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Authors

Orloff, Marshall J

Hye, Robert J

Wheeler, Henry O

et al.

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Randomized trials of endoscopic therapy and transjugular intrahepatic portosystemic shunt versus portacaval shunt for emergency and elective treatment of bleeding gastric varices in cirrhosis

Marshall J. Orloff, MD[a], **Robert J. Hye, MD**[a], **Henry O. Wheeler, MD**[b], **Jon I. Isenberg, MD**[b], **Kevin S. Haynes, MD**[b], **Florin Vaida, PhD**[c], **Barbara Girard, MS**[a], and **Karen J. Orloff, MSW**[a]

[a]Department of Surgery, the Division of Gastroenterology and Hepatology, San Diego, CA

[b]Department of Surgery, Department of Medicine, and the Department of Family and Preventive Medicine/Biostatistics and Bioinformatics, San Diego, CA

[c]Department of Surgery,University of California, San Diego Medical Center, San Diego, CA

Abstract

Importance.—Bleeding esophageal varices has been studied extensively, but bleeding gastric varices (BGV) has received much less investigation. However, BGV has been reported in ≤30% of patients with acute variceal bleeding. In our studies of 1,836 bleeding cirrhotics, 12.7% were bleeding from gastric varices. BGV mortality rate of 45–55% has been reported. The BGV literature has mainly involved retrospective case reports, often with short-term follow-up.

Objective.—*We sought to describe the results of a prospective, randomized, controlled trial (RCT) in unselected, consecutive patients with BGV comparing endoscopic therapy (ET) with portacaval shunt (PCS;* n = *518), and later comparing emergency transjugular intrahepatic portosystemic shunt (TIPS) with emergency portacaval shunt (EPCS;* n = *70).*

Design, setting, and participants.—*Initially, our RCT involved 518 patients with BGV comparing ET with direct PCS regarding control of bleeding, mortality rate, and disability. When*

Reprint requests: Marshall J. Orloff, MD, Distinguished Professor of Surgery and Founding Chair of Surgery, Emeritus, UCSD Medical Center, 200 West Arbor Drive, San Diego, CA 92103-8999. morloff@ucsd.edu.

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External Advisory, Data Monitoring, and Safety Committee—1977–2011: Professor Harold O. Conn, MD (deceased), Professor of Medicine (Hepatology), Yale University; Professor Haile T. Debas, MD, Emeritus Chair of Surgery; Dean and Chancellor, University of California, San Francisco, School of Medicine; Professor Paul A. Saltman, PhD, Professor of Biology and Vice-Chancellor, University of California, San Diego (deceased); Professor Kenneth Moser, MD, Professor of Medicine, University of California, San Diego (deceased); Professor Philip Sandblom, MD, Chair of Surgery and President, University of Lund, Sweden, Visiting Professor of Surgery, UCSD (deceased).

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*entry of patients ended, the RCT was expanded to compare emergency TIPS with EPCS (*n = *70). This RCT of BGV was separate from our other RCTs of bleeding esophageal varices.*

Interventions.—Initially, ET was compared with PCS. In the second part of our RCT, emergency TIPS was compared with emergency PCS (EPCS).

Main outcome measures.—*Outcomes were survival, control of bleeding, portal-systemic encephalopathy (PSE), quality of life, and direct costs of care. In the RCT of ET versus PCS, 28 and 30%, respectively, were in Child class C. In the expanded RCT of TIPS versus EPCS, 40 and 41%, respectively, were in Child class C. Permanent control of BGV was achieved in 97–100% of patients treated by emergency or elective PCS, compared with 27–29% by ET. TIPS was even less effective, achieving long-term control of BGV in only 6%. Survival rates after PCS were greater at all time intervals and in all Child classes (*P < *.001). Repeated episodes of PSE occurred in 50% of TIPS patients, 16–17% treated by ET, and 8–11% treated by PCS. Shunt stenosis or occlusion occurred in 67% of TIPS patients, in contrast with 0–2% of PCS patients.*

Conclusion.—These results support the conclusion that PCS is uniformly effective, whereas ET and TIPS are not very effective.

VARICEAL HEMORRHAGE is the most lethal form of gastrointestinal bleeding and the most common cause of death in patients with cirrhosis of the liver. Bleeding from ruptured esophageal varices has been studied extensively, but much less investigation has been directed at the problem of bleeding gastric varices (BGV). Yet, gastric varices have been observed in as many as 65% of patients with portal hypertension,[1–4] and bleeding from gastric varices has been reported to occur in as many as 30% of patients with acute variceal bleeding.[5–7] In our ongoing prospective studies of 1,836 cirrhotic patients who underwent portacaval shunt (PCS) for portal hypertension-related bleeding, 12.7% were bleeding from gastric varices. The mortality rate of BGV has been reported to be as great as 45–55%.[5–8]

Treatment of BGV has been uncertain and often empiric. Much of the literature on treatment of BGV has involved retrospective evaluations of small series of cases or case reports, often with short-term follow-up.[5,6,9–15] Moreover, analysis of the results of treatment often has been based on series of cases that included patients with gastric varices caused by disparate underlying diseases as if they were a single condition.

To determine the effectiveness of treatment of BGV in cirrhosis, we conducted a prospective randomized, controlled trial (RCT) in 518 consecutive unselected patients in whom we compared 2 established forms of therapy with regard to control of bleeding, mortality rate, and disability. One-half of the patients underwent endoscopic therapy (ET), consisting of variceal sclerotherapy and/or variceal band ligation, and one-half endoscopic therapy direct PCS. After entry of patients into the RCT of ET versus PCS was concluded, the RCT was expanded to compare emergency transjugular intrahepatic portosystemic shunt (TIPS) versus emergency PCS (EPCS). Seventy patients with acute active bleeding were randomized in the expanded RCT, 36 to TIPS and 34 to EPCS. This is a report of the results of our RCT. We wish to make it clear that this RCT of BGV was separate and distinct from our other recent RCTs, both of which dealt with bleeding esophageal varices. It was started >10 years before our RCT of endoscopic sclerotherapy versus EPCS[16] and 19 years before our RCT of TIPS

versus EPCS,[17] both of which dealt with the emergent treatment of bleeding esophageal varices.

PATIENTS AND METHODS

Design of study.

The study was conducted at University of California, San Diego (UCSD) Medical Center and the UCSD-affiliated San Diego Veterans Administration Hospital. All physicians involved in the study cared for patients at both hospitals. By prior agreement, patients were referred to the 2 UCSD hospitals by physicians caring for patients in hospitals in the counties of San Diego, Imperial, Orange, Riverside, and Kern, with a combined population of 9.5 million. The addition of patients referred from the 5 adjacent counties made it possible to enter in the RCT a substantial number of patients with BGV, a form of variceal hemorrhage that is substantially less common than bleeding esophageal hemorrhage. The objectives were to compare in unselected, consecutive patients with BGV resulting from cirrhosis of the liver, the influence on survival rate, control of bleeding, quality of life (QOL), and economic costs of 2 standard forms of treatment: ET, consisting of repetitive sessions of intravariceal injection sclerotherapy, or variceal band ligation or both modalities aimed at variceal obliteration, and direct PCS. By “unselected,” we mean that all patients, without exception, who entered the 2 UCSD hospitals with BGV and cirrhosis were included. The 2 forms of treatment were compared in 220 patients who were bleeding actively and required emergent therapy, and separately in 298 patients who were referred for elective treatment having recovered from ≥1 episodes of BGV elsewhere. Eligibility for the study included bleeding of a magnitude that required ≥2 units of blood transfusion. Diagnosis was based on endoscopic demonstration of BGV, absence of bleeding from esophageal varices, and absence of any other lesion that could account reasonably for the bleeding. All patients underwent the same diagnostic workup and initial therapy, and were randomized to the 2 treatment groups after the diagnosis of cirrhosis-related BGV was made. The study protocol and consent forms were approved by the UCSD Human Subjects Committee (Institutional Review Board) and the National Institutes of Health before the start of the study and at regular intervals thereafter. Patients were entered in the RCT from August 15, 1977, until December 15, 1997, and follow-up was continued until July 31, 2011. After entry of patients into the RCT of ET versus PCS ended on December 15, 1997, the RCT was expanded to compare TIPS with EPCS. Seventy patients were randomized in the expanded RCT (36 to emergency TIPS and 34 to EPCS) and follow-up was continued until July 31, 2011. Figure 1 is a consort flow diagram that shows the overall design and conduct of the RCT.[18–20]

Informed consent.

Voluntary consent to participate in the study was obtained in writing by a physician co-investigator from every patient before randomization to the treatment groups, and witnessed by a third party who was not involved in the study. Consent was obtained after the patient received a thorough explanation of the study that included the risks and benefits of all treatment options, including those not provided by the study. When it was not possible to obtain informed consent because of an altered sensorium, 2 patient advocates were assigned

to the patient from a panel of senior faculty physicians who were not involved in the study to determine whether consent should be given. The procedure for obtaining consent and the consent form were regularly reviewed and approved by the Human Subjects Committee (Institutional Review Board) and the National Institutes of Health.

Randomization.

Patients were randomized after BGV was proven by emergency endoscopy, and after cirrhosis was indicated by history, physical examination, results of liver function tests, and, in many cases, previous liver biopsy, and after informed consent was obtained. Emergency endoscopy showed that only BGV and no other lesion could reasonably account for the bleeding. Randomization was accomplished by drawing an instruction card from a serially numbered, opaque, sealed envelope prepared by a biostatistician according to a block randomization design that was unknown to the physicians conducting the study. Informed consent for participation in the study was obtained from every patient before endoscopy. There were no escape clauses or crossover provisions in the protocol; 259 patients were randomized to each treatment group. In the ET groups, 105 patients underwent emergency treatment, and 154 patients had elective treatment. In the PCS group, 115 patients underwent emergency operation, and 144 patients had an elective shunt. In the expanded RCT, 36 patients were randomized to emergency TIPS and 34 patients to EPCS. Before randomization, all patients had received ≥2 units of blood transfusion.

Emergency diagnostic workup.

All patients underwent the same diagnostic workup that has been described in detail in our previous RCTs of bleeding esophageal varices published in 2009, 2012, and 2014.[16,17,21] In addition, Doppler duplex ultrasonography was performed at the bedside in the intensive care unit to determine the patency of the portal vein (PV) and to estimate the volume of ascites. In patients who required emergency treatment, the diagnostic workup was completed within 2–7 hours. Patients in the ET group underwent ultimately a percutaneous or transjugular needle liver biopsy if they had not previously had a liver biopsy.

