

Pathogenesis of portal hypertensive gastropathy: translating basic research into clinical practice

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SUMMARY

Portal hypertensive gastropathy (PHG) is often seen in patients with portal hypertension, and can lead to transfusion-dependent anemia as well as acute, life-threatening bleeding episodes. This Review focuses on the mechanisms that underlie the pathogenesis of PHG that provide reasonable grounds for the treatment of this condition, and ultimately enable translation of basic research into clinical practice. Increased portal pressure associated with cirrhosis and liver dysfunction is critical for the development of clinically significant PHG, and leads to impaired gastric mucosal defense mechanisms that render the stomach susceptible to mucosal injury. The use of pharmacological agents such as β -blockers reduces the frequency of bleeding episodes in PHG. As a last resort, surgical decompression of the portal system, transjugular intrahepatic stent placement and liver transplantation can resolve this condition. Elimination of known risk factors for gastric injury such as alcohol, aspirin and traditional NSAIDs is critical. The role of *Helicobacter pylori* colonization of the gastric mucosa in PHG is not clear. Careful and critical interpretation of human and experimental data can be helpful to establish a rationale for the medical management of this important condition.

KEYWORDS bleeding, cirrhosis, pathogenesis, portal hypertension, portal hypertensive gastropathy

REVIEW CRITERIA

PubMed was searched in April 2008 for original articles on portal hypertensive gastropathy. Clinical and experimental studies that explored the pathogenesis of portal hypertensive gastropathy were included. Where available, level one evidence studies, such as randomized controlled trials of therapy were reviewed. The search was performed using the following keywords alone or in combination: "portal hypertension", "portal hypertensive gastropathy", "cirrhosis", "bleeding", "GAVE", "watermelon stomach", "stomach", "mucosal defense", "acid", "proton pump inhibitor", "*Helicobacter pylori*", "gastric antral vascular ectasia", "physiopathology", "management", "therapy", "randomized controlled trials", "human", "animal". Original articles published in the following languages were included: English, Spanish and Portuguese. The reference list was updated in November 2008.

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INTRODUCTION

Patients with liver cirrhosis and portal hypertension are widely accepted to be at risk of developing acute upper gastrointestinal bleeding.^{1,2} This risk is believed to be dependent on the severity of liver dysfunction and the degree of portal hypertension. Ruptured esophageal and/or gastric varices account for the majority of bleeding episodes in these patients, whereas gastroduodenal ulcers, portal hypertensive gastropathy (PHG), Mallory–Weiss tear and duodenal varices are less frequent causes of bleeding.^{1–3} This review will focus primarily on the pathogenesis of PHG and will provide practicing clinicians with a rationale for some of the therapeutic options available for this condition.

The stomach is a target organ in patients with cirrhosis and portal hypertension and these conditions possibly contribute to acute and/or chronic gastrointestinal blood loss, which can influence short-term and long-term outcome. An increased risk for the development of peptic ulcers has been suggested in patients with cirrhosis; these ulcers have been termed hepatogenic ulcers.⁴ Gastroduodenal ulcers can also develop as an adverse reaction to the use of aspirin and/or traditional NSAIDs. Other non-ulcer-related morphological changes in patients with cirrhosis and portal hypertension can be detected by endoscopy. PHG is a condition characterized by changes in the mucosa of the stomach. Endoscopic evaluation shows a mosaic-like mucosal appearance, accompanied by lesions of variable severity (Figure 1). These findings are associated with histological evidence of dilated submucosal and/or mucosal blood vessels and, possibly the presence of lymphatic vessel ectasia. Intra-arterial thrombi and features consistent with acute or chronic inflammation are absent.⁵ These findings define PHG and are critical in distinguishing it from gastric vascular antral ectasia (GAVE), which also occurs in patients with cirrhosis and portal hypertension. GAVE is characterized by dilated small blood vessels in the antrum, and

is also termed 'watermelon stomach' because streaky, elongated, red areas can be present in the stomach that resemble the markings on a watermelon.^{5–8}

