Management of variceal and nonvariceal upper gastrointestinal bleeding in patients with cirrhosis

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Isabelle Cremers and Suzane Ribeiro

***Abstract*:** Acute upper gastrointestinal haemorrhage remains the most common medical emergency managed by gastroenterologists. Causes of upper gastrointestinal bleeding (UGIB) in patients with liver cirrhosis can be grouped into two categories: the first includes lesions that arise by virtue of portal hypertension, namely gastroesophageal varices and portal hypertensive gastropathy; and the second includes lesions seen in the general population (peptic ulcer, erosive gastritis, reflux esophagitis, Mallory–Weiss syndrome, tumors, etc.). Emergency upper gastrointestinal endoscopy is the standard procedure recommended for both diagnosis and treatment of UGIB. The endoscopic treatment of choice for esophageal variceal bleeding is band ligation of varices. Bleeding from gastric varices is treated by injection with cyanoacrylate. Treatment with vasoactive drugs as well as antibiotic treatment is started before or at the same time as endoscopy. Bleeding from portal hypertensive gastropathy is less frequent, usually chronic and treatment options include β-blocker therapy, injection therapy and interventional radiology.
The standard of care of UGIB in patients with cirrhosis includes careful resuscitation, preferably in an intensive care setting, medical and endoscopic therapy, early consideration for placement of transjugular intrahepatic portosystemic shunt and, sometimes, surgical therapy or hepatic transplant.

Keywords: cirrhosis, upper gastrointestinal bleeding, management

Introduction

Upper gastrointestinal bleeding (UGIB) is a major public health problem, its prevalence being around 150 per 100,000 adults per year [Palmer, 2002; Hopper and Sanders, 2011]. This condition is the commonest emergency medical admission for gastroenterology worldwide and has a significant inpatient mortality of 10% [Hearnshaw *et al.* 2011] that has remained unchanged over the past 30 years, in spite of the modern methods of diagnosis and treatment [Palmer, 2002; Amitrano *et al.* 2012; Hearnshaw *et al.* 2011]. UGIB results in 250,000–300,000 hospitalizations and 15,000–30,000 deaths per year in the USA [Gilbert, 1990]. Using the National Inpatient Sample from USA (restricted to patients who survived to discharge), the costs for an uncomplicated nonvariceal bleed were $3402 and when associated with complications $5632; for variceal haemorrhage, the costs were $6612 and $23,207, respectively [Viviane and Alan, 2008]. A recent study has shown that UGIB bleeding events result in significant mortality, similar to that of an acute myocardial infarction (0.64% *versus* 0.77%) after adjusting for the initial hospitalization [Wilcox *et al.* 2009].

Variceal bleeding represents 60–65% of the bleeding episodes in patients with cirrhosis [Garcia-Tsao *et al.* 2007]. The outcome for patients with variceal haemorrhage is closely related to the severity of the underlying liver disease. The 6-week mortality with each episode of variceal haemorrhage is approximately 15–20%, ranging from 0% among patients with Child-Pugh class. A disease to approximately 40% among patients with Child-Pugh class C disease [Villanueva *et al.* 2006; Abraldes *et al.* 2008; Bosch *et al.* 2008].

Correspondence to:
Isabelle Cremers, MD
Centro Hospitalar de Setúbal,
R Camilo Castelo Branco,
Setubal 2910-446,
Portugal
cremers_tavares@hotmail.com

Suzane Ribeiro, MD
Centro Hospitalar de Setúbal, Setubal, Portugal

Variceal bleeding in patients with cirrhosis

General considerations

Variceal haemorrhage is a true medical emergency and a lethal complication of cirrhosis, particularly in patients in whom clinical decompensation (i.e. ascites, encephalopathy, a previous episode of haemorrhage, or jaundice) has already developed and especially in patients with Child–Pugh B or C disease in whom bleeding only stops spontaneously in about 50% of cases [D'Amico *et al*. 1999]. For these reasons, management of those patients has to be rapid and efficient to lower both morbidity and mortality.

