Current Role of Surgery in Portal Hypertension

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Abstract Treatment for portal hypertension (PHT) has evolved from surgery being the only option during the 1970s to the wide range of options currently available. Surgery has not vanished from the therapeutic armamentarium, but its role has changed and is constantly evolving. The present review primarily focuses on the role of surgery in tackling patients with PHT and varices with regard to the Indian scenario and also looks at its relevance, given the availability of a host of other therapeutic options.

Keywords Portal hypertension · Portosystemic shunt · Surgery · Variceal haemorrhage

Pathophysiology of PHT

For understanding how surgery can help modify the natural course in patients with PHT, it is necessary to understand its pathophysiology and the natural history of varices in such patients. PHT is usually the consequence of increased resistance to portal blood flow coupled with increased blood flow through the splanchnic circulation because of a hyperdynamic circulatory state that exists both in cirrhotics and to some extent in noncirrhotic etiologies (large congested splenomegaly) as well. Traditionally, at the ultrastructural level, PHT has been classified into presinusoidal, sinusoidal, and postsinusoidal. It is for the sinusoidal and postsinusoidal blocks that there is an accurate but invasive way of monitoring the portal pressure by using the

method to estimate the hepatic venous pressure gradient (HVPG) in the vascular/hemodynamic lab [1–3]. In cirrhotic patients, as about a third to half of them will actually have PHT; HVPG >5 mmHg indicates PHT. PHT becomes *clinically significant* when the HVPG is ≥ 10 mmHg [1–3]. This is the pressure threshold when PHT leads to the formation of esophagogastric varices, retroperitoneal and periportal collaterals, hypersplenism, low serum albumin-ascitic albumin gradient ascites, spontaneous bacterial peritonitis, etc. Varices rupture and bleed only when the HVPG >12 mmHg [1–3].

Natural History of PHT

It has been estimated that varices are present in about 30–40% of compensated cirrhotics and nearly two-thirds of the decompensated patients. In cirrhotic patients without varices on the first endoscopy, the annual incidence of new varices is between 5% and 10% [1, 4]. Once developed, the progression of varices from small to large depends on the deterioration of liver function and continued hepatic insult (virus-, alcohol-, metabolic-, drug-induced, etc.). The overall annual incidence of bleeding is about 4% and this increases to 15% per year in those with large varices, red signs, and poor Child's status [1, 4–6]. About a third of the cirrhotic patients with varices will bleed and the mortality following each episode of bleeding is about 20% (maybe higher) in experienced tertiary health centers. Early mortality (within 6 weeks) following an acute episode of variceal bleeding depends on the etiology of PHT, the severity of underlying liver disease (Child's C, model for end-stage liver disease [MELD] >18), actively bleeding varices, bleeding gastric varices (GVs), presentation with shock, failed control with very early rebleeding (within

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5 days of the index bleeding), spontaneous bacterial peritonitis, and HVPg >20 mmHg [1, 4–6].

Although the natural history of varices due to cirrhotic PHT has been characterized in considerable detail, little is known about the natural history of varices due to non-cirrhotic causes of PHT prevalent in our country. *Extrahepatic portal venous obstruction* (EHPVO) and *noncirrhotic portal fibrosis* (NCPF) together account for 40–50% of acute variceal hemorrhage (AVH) presenting to the emergency services in our country [7]. The etiology of these presinusoidal causes of PHT has remained obscure, and these diseases are also not prevalent in the West (<10% of PHT cases) [1, 3, 4]. In our country, EHPVO affects the young (age of onset <20 years) with the first bleeding episode occurring before puberty in most patients [7–9]. Patients with EHPVO have good liver function, which remains preserved over the long term; amoderately enlarged spleen; tolerate variceal bleeding episodes well; rarely develop ascites (except during an acute bleed or in children <5 years); and do not show signs of liver decompensation such as encephalopathy. Children and young adults with EHPVO may have significant growth retardation (50%), symptomatic hypersplenism (15–20%), and may develop symptomatic portal biliopathy in the long run as a consequence of the periportal cavernoma compressing on the extrahepatic bile duct [8–10]. The block in portal vein mainly affects the junction of superior mesenteric vein and splenic vein in 85–90% of cases with EHPVO, whereas the entire splenoportal axis is obliterated in 10–15% [8, 9]. The hypothesis that patients with EHPVO outgrow their PHT in their teens by developing spontaneous splenorenal collaterals has not been substantiated. Instead, it is known that patients with long-standing EHPVO may have their course of disease altered due to superadded posttransfusion viral hepatitis (B, C) or portal biliopathy with secondary biliary cirrhosis [8–10]. In the west, EHPVO presenting in adults has been ascribed to latent or overt thrombophilic states such as protein C/S deficiency, latent myeloproliferative disorders, and factor V Leiden mutation; prognosis in these individuals is related, in part, to the management of their thrombophilic state [11].

In contrast, NCPF is characterized by huge splenomegaly (average weight 1,500 g), predominantly affects people of the lower socioeconomic strata in the fourth decade of life, has a patent splenoportal axis with dilated portal vein and splenic vein with large perisplenic, retroperitoneal collaterals, and these patients commonly develop esophagogastric varices with a high incidence of variceal bleeding [12–16]. Ultrastructurally, the liver has obliteration of the portal venules and increased periportal fibrosis in the absence of liver regeneration [12, 13]. Majority of these patients (>95%) have good liver function [12–14], but some may decompensate to develop ascites and encephalo-

pathy spontaneously and may end up needing a liver transplantation [17]. Generally speaking, these patients tend to have a liver function capacity that lies in between normal as in EHPVO and the cirrhotic liver. There is also evidence that the incidence of this disease is decreasing in our country as has been the case with ‘idiopathic PHT’, a disease with similar features, in Japan [16, 18]. Many of the clinical features also overlap with schistosomiasis-induced liver disease and PHT seen commonly in Egypt and Middle Eastern countries.

Management of Portal Hypertension

Management of PHT mainly revolves around the management of the underlying cause of liver disease (e.g., alcohol abstinence, antiviral therapy) and prophylaxis of variceal bleeding, as this can be fatal and in addition can cause significant decompensation of liver function in cirrhotics. By convention, management of this complication of PHT involves the following different clinical scenarios:

1. Preprimary prophylaxis [1]: prevention of variceal formation
2. Primary prophylaxis: prevention of first variceal bleed
3. Treatment of acute variceal bleeding
 - a. Bleeding esophageal varices
 - b. Bleeding GVs
 - c. Bleeding from ectopic varices
 - d. Bleeding from portal hypertensive gastropathy (PHG)
4. Secondary prophylaxis: preventing recurrence of variceal bleeding

The therapeutic armamentarium includes the following modalities:

1. Pharmacotherapy [3, 4, 19]
 - a. Splanchnic vasoconstrictors: terlipressin, vasopressin (acute use)
 - b. Inhibitory hormones: somatostatin, octreotide, vapreotide (acute use)
 - c. Nonselective β -blockers: propranolol, nadolol (chronic use)
 - d. Nonselective β -blocker with α -activity: carvedilol (chronic use)
 - e. Vasodilator: isosorbide mononitrate (in conjunction with β -blockers)
2. Endoscopic treatments [3, 4, 19]
 - a. Endoscopic sclerotherapy (EST), with or without ‘glue’
 - b. Endoscopic variceal ligation (EVL)
 - c. Deployment of covered expandable esophageal stents for variceal tamponade

