Portal Hypertension

Bimaljit S. Sandhu, MBBS, MD, DM
Arun J. Sanyal, MBBS, MD

Cirrhosis of the liver causes nearly 32,000 deaths and more than 20 million lost workdays annually in the United States, most of which are directly related to the development of portal hypertension and its complications.[1] Normal portal vein pressure is between 5 and 10 mm Hg. Portal hypertension occurs when the portal vein pressure gradient increases by 5 mm Hg or more. The principal consequences of portal hypertension include the development of varices, variceal hemorrhage, and/or ascites, all of which are major complications of cirrhosis. Given the contribution of portal hypertension to the outcome of cirrhosis, appropriate management of portal hypertension is a cornerstone of managing cirrhosis. This article reviews the pathophysiology of portal hypertension and the primary and secondary prophylaxis of variceal bleeding.

TAKE HOME POINTS

- Hepatic stellate cells and vasoactive cytokines, such as nitrous oxide, play an important role in the development of portal hypertension.
- Esophagogastric variceal bleeding is the most common and dreaded complication of portal hypertension. Varices develop when the portal pressure exceeds 12 mm Hg.
- All patients with cirrhosis must undergo screening endoscopy to identify varices at risk for bleeding.
- Nonselective β-blockers should be used for primary prophylaxis of variceal hemorrhage in high-risk varices. Endoscopic variceal band ligation may be used as an alternative in patients who have side effects from or contraindications to the use of β-blockers.
- Endoscopic variceal band ligation should be used for secondary prophylaxis of variceal hemorrhage to eradicate varices, although β-blockers are also effective.

ANATOMY OF THE PORTAL SYSTEM

The portal vein is formed by the confluence of the left gastric vein, superior and inferior mesenteric veins, splenic vein, and the veins from the pancreatic bed. The portal venous system communicates with other veins that directly drain into the systemic circulation at the lower end of esophagus and gastric cardia via the extrinsic and intrinsic veins; at the anal canal via anastomoses between the superior and the middle hemorrhoidal veins; at the splenic venous bed and the left renal vein or adrenal vein; at the umbilical and paraumbilical veins; and in the retroperitoneum. In addition, the falciform ligament is a well-known site for development of portal hypertension due to recanalization of the paraumbilical vein. Recanalization opens the primitive circulation sites that were once important to fetal circulation. These portasystemic venous communications allow blood to flow into the systemic circulation only when portal pressure rises above the normal level. Increased blood pressure leads to enlargement of these collaterals, which become varicose and sometimes bleed.[2–4]

Of the collateral varices, the gastroesophageal are most important given their propensity to bleed. Gastroesophageal varices divert portal venous inflow by accommodating blood from the left gastric vein and the splenic hilus through the short gastric veins. The veins draining the esophagus are called the intrinsic, extrinsic, and vena comitantes of the vagus. Vianna and colleagues[5] divided the intrinsic veins of the gastroesophageal junction into 4 zones: gastric, palisade, perforating, and truncal. The perforating veins penetrate from the submucosa at random intervals to drain into the extrinsic veins. Portasystemic shunting via the gastroesophageal collaterals partially compensates for the increased resistance to portal outflow seen in portal hypertension; with shunting, the valves in the perforating veins become incompetent, which allows reverse flow from the extrinsic to the intrinsic veins. The intrinsic veins at the gastroesophageal junction become dilated and

Dr. Sandhu is an assistant professor, and Dr. Sanyal is chairman, Division of Gastroenterology, Hepatology and Nutrition, VCU Medical Center, Richmond, VA.

tortuous, forming gastroesophageal varices, which occur in 4 patterns: (1) fundal varices that are fed by short gastric veins but may also be fed by the left gastric vein; (2) gastric and palisade zone varices (the most commonly seen varices in clinical practice); (3) varices in the perforating zone; and (4) paraesophageal varices that involve the extrinsic veins and are not at risk for bleeding.

PATHOPHYSIOLOGY OF PORTAL HYPERTENSION

Portal venous pressure is a product of the portal venous inflow and resistance to outflow (Ohm's law): $P = Q \times R$, where P is portal vein pressure, Q is blood flow, and R is resistance to outflow. Portal hypertension develops in patients with cirrhosis because there is increased resistance to the portal venous outflow at the level of the sinusoids, primarily due to architectural changes. Clinically, portal pressure is measured from the hepatic venous pressure gradient (HVPG): HVPG = WHVP – FHVP, where the wedged hepatic vein pressure (WHVP) reflects the sinusoidal pressure and the free hepatic venous pressure (FHVP) is the correction for the intra-abdominal pressure. The HVPG most closely reflects the portal pressure when the portal vein is patent.

