC transfusions, usually because of recurrent BEV in the EST group, was greatest in the first year after discharge from the index hospital admission. Table 3 shows the yearly requirement for PRBC transfusions in survivors who were discharged from the index hospitalization after undergoing EST or EPCS.

Number of hospital readmissions.

Readmission to the hospital because of recurrent bleeding, a complication of treatment, or cirrhosis has a significant and highly negative effect on the DI. In the first year after entry in the trial, the number of patients who survived to the point of discharge from the index admission was 96 in the EST group and 90 in the EPCS group. The 96 EST patients required 233 readmissions to the hospital, or 2.43 readmissions per patient. In contrast, the 90 EPCS patients were readmitted 83 times, or .92 readmissions per patient. This difference was highly significant ($P < .001$).

Similar calculations of mean readmissions for subsequent years in the EST and EPCS groups, respectively, were as follows: 1.21 versus .65 in year 2, .85 versus .60 in year 3, .68 versus .44 in year 4, and .62 versus .53 in year 5, at which time only 21 EST patients were still alive compared with 74 EPCS survivors. The yearly hospital readmissions were significantly fewer in the EPCS group ($P < .001$ for each year). The main causes of hospital readmission were BEV in the EST group, PSE, infection, liver failure, and alcohol intoxication. Table 4 summarizes data on the number of hospital readmissions and resultant days of hospitalization.

Hospital readmission days.

Days in the hospital during readmissions corresponded to the number of readmissions (Table 4). In the first year after entry in the BEV trial, the 96 patients in the EST group spent 1,517 days in the hospital during readmissions, or a mean of 15.8 days per patient. In contrast, the 90 patients who underwent EPCS were rehospitalized for 784 days, or a mean of 8.71 days per patient, which was close to half as many days as the EST patients ($P < .001$). Similar calculations of readmission days per patient during subsequent years in the EST and EPCS groups, respectively, were 8.17 versus 5.19 in year 2, 7.04 versus 3.88 in year 3, 4.84 versus 3.90 in year 4, 5.81 versus 3.24 in year 5, and 6.0 versus 2.61 beyond year 5. Similar to the number of hospital readmissions, the EPCS patients spent significantly fewer days in the hospital than the EST patients ($P < .001$ for each year), and their lives experienced less disruption.

Return to work.

Patients aged 65 or older were considered retired and were not included in the analysis of return to work. There were 10 such surviving patients in the EST group and 13 such survivors in the EPCS group. By definition, return to full-time housekeeping was considered a return to work. Overall, during the 5 years after discharge from the index hospital admission, 40% of the EPCS group and 42% of the EST group returned to full-time work. This difference was not significant. Alternatively, 54% of the EPCS patients and 51% of the

EST patients did not return to work. The remaining patients, who constituted 12% to 16% of the total, returned to work part time or irregularly. During the 5 postdischarge years, 22 EST patients (9%) died after returning to work. Return to work was not a factor in the DI comparison of EST versus EPCS.

Abstinence from alcoholism.

Sixty-nine patients in the EST group and 72 patients in the EPCS group had a history of chronic alcoholism at entry in the randomized trial. During the 5 years after the index hospital admission, taking into account the patients who died, 55% of the EST patients and 63% of the EPCS patients abstained from alcoholism. Abstinence was similar in the 2 treatment groups. At the same time, 28% of the patients in each group returned to chronic alcoholism. The remaining patients, 17% in the EST group and 11% in the EPCS group, engaged in 1 to more than 4 episodes of alcohol consumption. Although abstinence from alcoholism undoubtedly improved the DI, there was no difference between EST and EPCS in the influence of this factor.

Portacaval shunt patency.

Patency and function of the portacaval shunt was determined by yearly Doppler duplex ultrasonography in the survivors of EPCS and of rescue PCS in the EST group. Two patients, both of whom underwent EPCS, developed occlusion of the shunt, one occurred 46 days postoperatively and the other occurred during the second year postoperatively. In each case, patency of the shunt was restored by reoperation. One of the patients remained alive for 7 years and the other patient survived until the end of the follow-up evaluation approximately 12 years after entering the trial. Overall, patency of the portacaval shunt was a positive factor in the DI.

DI

Table 5 and Figure 2 present an overall picture of disability, comparing EST and EPCS. It incorporates all the objective factors that determine the DI in this study. The key at the bottom of Table 5 explains how the scores were calculated. Some factors, such as change in Child risk class and recurrent PSE, were assigned a weighted number that changed with the severity of the factor. Other factors such as PRBC transfusions, number of readmissions, and days of readmission used actual data numbers. The DI is presented for each of the DI factors for 5 years of follow-up evaluation. Also, mean scores for all the factors together are presented year by year as well as for the overall study. After 5 years there were too few survivors of EST to allow a meaningful comparison with EPCS.