3. Balloon tamponade: Sengstaken–Blakemore tube (double balloon), Linton–Nachlas tube (single gastric balloon) [3, 4, 19]
4. Interventional radiology [3, 4, 19, 20]
 - a. Transjugular intrahepatic portocaval stent shunt (TIPS)
 - b. Balloon-occluded retrograde transvenous obliteration (BORTO)
 - c. Transhepatic portal vein cannulation and direct variceal embolization (with or without TIPS)
5. Surgery
 - a. Esophagogastric devascularization, with or without splenectomy, and with or without direct ligation of varices or esophageal transection
 - i. Sugiura procedure [21]
 - ii. Modified Hassab's procedure [(splenectomy with esophagogastric devascularisation (SED)) [22]
 - iii. Johnston's stapled esophageal transection and reanastomosis [23]
 - iv. Transabdominal esophagogastric devascularization with gastroesophageal stapling with or without splenectomy (Mathur et al. [24])
 - b. Nonselective portosystemic shunts
 - i. Side-to-side portocaval shunts (s-s PCS) [13, 25]
 - ii. Proximal splenorenal shunt (PSRS) with splenectomy [9, 26]
 - iii. S-side splenorenal shunt without splenectomy (Mitra et al. [27])
 - c. Selective or partial portosystemic shunts
 - i. Distal splenorenal shunt (DSRS) [28]
 - ii. Sarfeh's small diameter (8 mm) interposition (H graft) PCS [29]
 - iii. Inokuchi's coronary caval shunt [30]
 - d. Liver transplantation: the only 'curative' treatment [31]

4, 32, 33]. By and large, β -blockers and EVL are preferred in this setting [2–4]. Also, there is evidence from controlled trials that prophylactic shunt surgery in cirrhotics is associated with faster decompensation and higher rate of liver failure despite protection from variceal bleeding [34–36]. But the results are different when Sugiura devascularization technique is used for prophylactic indications. Two previous reports from Japan, one uncontrolled (noncirrhotics; $n=137$) [21] and the other a randomized controlled trial (RCT) (cirrhotics only; $n=103$) [37] in a mixed group of cirrhotic and noncirrhotic patients with PHT, have shown that prophylactic devascularization is effective in preventing variceal bleeding in both cirrhotics and noncirrhotics (5% bleeding rate) with enhanced survival in both groups of patients (10-year actuarial survival: 72% in cirrhotics; 95% in noncirrhotics).

There is no RCT comparing surgery and endotherapy in the prophylaxis of variceal bleeding in the setting of NCPH. Our group has previously published experience with prophylactic surgery (predominantly PSRS; few Hassab's SED) in EHPVO ($n=74$) and NCPF ($n=45$) [38, 39]. Although the reports are based on retrospective analysis of prospectively collected data over 25 years, we were able to show that prophylactic shunt surgery (few SEDs) was effective in reducing variceal bleeding rates (NCPF: 6.6%; EHO: 2%) with a low operative mortality (<1%). But the long-term results were better in EHPVO (90% symptom free, none had portosystemic encephalopathy; mean follow up: 60 months) than NCPF, as in the later more than half of the patients followed up (mean follow up: 49 months) showed significant systemic morbidity such as portosystemic encephalopathy, nephropathy, myelopathy, etc. We believe that prophylactic shunt surgery is worthwhile in patients with EHO who have high risk of esophagogastric varices and/or hypersplenism and come from remote areas of the country with poor access to tertiary health care facilities. In selected patients with NCPF perhaps, EVL with β -blockers or devascularization can be tried [40].

Surgery for Primary Prophylaxis in PHT

In cirrhotics, apart from variceal size and red signs, HVPg is a good predictor of the risk of first variceal bleed. It has been shown that reduction of HVPg to 12 mmHg or less or 20% reduction from baseline reduces the risk of first bleed [1–5]. HVPg has been used to identify patients with high risk of variceal bleeding and nonresponders to pharmacotherapy in clinical trials [1–5]. However, HVPg has limitations of being invasive and not being widely available.

It is generally believed that surgery and EST have no important role to play in the *preprimary* and *primary* prophylaxis of variceal bleeding in PHT due to cirrhosis [2,

Surgery for Acute Variceal Hemorrhage (AVH)

Mortality associated with each episode of AVH in cirrhotics has decreased to approximately 20%, but can be as high as 70% [3–6, 19, 20, 32, 33, 41]. Several risk factors have been identified that are associated with increased mortality risk for an episode of AVH, including active bleeding at initial endoscopy, infection, HVPg >20 mmHg, hematocrit level, platelet count, aminotransferase levels, presence of portal vein thrombosis, alcoholic liver disease, serum bilirubin and albumin levels, hepatic encephalopathy, hepatocellular carcinoma, and a high Child–Turcotte–Pugh (CTP) score [3–6, 19, 20, 32, 33, 41]. In a recent multicenter

study, MELD score >18 was found to be a strong predictor of short-term mortality at 5 days and 6 weeks after an AVH [6].

Clinical examination should be directed to ascertain the possible cause and severity of the bleeding episode. In a previously diagnosed patient with cirrhosis, variceal bleeding would be the likely cause of upper gastrointestinal hemorrhage (GIH) in 70% of the cases, whereas in patients with EHPVO/NCPF the source of bleeding should be considered variceal unless proved otherwise [3, 4, 7, 8, 14]. In addition, hyperactive bowel sounds on abdominal auscultation indicate upper gastrointestinal source of bleeding, and splenomegaly is an important clinical indicator toward the presence of PHT. The diagnosis of AVH is dependent on upper gastrointestinal endoscopy that allows direct visualization of bleeding esophageal/gastric varix, or signs of recent bleeding such as (white nipple or overlying clot) or red signs associated with blood in the stomach [3, 4, 7, 8, 14].

Prompt initial management is the key to therapeutic success in AVH. For protection of airway, elective intubation is recommended in patients with grade III–IV encephalopathy, severe uncontrolled hemorrhage, aspiration pneumonitis, or in the patients in whom oxygen saturation is low ($<90\%$). Two large-bore (16 G) IV lines should be established in the upper extremities for fluid resuscitation. Volume resuscitation should aim to maintain a systolic BP of 90 mmHg, pulse <100 beats/min, Hb around 7–8 g/dl (hematocrit around 25%). Overaggressive resuscitation may induce or perpetuate UGIH by causing an increase in PHT. Fresh frozen plasma and platelets (if $<50,000/\text{ml}$) should be used when indicated to correct coagulopathy. Use of recombinant factor VII improves hemostasis, but does not enhance survival. In cirrhotics, a short-term broad-spectrum antibiotic prophylaxis should be initiated early during the treatment. This has been shown to reduce bacteremia, variceal rebleeding, and mortality [14, 41].

Pharmacotherapy is always instituted first, followed by endoscopy and attempt at control of hemorrhage by variceal ligation/sclerotherapy or glue injection [3, 4]. Surgery has traditionally been reserved for endotherapy failures. In case of inadequate control with endotherapy, a Sengstaken–Blakemore tube should be inserted and the gastric balloon inflated for maintaining variceal tamponade for 12 h. This buys time for resuscitation and allows a semielective shunt surgery, as emergency shunt surgery (PSRS) carries a much higher mortality in both cirrhotics and noncirrhotics ($>10\%$; NCPF $>$ EHO patients) [3, 4, 8, 14].

At surgery, a gastrotomy is often required to directly under run the esophagogastric varices with interlocking nonabsorbable sutures to arrest the hemorrhage before constructing the decompressive portosystemic shunt [7, 9, 26]. In centers where expertise is available, surgical shunt should be considered in patients with Child's A status and

patients with noncirrhotic portal hypertension (NCPH) once the other modalities have failed to arrest the variceal bleeding. Some selected patients with Child's B and Child's C cirrhosis may also be salvaged by advocating early shunt/devascularization surgery [25, 41, 42]. The selected surgical procedure depends on the available surgical expertise, hepatic functional reserve, patency of the splenoportal venous axis, and transplant candidacy. For example, a peripheral shunt (PSRS, DSRS) or an interposition H-graft PCS (Sarfeh's) is preferable to PCS in a patient who is likely to be a future transplant candidate [41, 42]. It must be borne in mind that in cirrhotics the major factor determining survival is the status of the liver disease at the time of surgery rather than the type of procedure performed, whereas in the case of NCPH, whenever feasible, surgery should be chosen with regard to its efficacy in immediate control of bleeding. In general, patients with NCPH are better treated with decompressive shunts [7, 9, 26, 43]. If suitable shuntable veins are not available, devascularization may be the only option [21, 24].