Shortly after initial contact, as soon as the results of the diagnostic workup were known, the patients were assigned to Child risk classes using the 5 criteria originally proposed by Child and Turcotte for assessing hepatic functional reserve.[22] The widely used quantitative method of Campbell and associates,[23] use of which we have reported previously,[16,17,21] was used to decrease subjectivity by assigning points to each of Child's 5 criteria.

Liver transplantation evaluation.

Bleeding varices in cirrhosis has been considered an indication for liver transplantation (LT). It has been proposed that LT be considered the treatment of choice for "patients with advanced liver disease after failure of EST,"[24,25] and for "all patients with end-stage liver disease (Child group C) and variceal bleeding …in the absence of any contraindications."[24–26] Regrettably, there have been no RCTs of LT after any of the emergency modalities of therapy for BGV to support or contradict these proposals.

In our RCT, beginning with the index admission and regularly thereafter, all patients were evaluated by the UCSD LT program for indications for LT. If and when patients exhibited progressive liver failure, they underwent extensive evaluation for LT. As part of our analysis, we examined the question of the need for LT after the life-threatening problem of BGV had been addressed.[27] In addition, the effect of EST or EPCS on the conduct and outcome of LT was examined. As a supplement to the RCT data, we analyzed our results regarding LT in 1,300 unrandomized patients in whom we performed PCS beginning in 1978, 600 as an EPCS and 700 electively.

Hepatocellular carcinoma.

In patients with cirrhosis, hepatocellular carcinoma (HCC) is a frequent cause of death.[28–30] Detection of HCC in cirrhotic patients with BGV has not been studied. All patients underwent screening for HCC by serial abdominal ultrasonography at study entry and whenever possible every 6 months, and serial measurements of serum α-fetoprotein at study entry and monthly for the first year, then every 3 months thereafter. Additionally, CT was performed during the index admission and subsequently when a questionable or suspicious abnormality was found on ultrasonography.

Direct cost of care.

There have been no reports of the costs of any of the widely used forms of emergency treatment of BGV. In this RCT, the 2 groups were compared with regard to charges as a reflection of the direct costs of care. Complete UCSD charges were obtained for every patient entered in each RCT continuously for >10 years. In addition, all referring hospitals and referring physicians signed agreements to provide complete records of charges as they occurred. Before initiation of the study, the UCSD Medical Center agreed to provide promptly copies of all hospital and outpatient charges on all patients at the time when the patients and insurance carriers were billed. Similarly, the UCSD Medical Group, which does the professional fee billing for all physicians who care for patients at UCSD Medical Center, agreed to provide promptly copies of all professional fee bills.

Initial emergency therapy.

The 290 patients who required emergency treatment for active BGV received the same initial therapy while the diagnostic workup was in progress. The initial therapy regimen has been described in detail in ou0072 previous publications.[16,17,21,22] In the later years of the study, octreotide acetate, a somatostatin analog, was given as a continuous intravenous infusion at a rate of 50 μg/h to temporarily control bleeding. Emergency ET was undertaken at the bedside in the intensive care unit within 8 hours of study entry. EPCS and TIPS were undertaken within 24 hours of initial contact and usually within <8 hours. Broad-spectrum antibiotics before and for 3 days after primary therapy were given routinely to patients in both groups.

ET.

From 1977 to 1990, all patients randomized to ET received endoscopic sclerotherapy. ET consisted of intravariceal injection of each varix with <1 mL of 1.5% sodium tetradecyl

sulfate at a time. Variceal band ligation became available in 1990. Initially, the device that was available delivered only 1 band at a time (Bard Interventional Products, Tewksbury, MA). Subsequently, a multiband ligating device was used (Endoloop; Olympus Optical Co., Center Valley, PA). From 1990 to 1997, depending on the findings initially and at each follow-up session, a given patient underwent either variceal sclerotherapy or band ligation. The senior gastroenterologist/endoscopist made the decision on which endoscopic modality to use. ET was repeated 8 days, then 22 days, then 6 weeks after initial treatment, and then every 3 weeks until varices were obliterated. ET was performed by board-certified attending gastroenterologists experienced in this form of treatment. A needle liver biopsy was performed in patients who did not have a previous biopsy and confirmed the diagnosis of cirrhosis in each patient.

PCS.

Our technique of direct PCS has been described previously.[31] Side-to-side PCS was performed in 246 patients (95%), and end-to-side PCS was done in 13 patients. Intraoperative pressure measurements were made before and after PCS by direct needle puncture of the PV and inferior vena cava (IVC), using a saline solution manometer positioned at the level of the IVC. Post-shunt PV-IVC pressure gradient was <50 mm saline solution in 258 of the 259 patients. A large, wedge liver biopsy was obtained from all patients and confirmed the diagnosis of cirrhosis in each case. EPCS was undertaken within 24 hours of initial contact and usually within <8 hours in the 115 patients who were bleeding actively.

TIPS.

A standard, widely used TIPS procedure was performed beginning with right jugular vein access through which a 40-cm long, 10-F sheath was advanced into the right atrium.[17] After pressure measurements were obtained, the 10-F sheath was advanced into the right or middle hepatic vein (HV), and ≥4 liver biopsy specimens were obtained. Next, a 45-cm-long, 16-gauge Roösch-Uchida needle system was advanced into the HV over a guidewire, and the catheter–trochar apparatus was advanced toward the expected location of the right PV or left PV if the middle HV was used. Next, a direct portal venogram and portal pressures were obtained. Then, the intrahepatic track was dilated with a balloon catheter, and the 10-F sheath system was advanced into the PV. A 12-mm diameter Wallstent was inserted, and the stent was dilated with a balloon. Additional stents were inserted to produce a smooth track from the PV bifurcation to the right HV. The portosystemic gradient was measured, and, if necessary, the shunt was dilated with a balloon until the gradient was <10 mmHg. If necessary, additional stents were placed. If varices still opacified, variceal embolization was performed through the catheter in the PV.

Posttreatment therapy.

All patients in the PCS and TIPS groups and patients in the emergency ET group were admitted to the same surgical intensive care unit to which they had been admitted initially. They received a monitoring and therapy regimen that has been described in detail in our previous publications.[16,17,21] The patients and their families were given detailed dietary instructions by a dietitian and received repeated counseling about abstinence from alcohol.

The patients were tested for dietary protein tolerance of ≤80 g/d and were discharged from the hospital with a diet limited to 60 g protein and 2 g sodium salt per day.

Lifelong follow-up.

All patients were followed in a designated portal hypertension clinic, biweekly for the first 4 weeks, monthly for the remaining 11 months of the first postoperative year, and every 3 months thereafter. At each clinic visit, clinical status was evaluated and the presence or absence of portal-systemic encephalopathy (PSE) was determined by a battery of tests that included a series of timed number connection tests, evaluation of mental status by a senior attending faculty physician, examination for asterixis, and measurement of arterial blood ammonia. In addition, measurements were made of blood count, hepatic function, renal function, psychomotor function, and fluid and electrolyte balance. A dietitian employed full-time by the RCT counseled the patients and their families at each clinic visit on restricting dietary protein intake to 60 g/d and sodium salt intake to 2 g/d. Abstinence from alcohol was emphasized at each clinic visit. Biochemical serum markers for HCC were measured at regular intervals. Each year, PCS patency and function were assessed by Doppler duplex ultrasonography or shunt catheterization with pressure measurements and angiography. In the ET group, upper endoscopy was performed by a board-certified attending gastroenterologist every 6 months and, if indicated, ET was applied. A concerted and highly successful effort was made to ensure regular follow-up and to trace patients who missed appointments. Two research study nurses and a social worker were employed full time by the RCT to assist with follow-up. The few patients ($n = 6$) who moved from the referral area were put in contact with a physician well-known to us who agreed to see the patient regularly and return completed study data forms to us. The 1-, 5-, 10-, and 15-year follow-up rates were 100%, 97%, 97%, and 92%, respectively. All patients were operated on >10 years ago. There were no dropouts or withdrawals from the study, largely as a result of the concerted efforts of the entire BGV treatment team.

Criteria for failure of therapy.

Failure of therapy was defined as persistent or recurrent portal hypertension-related bleeding (1) requiring transfusion of ≥4 units of packed red blood cells or whole blood during the first 7 days after initial ET or PCS, or (2) after the first 7 days, requiring transfusion of ≥8 units of blood during any 12-month period, or (3) after the attending faculty endoscopist had previously declared the gastric varices obliterated or gone.

Quantitation of PSE.

PSE was quantitated during hospitalizations and at each clinic visit by grading 4 variously weighted components on a scale of 0 to 4: mental state, asterixis, number connection test, and arterial blood ammonia. A PSE index was calculated according to the method of Conn and Liberthal,[32] in which the scores of the 4 components were added to yield a PSE sum, which was then divided by the maximum possible PSE sum. Mental state was given a weight of 3 and the other components a weight of 1. To increase objectivity, a senior faculty hepatologist/gastroenterologist who was not otherwise involved in the bleeding esophageal varices study evaluated the patients for PSE during the clinic visits. The hepatologist/

gastroenterologist was “blinded” in that he was not told what therapy the patient had received. Details of our assessment of PSE have been described in a recent publication.[33]

Data collection.

Sixteen data forms pertinent to the events in the course of each patient were completed by attending physicians, residents, nurses, and social workers at the time that each event occurred. Beginning with initial contact and continuing through follow-up, detailed data obtained from the history, physical examination, laboratory tests, endoscopic findings, x-ray studies, and operative findings were recorded and analyzed. Throughout the study, 220 categories of data were recorded on standard forms and entered into a computer program for analysis. In addition to the hospital medical record, an individual patient research study file was maintained and brought to the portal hypertension clinic at each visit. Autopsies were obtained on all patients who died in the study hospital and were attended by ≥1 co-investigators in the study.

Statistical analysis.

Primary outcomes were mortality and treatment failure. Sample size computations assumed that patients would be followed for a minimum of 5 years, and that a log-rank test for survival would be conducted at the 2-sided 5% level. Based on a power of 0.9 to detect a significant difference between groups, it was estimated that 250 patients per group would be required, or a total of 500 patients. Comparison between treatment groups, separately for emergency interventions and elective interventions, used the Student *t* test for numeric variables and Fisher’s exact test for categorical variables.

Overall comparisons of the 2 treatment arms involving all subjects were done as follows: for the primary endpoint, overall survival was determined using Kaplan–Meier analysis, and the comparison between groups via the log-rank test. Overall survival at each time point (30 days, and 1, 5, 10, and 15 years) was done using the Mantel–Haenszel test, stratified by type of intervention (emergency or elective). Comparison of survival among alcohol abstainers was done using the Fisher exact test. Comparisons of control of bleeding, incidence of recurrent PSE, improvement of liver function, distribution of Child class, and return to work or housekeeping were done using the Mantel–Haenszel test stratified by type of intervention. All analyses were performed using the R statistical platform. All randomized patients were included on the basis of intention to treat.