Increased Vascular Resistance

In patients with cirrhosis, dynamic changes in the vasculature and fixed changes in the hepatic architecture lead to decreased compliance in the portahepatic circulation, which increases outflow resistance. The fixed architectural changes in the cirrhotic liver are produced by collagen deposition in the perisinusoidal space (capillarization of the sinusoids). Hepatic stellate cells that surround the hepatic sinusoids also play an active role in modifying resistance to hepatic blood flow. These cells exhibit a contractile response to vasoconstrictors, which are found in increased levels in the blood and liver tissue of patients with cirrhosis.[6,7] A relative deficiency of the vasodilator nitric oxide (NO) in the intrahepatic circulation also has been found and can lead to worsening of intrahepatic vasoconstriction.[8] High circulating levels of noradrenaline, angiotensin II, and vasopressin potentially contribute to the increased intrahepatic vascular resistance. Finally, the extrahepatic portosystemic collateral system exhibits a contractile response to various vasoactive substances, which further worsens the preexisting resistance to portal venous outflow.

Increased Portal Venous Inflow

Increased portal venous inflow contributes to the development and aggravation of portal hypertension in patients with cirrhosis. This aspect of portal hypertension is characterized by increased vascular capacity and decreased systemic vascular resistance, which produces hemodynamic disturbances including an increased cardiac index and absolute circulatory volume as well as a decrease in effective circulating volume.

Endogenous Vasoactive Mediators

Humoral factors such as NO, glucagon, eicosanoids, adenosine, bile salts, platelet-activating factor, and gamma-aminobutyric acid have a role in the pathophysiology of portal hypertension. Glucagon causes splanchnic vasodilation, and its levels are increased in portal hypertension. NO, a vascular endothelium-derived relaxant factor and a very potent vasodilator, may play a role in the hyperdynamic circulation seen in cirrhosis patients.[9] NO relaxes the vascular smooth muscle by activating soluble guanylate cyclase. Cirrhotic patients have been shown to have high levels of the metabolic products of NO, and inhibition of NO synthesis by methylene blue restores the splanchnic vascular reactivity to vasoconstrictors, ameliorates the systemic hemodynamic changes, increases blood pressure, and improves oxygenation in hepatopulmonary syndrome.[10]

ENDOSCOPIC CLASSIFICATION OF GASTROESOPHAGEAL VARICES

Esophageal Varices

Esophageal varices are classified on the basis of their endoscopic appearance, location, and the extent to which they protrude into the esophageal and gastric lumen. The classification proposed by the North Italian Endoscopic Club (NIEC) is widely used because it is simple and has fair to excellent interobserver concordance.[11] Varices are categorized as: F1, small, straight varices; F2, enlarged, tortuous varices occupying less than one third of the esophageal lumen; or F3, large, coil-shaped varices occupying more than one third of the esophageal lumen.[12]

Gastric Varices

Gastric varices are classified according to the Sarin classification system based on their location in the stomach and their relationship with the esophageal varices.[13] Gastroesophageal varices (GOV) are those that extend from the esophagus to the stomach. They are further classified as: type 1 (GOV1) when they extend from the esophagus to the lesser curve of the stomach 2 to 5 cm below the gastroesophageal junction; and type 2 (GOV2) when the varices are long and tortuous and extend from the esophagus towards the fundus of the stomach. Isolated gastric varices (IGV) are those that

are not directly continuous with esophageal varices and are further classified as: type 1 (IGV1) when the varices are located in the fundus and are tortuous and complex in shape; and type 2 (IGV2) when the varices are located in the body, antrum, or around the pylorus.

Portal Hypertensive Gastropathy Classification

Portal hypertensive gastropathy is classified as mild when a mosaic-like pattern of mild degree is present (without redness at the areola) and severe when a mosaic-like pattern is superimposed by any red color signs.[14]

Table 1. Intravariceal Pressure and Risk of Variceal Bleeding

Variceal Pressure (mm Hg)	Incidence of Variceal Bleeding (%)
≤ 13	0
13.1–14	9
14.1–15	17
15.1–16	50
> 16	72

Data from Nevens F, Bustami R, Scheys I, et al. Variceal pressure is a factor predicting the risk of a first variceal bleeding: a prospective cohort study in cirrhotic patients. Hepatology 1998;27:15–9.

