Role of Emergency Transjugular Intrahepatic Portosystemic Shunts

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ABSTRACT

Transjugular intrahepatic portosystemic shunts (TIPS) is a highly effective treatment for bleeding esophageal varices, with control of the bleeding in over 90% of the patients. TIPS is recommended as “rescue” treatment if primary hemostasis cannot be obtained with endoscopic and pharmacological therapy, or if uncontrollable early rebleeding occurs within 48 hours. TIPS is also a very effective technique for patients presenting with severe refractory bleeding gastric and ectopic varices, cases where endoscopic techniques are less effective. Emergency TIPS should be considered early in patients with refractory variceal bleeding once medical treatment and sclerotherapy fail, before the clinical condition worsens. Every effort should be made to stabilize the patient before TIPS, including the use of tamponade tubes and aggressive correction of coagulopathy. Patients with acute variceal bleeding with a Child-Pugh score > 12, Apache score II > 18 points, hemodynamically unstable, receiving vasopressors and coagulopathy, and/or bilirubin > 6 mg/dL have a high risk of early death after TIPS. Expedite liver transplantation after emergency TIPS should be considered for high-risk patients.

KEYWORDS: Hypertension—portal, liver—interventional procedures, shunts—portosystemic, varices

Objectives: Upon completion of this article, the reader should be able to (1) review the current treatment alternatives for patients with bleeding esophageal varices, (2) review the role of TIPS in the setting of acute refractory esophageal varices bleeding, (3) discuss the prognostic factors that might influence patient selection for emergency TIPS, and (4) review the role of TIPS in the treatment of gastric and ectopic varices.

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The role of transjugular intrahepatic portosystemic shunts (TIPS) for the prevention of rebleeding of esophageal varices and control of refractory ascites has become more precisely defined in the past 10 years with several comparative studies showing better control of these complications of portal hypertension with TIPS

than with standard forms of therapy.¹ However, the role of the TIPS as an emergency, lifesaving procedure is less well defined and remains highly controversial.

The purpose of this article is to describe the different treatment options for patients with refractory esophageal and gastric varices bleeding and the role of

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TIPS as a "rescue therapy." The factors associated with mortality after emergency TIPS and the main criteria for patient selection are also discussed.

TREATMENT OPTIONS

Esophageal varices are the most feared complication of portal hypertension. Variceal hemorrhage carries a death rate between 30 and 50% during each bleeding episode.² The high mortality of these patients is due to a combination of massive bleeding due to the elevated portal pressure, compromised hepatic reserve, and multiorgan failure.³ Patients with massive hemorrhage from esophageal varices represent a considerable challenge to clinicians. No single therapy is appropriate for all patients with bleeding varices. Ideally, patients with esophageal bleeding should be treated by a multidisciplinary team with extensive experience. The optimal management will depend on the clinical circumstance of the patient, cause and severity of the underlying liver disease, extent and location of the bleeding varices, and the local availability of endoscopic, radiological, and surgical teams with expertise in this area.

Emergency therapy in patients with bleeding esophageal varices requires a rapid response to allow clinical stabilization of the patient to prevent hypovolemia, shock, and death. Rapid resuscitation with replacement of blood products, clotting factors, and intravenous fluids is essential. Severe hypovolemia may jeopardize hepatic and renal function. Overreplacement of intravenous volume should also be avoided because this may precipitate rebleeding.⁴ The use of injections of recombinant activated factor VIIa has been shown to practically normalize the impaired coagulation of decompensated cirrhotics.⁵

Prevention of hepatic encephalopathy with the administration of lactulose or lactitol and prevention of hypoglycemia are also important. Prophylactic antibiotics should be administered as soon as possible in patients with acute variceal bleeding because it has been shown that within 2 days of variceal bleeding, 20% of cirrhotic patients develop bacterial infections.⁶ Patients with massive bleeding are usually intubated to prevent aspiration and facilitate other therapies.

Pharmacological therapy using vasopressin and somatostatin, and their longer-acting analogs terlipressin and octreotide/vapreotide, is effective in the treatment of acute variceal bleeding. These vasoconstrictors reduce portal blood flow and are useful for the short-term control of acute variceal hemorrhage. Somatostatin and its analogs decrease portal pressure and portal blood flow without the systemic effects of vasopressin.³ Pharmacological therapy is as effective as sclerotherapy for the control of acute variceal bleeding, and it is often used in combination with endoscopic techniques.

Endoscopic examination of the upper gastrointestinal tract should be performed as soon as possible.

Early and precise identification of the bleeding source is important. Up to 30% of patients with esophageal varices may be bleeding from another source such as a Mallory Weiss tears or peptic ulcers.^{3,7} Endoscopic techniques are accepted first-line treatment of variceal bleeding. Sclerotherapy is the treatment of choice when there is evidence of active bleeding. Both sclerotherapy and variceal band ligation are equally effective in stopping bleeding, but band ligation is associated with fewer complications. Several recent studies showed a reduction of ~33% in the number of treatment sessions required to obliterate varices by banding compared with sclerotherapy.^{8,9}

Endoscopic sclerotherapy and pharmacological therapy achieve primary hemostasis in more than 80% of the cases. However, in 25 to 30% of the cases bleeding persists or recurs, requiring other therapeutic options.⁷ In patients with refractory bleeding to endoscopic techniques, treatment alternatives include the use of balloon tamponade, TIPS, or emergency surgery.