Crossover treatment.

When the protocol of our study was designed and approved by the Institutional Review Board, the External Advisory, Data Monitoring and Safety Committee recommended that crossover rescue therapy for failed ET or PCS not be included, because it was anticipated that it would not be possible to apply crossover therapy uniformly. The anticipated lack of uniformity proved to be true, because many patients who failed primary ET rebled and died outside of our institution where PCS was not available, for example, at home or at a hospital near their home to which they were taken by ambulance, as required by law. In contrast, when ETor PCS failed, patients were urged to undergo whatever potentially life-saving pharmacologic, radiologic, or operative therapy was available to them. Every effort was

made to save the lives of patients who developed recurrent bleeding. Whenever possible, every effort was made to facilitate rescue treatment.

RESULTS

Rapidity of emergency therapy.

In all, 290 patients were actively bleeding and required emergency therapy. The median time from onset of bleeding to entry in a referring hospital was 6.5 hours in the 149 patients randomized to ET. The median time in the referring hospital before arrival at UCSD was 13.4, 14.0, and 12.8 hours, respectively. The median time from entry in the RCT at UCSD to EPCS, EST, or TIPS was 10.4, 13.8, and 14.0 hours, respectively, but was <24 hours in all patients. Active bleeding had been observed within 4 hours before entry in the RCT in all patients. Obviously, in this RCT of acute BGV, the diagnostic workup and emergency treatment were accomplished rapidly.

Patient characteristics.

Table I summarizes the clinical characteristics at the time of initial contact in the 588 patients with BGV, 290 of whom received emergency treatment and 298 of whom were referred for elective treatment. Ages ranged from 25 to 78 years. Mean age was 49 years in ET patients and 50 years in PCS patients. There were no differences in any of the clinical variables between patients who received ET, those who unde0072went PCS either emergently or electively, and patients who received emergency TIPS. All patients had proof of BGV by endoscopy and of cirrhosis by liver biopsy. A history of alcoholism was obtained from 84 to 90% of the patients, and positive serologic tests for hepatitis were obtained in 15–16% of patients in the main RCT. Because serologic tests for hepatitis, particularly hepatitis C, were not available in the early years of the study, it is likely that the incidence of posthepatitic cirrhosis with or without alcoholism was greater. The incidence of serious risk factors, such as ascites, jaundice, and PSE, was substantial. The number of patients in quantitative Child risk class C ranged from 28 to 41%.

Gastric varices were classified during initial endoscopy according to the system proposed by Sarin et al[5] (Fig 2), which also shows the incidence of the various types in patients randomized to ET or PCS. Patients who underwent endoscopy in the years before the Sarin classification was reported were classified retrospectively from detailed notes recorded at each endoscopic examination. Those detailed observations maintained in the patient research medical record made it possible to apply the Sarin classification accurately in retrospect. Gastroesophageal varices (GOV), which appear as continuations of esophageal varices. Junctional GOV extending along the lesser curvature of the stomach, classified as GOV_1, were found in 13– 14% of patients. GOV extending into the gastric fundus along the greater curvature classified as GOV_2 were observed in 60–62% of patients. Isolated gastric varices (IGV) in the absence of esophageal varices were found in the fundus of the stomach in 20–22% of patients (IGV_1), and in the corpus, antrum, or pylorus in 3–6% of patients (IGV_2). Esophageal varices were present on admission or had been treated previously by ET in 73–76% of patients. BGV of the types reported to be of greatest risk for hemorrhage and death, namely GOV_2, IGV_1, and IGV_2, occurred in 87% of patients.

Findings at surgery.

Table II summarizes important findings at operation in the 293 patients who underwent emergency (n = 149) or elective (n = 144) PCS. Direct PCS was performed in all patients and was a side-to-side anastomosis in 95%. All patients had portal hypertension with a PV-IVC pressure gradient that averaged 257 mm saline in the EPCS group and 259 mm saline in the elective PCS group. PCS decreased the mean PV-IVC gradient to 22 mm saline in the patients treated emergently and 20 mm saline in the patients treated electively. The PV-IVC gradient decreased to <50 mm saline in all but 1 patient. Cardiac output measured intraoperatively before and after PCS indicated a hyperdynamic circulation in more than three-fourths of the patients. Skin-to-skin operative time was <4 hours in 89% of the EPCS group (mean, 3.3 hours) and 96% of the elective PCS group (mean, 3.1 hours). All patients had cirrhosis on gross examination and on liver biopsy.

Control of bleeding.

Data on control of bleeding are presented in Table III. EPCS promptly controlled BGV permanently in 97% of 115 patients. In ≤25 years of follow-up of patients who underwent EPCS, only 2 patients developed recurrent portal hypertension-related bleeding. Similarly, elective PCS prevented recurrent variceal bleeding for ≤25 years in all but 1 of 144 patients.

In contrast, ET was of limited effectiveness in controlling BGV and in preventing recurrent bleeding. Emergency ET controlled active BGV initially in 82% of 105 patients, but 33% developed recurrent bleeding within 30 days of admission to the hospital, and 77% had recurrent variceal hemorrhage during 5 years of follow-up after randomization. Only 27% of the patients who underwent emergency and then repeat ET had permanent control of bleeding for ≤5 years or until death. Among the 154 patients who underwent elective ET, 71% developed recurrent variceal bleeding, and only 29% had permanent control of bleeding for ≤5 years or until death.

In the expanded study of TIPS in 36 patients, the median PV-IVC pressure gradient before TIPS was 24 mmHg (range, 12–44) and after TIPS had decreased to 6.5 mmHg (range, 0–18). At the conclusion of the procedure, TIPS was considered a technical success in 94% of the patients and indeterminate in 6%. TIPS-specific follow-up by color Doppler ultrasonography, angiography, esophagogastroduodenoscopy, and regular clinical examinations was conducted rigorously. TIPS stenosis or occlusion was demonstrated in 34 of these patients (94%). They developed a mean of 3 episodes of TIPS stenosis or occlusion, a total of 32 episodes in thefirst postentry year, and 26 episodes in the second year after entry. Of these 34 patients, 30 (88%) with TIPS malfunction underwent revision of the TIPS by balloon angioplasty or insertion of ≥1 additional stents. The revisions failed in 93% of the patients, and success was indeterminate in an additional 7%. The durability of TIPS was disappointing.

Survival.

Table IV presents the survival and follow-up rates of patients with BGV. Figure 3 illustrates the 15-year Kaplan–Meier survival plots for patients treated by ET and those treated by PCS and TIPS. All patients were eligible for ≥8 years of follow-up. Follow-up rates for both

treatment groups at 1, 5, 10, and 15 years were 100%, 97%, 97%, and 92%, respectively. Survival of patients who required emergency treatment for active bleeding was greater at all time points after EPCS than after emergency then repetitive ET ($P < .001$). Almost twice as many patients both survived 30 days and left the hospital alive after EPCS than after emergency ET. Five and 10 years after entry in the study, survival of patients treated by EPCS was 3-fold greater than that of patients treated by emergency ET.

The initial survival rates of patients treated electively by ET and PCS were similar, at 93% and 99%, respectively; however, within 1 year and thereafter, there was a greater survival rate in the PCS group than in the ET or TIPS groups ($P < .001$), largely because of recurrent variceal hemorrhage in patients who received ET or TIPS. Five, 10, and 15 years after entry in the study, there was a 2-fold greater survival rate in the elective PCS group than in the elective ET group.

Patients with alcoholic cirrhosis in both treatment groups who abstained from drinking had a substantially greater survival rate than those who continued to drink alcohol. Five-year survival rate in the ET treatment group was 62% in the 42 patients who abstained versus 24% in the remainder of the ET group. Similarly, the 5-year survival rate in the PCS treatment group was 88% in the 86 patients who abstained versus 61% in the remainder of the PCS group.

In the expanded RCT of TIPS versus EPCS involving 70 patients over 10.5 years, survival after EPCS was similar to that observed in the preceding RCT of EPCS versus EST. In striking contrast, the survival rate of the 36 patients randomized to TIPS was 55% at 1 year, 36% at 3 years, 20% at 5 years, and 15% at 7 years.

QOL.

QOL was defined in our RCT as freedom from PSE, long-term PCS patency, abstinence from alcohol, improvement in liver function, improvement in Child class, return to work or housekeeping, and avoidance of the need for LT. Table V presents data on QOL during the first 5 years after treatment for BGV. Approximately one-third of the patients in each group had PSE preoperatively on initial contact, by past history documented in the medical record, or at both times. Before discharge from the hospital, all patients were tested for dietary protein tolerance, and all were observed to tolerate 80 g/d of protein intake. During followup, a concerted effort was made at each clinic visit to identify PSE by evaluation of mental status, testing for asterixis, use of a series of timed number connection tests, and measurement of arterial blood ammonia. Ten percent of patients had a single episode of PSE usually during the first few months after discharge from the hospital, and then had no further problems as hepatic function improved. These patients did not require prolonged treatment with lactulose, neomycin, or more than the usual 60 g/d dietary protein restriction. Recurrent postdischarge PSE that required dietary protein restriction to <60 g/d and chronic therapy with lactulose and neomycin occurred in 16–17% of patients treated by ET and 8–10% of patients who underwent PCS. Recurrent PSE was defined as ≥2 episodes of PSE in patients who were discharged from the index hospital admission and survived ≥30 days. Eighty percent of patients in each group who had recurrent PSE had PSE pre-operatively. Onset was in the first postoperative year in 70% of patients with recurrent PSE. Patients with recurrent

PSE required hospitalization ≥1 times. Hospitalizations were usually precipitated by dietary indiscretion, alcohol abuse, or occasionally by infection. Patients who abstained from alcohol and adhered to simple dietary instructions that restricted protein intake to 60 g/d had a negligible incidence of PSE.

The PCS was shown to be patent by Doppler duplex ultrasonography or by angiographic studies in all but 3 of the 293 patients who underwent PCS. Those 3 patients were the only ones among the 293 patients who developed recurrent variceal bleeding after PCS, an incidence of 1%. In contrast, 73% of the patients treated by emergency ET and 71% of those who underwent elective ET had recurrent variceal hemorrhage. No patient with a PCS who died was found to have thrombosis of the shunt at autopsy.

A history of chronic alcoholism was obtained in 419 of the 518 patients with BGV. Abstention from alcohol during 5 years of follow-up occurred in 65% of the patients in each treatment group.

Results of liver function tests in patients who survived 1 and 5 years after initial ET showed improvement in 48% and 50%, respectively. In patients treated by PCS, results of liver function tests showed improvement in 75% who survived 1 year and 78–80% who survived 5 years.