Role of Surgery in AVH: Challenging the Dogma

In a recent RCT by Orloff et al. [25], a total of 211 unselected, consecutive patients with cirrhosis and acutely bleeding esophageal varices who required at least 2 units of blood transfusion were randomized to EST ($n=106$) or emergency portocaval shunt [EPCS; $n=105$]. EST or EPCS was initiated within 8 h of initial presentation. EST achieved permanent control of bleeding in only 20% of patients, whereas emergency PCS controlled bleeding in all patients ($P\leq 0.001$). Compared with EST, survival after EPCS was significantly higher at all time intervals and in all Child's classes ($P\leq 0.001$). Interestingly, recurrent episodes of portal-systemic encephalopathy were also significantly less in the EPCS group (15 vs. 35%) patients ($P\leq 0.01$). The authors therefore concluded that EPCS permanently stopped variceal bleeding, rarely became occluded, was accomplished with a low incidence of portal-systemic encephalopathy, and compared with EST, produced greater long-term survival.

In another recently published RCT [44] that recruited patients with Child's B and Child's C cirrhosis ($n=63$) who were hospitalized with active variceal bleeding and had high risk for endoscopic treatment failure, it was shown that the early use of TIPS (within 72 h) was associated with significant reductions in treatment failure and mortality. During a median follow-up of 16 months, rebleeding or failure to control bleeding occurred in 14 patients in the pharmacotherapy–EVL group as compared with 1 patient in the early-TIPS group ($P=0.001$). The 1-year actuarial survival was 61% in the pharmacotherapy–EVL group versus 86% in the early-TIPS group ($P<0.001$) [44]. Like

the case of conventional shunt surgery it is now well accepted that wherever the expertise is available, TIPS with a covered stent can be advocated in cirrhotics with poor liver reserve (Child's B or C) for salvaging endotherapy/pharmacotherapy failures, especially in those with high HVPG [3, 4, 20, 44]. It is worth mentioning here that the role of TIPS in NCPF and EHPVO has not yet been defined.

The studies mentioned above have shown that a portosystemic shunt (either surgical or TIPS) decompression may result in better control of bleeding and long-term survival even in patients with advanced cirrhosis. These results need to be reproduced by further studies on similar lines. Nevertheless, the dogma that a decompressive shunt should be advocated as a salvage procedure only when endoscopy and pharmacotherapy fails to control AVH has been challenged. The management protocol for AVH should therefore be designed keeping the above and local available expertise in mind.

Surgery for Secondary Prophylaxis

Although EVL is the first-line treatment for the control of active bleeding from esophageal varices [3, 4, 19], up to 80% of these patients rebleed in the absence of secondary prophylaxis [3, 4, 19]. Hence, secondary prophylaxis of variceal bleeding is routinely recommended. In cirrhotics, β -blockers have been reported to reduce the risk of rebleeding of esophageal varices by ~40% and risk of death by 20% [3, 4, 19]. Endoscopic therapy is effective and EVL is preferred due to its better safety profile and efficacy [32, 45]. In NCPH, a recent RCT has shown that β -blockers are as effective as EVL for long-term secondary prophylaxis [46].

Even though endoscopic variceal obliteration has good long-term outcomes there are certain caveats that should be kept in mind:

1. Although EST/EVL is effective therapy, the protective effect against an episode of rebleeding is not achieved until the varices have been completely obliterated, which may take between 4 and 10 sessions over 8–20 weeks [32, 45, 47, 48].
2. Sclerotherapy has been extensively studied in preventing variceal rebleeding in patients with NCPH. Studies had shown that sclerotherapy reduced the rebleeding rate in patients with NCPH, suggesting a rebleed rate of approximately 25% at 2 years and 35% at 5 years [47, 48]. EVL has been reported to be more effective [32, 45].
3. Lifelong follow-up is necessary as rebleeding can occur after 5 years and can continue to occur as late as 15 years after endoscopic variceal obliteration [47].

4. In the long run following endotherapy, there is a higher risk of developing GV's, ectopic varices, PHG, and portal biliopathy [45].
5. Morbidity in the form esophageal stenosis (15%) can impact the quality of life of these patients and increase the requirement of hospital attendance [47, 48].
6. Growth retardation (in EHPVO) and hypersplenism remains unaddressed.

Role of Surgery for Secondary Prophylaxis in NCPH

Evidence in the Western literature indicates that if shunt surgery has a role in treatment of PHT, it is in patients with NCPH [41, 42]. From India too, excellent long-term results of PSRS have been reported in such patients [9, 26, 38]. Of the 160 children who underwent PSRS with splenectomy at our institution, the overall mortality was 1.9% (elective: 1/140 [0.7%]; emergency 2/20 [10%]), rebleeding rate was 11% and actuarial survival at 15 years by life-table analysis was 95% [9, 26]. None of these patients developed encephalopathy. The procedure cured hypersplenism in all the patients who had this. Only one patient developed meningococcal meningitis, which recovered following treatment. Similarly, a study from Chandigarh that included 104 patients with NCPH who had undergone side-to-side splenorenal shunt showed a shunt patency rate of 87%, a rebleeding rate of 10%, and no occurrence of encephalopathy after a mean follow-up of 54 months [27]. Thus, surgery is a one-time treatment procedure with durable, long-term efficacy in preventing variceal rebleeding. Long-term studies (15–40 years) from the West have also repeatedly shown that shunt surgery with or without splenectomy (proximal splenorenal, side-to-side splenorenal, distal splenorenal, or mesocaval) for EHPVO in children and adults is associated with shunt patency rates between 90% and 95%, rebleeding rates of 5–10%, absence of portosystemic encephalopathy and 15-year actual survival rates of 95% [49–52]. These studies have found portosystemic shunts to be consistently effective for bleeding esophagogastric varices due to EHPVO. A shunt also ameliorates the ectopic varices/PHG and portal biliopathy and reverses growth retardation [53]. In a prospective study of patients with EHPVO undergoing shunt surgery, there was an overall improvement in scholastic abilities, physical activity, and social interaction in a majority of the patients [53]. For patients with portal biliopathy shunt surgery is required following failure of nonsurgical means of biliary intervention [54–57]. If this does not help, a surgical bilioenteric bypass will be required [57]. Thus, the major benefit of surgical treatment is its being a one-time therapy that provides excellent long-term results and has the potential to beneficially modify the natural course of the disease [58].

It is also cost-effective in the long run. Nonsurgical shunts such as TIPS have no role in EHPVO yet.

The surgical options in EHPVO have been recently bolstered by the development of a new type of shunt, the mesenterico-left portal vein bypass (Rex shunt) in children [59]. This is a new paradigm in surgical treatment. This procedure decompresses the portal venous system while simultaneously restoring portal blood flow to the liver. Follow-up results ranging between 1 and 7 years are available. In the largest study reported till date, 34 patients underwent this procedure with a success rate of 91%, good shunt patency rate, and rebleeding rate of 8% with amelioration of hypersplenism in most patients [59]. Although promising, long-term follow-up studies are needed to confirm its efficacy.

Furthermore, in our previously published data [43], a retrospective analysis of our prospectively maintained NCPF database was done. The records of 317 consecutive patients (200 males) with NCPF treated between 1975 and 2000 were studied. Overall, 226 (71.3%) belonged to Child's A, 87 (27.4%) to Child's B, and 4 (1.3%) to Child's C. A total of 322 operations were done to treat PHT. Of these 251 (78%) were elective and 71 had emergency operations. PSRS was the commonest procedure done in 285 (88%) patients. The elective operative mortality was 0.8%. Rebleeding occurred in 9.6% (PSRS 8%, devascularization 11.5%). An emergency procedure ($P<0.001$), poor Child's class ($P=0.005$), and blocked shunt ($P=0.014$) were all associated with high likelihood of rebleed. Encephalopathy occurred in 13.2%. The presence of nodular or shrunken liver, low preoperative albumin (<3.5 g/dl), and large shunt size (>1.2 cm) were significantly associated with a higher occurrence of postoperative encephalopathy ($P<0.001$, 0.03, 0.03, respectively). The mean follow-up was 50 months (6 months–234 months). Twenty-five patients died during follow-up, most due to rebleed (10) or liver failure. The overall median actuarial survival was 234 months. A poor preoperative Child's status ($P=0.0001$) and occurrence of rebleeding ($P=0.005$) were significantly associated with delayed death. By Cox-regression multivariate analysis the odds ratio for death during follow-up for a patient with Child's B or C status was 8.9 (CI: 2.98–27.03) and for a patient with a rebleed was 4.8 (CI: 1.5–14.3). As per our experience and that of others (APASL guidelines on NCPF), shunt surgery (PSRS) is effective and yields good short- and long-term results with acceptable morbidity in a majority of NCPF patients and is recommended for secondary prophylaxis of variceal bleeding [14, 60]. The long-term survival in these patients is related to the preoperative liver function status and patency of the shunt [14, 43, 60].