The factors that had the greatest impact on DI were liver function as measured by Child risk class, recurrent PSE, requirement for PRBC transfusions because of recurrent variceal bleeding, and requirement for readmission to the hospital. Each of these factors had a significantly lower (ie, better) DI year by year and overall in the patients treated by EPCS. No significant differences between EST and EPCS were observed in alcohol abstinence, PCS patency, and return to work. However, less than one third of the alcoholic patients in each group returned to chronic alcoholism, and only 2 of the 155 patients with surgical

shunts developed occlusion of the shunt. Overall, during each year and for the entire 5-year period of study, DI was significantly better in patients treated by EPCS than in those who received EST ($P < .001$).

Comments

Explanatory comments are indicated about 2 aspects of our RCT, namely, (1) use of EST rather than endoscopic variceal ligation (EVL) as the emergency endoscopic treatment of BEV, and (2) absence of transjugular intrahepatic portal-systemic shunt (TIPS) in our study of disability. For more than 30 years EST has been used throughout the world as a primary emergency and long-term treatment of BEV, and such use continues to this day. Nevertheless, comment is warranted regarding whether or not clinicians consider EST to be the current therapy of choice. Some workers have suggested that EST has been replaced by EVL and vasoactive drug therapy as the treatment of choice for BEV in both emergency and elective circumstances. It has been concluded by some that, compared with EST, EVL eradicates varices more rapidly, results in a lower rate of recurrent bleeding, and causes fewer complications. Nevertheless, our use of EST has received strong support from studies published in 2003, 2005, and 2006 that have questioned replacement of EST by EVL.^{10–13} We discussed this issue and the justification for our use of EST in our recent publications.^{3–7} It is noteworthy that, currently, in our 4-county community of 8.5 million people, gastroenterologists with whom we have had regular and frequent contact use EST more frequently than EVL. At the time when EVL was introduced at our institution, we were well into our RCT and made the decision not to change from EST to EVL.

As for TIPS, which was popularized long after our RCT was initiated, it has become the most widely used rescue procedure when endoscopic and pharmacologic measures have failed to control bleeding. However, as we have pointed out previously, TIPS has a high rate of stenosis and occlusion, a resultant high incidence of PSE, and limited durability. The TIPS occlusion rate appears to have been reduced by the recent introduction of the polytetrafluorethylene-coated stent, but the high incidence of PSE has not changed and the rates of occlusion and PSE are still much higher than the incidences of these serious complications after portacaval shunt observed in all of our studies. Recently, we completed a RCT comparing TIPS and EPCS in 154 patients and have submitted a report of this study for publication.

Survival rate and control of bleeding are the most important determinants of effectiveness of emergency treatment of BEV in cirrhosis. After these 2 determinants, a disability index is an important measure of therapeutic effectiveness. Unfortunately, few observations on DI after emergency or elective treatment of BEV have been reported.¹⁴

DI is determined by a number of objective factors. The most important factor is improvement, stabilization, or worsening of liver function, which can be determined by serial quantitative measurements of Child risk class. Other important factors are recurrent PSE, requirement for blood transfusions, number of readmissions to the hospital and days of hospitalization, abstinence from alcoholism, and patency of the primary or rescue PCS. In the current RCT there was no statistically significant difference between EST and PCS in the

incidence of abstinence from alcohol although, undoubtedly, resumption of alcoholism had a similar negative effect on DI in both groups. Similarly, patency of the PCS was a positive determinant of DI in both treatment groups because 98% of the shunts remained patent and patency was restored by reoperation in the 2 of 155 patients with shunts (1%) who developed occlusion of the portal venous system.

Except for the incidence of abstinence from alcohol and PCS patency in which there was no difference between EST and EPCS, all the other determinants of DI were significantly better after EPCS than after treatment by EST. Liver function improved in 59% of the measurements obtained in the EPCS group, compared with 33% in the EST group, and liver function worsened in only 10% of the determinations after EPCS compared with 31% after EST. The difference favoring EPCS was most marked in patients in Child class C who entered the study with the poorest liver function. The mean DI for all the factors together was significantly lower in the EPCS group year by year as well as for the overall study.