Quantitative Child risk class was determined at each clinic visit and compared with the risk class assigned before treatment. Five years after emergency ET, 21% of the survivors were in class A (versus 10% before ET), 42% were in class B (versus 62% before ET), and 37% were in class C (versus 28% before ET). In the elective ET group, 5 years after ET, 40% were in class A, 40% were in class B, and 20% were in class C. Generally, there was a decline in hepatic function in the emergency ET patients and a modest improvement in hepatic function in survivors of elective ET. Worsening liver function was related to recurrent BGV. In contrast, patients treated by PCS had a marked improvement in hepatic function throughout the 5 years post-operatively, related likely to freedom from recurrent hemorrhage. In the EPCS group, 75% of patients were in class A (versus 10% before PCS), 18% were in class B (versus 60% before PCS), and 7% were in class C (versus 30% before PCS). Similarly, 5 years after elective PCS, 80% were in class A, 15% were in class B, and 5% were in class C.

Excluding patients who were ≥65 years of age and who were classified as retired, 41–43% of the 5-year survivors of ET, and 64–65% of the 5-year survivors of PCS were employed gainfully or engaged in full-time housekeeping for part or all of the first 5 years of follow-up.

LT has been used with some frequency as treatment in patients with end-stage alcoholic cirrhosis and bleeding esophagogastric varices. Of the 419 patients in this study who survived 30 days and were discharged alive from the hospital, only 6 (1.4%) became candidates for LT. Alcoholism was the reason why some patients were not LT candidates. Furthermore, control of bleeding and improvement in liver function, particularly in patients who underwent PCS, obviated the need to consider LT.

Direct costs of care.

The total post-index charges were greater in patients who were treated by EST or TIPS compared with those who underwent PCS ($P < .001$), and the total overall charges for emergency and long-term care required over a number of years were greater in patients who received emergency followed by long-term repetitive EST, or by TIPS related to duration of survival and, therefore, days or years during which care was required. PCS was significantly less expensive than EST or TIPS in every aspect of care except for the index admission. Charges for post-index care per year in the emergency EST and EPCS groups, respectively, were a mean $108,500 versus $25,100 ($P < .001$). Total overall charges were a mean $168,100 per year in the emergency EST group versus $39,400 per year in the EPCS group ($P < .001$).

Of particular note were the charges for patients who failed emergency EST and underwent a rescue PCS. Charges for such patients were significantly greater than the charges required by emergency EST patients who did not have a rescue shunt as well as by the patients who underwent EPCS. This finding is noteworthy because the main use of surgical shunts in recent years in the United States and abroad has been as elective rescue treatment for failure of ET and other forms of treatment of esophageal varices. Our study indicates that such use of surgical shunts is not only substantially less effective than EPCS, but also is much more costly.

The reasons why EPCS was less costly than emergency EST and TIPS are very likely a consequence of differences in effectiveness of emergency treatment of BGV. The most important determinants of the effectiveness of therapy are survival rate, control of bleeding, and incidence of recurrent PSE. As we have observed in our recent reports, compared with emergency EST and TIPS, EPCS produced a significantly greater survival rate, was much more effective in controlling bleeding, and was followed by less than one-half the incidence of PSE.[16,17,21]

DISCUSSION

BGV can be a serious problem in cirrhotic patients with portal hypertension. Although the reported incidence has varied widely, there is no doubt that gastric varices occur with considerable frequency, they often bleed, and they are associated with a high mortality when they bleed. The treatment of BGV has been uncertain. No acceptable, standard therapy has been established by definitive investigations. Various therapeutic measures have been used, most of them derived from experience with treatment of bleeding esophageal varices. These measures include endoscopic, radiographic, and operative procedures. Current management of BGV has been summarized in informative reviews by Irani, Tripathi, and Ryan and their associates[13–15] in 2011, 2006, and 2004. These reviews contain 122, 80, and 161 references, respectively. The reader should consult these reviews for literature references to reports of the results of the various forms of therapy.

Endoscopic variceal sclerotherapy has been the most widely used method of treating BGV. Sodium tetradecyl sulfate, ethanolamine oleate, 50% glucose solution, and absolute alcohol have been used as sclerosants. Control of acute BGV has been reported in 40–100% of

patients, but rebleeding occurred in 16–90% of patients, often from deep sclerotherapy-induced ulcers, and these ulcers have been difficult to control by repeated endoscopic variceal sclerotherapy. Complication rates have been high, ranging from 19 to 82%. Elective endoscopic variceal sclerotherapy as prophylaxis to prevent recurrent bleeding has been followed by rebleeding in 16–70% of patients. In most of the studies, the period of follow-up has been short.

Endoscopic variceal ligation with a multiband ligator has been used in a small number of patients with gastric varices to control active bleeding and, electively, to prevent bleeding. Follow-up periods have been short; in 1 randomized trial, almost one-half of the patients had HCC. Because of difficulty in ligating large varices, a detachable snare has been introduced to occlude the base of the varix. Initial control of bleeding has been reported to be high, but still, recurrent bleeding has been reported in ≤72% of patients.

Endoscopic variceal injection of bovine and human thrombin, called fibrin glue, has been used in treatment of BGV in a small number of patients, most of whom had follow-up of <1 year. The reports do not permit a meaningful analysis of the effectiveness of thrombin injections. Thrombin produces rapid blood clotting by converting fibrinogen to fibrin and promoting aggregation of platelets. Bovine thrombin is no longer used because of the risk of prion transmission. The cost of human thrombin is substantial, the substance is difficult to obtain, and the US Food and Drug Administration has not yet approved the commercial product.

Endoscopic variceal injection of cyanoacrylate (*N*-butyl-2-cyanoacrylate or histoacryl), a tissue adhesive that polymerizes rapidly on contact with blood to form a hard substance, has been used with increasing frequency to treat BGV in other countries, but has not been approved by the US Food and Drug Administration. Some authors consider it to be the most effective agent in controlling bleeding, and the treatment of choice in BGV. In the largest series of actively bleeding patients reported to date, Kind et al[11] reviewed retrospectively their 12-year experience with emergency and repetitive endoscopic variceal injection of cyanoacrylate in 174 cirrhotic patients with BGV who were followed for a mean of 36 months. Initial hemostasis was obtained in 97.1% of the patients. Early rebleeding (within 30 days) occurred in 15.5% of the patients, and the 30-day mortality rate was 19.5%. Of the 140 patients who left the hospital alive, 18.6% experienced late rebleeding. The overall incidence of recurrent bleeding based on the entire group of 174 patients was 30.4%. The 3-year survival rate was 45.7%.

Use of cyanoacrylate has been associated with some serious complications. Thromboembolic events have been reported and include cerebral infarction, pulmonary embolism, portal and splenic vein thrombosis, and splenic infarction. Septic complications have included bacteremia, mediastinitis, retrogastric abscess, and perforation of the stomach and esophagus. In addition, damage to the endoscope from polymerization of the cyanoacrylate is an ever-present risk.

Recently, 2-octyl cyanoacrylate, an agent related to histoacryl, was approved by the US Food and Drug Administration for skin closure, and a short-term investigational study of use of

this agent to treat 25 patients with BGV has been conducted with US Food and Drug Administration approval. Data to determine the effectiveness and safety of this agent are insufficient.

Two radiographic techniques have been used to treat BGV, namely, balloon-occluded retrograde transvenous obliteration of gastric varices (BRTO) and TIPS. BRTO has been used mainly in Japan but not in the United States. Based on the observation that a spontaneous gastrorenal shunt is often present in patients with fundal varices, catheterization of the shunt and occlusion by a balloon is possible. With the shunt occluded, a sclerosant such as ethanolamine oleate is injected into the gastric varices and allowed to remain for several hours until blood clots have occluded the varices. Most of the patients who underwent BRTO had gastric varices that had not bled. BRTO has not been tested sufficiently in the emergency control of BGV or in the prevention of recurrent bleeding. In reports from Japan, BRTO is described as being successful in obliterating non-BGV and in preventing recurrence of the varices. A negative feature of BRTO has been worsening of esophageal varices in as many as 67% of patients because of increase in portal pressure resulting from occlusion of the gastrorenal shunt.

Unlike all the measures of therapy described thus far, TIPS is a definitive treatment of portal hypertension and in that regard is similar to surgical portosystemic shunts. TIPS has been very effective initially in controlling active bleeding from esoph-ageal varices,[17] and in a small number of patients, most of whom were unresponsive to endoscopic and pharmacologic therapy, TIPS was similarly effective initially in controlling BGV. The main problem with TIPS is the high rate of stenosis or occlusion, which approaches 100% by 3 years.

Recently, we completed and in 2012 reported the results of a 10-year-long RCT of emergency treatment of bleeding esophageal varices in which we compared TIPS versus EPCS in 154 unselected, consecutive patients with cirrhosis and acute bleeding esophageal varices.[17] EPCS was superior to TIPS in all outcome measures ($P < .001$). Permanent control of bleeding was achieved in 97% of patients treated by EPCS but in only 22% treated by TIPS. Median survival was >10 years after EPCS versus 1.99 years after TIPS. Recurrent PSE was 3 times more frequent in the TIPS patients than in the EPCS group (61% vs 21%). Importantly, the shunt remained permanently patent in 99% of patients after EPCS but in only 16% of patients treated by TIPS. Moreover, TIPS revision failed in 80% of the patients in this group.

It was hoped that the TIPS patency rate would be improved by the use of a polytetrafluorethylene-covered stent, but such has not proved to be the case. Studies of TIPS in which covered stents were compared with bare stents were summarized recently (in 2010 and 2011) by Clark et al under the direction of Rosemurgy, a group that has been involved for more than a decade in studies of TIPS and surgical portosystemic shunts.[34,35] Clark et al concluded that “the early data with covered stents indicate no differences in rates of encephalopathy or survival between covered and noncovered TIPS.” There is no reason to believe that the results of TIPS treatment of BGV in patients with cirrhosis would be any

better or that the rate of TIPS patency and prevention of rebleeding will approach that of surgical PCS.