PHG develops in response to increased resistance to portal blood flow, which occurs in several diseases that affect the liver and/or portal circulation, and leads to complex hemodynamic changes in the splanchnic and systemic vascular territory that can ultimately affect function in the stomach and other organ systems.⁹ Impaired or disturbed regulation of central blood volume, renal and cardiac function have been reported in association with cirrhosis, portal hypertension and liver dysfunction. The lungs, small bowel and large bowel can also be involved. The immune system and the ability of the patient to respond to infections can also be affected as a result of profound changes in the production and/or release of vasoactive and proinflammatory mediators in the setting of endotoxemia.^{10,11} Increased cardiac output and heart rate with reduced mean arterial blood pressure are classic manifestations of the hemodynamic changes that can be detected in patients with cirrhosis and portal hypertension.

PHG rarely leads to severe, acute bleeding, and is more often associated with chronic blood loss, which leads to anemia and the requirement for multiple blood transfusions that can have a significant and negative effect on a patient's quality of life.¹² The incidence of PHG in patients with cirrhosis and portal hypertension ranges from 9% to 80%.^{1,13–16} The documented natural history of PHG is variable given a lack of uniform diagnostic criteria for the condition. Furthermore, interobserver and intraobserver variability in the identification and characterization of gastric mucosal changes make comparisons of research findings reported by different groups virtually impossible.^{12,13,15}

CLASSIFICATION

PHG can affect the whole stomach, despite suggestions that it is normally only detected in the gastric body and fundus. Mucosal changes in the stomach associated with PHG are characterized endoscopically by the presence of four main findings, as described by the New Italian Endoscopic Club: a mosaic-like pattern, red point lesions, cherry-red spots and black–brown spots (Box 1, Figure 1).^{13,17,18} Similar mucosal changes to those found in the stomach might also be seen in the small intestine (portal hypertensive

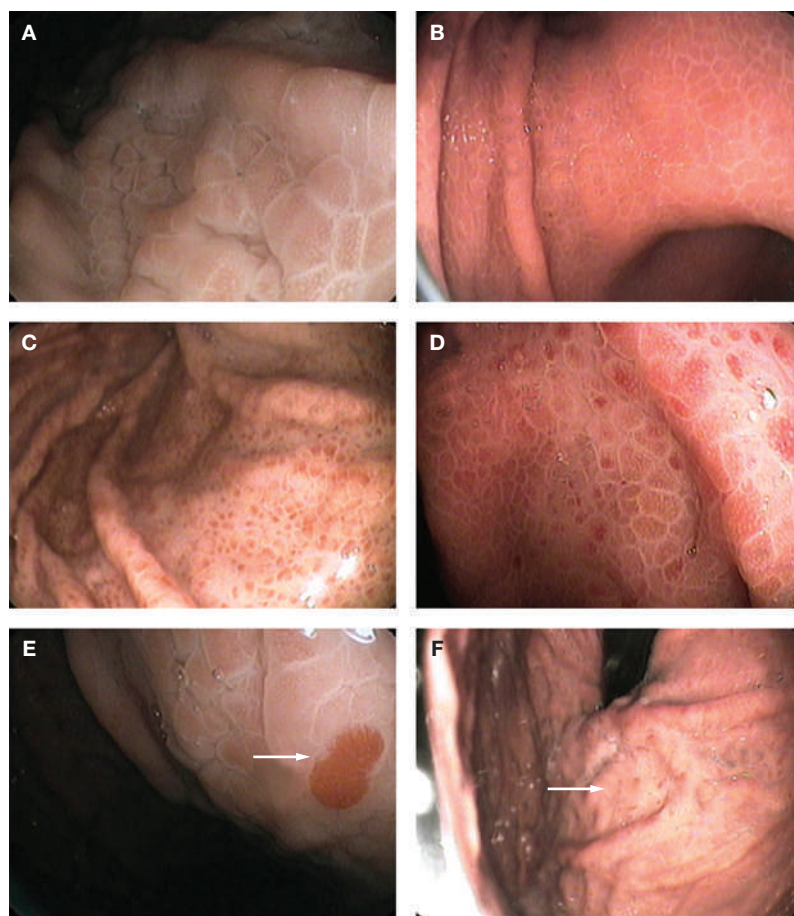


Figure 1 Endoscopic images of portal hypertensive gastropathy that show the four main findings of this condition. Mild (A) and moderate (B) mosaic-like gastric mucosal pattern, red point lesions (C), cherry-red spots (D), and black–brown spots, including an intramucosal hemorrhage (E) and a brown spot (F).

duodenopathy and portal hypertensive enteropathy)¹⁹ and colon (portal hypertensive colopathy)²⁰ of patients with portal hypertension and cirrhosis.