The overall mortality of variceal bleeding in patients with cirrhosis is between 10% and 20% [Carbonell *et al*. 2004]. This mortality has decreased steadily since the 1980s, when the overall mortality was about 40%, due to aggressive resuscitation in the intensive care setting, increasing use of vasoactive drugs, therapeutic endoscopy, and antibiotic prophylaxis [Carbonell *et al*. 2004]. However, early (first 6 weeks) mortality is still high (around 40%) in Child–Pugh C patients. Risk factors for early mortality include Child–Pugh and Meld score [D'Amico and De Franchis, 2003], active bleeding on admission [Goulis *et al*. 1998], the presence of infection [Bernard *et al*. 1995], portal vein thrombosis [D'Amico and De Franchis, 2003] and an initial hepatic-venous portal gradient (HVPG) higher than 20 mmHg [Abraldes *et al*. 2008]. Although HPVG is a powerful indicator of the severity of the bleeding, it is not possible to use in everyday practice.

When addressing the management of variceal bleeding in patients with cirrhosis, we must always bear in mind that there are two essential steps for success: the management of acute bleeding and the prevention of rebleeding. After stopping the acute bleeding, if left untreated, 60% of these patients will rebleed, with a mortality of 33% [Bosch and Garcia-Pagán, 2003].

Management of acute bleeding

The optimal management of acute bleeding (Figure 1) requires a multifactorial approach, including evaluation and resuscitation, blood transfusion, use of vasoactive drugs, performance of early diagnostic and therapeutic endoscopy (less than 12 h after admission), administration of prophylactic antibiotics, and consideration of placement of a covered transjugular intrahepatic portosystemic shunt (TIPS) in case of failure of endoscopic treatment. However, this step-by-step approach is not usually possible in an acutely bleeding patient who is decompensated and most, if not all, of these steps must be considered or performed almost simultaneously to succeed.

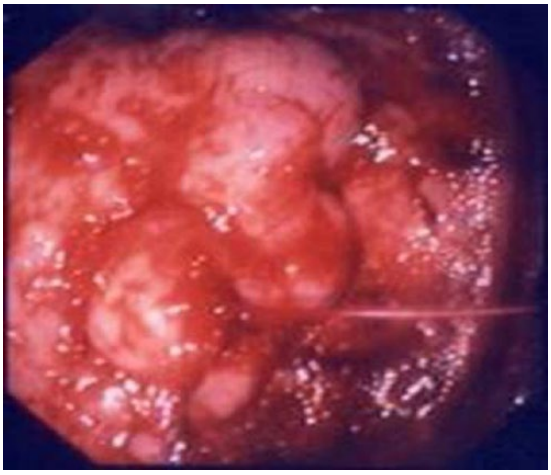

Figure 1. Active bleeding from a gastric varix.

Evaluation and resuscitation. The first step is evaluation and resuscitation, which should take place in an intensive care unit by a multidisciplinary team, including trained hepatogastroenterologists/endoscopists, intensivists, and nurses [Biecker, 2013]. However, in real life, patients are treated first in the emergency department, while procedures for admission in an intensive care unit are undertaken. This means that the team that receives and treats these acutely ill patients must be well trained in all the emergency procedures involved in variceal haemorrhage, always including a hepatogastroenterologist from the start.

When these patients are admitted to the hospital, one of the most important steps is to try to establish if the patient has cirrhosis, either from the history and clinical data, or from laboratory tests, showing thrombocytopenia, altered coagulation, or abnormal liver tests. The suspicion of bleeding varices places the patient in a high-risk group and makes it mandatory to perform immediate procedures, as explained later.

Airway protection must be considered, but there are no strong data in the literature to recommend prophylactic endotracheal intubation, as it has not been shown to decrease the incidence of cardiovascular events, aspiration pneumonia, or mortality [Rudolph *et al*. 2003; Koch *et al*. 2007;

Rehman *et al*. 2009; Waye, 2000]. Experts advise that endotracheal intubation should be performed before endoscopy in patients with ongoing haematemesis, haemodynamic instability in spite of volume loading, agitation with the absence of cooperation during the exam, or Glasgow Coma Scale less than 8 [Garcia-Tsao and Lim, 2009].

Peripheral venous access must be provided and the placement of a venous central line must be considered. Volume replacement should be given in order to obtain a systemic blood pressure greater than 100 mmHg [Dellinger *et al*. 2008]. This must be done with caution to obtain haemodynamic stability and not to overload these patients, as it might lead to failure of bleeding control and rebleeding [Dellinger *et al*. 2008].