Balloon tamponade is a useful alternative for patients with refractory massive bleeding and it can be a lifesaving step. Balloon tamponade achieves control of variceal bleeding by direct pressure on the varices. Dual tubes with both gastric and esophageal balloons such as the Sengstaken-Blakemore are used commonly; the gastric balloon is inflated first and the esophageal balloon is inflated only if bleeding is not controlled. If gastric varices are the source of bleeding, a tube with a single large (600 mL) gastric balloon (Linton-Nachlas) is more effective in stopping hemorrhage. Initial control of bleeding is seen in 90% of cases. However, up to 50% of patients rebleed when the tube is deflated. The complication rate is 25 to 30%.⁴ Usually, these tubes are used as a temporizing treatment to stabilize the patient while repeat sclerotherapy, TIPS, or surgery is performed.

Surgical techniques with extensive operations such as esophageal transection or transgastric plication are rarely used today because most of the patients are too unstable to tolerate major surgical interventions.^{10,11} Many patients who would naturally be excluded from emergent or elective shunt surgery because of poor clinical status or advanced liver disease now undergo TIPS creation. In a nonrandomized comparative study of emergency TIPS and esophageal transection in the management of uncontrolled variceal hemorrhage, Jalan et al reported a 30-day mortality of 42% in the TIPS group compared with 79% in the esophageal transection group. Rebleeding occurred in 15.6% patients with TIPS, compared with 26.2% in the surgical group. Encephalopathy in the two groups of patients was not significantly different.¹²

Surgical portocaval shunts to decompress the portal system for patients with failed sclerotherapy are associated with a 35 to 50% mortality for patient with

cirrhosis Child A or B patients, and 70 to 100% for cirrhosis Child C patients.¹³ More recent uncontrolled data, however, has shown reduced perioperative mortality in patients undergoing early shunt procedures. Elective selective surgical shunts play an important role for the long-term control of the variceal bleeding in younger patients with well-preserved liver function who are not considered to require liver transplantation for at least 12 months.^{14,15}

Liver transplantation is the ultimate goal for many patients with advanced liver dysfunction. Most patients with advanced Child C cirrhosis who bleed from varices do not survive for 1 year, regardless of whether they receive sclerotherapy, TIPS, or surgical shunts. Transplantation is the only therapy that has shown to significantly improve survival in patients with advanced liver failure. A 5-year actuarial survival of 70% has been reported in Child C patients with variceal bleeding.¹⁶ Although emergent orthotopic liver transplantation effectively treats acute variceal bleeding, unfortunately due to limited availability of donor organs, liver transplantation is less useful as an emergency procedure, and many patients don't qualify for transplantation for other medical reasons. TIPS has been reported as a useful method to control acute variceal bleeding in patients awaiting liver transplantation, and it is commonly used as a nonsurgical "bridge" procedure, stabilizing patients until a suitable donor organ is available.^{13,17}

TIPS FOR ACUTE VARICEAL BLEEDING

At the present time the recommended standard treatment for acute variceal bleeding consists of immediate pharmacological treatment with early endoscopic band ligation and/or sclerotherapy.^{18,19} TIPS is recommended as "rescue" treatment if primary hemostasis cannot be obtained with endoscopic and pharmacological therapy, or if uncontrollable early rebleeding occurs within 48 hours. Reasons for failed endoscopy therapy include massive bleeding rendering visualization of the bleeding vessels impossible, unsuccessful hemostasis of an actively bleeding vessel, or recurrent bleeding after two attempts at endoscopic hemostasis.²⁰ Patients with contraindications to endoscopy, such as patients with esophageal strictures or tumors, are considered primary candidates for TIPS.²¹ TIPS is also useful for patients bleeding from portal hypertensive gastropathy or from other sites that are endoscopically inaccessible such as gastric, duodenal, ileal, and other ectopic varices.¹

TIPS has been extensively studied and compared with other forms of therapy for the prevention of rebleeding from esophageal varices. Multiple controlled trials comparing TIPS with pharmacological and endoscopic therapies have shown better control of the

bleeding with TIPS than with endoscopic or pharmacological treatments.^{1,22-27} TIPS usually achieves a one-time, immediate decompression of the varices. On the other hand, endoscopic obliteration of esophageal varices usually requires multiple⁶⁻¹² endoscopic sessions. Until complete obliteration of the varices is achieved, the patient is at risk of rebleeding. Although less incidence of rebleeding is seen with TIPS, no difference in survival between TIPS and sclerotherapy-treated patients has been demonstrated. Most studies have also shown an increase in the incidence of encephalopathy after TIPS compared with sclerotherapy.^{1,28} In patients with acute variceal bleeding receiving TIPS, Cello et al also demonstrated that patients undergoing TIPS were significantly less likely to rebleed from esophageal varices than patients undergoing sclerotherapy; however, TIPS did not improve health costs or decrease morbidity after randomization.²¹ Current evidence supports the use of TIPS as a "rescue" treatment for patients with bleeding esophageal varices who failed pharmacological and endoscopic treatments, and not as a primary form of treatment.²⁷

PATIENT EVALUATION FOR EMERGENCY TIPS

A complete evaluation of the patient is essential before the TIPS procedure. In particular the degree of physiological derangement and comorbidities at the time of TIPS are very important as they can have marked effects on early outcome.²⁷

In an emergent situation the following conditions should be noted:

1. Time of initial bleeding.
2. Degree of hemodynamic stability including the use of vasopressors and the need for continuing red blood cell and plasma transfusion requirement within 24 hours prior to TIPS.
3. Results of the endoscopic examination noting the location of varices, previous endoscopic therapies, and possible additional sites of bleeding.
4. Use of pharmacological therapies to reduce portal pressure.
5. Endotracheal intubation.
6. Use of balloon tamponade.
7. Comorbid conditions including: presence of hepatic or renal failure, sepsis, bacteremia, pneumonia, adult respiratory distress syndrome, bacterial peritonitis, ascites, pulmonary edema, or heart failure.
8. Serum laboratory parameters should include: hemoglobin, white blood cell count, platelet count, coagulation profile, liver function tests (albumin, bilirubin, alanine aminotransferase [ALT/SGPT], aspartate aminotransferase [AST/SGOT], alkaline

- phosphatase), ammonia level, electrolytes (sodium, potassium), and renal function test.
9. A review of previous imaging tests specially ultrasound and computed tomography scans is important. A bedside Doppler ultrasound of the abdomen, if the clinical condition of the patient allows, is very useful to determine patency of the portal vein, to rule out biliary obstruction and liver tumors, and to evaluate the amount of ascites.
 10. Consider the presence of absolute contraindications for TIPS, including severe congestive heart failure, severe tricuspid regurgitation, and severe pulmonary hypertension (mean pulmonary pressures > 45 mm Hg), or relative contraindications, such as portal venous and hepatic vein obstruction, large hepatic tumors, and extensive polycystic liver disease.
 11. After a complete evaluation of the patient, a discussion with the patient and/or the family with realistic expectations explained, and informed consent is obtained. Patients with predicted high-risk mortality after TIPS should be informed of the prognosis. Early consultation for liver transplantation should also be considered.
 12. Patients who are hemodynamically unstable and with active bleeding should be stabilized medically as much as possible before the procedure. Endotracheal intubation for airway control and general anesthesia are also essential parts of the procedure in an emergency situation.

TIMING OF EMERGENCY TIPS

There is little doubt that TIPS is effective for the treatment of bleeding esophageal varices, with most series reporting control of the bleeding in over 90% of the patients.^{1,27} However, it is unclear if early TIPS within few hours of the index bleeding will be associated with a better prognosis or if the patient should be medically stabilized first and later undergo TIPS in a semielective fashion.

Any interventional radiologist is familiar with the frustrating problem of a critically ill, hemodynamically unstable, and intubated patient with massive variceal bleeding who is referred for an emergency TIPS as the last-resort therapy after failed medical and endoscopic therapy. It has been demonstrated that after multiple unsuccessful attempts to stop the bleeding with less invasive treatments, the liver function deteriorates, complications supervene, and the outcome worsens regardless of the type of definitive therapy.^{20,29} It is not surprising to find a disappointing high mortality rate after "rescue" TIPS despite successful control of bleeding in many patients in whom other treatment options have already exhausted.²⁹

Many authors recommend performing TIPS early if bleeding continues or significant bleeding recurs

within 48 hours after standard medical and endoscopic treatment. A generous indication to early TIPS implantation before multiorgan failure occurs may decrease the high mortality of acute variceal bleeding.^{18,19} Bizollon and coworkers reported a series of 28 patients with refractory variceal bleeding in whom TIPS was performed early, within 48 hours following failed endoscopic and medical treatment. The 40-day mortality was 25%; 17 (61%) of the patients were Child C cirrhosis. The survival at 1 year was 75% and 52% at 2 years.¹³ Sanyal et al performed TIPS semiemergently within 12 hours in patients with actively bleeding esophageal or contiguous gastric varices despite sclerotherapy, after stabilization by balloon tamponade and vasopressin/nitroglycerin. TIPS was successfully placed in 29 of 30 patients and achieved hemostasis in all. Thirty-day and 6-week survival rates were 63 and 60%, respectively.³⁰ Azoulay and coworkers performed TIPS within 3 hours after the diagnosis of uncontrollable bleeding. TIPS controlled the hemorrhage in 90% of cases, and the 60-day mortality was 34.5%, mainly due to the advanced liver dysfunction in the majority of their patients.²⁰ These authors found a significant correlation between early mortality after TIPS and the delay between the index bleed and transfer to intensive care unit (ICU), number of sclerotherapy sessions before TIPS, and the use of balloon tamponade. With the use of multivariable analysis they found that when three variables—the presence of ascites, the use of catecholamines, and balloon tamponade—were present, the risk of death within 60 days after TIPS was 95.7%, but only 1.7% if none of these three factors was present.

Monescillo and coworkers measured the hepatic venous pressure (HVPG) gradient within the first 24 hours after admission in 116 consecutive patients with cirrhosis with acute variceal bleeding.²⁹ Patients with HVPG greater than or equal to 20 mm Hg were classified as high-risk group and randomly allocated into those receiving TIPS ($n=26$) within the first 24 hours after admission and those not receiving TIPS ($n=26$). The high-risk non-TIPS group had more treatment failures (50 versus 12%, $P=0.0001$), transfusional requirements (3.7 ± 2.7 versus 2.2 ± 2.3 , $P=0.002$), need for intensive care (16 versus 3%, $P<0.05$), and worse actuarial probability of survival than the low-risk group. Early TIPS placement reduced treatment failure (12%, $P=0.003$) and in-hospital and 1-year mortality (11 and 31%, respectively; $P<0.05$). The authors postulate that increased portal pressure estimated by early HVPG measurement is a main determinant of treatment failure and survival in variceal bleeding, and early TIPS placement reduces treatment failure and mortality in high-risk patients defined by hemodynamic criteria.²⁹

Although an early indication for emergency TIPS is recommended, it is very important to institute aggressive medical therapy to try to stabilize the patient

before TIPS. Helton et al reported a high 56% in-hospital mortality in 23 patients actively bleeding at the time of TIPS. In their review, 35% of the patients did not receive endoscopic therapy, vasopressor administration, or balloon tamponade prior to TIPS, and many patients underwent TIPS while actively bleeding, hemodynamically unstable, acidotic, and coagulopathic.³¹ Encarnacion et al reported better prognosis for patients who were stable at the time of the TIPS; the 30-day mortality for patients who continued to bleed despite medical treatment and sclerotherapy was 28% while the mortality in patients whose bleeding was controlled in the 24 hours before the TIPS was 4% ($P = 0.013$). They recommended to stabilize the patient and improve the metabolic condition before the TIPS.³²

EMERGENCY TIPS MORTALITY

Several series have demonstrated that critically ill patients with chronic liver disease admitted to the ICU with liver failure, variceal bleeding, hepatic encephalopathy, or hepatorenal syndrome have a very low survival rate. Gildea et al reported that an acute physiology, age, and chronic health evaluation (APACHE) III score of 90, the use of pressors, mechanical ventilation, and the presence of renal failure were predictors of short-term medical ICU and hospital mortality. Patients with all three risk factors, APACHE III score of 90, the use of pressors, and jaundice had a 92% 1-month mortality rate compared with 11.2% for patients with no risk factors. Those patients with an APACHE III score of < 90 who had been discharged to home had a median survival time of 17 months. This group reported a long-term follow-up in these patients with a 1-year mortality rate of 69% and 5-year mortality rate of 77%. The median survival time was 1 month.³³ Another study by Shellman and coworkers reported that patients with Child-Pugh C receiving mechanical ventilation and serum creatinine > 1.3 mg/dL during the first 72 hours in the ICU had only a 2% survival rate.³⁴

Most of the deaths of patients after emergency TIPS are related to hepatic failure, multiorgan failure, and sepsis, often accompanied by variceal and nonvariceal bleeding; a minority of the deaths are related to isolated recurrent variceal bleeding.^{35,36} Early death occurring within 30 days is most commonly caused by multiorgan failure, and late death after 30 days is most commonly related to liver failure.³⁷

Many studies reporting on emergency TIPS for the "rescue" treatment of acute esophageal varices bleeding have shown low survival rates and significantly higher mortality rates than patients undergoing elective TIPS. Rajan et al reported 123 patients who were acutely bleeding at the time of TIPS creation. Of these, 42 (34.1%) died within 30 days of TIPS creation, compared with 16 of 97 patients (16.5%) undergoing elective TIPS creation. As an independent predictor of mortality,

bleeding at the time of TIPS creation was associated with odds of death that were 2.9 times greater than those associated with elective TIPS placement.³⁸ Similar findings have been reported by Helton et al, who reported 56% in-hospital mortality for patients who were actively bleeding or hemodynamically unstable at the time of the TIPS versus 5.5% following nonemergent procedures.³¹

Table 1 summarizes the results of several publications on the role of emergency TIPS.^{7,13,20,30–32,39–46} The reported mortality associated with TIPS varies widely because the inclusion criteria, timing of the TIPS, and the severity of liver disease varies in the different series. Many of these reports combine the results of patients actively bleeding during TIPS with those of the patients who were stable during the procedure.

Several reports describing different prognostic factors associated with mortality after TIPS have been published. Prognostic factors are not intended to predict outcome or management on individual basis or to deny a patient a potentially lifesaving intervention, but are useful as guidelines for prognostic purposes, to develop appropriate expectations, and to weigh different therapeutic options. Final decisions are based on the individual patient needs and overall clinical condition.^{29,39} Many of these prognostic factors correlate well with the mortality of patients undergoing elective TIPS. In patients with acute variceal bleeding, however, these predictors may fail because the hepatic reserve and renal function are difficult to evaluate in the acute setting.²⁹ Events such as bleeding, infection, and high-dose diuretic therapy may affect the renal and liver function in a transient way.⁴⁰ No single prognostic criteria has been demonstrated to be able to help to accurately select those patients with a very high risk of dying.⁴⁷ However, several selection criteria have been recently described as more experience has been obtained over the years in regards to the emergency TIPS procedure.⁴⁸

A prognosis index (PI) was created by Patch et al as a model for patients undergoing emergency TIPS after failed endoscopic therapy for acute variceal bleeding.⁴⁴ Factors associated with markers of advanced liver disease, sepsis, and multiorgan failure were related to early mortality after TIPS. A PI was created using this formula:

$$\begin{aligned} &\text{Presence of moderate/severe ascites, or need} \\ &\quad \text{for ventilation, scored 1.} \\ &\text{PI} = 1.54 (\text{ascites}) + 1.27 (\text{ventilation}) \\ &\quad + 1.38 \log e (\text{white blood count}) \\ &\quad + 2.48 \log e (\text{partial thromboplastin time}) \\ &\quad + 1.55 \log e (\text{creatinine}) - 1.05 \log e (\text{platelets}) \end{aligned}$$

Using this equation, 42% of deaths occurred in patients with $\text{PI} \geq 18.52$, where the mortality was 100%. The score had a 100% positive predictive value. No survivors had a $\text{PI} > 18.3$. They concluded that the use

Table 1 Summary of Series on Emergency TIPS

Reference	Child's A/B/C	No. of patients	Initial Control of Bleeding (%)	30-Day Mortality (%)	Persistent/Recurrent Bleeding	Prognostic Factors	Survival (%)
Banares et al ⁷	11/22/23	56	95	28	22% (at 1 mo) Early (< 30 days) <i>n</i> = 8 V	Child C Ascites Encephalopathy Albumin < 2.7 g/L Bilirubin > 2 mg/dL Creatinine	NS
Bizollon et al ¹³	0/11/17	28	96	25 (at 40 d)	18% Early (< 14 days) <i>n</i> = 2 Late <i>n</i> = 8 (6 V)	Bilirubin Creatinine	75 (at 12 mo) 52 (at 24 mo)
Azoulay et al ²⁰	3/8/47	58	90	29	17% Persistent <i>n</i> = 6 Recurrent <i>n</i> = 4 18%	Sepsis Catecholamines Balloon tamponade Pulmonary infiltrate	51.7 (at 12 mo) 40 (at 60 mo)
Sanyal et al ³⁰	1/7/22	32	100	27	39%	Emergent procedure Presence of bleeding at time of TIPS	60 (at 1.5 mo) 46 (at 30 mo) NS
Helton et al ³¹	0/5/18	23	74	56 (in hospital)		Unstable Bilirubin	56 (at 12 mo)
Encarnacion et al ³²	2/32/31	64	98	19	29% (at 6 mo) 50% (at 1 year)	NS	30 (at mo) 58 (at 12 mo) 10 (at 36 mo)
McCormick et al ³⁹	1/7/12	20	100	60 (at 40 d)	40%	Low albumin < 2.5 Increased bilirubin > 3 Increase PT > 15 s	NS
Tyburski et al ⁴⁰	0/5/28	33	NS	27	42% Early <i>n</i> = 5 Late (> 30 days) <i>n</i> = 9	None NS	73 (at 12 mo) 29 (at 5 mo) 53 (at 6 mo)
LaBerge et al ⁴¹	NS	32	97	NS	NS	WBC	
Gerbes et al ⁴²	1/2/7	11	91	27	27%	Platelet count	
Le Moine ⁴³	3/13/9	24	96	17	25% (at 5 mo)	Partial	
Patch et al ⁴⁴	5/20/29	54	91	48 (at 6 wk)	11% Early <i>n</i> = 5 (5 NV) Late <i>n</i> = 11 (6 V)	Thromboplastin time Creatinine	62 (at 6 mo)
Chau et al ⁴⁵	4/17/63	84	98	34	30% (at 30 d) 36% (at 6 mo) Early (< 7 days) <i>n</i> = 11 (3 V) Late <i>n</i> = 9 (8 V)	NS	
Jalan et al ⁴⁶	17/30/21	68	89	20	20% <i>n</i> = 19 (14 V) Early (< 10 days) <i>n</i> = 10	Hyponatremia Child C	67 (at 10 mo)

Persistent/recurrent bleeding is given as a percentage of the total. When available it was divided in early or late bleedings with the time definition in parenthesis. Abbreviations: V, the number of patients with variceal bleeding; NV, nonvariceal bleeding; PT, prothrombin time; NS, not specified.

Table 2 APACHE II Score System

Parameter	Score Points						
	4	3	2	1	0	1	2 3 4
Mean arterial pressure (mm Hg)	≥ 160	130–159	110–129		70–109		50–69 40–54 ≤ 49
Heart rate	> 180	140–179	110–139		70–109		55–69 40–54 ≤ 39
Ventilation	≥ 50	35–49		25–34	12–24	10–11	6–9 ≤ 5
Oxygenation	A-aDO ₂ ≥ 500 and FIO ₂ ≥ 0.5	A-aDO ₂ 350–499 and FIO ₂ ≥ 0.5	A-aDO ₂ 200–349 and FIO ₂ ≥ 0.5		A-aDO ₂ < 200 and FIO ₂ ≥ 0.5	PaO ₂ 61–70 and FIO ₂ < 0.5	PaO ₂ 55–60 and FIO ₂ < 0.5
Arterial pH	≥ 7.7	7.6–7.69		7.5–7.59	7.33–7.49		7.25–7.32 7.15–7.24 < 7.15
Serum sodium	≥ 180	160–179	155–159	150–154	130–149		120–129 111–119 ≤ 110
Serum potassium	≥ 7.0	6.0–6.9		5.5–5.9	3.5–5.4	3.0–3.4	2.5–2.9 < 2.5
Serum creatinine (mg/dL)	≥ 3.5	2.0–3.4	1.5–1.9		0.6–1.4		< 0.6
Hematocrit (%)	≥ 60		50–59.9	46–49.9	30–45.9		20–29.9 < 20
WBC count (thousands)	≥ 40		20–39.9	15–19.9	3–14.9		1–2.9 < 1
Rectal temp (°C)	≥ 41	39–40.9		38.5–38.9	36–38.4	34–35.9	32–33.9 30–31.9 ≤ 29.9
Glasgow Coma score	score = 15 minus actual Glasgow Coma Score						

Total acute physiology score (APS) = sum of the 12 individual variable points.

Age points: ≤ 44 years = 0 points; 45–54 = 2 points; 55–64 = 3 points; 65–74 = 5 points; ≥ 75 = 6 points.

Chronic health points: cirrhotic patients who are nonoperative or emergency postoperative accumulate 5 points.

APACHE II Score is the sum of the APS, age, and chronic health points.

of TIPS is probably not justified in this subgroup of patients. This model has not been validated yet in other institutions performing emergency TIPS.

The APACHE II score (Table 2) is a system developed to predict risk of death of patients admitted to the ICU.⁴⁹ It is calculated by obtaining an acute physiology score based on the sum of 12 individual variables, patient's chronological age, and a chronic health point based on the patient's baseline disease. The scores should be calculated from physiological data from the 24 hours preceding shunt placement. Rubin et al found that APACHE II scores of >18 was associated with high risk of mortality (odds ratio = 21.7). With use of univariate logistic regression, APACHE II scores >18 , Child-Pugh class, intubated versus nonintubated patients, and active bleeding were also found to be predictive of 30-day mortality. In their study only one of 13 patients (7.7%) with Child class C cirrhosis and APACHE II score >18 survived more than 30 days after the TIPS, with none of the patients with an APACHE >30 survived.³⁶

The Emory score was also described.⁵⁰ Chalasani et al, using the Cox proportional hazards model, identified four factors associated with 30-day mortality after TIPS: emergency TIPS creation, elevation of the alanine aminotransferase and bilirubin levels, and pre-TIPS encephalopathy. Using these four variables a scoring system was created:

Emergent TIPS: 2 points
ALT >100 IU/L: 1 point
Bilirubin >3.0 mg/dL: 1 point
Pre-TIPS encephalopathy: 1 point
High risk: 4 to 5 points
Medium risk: 1 to 3 points
Low risk: 0 points

The 1-year survival rates were 10, 43, and 70% for high-, medium-, and low risk patients, respectively. The strongest predictor of mortality was variceal hemorrhage requiring emergent TIPS (hazard ratio, 5.1; 95% confidence interval, 2.2 to 9.1). The high-risk cirrhotic group had a $\sim 90\%$ mortality within a few weeks after TIPS.⁵⁰

Rajan et al reported that an elevated pre-TIPS bilirubin level is a powerful independent predictor

of 30-day mortality after TIPS creation with a 40% increased risk of death for each 1-mg/dL increase above 3.0 mg/dL.³⁸ In their study only one of 20 patients (5%), with a pre-TIPS bilirubin level >6.0 mg/dL survived more than 30 days after TIPS creation. They suggest that the use of bilirubin alone allows predicting mortality with the magnitude of the effect on mortality similar to that of APACHE II scores and modified Child-Pugh class but is simpler to ascertain. Bilirubin levels are a marker of underlying liver function; however, in some special clinical conditions such as obstructive jaundice, sclerosing cholangitis, and acute alcoholic hepatitis, bilirubin levels may not accurately predict patient's prognosis. With use of univariate logistic regression, APACHE II scores >18 , Child-Pugh class, intubated versus nonintubated patients, and active bleeding were also found to be predictive of 30-day mortality.³⁸ Tyburski et al reported a 71% mortality after 18 months when patients had a pre-TIPS total bilirubin level >3.0 mg/dL ($P < 0.001$). Other threshold markers in their review of 33 patients included albumin <2.2 g/L ($P < 0.005$) and elevated prothrombin time ($P < 0.05$).⁴⁰

A Bonn TIPS early mortality (BOTEM) score system (Table 3) has been described by Brensing et al.⁵¹ These authors studied 103 patients, 75 patients with refractory variceal bleeding, 26 with refractory ascites, and two with hypertensive gastropathy, admitted for TIPS. A BOTEM score >6 was the best mortality predictor ($P < 0.001$) in this study, which was first tested in 30 patients in whom early mortality (30%) depended primarily on bilirubin ($P < 0.005$), APACHE-II ($P < 0.001$), and TIPS urgency ($P < 0.001$). A BOTEM score >6 had a 56% sensitivity, 100% specificity, 100% positive predictive value, 84% negative predictive value, and 87% accuracy in the first 30 patients. The score was further tested prospectively in a cohort of 73 patients; early mortality (8.2%) was again best predicted by BOTEM ($P < 0.01$) with the same cutoff and 67% sensitivity, 99% specificity, 80% positive predictive value, 97% negative predictive value, and 96% accuracy. APACHE score >20 , serum bilirubin >6 mg/dL, and need for emergency TIPS were variables associated with very high 60-day mortality rate after TIPS. Patients in the BOTEM status III category had a 90% increase in

Table 3 Bonn TIPSS Early Mortality (BOTEM) Score System

Bilirubin (mg/dL)	APACHE-II	Variceal Bleeding	BOTEM Score Points
<3	<10	Elective	1
3–6	10–20	Urgent (salvage TIPS within 36 hours after last life-threatening bleeding)	2
>6	>20	Actively bleeding + balloon tamponade	3

BOTEM status I or low risk (3–4 points).

Status II or medium risk (5–6 points).

Status III or high risk (7–9 points).