Given the substantial failure rate of all forms of endoscopic and radiographic therapy of BGV, it is surprising that the reported experience with surgical treatment is meager. There are 2 categories of surgical therapy, namely, devascularization procedures and portal-systemic shunts. Devascularization procedures have involved devascularization of the distal esophagus and proximal stomach, or proximal gastrectomy, combined with splenectomy.[36–41] The largest series reported to date has involved 42 patients who underwent gastric devascularization and splenectomy as an emergency in 4, electively in 15, and prophylactically before any bleeding occurred in 12. During a mean follow-up period of 46 months, there was no recurrent bleeding and the actuarial 5-year survival rate was 76%. In reports of smaller series of patients, elective use of devascularization procedures has been quite successful, but emergency surgery has been associated with a high operative mortality rate.[36,37]

Although there are many reports of prospective studies of portal-systemic shunts in treatment of bleeding esophageal varices,[16,17,21,31] almost no information has been reported on the specific use of surgical shunts in the emergency or elective treatment of BGV in cirrhosis. In this report, we believe for the first time, we have presented results of a study comparing PCS with ET in a prospective RCT involving 518 unselected patients with cirrhosis and BGV. In this RCT, the results of PCS were impressively superior to those of ET in every respect, and the differences were highly significant (Table VI). ET was effective in emergency control of active BGV (82% control), although not as effective as PCS (98% control); however, 33% of the emergency ET group developed recurrent bleeding within 30 days, whereas none of the patients treated by EPCS had recurrent bleeding. The results of PCS are consistent with our previously reported experience with PCS in treatment of bleeding esophageal varices.[16,17,21] Permanent control of bleeding in the entire group of 518 patients was achieved by PCS in 98%, but by ET in only 28%. Recurrent bleeding played a major role in the high mortality rate associated with ET.

The 30-day survival rate, which included discharge alive from the hospital, was 78% for patients treated by EPCS, but only 41% for patients who underwent emergency ET. The survival rate for EPCS is similar to our previously reported 30-day survival rate for EPCS in the treatment of bleeding esophageal varices.[16,17,21] In the entire group of 518 patients, survival rates after 1, 5, 10, and 15 years in the ET group were 51, 30, 25, and 19%, respectively, and in the PCS group were 84, 70, 63, and 56%, respectively, all significant differences. As we have reported previously, alcoholic patients who abstained from drinking had an enhanced 5-year survival rate-−−62% in the ET group and 88% in the PCS group.

QOL was significantly better in patients treated by PCS than in those treated by ET, in large part owing to freedom from recurrent bleeding. Approximately one-third of the patients in each group had preoperative PSE. Recurrent PSE that required treatment and diminished the QOL occurred in 17% of the patients treated by ET and 9% of those treated by PCS. The low incidence of recurrent PSE in the PCS group is consistent with our previously reported experience that includes a study of patients in Child risk class C.[16,17,21,33,42] We attributed

the low incidence of PSE to the uniform prevention of recurrent gastrointestinal bleeding, improvement in hepatic function in a majority of the patients, and the intense, concerted, rigorous follow-up that emphasized restriction of dietary protein intake to 60 g/d.

An important factor in the effectiveness of PCS was the low incidence of long-term shunt thrombosis. Only 3 of the 259 patients treated by PCS developed occlusion of the PCS, an incidence of 1%. This low incidence of shunt thrombosis is similar to our previously reported experience.[16,17,21,42] Shunt occlusion is a failure of operative therapy and is usually followed by recurrence of bleeding. Shunt occlusion rates of 12, 15, and 29% for conventional portal-systemic shunts, and 14, 17, and 23% for distal splenorenal shunts have been observed in RCTs.[43] Reports of mesocaval interposition shunt from respected centers have described occlusion rates of 24, 33, and 53%.[44–46] As mentioned previously, the major shortcoming of TIPS has been a high rate of stenosis and occlusion.

Other factors that influence QOL are abstinence from alcohol and improvement in liver function. There is no doubt that resumption of alcoholism decreases the long-term survival rate.[47–49] Sixty-five percent of the patients in both groups abstained from alcohol for ≤5 years. Abstention was emphasized at each follow-up clinic visit. Liver function tests were performed at each of the regular outpatient follow-up visits. Results of liver function tests showed improvement after 1 year in 48% of the ET group and 75% of the PCS group, and after 5 years in 50% of the ET patients and 74% of the PCS patients. Improvement in liver function was reflected in improvement in quantitative Child risk class. In the 5-year survivors, 68% of patients treated by PCS and 23% of patients who underwent ET improved their Child risk class. In the PCS group after 5 years, 78% of the patients were in risk class A and only 6% remained in risk class C. Finally, 65% of the PCS patients and 42% of the ET patients who were not of retirement age were employed gainfully or engaged in full-time housekeeping for part or all of the initial 5-year follow-up period.

LT is an important measure of treatment for patients with end-stage alcoholic cirrhosis who have abstained from drinking for a considerable duration of time and who are unlikely to survive for >1 year despite control of variceal bleeding. Such patients are few. Only 6 of the 419 patients in our study who were discharged alive from the hospital (1.4%) became candidates for LT. The reasons for the small number include recent or continued alcoholism, patient refusal, unavailability of a donor liver, and, most important, improvement in liver function with control of bleeding, particularly in the PCS group, which obviated the need to consider LT.

The suggestion has been made frequently that direct PCS compromises subsequent LTand should be avoided in potential LT candidates. Further-more, if a surgical shunt is necessary, it has been proposed that the hepatic hilum be avoided and a mesocaval or splenorenal shunt be used. These suggestions are refuted by available data. At least 8 studies have shown that a previous portal-systemic shunt, regardless of type, had no influence on the outcome of LT.[24,26,50–55] Furthermore, the incidence of shunt thrombosis, a critical factor in the selection of the type of shunt, has been <1% in all of our studies of direct PCS including the current one,[16,17,21,42] compared with 24–53% for mesocaval interposition shunts using synthetic grafts.

[44–46] Most important, the vast majority of patients with BGV do not become candidates for LT.

In conclusion, results of the RCT reported herein support the conclusion that PCS, under both emergency and elective circumstances, is very effective treatment of BGV owing to cirrhosis, whereas ET is not very effective. Of the 293 patients entered in the PCS arms of the trial, only 3 had portal hypertension-related bleeding at any time after PCS. Furthermore, PCS had a 99% permanent patency rate, led to 5-and 10-year survival rates of 70 and 65%, respectively, had a low incidence of recurrent PSE, and in many patients led to an acceptable QOL with improvement in liver function in 79% and in quantitative Child risk class in 68%. These results of PCS are superior to the reported results of all forms of endoscopic and radiographic therapy of BGV. Table VI summarizes the results of our RCT.

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REFERENCES

1. Hashizume M, Kitano S, Yamaga H, et al. Endoscopic classification of gastric varices. Gastrointest Endosc 1990;36: 276–80. [PubMed: 2365213]
2. Watanabe K, Kimura K, Matsutani S, et al. Portal hemodynamics in patients with gastric varices: a study of 230 patients with oesophageal and gastric varices using portal vein catheterization. Gastroenterology 1988;95:434–40. [PubMed: 3391371]
3. Evans JA, Delany F. Gastric varices. Radiology 1953;60:40–52.
4. Yasumoto M Clinical observations on 100 cases of gastric varices. Jpn J Gastroenterol 1971;68:721–39.
5. Sarin SK, Lahoti D, Saxena SP, et al. Prevalence, classification and natural history of gastric varices: a long-term follow-up study in 568 portal hypertension patients. Hepatology 1992;16:1343–9. [PubMed: 1446890]
6. Korula J, Chin K, Ko Y, et al. Demonstration of two distinct subsets of gastric varices observed during a 7-year study of endoscopic sclerotherapy. Dig Dis Sci 1991;36:303–7. [PubMed: 1995266]
7. Kotfila R, Trudeau W. Extraesophageal varices. Dig Dis 1998;16:232–41. [PubMed: 9732183]
8. Trudeau W, Prindiville T. Endoscopic injection sclerosis in bleeding gastric varices. Gastrointest Endosc 1986;32:264–8. [PubMed: 3488937]

9. Sarin SK, Agarwal SR. Gastric varices and portal hypertensive gastropathy. Clin Liver Dis 2001;5:727–67. [PubMed: 11565139]
10. Stanley AJ, Jalan R, Ireland HM, et al. A comparison between gastric and oesophageal variceal haemorrhage treated with transjugular intrahepatic portosystemic stent shunt (TIPSS). Aliment Pharmacol Ther 1997;11:171–6. [PubMed: 9042990]
11. Kind R, Guglielmi A, Rodella I, et al. Bucrylate treatment of bleeding gastric varices: 12 years' experience. Endoscopy 2000;32:512–9. [PubMed: 10917182]
12. Lee YT, Chan FKL, Ng EKW, et al. EUS-guided injection of cyanoacrylate for bleeding gastric varices. Gastrointest Endosc 2000;52:168–74. [PubMed: 10922086]
13. Irani S, Kowaley K, Kozarek R. Gastric varices. An updated review of management. J Clin Gastroenterol 2011; 45:133–48. [PubMed: 21135706]
14. Tripathi D, Ferguson JW, Therapondos G, Plevris JN, Hayes PC. Review article. Recent advances in the management of bleeding gastric varices. Aliment Pharmacol Ther 2006;24:1–17.
15. Ryan BM, Stockbrugger RW, Ryan JM. A pathophysiologic, gastroenterologic, and radiologic approach to the management of gastric varices. Gastroenterology 2004;126:1175–89. [PubMed: 15057756]
16. Orloff MJ, Isenberg JI, Wheeler HO, et al. Randomized trial of emergency endoscopic sclerotherapy versus emergency portacaval shunt for acutely bleeding esophageal varices in cirrhosis. J Am Coll Surg 2009;209:25–45. [PubMed: 19651060]
17. Orloff MJ, Vaida F, Haynes KS, Hye RJ, Isenberg JI, JinichBrook H. Randomized controlled trial of emergency transjugular portosystemic shunt versus emergency portacaval shunt treatment of acute bleeding esophageal varices in cirrhosis. J Gastrointest Surg 2012;16:2094–111. [PubMed: 23007280]
18. Moher D, Schulz KF, Altman D. The CONSORT statement: revised recommendations for improving the quality of reports of parallel-group randomized trials. JAMA 2001;285: 1987–91. [PubMed: 11308435]
19. Altman DG, Schulz KF, Moher D, et al. The revised CONSORT statement for reporting randomized trials: explanation and elaboration. Ann Intern Med 2001;134:663–94. [PubMed: 11304107]
20. Schulz KF, Altman DG, Moher D, for the CONSORT Group. CONSORT 2010 Statement: updated guidelines for reporting parallel group randomized trials. BMJ 2010;340:c332. [PubMed: 20332509]
21. Orloff MJ. Fifty-three years' experience with randomized clinical trials of emergency portacaval shunt for bleeding esophageal varices in cirrhosis: 1958–2011. JAMA Surg 2014;149:155–69. [PubMed: 24402314]
22. Child CG III, Turcotte JG. Surgery and portal hypertension. In: Child CG III, editor. The liver and portal hypertension Philadelphia: Saunders; 1964 p. 1–85.
23. Campbell DP, Parker DE, Anagnostopoulos CE. Survival prediction in portacaval shunt: a computerized statistical analysis. Am J Surg 1973;126:748–51. [PubMed: 4543312]
24. Iwatsuki S, Starzl TE, Todo S, et al. Liver transplantation in the treatment of bleeding esophageal varices. Surgery 1988; 104:697–705. [PubMed: 3051474]
25. Reyes J, Iwatsuki S. Current management of portal hypertension with liver transplantation. Adv Surg 1992; 25:189–208. [PubMed: 1536096]
26. Bismuth H, Adam R, Mathur S, Sherlock D. Options for elective treatment of portal hypertension in cirrhotic patients in the transplantation era. Am J Surg 1990;160: 105–10. [PubMed: 2368870]
27. Orloff MJ, Isenberg JI, Wheeler HO, Haynes KS, JinichBrook H, Rapier R, et al. Liver transplantation in a randomized controlled trial of emergency treatment of acutely bleeding esophageal varices in cirrhosis. Transplant Proc 2010;42:4101–8. [PubMed: 21168637]
28. Benvegnu L, Gios M, Boccato S, et al. Natural history of compensated viral cirrhosis: a prospective study on the incidence and hierarchy of major complications. Gut 2004;53: 744–9. [PubMed: 15082595]
29. Degos F, Christidis C, Ganne-Carrie N, et al. Hepatitis C virus related cirrhosis: time to occurrence of hepatocellular carcinoma and death. Gut 2000;47:131–6. [PubMed: 10861275]

