Review

Management of variceal bleeding

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SUMMARY

Portal hypertension, a common clinical syndrome of chronic liver disease, is characterised by a pathologic increase in portal pressure, that causes dilation of portosystemic collateral vessels, leading to the formation and bleeding of oesophagogastric varices. Large varices, measuring more than 5 mm in diameter, have a greater predisposition to spontaneouse rupture than small varices below this level (<10% bleeding risk at 2 years). At endoscopy, bleeding can be attributed to varices if there is a venous spurt or a venous ooze or an adherent clot (cherry red spots, red wale markings, hemocystic spots) or if a 'platelet aggregate' (white in colour) is doserved. The management of variceal bleeding includes surgical, endoscopical and medical procedures and can be considered in three different distinct situations: a) acute bleeding episodes (emergency treatment), b) prevention of variceal rebleeding (secontary prophylaxis) and c) prevention of the first variceal bleeding episode (primary prophylaxis).

Key words: Variceal bleeding, Sclerotherapy, TIPS, Variceal ligation, b-blockers, Shunt surgery, Octreotide.

INTRODUCTION

The first variceal bleeding was described in 1840 and the relationship of esophageal varices, bleeding and liver disease in 1900.[1] Variceal bleeding is the most frequent severe complication of portal hypertension (affects 30-60% of cirrhotic patients) and a leading cause of death and liver transplantation in patients with cirrhosis.[2,3] About one third of patients bleed within 2 years after

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the diagnosis of varices.[4] Patients with compensated liver disease bleed in only 30% of cases, while those with decompensated liver disease bleed in 60% of cases with oesophagogastric varices.[5] Patients surviving variceal bleeding are at high risk of rebleeding, about 60% at 1 year.[6] Patients with cirrhosis surviving a variceal bleed are at higher risk of rebleeding, (over 70% at 1 year) and mortality from each rebleeding episode is about 20%.[6,7] The most important factor predicting mortality of variceal bleeding is liver disease. Most studies have found a correlation between the extent of liver failure in patients with bleeding oesophageal varices, as expressed by the Child-Pugh-Classification (Table 1) and mortality.[7] Survival statistics are best for patients with minimal liver dysfunction (Child's group A) and worst (mortality 70-80%) for the sickest patients (Child's group C).[7,8]

GENERAL MANAGEMENT

The important points, in order to reduce mortality in variceal bleeding, is accurate diagnosis and early treatment. The specific aims should be: 1) correct hypovolaemia, 2) bleeding cessation as soon as possible, 3) prevention of early rebleeding, 4) prevention complications associated with bleeding, 5) prevention deterioration in liver function.[9] Clinical and laboratory evidence of both severity of haemorrhage and liver disease should be included in the initial assessment, as these have prognostic significance. The keystone of therapy for variceal bleeding remains aggressive resuscitation with blood products.[10] It is essential to avoid over-transfusion, because it increases portal pressure and can, therefore, negatively influence hemorrhage control.[11] Large volume transfusion may also lead to impaired haemostasis and throbocytopenia.[11] Based on a consensus at the Baveno III meeting, blood volume restitution should be done cautiously, in order to maintain the haematocrit level between 25-30% and haemodynamic stability[3] (systolic blood pressure >85-90 mmHg and heart rate <100-110

Table 1. Child's-Pugh Classification of cirrhosis

Feature	1 Point	2 Points	3 Points
Encephalopathy (Stage)	0 (absent)	1-2	3-4
Ascites	absent	slight	poorly controlled
Bilirubin (mg/dL)	<2.0	2.0-3.0	>3.0
Albumin (g/dL)	>3.5	2.8–3.5	<2.8
INR	<1.7	1.7–2.3	>2.3

Class A: 5–6 points, Class B: 7–9 points, Class C: 10–15 points

b.p.m.). Bacterial infection is an independent prognostic factor of failure to control bleeding or early rebleeding.[12] Bacterial infections have been documented in 35%-66% of patients with cirrhosis who have variceal bleeding.[13] A recent meta-analysis has demonstrated that antibiotic prophylaxis significantly increased the mean survival rate and also increased the mean percentage of patients free of infection.[12,13] All cirrhotics with upper gastrointestinal bleeding should receive prophylactic antibiotics whether sepsis is suspected or not.[14] This includes the administration of oral nonabsorbable antibiotics (norfloxacin or others) over 5 days, in order to reduce the incidence of severe bacterial infections produced by microorganisms of enteric origin.[14,15]

