

# Acute upper gastrointestinal haemorrhage

Eliana Saffouri

A John Morris

## Abstract

Acute upper gastrointestinal bleeding (UGIB) is a common hospital presentation with high mortality. Presentation is across age groups and affected by increasingly complex underlying multimorbidity. New developments in the pharmacology of thrombotic disorders can lead to increased bleeding risk. Risk stratification scoring systems can identify patients at risk of adverse outcomes and facilitate early discharge in patients deemed at low risk. Initial management focuses on appropriate early resuscitation. The need for blood transfusion must be carefully considered, with target haemoglobin guided by pre-existing medical conditions and response to initial resuscitation measures. The diagnosis of underlying cirrhosis should prompt administration of intravenous antibiotics before endoscopy. During endoscopy, the standard of care for bleeding peptic ulcers is dual-endoscopic therapy followed by intravenous proton pump inhibition infusion. When the cause of bleeding is determined to be oesophageal varices, band ligation is the treatment of choice. Newer developments in the treatment of UGIB, such as topical haemostatic agents, have been used, with encouraging results. Over-the-scope clips, previously used to manage gastrointestinal perforation, are now used in the management of UGIB refractory to standard treatment. When haemorrhage is not controlled endoscopically, referral to interventional radiology is recommended to facilitate catheter embolization of bleeding vessels.

**Keywords** Antibiotics; band ligation; blood transfusion; endoscopy; gastrointestinal bleeding; Hemospray®; intravenous proton pump inhibitors; MRCP; oesophageal varices; peptic ulcer

## Introduction

Acute upper gastrointestinal bleeding (UGIB) is common, accounting for 85,000 presentations to UK hospitals each year. The

*Eliana Saffouri MB ChB MRCP PG Cert Med Ed is a Specialty Trainee in Gastroenterology and Advanced Endoscopy Fellow at Glasgow Royal Infirmary, UK. Competing interests: Dr Saffouri has received educational sponsorship from Gilead.*

*A John Morris MB FRCP is Consultant Gastroenterologist, Clinical Lead for Gastroenterology at Glasgow Royal Infirmary and Director of the West of Scotland Endoscopy Training Centre, Glasgow, UK. Competing interests: Dr Morris has received speaker and consulting fees from Cook Medical, Ferring, Falk, Vifor and Takeda Pharmaceuticals.*

## Key points

- Many patients who present with acute upper gastrointestinal bleeding have peptic ulcer disease
- The Rockall and Blatchford scores can aid in risk stratification, with a low Blatchford score strengthening a decision for early discharge
- IV crystalloid is the preferred resuscitation fluid; there is evidence that a 'restrictive' blood transfusion practice is beneficial
- Dual-endoscopic therapy is the standard for bleeding from peptic ulcer disease
- Aspirin should be continued, as the cardiovascular benefits conferred outweigh the risk of further bleeding

2015 National Confidential Enquiry into Patient Outcome and Death (NCEPOD) report determined that the management of this presentation was highly variable, and that efforts should be made to standardize practice to improve patient outcomes. Key messages from this report suggest that patients admitted with acute gastrointestinal bleeding should only be admitted to hospitals with 24/7 access to on-site endoscopy, critical care and interventional radiology; the report also provides guidance on resuscitation and the timing of endoscopy.<sup>1</sup>

## Aetiology

Many patients with acute UGIB are found to have peptic ulcer disease, which has been implicated in 36% of presentations. Variceal bleeding – either oesophageal or gastric – accounts for a significant proportion of the remaining presentations. Other causes of acute UGIB include oesophagitis, Mallory–Weiss tear, gastritis, duodenitis, arteriovenous malformations and upper gastrointestinal malignancies. Risk factors for these pathologies include non-steroidal anti-inflammatory drugs, *Helicobacter pylori* infection, recurrent vomiting and the use of a range of medications predisposing patients towards bleeding. Antiplatelet therapy, particularly as dual therapy, for example aspirin and clopidogrel, along with warfarin and newer direct-acting oral anticoagulants (DOACs), is also implicated in acute UGIB.