Comparative studies of long-term outcomes of surgery versus EVL in patients with EHPVO and NCPF are sorely needed. But available data does suggest that shunt surgery

is an effective modality for secondary prophylaxis in these patients.

Devascularization Procedures in NCPH

It has been argued that a surgical option does not exist for the 10–15% of patients with EHPVO who have no shuntable vein or a thrombosed splenoportal and mesentericoportal axis. In a series of 68 patients (44 EHO, 22 NCPF), transabdominal extensive esophagogastric devascularization with gastro-esophageal stapling was done (emergency 38; elective 30) and were followed up for a mean period of 54 months. An operative mortality of 4%, rebleeding rate of 11% (5% variceal), esophageal stricture rate of 15% and a 5-year survival of 88% were reported [24]. The authors concluded that this modified Sugiura procedure was safe and effective for long-term control of variceal bleeding in NCPH, especially in the emergency setting and in patients with anatomy unsuitable for shunt surgery or if surgical expertise for a shunt operation is not available [24]. Orozco et al. [61] from Mexico reported similar results in a selected group of patients with EHPVO ($n=38$) undergoing the one-stage or two-stage Sugiura procedure. Goyal et al. [62] reported a rebleeding rate of 10% and a 95% overall survival among 22 patients with NCPH undergoing esophagogastric devascularization who were followed for a mean duration of 4 years.

The above results coupled with the Japanese experience quoted earlier suggests that whenever shunt is not feasible, devascularization will remain an effective surgical option in the management of acute variceal bleeding as well as prevention of rebleeding.

Role of Surgery for Secondary Prophylaxis in Cirrhosis

A meta-analysis of all randomized clinical trials comparing total shunts, DSRS, or TIPS with endoscopic therapy in patients who had recovered from an episode of variceal hemorrhage and were known to be cirrhotic included 22 trials evaluating 1,409 patients [63]. Shunt therapy compared with endoscopic therapy demonstrated significantly less rebleeding (OR 0.24, 95% CI: 0.18–0.30), but at the cost of significantly increased acute hepatic encephalopathy (OR 2.07, 95% CI: 1.59–2.69), and chronic encephalopathy (OR 2.09, 95% CI: 1.20–3.62). There were no significant differences regarding mortality and duration of in-patient stay. The proportion of patients with shunt occlusion or dysfunction was 3.1% (95% CI: 0.4–10.7) following TS (two trials), 7.8% (95% CI: 3.8–13.9) following DSRS (four trials), and 59% (range: 18–72%) following TIPS (14 trials) [63]. The meta-analysis concluded that all portosystemic shunts resulted in a significantly lower rebleeding rate at the expense of a higher incidence of encephalopathy and TIPS was complicated by a high incidence of shunt

dysfunction. No survival advantage over endotherapy was demonstrated with any shunt.

Devascularization Procedures in Cirrhosis

To obviate the high incidence of encephalopathy following shunts, many centers have deliberately employed devascularization procedures such as extensive two-stage esophagogastric devascularization (transthoracic and transabdominal; Sugiura–Futgawa technique) [21], modified Hassab's (transabdominal esophagogastric devascularization with splenectomy, without esophageal transection) [22] or spleen-preserving esophagogastric devascularization with stapled esophageal/cardial transection [23, 24] for secondary prophylaxis as well as for managing acute variceal bleeding (see above).

In a study from Chennai [64], 52 Child's A/B cirrhotic and noncirrhotic patients who had variceal bleeding and failed endotherapy underwent esophagogastric devascularization (14 with stapled esophageal transection [group I]; 38 nonstapled [group II]; emergency devascularization: 16) with a postoperative mortality of 7.1% in group I, 10.5% in group II ($P>0.05$). Although emergency surgery had a mortality of 31.2% (5/16), there were no deaths in the elective surgery group. Overall morbidity was 57.1% in group I and 21.0% in group II ($P<0.05$). The rates of variceal rebleeding were 7.1% and 7.8%; residual varices were 30.7% and 32.3%; recurrent varices were 7.6% and 5.8% following the group I and group II procedures, respectively, over a mean follow-up period of 40 months. Esophageal transection-related morbidity (leak, stricture, and bleeding) was 21.4% (3/14) in group I. It was concluded by the authors that esophagogastric devascularization without esophageal stapled transection was a safe and effective procedure for adequate (urgent and long-term) control of variceal bleeding with similar results and lesser morbidity when compared with devascularization with esophageal transection.

In another study from Egypt [65], 219 patients (child's A/B) with PHT due to schistosomiasis (40%) and nonalcoholic cirrhosis (60%) underwent either DSRS ($n=123$) or splenectomy with esophagogastric devascularization (SGD; $n=96$) electively. Rebleeding occurred significantly ($P<0.05$) more frequently after SGD (27%) compared with DSRS (5.7%). EST salvaged 65% of SGD rebleeders. Encephalopathy developed significantly ($P<0.05$) more after DSRS (18.7%) compared with SGD (7.3%). Following a mean follow-up of over 6 years, the overall survival was 80% in both the groups of patients, with liver failure as the main cause of death in the long term. However, in the schistosomal patients, survival was better after DSRS (90%) compared with SGD (75%), with no difference among the cirrhotic patients (DSRS 73%, SGD 72%). Although non-

randomized, it was a unique comparative study of two different surgical modalities in PHT. It was concluded by the authors that (1) both DSRS and SED have low mortality rate in the elective setting, (2) DSRS is superior to SGD in the schistosomal patients, and (3) SED backed by EST/EVL for rebleeding is a good surgical alternative to selective shunt in the nonalcoholic cirrhotics.

The same Egyptian group subsequently published their experience with surgical management of variceal bleeding in a cohort of 272 consecutive patients with chronic active hepatitis of varying severity (high grade: 60%) [66]. The overall mortality for DSRS and SED was similar (~5%), but the rebleeding rate was significantly lower with DSRS (5 vs. 17%). In the long term, the encephalopathy rate following DSRS was significantly higher (28 vs. 6%). The patients with low-grade hepatitis activity had minimal long-term morbidity. Although the overall 5-year survival was similar in both surgical groups at ~75% the long-term deaths following DSRS were mainly due to liver failure. The authors concluded that in patients with chronic active hepatitis with high-grade activity and variceal bleeding a *nonshunt* surgical option backed by endotherapy for rebleeding was a better long-term option, whereas for patients with low-grade hepatitis either option was suitable [66].

We believe, as do others [67], that the essential components of an effective esophagogastric devascularization for variceal bleeding include ligation of esophageal/GVs with continuous nonabsorbable sutures through an early gastrotomy (in actively bleeding patients), splenectomy to reduce the portal pressure followed by a standard transabdominal devascularization (as described by Hassab) [22] involving the lower 5 cm of esophagus and upper half of the stomach. Pyloroplasty and esophageal transection are unnecessary. Splenectomy with esophagogastric devascularization (SED) remains an effective surgical tool in Child's A/B cirrhotics who are endotherapy failures and in NCPH patients with no shuntable veins.

