

Clinical Management of Chronic Portal/Mesenteric Vein Thrombosis: The Surgeon's Point of View

Tim R. Glowka · Jörg C. Kalff · Nico Schäfer

Department of Surgery, University of Bonn, Bonn, Germany

Keywords

Portal hypertension · Portal/mesenteric vein thrombosis · Surgical portocaval shunt · Cirrhosis · Esophageal varices

Summary

Background: Bleeding from esophageal varices is a life-threatening complication of chronic portal hypertension (PH), occurring in 15% of patients with a mortality rate between 20 and 35%. **Methods:** Based on a literature review and personal experience in the therapy of PH, we recommend a therapy strategy for the secondary prophylaxis of variceal bleeding in PH. **Results:** The main causes for PH in western countries are alcoholic/viral liver cirrhosis and extrahepatic portal/mesenteric vein occlusion, mainly caused by myeloproliferative neoplasms or hypercoagulability syndromes. The primary therapy is medical; however, when recurrent bleeding occurs, a definitive therapy is required. In the case of parenchymal decompensation, liver transplantation is the causal therapy, but in case of good hepatic reserve or without underlying liver disease, a portal decompressive therapy is necessary. Transjugular intrahepatic portosystemic shunt has achieved a widespread acceptance, although evidence is comparable with or better for surgical shunting procedures in patients with good liver function. The type of surgical shunt should be chosen depending on the patent veins of the portovenous system and the personal expertise. **Conclusion:** The therapy decision should be based on liver function, morphology of the portovenous system, and imminent liver transplantation and should be made by an interdisciplinary team of gastroenterologists, interventional radiologists, and visceral surgeons.

Schlüsselwörter

Portale Hypertension · Pfortaderthrombose · Portokavaler Shunt · Zirrhose · Ösophagusvarizen

Zusammenfassung

Hintergrund: Eine Blutung aus Ösophagusvarizen ist eine lebensbedrohliche Komplikation der chronischen portalen Hypertension. Sie tritt bei 15% der Patienten auf und führt in 20–35% der Fälle zum Tod. **Methoden:** Basierend auf einer Literaturrecherche und der persönlichen Erfahrung in der Therapie der portalen Hypertension schlagen wir einen Therapiealgorithmus für die Sekundärprophylaxe der Varizenblutung vor. **Ergebnisse:** Die Hauptursachen für eine portale Hypertension in den Industrienationen sind eine äthyltoxische/virale Leberzirrhose und eine extrahepatische Pfortaderthrombose, meist auf dem Boden einer hämatologischen oder gerinnungsphysiologischen Erkrankung. Die primäre Therapie ist hier konservativ; im Fall des Blutungsrezidivs muss eine definitive Therapie erfolgen. Bei zugrunde liegender Lebererkrankung besteht diese in der Lebertransplantation, während bei guter Leberreserve oder gesundem Parenchym eine portale Dekompression angezeigt ist. Der transjuguläre intrahepatische portosystemische Shunt wird weitverbreitet eingesetzt, allerdings ist die Evidenz für die chirurgisch angelegten Shunts bei kompensierter Leberfunktion vergleichbar bis besser. Die Art des chirurgischen Shunts sollte anhand der Offenheit des portalvenösen Systems und der chirurgischen Expertise gewählt werden. **Schlussfolgerung:** Die Therapieentscheidung sollte in einem interdisziplinären Team aus Gastroenterologen, interventionellen Radiologen und Viszeralchirurgen getroffen werden und die residuelle Leberfunktion, eine anstehende Lebertransplantation und die Morphologie des portalvenösen Systems berücksichtigen.