Blood transfusion is given in order to obtain a haemoglobin level between 7 and 8 g/dl [Garcia-Tsao *et al*. 2007]. A restrictive blood transfusion is associated with a reduction in further bleeding and rebleeding, a reduction in complication rate, and increased survival [Garcia-Tsao *et al*. 2007]. This has received consensus in the Baveno V conference [De Franchis, 2010] and has been demonstrated again in a recently published study [Villanueva *et al*. 2013].

Correction of coagulopathy and thrombocytopenia, which are usually present in variceal bleeding in patients with cirrhosis, are not indicated by experts, as discussed in the Baveno V meeting [De Franchis, 2010]. Overtransfusion with fresh frozen plasma and platelets causes an increase in portal pressure and may lead to continued bleeding and rebleeding.

Vasoactive therapy. Vasoactive drugs should be administered immediately, ideally during transport to the hospital or on admission, before endoscopy, if variceal bleeding is suspected [De Franchis, 2005, 2010] [Garcia-Tsao and Bosch, 2010], and should be continued for 5 days [De Franchis, 2010]. This is one of the most important procedures to diminish mortality and it achieves haemostasis in 80% of patients [D'Amico *et al*. 2003].

Vasoactive drugs include vasopressin (not used anymore for variceal bleeding due to its many side effects), terlipressin, octreotide, somatostatin, and vapreotide, with different availability among countries. In the USA, the only drug approved for variceal bleeding is octreotide. Vasoactive drugs cause splanchnic vasoconstriction, thereby decreasing portal pressure and reducing or stopping variceal bleeding.

Terlipressin is a synthetic vasopressin analogue with a longer half life and fewer side effects. Similarly to vasopressin, it may cause ischaemic complications and dysrhythmias in patients with ischaemic heart disease or peripheral vascular disease [Escorsell *et al*. 1997]. Several studies have shown that terlipressin is effective in bleeding control and it was the only vasoactive drug that diminished mortality in these patients [Levacher *et al*. 1995; Ioannou *et al*. 2003]. It is given at a dose of 2 mg intravenously every 4 h during the first 48 h, reducing to 1 mg every 4 h for another 3 days, if the bleeding is controlled [Escorsell *et al*. 1997].

Somatostatin causes splanchnic vasoconstriction and it inhibits the postprandial increase in portal blood flow and portal pressure [Burroughs *et al*. 1990]. It is given as an initial bolus of 250 μg followed by 250–500 μg/h in continuous infusion. Octreotide is a synthetic analogue of somatostatin with a longer half life, which is not reflected by longer haemodynamic effects, which may be caused by rapid desensitization or tachyphylaxis [Escorsell *et al*. 2001]. It is administered as an initial bolus of 50 μg followed by a continuous infusion of 50 μg/h [Garcia-Tsao *et al*. 2007]. Vapreotide (another somatostatine analogue) is given as a 50 μg bolus followed by an infusion of 50 μg/h [Garcia-Tsao *et al*. 2007] (Table 1).

A Cochrane review of 21 trials involving 2588 patients with active variceal haemorrhage found no difference in mortality rate or risk of rebleeding with somatostatin and its derivatives (e.g. octreotide) [Gøtzsche and Hróbjartsson, 2008] and a recent study comparing terlipressin, somatostatin, and octreotide in the control of acute esophageal variceal haemorrhage showed no difference in the haemostatic efficacy between these drugs [Seo *et al*. 2014]. Furthermore, the same study showed that the mortality rate does not differ significantly between these three drugs in the setting of combination therapy with endoscopic treatment. Therefore, any of these drugs may be used in combination with endoscopic therapy to control bleeding from esophageal varices.

Antibiotic prophylaxis. For the past two decades it has been widely known that patients with cirrhosis with variceal haemorrhage have a high risk of bacterial infections, which relates to early rebleeding rates and to a high mortality [Goulis

Table 1. Vasoactive drugs.