Management of Gastric Variceal Bleeding

GVs are less common than esophageal varices, occurring in 20–25% of patients with PHT [2, 8]. GV bleed less frequently than esophageal varices [2, 8]; however, bleeding tends to be more severe, requires more transfusions, and has a higher mortality rate than esophageal variceal bleeding [2–4, 68]. After control of acute bleeding, GV have a high rebleeding rate (34–89%) and treatment modalities to prevent rebleeding have not been properly delineated. The frequency and severity of bleeding from GV depend on their location and size. GV could be associated with esophageal varices (GOV1 along the lesser curve, or type 2 [GOV2] along the fundus) or are present in

isolation (isolated gastric varix type 1 [IGV1]), in the fundus or at ectopic sites in the stomach or the first part of the duodenum ([IGV type 2]) [68]. The 2-year incidence of variceal bleeding from IGV1 and GOV2 type of varices is more frequent and profuse (78 and 54%, respectively) than the lesser curve (GOV1) varices (28%) [1]. In the presence of factors indicating a high risk of bleeding, the 2-year probability of GV bleeding is as high as 65% [69].

Based on the results of a recently published RCT in cirrhotics [69], it was concluded that *primary prophylaxis* is recommended in patients with large (>2 cm) and high-risk gastric varices (GOV2 and IGV1) to reduce the risk of first bleeding and mortality. Associated congestive gastropathy and MELD score ≥ 17 also contributed to the increased risk of bleeding. Cyanoacrylate injection was found to be more effective than β -blocker therapy in preventing first gastric variceal bleeding. In another randomized trial [70], which recruited cirrhotics with gastric varices which had bled, it was shown that the probability of rebleeding and mortality from large gastroesophageal varices type 2 (GOV2) or IGV1 was significantly lower in the endoscopic cyanoacrylate injection group (15% and 3%) compared with the β -blocker group (55% and 25%) [70]. The majority of patients with such gastric varices have an elevated HVPG >12 mmHg. It was also demonstrated that cyanoacrylate injection increases the HVPG, and β -blocker decreases HVPG significantly on follow-up. It was therefore concluded that endoscopic injection of cyanoacrylate should be used to prevent rebleeding from large GOV2 and IGV1 and improve survival, whereas β -blockers are not effective despite the fact that they decrease HVPG in these patients [70].

Although endoscopic variceal obliteration is the first-line treatment for acute GV bleeding, other treatment modalities need further evaluation. Both surgical shunting and TIPS are considered as valuable adjuncts in the management of acute refractory or recurrent GV bleeding [71]. The role of TIPS in managing patients with a low HVPG <12 mmHg and its appropriateness in patients with advanced liver disease remain unclear. TIPS has been found to be quite effective in the prevention of GV rebleeding, not only by reducing the portal pressure but also by allowing the possibility of transhepatic obliteration of gastric variceal channels [72]. A number of radiologic or combination endoscopic-radiologic techniques such as BORTO (balloon-occluded retrograde transvenous obliteration and percutaneous transhepatic obliteration) and balloon-occluded endoscopic injection sclerotherapy have been pioneered in Japan, but need further evaluation [73].

Only few surgical studies have addressed the issue of bleeding gastric varices exclusively. High-risk gastric varices, especially in patients with NCPH and Child's A cirrhosis are best addressed by a decompressive shunt surgery whenever feasible [74]. Although glue injections

remain effective, surgery offers a one-time therapy with durable long-term outcome [71]. At times, during emergency surgery for control of gastric variceal bleeding following a failed glue injection the fundus of the stomach may need to be excised to effect control of bleeding.

Surgical Portosystemic Shunts Versus TIPS

There have been only a few studies in the literature reporting a prospective comparison of a surgical shunt with TIPS in the setting of variceal bleeding in cirrhotics. Long-term outcomes of patients undergoing prosthetic 8-mm H-graft portacaval shunts (HGPCS) or TIPS were reported by Rosemurgy et al., in 2005 [75–77]. Patients undergoing HGPCS ($N=66$) or TIPS ($N=66$) were very similar with regard to Child's class and MELD scores. The actual survival was superior to predicted survival for both intervention groups. Compared with TIPS, survival was superior after HGPCS for patients of Child's class A and B and with MELD scores <13 with follow-up of 5–10 years. Shunt failure was significantly less following HGPCS. TIPS was more often associated with shunt stenoses/occlusions, recurrent hemorrhage, shunt revisions, and shunt failure. For Child's class C patients undergoing HGPCS or TIPS, though long-term survival was similar, it was at the cost of high periprocedural 30-day mortality of 20% and 15%, respectively. But measures of resource consumption and cost of postprocedure health care favored HGPCS over TIPS. The authors therefore concluded that HGPCS should be preferentially applied for acceptable patients without easy access to skilled post-shunt care or without definitive plans for early transplantation. For patients with MELD scores ≥ 14 , TIPS should be considered and should be used as a bridge to liver transplantation. In addition, TIPS may also be offered to patients in need of portal decompression who are unacceptable operative candidates such as patients with histories of multiple right upper quadrant abdominal operations or super obesity.

Another prospective multicenter randomized controlled clinical trial enrolled 140 patients with Child-Pugh class A and B cirrhosis and refractory variceal bleeding and randomized them to undergo DSRS (73) or TIPS (67) [78]. After a mean follow-up of 46 months there was no significant difference in rebleeding (DSRS, 5.5%; TIPS, 10.5%; $P=0.29$) or first encephalopathy event (DSRS, 50%; TIPS, 50%). Procedure-related 30-day mortality was 6.8% and 1.5%, respectively. Survival at 2 and 5 years (DSRS, 81% and 62%; TIPS, 88% and 61%, respectively) were not significantly different ($P=0.87$). Thrombosis, stenosis, and reintervention rates (DSRS, 11%; TIPS, 82%) were significantly ($P<0.001$) higher in the TIPS group. Ascites, need for transplant, quality of life, and costs

were not significantly different. This study showed that DSRS and TIPS are similarly efficacious in the control of refractory variceal bleeding in Child-Pugh class A and B patients, but reintervention was significantly greater for TIPS compared with DSRS. Since both procedures had equivalent outcomes, the choice should depend on available expertise and ability to monitor the shunt and reintervene when needed.

Combining the outcome of the two studies quoted above, it would seem that surgical shunting does have a role in cirrhosis (Child's class A and B) for prevention of variceal rebleeding and may offer a more durable long-term solution, which is cost effective and avoids frequent hospital visits/admissions. Surgical option is especially suited to those patients in whom transplant is not imminent or not indicated.

Portal Hypertension due to Hepatic Venous Outflow Tract Obstruction

Hepatic venous outflow tract obstruction (HVOTO) is a rare cause of PHT accounting for 7–9% of cases with PHT in India [79]. Hepatic vein obstruction is the predominant lesion in the West, whereas inferior vena cava (IVC) obstruction is the more common lesion in Southern Asia, Far East, and Africa [79, 80]. The latter follows a more indolent clinical course. The etiology of HVOTO is membranous obstruction of vena cava in Japan, whereas in India IVC thrombosis is more frequent [79]. A combination of hepatic vein and IVC obstruction is not uncommon in India. In general, the treatment of patients with HVOTO depends mainly on the rapidity of onset and severity of symptoms at presentation, extent of liver damage, refractory ascites, signs of liver failure (other than ascites), and failure of prior treatment (medical, radiological, or surgical) with disease progression [80]. The presence of a documented thrombophilic state also determines the likely outcome of such patients, although in India such associations are rarely encountered. Patients with fulminant presentation with rapid onset of encephalopathy within weeks of onset, patients with end stage liver disease (ESLD), with failed previous TIPS/surgery, and with underlying metabolic deficiencies promoting thrombophilic states (Protein C and S deficiencies, antithrombin III deficiency) are candidates for transplantation, which may yield 5-year survival rates between 50% and 95% [81, 82]. The graft survival rate is poorer and patients are required to be on lifelong anticoagulant therapy.