Introduction

Chronic portal hypertension (PH) is a challenging disease for the gastroenterologist/hepatologist, radiologist, and visceral surgeon. The main cause for PH in western countries is liver cirrhosis, accounting for 90% of PH, followed by non-cirrhotic PH, i.e. mainly extrahepatic portal vein thrombosis (PVT) [1]. Variceal bleeding (VB) is a life-threatening complication of chronic PH, occurring in 15% of the patients with PH independently of the underlying disease [2–4]. Following the Baveno V guidelines, the primary therapy for VB is medical [5]; however, despite the medical advances, the 6-week mortality after VB is still 20–35% [6]. Medical failure with rebleeding occurs in 20–30% of the patients with VB requiring variceal decompression as the only effective therapy [7–10]. For decades, surgical shunt procedures were the only option for portal decompression. In 1988, the transjugular intrahepatic portosystemic shunt (TIPS) was established [11], profoundly changing the therapy of VB. Due to the now widespread availability of TIPS, most patients will first be treated interventionally, severely reducing the frequency of surgical shunt procedures (e.g. currently 12 times more TIPS than surgical shunts in the USA [12]). In most instances the visceral surgeon will not be involved in the therapy of VB, leading to a comprehensive decline in the expertise in portocaval shunt surgery [12–14]. TIPS has achieved widespread acceptance, although the superiority of TIPS over operative shunting techniques has never been shown [10, 15–18]. The correct therapy algorithm for variceal decompression should be chosen in an interdisciplinary way while considering liver function, rebleeding frequency, long-term outcome, graft patency, and cost-effectiveness. Especially in patients with noncirrhotic PH surgical shunting procedures still have a high significance, not only providing excellent secondary prophylaxis for VB but also preventing ongoing thrombosis of the portovenous system ('panthrombosis').

Definition and Classification of Portal Hypertension

PH is defined as an increase in the portal pressure gradient measured clinically as an increase in the hepatic venous pressure gradient (HVPG) between the portal vein and the inferior vena cava of more than 5 mm Hg. Gastroesophageal varices develop above 10 mm Hg, and bleeding occurs at 12 mm Hg [1]. The underlying cause for PH is crucial for the following therapy. Causes for PH can be classified according to their anatomical location: prehepatic, intrahepatic, and posthepatic. The leading cause for PH in western countries, accounting for 90% of PH, is liver cirrhosis, predominantly caused by alcoholic liver disease and viral hepatitis. Extrahepatic PVT is less common (8–10%), and its course is regularly not being complicated by liver dysfunction [1]. Rare causes are posthepatic disorders such as Budd-Chiari syndrome [19].

The complications arising from PH in cirrhosis dominate its further course: ascites, spontaneous bacterial peritonitis, hepatorenal syndrome, portopulmonary hypertension, hepatopulmonary syndrome, hepatic encephalopathy, portal hypertensive gastropathy, enteropathy, colopathy, and, last but not least, the formation of esophagogastral varices [1]. Two thirds of the patients with cirrhosis develop varices, and bleeding occurs in 30–40% of cirrhotics [6]. The mortality secondary to VB is mainly related to the degree of hepatic decompensation: the average mortality after the first hemorrhage is 20–35% but can be 50% in Child-Pugh grade C patients [6, 20, 21]. The severity of liver dysfunction is also a risk factor for early rebleeding [21], demonstrating the importance of quantifying the hepatic reserve in the therapy of VB. Different scores predicting bleeding and rebleeding have been described [6, 21], but the Child-Pugh score is still essential for planning the further decompressive therapy [6]. In the case of noncirrhotic PVT, it is important to determine the stage of PVT (recent vs. chronic), which can sometimes be difficult. Generally, recent PVT is assumed when patients present with symptoms (abdominal pain, ascites, fever) in the absence of porto-systemic collaterals or portal cavernoma. These are usually detectable in the chronic stage [5], where the initial acute event is often asymptomatic and the disease as well as its underlying cause is often not detected until the first bleeding episode [13].

Diagnostics

PH requires an interdisciplinary approach in diagnostics. The assessment of the clinical condition includes typical complications of PH or the underlying liver disease and the history of gastrointestinal hemorrhages. Upper gastrointestinal endoscopy is crucial for the diagnosis of esophageal or gastric varices and for the exclusion of other sources of gastrointestinal bleeding. Localization, size, color, and stigmata are documented and used for the classification of bleeding risk [6]. A special importance lies in the exact quantification of liver function. Clinical biochemistry, Child-Pugh, MELD (model of end-stage liver disease) score, and transient elastography (Fibroscan®; Echosens™, Paris, France) [22, 23] can assess the severity of liver fibrosis/cirrhosis. In complex cases, liver biopsy can provide histological information [24]. If new-onset PVT occurs in known cirrhosis, alpha-fetoprotein levels combined with imaging should be performed to exclude hepatocellular carcinoma formation. For noncirrhotic PH a hypercoagulability syndrome or a myeloproliferative neoplasm must be evaluated. As summarized in more detail in the article by Trebicka and Strassburg [25], this includes measurements of protein C, protein S, antithrombin III, total homocysteine serum levels, anti-cardiolipin antibodies, lupus-like anticoagulant, and anti-beta-2 glycoprotein antibodies. Genetic studies for factor V Leiden, prothrombin G20210A, and JAK-2 gene mutations