PRIMARY PROPHYLAXIS

Patients who have esophageal varices but who have never had a bleeding episode may be treated medically or endoscopically (primary prophylaxis). Without treatment, 30-60% of cirrhotic patients with varices bleed, and this risk is reduced by approximately 50% with therapy.[6] Medical therapy includes non-selective beta blockers with or without nitrates. Compliance and side effects limit efficacy.[16] Endoscopical treatment includes variceal ligation (EVL) and sclerotherapy (ES).[17] Studies of endoscopic therapy with ligation demonstrate that in select patients, those with large varices, endoscopic banding may reduce the risk of first bleeding episode when compared with b-blockers.[18] Primary prophylaxis with ES is not warranted because of evidence suggesting that complications outweigh benefits.[17] Based on a consensus at the Baveno III meeting, measurement of hepatic venous pressure gradient-HVPG should be used routinely in the initial investigation of cirrhotic patients, as it is a very useful clinical marker of portal pressure and predicts survival in prophylaxis for variceal haemorrhage.[19] Clinically significant portal hypertension is defined as HVPG >12 mmHg and a value of 16 mmHg may be a threshold

portal pressure for survival, while normal HVPG is below 5 mmHg.[20] Many studies show that if drug therapy achieves a reduction in HVPG of at least 20% of the baseline value, even without reaching values below 12 mm Hg, the residual risk of variceal bleeding is low, about 10% at 2 years.[19,20] Although it has been customary to adjust the dose of b-blockers to achieve a 25% fall in the resting heart-rate, this reduction by no means guarantees an effective fall in HVPG and there is no correlation between changes in heart rate and changes in HVPG.[19] Once pharmacologic therapy is initiated, follow-up measurements of HVPG should be made every 3 months.[20] Beta-blockers and EVL are the best options for primary prophylaxis of variceal bleeding.

SECONTARY PROPHYLAXIS

After an initial variceal bleed the risk of a second bleed is high and therapy is warranted to reduce the risk of rebleeding (secondary prophylaxis). It is estimated that 17-42% of patients with early hemostasis will rebleed within 5–10 days of their initial hemorrhage.[6] The likelihood of rebleeding in untreated patients is 55-67%.[6] Early rebleeding is significantly associated with worsening mortality.[21] Thus treatments regime should be evaluated in terms of providing a bleed-free interval of at least 5 days, which allows some recovery of the patient and provides an opportunity for secondary preventative therapy to be instituted.[21] The options are similar to those for primary prophylaxis and, in addition to medical and endoscopic therapy, transjugular intrahepatic portosystemic shunts (TIPS) and surgical shunts are therapeutic options.[22] The combination of endoscopic therapy (EVL and/or ES) with medical therapy is the initial approach to prevent variceal rebleeding.[21,25] If pharmacological treatment is chosen, vasoactive drugs are the drugs of choice.[23] Based on a consensus at the Baveno III meeting, the final agreement for the duration of *iv* vasoactive drug administration for preventing a rebleeding episode was to give pharmacological treatment for at least 48h and until 5 days.[3] Assessment of the HVPG response is advised during pharmacological therapy for the prevention of rebleeding.[24,79] EVL is preferred to ES because banding is associated with lower bleeding rates and fewer complications.[26] TIPS is useful in cases refractory to endoscopic therapy or in uncontrolled variceal hemorrhage.[27] Surgical shunts are typically reserved for patients in whom TIPS cannot be performed for technical reasons or for well-compensated cirrhotic patients.[28] In conclusion, drug therapy is a simple and safe way to prevent variceal rebleeding, provided target reductions in HVPG

are achieved and EVL seems to be superior to ES for obliteration of esophageal varices.

ACUTE BLEEDING

Acute bleeding from esophageal varices requires an endoscopic evaluation and therapeutic intervention (emergency treatment). EVL and ES are equally effective for treatment of active bleeding.[29] Moreover, some studies demonstrate that in some patients EVL may not be possible because of limited visualization from bleeding and ES is used because it is easier to perform in this setting.[30] Drug therapy with terlipressin, vasopressin plus nitroglycerin, somatostatin or octreotide have been shown to be effective and may be used as initial treatment before sclerotherapy or ligation for the treatment of acute variceal bleeding.[31] Octreotide and terlipressin were shown to be as effective as sclerotherapy in achieving initial hemostasis.[32] If variceal bleeding cannot be controlled, then a Minnesota or a Sengstaken-Blakemore tube should be placed.[33] TIPS is effective rescue therapy for controlling acute variceal hemorrhage in circumstances when other methods fail.[34]

A. ENDOSCOPIC PROCEDURES

1. Endoscopic Variceal Ligation (EVL)

EVL was introduced in the late 1980s and has achieved wide application and confirmation of efficacy.[35] During EVL a standard endoscope is outfitted with a special ligating chamber at its tip.[36] After a varix is identified, an elastic "O" ring around the neck of the varix is released, creating a "polyp".[36] This results in the coagulative necrosis of the ensnared polyp with eventual sloughing.[36] The performance of EVL may be technically difficult in an esophagus awash in blood.[37] High recurrence rates following EVL could be related to inability to further ligate varices once they became small and lack of effect on perforating veins and paraesophageal collaterals.[38] At follow-up endoscopy sessions, it becomes increasingly difficult to ligate residual, partially-treated varices. A combination of EVL for large varices and ES for small varices may be warranted.[39] Sequential and simultaneous ligation and sclerotherapy were more effective than ligation alone, in reducing the recurrence rate after variceal obliteration.[40]

2. Endoscopic Sclerotherapy (ES)-Tissue Adhesives

In ES, an irritant solution (sodium morrhuate, ethanolamine or polidocanol) or a dehydrating chemical (so-

dium tetradecyl sulfate) is injected into an esophageal varix or its adjacent supporting tissues.[41] The goal is the acute induction of vascular spasm with subsequent development of intravariceal thrombosis, intimal thickening and perivenous fibrosis. By the mid-1980s, it was recognized that ES could achieve early hemostasis in up to 95% of patients suffering from variceal bleeding.[42] ES has a number of important problems. First, it usually takes 3-6 sessions to obliterate esophageal varices.[43] Furthermore, ES is rarely successful in the emergent control of bleeding from large gastric varices and plays no role in treating the bleeding which may develop from portal hypertensive gastropathy.[44] Finally, side effects and procedural complications are common. The most common complications result from the development of post-sclerotherapy esophageal ulcers.[45] Patients may experience chest pain or odynophagia in the early post-ES period.[46] ES-induced strictures occasionally necessitate additional endoscopy to facilitate esophageal dilation. Other important complications of ES include esophageal perforation, systemic infection, pleural effusion, aspiration pneumonia, adult respiratory distress syndrome, mediastinitis and portal and mesenteric venous thrombosis.[47] We use sclerotherapy technique to inject the tissue adhesives in an attempt to occlude the lumen of bleeding varices.[48] Two types of tissue adhesives, n-butyl-2-cyanoacrylate (Histoacryl) and isobutyl-2-cyanoacrylate (Bucrylate), have been used for the control of variceal bleeding.[48] Studies employing cyanoacrylate injection for treatment of large varices with simultaneous traditional sclerotherapy for treatment of small varices have been associated with rebleeding rates of 10% or less.[49] Finally, a biological fibrin glue (Tissucol) was more effective than sclerotherapy with polidocanol in the prevention of early rebleeding and had a significantly lower incidence of complications.[50] More studies are necessary to confirm these data and examine the potential risks of activation of coagulation, systemic embolism and transmission of infections with the human plasma derived fibrin glue.[51] Recently, argon plasma-coagulation has been used to induce superficial burns and fibrosis on the esophageal mucosa after eradication of varices.[52] A circumferential burn at the lower esophagus is made with the aim of inducing fibrosis in the submucosa to prevent recurrence of varices. While the procedure seems quite safe in patients after all varices are obliterated, the long-term effect of argon plasma coagulation remains to be confirmed.