Portosystemic Shunt Surgery

Portosystemic shunt surgery (PSS) is usually indicated in the acute and subacute cases of HVOTO with refractory ascites and ongoing liver necrosis, but no evidence of

cirrhosis [79, 80]. Such patients are most commonly treated with s-s PCSmesocaval shunts (MCS), cavoatrial shunt (CAS), and mesoatrial shunts (MAS). Patients with isolated hepatic vein blocks require a s-s PCS where the portal vein forms the outflow tract for the congested liver. The long-term results are good with 81–94% symptom-free survival [80, 83]. But the results have not been reproducible and often a MCS is preferred, as it avoids hilar dissection (ensuring safety if a future transplant is required) and is technically simpler to construct even in the presence of a hypertrophied caudate lobe [83]. The best results and long-term patency rates are obtained with autologous jugular vein interposition grafts with a 5-year survival rate varying between 55% and 95% [83]. A MAS is indicated in selected patients with IVC block or mixed HV-IVC blocks, where there is severe narrowing of IVC (>75% of the luminal diameter) that is not amenable to stenting. A pressure gradient of 15 mmHg or more between the right atrium and the IVC is one of the prerequisites for this shunt. Although technically demanding with high operative mortality (15–20%), satisfactory long-term results with 75% long-term survival have been achieved in specialized centers [80, 83]. A long reinforced or ringed PTFE graft (16–20 mm diameter) is preferred. Combined blocks have also been treated with a CAS in tandem with a s-s PCS, exponents of this operation claim good results. The high graft thrombosis rates in MAS/CAS (up to 50%) mandates carefully monitored lifelong anticoagulation therapy with radiological rectification of thrombosis as and when detected.

Until the 1990s, portosystemic shunt surgery (PSS) formed the mainstay of the management. The main limitations of shunt surgery are declining expertise and high perioperative mortality of 10–20% [79, 80, 83]. Further, on the basis of our experience with 75 cases of HVOTO, it was felt that hepatic vein blocks are best treated surgically with a s-s PCS, provided that liver failure had not set in, and IVC blocks were best treated by balloon IVC venoplasty with or without stenting [79]. With such an approach 60% of the patients were rendered asymptomatic. But this was a pretransplant and pre-TIPS era experience, and with accumulating evidence it is now becoming clear that many HVOTO patients, including those with combined blocks, can be salvaged with balloon venoplasty and/or IVC stenting or TIPS [84, 85]. An impressive 5-year survival of 74% following TIPS for HVOTO seems to support this [85]. Currently, the indications for TIPS are as a bridge for liver transplantation for ESLD and liver decompression in patients with HVOTO due to isolated hepatic vein thrombosis with acute presentation. But one should keep in mind that the main limiting factors for this modality are procedure-related complications of approximately 10%, stent dysfunction of more than 50% at 1 year, and limited availability of expertise [83, 85].

Hence, keeping the above in perspective PSS, TIPS, or liver transplantation should be considered complimentary modalities for the treatment of patients with HVOTO. The choice, as is also the case in other types of PHT, is best determined by presentation, liver function tests, level of block, and the available local expertise.

Conclusions

The last word in the optimal management of PHT is yet to be written. The role of surgery continues to be redefined with the advent of the newer interventional radiology techniques and refinements in the nonoperative management of PHT [41, 42]. Far from becoming obsolete, surgery in its various forms continues to have a place in the management of variceal bleeding due to PHT in noncirrhotics as well as cirrhotics. Modest success has been achieved in the treatment of NCPH in which surgery has a significant role to play, but in cirrhotics the struggle for therapeutic supremacy continues! Of course in patients with advanced liver disease with recurrent variceal bleeding, liver transplantation still remains the ultimate 'surgical' option!

References

- Groszmann RJ, Garcia-Tsao G, Bosch J, Grace ND, Burroughs AK, Planas R et al (2005) Portal hypertension collaborative group. Beta blockers to prevent gastroesophageal varices in patients with cirrhosis. *N Engl J Med* 353:2254–2261
- Sarin SK, Kumar A, Angus PW, Bajjal SS, Chawla YK, Sahni P et al (2008) APASL working party on portal hypertension. Primary prophylaxis of gastroesophageal variceal bleeding: consensus recommendations of the Asian Pacific Association for the Study of the Liver. *Hepatol Int* 2(4):429–439
- de Franchis R, Baveno V Faculty (2010) Revising consensus in portal hypertension: report of the Baveno V consensus workshop on methodology of diagnosis and therapy in portal hypertension. *J Hepatol* 53(4):762–768
- Bosch J, Berzigotti A, Garcia-Pagan JC, Abraldes JG (2008) The management of portal hypertension: rational basis, available treatments and future options. *J Hepatol* 48(Suppl 1):S68–S92
- D'Amico G, Luca A (1997) Natural history clinical-haemodynamic correlations. Prediction of the risk of bleeding. *Baillieres Clin Gastroenterol* 11:243–256
- Bambha K, Kim WR, Pedersen R, Bida JP, Kremers WK, Kamath PS (2008) Predictors of early re-bleeding and mortality after acute variceal haemorrhage in patients with cirrhosis. *Gut* 57(6):814–820
- Rao TH, Pande GK, Sahni P, Nundy S (1991) The management of upper gastrointestinal haemorrhage in a tropical country. *Arch Emerg Med* 8(3):169–176
- Sarin SK, Sollano JD, Chawla YK, Amarapurkar D, Hamid S, Hashizume M et al (2006) Members of the APASL working party on portal hypertension. Consensus on extra-hepatic portal vein obstruction. *Liver Int* 26(5):512–519
- Pande GK, Reddy VM, Kar P, Sahni P, Berry M, Tandon BN, Nundy S (1987) Operations for portal hypertension due to extrahepatic obstruction: results and 10 year follow up. *Br Med J (Clin Res Ed)* 295(6606):1115–1117
- Sarin SK, Bansal A, Sasan S, Nigam A (1992) Portal-vein obstruction in children leads to growth retardation. *Hepatology* 15:229–233
- Valla DC, Condat B, Lebrech D (2002) Spectrum of portal vein thrombosis in the West. *J Gastroenterol Hepatol* 17(Suppl 3):S224–S227
- Basu AK, Boyer J, Bhattacharya R, Basu Mallick KC, Sengupta KP (1967) NCPF with PHT—a new syndrome. Part I. *Indian J Med Res* 55:336–350
- Mallick KC, Sengupta KP, Basu AK, Biswas SK, Pal NC, Boyer J (1967) NCPF with PHT—a new syndrome. Part II. *Indian J Med Res* 55:351–359
- Sarin SK, Kumar A, Chawla YK, Bajjal SS, Dhiman RK, Sahni P et al (2007) Members of the APASL working party on portal hypertension. Noncirrhotic portal fibrosis/idiopathic portal hypertension: APASL recommendations for diagnosis and treatment. *Hepatol Int* 1(3):398–413
- Sarin SK (2002) Non-cirrhotic portal fibrosis. *J Gastroenterol Hepatol* 17(Suppl 3):S214–S223
- Chawla Y, Duseja A (2003) Non-cirrhotic portal fibrosis (NCPF) is a vanishing disease in India. *Trop Gastroenterol* 24(2):45–46
- Saigal S, Nayak NC, Jain D, Kumaran V, Mohanka R, Saraf N, Rastogi A, Mehta N, Nundy S, Soia A (2011) Non-cirrhotic portal fibrosis related end stage liver disease in adults: evaluation from a study on living donor liver transplant recipients. *Hepatol Int* [Epub ahead of print]
- Okuda K, Obata H (1991) Idiopathic portal hypertension (hepatoportal sclerosis). In: Okuda K, Benhamou JP (eds) *Portal hypertension: clinical and physiological aspects*. Springer, Tokyo, pp 271–287
- Sarin SK, Kumar A, Angus PW, Bajjal SS, Baik SK, Sahni P, Asian Pacific Association for the Study of the Liver (APASL) Working Party on Portal Hypertension et al (2011) Diagnosis and management of acute variceal bleeding: Asian Pacific Association for Study of the Liver recommendations. *Hepatol Int* 5(2):607–624
- Luca A, D'Amico G, La Galla R, Midiri M, Morabito A, Pagliaro L (1999) TIPS for prevention of recurrent bleeding in patients with cirrhosis: meta-analysis of randomized clinical trials. *Radiology* 212:411–421
- Sugiura M, Futagawa S (1984) Esophageal transection with paraesophagogastric devascularizations (the Sugiura procedure) in the treatment of esophageal varices. *World J Surg* 8(5):673–679
- Hassab MA (1998) Gastro-esophageal decongestion and splenectomy GEDS (Hassab), in the management of bleeding varices. Review of literature. *Int Surg* 83(1):38–41
- Spence RA, Johnston GW (1985) Results in 100 consecutive patients with stapled esophageal transection for varices. *Surg Gynecol Obstet* 160(4):323–329
- Mathur SK, Shah SR, Nagral SS, Soonawala ZF (1999) Trans-abdominal extensive esophagogastric devascularization with gastroesophageal stapling for management of noncirrhotic portal hypertension: long-term results. *World J Surg* 23(11):1168–1174
- Orloff MJ, Isenberg JI, Wheeler HO, Haynes KS, Jinich-Brook H, Rapier R, Vaida F, Hye RJ (2009) Randomized trial of emergency endoscopic sclerotherapy versus emergency portacaval shunt for acutely bleeding esophageal varices in cirrhosis. *J Am Coll Surg* 209(1):25–40
- Prasad AS, Gupta S, Kohli V, Pande GK, Sahni P, Nundy S (1994) Proximal splenorenal shunts for extrahepatic portal venous obstruction in children. *Ann Surg* 219(2):193–196
- Mitra SK, Rao KL, Narasimhan KL, Dilawari JB, Batra YK, Chawla Y et al (1993) Side-to-side lienorenal shunt without splenectomy in noncirrhotic portal hypertension in children. *J Pediatr Surg* 28:398–401