Differences in endoscopic findings might reflect differences in the severity of PHG, however, no clear association has been found between endoscopic findings and hemodynamic parameters or clinical features of this condition. Histological analysis might be helpful when lesions are not characteristic of PHG or when concomitant processes such as *Helicobacter pylori* colonization of the gastric mucosa, acute drug-induced mucosal damage and GAVE are suspected. As mentioned previously, histological findings of ectasia in gastric mucosal capillaries and submucosal veins in the absence of inflammation, erosions, or fibrinous thrombi can be critical to discriminate PHG from GAVE.⁵

Box 1 Mucosal changes in the stomach associated with portal hypertensive gastropathy.^a

Mosaic-like mucosal pattern

Small, polygonal areas surrounded by a whitish–yellow depressed border (snake-skin appearance)
Can be categorized as mild (pink mucosa), and moderate (diffuse red mucosa)

Red point lesions

Small (<1 mm), red, flat, point-like marks

Cherry-red spots

Large (>2 mm), round, red-colored, protruding lesions

Black–brown spots

Irregularly shaped black and brown flat spots that do not fade upon washing (these changes might represent intramucosal hemorrhage)

^aThese changes are characterized endoscopically by the presence of four main findings, as described by the New Italian Endoscopic Club (NIEC).¹³

Significant variability in grading the severity of PHG among investigators and physicians in clinical practice has been suggested, and a modified grading system has been proposed by the Baveno III meeting on portal hypertension:²¹ PHG is mild when a pink mosaic-like mucosal pattern with no red signs or black–brown spots is present, and severe when the mosaic-like mucosal pattern is red and superimposed by any red sign (red point lesions and/or cherry-red spots) or black–brown spots. Although the intensity of the mosaic-like pattern and the presence of red point lesions and/or cherry-red spots has been associated with an increased risk of acute bleeding, chronic bleeding occurs irrespective of the extent of mucosal changes, presence and grading of red signs, and Child–Turcotte–Pugh score.¹³

PATHOGENESIS

Increased resistance to portal blood flow in patients with liver disease (with and without cirrhosis) and the consequent elevation in portal pressure is believed to be a prerequisite for the development of PHG.⁹ Amelioration of PHG with no subsequent recurrence has been reported in patients with cirrhosis who have undergone transjugular intrahepatic portosystemic shunt (TIPS) placement, and in patients without cirrhosis who have undergone surgical decompression of the portal system.^{22–24} However, numerous studies have failed to demonstrate a

linear correlation between the severity of portal hypertension and that of PHG.^{5,6,22,25–28}

PHG has been associated with increased hepatic portal venous pressure gradient (HVPG), but no difference has been shown in HVPG between patients with PHG and mild or severe forms of liver disease.¹⁴ In patients with cirrhosis, PHG does not seem to correlate with the degree of increased portal pressure, nor are the prevalence and severity of PHG influenced by underlying liver function or size of esophageal varices.³¹ Moreover, some data suggest that endoscopic treatment of esophageal varices leads to the development of PHG, or worsens pre-existing PHG; however, no clear, reproducible evidence indicates that prophylactic or therapeutic endoscopic treatment of varices, and the method employed to achieve it, affects the stomach.^{19,27,30–35}