3. Balloon Temponate

The Sengstaken-Blakemore tube was first introduced

in 1950.[53] This device and its subsequent variations, the Minnesota and Linton-Nachlas tube, are passed per nares or per os in an intubated patient.[54] Correct positioning of the tube is documented by chest and abdominal X-ray. Sengstaken-Blakemore and Minnesota tubes are also equipped with an esophageal balloon which can permit balloon tamponade directly to bleeding esophageal varices.[55] Balloon tamponade induces initial hemostasis in 40-90% cases of bleeding esophageal varices.[56] However, fatal complications arise in 6-20% of cases.[57] They include necrosis of the gastroesophageal wall, rupture of the esophagus and aspiration pneumonia.[57] In spite of these problems, balloon tamponade should be employed as a temporizing measure when patients with massive hemorrhage fail emergent endoscopic and medical therapies.[58] Balloon tamponade with Linton-Nachlas and Sengstaken-Blakemore tubes were equally effective in stopping bleeding from oesophageal varices but the first was more effective in gastric variceal bleeding.[59] Providing the balloon is in the correct position, bleeding from oesophageal and subcardial varices is always stopped. If the correct position is achieved, continued bleeding indicates bleeding from other lesions, including fundal varices and portal hypertensive gastropathy, usually in septic patients.[60] The problem is that rebleeding following removal of tamponade is very frequent, thus the rationale for its use is only as part of a therapeutic regimen, acting as a temporizing measure before sclerotherapy or surgery.

B. DRUG THERAPY IN VARICEAL BLEEDING

1. Vasopressin

Vasopressin, a hormone of the posterior lobe of the hypophysis, was the first vasoconstrictor used in the treatment of bleeding due to portal hypertension and proved to be effective.[61] It binds to the V1 receptor of vascular smooth muscle cells and induces vasoconstriction in the mesenteric arterial circulation.[62] As a result, there is decreased portal venous inflow and a subsequent reduction in portal pressure. Disparate studies have demonstrated that acute variceal bleeding is controlled in 29-71% of cases treated with vasopressin alone and in 45-73% of cases when vasopressin is combined with nitroglycerin.[63] Typical vasopressin dosing is 0.4 units/min intravenously (iv), used in combination with nitroglycerin 50μg/min. [64] Treatment with vasopressin and nitroglycerin is tapered once bleeding has stopped and the patient no longer has an ongoing need for blood transfusion. If bleeding does not cease, the vasopressin dose may be increased to as high as 1.0 units/min.[63] However, higher doses are associated with increased side effects, including myocardial and gastrointestinal ischemia.[64] This causes discontinuation of the treatment in up to 30% of cases.[63] The incidence of these severe side effects is reduced by co-administration of nitroglycerin.[64]

2. Terlipressin (Glypressin)

Terlipressin (N-triglycyl-8-lysine-vasopressin) is a synthetic analogue of vasopressin, developed in 1964.[65] It causes splanchnic vasoconstriction with a consequent decrease of the portal pressure and blood flow in porto-systemic collaterals.[65] In comparison with vasopressin, it has minimum side effects and a prolonged biological turnover (half-time 3-4h) that enables intermittent administration.[66] In sufficient dose, it decreases significantly not only the pressure in hepatic veins but also the intravariceal pressure.[66] Its efficacy is similar to balloon tamponade, somatostatin, octreotide or endoscopic sclerotherapy.[67] Terlipressin, a powerful splanchnic vasoconstrictor, may preserve renal blood flow and hence prevent the development of hepatorenal syndrome.[68] Terlipressin's theoretical advantages over vasopressin include the convenience of bolus administration as opposed to continuous iv infusion, the drug's decreased cardiotoxicity and its ability to control up to 70% of variceal hemorrhages.[67,68]

3. Somatostatin

Somatostatin, a 14 amino acid hormone produced in the hypothalamus and in the gastrointestinal tract, was first isolated in 1973.[69] It is considered to be at least as effective as vassopressin without any serious complications.[70] Somatostatin has a half-life of one minute, which necessitates administration via continuous iv infusion.[70] Administration of somatostatin (typically at doses of 250 μg/hr) controls variceal bleeding in 40–90% of cases.[69,70] In general, treatment is continued for 2–5 days.[71] Its ease of administration, safety and efficacy lead us to recommend the use of somatostatin as soon as variceal bleeding is suspected. Its efficacy has proved to be similar to endoscopic measures but optimal in their combination.[72]