30. Sangiovanni A, Del Ninno E, Fasani P, et al. Increased survival of cirrhotic patients with a hepatocellular carcinoma detected during surveillance. Gastroenterology 2004;1265: 1005–14.
31. Orloff MJ, Orloff SL, Orloff MS. Portacaval shunts: side-to-side and end-to-side. In: Clavien PA, Saar MG, Fong Y, editors. Atlas of upper gastrointestinal and hepato-pancreato-biliary surgery Berlin: Springer-Verlag; 2007 p. 687–702.
32. Conn HO, Liberthal MM. The hepatic coma syndromes and lactulose Baltimore: Williams & Wilkins; 1978.
33. Orloff MJ, Isenberg JI, Wheeler HO, Haynes KS, Jinich-Brook H, Rapier R, et al. Portal-systemic encephalopathy in a randomized controlled trial of endoscopic sclerotherapy versus emergency portacaval shunt treatment of acutely bleeding esophageal varices in cirrhosis. Ann Surg 2009;250:598–610. [PubMed: 19730244]
34. Clark W, Hernandez J, McKeon B, Villadolid D, Al-Saadi S, Mullinax J, et al. Surgical shunting versus transjugular intrahepatic portosystemic shunting for bleeding varices resulting from portal hypertension and cirrhosis: a meta-analysis. Am Surg 2010;76:857–64. [PubMed: 20726417]
35. Clark W, Golkar F, Luberice K, Toomey P, Paul H, Marcadis A, et al. Uncovering the truth about covered stents: is there a difference between covered versus uncovered stents with transjugular intrahepatic portosystemic shunts? Am J Surg 2011;202:561–4. [PubMed: 21944293]
36. Hosking S, Johnson A. Gastric varices: a proposed classification leading to management. Br J Surg 1988;75:195–6. [PubMed: 3349325]
37. Greig ID, Garden OJ, Anderson JR, et al. Management of gastric variceal hemorrhage. Br J Surg 1990;77:297–9. [PubMed: 2322791]
38. Hsieh J-S, Huang C-J, Huang T-J. Management of isolated gastric varices by devascularization and proximal gastrectomy in cirrhotic patients. HPB Surg 1994;7:201–9. [PubMed: 8155586]
39. Kollias J, Jeans PL, Padbury RTA, Toouli J. Gastric devascularization and splenectomy for bleeding gastric varices. Aust N Z J Surg 1995;65:804–7. [PubMed: 7487731]
40. Tomikawa M, Ha M, Hashi M, et al. Effectiveness of gastric devascularization and splenectomy for patients with gastric varices. J Am Coll Surg 2000;191:498–503. [PubMed: 11085729]
41. Chaudhary A, Dhar P, Aggarwal A, et al. Long-term outcome of surgical treatment for gastric varices. Hepatology 2000;32:519A.
42. Orloff MJ, Orloff MS, Rambotti M, Girard B. Is portalsystemic shunt worthwhile in Child's class C cirrhosis? Long-term results of emergency shunt in 94 patients with bleeding varices. Ann Surg 1992;216:256–68. [PubMed: 1417175]
43. Grace ND, Conn HO, Resnick RH, et al. Distal splenorenal versus portal systemic shunts after haemorrhage from varices: a randomized controlled trial. Hepatology 1988;8: 1475–81. [PubMed: 3056820]
44. Terpstra OT, Ausema B, Bruining HA, et al. Late results of mesocaval interposition shunting for bleeding oesophageal varices. Br J Surg 1987;74:787–90. [PubMed: 3499203]
45. Smith RB, Warren WD, Salam AA, et al. Dacron® interposition shunts for portal hypertension. An analysis of morbidity correlates. Ann Surg 1980;192:9–17. [PubMed: 6447485]
46. Fletcher MS, Dawson JL, Williams R. Long-term follow-up of interposition mesocaval shunting in portal hypertension. Br J Surg 1981;68:485–7. [PubMed: 6972793]
47. Borowsky SA, Stroma S, Lott E. Continued heavy drinking and survival in alcoholic cirrhotics. Gastroenterology 1981; 80:1405–9. [PubMed: 6971772]
48. Powell WJ, Klatskin G. Duration of survival in patients with Laennec's cirrhosis. Am J Med 1986;98:695–716.
49. Capone RR, Buhac I, Kohberg RC, Balint JA. Resistant ascites in alcoholic liver cirrhosis. Dig Dis Sci 1978;23: 867–71.
50. Boillot O, Houssin D, Santoni P, et al. Liver transplantation in patients with a surgical portosystemic shunt. Gastroenterol Clin Biol 1991;15:876–80. [PubMed: 1783246]
51. Langnas AN, Marujo WC, Stratta RJ, et al. Influence of a prior porta-systemic shunt on outcome after liver transplantation. Am J Gastroenterol 1992;87:714–8. [PubMed: 1590306]
52. Mazzaferro V, Todo S, Tzakis AG, et al. Liver transplantation in patients with previous portosystemic shunt. Am J Surg 1992;160:111–5.

53. Minegaux F, Keefe EB, Baker E, et al. Comparison of transjugular and surgical portosystemic shunts on the outcome of liver transplantation. Arch Surg 1994;129: 1018–24. [PubMed: 7944930]

54. Turrion VS, Mora NP, Cofer JB, et al. Retrospective evaluation of liver transplantation for cirrhosis: a comparative study of 100 patients with or without previous portosystemic shunt. Transplant Proc 1991;23:1570–1. [PubMed: 1989295]

55. Aboujaoude MM, Grant DR, Ghent CN, et al. Effect of portosystemic shunts on subsequent transplantation of the liver. Surg Gynecol Obstet 1991;172:215–9. [PubMed: 1994497]

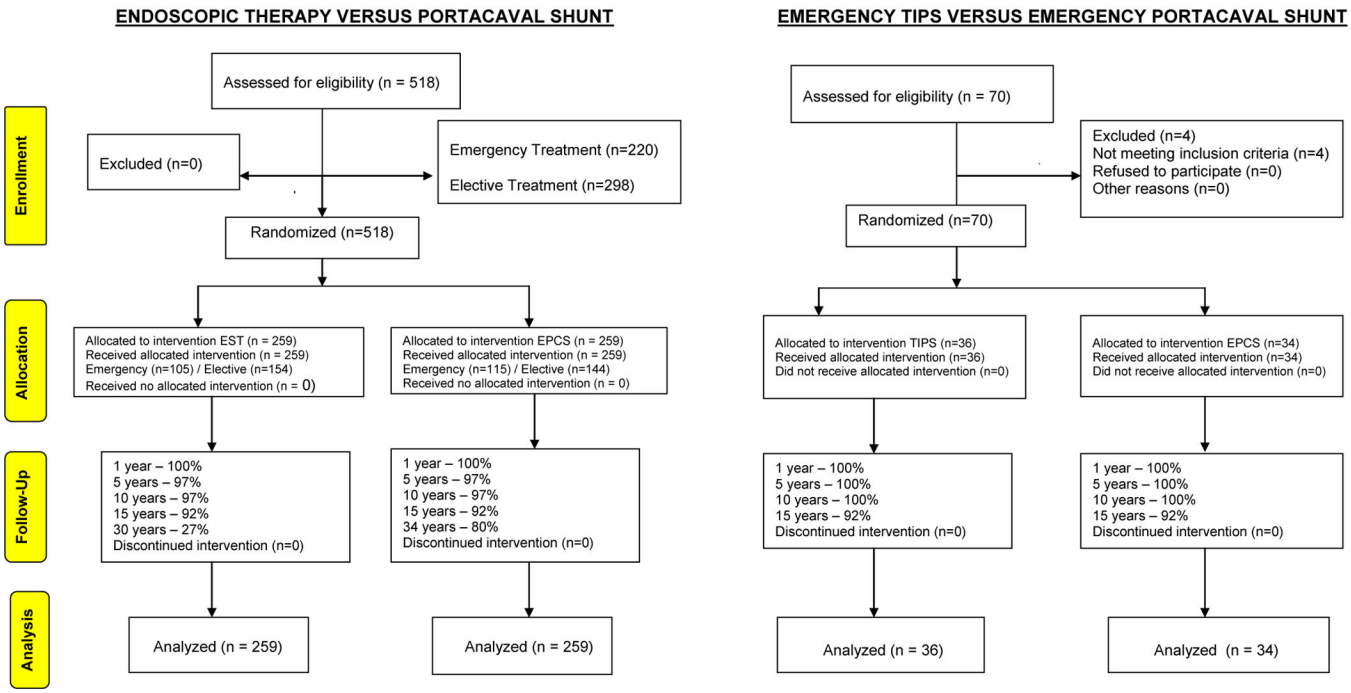

Fig 1.