NATURAL HISTORY OF GASTROESOPHAGEAL VARICES

Gastroesophageal varices are seen in 50% to 60% of cirrhotic patients at presentation; 20% of these patients present with large varices.[15] In those without varices at presentation, varices develop at highly variable rates, ranging from 5% to 15% annually.[16] Small varices develop into large varices at a rate of 4% to 10% annually. Approximately 25% to 35% of cirrhotic patients with gastroesophageal varices will eventually bleed within 2 years of diagnosis of varices, with the risk being greatest within 6 to 12 months of detection.[12,17]

Predictive Factors for Variceal Bleeding

Varices develop when the HVPG exceeds 12 mm Hg, but there is a poor correlation between an HVPG exceeding 12 mm Hg and risk of variceal bleeding.[18] However, once bleeding occurs, patients with a HVPG exceeding 20 mm Hg are more likely to continue to bleed and fail first-line therapy.[19] High intravariceal pressure has also been correlated with the risk of bleeding (**Table 1**),[20] and in a study of patients with cirrhosis, those who bled had a higher variceal pressure than patients who did not bleed even though the HVPGs in the 2 subgroups were similar.[21]

The frequency of bleeding from large varices is 50% to 53% as compared with 5% to 18% with small varices.[12,22] The presence of red color signs identified during endoscopy, such as red wale marks (longitudinal red streaks on the varices), cherry red spots (discrete cherry-colored flat spots on the varices), and hematocystic spots (raised discrete red spots on varices resembling blisters), in addition to the size of the varices and the severity of cirrhosis can predict the probability of variceal bleeding fairly reliably (**Table 2**).[12] A patient with Child-Pugh class C cirrhosis with NIEC class F3 varices and extensive red wale marks has a 76% likelihood of bleeding within 1 year of diagnosis.

The risk of rebleeding is quite high for the 6 weeks following an index bleeding episode; over 50% of such episodes occur within 3 to 4 days from admission for bleeding.[23–25] The risk factors for early rebleeding are severe initial bleeding (defined as hemoglobin < 8 g/dL), gastric variceal bleeding, thrombocytopenia, encephalopathy, alcohol-related cirrhosis, large varices, active bleeding during endoscopy, and a high HVPG (**Table 3**).[13,24–26]

Gastric varices have a higher frequency of bleeding (nearly 25%), and the risk of bleeding is related to their location.[13] Although more than 70% of gastric varices are classified as GOV1, bleeding occurs in only 11%. Yet IGV1 varices, which constitute only 8% of all gastric varices, account for 80% of varices that bleed.[18] In the case of IGV1, the risk of variceal bleeding is directly proportional to variceal size (> 10 mm), severity of liver disease, and presence of red color signs.[13] After obliteration of the esophageal varices by sclerotherapy or endoscopic variceal band ligation (EVL), GOV1 spontaneously regress in approximately 60% of cases. Esophageal variceal obliteration has no effect on GOV2.

Variceal Screening

All patients with cirrhosis must undergo screening endoscopy to identify varices at risk for bleeding. Patients with no varices on screening endoscopy should be screened every 2 years if they have stable liver function and yearly if deterioration of liver function occurs.[16,27] Patients with small varices at screening should also be screened annually.

MANAGEMENT OF PORTAL HYPERTENSION

Management may be considered in 3 phases: (1) primary prophylaxis, (2) control of acute bleeding episode, and (3) prevention of rebleeding. The various management tools available either attempt to correct portal hypertension or provide local treatment for varices.

Table 2. Probability of Variceal Bleeding According to the North Italian Endoscopy Club (NIEC) Index

	Child-Pugh Class								
	A			B			C		
Red Wale Marks	**F1**	**F2**	**F3***	**F1**	**F2**	**F3***	**F1**	**F2**	**F3***
None	6	10	15	10	16	26	20	30	42
Present	8	12	19	15	23	33	28	38	54
Extensively present	16	23	34	28	40	52	44	60	76

NOTE: Probability is in percentage.

Adapted with permission from Prediction of the first variceal hemorrhage in patients with cirrhosis of the liver and esophageal varices. A prospective multicenter study. The North Italian Endoscopic Club for the Study and Treatment of Esophageal Varices. N Engl J Med 1988;319:983–9. Copyright © 1988 Massachusetts Medical Society.