The incidence of recurrent PSE, an important factor in the DI, was more than twice as great after EST than after EPCS (36% vs 15%). Beginning with the animal experiments more than a century ago by Eck¹⁵ and of Hahn et al¹⁶ in Pavlov's laboratory it has been suggested repeatedly that a direct portacaval shunt diverts essential portal blood away from the liver and, consequently, may cause progressive liver damage. That suggestion ignores 2 important hemodynamic facts. The first is that, whether or not a PCS is constructed, BEV arise as a consequence of progressive diversion of a substantial portion of portal venous blood flow away from the liver and into portal-systemic collaterals so that, with regard to insertion of a PCS, the cirrhotic liver with BEV is markedly different from the normal liver. The second important hemodynamic fact is that a fundamental physiological response to diversion of portal venous flow is a compensatory increase in hepatic arterial blood flow to the liver.¹⁷⁻²² It is not possible by any currently available practical method to predict the adequacy of hepatic arterial compensation before performance of a PCS. Substantial data from preoperative and intraoperative measurements of both pressure and blood flow in the portal vein in large numbers of patients have failed to show a correlation between any hemodynamic measurements performed before PCS and survival, hepatic function, or development of PSE after PCS.²⁰⁻²⁴ Our studies of portal vein hemodynamics before PCS showed no statistically significant correlation between preshunt maximum perfusion pressure and posts-hunt survival, liver function, hepatic failure, or development of PSE.²² In the final analysis, the long-term improvement in liver function after EPCS observed in the current trial provides the most meaningful information regarding the effect of portal venous flow diversion on the cirrhotic liver.

The effects of EPCS and, therefore, the significantly better DI were the result of several critical aspects of care in our RCT: (1) simplification of the diagnostic work-up of 4.4 hours; (2) development of an organized system of pre-therapy and post-therapy care; (3) a rigorous, life-long program of follow-up evaluation with intensification of efforts to obtain dietary protein control and abstinence from alcohol; and (4) permanent (99%) long-term patency of the portacaval shunt.

Conclusions

In this RCT of emergency treatment of acute BEV in 211 unselected, consecutive patients with cirrhosis of all grades of severity, EPCS resulted in a markedly better DI than EST, even when failure of EST to control bleeding was treated by cross-over PCS as salvage therapy. When added to the other benefits of EPCS observed in this trial, specifically a significantly higher and longer survival rate, a markedly better control of bleeding, and a significantly lower incidence of recurrent PSE, these results provide support for the use of EPCS as a first-line emergency treatment of patients with BEV. Moreover, these results call into question the widespread practice of using portal-systemic shunt mainly or only as salvage for failure of endoscopic therapy of BEV.

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Figure 1.

Consort flow diagram showing the overall design and conduct of the prospective randomized controlled trial.^{8,9}

Figure 2. Mean DI yearly for 5 years in patients who were randomized to EST or EPCS and were discharged from the index hospital admission.

Table 1

Changes in Child class compared with Child class on study entry (increase or decrease of 2 Child class points indicates a change)

Time after study entry,	Change in Child class	Child class A on entry, n (%)			Child class B on entry, n (%)			Child class C on entry, n (%)			Overall for all classes, n (%)		
		EST	EPCS	P	EST	EPCS	P	EST	EPCS	P	EST	EPCS	P
0-1	N	28	25	.25	42	45	<.001*	19	19	.005*	89	89	<.001*
	Improved	9 (32)	4 (16)		15 (36)	32 (71)		8 (42)	17 (89)		32 (36)	53 (60)	
	Unchanged	15 (54)	16 (64)		16 (38)	10 (22)		3 (16)	0 (0)		34 (38)	26 (29)	
	Worse	4 (14)	5 (20)		11 (26)	3 (7)		8 (42)	2 (11)		23 (26)	10 (11)	
2	N	26	25	.83	36	42	<.001*	12	16	.006*	74	82	<.001*
	Improved	7 (27)	4 (17)		11 (31)	31 (74)		6 (50)	15 (94)		24 (32)	50 (61)	
	Unchanged	13 (50)	15 (62)		14 (39)	8 (19)		2 (17)	1 (6)		29 (39)	24 (29)	
	Worse	6 (23)	5 (21)		11 (31)	3 (7)		4 (33)	0 (0)		21 (28)	8 (10)	
3	N	21	23	.74	26	38	.020*	8	16	.044*	55	77	.006*
	Improved	3 (14)	2 (9)		12 (46)	28 (74)		4 (50)	14 (88)		19 (35)	44 (57)	
	Unchanged	15 (71)	17 (74)		7 (27)	7 (18)		1 (12)	1 (6)		23 (42)	25 (32)	
	Worse	3 (14)	4 (17)		7 (27)	3 (8)		3 (38)	1 (6)		13 (24)	8 (10)	
4	N	20	23	1.0	21	37	.002*	4	15	.035*	45	75	<.001*
	Improved	5 (25)	2 (9)		8 (38)	28 (76)		2 (50)	15 (100)		15 (33)	45 (60)	
	Unchanged	10 (50)	18 (78)		4 (19)	6 (16)		0 (0)	0		14 (31)	24 (32)	
	Worse	5 (25)	3 (13)		9 (43)	3 (8)		2 (50)	0		16 (36)	6 (8)	
5	N	19	23	.046*	12	37	<.001*	2	16	1.0	33	76	<.001*
	Improved	4 (21)	3 (13)		3 (25)	26 (70)		2 (100)	16 (100)		9 (27)	45 (59)	
	Unchanged	3 (16)	16 (70)		3 (25)	9 (24)		0	0		6 (18)	25 (33)	
	Worse	12 (63)	4 (17)		6 (50)	2 (5)		0	0		18 (55)	5 (8)	
1-5 y average	N	28	25	.73	42	45	<.001*	19	19	<.001*	89	89	<.001*
	Improved	12%	6%		33%	59%		49%	94%		33%	59%	
	Unchanged	49%	69%		36%	31%		13%	2%		36%	31%	
	Worse	26%	18%		31%	10%		38%	4%		31%	10%	