Somatostatin	250 µg bolus followed by an infusion of 250–500 µg/h
Terlipressin	2 mg intravenously every 4 h during the first 48 h, reducing to 1 mg every 4 h for another 3 days
Octreotide	50 µg bolus followed by an infusion of 50 µg/h
Vapreotide	50 µg bolus followed by an infusion of 50 µg/h

et al. 1998; Bernard *et al.* 1995], mainly in more decompensated patients with cirrhosis, Child–Pugh B and C [Pauwels *et al.* 1996]. However, bacterial infections, early rebleeding and mortality are reduced when patients are given prophylactic antibiotics, which are nowadays a part of the standard of care of these patients [Soares-Weiser *et al.* 2002]. The recommended antibiotic is norfloxacin, in a dose of 400 mg orally twice a day [Rimola *et al.* 2000], or ciprofloxacine 200 mg intravenously twice a day if the oral route is not possible. In patients with advanced cirrhosis, Child–Pugh B or C, ceftriaxone proved to be more effective than oral norfloxacine [Fernandez *et al.* 2006].

A review of 12 trials involving 1241 patients with variceal haemorrhage found that broad-spectrum antibiotics (e.g. ceftriaxone, norfloxacin, ciprofloxacin) reduced overall mortality [relative risk (RR) = 0.79] and risk of rebleeding (RR = 0.53) [Chavez-Tapia *et al.* 2010].

Endoscopic treatment. Upper gastrointestinal endoscopy should be performed early, in the first 12 h after admission, and endoscopic therapy should be performed at once if there is a diagnosis of variceal bleeding [Garcia-Tsao *et al.* 2007], which is made using the following criteria: active bleeding from a varix; presence of a 'white nipple' fibrin clot overlying a varix; a clot on a varix; the presence of varices without other potential source of bleeding; and fresh blood in the stomach [Garcia-Tsao and Lim, 2009].

Endoscopy should ideally be performed on an empty stomach. Nasogastric lavage is usually performed to that purpose, but it is associated with complications and is not efficient in half of cases. The use of erythromycin at a dose of 250 µg intravenously over 5 min, 20 min before endoscopy, acting as a motilin agonist, has been shown to result in an empty stomach, decreasing the time of endoscopy [Frossard *et al.* 2002].

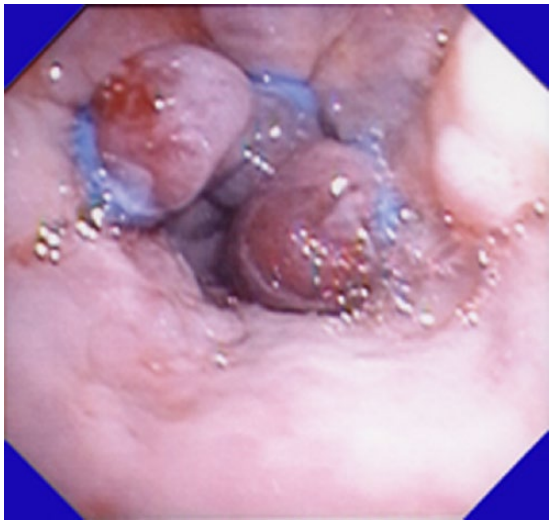

Figure 2. Band ligation of esophageal varices.

Regarding endoscopic therapy, endoscopic band ligation (Figure 2) is preferred as it provides better bleeding and rebleeding control and has fewer adverse events compared with sclerotherapy. The most frequent complications of band ligation are superficial ulcerations, oesophageal strictures, and delayed bleeding after falling of the rubber rings [Biecker, 2013]. Sclerotherapy is used when band ligation is technically difficult (for example, when there is too much blood for good visibility) or not available [Garcia-Tsao and Lim, 2009; Garcia-Tsao *et al.* 2007; De Franchis, 2005]. Sclerotherapy is less expensive than band ligation.

Combined therapy (vasoactive drugs and endoscopic therapy) is more effective than either treatment alone, as has been showed by several randomized controlled trials and meta-analysis of these trials [Augustin *et al.* 2010; Sung *et al.* 1995].

Failure of bleeding control or rebleeding. Failure to control bleeding or rebleeding implicates a change in treatment. For oesophageal varices, a second therapeutic endoscopy is indicated if the patient is stable [Garcia-Tsao *et al.* 2007]. For gastric varices, only one endoscopic treatment is allowed and if the patient rebleeds or continues to bleed, then another treatment must be performed [Garcia-Tsao *et al.* 2007]. Vasoactive medication should be given at maximum doses. If endoscopic treatment and vasoactive drugs fail, then other steps must be taken.