Table 1. Studies comparing TIPS with surgical shunt (modified according to [15])

	Khaitiyar 2000		Helton 2001		Henderson 2006		Rosemurgy 2012		Orloff 2012	
	TIPS	DSRS	TIPS	14 PCS/6 DSRS	TIPS	DSRS	TIPS	HGPCS	TIPS	EPCS
n	35	32	20	20	67	70	66	66	78	76
CHILD A/B, %	100		100		100		56	50	71	68
Follow-up	30 months		19 months	23 months	45 months		13.4–18 years		7 years	
Mortality 30 days, %	6	6	20	0	2	6	15	20	22	23
Survival 2 years, %	80	81	80	90	88	81	53	68 ^a	49	68 ^a
Mortality 5 years, %	–	–	–	–	61	62			20	61 ^a
Recurrence of VB, %	26	6	50	5 ^a	11	6	30	0 ^a	78	3 ^a
Shunt revision/ stenosis, %	69	6 ^a	60	10 ^a	82	11 ^a	48	11 ^a	84	3 ^a
Total charge, USD			111,573	61,934 ^a	74,267	54,975 ^a			264,800	39,000 ^a

^aSignificant difference.

TIPS = Transjugular intrahepatic portosystemic shunt; DSRS = distal splenorenal shunt; PCS = portocaval shunt; HGPCS = H-graft portocaval shunt; EPCS = emergency portocaval shunt; VB = variceal bleeding.

should be conducted; eventually, bone marrow biopsy is useful [26, 27]. Abdominal ultrasonography combined with color Doppler ultrasound is the first-line imaging technique for the diagnosis of PH. Cirrhosis and PVT can be detected with high sensitivity. Especially in compensated patients the sensitivity for PH is lower; however, indirect signs of PH like splenomegaly or ascites can be detected [1]. Computed tomography and magnetic resonance imaging can accurately visualize the portal system including the extent of PVT, map collateral circulation, and identify rare causes for PH such as intra-abdominal inflammation or tumor growth [1, 26]. In selected cases with extended PVT visceral angiography can still be used to evaluate the extent of thrombosis, to map the collateral circulation, and to assess the direction of blood flow in order to evaluate the feasibility of a selective surgical shunt [9].

Indication for Portal Decompression

Nonselective beta-blockers or endoscopic band ligation are recommended for the primary prophylaxis of VB in medium and large varices in the latest Baveno consensus [5]. There is no indication for prophylactic portal decompression (either TIPS or surgical shunt) in asymptomatic varices [5, 8, 28, 29].

The emergency therapy of VB is primarily endoscopic [5]; a successful primary hemostasis can be achieved in 80–90% [29, 30]. Emergency portal decompression (TIPS or surgical shunt) is seldom indicated as there is no survival advantage [31]. Nonetheless, a few groups report excellent outcomes for early TIPS [32] or operative portocaval shunt procedures [18], so these procedures should be kept in mind for salvage procedures in unstoppable bleeding. Medical failure with rebleeding occurs at a rate of 20–30% after VB in patients with PH requiring definitive therapy [7–10]. For the further therapeutic strategy, the assessment of the liver function is crucial.

Liver Cirrhosis

Liver transplantation is undoubtedly the only causal therapy; however, 20–30% of the cirrhotics suffering from variceal rebleeding have an excellent liver function and do not require transplantation [29]. These patients are now widely treated with TIPS as a bridging procedure to transplantation, although less than 10% of the patients are transplanted following TIPS [33, 34]. Compared to TIPS, surgical shunting procedures show a comparable or even better outcome in patients with good liver function (Child-Pugh A and B), so perhaps the decision for TIPS is often not an interdisciplinary approach. Liver transplantation, however, does not occur more frequently following surgical shunt [35, 36].

Noncirrhotic Portal Vein Thrombosis

Decompressive therapy of the portal system, such as in cirrhotic PH, is indicated if endoscopic and pharmacological therapy fails in the treatment of VB [13, 37]. The outcome for shunting procedures after VB without underlying liver disease is better [38], and the results for surgical shunts are excellent with rebleeding rates of 10% after 5 years [13]. Especially for children and young adults other indications than the secondary prophylaxis of VB should be considered. Symptomatic hypersplenism, severe thrombocytopenia, or growth retardation are reasons for decompression of the portal system [37]. The risk for ongoing thrombosis with intestinal infarction in PVT is as high as for VB [38]. An appositional thrombus of superior mesenteric vein and splenic vein is present in 37% [39]. Therefore, shunting procedures should be considered ‘early’ in patients with symptomatic PVT, providing a patent portovenous system in addition to rebleeding prophylaxis. Additionally, they allow an aggressive anticoagulation therapy in the case of myeloproliferative neoplasms or hypercoagulability syndromes. If PVT is caused by malign tumor growth (pancreatic cancer, hepatocellular carcinoma), no decompressive

Table 2. Surgical shunting procedures, classified into selectivity

	Total shunts	Partial shunts	Selective shunts
Portocaval	end-to-side	side-to-side interposition (SARFEH)	
Mesocaval		side-to-side interposition (DRAPANAS)	
Mesorenal			side-to-side
Splenorenal	side-to-side (COOLEY)	proximal end-to-side (LINTON)	distal end-to-side (WARREN)
Coronary-caval			INOKUCHI

therapy should be undertaken since the prognosis is poor [13]. The most common cause for posthepatic PH in western countries is Budd-Chiari syndrome [19]. Surgical or radiological shunting should be performed as early as possible, preserving liver function and leading to a 5-year mortality of less than 25%. If cirrhosis is present, liver transplantation is the only curative therapy [14].

Comparison Surgical Shunt versus TIPS

In the Baveno V consensus, polytetrafluoroethylene (PTFE)-covered TIPS is the preferred therapy for patients failing medical treatment for the prevention of rebleeding. Surgical shunts are considered in Child-Pugh A and B patients only if TIPS is unavailable [5]. This is surprising as scientific evidence for this decision is missing. Five studies exist that compare TIPS with surgical shunting procedures, as shown in table 1. In a recent meta-analysis on four of these studies, a significant superiority in terms of rebleeding frequency and shunt patency was shown for the surgical shunts [40]. In most studies, the cost-effectiveness of surgical shunts is also better compared to TIPS, mostly because of the higher rate of reinterventions after TIPS. In addition, a recent German study reported better results for surgical shunts compared with TIPS in a collection of case series, i.e. a rebleeding rate of 10.5–30% for TIPS versus 1–11% (surgical shunt), a reintervention rate of 48–82% (TIPS) versus 6.3–11% (surgical shunt), and a 30-day mortality of 15–40% (TIPS) versus 8–20% (surgical shunt) [14].

A critical point discussed in these trials was the use of bare-metal-stent TIPS rather than the now used PTFE-covered TIPS, which show a reduced rate of reinterventions due to shunt occlusion. However, most studies evaluating PTFE-covered TIPS are retrospective, pure case series or present poor follow-up rates [41–44]. The findings for an overall survival benefit of PTFE-covered vs. uncovered TIPS differ [45, 46]. For noncirrhotic PVT, only few studies applying TIPS exist, showing a reintervention rate of 35% [47]. Only in Budd-Chiari syndrome a comparable result for TIPS compared with surgical shunt was shown [48].

Nowadays, TIPS is popular, widespread, and generously applied as first-line decompressive therapy after VB but the evidence is weak. As a consequence, the general knowledge as well as the surgical technical expertise to treat the patients with a surgical shunt procedure is continuously diminishing. Prospective randomized multicenter studies comparing surgical shunts with TIPS are needed to clarify this discrepancy between available evidence and clinical reality.

Selection and Technique of Surgical Therapy

A multitude of operative shunting procedures have been described, and these can be divided in total, partial, and selective shunts (table 2). For the selection of the best applicable shunt, three aspects are crucial: a good hepatic reserve, imminent liver transplantation, and the morphology and patency of the portovenous system.