## Initial assessment and management

Appropriate and timely resuscitation remains the initial focus of the first assessment of patients with acute UGIB. Initial observations such as pulse and blood pressure suggest the need for immediate intravascular volume replacement and are also used in pre-endoscopic scoring. Regular review of these parameters informs the clinician of the patient's response to resuscitation.

Increased American Society of Anesthesiologists (ASA) grade, a measurement of co-morbidity and predictor of perioperative morbidity and mortality, has been associated with increased risk of adverse events at endoscopy. It can therefore be a useful tool

to aid risk stratification and determine optimal timing for emergency endoscopy.

### Risk stratification

Part of the initial assessment must be a determination of a patient's underlying co-morbidities and the potential risks of an endoscopic procedure. It can be difficult to determine a patient's risk of further bleeding or other morbidity, or indeed mortality, after presentation with acute UGIB. Additionally, there is the question of timing of endoscopy and potential endoscopic intervention.

The Rockall and Blatchford scoring systems are both well validated and straightforward to use. The Rockall system has both a pre- and a post-endoscopic value. The initial Rockall score is calculated from age, presence of clinical signs of shock, and co-morbidities; the post-endoscopic score also includes endoscopic findings. Low pre-endoscopic Rockall scores are associated with low risk of rebleeding or death within the 30 days after an UGIB. Recent work has also linked full Rockall scores  $\geq 6$  with a risk of long-term recurrent peptic ulcer bleeding.

The Glasgow Blatchford Score (GBS) acknowledges objective measurements such as blood results and clinical observations, and is a useful predictor of the need for inpatient endoscopy (Table 1). Its component values include information readily available in the immediate post hospital admission phase, making it a useful tool early in a patient's admission.

In a recently-published study of acute admissions in the emergency department setting, the GBS proved superior to the pre-endoscopic Rockall for predicting 30-day mortality (see Further reading). It has also been shown to be superior to the pre-endoscopic Rockall score in predicting both rebleeding and the need for endoscopic therapy (see Further reading).

### Glasgow Blatchford Score

Factor	Value	Score
Urea (mmol/dl)	6.5–8.0	2
	8.0–10.0	3
	10.0–25.0	4
	>25	6
Haemoglobin – men (g/litre)	120–129	1
	100–119	3
	<100	6
Haemoglobin – women (g/litre)	100–119	1
	<100	6
Systolic blood pressure (mmHg)	100–109	1
	90–99	2
	<90	3
Pulse (per minute)	$\geq 100$	1
Presence of melaena		1
Syncope		2
Underlying liver disease		2
Heart failure		2

Components of the Glasgow Blatchford Score. A score of 0 or 1 suggests that a patient may be suitable for discharge and outpatient endoscopy.

Table 1

ASA grade has recently been shown to be a key factor in determining timing of endoscopy. In a study of >12,000 patients, endoscopy 12–36 hours after admission was associated with lower in-hospital mortality in haemodynamically stable patients with an ASA score of 3–5. Patients who were haemodynamically unstable had a lower in-hospital mortality when undergoing endoscopy 6–24 hours after admission, regardless of ASA grade.

### Resuscitation

Intravenous (IV) crystalloid should initially be used as volume replacement in patients with acute UGIB. Monitoring the patient for clinical signs of shock (confusion, tachycardia, hypotension, reduced urine output) will guide continuing volume replacement.

The use of red blood cells for resuscitation in acute UGIB has been extensively debated. A randomized controlled trial demonstrated improved outcomes with a 'restrictive' transfusion policy (transfusion if haemoglobin is <70 g/litre) versus a 'liberal' one (transfusion if haemoglobin is <90 g/litre), with reduced rebleeding rates and fewer adverse events. Within the subgroup of patients suspected to be bleeding from causes related to portal hypertension, a target of 70–80 g/litre is recommended, as more aggressive transfusion has been associated with an increase in portal pressure and thus further bleeding.<sup>2</sup>

Platelets should be transfused if the patient is actively bleeding and has a platelet count  $<50 \times 10^9$ /litre.

### