

Primary and secondary prophylaxis of gastric variceal bleeding

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Abstract

Gastric variceal bleeding is a common problem in patients with cirrhosis and is associated with increased morbidity and mortality. Management is complex and includes pharmacotherapy, endoscopic therapy, and shunt placement. Recent studies indicate that endoscopic therapy with tissue adhesives has similar hemostasis rates and outcomes in terms of mortality as shunt placement but has a lower complication rate and therefore could be considered the first line therapy for acute bleeding and secondary prophylaxis of gastric varices.

Introduction and context

Variceal bleeding is the most common lethal complication of cirrhosis, with a mortality rate of 20% [1,2]. Gastroesophageal varices (GOVs) are present in 50% of cirrhotics, and approximately 25% of patients with portal hypertension have gastric varices [3,4]. Gastric varices are commonly classified as GOVs (gastric varices in continuity with esophageal varices) and isolated gastric varices (IGVs). These are further divided into GOV1 (GOVs along the lesser curve of the stomach), GOV2 (GOVs along the fundus), IGV1 (IGVs in the fundus), and IGV2 (IGVs in the gastric body, pylorus, or antrum). Although the prevalence and risk of bleeding of gastric varices are lower than those of esophageal varices, gastric variceal bleeding tends to be more severe, requires more transfusions, and is associated with higher mortality (~45%) [5]. Gastric varices tend to be larger and more tortuous compared with esophageal varices, characteristics that, combined with their anatomical location (particularly fundic varices), make endoscopic management more challenging. Current management strategies for gastric varices include pharmacotherapy (β -blockers and vasoactive agents), endoscopic therapy (band ligation, thrombin, and tissue adhesives), transjugular intrahepatic portosystemic shunt (TIPS) placement, and surgical intervention. Large, well-conducted trials comparing these therapeutic modalities are lacking. Therefore, recommendations for

management of gastric varices are based on recent prospective and retrospective studies, expert consensus opinion, and experience with esophageal varices.

Recent advances

Primary prophylaxis

The pathophysiology of gastric varices is not as well understood as that of esophageal varices; however, the former are mostly seen in patients with cirrhotic portal hypertension. IGV1 gastric varices are an exception and frequently result from isolated splenic vein thromboses. Therefore, the treatment of choice for IGV1 varices is splenectomy. No studies to evaluate pharmacologic therapy or endoscopic therapy for primary prophylaxis of gastric varices have been performed, and recommendations are based primarily on the guidelines for managing esophageal varices. Large gastric varices with red color signs, especially in patients with advanced liver disease (Child's class C), are most likely to bleed [4,6]. These patients may be treated with non-selective β -blockers to prevent variceal hemorrhage. Endoscopic treatment or TIPS is not currently recommended for primary prophylaxis of gastric varices.

Treatment of acute bleeding and secondary prophylaxis

Endoscopic therapy and TIPS are both considered first-line treatments for gastric variceal bleeding; however, current

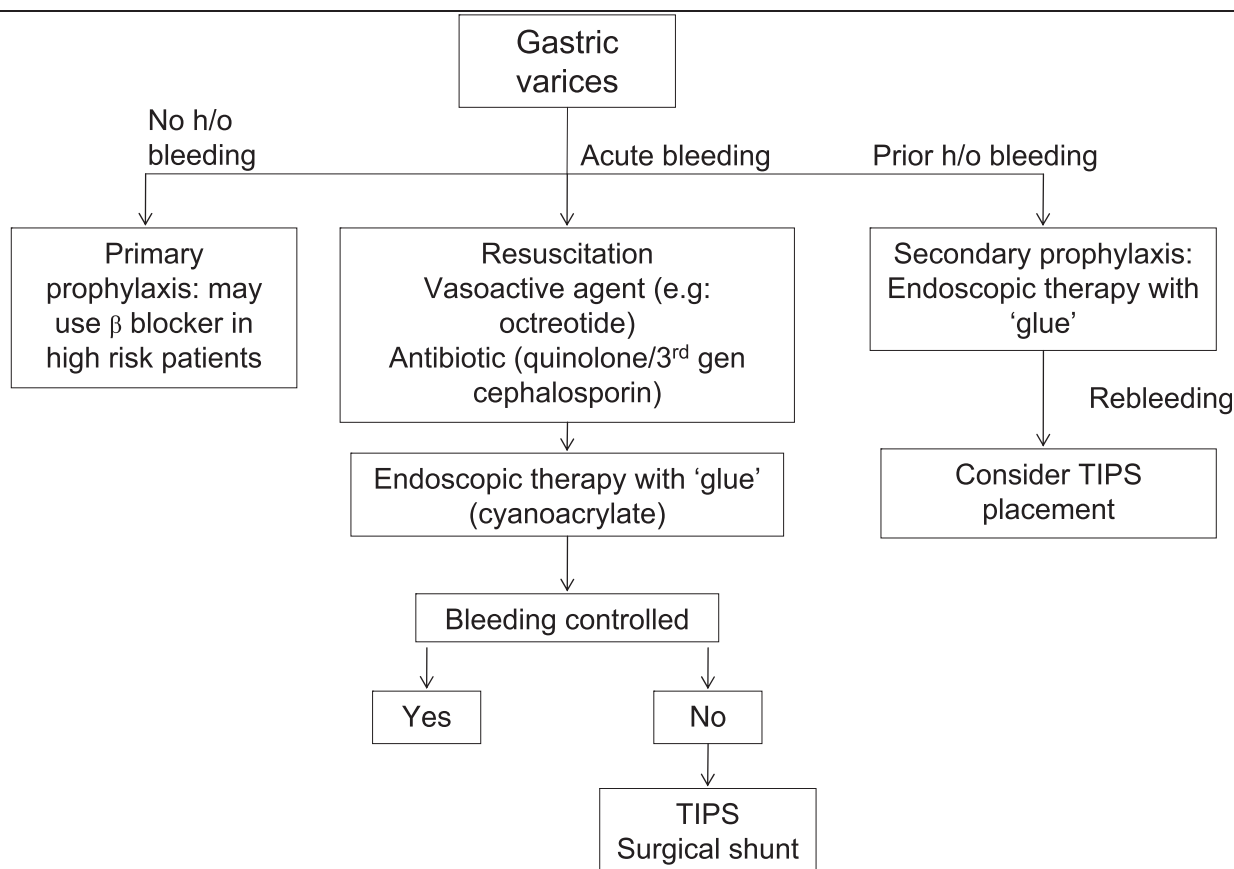
guidelines favor endoscopy as the preferred initial intervention [7,8]. Endoscopic therapeutic options for gastric variceal bleeding include band ligation, tissue adhesives, thrombin, and sclerotherapy. The greatest evidence exists for tissue adhesives such as cyanoacrylate (*N*-butyl-2-cyanoacrylate, 'glue'); however, cyanoacrylate is not routinely available in the US. Cyanoacrylate undergoes rapid polymerization on contact with living tissues and obliteration of varices occurs when the injected cyanoacrylate adhesive hardens on contact with blood. The mucosa overlying the varix eventually sloughs and the polymer is extruded. Two randomized controlled trials have compared cyanoacrylate injection with variceal band ligation, showing mixed results for initial hemostasis but reduced rebleeding rates with cyanoacrylate (22% versus 44% and 31% versus 54%) [9,10]. There was no difference in mortality rates. Another study compared cyanoacrylate injection with sclerotherapy and found better control of initial hemostasis as well as lower rebleeding rates with cyanoacrylate [11]. Meticulous adherence to technique is crucial when using tissue adhesives to prevent irreversible damage to endoscopes caused by polymerization. A recent

study reported the use of endoscopic ultrasound to guide injection of feeding veins with excellent results; however, the risk of damaging expensive equipment may prevent its widespread usage [12]. Complications of tissue adhesives include embolization, with case reports of portal vein embolization, coronary emboli, splenic infarction, pulmonary emboli, and cerebral stroke [13-16].

Thrombin is a promising agent that does not carry the risk of embolization and damage to equipment. A recent study using bovine thrombin to control gastric variceal bleeding demonstrated a hemostasis rate of 92% and no episodes of rebleeding [17]. Several other studies with thrombin have shown promising results [17-19]. However, controlled trials comparing thrombin with other agents are required before it is universally accepted.

The role of TIPS in the management of gastric varices alone or in comparison with esophageal varices has been investigated in multiple studies. Chau *et al.* [20] reported a 96% initial hemostasis rate and 29% rebleeding rate with TIPS in patients with fundal varices, and these were

Figure 1. Algorithm for management of gastric varices



h/o, history of; TIPS, transjugular intrahepatic portosystemic shunt.

similar to the rates for cirrhotics with esophageal varices. In another retrospective series comparing TIPS in 40 cirrhotics with gastric variceal bleeding and 232 patients with esophageal variceal bleeding, the rates of rebleeding were similar (20% versus 15%) [21].

Clearly, with hemostasis rates over 90%, tissue adhesives and TIPS are both highly effective management options for gastric variceal bleeding. Very few studies have compared the two therapies. Lo *et al.* [22] carried out a randomized controlled trial comparing TIPS (n = 35) and cyanoacrylate glue (n = 37) for secondary prophylaxis of gastric variceal bleeding. There was no difference in survival or complication rates. However, the rebleeding rate was significantly higher in the cyanoacrylate arm compared with the TIPS arm (38% versus 11%). In a UK-based retrospective study, the two therapies were equally effective for initial hemostasis but patients with TIPS had a lower rebleeding rate (20% versus 35%) [23]. However, TIPS was considerably more expensive than cyanoacrylate therapy. Finally, in a recent retrospective study comparing TIPS (n = 44) and cyanoacrylate therapy (n = 61) for gastric variceal bleeding, rebleeding rates and mortality rates were similar between the two groups. However, the TIPS group had increased morbidity requiring hospitalization and had a higher incidence of encephalopathy (11 versus 1) [24].

Implications for clinical practice

The initial steps in the management of gastric variceal bleeding are similar to esophageal varices and include attention to airway and obtaining intravenous access with prompt hemodynamic resuscitation, institution of vasoactive medications (somatostatin analogues, octreotide, vasopressin, and terlipressin) to reduce portal pressure by splanchnic vasoconstriction and prophylactic antibiotics followed by diagnostic and potentially therapeutic upper endoscopy (Figure 1). The next step in the management may be endoscopic injection of tissue adhesives or TIPS placement. With a lower complication rate, comparable hemostasis and survival rates, and lower cost, endoscopic therapy with tissue adhesives is likely to be the treatment of choice for acute bleeding and secondary prophylaxis in most patients. On the other hand, TIPS will remain an important second-line modality in patients who fail endoscopic therapy. However, additional controlled studies are needed before valid conclusions can be made, and individual patient characteristics must be considered in management decisions. Primary prophylaxis may be instituted with β -blockers in patients with large varices with red color signs and advanced liver disease. Further research on management of acute bleeding, primary prophylaxis, and comparisons between tissue adhesives and thrombin would be welcome.

Abbreviations

GOV, gastroesophageal varix; IGV, isolated gastric varix; TIPS, transjugular intrahepatic portosystemic shunt.

Competing interests

The authors declare that they have no competing interests.

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