28. Warren WD, Salam AA, Hutson D, Zeppa R (1974) Selective distal splenorenal shunt. Technique and results of operation. *Arch Surg* 108(3):306–314
29. Collins JC, Rypins EB, Sarfeh IJ (1994) Narrow-diameter portacaval shunts for management of variceal bleeding. *World J Surg* 18(2):211–215
30. Inokuchi K, Beppu K, Koyanagi N, Nagamine K, Hashizume M, Iwanaga T, Sugimachi K (1984) Fifteen years' experience with left gastric venous caval shunt for esophageal varices. *World J Surg* 8(5):716–721
31. Hillert C, Fischer L, Broering DC, Rogiers X (2003) Liver transplantation in patients with liver cirrhosis and esophageal bleeding. *Langenbecks Arch Surg* 388(3):150–154
32. Imperiale TF, Chalasani N (2001) A meta-analysis of endoscopic variceal ligation for primary prophylaxis of esophageal variceal bleeding. *Hepatology* 33:802–807
33. The Veterans Affairs Cooperative Variceal Sclerotherapy Group (1991) Prophylactic sclerotherapy for esophageal varices in men with alcoholic liver disease. A randomized, single-blind, multicenter clinical trial. *N Engl J Med* 324:1779–1784
34. Burroughs AK, D'Heygere F, McIntyre N (1986) Pitfalls in studies of prophylactic therapy for variceal bleeding in cirrhotics. *Hepatology* 6:1407–1413
35. Jackson FC, Perrin AB, Smith AG, Dagradi AE, Nadal HM (1968) A clinical investigation of the portocaval shunt. II—Survival analysis of the prophylactic operation. *Am J Surg* 115:22–42
36. Resnick RH, Chalmers TC, Ishihara AM, Garceau AJ, Callow AD, Schimmel EM et al (1969) A controlled study of the prophylactic porto-caval shunt—A final report. *Ann Intern Med* 70:675–688
37. Inokuchi K (1990) Improved survival after prophylactic portal non decompression surgery for esophageal varices: a randomized clinical trial. Cooperative Study Group of Portal Hypertension of Japan. *Hepatology* 12(1):1–6
38. Pal S, Radhakrishna P, Sahni P, Pande GK, Nundy S, Chattopadhyay TK (2004) Prophylactic operations in portal hypertension due to extrahepatic portal venous obstruction in India: lessons learnt over two decades of experience. (APASL\Abstract\100). *J Gastroenterol Hepatol* 19(Suppl):A733
39. Pal S, Radhakrishna P, Sahni P, Pande GK, Nundy S, Chattopadhyay TK (2005) Prophylactic surgery in non-cirrhotic portal fibrosis: is it worthwhile? *Indian J Gastroenterol* 24(6):239–242
40. Sarin SK, Wadhawan M, Agarwal SR, Tyagi P, Sharma BC (2005) Endoscopic variceal ligation plus propranolol versus endoscopic variceal ligation alone in primary prophylaxis of variceal bleeding. *Am J Gastroenterol* 100:797–804
41. Henderson JM, Yang Y (2005) Is there still a role for surgery in bleeding portal hypertension? *Nat Clin Pract Gastroenterol Hepatol* 2:246–247
42. Rikkers LF, Jin G, Langnas AN, Shaw BW Jr (1997) Shunt surgery during the era of liver transplantation. *Ann Surg* 226:51–57
43. Pal S, Desai PR, Rao YG, et al (2002) Non-cirrhotic portal fibrosis: results of surgery in 317 consecutive cases over a 25-year period from an Indian center (abstract). *J Hepatobiliary Pancreat Surg* 9(Suppl1):F-278, p135 also in *Gastroenterology* 2002;122(Supplement 4), July/August
44. García-Pagán JC, Caca K, Bureau C, Laleman W, Appenrodt B, Luca A, Abraldes JG, Nevens F, Vinel JP, Mössner J, Bosch J, Early TIPS (Transjugular Intrahepatic Portosystemic Shunt) Cooperative Study Group (2010) Early use of TIPS in patients with cirrhosis and variceal bleeding. *N Engl J Med* 362(25):2370–2379
45. Sarin SK, Govil A, Jain AK, Guptan RC, Issar SK, Jain M et al (1997) Prospective randomized trial of endoscopic sclerotherapy versus variceal band ligation for esophageal varices: influence on gastropathy, gastric varices and variceal recurrence. *J Hepatol* 26:826–832
46. Sarin SK, Gupta N, Jha SK, Agrawal A, Mishra SR, Sharma BC, Kumar A (2010) Equal efficacy of endoscopic variceal ligation and propranolol in preventing variceal bleeding in patients with noncirrhotic portal hypertension. *Gastroenterology* 139(4):1238–1245
47. Thomas V, Jose T, Kumar S (2009) Natural history of bleeding after esophageal variceal eradication in patients with extra hepatic portal venous obstruction: a 20 year follow-up. *Indian J Gastroenterol* 28:206–211
48. Bhargava DK, Dasarathy S, Atmakuri SP, Dwivedi M (1990) Comparative efficacy of emergency endoscopic sclerotherapy for active variceal bleeding due to cirrhosis of the liver, non-cirrhotic portal fibrosis and extrahepatic portal venous obstruction. *J Gastroenterol Hepatol* 5:432–437
49. Orloff MJ, Orloff MS, Girard B, Orloff SL (2002) Bleeding esophagogastric varices from extrahepatic portal hypertension: 40 years' experience with portal-systemic shunt. *J Am Coll Surg* 194:717–728
50. Bismuth H, Franco D, Alagille D (1980) Portal diversion for portal hypertension in children: the first ninety patients. *Ann Surg* 192:18–24
51. Alvarez F, Bernard O, Brunelle F, Hadchouel P, Odièvre M, Alagille D (1983) Portal obstruction in children. II. Results of surgical portosystemic shunts. *J Pediatr* 103:703–707
52. Mohapatra MK, Mohapatra AK, Acharya SK, Sahni P, Nundy S (1992) Encephalopathy in patients with extrahepatic obstruction after lienorenal shunts. *Br J Surg* 79(10):1103–1105
53. Menon P, Rao KL, Bhattacharya A, Thapa BR, Chowdhary SK, Mahajan JK et al (2005) Extrahepatic portal hypertension: quality of life and somatic growth after surgery. *Eur J Pediatr Surg* 15:82–87
54. Desai P (2000) Role of MRCP in delineating biliary abnormalities in patients with EHO before and after proximal lienorenal shunt [MCh (GI Surgery) dissertation]. All India Institute of Medical Sciences, New Delhi
55. Dhiman RK, Behera A, Chawla YK, Dilawari JB, Suri S (2007) Portal hypertensive biliopathy. *Gut* 56:1001–1008
56. Singh RK, Pal S, Sahni P, Acharya SK, Chattopadhyay TK (2004) Obstructive jaundice due to portal biliopathy—our experience with shunt surgery. (APASL\Abstract\42). *J Gastroenterol Hepatol* 19(Suppl):A691
57. Chaudhary A, Dhar P, Sarin SK, Sachdev A, Agarwal AK, Vij JC et al (1998) Bile duct obstruction due to portal biliopathy in extrahepatic portal hypertension: surgical management. *Br J Surg* 85:326–329
58. Pal S, Sahni P (2009) Extrahepatic portal venous obstruction: is the knife irrelevant? *Indian J Gastroenterol* 28(6):198–200
59. Superina R, Bambini DA, Lokar J, Rigsby C, Whittington PF (2006) Correction of extrahepatic portal vein thrombosis by the mesenteric to left portal vein bypass. *Ann Surg* 243:515–521
60. Sharma BC, Singh RP, Chawla YK, Narasimhan KL, Rao KL, Mitra SK (1997) Effect of shunt surgery on spleen size, portal pressure and esophageal varices in non cirrhotic portal fibrosis. *J Gastroenterol Hepatol* 12:582–584
61. Orozco H, Takahashi T, Mercado MA, Garcia-Tsao G, Hernandez-Ortiz J (1991) The Sugiura procedure for patients with haemorrhagic portal hypertension secondary to extrahepatic portal vein thrombosis. *Surg Gynecol Obstet* 173:45–48
62. Goyal N, Singhal D, Gupta S, Soin AS, Nundy S (2007) Transabdominal gastroesophageal devascularization without transection for bleeding varices: results and indicators of prognosis. *J Gastroenterol Hepatol* 22:47–50
63. Khan S, Tudor Smith C, Williamson P, Sutton R (2006) Portosystemic shunts versus endoscopic therapy for variceal