4. Octreotide

Octreotide is a synthetic octapeptide derivate of somatostatin, first described in 1982.[73] Octreotide has a similar pharmacological effect to somatostatin.[73] The differences are dependent on its binding to three out of five somatostatin receptors. In comparison to somatostatin, its advantages are its longer half-life (90–120 min) and, especially, longer pharmacological action (8–12 h).[74] Its mechanism of action is believed to be due to inhibition

of vasodilatory gastrointestinal peptides, including glucagon, vasoactive intestinal peptide, calcitonin gene related peptide, and substance P.[75] Meta-analysis studies using octreotide or somatostatin have shown a lower rate of complications and a similar effect to sclerotherapy or balloon tamponade, for the treatment of variceal bleeding.[76] The administration of octreotide after sclerotherapy reduces portal pressure and rebleeding rate compared to sclerotherapy alone, but the effect on mortality is not yet proved.[77] Octreotide by continuous iv infusion has demonstrated effectiveness in reducing blood loss and transfusion requirements.[78] Additionally, octreotide is relatively free of significant adverse effects.

5. b-blockers

The ability of b- blockers to decrease splanchnic blood flow has been known since the 1960s.[80] Non-selective b-blockers like propranolol and nadolol are particularly effective in reducing portal pressures in cirrhotics.[81] Although b-blocker therapy does not play a role in the patient with acutely bleeding varices, a meta-analysis of heterogeneous studies comparing propranolol or nadolol to placebo showed a reduction in the relative risk of recurrent variceal bleeding.[82] Taking into consideration the safety and low cost of b-blocker therapy, we routinely recommend it as primary and secontary prophylaxis against variceal bleeding. Combination of beta-blockers and nitrates looks promising but needs further evaluation. EVL compares favourably with non-selective beta-blockers in preventing the first bleeding episode in cirrhotic patients and may be an alternative for patients who cannot tolerate, or have contraindications to beta-blockers.[83] Congestive heart failure, severe asthma, chronic obstructive lung disease and insulin–dependent diabetes mellitus are relative contraindications to the use of b-blockers.[83,84] Patients with medium or large varices should be treated with a non-selective beta-blocker with the dose titrated to achieve a 20% decrement in HVPG.[83] The most common adverse effects are depression, fatigue and cold extremities.[82] Carvedilol is a new non-selective b-blocker with additional anti-a-adrenergic activity that reduces portal pressure gradient, arterial blood pressure and peripheral resistanse.[84] Carvedilol therapy was associated with a mean reductions of 16-43% in portal pressure, assessed by HVPG, after single and multiple doses.[85] Further multiple-dose trials comparing carvedilol with standard therapy are needed to assess the agent's long-term safety and effectiveness in preventing variceal bleeding.

6. Nitroglycerin

Nitrates, administered either iv or per os, help overcome sinusoidal resistance.[86] Nitrates are not effective as single agents in the control of acute variceal bleeding and their use is limited, due to their hypotensive effects.[87] However, they are often used in combination with other drugs such as vasopressin and b-blockers.[87] In the mid 1980s, it was demonstrated that nitroglycerin (glyceryl trinitrate), administered iv at a rate of 50 μg/min, significantly improved the rate of control of variceal hemorrhage when added to a regimen of vasopressin.[87] A decade later, many investigators showed that the addition of isosorbide-5-mononitrate to a regimen of propranolol or nadolol significantly improved portal hypertension and increased the efficacy of oral b-blockers in preventing recurrent variceal bleeding.[86,87]