Overall design and conduct of the 2-part, prospective, randomized, controlled trial is shown in a consort flow diagram. *EPCS*, Emergency portacaval shunt; *EST*, endoscopic sclerotherapy; *TIPS*, transjugular intrahepatic portosystemic shunt.[18–20]

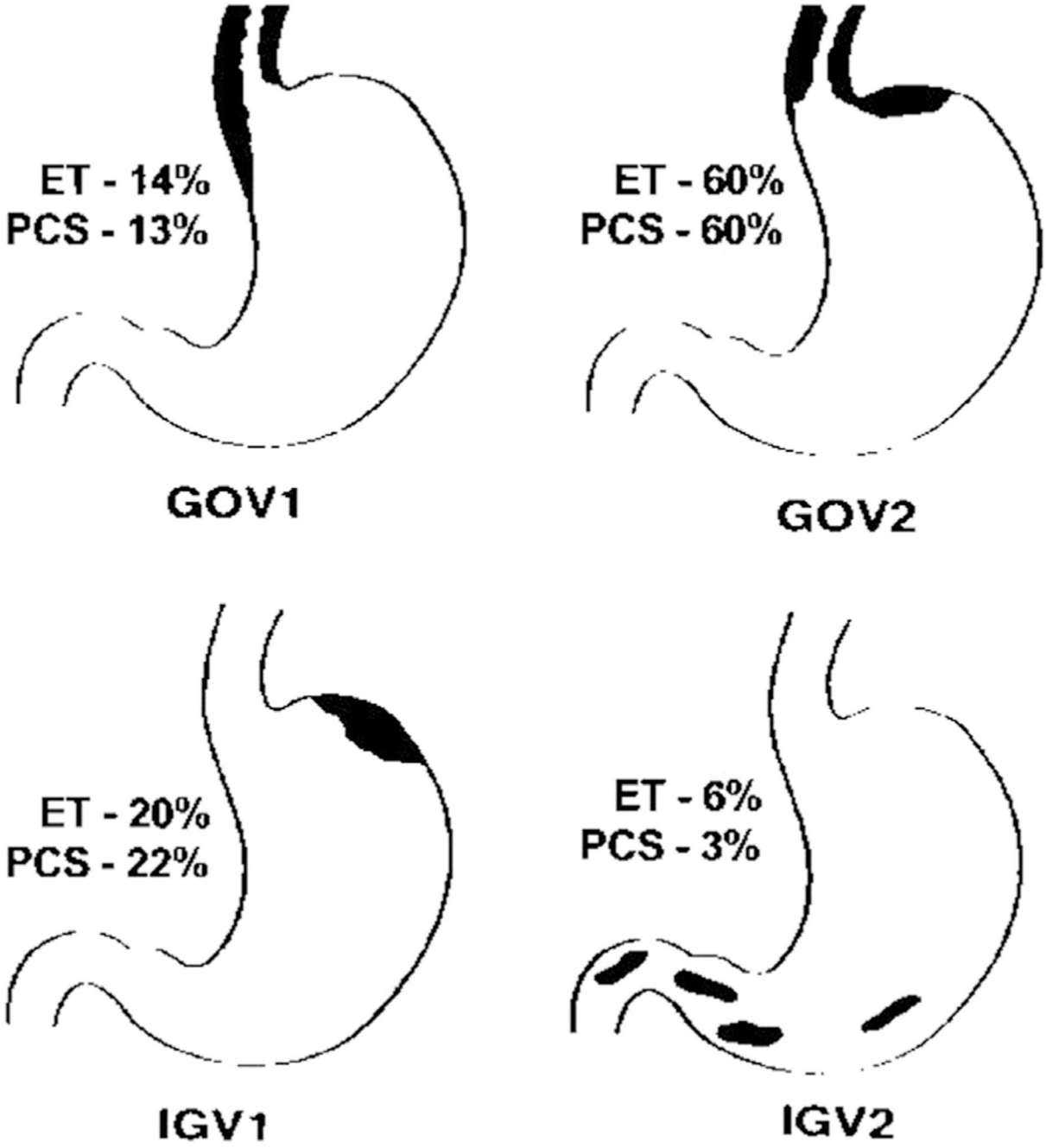

Fig 2.

Classification of types of gastric varices according to the system of Sarin et al[5] and incidence of the various types in 518 patients with bleeding gastric varices randomized to treatment by endoscopic therapy (ET) or portacaval shunt (PCS). *GOV_1*, Junctional gastroesophageal varices extending along the lesser curvature of the stomach; *GOV_2*, gastroesophageal varices extending into the gastric fundus along the greater curvature; *IGV_1*, isolated gastric varices in the fundus of the stomach; *IGV_2*, isolated gastric varices in the corpus, antrum, or pylorus of the stomach.

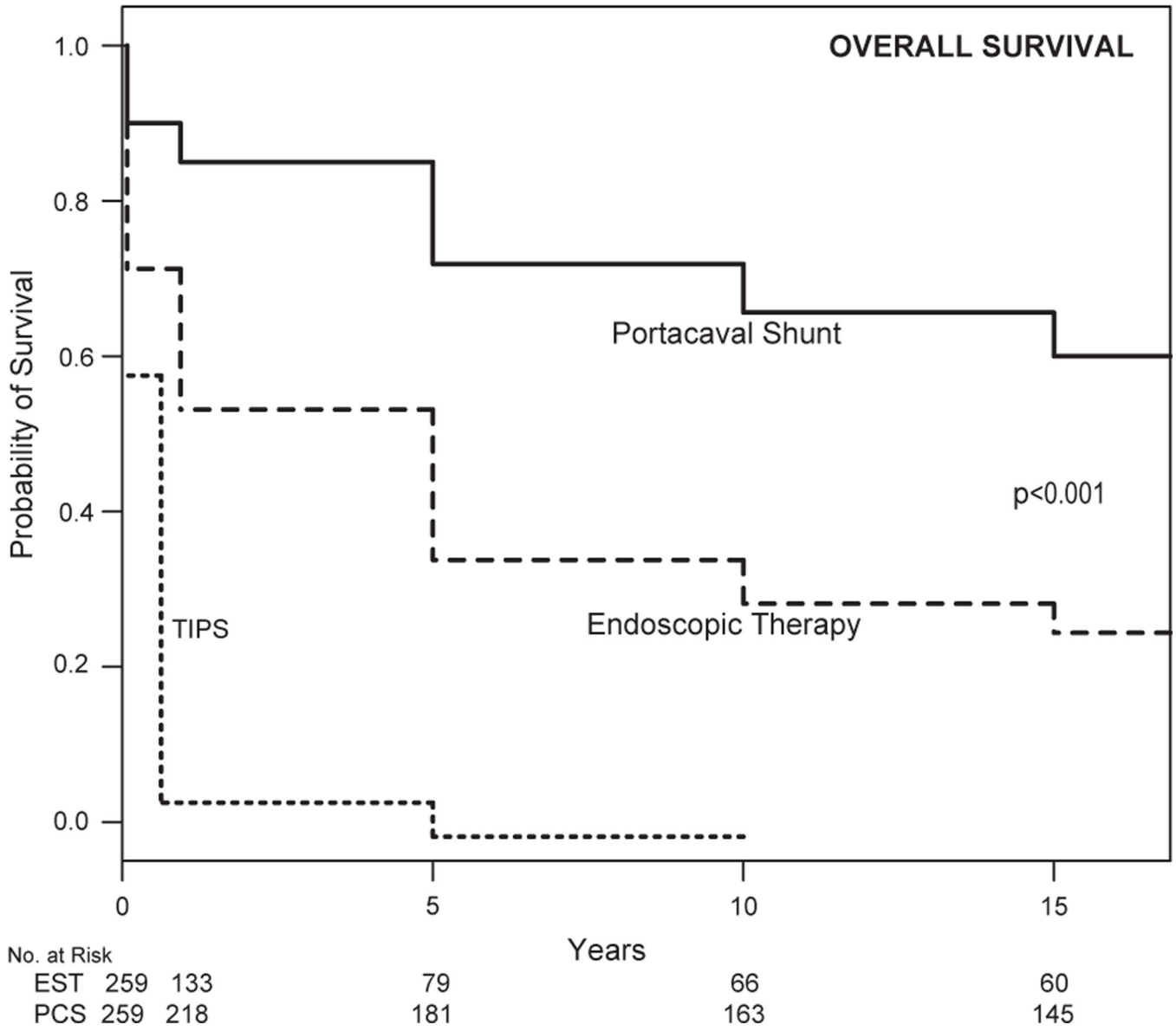

Fig 3.

Fifteen-year Kaplan–Meier survival plots for 588 patients treated emergently and electively by endoscopic therapy (EST; $n = 259$), portacaval shunt (PCS; $n = 293$), and transjugular intrahepatic portosystemic shunt ($n = 36$).

Table I.

Clinical characteristics at time of study entry of 588 patients with cirrhosis and bleeding gastric varices

	Emergency treatment (n = 220)					*RCT of expanded emergency treatment* (n = 70)					*Elective treatment* (n = 298)				
	ET (n = 105)		*PCS (n = 115)*			*TIPS (n = 36)*		*EPCS (n = 34)*			*ET (n = 154)*		*PCS (n = 144)*		
Characteristic	n	%	n	%	P *value*	n	%	n	%	P *value*	n	%	n	%	P *value*
Male sex	68	65	75	65	.99	25	70	24	71	.99	100	65	94	65	.99
Bleeding episode					.97					.99					.98
First	41	39	47	41		7	19	6	18		63	41	58	40	
Second	43	41	46	40		20	56	19	56		60	49	58	40	
Third or more	21	20	22	19		9	25	9	26		31	20	28	20	
Hematemesis	105	100	115	100	.99	36	100	34	100	.99	154	100	144	100	.99
Blood in gastric aspirate, stool, or both	105	100	115	100	.99	36	100	34	100	.99	154	100	144	100	.99
Recent alcohol ingestion (≤7 d)	68	65	80	70	.47	25	70	24	70	.99	0	0	0	0	.99
Ascites	68	65	75	65	.99						62	40	56	39	.81
Jaundice	59	56	66	57	.95						52	34	50	35	.90
Portosystemic encephalopathy on initial contact, or past history, or both times	36	34	40	35	.99	13	36	14	41	.99	51	33	50	35	.81
Severe muscle wasting	42	40	47	41	.96	18	50	18	53	.99	62	40	60	42	.81
Delirium tremens on initial contact, or past history, or both	18	17	20	17	.99	7	19	6	18	.99	26	17	26	18	.92
Hyperdynamic cardiac output ≥6 L/min	95	90	105	91	.99	32	90	31	91	.99	106	69	101	70	.90
Gastric varices on	105	100	115	100	.99	36	100	34	100	.99	154	100	144	100	.99
endoscopy															
Cirrhosis proven by biopsy	105	100	115	100	.99	36	100	34	100	.99	154	100	144	100	.99
Alcoholic	88	84	98	85	.85	32	90	31	90	.99	129	84	121	84	.99
Posthepatitic or other (± alcoholic)	16	16	17	15	.99	16	44	15	44	.99	25	16	23	16	.99
Child's risk class					.81					.99					.89
A	11	10	11	10		0	0	0	0		15	10	14	10	
B	65	62	69	60		22	61	20	59		95	62	86	60	
C	29	28	25	30		14	40	14	41		44	28	44	30	

ET, Endoscopic therapy; *PCS*, portacaval shunt; *RCT*, randomised controlled trial; *TIPS*, transjugular intrahepatic portosystemic shunt.

Table II.

Operative data in 293 patients who underwent emergency or elective portacaval shunt (PCS) for bleeding gastric varices

Characteristic	*Emergency PCS (n = 115)*	*Elective PCS (n = 144)*	*Expanded RCT of emergency PCS (n = 34)*
Type of PCS, *n* (%)			
Direct side-to-side	109 (95)	137 (95)	34 (100)
Direct end-to-side	6 (5)	7 (5)	0
Mean PV-IVC pressure gradient, mm saline			
Pre-PCS	257	259	284
Post-PCS	22	20	18
Post-PCS PV-IVC pressure gradient <50 mm saline, *n* (%)	114 (99)	144 (100)	34 (100)
Mean cardiac output, L/min			
Pre-PCS	8.6	8.0	8.8
Post-PCS	7.9	7.9	8.0
Post-PCS cardiac output $6 L/min, *n* (%)	102 (89)	111 (77)	34 (100)
Mean duration of operation (h)	3.3	3.1	3.6
Duration of operation <4 h, *n* (%)	91 (79)	138 (96)	33 (97)

PV-IVC, Portal vein-inferior vena cava; *RCT*, randomised controlled trial.

Table III.

Control of variceal bleeding in 588 patients with bleeding gastric varices

Characteristic	*Emergency treatment* (n = *220*)			*Expanded RCT of emergency treatment* (n = *70*)			*Elective treatment* (n = *298*)		
	ET (n = *105*)	*PCS* (n = *115*)	P *value*	*TIPS* (n = *36*)	*EPCS* (n = *34*)	P *value*	*ET* (n = *154*)	*PCS* (n = *144*)	P *value*
Temporary control during emergency diagnostic workup, *n* (%)	53 (50)	103 (90)	<.001	18 (50)	31 (90)	<.001		—	
Initial control by emergency ET, PCS, or TIPS, *n* (%)	86 (82)	112 (97)	<.001	30 (83)	34 (100)	.81			
Recurrent bleeding within 30 d, *n* (%)	35 (33)	0	<.001	12 (33)	0	<.001			
Bleeding controlled 30 d and survived to leave hospital, *n* (%)	43 (41)	90 (78)	<.001	20 (56)	29 (85)	<.001			
Recurrent bleeding at any time, *n* (%)	77 (73)	2 (2)	<.001	34 (94)	0	<.001	109 (71)	1 (0.7)	<.001
Permanent control up to 5 y or until death, n (%)	28 (27)	112 (97)	<.001	2 (6)	34 (100)	<.001	45 (29)	143 (99)	<.001
Blood transfusions (U), mean (range)									
Before and during emergency treatment	9.6 (3–46)	9.1 (2–44)		10.0 (4–22)	9.0 (3–18)		—	—	
During PCS surgery		3.0 (0–12)			3.5 (2–10)			2.1 (0–8)	

ET, Endoscopic therapy; *PCS*, portacaval shunt; *EPCS*, emergency portacaval shunt; *RCT*, randomised controlled trial; *TIPS*, transjugular intrahepatic portosystemic shunt.

Table IV.

Survival and follow-up of 588 patients with bleeding gastric varices

	Emergency treatment (n = *220*)				*Expanded RCT of emergency treatment* (n = *70*)				*Elective treatment* (n = *298*)			
Follow-up	*ET* (n = *105*), n *(%)*	*PCS* (n = *115*), n *(%)*	*Follow-up (%)*	P *value*	*TIPS* (n = *36*), n *(%)*	*PCS* (n = *34*), n *(%)*	*Follow-up (%)*	P *value*	*ET* (n = *154*), n *(%)*	*PCS* (n = *144*), n *(%)*	*Follow-up (%)*	P *value*
30 d and left hospital	43 (41)	90 (78)	100	<.001	20 (56)	29 (85)	100	<.001	143 (93)	142 (99)	100	.021
1 y	28 (27)	81 (70)	100	<.001	18 (50)	29 (85)	100	<.001	105 (68)	135 (94)	100	<.001
5 y	24 (23)	79 (69)	97	<.001	2 (6)	28 (82)	100	<.001	55 (36)	102 (70)	97	<.001
10 y	21 (20)	68 (59)	97	<.001	1 (3)	24 (71)	100	<.001	45 (29)	94 (65)	97	<.001
15 y	21 (20)	59 (51)	92	<.001	—	—	—	—	39 (25)	86 (60)	92	<.001

ET, Endoscopic therapy; *PCS*, portacaval shunt; *RCT*, randomised controlled trial; *TIPS*, transjugular intrahepatic portosystemic shunt.

Table V.

Quality of life during 5 years after treatment for bleeding gastric varices

	Emergency treatment			*Expanded RCT of emergency treatment*			*Elective treatment*		
	ET* (n = *105*), n *(%)	***PCS* (n = *115*), n *(%)***	**P *value***	***TIPS* (n = *36*), n *(%)***	***PCS* (n = *34*), n *(%)***	**P *value***	***ET* (n = *154*), n *(%)***	***PCS* (n = *144*), n *(%)***	**P *value***
Survived 30 d and left hospital	43/105 (41)	90/115 (78)	<.001	20 (56)	29 (85)	<.001	143/154 (93)	142/144 (99)	.021
Portosystemic encephalopathy									
Pretreatment (*n* = 518)	36/105 (34)	40/115 (35)	.99	13 (36)	14 (41)	.99	51/154 (33)	50/144 (35)	.81
Posttreatment during 5 y									
Recurrent	7/43 (16)	9/90 (10)	.39	9/18 (50)	3/28 (11)	<.001	24/143 (17)	11/142 (8)	.029
Single episode	4/43 (10)	9/90 (10)	.99	1/18 (6)	1/28 (4)	.01	14/143 (10)	14/142 (10)	.99
PCS patency during 5 y (*n* = 259)	—	113/115 (98)	—	2/6 (33)	28/28 (100)	<.001	—	143/144 (99)	—
Variceal rebleeding up to 5 y (*n* = 518)	77/105 (73)	2/115 (2)	<.001	8/8 (100)	0/32 (0)	<.001	109/154 (71)	1/144 (0.7)	<.001
Alcohol abstention up to 5 y (*n* = 419)	28/43 (65)	59/90 (65)	.99	100%	100%	.99	93/143 (65)	92/142 (65)	.99
80 g protein tolerance in 30-d survivors (*n* = 419)	43/43 (100)	90/90 (100)	.99	100%	100%	.99	143/143 (100)	142/142 (100)	.99
Liver function tests									
1-y survivors (*n* = 349)			.005	(*n* = 18)	(*n* = 29)				<.001
Improved	13/28 (48)	61/81 (75)		5/18 (28)	29/29 (100)	<.001	50/105 (48)	101/135 (75)	
Same	10/28 (34)	14/81 (18)		2/18 (11)	0 (0)	<.001	36/105 (34)	24/135 (18)	
Worse	5/28 (18)	6/81 (7)		11/18 (61)	0 (0)	<.001	19/105 (18)	9/135 (7)	
5-y survivors (*n* = 260)			.009	(*n* = 12)	(*n* = 29)				<.001
Improved	12/24 (50)	62/79 (78)		0	0	—	27/55 (50)	82/102 (80)	
Same	9/24 (36)	12/79 (15)		0	27/29 (93)	<.001	20/55 (36)	15/102 (15)	
Worse	3/24 (14)	5/79 (7)		12/12 (100)	2/29 (7)	<.001	8/55 (14)	5/102 (5)	
Child's class at baseline and in 5-y survivors									
A									
Pretreatment (*n* = 518)	11/105 (10)	11/115 (10)	.64	0	0	.99	15/154 (10)	14/144 (10)	.70
Posttreatment (*n* = 260)	5/24 (21)	59/79 (75)	<.001	0	26 (76)	<.001	22/55 (40)	82/102 (80)	<.001
B									
Pretreatment (*n* = 518)	65/105 (62)	69/115 (60)		22/36 (61)	20/34 (59)	.99	95/154 (62)	86/144 (60)	
Posttreatment (*n* = 260)	10/24 (42)	14/79 (18)					22/55 (40)	15/102 (15)	<.001

	Emergency treatment			*Expanded RCT of emergency treatment*			*Elective treatment*		
	ET* (n = *105*), n *(%)	***PCS* (n = *115*), n *(%)***	**P *value***	***TIPS* (n = *36*), n *(%)***	***PCS* (n = *34*), n *(%)***	**P *value***	***ET* (n = *154*), n *(%)***	***PCS* (n = *144*), n *(%)***	**P *value***
C									
Pretreatment (*n* = 518)	29/105 (28)	35/115 (30)		14/36 (40)	14/34 (41)	.99	44/154 (28)	44/144 (30)	
Posttreatment *(n* = 260)	9/24 (37)	6/79 (7)		11/18 (60)	1/34 (3)	<.001	11/55 (20)	5/102 (5)	<.001
Work status in 5-y survivors (*n* = 260)									
Retired because of age (*n* = 41)	5/24 (21)	17/79 (22)	.99	—	—	—	7/55 (13)	12/102 (12)	.99
Employed or housekeeping in those not retired (*n* = 219)	8/19 (41)	40/62 (64)	.11	1/18 (6)	23/29 (80)	<.001	21/48 (43)	59/90 (65)	.018

ET, Endoscopic sclerotherapy; *PCS*, portacaval shunt; *EPCS*, emergency portacaval shunt; *TIPS*, transjugular intrahepatic portosystemic shunt.

Table VI.

Overall comparisons of outcome of treatment in a randomized controlled trial of endoscopic therapy (ET) and portacaval shunt (PCS), and in expanded RCT of emergency transjugular intrahepatic portosystemic shunt (TIPS) and emergency PCS (EPCS)

Outcome	*ET* (n = *259*), %	*PCS* (n = *259*), %	P *value*	*TIPS* (n = *36*), %	*EPCS* (n = *34*), %	P *value*
Survival						
30 d and left hospital	72	90	<.001	56	85	<.001
1 y	51	83	<.001	50	85	<.001
5 y	31	70	<.001	50	85	<.001
10 y	25	63	<.001	3	71	<.001
15 y	23	56	<.001	—	—	—
5 y in alcohol abstainers	62	88	<.001	60	92	<.001
Control of bleeding						
Permanent	28	98	<.001	6	100	<.001
Variceal rebleeding	72	1	<.001	94	0	<.001
Recurrent PSE	17	9	.018	15	7	<.001
Quality of life						
Improved liver function	47	75	<.001	32	82	<.001
Child’s class in 5-y survivors			<.001			<.001
A	34	78		0	76	
B	41	16		40	20	
C	25	6		60	4	
Resumed work/housekeeping	43	65	.004	6	76	<.001

PSE, Portal-systemic encephalopathy.