- rebleeding in patients with cirrhosis. *Cochrane Database Syst Rev* (4):CD000553
64. Johnson M, Rajendran S, Balachandar TG, Kannan D, Jeswanth S, Ravichandran P, Surendran R (2006) Transabdominal modified devascularization procedure with or without esophageal stapler transection—an operation adequate for effective control of a variceal bleed. Is esophageal stapler transection necessary? *World J Surg* 30(8):1507–1518
 65. Ezzat FA, Abu-Elmagd KM, Aly MA, Fathy OM, El-Ghawlby NA, El-Fiky AM, El-Barbary MH (1990) Selective shunt versus nonshunt surgery for management of both schistosomal and nonschistosomal variceal bleeders. *Ann Surg* 212(1):97–108
 66. Abu-Elmagd KM, Aly MA, Fathy OM, El-Ghawlby NA, El-Fiky AM, El-Barbary MH, El-Hak NG, El-Ebady GE, Sultan A, Bahgat OO et al (1993) Ten years of experience with patients with chronic active liver disease variceal bleeding: ablative versus selective decompressive therapy. *Surgery* 114(5):868–881
 67. Singhal D, Goyal N, Soin AS, Gupta S, Nundy S (2007) What are the essential components of a transabdominal devascularization procedure for bleeding esophageal varices? *World J Surg* 31(4):861–862, Letter
 68. Sarin SK, Lahoti D, Saxena SP, Murthy NS, Makwana UK (1992) Prevalence, classification and natural history of gastric varices: a long-term follow-up study in 568 portal hypertension patients. *Hepatology* 16:134–139
 69. Mishra SR, Sharma BC, Kumar A, Sarin SK (2011) Primary prophylaxis of gastric variceal bleeding comparing cyanoacrylate injection and beta-blockers: a randomized controlled trial. *J Hepatol* 54(6):1161–1167
 70. Mishra SR, Sharma BC, Kumar A, Sarin SK (2010) Endoscopic cyanoacrylate injection versus beta-blocker for secondary prophylaxis of gastric variceal bleed: a randomised controlled trial. *Gut* 59(6):729–735
 71. Ryan BM, Stockbrugger RW, Ryan JM (2004) A pathophysiologic, gastroenterologic, and radiologic approach to the management of gastric varices. *Gastroenterology* 126(4):1175–1189
 72. Lo GH, Liang HL, Chen WC, Chen MH, Lai KH, Hsu PI et al (2007) A prospective, randomized controlled trial of transjugular intrahepatic portosystemic shunt vs. cyanoacrylate injection in the prevention of gastric variceal rebleeding. *Endoscopy* 39:679–685
 73. Hong CH, Kim HJ, Park JH (2009) Treatment of patients with gastric variceal hemorrhage: endoscopic N-butyl-2-cyanoacrylate injection versus balloon-occluded retrograde transvenous obliteration. *J Gastroenterol Hepatol* 24:372–378
 74. Thomas PG, D'Cruz AJ (1994) Distal splenorenal shunting for bleeding gastric varices. *Br J Surg* 81:241–244
 75. Rosemurgy AS, Serafini FM, Zweibel BR, Black TJ, Kudryk BT, Nord HJ, Goode SE (2000) Transjugular intrahepatic portosystemic shunt vs. small-diameter prosthetic H-graft portacaval shunt: extended follow-up of an expanded randomized prospective trial. *J Gastrointest Surg* 4(6):589–597
 76. Rosemurgy AS, Zervos EE, Bloomston M, Durkin AJ, Clark WC, Goff S (2003) Post-shunt resource consumption favors small-diameter prosthetic H-graft portacaval shunt over TIPS for patients with poor hepatic reserve. *Ann Surg* 237(6):820–825, discussion 825–827
 77. Rosemurgy AS, Bloomston M, Clark WC, Thometz DP, Zervos EE (2005) H-graft portacaval shunts versus TIPS: ten-year follow-up of a randomized trial with comparison to predicted survivals. *Ann Surg* 241(2):238–246
 78. Henderson JM, Boyer TD, Kutner MH, Galloway JR, Rikkers LF, Jeffers LJ, Abu-Elmagd K, Connor J, DIVERT Study Group (2006) Distal splenorenal shunt versus transjugular intrahepatic portal systemic shunt for variceal bleeding: a randomized trial. *Gastroenterology* 130(6):1643–1651
 79. Kohli V, Pande GK, Dev V, Reddy KS, Kaul U, Nundy S (1993) Management of hepatic venous outflow obstruction. *Lancet* 342:718–722
 80. Zeitoun G, Escolano S, Hadengue A, Azar N, El Younsi M, Mallet A et al (1999) Outcome of Budd-Chiari syndrome: a multivariate analysis of factors related to survival including surgical portosystemic shunting. *Hepatology* 30:84–89
 81. Srinivasan P, Rela M, Prachalias A, Muiesan P, Portmann B, Mufti GJ, Pagliuca A, O'Grady J, Heaton N (2002) Liver transplantation for Budd-Chiari syndrome. *Transplantation* 73:973–977
 82. Mentha G, Giostra E, Majno PE, Bechstein WO, Neuhaus P, O'Grady J et al (2006) Liver transplantation for Budd-Chiari syndrome: a European study on 248 patients from 51 centres. *J Hepatol* 44:520–528
 83. Singhal D, de Castro S, Goyal N, Gouma DJ, Chaudhary A, van Gulik TM (2006) Current role of PSS in the management of HVOO. *Dig Surg* 23:358–369
 84. Kaul U, Agarwal R, Jain P, Sharma S, Sharma S, Wasir HS (1996) Management of idiopathic obstruction of the hepatic and suprahepatic inferior vena cava with a self-expanding metallic stent. *Cathet Cardiovasc Diagn* 39:252–257
 85. Rossle M, Olschewski M, Siegerstetter V, Berger E, Kurz K, Grandt D (2004) The Budd-Chiari syndrome: outcome after treatment with the transjugular intrahepatic portosystemic shunt. *Surgery* 135:394–403