C. SHUNT SURGERY

Shunt surgery has been used for almost 50 years and is based on the simple concept of bypassing the site of increased resistance.[88] Basically, there are 2 types of shunts, a) central (or non-selective) shunts and b) non-central (or selective) shunts.[89] Central shunts, such as end-to-side and side-to-side portacaval shunt, mesocaval shunt, proximal and interposition splenorenal shunt, decompress the portal system directly and decompress the esophagogastric variceal complex only by lowering portal pressures.[88] Noncentral shunts, such as distal splenorenal shunt, selectively decompress the esophagogastric variceal complex and therefore may not reduce portal pressures at all.[89] Shunt surgery is used for the control of acute variceal bleeding and for the prevention of vericeal rebleeding when pharmacologic therapy and endoscopic therapy have failed.[88] Data indicate 90% control of bleeding with all types of surgical shunt and only 9-22% of patients experience late episodes of rebleeding.[88,90] Shunt surgery is effective at decreasing the risk of variceal rebleeding, but has the disadvantage of enhancing encephalopathy and worsening liver failure.[88] Selective shunts, or "calibrated" shunts, aim to reduce this problem.[89] Encephalopathy and liver failure rates are dependent on the underlying liver disease and the loss or maintenance of portal perfusion.[91] Emergency shunts may not be very effective because they often are followed by early rebleeding due to acute thrombosis in the shunt.[91] Shunt surgery should be considered when emergent portal decompression is required in a relatively well-compensated cirrhotic patient[89] (patients with Child class A status and well selected patients with Child class B status).

D. TIPS (TRANSJUGULAR INTRAHEPATIC PORTOSYSTEMIC SHUNT)

Work by Rosch, Colapinto, Palmaz and colleagues in the 1970s and 1980s laid the groundwork for the first successful creation of TIPS in humans in 1989.[92] TIPS is physiologically equivalent to a side-to-side portocaval shunt[92] (Figure 1), and is used for the control of refractory ascites, acute variceal bleeding and for the prevention of variceal rebleeding when pharmacologic therapy and endoscopic therapy have failed.[93] Also promising indications for TIPS are a) Budd-Chiari syndrome uncontrolled by medical therapy, b) severe portal hypertensive gastropathy, c) refractory hepatic hydrothorax and d) hepatorenal syndrome.[94] The major limiting factors for TIPS success are shunt dysfunction and hepatic encephalopathy.[95] TIPS stent occlusion occurs in more than 50% of patients within a year, mainly related to vascular endothelial ingrowth.[96] Most cases of severe stenosis or occlusion can be detected if patients are enrolled in a programme of surveillance with Doppler ultrasonography, usually scheduled every 3 months after TIPS placement.[97] In the vast majority of cases of TIPS stenosis, repeat angiographic intervention can successfully re-establish patency.[98] TIPS procedures fail to create a shunt in up to 10% of cases.[99] In an effort to improve the efficacy and safety of the procedure, an alternative transmesenteric-transfemoral method (tmTIPS) is used.[100] Although the transmesenteric-transfemoral technique necessitates general anesthesia and mini-laparotomy, operative complications have been minimal. Some authors recommend routine venography to follow TIPS patency. TIPS can give rise to various procedure-related complications such as hepatic arterial injury and hemoperitoneum due to
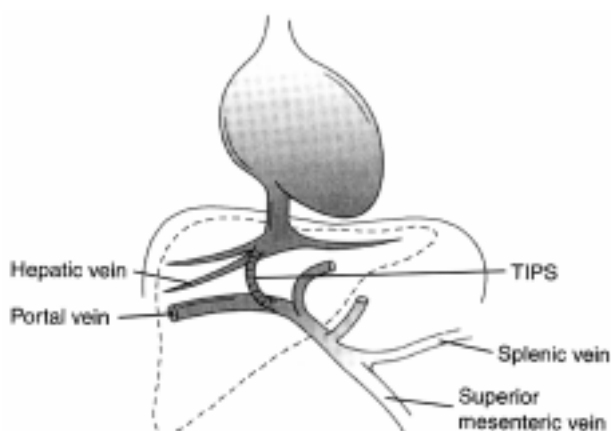
Figure 1. Transjugular Intrahepatic Portosystemic Shunt (TIPS).

extrahepatic puncture.[97] In comparison with surgical shunts, TIPS is a significantly less invasive procedure that can be done in poor surgical candidates with advanced cirrhosis.[92] The advent of TIPS provides us with an additional option in patients with advanced Child class B and C cirrhosis, particularly those who are candidates for liver transplantation.[98] TIPS and surgical shunts produce comparable survival rates and have their place in the treatment of gastroesophageal variceal hemorrhage unresponsive to endoscopic therapy.[92]