On the basis of the above findings one could speculate (and most investigators might agree) that portal hypertension is necessary, but perhaps not sufficient for the development of clinically significant PHG. This theory raises the question of what the additional or determinant factors are that lead to bleeding episodes in the clinical setting of PHG, and whether the gastric mucosa is actually prone to spontaneous bleeding or becomes susceptible to injury induced by luminal irritants such as ethanol, bile salts, aspirin or traditional NSAIDs.³⁶ The mechanism of spontaneous bleeding is not well understood, but is possibly related to a state of chronic endotoxemia; the mechanism of susceptibility to mucosal injury is thought to be related to an imbalance between gastric mucosal aggressive and defensive factors.^{37,38} Investigation of gastric mucosal defense mechanisms involved in the maintenance of gastric mucosal integrity has improved the understanding of PHG. This understanding has been achieved via studies of animal models of portal hypertension with or without liver dysfunction and cirrhosis, and a limited number of human studies. Increased susceptibility of the gastric mucosa to injury induced by the administration of ethanol, bile salts, aspirin or traditional NSAIDs has been reported in patients with cirrhosis and in experimental models.³⁷ The ability of the gastric mucosa to repair itself following injury is also compromised in these individuals.³⁸

Colonization of the gastric mucosa by *H. pylori* might have an indirect role in PHG as

such colonization is theoretically important in associated peptic ulcer disease.^{26,39–43} Whether aspirin-induced and/or NSAID-induced gastric injury exacerbate the risk of bleeding in patients with cirrhosis who are infected with *H. pylori* remains unclear.

Reduced delivery of oxygen to the gastric mucosa, a phenomenon related to the modified tissue architecture (vascular congestion) and blood flow regulation of the stomach and lungs in portal hypertension, has a role in the reduced resistance of gastric mucosa to irritants in patients with cirrhosis and portal hypertension.^{44–46} Moreover, reduced basal or stimulated gastric acid secretion, a phenomenon probably secondary to a compensatory adaptation to cirrhosis and portal hypertension, has been reported in both human and experimental models.^{47–50} Acid secretion blockade is believed to be a beneficial treatment for peptic ulcer disease in patients with cirrhosis, but its benefit in PHG is not clear.⁵¹ The clinically relevant question remains the same: are bleeding episodes (acute and chronic) related to PHG itself or to an increased susceptibility of the gastric mucosa to injury induced by a noxious agent?

Experimental models of portal hypertension have generated critical information that might be applicable in a clinical setting; however, we must emphasize that these data are derived from basic studies and, therefore, require careful interpretation when extrapolating the findings to clinical practice. For example, rats that have been subjected to portal vein stenosis develop portal hypertension, and their stomachs exhibit several, if not all, of the macroscopic changes that are seen in patients with PHG.⁵² Ethanol-induced gastric damage is increased in experimental models of portal hypertension compared with controls; however, the concentration of ethanol required to achieve this increased damage is relatively high.^{52,53} By contrast, spontaneous bleeding or mucosal injury secondary to exposure of the gastric mucosa to ethanol followed by topical application of hydrochloric acid causing acid back-diffusion is shown to be comparable between rats subjected to portal vein stenosis and controls (Camara PR, unpublished data). The presence of portal hypertension alone, without liver dysfunction, does not, therefore, increase the susceptibility of the gastric mucosa to injury or bleeding, and a relatively high concentration of a given topical irritant is required to induce acute damage. These studies indicate that rats

with portal vein stenosis are unlikely to develop chronic, slow, gastric bleeding. A parallel can be drawn between this experimental finding and the clinical setting in which the frequency and severity of bleeding episodes seem to be reduced in patients with PHG whose portal hypertension is secondary to pure schistosomiasis.⁵⁴ This observation suggests that liver dysfunction might have an important role in susceptibility of the gastric mucosa to injury induced by irritants, as well as in the development of spontaneous bleeding episodes.