* Statistically significant.

Table 2

Recurrent PSE in patients who survived more than 30 days and were discharged from the hospital

	EST (n = 93)	EPCS (n = 89)	P value
Incidence of recurrent PSE, n (%)	33 (36)	13 (15)	.001 [*]
Incidence of transient PSE, n (%)	3 (3)	3 (3)	1.0
Length of survival			
Total days	133,163	267,899	<.001 [*]
Total years	364.6	733.5	
Total days per patient	1,463.3	3,044.3	
Total years per patient	4.0	8.3	
Episodes of recurrent PSE			
Total episodes, n (n/person)	179 (1.97)	94 (1.06)	.003 [*]
Episodes per year of follow-up evaluation	.49	.13	
Interval between episodes, y	2.03	7.74	
Hospital readmissions for recurrent PSE			
Total readmissions, n (n/person)	146 (1.60)	87 (.99)	.003 [*]
Readmissions per year of follow-up evaluation	.40	.12	
Interval between readmissions, y	2.50	8.43	
Cause of recurrent PSE episodes, n (%)			<.001 [*]
Dietary protein indiscretion	75 (39)	60 (61)	
UGI bleeding	57 (30)	8 (8)	
Infection	18 (9)	12 (12)	
Alcoholism	28 (15)	4 (4)	
Uncontrolled diabetes	2 (1)	11 (11)	
Hepatic failure	5 (3)	0 (0)	
Other	5 (3)	3 (3)	

^{*} Statistically significant.

Yearly requirement for PRBC blood transfusions in survivors who were discharged from the index hospitalization after undergoing EST or EPCS

Table 3

	EST			EPCS			P value
	Surviving patients, n	Total PRBC, U	Mean PRBC, U	Surviving patients, n	Total PRBC, U	Mean PRBC, U	
Years after study entry							
1	94	679	7.22	84	55	.65	* <.001
2	58	163	2.81	82	19	.23	* <.001
3	47	70	1.49	78	0	0	* <.001
4	36	18	.5	78	6	.08	* .006
5	20	0	0	78	0	0	NA
>5	19	0	0	70	0	0	NA
Source							
Variceal	93	647	6.957	88	31	.357	* <.001
Nonvariceal	93	358	3.849	88	289	3.542	.32
Total PRBC	93	1,005	10.81	88	320	3.81	* <.001

* Statistically significant.

Hospital readmissions and readmission days in survivors who were discharged from the index hospitalization after undergoing EST or EPCS

Table 4

Years after study entry	Treatment group	Patients discharged, n	Re-admits			Readmit days		
			n	Mean	P value	n	Mean	P value
1	EST	96	233	2.43	<.001	1,517	15.80	*
	EPCS	90	83	.92		784	8.71	
2	EST	58	70	1.21	<.001*	414	8.17	*
	EPCS	81	53	.65		420	5.19	
3	EST	46	39	.85	.11	324	7.04	*
	EPCS	80	48	.60		310	3.88	
4	EST	37	25	.68	.097	179	4.84	*
	EPCS	80	35	.44		312	3.90	
5	EST	21	13	.62	.61	122	5.81	*
	EPCS	78	41	.53		253	3.24	
>5	EST	21	7	.33	.53	126	6.00	*
	EPCS	74	32	.43		193	2.61	

* Statistically significant.