If the patient has unstable disease, a balloon tamponade (Sengstaken-Blackemore for oesophageal

varices or Linton for both oesophageal and gastric varices) is indicated in order to control the bleeding and while the team prepares a more definitive therapy [Garcia-Tsao *et al*. 2007]. Balloon tamponade is effective in bleeding control in about 80% of patients, but they will rebleed in about half of cases after balloon deflation. There are several frequent complications, such as aspiration, migration, necrosis and perforation of the oesophagus, and a high mortality. To reduce those complications, the balloon should only stay in place for 24 h [Garcia-Tsao *et al*. 2007]. Balloon tamponade is a bridge therapy, usually while arranging for a TIPS.

Another bridge therapy is the placement of covered oesophageal stents, which has been studied in several reports [Garcia-Tsao and Lim, 2009; De Franchis, 2010; Hubmann *et al*. 2006]. Those stents seem to have fewer complications than balloon tamponade, but there are no recommendations from the Baveno V consensus meeting [De Franchis, 2010].

Covered TIPS can be used as a salvage therapy if the oesophageal or gastric variceal bleeding is not controlled with conventional endoscopic and medical therapy, when oesophageal variceal bleeding recurs despite two endoscopic treatments associated with medical therapy and if gastric variceal bleeding occurs after a single failure endoscopy [Garcia-Tsao and Lim, 2009; Garcia-Tsao *et al*. 2007]. Placement of TIPS in these patients is sometimes performed too late, when patients have become more decompensated and survival is poor. The same is true for a late shunt surgery [Garcia-Tsao and Lim, 2009; Garcia-Tsao *et al*. 2007].

Transplant should be considered in selected patients as soon as possible during the bleeding episode [Garcia-Tsao *et al*. 2007].

Importance of early TIPS in selected patients. Recent studies have identified a group of high-risk patients in whom the early placement of a covered TIPS, within 72 h of admission, was associated with a better prognosis [Monescillo *et al*. 2004; Garcia-Pagán *et al*. 2010]. These high-risk patients include patients with Child B cirrhosis and active bleeding at endoscopy and patients with Child C cirrhosis with less than 14 points, after medical and endoscopic treatment has been administered. A follow-up study published in 2013 has confirmed that the use of early covered TIPS in these high-risk patients is associated with a much lower risk of failure to control bleeding and of rebleeding, and also with a significant lower mortality [Garcia-Pagán *et al*. 2013]. The importance of these studies cannot be overstressed and professionals in charge of these patients should organize referral to specialized centres.

Gastric variceal bleeding. Bleeding from gastric varices is less frequent than from oesophageal varices, accounting for about 3% of variceal bleeds. However, bleeding from gastric varices is usually more severe and difficult to control and the mortality is higher [Bosch, 2009]. There are four types of gastric varices. Type one varices are an extension of oesophageal varices along the lesser curvature and can be treated as oesophageal varices [Sarin, 2009]. The other gastric varices should be treated by obliteration with a tissue adhesive, such as cyanoacrylate [Garcia-Tsao *et al*. 2007; De Franchis, 2010].

Cyanoacrylates are a family of compounds that have been used as haemostatic agents. Over the past 30 years, the use of cyanoacrylate injection has been established in many parts of the world to achieve gastric varix obliteration. In the meantime, several comparative studies have emerged. A randomized, controlled trial with cyanoacrylate (enbucrilate mixed 1:1 with lipiodol) *versus* band ligation has demonstrated a 27% rebleed rate in the cyanoacrylate group *versus* 63% rebleeding in the ligation group, with no difference in long-term survival [Tan *et al*. 2006]. Another randomized trial has found that cyanoacrylate injection was more effective than β-blocker treatment for the prevention of gastric variceal rebleeding, with a lower mortality rate (3% *versus* 25%) [Mishra *et al*. 2010]. In a cohort study, comparing cyanoacrylate (enbucrilate mixed with lipiodol 1:1.5) with TIPS, similar rebleeding rates with a slight (nonsignificant) advantage to a TIPS have been shown, as well as a 50% cost reduction in the cyanoacrylate group [Mahadeva *et al*. 2003]. However, if the injection of cyanoacrylate is too difficult due to obscured view from excessive bleeding or if it fails, then the patient should be referred for TIPS, which has been proved highly effective, stopping the bleeding in about 90% of patients [Garcia-Tsao *et al*. 2007]. A Linton balloon can be placed as a bridge before more definitive therapy [Sarin, 2009]. Figure 3 shows a treatment algorithm for upper gastrointestinal bleeding in patients with cirrhosis.