*F1, F2, F3 are NIEC categories that denote progressively larger varices. F1 = small, straight varices; F2 = enlarged, tortuous varices occupying less than one third of esophageal lumen; F3 = large, coil-shaped varices occupying more than one third of the esophageal lumen.[5]

Primary and secondary prophylaxis of variceal bleeding are discussed below.

Primary Prophylaxis of Variceal Bleeding

Nonselective β-adrenergic receptor antagonists and nitrates are the mainstay of therapy in the prevention of a first variceal bleeding episode. EVL has emerged as a modality for the primary prophylaxis of variceal bleeding and appears promising but needs further confirmation in clinical trials.

Pharmacologic therapy. Nonselective β-blockers (propranolol and nadolol) are the most widely used and studied drug in the prevention of a first variceal bleeding episode. These agents block the β-adrenergic receptor–mediated vasodilation of the mesenteric arterioles and promote unopposed β-receptor–mediated vasoconstriction, thereby decreasing portal venous inflow and ultimately portal pressure. At high doses, β-blockers decrease blood pressure and cardiac output, further decreasing portal venous inflow and hence portal pressures.[28,29] The dose of β-blockers is titrated to achieve a target resting heart rate between 55 and 60 bpm or a 25% decrease in the resting basal heart rate. In patients who cannot achieve these targets, the dose is titrated to maximal tolerated doses. The dose of propranolol required for adequate β-receptor blockade varies from 80 to 160 mg/day, usually given in 2 divided doses, whereas the dose for nadolol varies from 40 to 80 mg/day. However, none of the above targets correlate well with decreases in portal blood pressure. Patients whose HVPG decreases below 12 mm Hg or by 25% have a high probability of remaining free of variceal bleeding.[30,31]

A meta-analysis of 9 randomized controlled trials concluded that the use of nonselective β-blockers decreases the risk of initial hemorrhage in patients with cirrhosis and gastroesophageal varices.[32] A decreased risk of variceal bleeding was observed in 7 trials and was statistically significant in 4 of these trials. The risk of death was decreased (odds ratio, < 1.0) in 7 of the 9 trials, and reached statistical significance in 1 trial.[33] These data have been corroborated by 2 recent meta-analyses,[34,35] which confirm that nonselective β-blockers reduce the incidence of initial variceal bleeding by 45% and decrease bleeding-related mortality by 50%.

Propranolol is the most cost-effective therapy for primary prophylaxis of variceal bleeding in cirrhotic patients who have esophageal varices regardless of their Child-Pugh class and risk of bleeding.[36] As most studies have recruited patients with medium to large varices, these results cannot be extrapolated for using β-blockers in patients with small varices. Between 50% and 70% of patients receiving propranolol fail to decrease HVPG below 12 mm Hg or sustain a decrease in portal pressures by 20% of the baseline portal pressure.[28,30,31,37] β-Blocker therapy is associated with many side effects, including bronchospasm, heart failure, and sexual dysfunction (which accounts for discontinuation of therapy in around 20% of patients).[38] On discontinuation, the risk of variceal bleeding returns to the level in an untreated patient; however, mortality is increased compared with those who continue treatment.[39]

Isosorbide dinitrate, isosorbide 5-mononitrate (ISMN), and nitroglycerine are the most frequently evaluated vasodilators for controlling portal hypertension. Nitrates are predominantly systemic venous dilators at usual doses and decrease the cardiac output by decreasing venous return as well as postsinusoidal

resistance, which thereby reduces portal pressure. At high doses, there is arterial dilation and systemic hypotension that triggers splanchnic arterial constriction, further decreasing the portal blood inflow and the portal pressures. Nitrates decrease portal and collateral outflow resistance by venodilation, further decreasing portal and variceal pressure and counteracting the increased portal-collateral resistance associated with the use of β-blockers.

Various randomized controlled trials have evaluated the role of nitrates for primary prophylaxis of variceal hemorrhage.[40–46] Although ISMN monotherapy was as effective as nadolol in preventing variceal hemorrhage,[47] it was also associated with a higher mortality rate, especially in patients older than age 51 years. A combination of ISMN and nadolol has been shown to be superior to nadolol alone (12% versus 29%) for the primary prophylaxis of variceal bleeding.[42] The current role of nitrates is restricted to combination therapy along with a nonselective β-blocker in selected individuals with high-risk varices who have relatively preserved liver function.