Table 4 Child Pugh Score (CPS)

Score	Bilirubin (mg/dL)	Albumin (gm/dL)	PT (s)	Hepatic Encephalitis	Ascites (grade)
1	< 2	> 3.5	1–4 (< 1.7)	None	None
2	2–3	2.8–3.5	4–6 (1.7–2.3)	Mild (I–II)	Mild
3	> 3	< 2.8	> 6 (> 2.3)	Severe (III–IV)	Severe

PT, prothrombin time. Interpretation: Class A: 5–6; Class B: 7–9; Class C: 10–15.

the 60-day mortality, and 96% of patients in the BOTEM status I category survived for 60 days after TIPS.⁵¹

Jalan et al reported also described that hyponatremia ($P < 0.001$), a marker of multiorgan failure and advanced liver dysfunction, was an independent factor of 30-day mortality in their series of 68 patients who underwent TIPS for variceal hemorrhage. The risk of early mortality in hyponatremic patients with Child C cirrhosis was 80%. They found a 22% mortality rate for patients with total bilirubin levels > 50 mol/L ($P < 0.01$).⁴⁶

Azoulay and coworkers reported that the main clinical variables correlating with death within 60 days of the procedure were on univariate analysis: the delay between index bleeding and admission to ICU, presence of ascites, use of catecholamine for hemodynamic support, use of mechanical ventilation, and the presence of infection. Using logistic regression, the combined presence of sepsis, use of catecholamines, and use of balloon tamponade gave a risk of death of 95.7%, and the risk was 1.7% when none of these risk factors was present.²⁰ Russo et al described that creatinine level greater than 1.7 mg/dL and uncontrollable variceal bleeding as an indication for TIPS placement were independently associated with 30-day mortality. Patients with both coagulopathy (prothrombin time greater than 17 seconds) and renal insufficiency had a 30-day mortality of 78%.⁵²

The Child-Pugh classification and the Child Pugh Score (CPS) have been used as independent predictors of mortality after TIPS (Table 4). Higher mortality rates have been consistently reported after TIPS in patients with Child C cirrhosis.^{39,46,53} A threshold of CPS > 11 has been described for high-risk patients with a median survival of 3 months or less after TIPS.⁴⁰ In Banares study the operative mortality after emergency TIPS was 28%. All but one of the patient with a CPS > 11 points died during the first 30 days after the procedure versus 11% of patient with score < 11 . They also observed an 81% 30-day mortality rate with bilirubin serum levels > 2.0 mg/dL.⁷ Bosch describes that no patient with a CPS of 13 or above has survived a TIPS procedure.⁴⁷ LaBerge et al also reported that most patients with a CPS of 12 to 15 died within 90 days of TIPS, whereas patients with scores of 10 or 11 did as well as patients with CP class A or B.³⁷

Although the CPS and the Child-Pugh are easily calculated, the inclusion of the relatively subjective variables of degree of ascites and encephalopathy⁴⁸ and the lack of inclusion of the renal function are significant disadvantages of the CPS system as a predictor model for patients with variceal bleeding.⁵⁴ Also the so-called ceiling effect, whereby once the bilirubin level is > 5 mg/dL the patient is assigned a score of 3, regardless of the actual bilirubin number, is another disadvantage of this scoring system.⁴⁸

In patients undergoing elective TIPS, the use of the Model for End-stage Liver Disease or MELD score, has been recently validated as useful scoring system to predict outcomes.⁵⁴ A high MELD score has been associated with increased mortality. Patients with MELD scores of 18 or more have a significantly lower survival rate than do patients with MELD scores of 17 or less.^{55,56} Many authors report that both the MELD score and the CPS score are roughly equivalent as predictive models for patients undergoing elective TIPS.^{48,55–57} The MELD score was specifically designed for patients undergoing elective TIPS and probably its prognostic ability is not accurate in emergency population.

OTHER MANAGEMENT ALTERNATIVES IN PATIENTS WITH ACUTE VARICEAL BLEEDING

Embolization of Varices

Embolization of esophageal varices using a transhepatic approach was once used for the control of bleeding esophageal varices; however, this procedure has been almost completely abandoned due to the high recurrence rate, technical difficulties, and risk of portal vein thrombosis.^{13,58} Embolization of the esophageal varices at the time of the TIPS is easily accomplished but its routine application has been also controversial. Embolization after TIPS has been reported in some series in 24 to 48% of patients.^{20,36} Currently, it is not clear whether the combination of TIPS and variceal embolization is more effective than TIPS alone. Some authors recommend transjugular embolization of the varices to increase the effect of the shunt with respect to acute hemostasis,^{18,59} and other authors don't perform any embolization during the TIPS procedure.¹³ In our clinical

practice we perform embolization of varices only if we observe persistent contrast flow into the varices in the control portography after TIPS. Variceal embolization is also indicated for patients with recurrent esophageal bleeding despite a patent shunt.⁵⁸ Embolization of esophageal varices is most commonly performed with the use of metallic coils, but the use of liquid agents such as opacified enbucrylate and ethanol have also been described.²⁰ The use of absolute ethanol is not recommended due to the possible adverse effects including cardiovascular collapse due to the possible venous channels between the portal system and the pericardium, mainly from the pericardiophrenic vein.