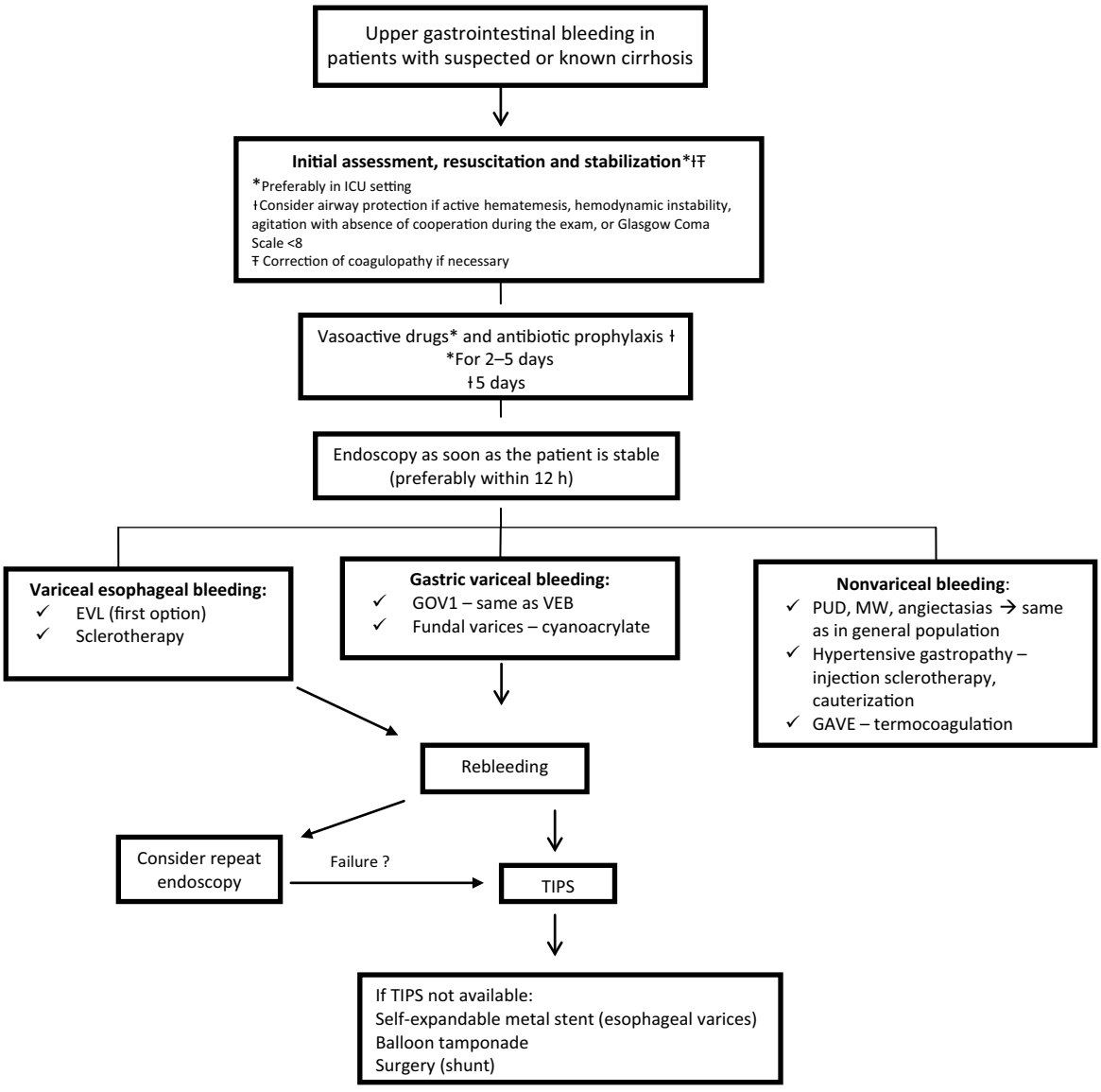

Figure 3. Treatment algorithm for upper gastrointestinal bleeding in patients with cirrhosis.
EVL, endoscopic variceal ligation; ; GAVE, gastric antral vascular ectasia; GOV, gastroesophageal varices; ICU, intensive care unit; MW: Mallory–Weiss; PUD, peptic ulcer disease; TIPS, transjugular intrahepatic portosystemic shunt; VEB, variceal esophageal bleeding.