A study using a rat model of bile duct ligation (in which treated rats developed secondary biliary cirrhosis, liver dysfunction and portal hypertension) has revealed that the gastric mucosa of rats with secondary biliary cirrhosis has areas of spontaneous bleeding that could potentially lead to anemia.⁵⁵ These animals develop significant liver fibrosis, portal hypertension, splenomegaly, ascites, jaundice, weight loss and wasting similar to that seen in patients with cirrhosis. In addition, the stomachs of these rats had increased susceptibility to injury after exposure of the gastric mucosa to a low concentration of ethanol or irritants followed by acid back-diffusion. Stomachs of bile-duct-ligated rats have also been shown to have susceptibility to injury induced by aspirin and traditional NSAIDs.⁵⁶ This observation suggests that, in this model, the gastric mucosa is prone to both spontaneous bleeding and injury induced by irritants followed by acid back-diffusion. These characteristics closely mimic the clinical presentation of patients with significant liver dysfunction and portal hypertension who develop transfusion-dependent PHG, or an acute bleeding episode. The rat bile-duct-ligation model of cirrhosis and portal hypertension seems to represent the observed scenario in human disease more closely than the rat model of portal vein stenosis. This model, therefore, seems to be a suitable tool for understanding the pathogenesis of PHG.

Beck and colleagues have demonstrated that the gastric mucosa of rats with cirrhosis has a reduced capacity to produce prostaglandins.^{56–58} Aspirin and NSAIDs are reported to induce significantly more damage to the gastric mucosa of rats with cirrhosis than to that of controls,⁵⁶ which suggests that the capacity to synthesize gastric prostaglandin is critical in the maintenance of mucosal integrity, as well as in regulation of gastric blood flow. Gastric microcirculation has a critical role in defense

against mucosal injury. An increase in gastric blood flow in response to the presence of acid or irritants on the mucosa enables neutralization of toxins or noxious agents and is termed the gastric hyperemic response.⁵⁹ Reduced responsiveness of the gastric microcirculation to injury is believed to be associated with diminished gastric prostaglandin production, a phenomenon related to the significantly increased nitric oxide production and release associated with the hyperdynamic circulation seen in portal hypertension.⁶⁰ An interesting point indicated by these data is that the gastric mucosa develops injury in response to topical exposure of the mucosa to a specific agent followed by acid back-diffusion and, therefore, a low gastric pH is necessary for damage to occur.

Investigation of the mechanisms that regulate the gastric hyperemic response to irritants in rats that have undergone bile duct ligation has generated an insight into how PHG can be managed clinically. Although patients with cirrhosis and portal hypertension have a low gastric acid output under basal or stimulated conditions, the notion that acid back-diffusion has an important role in damage to the stomach following administration of an irritant, aspirin or traditional NSAIDs makes a case for the therapeutic use of gastric acid secretion blockers to promote healing of the damaged mucosa. This notion does not, however, justify the use of these agents under circumstances where gastric mucosal damage is not suspected or documented, or in the absence of a known irritant. In addition, the fact that the increased susceptibility of the gastric mucosa to injury by ethanol in rats can be reduced by exogenous administration of a prostaglandin analog opens up the opportunity for testing this hypothesis in humans.⁵⁸ Acute or chronic administration of the prostaglandin analog misoprostol restores the responsiveness of the rat gastric microcirculation to acid and ethanol as well as to nitric oxide—a critical downstream mediator of the gastric hyperemic response to irritants.⁵⁸ In addition, administration of a prostaglandin analog has the potential to regulate tumor necrosis factor production and/or release by the gastric mucosa.⁶¹ This cytokine has been demonstrated to contribute, at least in part, to the increased susceptibility of the gastric mucosa to injury induced by ethanol in rats with cirrhosis.⁶³ Increased prostaglandin delivery to the stomach might increase or improve

resistance to mucosal injury, without restoring gastric mucosal tissue architecture to normal.

Sensory afferent neurons modulate the hyperdynamic circulation in cirrhosis,⁶² and participate in the development of complications such as renal dysfunction,⁶³ altered cardiac function⁶⁴ and, in particular, PHG.⁶⁵ Acute administration of capsaicin, a neurotoxin, to activate sensory afferent neurons in the stomach of a healthy rat triggers the gastric hyperemic response via release of calcitonin gene-related peptide (CGRP), which ultimately signals endothelial cells to release nitric oxide within the microcirculation.^{60,66} This phenomenon is blunted in rats with cirrhosis and portal hypertension, and failure to trigger the gastric hyperemic response is believed to be secondary to a reduced response to nitric oxide within the gastric microcirculation following CGRP release. This reduced response to nitric oxide potentially leads to profound changes in the signaling mechanisms for gastric prostaglandin and nitric oxide production, and ultimately affects the ability of the stomach to resist mucosal injury. Ablation of sensory afferent neurons in neonatal rats, followed by the induction of cirrhosis by bile duct ligation, prevents development of the hyperdynamic circulation, and has a positive effect on renal dysfunction. Furthermore, the susceptibility of the gastric mucosa to ethanol-induced injury in these rats was not different to that observed in controls.⁶⁵ Sensory afferent neurons, therefore, influence the ability of the gastric mucosa to resist injury in portal hypertension. Further animal studies have suggested that this phenomenon is probably mediated by substance P and tachykinins, which are increased in patients with cirrhosis and portal hypertension, as well as in animal models of these conditions.⁶⁵ These findings led to speculation that modulators of blood flow that can also interact with sensory afferent neuron function are candidates for the modulation of gastric mucosal defense mechanisms against injury in cirrhosis and portal hypertension.⁶⁵ For example, signaling for release and production of gastric endothelin 1 (a mediator that participates in regulation of vascular tone as well as neurogenic inflammation) is altered in portal hypertension.⁶⁷ The role of cannabinoid receptors has not yet been explored in PHG, but these receptors' roles have been investigated in portal hypertension, and in cardiac function in cirrhosis and liver fibrosis.⁶⁸

Finally, one might speculate that increased resistance to portal blood flow in the setting of portal hypertension, cirrhosis and chronic endotoxemia would potentially influence the ability of the gastric mucosa to defend against injury induced by luminal irritants, or even induce spontaneous bleeding that would parallel PHG findings in the clinical setting. This theory has not been fully investigated, but patients with portal hypertension and cirrhosis are accepted to be at risk of developing gastrointestinal bleeding if they have an infection of the urinary tract, lungs or spontaneous bacterial peritonitis.¹⁰ Bile-duct-ligated rats with cirrhosis do not survive acute or chronic administration of low doses of endotoxin, which limits the investigation of this hypothesis using this experimental model. However, preliminary data suggest that topical administration of ethanol followed by acid back-diffusion in rats with portal vein stenosis that are treated with endotoxin results in increased gastric damage compared with untreated control rats (Camara PR, unpublished data).

MANAGEMENT

The management of patients with PHG has been extensively reviewed elsewhere.⁷ Translation of research findings from experimental models of PHG, as well as from human studies, has established a theoretical framework for the use of pharmacological agents to treat PHG. Certainly, the prevention of development of liver fibrosis and cirrhosis is a key prophylactic strategy, and if achieved in conditions such as viral hepatitis, ethanol-induced liver disease and some autoimmune diseases that affect the liver, it might delay the onset of liver dysfunction and portal hypertension and, thereby, reduce the likelihood of development of PHG.

Treatment of an acute bleeding episode in patients with portal hypertension has traditionally aimed to identify the source by endoscopy, particularly for ruptured esophageal and/or gastric varices, and bleeding ulcers that require endoscopic treatment.³ Endoscopic hemostasis with appropriate methods (band ligation or sclerotherapy of esophageal varices, electrocoagulation, clipping, and the use of vasoconstrictors in the setting of bleeding ulcers or Dieulafoy lesions) is desirable once the source of bleeding is identified. Hemostatic treatment should be followed by administration of one of the following drugs: terlipressin,⁶⁹

octreotide,⁷⁰ somatostatin,⁷¹ vasopressin,⁷² and/or β -blockers.⁷³ These drugs could also be administered when the cause of bleeding is actually PHG. Clear and reproducible data on the benefit of these drugs in PHG are, however, lacking, except in the case of β -blockers, which confer a definite benefit and are strongly recommended in the literature.⁷³ The same lack of reproducible data applies to tranexamic acid; its use before endoscopic assessment is not suggested in the specific case of PHG, but might be considered if a patient has previously had GAVE.⁷⁴ Potential risk factors for peptic ulcer disease should be eliminated, such as the use of aspirin, traditional NSAIDs and *H. pylori* infection, the latter because of its status as a type I carcinogen, and not necessarily owing to its role in the development of peptic ulcer disease in this particular population of patients. The use of a PPI in the setting of peptic ulcer disease is supported (in theory) by the fact that acid back-diffusion has a role in the susceptibility of the gastric mucosa to injury in experimental models. The duration of PPI treatment required has not been established and current recommendations for the treatment of patients with non-*H. pylori* peptic ulcer disease without associated gastric hypersecretory conditions should be followed.⁷⁵ The use of PPIs in the absence of visible gastroduodenal damage is questionable, and treatment decisions should be made after considering the risk:benefit ratio. Unfortunately no reproducible data are available in the literature to facilitate an evidence-based approach in this particular situation. The decision to use a PPI, therefore, has to be made on an individual case-by-case basis and expert opinion.

Long-term β -blocker therapy should be considered in patients with cirrhosis and PHG.⁷³ The use of prostaglandin analogs has not been assessed in well-designed clinical trials and the decision to use these agents should be made on an individual basis by the patient and their attending physician. In addition, an angiotensin II receptor agonist has been reported to reduce the severity of PHG possibly by reducing portal pressure.⁷⁶

Decompression of the portal system with TIPS placement or surgery is potentially beneficial for patients with PHG,^{18,73,77–79} and TIPS placement seems to be a reasonable treatment for an acute bleeding episode in a patient in whom medical therapy has failed;

however, surgery is considered a last resort given its significant morbidity and mortality. Obliteration of the gastric vascular territory, including splenic artery embolization by interventional radiology, might also be a therapeutic option; however, the efficacy of this approach has been reported mainly for the treatment of bleeding gastric varices. Limited knowledge is available on the influence of this treatment on the gastric microcirculation and PHG.^{80,81} Ultimately, liver transplantation is the therapeutic solution to PHG as decompression of the portal system, resolution of the primary source of PHG (increased portal blood flow resistance) and liver dysfunction are resolved.⁸²

Endoscopic treatment of PHG has been reported using argon plasma coagulation, but its effect on long-term outcomes has not been decisively assessed—except in patients with GAVE—which limits its use to those patients who have not responded to all other treatment options.^{73,83,84} One could argue that TIPS placement is potentially a better approach than endoscopic treatment, even in patients who are not candidates for liver transplantation and despite the associated problems such as hepatic encephalopathy and shunt thrombosis, given the potential of this treatment to better reduce rates of rebleeding.

CONCLUSION

Understanding the mechanisms involved in pathogenesis and development of PHG via the findings of human and experimental studies has helped develop reasonable arguments that favor the use of pharmacological agents, as well as surgical strategies, to achieve control of acute or chronic gastrointestinal bleeding episodes in patients with PHG. However, the fundamental question remains as to whether bleeding episodes in patients with PHG are caused by the morphologic abnormalities of the gastric mucosa in the context of significant liver dysfunction, or arise from an increased susceptibility of the gastric mucosa to injury because of an impaired mucosal defense system. Data generated by experimental studies support the theoretical use of several pharmacological agents to treat this condition; however, the efficacy of these agents (with the exception of β -blockers, for which evidence is available in the literature) requires full investigation in clinical studies and their use should be decided upon by the individual physician.

KEY POINTS

- Portal hypertensive gastropathy (PHG) is frequently observed in patients with portal hypertension, with and without cirrhosis
- Patients with cirrhosis and portal hypertension often present with transfusion-dependent anemia, and the stomach of these patients is highly susceptible to injury induced by irritants such as ethanol, aspirin and traditional NSAIDs
- Portal hypertension is necessary but perhaps not sufficient for the development of clinically significant PHG
- Liver dysfunction has a role in the increased susceptibility of the portal hypertensive gastric mucosa to injury and spontaneous bleeding
- Several pharmacological agents can be employed to treat bleeding episodes associated with PHG— β -blockers seem to be beneficial in preventing recurrent bleeding and acid-secretion blockers are important in the treatment of documented gastric damage
- Endoscopic treatment of esophagogastric varices might enhance PHG
- Resolution of PHG can be achieved with surgical decompression of the portal system, placement of a transjugular intrahepatic shunt, or liver transplantation

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Competing interests

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