Table 5

Disability index based on 9 criteria in survivors who were discharged from the index hospitalization after undergoing EST or EPCS (lower score equals a better quality of life)

Years after study entry	Study group	Change in Child class	Recurrent PSE	PSE episodes	PRBC, U	Number of readmissions	Days of readmissions	Alcoholism	Return to work	Portacaval shunt patency	Overall (lower score equals a better DI)	Overall P value
1	EST, N	93	75	78	94	96	96	69	82	51		<.001 *
	Total points, mean	193 (2.08)	121 (1.61)	55 (.71)	679 (7.22)	233 (2.43)	303 (3.16)	119 (1.72)	190 (2.32)	51 (1.0)	1,944 (23.84)	
	EPCS, N	90	84	84	84	90	90	72	75	103		
	Total points, mean	144 (1.60)	102 (1.21)	31 (.37)	55 (.65)	83 (.92)	157 (1.74)	119 (1.65)	169 (2.25)	104 (1.0)	964 (11.24)	
2	EST, N	74	58	58	58	58	58	43	60	29		<.001 *
	Total points, mean	163 (2.2)	112 (1.93)	46 (.79)	163 (2.81)	70 (1.21)	94.8 (1.63)	77 (1.79)	118 (1.97)	29 (1.0)	872.8 (15.84)	
	EPCS, N	82	80	80	82	81	81	67	69	103		
	Total points, mean	126 (1.54)	113 (1.41)	32 (.40)	19 (.23)	53 (.65)	84 (1.04)	112 (1.67)	151 (2.19)	104 (1.02)	794 (9.86)	
3	EST, N	55	47	47	47	46	46	35	44	24		<.001 *
	Total points, mean	113 (2.05)	105 (2.23)	18 (.38)	70 (1.49)	39 (.85)	64.8 (1.41)	61 (1.74)	94 (2.14)	24 (1.0)	588.8 (13.55)	
	EPCS, N	77	78	78	78	80	80	64	67	79		
	Total points, mean	120 (1.56)	102 (1.31)	11 (.14)	0 (0)	48 (.60)	62 (.78)	109 (1.70)	145 (2.16)	79 (1.0)	676 (8.93)	
4	EST, N	45	36	36	36	37	37	25	35	18		<.001 *
	Total points, mean	101 (2.24)	94 (2.61)	15 (.42)	18 (.50)	25 (.68)	35.8 (.97)	43 (1.72)	72 (2.06)	18 (1.0)	421.8 (12.45)	
	EPCS, N	75	77	77	78	80	80	63	66	78		
	Total points, mean	112 (1.49)	101 (1.31)	14 (.18)	6 (.08)	35 (.44)	62.4 (.78)	106 (1.68)	142 (2.15)	78 (1.0)	656.4 (8.76)	
5	EST, N	33	22	22	20	21	21	14	21	12		<.001 *
	Total points, mean	90 (2.73)	66 (3.0)	4 (.18)	0 (0)	13 (.62)	24.4 (1.16)	20 (1.43)	46 (2.19)	12 (1.0)	275.4 (13.33)	
	EPCS, N	76	76	76	78	78	78	63	66	77		
	Total points, mean	114 (1.50)	100 (1.32)	1 (.01)	0 (0)	41 (.53)	50.6 (.65)	106 (1.68)	142 (2.15)	77 (1.0)	631.6 (8.51)	
0–5	EST, N	300	238	241	255	258	258	186	242	134		<.001 *
	Total points, mean	660 (2.20)	498 (2.09)	138 (.58)	930 (3.65)	380 (1.47)	523.2 (2.03)	320 (1.72)	520 (2.15)	134 (1.00)	4,103.2 (17.49)	
	EPCS, N	400	395	395	400	409	409	329	343	440		
	Total points, mean	616 (1.54)	518 (1.31)	89 (.25)	80 (.28)	260 (.64)	415.8 (1.02)	552 (1.68)	749 (.64)	442 (1.0)	3,721.8 (9.52)	

Key to point scores (lower score equals a better DI): Child class points are as follows: improved, 1; unchanged, 2; worse, 3; died, 4; recurrent PSE points are as follows: absent, 1; present, 3; return-to-work points are as follows: full time, 1; part time/irregular, 2; did not work, 3; died after return to work, 4; alcoholism points are as follows: abstained, 1; intermittent, 2; chronic, 3; portacaval shunt patency points are as follows: patent, 1; occluded, patency restored, 2; permanently occluded, 3. The PSE episodes, PRBC units, number of readmissions, and days of readmission are shown as actual data numbers.

* Statistically significant.

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