Operative decompression should only be undertaken in compensated liver function (Child-Pugh A and compensated Child-Pugh B) due to a high procedural mortality in Child-Pugh C patients of more than 50% as well as high encephalopathy rates [5, 13]. Of special importance for the preservation of liver function is the maintenance of an at least partial hepatopetal blood flow. If liver transplantation is planned, TIPS with the opportunity of avoiding an abdominal operation and preserving the hilar anatomy is widely favored. Nevertheless, transplantation complications due to TIPS misplacement have been described [49], and especially in patients with failed TIPS a distal splenorenal shunt can be applied without touching the hilar structures [50]. Mesocaval or mesorenal shunts which can easily be ligated during transplantation have also been recommended [9]. In patients with noncirrhotic PVT, selection of the surgical shunt is more dependent on the patency of the portovenous branches than on liver function as in almost all cases the function of the liver as well as its histological structure is not altered. Selective shunts or even devascularization procedures can be indicated when no portomesenteric veins are patent [13].

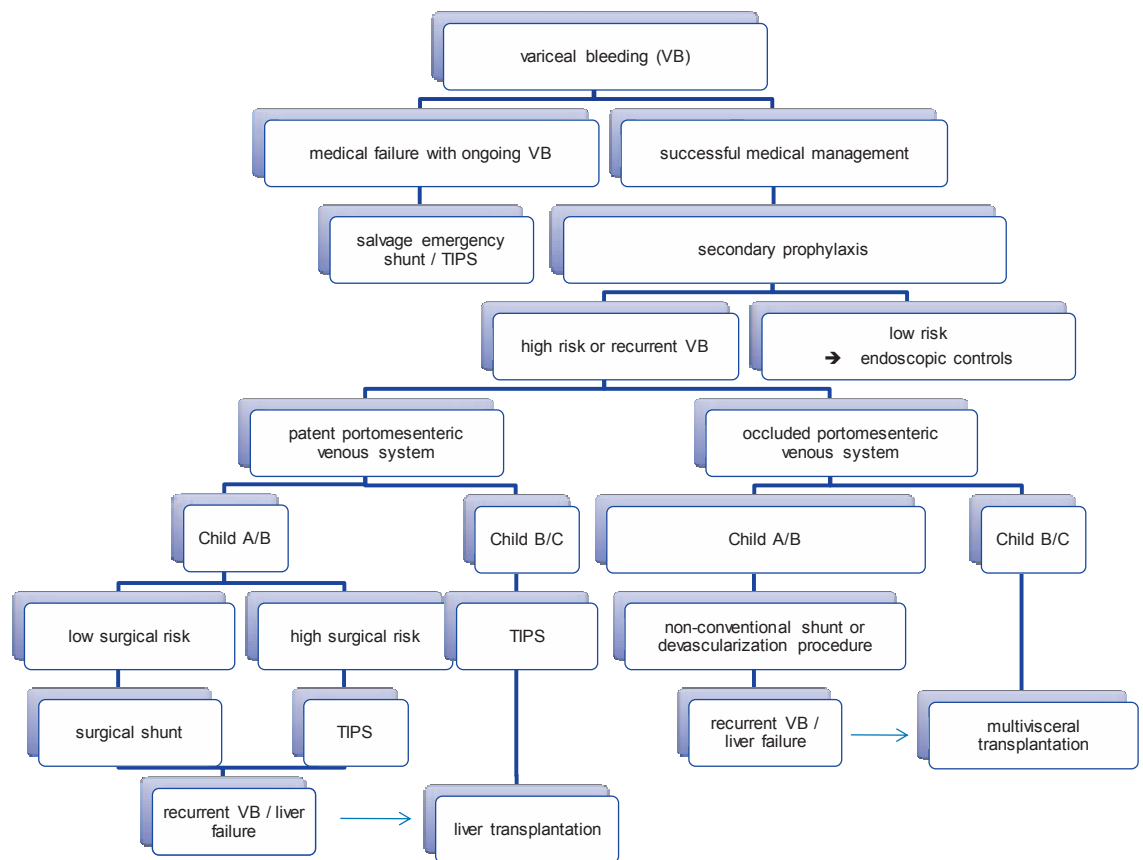


Fig. 1. Therapy algorithm for the secondary prophylaxis of variceal bleeding (modified according to [10]).