Endoscopic sclerotherapy (EST). EST is based upon the principle of variceal thrombosis and scarring by injection of a sclerosing agent. Various types of sclerosing agents are used. Tissue adhesives, such as N-butyl-2-cyanoacrylate (tissue glue), have been used successfully in the sclerosis of gastric varices.[47] EST trials were highly heterogeneous in regards to the treatment effects on both bleeding and mortality as well as the bleeding rate of untreated groups.[48,49] Primary prophylaxis of variceal bleeding with β-blockers is more cost-effective than EST.[36] Therefore, EST has no role in the primary prophylaxis of variceal hemorrhage.

Endoscopic variceal band ligation. EVL works by mechanically occluding varices and variceal flow. An elastic band is used to strangulate the varix, producing thrombosis, inflammation, necrosis, and finally sloughing of the mucosa, which heals with formation of a mural scar that is restricted to the mucosa and submucosa. The banding device consists of a cylinder preloaded with elastic bands. The varix to be ligated is suctioned into the cylinder and when complete obliteration of the field of vision by the varix ("red out") occurs, the band is released by the trigger wire. The bands are applied circumferentially starting from the gastroesophageal junction. Five to 10 bands are applied in each session. Esophageal varices are obliterated more rapidly with EVL compared with EST, and it is associated with fewer complications.[50]

EVL is effective in preventing the initial bleed when compared with no treatment,[51,52] but it is not superior to β-blockers.[53,54] Although 1 study found EVL to be superior to propranolol for primary prophylaxis,[55] other studies have failed to confirm this benefit.[53,54] The bleeding rates associated with the propranolol group[55] were higher than those reported with placebo in another study published by the same group in the same time period.[56] Recently, 2 studies have shown that the combination of EVL and β-blockers is as effective or even better than EVL alone in the primary prophylaxis of bleeding from high-risk varices.[57,58] In a meta-analysis that included 601 patients from 5 trials that compared prophylactic EVL with untreated controls, investigators found that prophylactic EVL was associated with a decreased risk of first variceal bleeding (relative risk [RR], 0.36), bleeding-related mortality (RR, 0.20), and all-cause mortality (RR, 0.55) compared with no treatment.[59] In this meta-analysis, a reduction in the risk of first variceal bleeding was still apparent when the analysis was limited to 4 trials in which prophylactic EVL was compared with β-blocker therapy (RR, 0.48). However, there was no effect on bleeding-related or all-cause mortality. Similar conclusions were reached in a subsequent meta-analysis that included 8 randomized controlled trials.[60] Currently, β-blocker therapy remains the first-line modality of primary prophylaxis for variceal bleeding, and EVL should be used in patients with contraindications or side effects to these medications.

Table 3. Risk Factors for Rebleeding in Esophageal Varices

Early rebleeding (< 6 weeks)	Late rebleeding (> 6 weeks)
Age > 60 years	Severity of liver failure
Severity of initial bleed	Ascites
Ascites	Hepatoma
Active bleeding on endoscopy	Active alcoholism
Red color signs	Red color signs
Platelet clot on varices	
Renal failure	

Recommendations

It is recommended that all patients with cirrhosis undergo screening endoscopy. Patients who do not have varices should have repeat endoscopy performed at 2- to 3-year intervals, whereas those with small varices should have endoscopy repeated every year. Patients with normal liver function (Child-Pugh class A) and NIEC class F2 or F3 varices or those with advanced liver failure and varices of any size should be considered for primary prophylaxis with a nonselective β-blocker. The dose should be titrated to achieve a resting heart rate

between 55 and 60 bpm. Patients with poor response and/or adverse reaction to β-blockers may be considered for EVL. Nitrates may be used in combination with a nonselective β-blocker in selected cases of young patients who have well-preserved liver function.