E. LIVER TRANSPLANTATION

Liver transplant has significantly improved the outcome of patients with end-stage liver disease.[101] Availability of donor organs is the major limiting factor in wider application, leading to the need for prudent patient selection and wise use of this limited resource. The indication for use of liver transplant for patients with portal hypertension and variceal bleeding is the end-stage liver disease.[101] Not every patient with variceal bleeding has end-stage disease, so it requires full evaluation and documentation of a patient's disease and its progression over time, to reach a decision to transplant such patients. Approximately 25% of patients receiving transplants have variceal bleeding as a component of their end-stage disease.[102] Liver transplantation is the only definitive treatment that can alter the course of the disease.[102]

GASTRIC VARICES

Gastric varices may be more difficult to identify at endoscopy because theye are generally situated deeper than oesophageal varices and may resemble rugal folds.[103] In much of the literature, gastric varices are reported together with oesophageal varices rather than as a separate entity.[104] Apart from oesophagogastric varices, duodenal varices are one of the more commonly reported digestive tract varices in portal hypertension.[103] The frequency with which gastric varices bleed is 3-30% and because of the greater and faster blood flow, the rupture of gastric varices results in a higher mortality rate (45-55%) than in cases in which esophageal varices rupture.[103] Endoscopic ultrasonography is useful in the prediction of recurrence of varices and facilitates visualization and guidance for further treatment of gastric varices.[104] For gastric varices, cyanoacrylate glue using the ES technique continues to be the first line of treatment, and band ligation is being assessed further.[104] Shunt surgery and TIPS have also been used for gastric varices.[105] Recently, a new radiological procedure for the obliteration of gastric

varices has been introduced known as balloon-occluded retrograde transvenous obliteration-BRTO. Involving a gastrorenal or gastrocaval shunt, the procedure increases portal blood flow in the liver, leading to improved liver function.[106] In BRTO a spontaneous portosystemic shunt is occluded and hepatic encephalopathy is thus not an obstacle.[107] Its possible side effects include pulmonary embolism, renal dysfunction, pleural effusion, pulmonary edema, hypersensitivity reaction, pyrexia, and disseminated intravascular coagulation syndrome.[108]

CONCLUSIONS

The meeting of BOVENO proposed that diagnostic endoscopic evaluation should take place at the time of diagnosis of liver cirrhosis and be repeated every two years in case of abscense of varices.[3] In those with small varices, the study may be repeated at 1 year intervals.[3] Also, measurement of HVPG should be used routinely in the initial investigation of cirrhotic patients.[79] Today the therapeutic approach in patients with varices must include the prophylactic use of vasoactive agents, early endoscopic diagnosis and endoscopic therapy. Beta-blockers and EVL are the best options for primary prophylaxis of variceal bleeding.[7] Once pharmacologic therapy is initiated, follow-up measurements of HVPG should be made every 3 months.[79] Clinical and laboratory evidence of both severity of haemorrhage and liver disease should be included in the initial assessment of accute variceal bleeding, as these have prognostic significance. Emergency endoscopy should be arranged if the patient remains hemodynamically unstable.[52] After endoscopic confirmation of the source of bleeding, banding ligation and/or injection sclerotherapy should be offered immediately.[30] Also, vasoactive agents should be administred in order to prevent early rebleeding and prophylactic antibiotics must be given.[14,16] When initial hemostasis is achieved, the patient can be scheduled for an endoscopic obliteration program with weekly or biweekly EVL or EST, until all varices are obliterated.[30] Patients who fail to respond to endoscopic therapy, or those who suffer from recurrent bleeding during the acute phase, should be offered balloon tamponade before a second session of therapeutic endoscopy.[53] If secure hemostasis still cannot be achieved, TIPS or surgery (when TIPS is not available or not feasible) offer the best salvage therapy.[92] Despite advances in the treatment of variceal bleeding, liver function remains the determining factor of patient survival. Liver transplantation is the only treatment that can alter the course of the disease.[102]

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