Direct Portocaval Shunt

The end-to-side portocaval shunt is a total portosystemic shunt with no remaining hepatopetal flow. It has a high patency rate and provides excellent prevention of rebleeding (less than 5%) but shows a high rate of encephalopathy of up to 40%, and ascites formation can occur due to missing sinusoidal decompression [50]. Other shunts have replaced the direct portocaval shunt in elective decompressive surgery. If at all, it is now mainly used in emergency situations due to its easy technical feasibility [51].

Portocaval H-Graft Interposition Shunt (Sarfeh)

Widely used is the portocaval interposition shunt using an 8-mm PTFE graft. It preserves a hepatopetal flow in about 80% due to the diameter of the PTFE graft [13], with an encephalopathy rate of 5%. Rebleeding occurs in 5%, and graft patency is about 95% over 7 years [17, 52].

Distal Splenorenal Shunt (Warren)

The most common selective shunt is the distal splenorenal shunt. It selectively decompresses gastroesophageal varices and can be used when portal vein and superior mesenteric vein are occluded. Hepatopetal flow is maintained in 70% [13]. The distal splenorenal shunt has a low rebleeding frequency (5–8%), shows a low mortality rate (less than 5%),

and provides a 3- to 5-year survival of 75–80% [10]. Shunt occlusion occurs in 6–11% of the patients [10, 15]. It is important to perform a complete splenopancreatic disconnection to prevent newly developing collateralization [9, 50]. The operation is technically demanding, especially when pancreatitis is apparent.

Splenorenal Side-to-Side Shunt (Cooley)

Patients with noncirrhotic PH can largely benefit from the splenorenal side-to-side shunt, especially if there is only a segmental PVT and a patent superior mesenteric vein. The procedure decompresses gastroesophageal varices as well as the mesenteric compartment and shows excellent patency (87%) and a low rebleeding frequency (10%) [53]. The few existing studies are in line with our personal experience with the Cooley procedure.

Mesocaval Shunt

Mostly used as a small-diameter shunt, it can be applied with or without PTFE interposition. The rates for rebleeding (5–15%) and patency (81–95%) differ [54, 55], suggesting a stronger operator dependency. We consider it a good alternative in cases of noncirrhotic PVT and patent superior mesenteric vein when splenic and portal vein are occluded.

Rex Shunt (Rex Bypass)

In children with segmental PVT and patent left intrahepatic portal vein requiring decompressive therapy, the Rex shunt between the left intrahepatic portal vein and the superior mesenteric vein is the first choice, with a rebleeding rate of 0% and a shunt patency between 75 and 100% [37, 56].

Occluded Portovenous System

In the case of total occlusion of the portovenous system, a portosystemic shunting procedure is not possible. In the case of recurrent VB and preserved liver function, a devascularization procedure can be performed with low rebleeding rates of 10% and a mortality rate of 22% [57]. The reported results from Japan are even better (rebleeding: 1.5–16%; mortality: 4–12%) [50]. Splenectomy is not routinely indicated [58]. We prefer spleen-preserving modifications of the Sugiura-Futagawa or Hassab-Paquet procedures without esophageal transection.

In cases of combined total portovenous occlusion and parenchymal decompensation, liver transplantation with cavoportal hemitransposition or multivisceral transplantation should be considered [9].

Conclusion

VB in PH is a life-threatening complication with high mortality. The primary therapy is medical; however, when recurrent bleeding occurs, an interdisciplinary approach should be followed. The gastroenterologist, interventional radiologist, and visceral surgeon should recommend a therapy based on liver function, portovenous morphology, personal expertise, and patient's will. At our tertiary center we direct the therapy according to a standardized algorithm (fig. 1) which can be modified in interdisciplinary agreement. The Warren shunt and the H-graft shunt are today the most recommendable surgical shunt procedures in the setting of cirrhotic PH. In non-cirrhotic PH, depending on the extent of thrombosis of the portovenous system, the Cooley shunt, the Warren shunt, and the mesocaval shunt are the most preferable shunt procedures.

Disclosure Statement

The authors declare that there are no conflicts of interest.

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