Secondary Prophylaxis of Variceal Bleeding

Combination therapy. Secondary prophylaxis is recommended in all the patients who survive an index episode of variceal hemorrhage due to a very high rate of rebleeding. Again, nonselective β-blockers are the most studied pharmacologic agents for the secondary prophylaxis of variceal bleeding. Most trials focusing on nonselective β-blockers showed improved rebleeding rates.[61–63] Overall, there was a 40% decreased risk of bleeding and a 20% decreased risk of death.[34,64] Presence of hepatocellular carcinoma, poor patient compliance, lack of persistent decrease in pulse, and continued alcohol abuse are associated with poor outcomes of β-blocker therapy.[65] EST is somewhat superior to β-blocker therapy in prevention of rebleeding, but EST does not confer a survival advantage.[32] Combination of ISMN and nadolol was found to be superior to EST as well as EVL with respect to the incidence of rebleeding, but the mortality rate between the 2 groups was not significantly different.[66]

Combination of pharmacologic therapy (nadolol or propranolol) and EST has been compared with EST alone in many clinical trials. In a meta-analysis, 10 clinical trials comparing the 2 treatment options showed that the combination is better than EST alone.[32] Combination of EST and propranolol was found to be superior to propranolol alone in decreasing the rebleeding rate and risk of death.[67] A recent randomized trial comparing the combination of EVL, sucralfate, and nadolol versus EVL alone showed that the combination is better than EVL alone in preventing rebleeding (23% versus 47%).[68]

Endoscopic therapy. EST is superior to placebo in decreasing both the rebleeding risk (from 70% to 40%–50%) and risk of death (from 50%–75% to 30%–60%).[63,67,69,70] However, EVL is superior to EST for the prevention of rebleeding and has fewer complications. Also, EVL requires fewer sessions to achieve variceal obliteration when compared with EST.[32] However, the recurrence of varices is higher with EVL than with EST. Variceal eradication rates with the combination of EVL and EST versus EST alone were similar, but the complication rate (3% versus 20%) and rebleeding rate (3% versus 16%) were lower with combination therapy. Other clinical trials, however, demonstrated a higher incidence of complications in the combination group, without reducing the number of sessions required to eradicate varices.[71] EVL is, therefore, the preferred endoscopic intervention for secondary prophylaxis.

Transjugular intrahepatic portosystemic shunts (TIPS). TIPS are more effective than endoscopic therapy for prevention of recurrent variceal bleeding, with a cumulative risk of bleeding at 1 year between 8% and 18%.[72–74] TIPS were associated with better long-term control of bleeding; however, there was no survival benefit with TIPS, and the risk of encephalopathy was significantly higher in patients after TIPS (25%–33%).[75] TIPS are used as a salvage therapy in the patients with bleeding refractory to endoscopic therapy. Presently, TIPS surgery is not a first-line modality for the secondary prophylaxis of variceal hemorrhage.

Shunt surgery. Surgical shunt is an excellent option to prevent recurrent variceal bleeding in patients who have failed on endoscopic and/or pharmacologic therapies. There are 4 published trials comparing distal splenorenal shunt (307 patients) with EST,[76–78] and 3 trials comparing central portal-caval shunts.[79,80] Shunt surgery when compared with EST significantly reduced the incidence of rebleeding (odds ratio, 0.18 [95% confidence interval {CI}, 0.12–0.28]) but failed to show a survival benefit and significantly increased the incidence of hepatic encephalopathy (odds ratio, 2.11 [95% CI, 1.1–4.0]). Recurrent bleeding after shunt surgery occurs in 10% to 20% of the patients, with the highest risk occurring in the first month after surgery.[77] Devascularization procedures are usually considered in patients with contraindications to shunts such as splanchnic vascular thrombosis and should be performed by experienced surgeons. The choice of surgical procedure should be individualized and must take into account the severity of the liver disease and the local expertise in the procedure.

Recommendations

The optimal approach to the prevention of recurrent variceal hemorrhage in patients with cirrhosis is uncertain. A decision analysis suggested that combination therapy with medications and EVL is an optimal strategy. Combined therapy is preferred because it showed resilience in patients who had poor compliance with medical therapy. However, patients are best served by medications, EVL, or a combination of both, depending, in part, upon the preferences of the treating physicians. TIPS surgery is reserved for those who have recurrent bleeding despite these options and are candidates for liver transplantation.

SUMMARY

Portal hypertension is an important complication of cirrhosis that is associated with a high rate of morbidity and mortality. Varices do not develop when HVPG is below 12 mm Hg. All patients with cirrhosis must undergo screening endoscopy to identify varices that are at risk of bleeding. Patients without varices on screening endoscopy should be screened every 2 years if they have stable liver function and yearly if their liver function deteriorates. Patients with small varices at screening should be re-screened on a yearly basis. For primary prophylaxis, nonselective β-blockers are first-line therapy; however, the role of EVL is still emerging. Secondary prophylaxis of variceal bleeding is accomplished using medications, EVL, or a combination of both depending, in part, upon the preferences of the treating physicians. **HP**

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