Gastric and Ectopic Varices

Gastric varices occur in 20% of patient with portal hypertension.⁶ Gastric varices are reported to have a lower bleeding risk than esophageal varices; however, once bleeding occurs, patients with a gastric variceal hemorrhage bleed more profusely and require more transfusions than patients with esophageal variceal bleeding.⁴⁵ The risk of rebleeding and the associated mortality are also higher.⁶ Emergency sclerotherapy in gastric variceal bleeding is associated with a highly variable initial success rate of between 25 and 89%. Endoscopic variceal obliteration with injection cyanoacrylates or thrombin is more effective than sclerotherapy in patients with gastric varices with control of over 90% of acute bleedings.⁶ However, the use of cyanoacrylates requires extensive experience and can be associated with distal embolization and damage to the endoscopic equipment. Balloon tamponade is also less effective in these patients due to the location of the varices. Emergency surgery for patient with fundal varices has been highly successful to control the bleeding but it is associated with high morbidity and mortality.⁴⁵ However, in patients with splenic vein obstruction causing isolated gastric varices, surgical splenectomy is the procedure of choice with a cure rate of almost 90% and low rebleeding rates.⁴⁵

TIPS has been successful for refractory bleeding gastric varices with success rates of 90 to 100% and rebleeding rates of 10 to 30% within 1 year.⁶ Reported survival rates vary from 50 to 85% at 1 month and 58 to 79% at 1 year.⁶ Barange et al reported a series of 32 patients with bleeding gastric varices unresponsive to vasoactive agents infusion, sclerotherapy, and/or tamponade and considered poor surgical candidates. Hemostasis was achieved with TIPS in 18 of 20 patients actively bleeding at the time of the procedure. Rebleeding rates were 14, 26, and 31%, respectively, at 1 month, 6 months, and 1 year. For the same periods of time, survival rates at 1 month, 6 months, and 1 year were 75, 62, and 59%.⁶⁰ Obideen et al treated 41 patients with

extraesophageal variceal bleeding (33 gastric varices and eight nongastric extraesophageal varices) with TIPS. Bleeding was controlled immediately in 90%. The mortality was 7% (3/41). The rebleeding rate was 10%.⁶¹ Chau et al treated 84 with esophageal varices (EV group) unresponsive to endoscopic and vasoconstrictor therapy and 28 with gastric fundal varices (GV group). During a median follow-up period of 7 months, 20 patients in the EV group (24%) and eight in the GV group (29%) developed clinical rebleeding. Their results suggest that emergency TIPS is equally effective in the immediate short-term control of gastric fundal variceal bleeding compared with esophageal variceal bleeding. Although the early rebleeding rate within 7 days in the GV group was 18%, only 1 (4%) episode was related to uncontrolled variceal bleeding. Most of the early rebleeding episodes were related to esophageal ulceration secondary to previous sclerotherapy or severe coagulopathy owing to hepatic failure and sepsis. The control of bleeding in this study was 95%.⁴⁵

In a significant proportion of patients with gastric varices, large gastrosplenic shunts are present. In some of these patients variceal bleeding is present with a portosystemic pressure gradient < 12 mm Hg. It is hypothesized that the pressure gradient may not be the critical determinant of the risk of bleeding in these patients. Therefore, TIPS in this subgroup of patients may not effectively prevent the risk of rebleeding.^{6,62} Balloon-occluded retrograde transvenous obliteration (B-RTO), a technique developed in Japan, has recently been recommended for the elective management of bleeding fundal varices associated with a gastrosplenic shunt, which accounts for 85% of the patients with gastric varices.⁶ This new interventional technique consists on the embolization of the gastric varices using a femoral venous approach with selective catheterization of the shunt between the renal vein and the gastric varices. Embolization of the gastric varices with 5% ethanolamine oleate iopamidol injected via a balloon catheter occludes the outlet of the gastrosplenic shunt. B-RTO was reported to eradicate 85 to 100% of gastric fundal varices and to have a low rate of rebleeding. A potential problem with this new technique is the development or worsening of esophageal varices in up to 50% of the patients treated.⁶ Major complications are rare even in patients with poor liver function. The major limitation of B-RTO in an emergency setting seems to be the requirement for the temporary control of bleeding.⁶³

TIPS has also been highly successful for bleeding ectopic varices including rectal, colonic, ileal, jejunal, and duodenal and stomal varices. Most of these ectopic varices are inaccessible by endoscopy and TIPS is an excellent alternative to surgical portal decompression.⁶⁴ Vangeli et al reported the results in 21 cirrhotic patients who underwent TIPS for bleeding ectopic varices. They observed that although TIPS was effective in

lowering the portal pressure, the rebleeding rate for patients with TIPS only was higher (42%) than in patients who received TIPS and embolization (28%). Simultaneous embolization of the varices in conjunction with the TIPS was recommended for patients with ectopic varices.⁶⁵

CONCLUSION

In conclusion, are there any prognostic factors to help decide whether an emergency TIPS should be performed in a particular patient? Although the factors are not 100% accurate and the clinical condition may change, patients with acute variceal bleeding with a Child-Pugh score > 12, APACHE score II > 18 points, hemodynamically unstable, receiving vasopressors and coagulopathy, and/or bilirubin > 6 mg/dL have a high risk of early death after TIPS. In specific, in some individual clinical situations it may be wise to withhold the TIPS in these patients because the mortality rate will be very high, regardless of the therapy given. Every effort should be done to stabilize the patient before TIPS, including the use of tamponade tubes and aggressive correction of coagulopathy. Once medical treatment and sclerotherapy fail, emergency TIPS should be considered early before the clinical condition worsens. Patients at high risk for early mortality after TIPS should be considered for expedite liver transplantation if this option is available.

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