Secondary prophylaxis

As stated above, patients who stop bleeding from varices have a risk of rebleeding of about 60% within 1–2 years if left untreated, with a mortality of 33% [Bosch and Garcia-Pagán, 2003]. Therefore, the second step of a successful treatment of variceal bleeding is prevention of recurrence and it should be started prior to discharge from hospital.

The consensus is to treat these patients with a combination of pharmacological therapy and endoscopic therapy [Garcia-Tsao *et al.* 2007]. The efficacy of this combined therapy has been demonstrated in two randomized studies [Lo *et al.* 2000; De La Pena *et al.* 2005].

Regarding pharmacological therapy, patients can be treated with a nonselective β blocker (e.g. nadolol and propranolol) alone or in combination with mononitrate ississorbide. A combination of these two drugs has been shown to be more effective but without reaching statistical significance [Gournay *et al.* 2000]. The median rebleeding rate of patients treated with this combination therapy is around 33–35% [D'Amico *et al.* 1999;

Bosch and Garcia-Pagán, 2003], lower than with a nonselective β blocker alone [D'Amico *et al.* 1999]. The problem with pharmacological combined therapy is the higher incidence of side effects compared with a nonselective β blocker [D'Amico *et al.* 1999; Gournay *et al.* 2000], leading to suspension of therapy and to treatment with a nonselective β blocker alone.

Pharmacological therapy should be used in combination with endoscopic therapy, usually endoscopic variceal ligation, which has been shown to be effective and have fewer side effects than sclerotherapy [Laine and Cook, 1995]. Ligation sessions are performed at 7–14-day intervals until variceal obliteration. Once eradicated, patients should be submitted to upper gastrointestinal endoscopy every 3–6 months to evaluate for variceal recurrence and need to repeat treatment. Complications of variceal ligation include transient dysphagia, chest discomfort, and ulcers at the site of ligation, which sometimes bleed [Saeed *et al.* 1997]. A small randomized study comparing pantoprazole and placebo showed smaller ulcers in the pantoprazole-treated patients and bleeding ulcers only in the placebo-treated group. Although the results of this study did not have statistical significance [Shahen *et al.* 2005], they support the use of pantoprazole in patients treated with endoscopic variceal ligation.

Ideally HVPG measurements should be used to evaluate response to pharmacological therapy. Patients with a reduction in HVPG to less than 12 mmHg or a reduction in HVPG by more than 20% have the lowest rate of variceal rebleeding, about 10% [D'Amico *et al.* 2006; Bosch and Garcia-Pagán, 2003]. It has been suggested that such patients could be treated with pharmacological treatment alone without endoscopic variceal ligation until eradication [Bureau *et al.* 2002; Gonzalez *et al.* 2006]. However, HVPG measurements are made only in referral centres and cannot be used for clinical practice.

Other treatments for prevention of variceal bleeding include the placement of covered TIPS, shunt surgery, and hepatic transplant. The placement of covered TIPS should be used as a rescue therapy for patients whose condition has failed to respond to pharmacological plus endoscopic treatment, as survival is identical, although rebleeding is less frequent in patients treated with TIPS [Boyer and Haskal, 2005]. Shunt surgery is very effective in preventing rebleeding, but has no effect on survival due to its complications [D'Amico *et al.* 1995]. Hepatic transplant should be offered to all candidates.

Portal hypertensive gastropathy and gastric vascular ectasia

Mucosal changes in the stomach in patients with portal hypertension include portal hypertensive gastropathy (PHG) and gastric antral vascular ectasia (GAVE). These are two clearly distinct clinical entities with different pathophysiology, endoscopic appearance, and treatment.

PHG is the characteristic mosaic-like gastric mucosa with or without red spots which is seen quite frequently in patients with cirrhosis. These changes are usually seen in the fundus or body of the stomach. Histopathologic features of portal hypertensive gastropathy are vascular ectasia of the mucosal and submucosal veins and capillaries [Cubillas and Rockey, 2010]. PHG is considered mild when only a mucosal mosaic pattern is present and severe when there are discrete red spots or diffuse haemorrhagic lesions [Cubillas and Rockey, 2010]. Although bleeding from PHG can be acute or chronic in nature, chronic bleeding presenting as iron deficiency anaemia or occult blood in stool is far more frequent than acute bleeding [Primignani *et al.* 2000]. The specific treatment options for significant PHG include nonselective β blockers, endoscopic therapy, TIPS, or surgical shunts [Thuluvath and Yoo, 2002]. Nonselective β blockers have been shown to reduce the risk of bleeding in patients who have PHG, however pharmacological therapy is not currently recommended to prevent bleeding (primary prophylaxis) in patients with severe PHG [Cubillas and Rockey, 2010]. Small studies have suggested that vasoactive drugs such as octreotide and terlipressin may be useful for controlling acute bleeding [Panés *et al.* 1994; Kouroumalis *et al.* 1998; Zhou *et al.* 2002]. B blockers are recommended for preventing chronic blood loss in patients who have bled from severe PHG [Perez-Ayuso *et al.* 1991]. Endoscopic therapy in the form of cauterization or injection sclerotherapy can be effective in patients who have acute bleeding caused by PHG and can be attempted for managing clinically significant chronic bleeding caused by PHG. TIPS should be considered as salvage therapy in patients with recurrent bleeding despite pharmacological and endoscopic therapy [Kamath *et al.* 2000].

In GAVE, aggregates of ectatic vessels can be seen on endoscopic examination as red spots without a mosaic background. As the name indicates, GAVE is typically located in the gastric antrum and contrarily to PHG, GAVE is also found in patients without portal or liver disease. Management of patients with bleeding GAVE is substantially different from PHG, as it does not respond to portal pressure reducing therapies, such as TIPS or shunt surgery. The mainstay of therapy in GAVE is the endoscopic ablation of the lesions [Herrera *et al.* 2008]. There are different endoscopic therapeutic methods which have been used in the setting of GAVE, including argon plasma coagulation (APC), heater probe, cryotherapy, band ligation, and laser therapy [Ripoll and Garcia-Tsao, 2011]. APC, which produces thermal coagulation by applying contact with mucosa, is easy to use and the risk of perforation is much lower than with laser therapy [Ripoll and Garcia-Tsao, 2011]. The sessions should be repeated every 2–6 weeks as needed. If endoscopic therapy fails, therapy with an oral oestrogen–progesterone combination may be useful in reducing transfusion requirement [Tran *et al.* 1999]. Surgery with antrectomy can be attempted when endoscopic therapy has failed. However, it has a high morbidity and mortality rate, particularly in patients with decompensated cirrhosis in whom GAVE usually presents [Spahr *et al.* 1999]. In contrast to PHG, TIPS does not reduce the bleeding risk in patients with GAVE and is associated with a substantial risk of hepatic encephalopathy [Kamath *et al.* 2000]. Therefore, TIPS placement is not recommended as therapy for GAVE.

Conclusion

Acute gastrointestinal bleeding is a potentially life-threatening emergency that remains a common cause of admission to hospital. In patients with liver cirrhosis, variceal haemorrhage is the most common source of acute upper gastrointestinal bleeding, a serious complication of portal hypertension, and an important cause of morbidity and mortality in these patients. Bleeding from portal hypertensive gastropathy and other lesions seen in the general population is also possible. Given the high recurrence rate, patients who survive an acute variceal haemorrhage should receive therapy to prevent recurrence before they are discharged from hospital.

Mortality after the index haemorrhage in patients with cirrhosis has been reported to be as high as 50%. Treatment of these patients is usually complex and requires a team approach with defined stepwise management. Endoscopic therapy is a key aspect, but pharmacological treatment with vasopressors and antibiotic treatment are also important components of successful patient care.

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Conflict of interest statement

The authors declare that there is no conflict of interest.

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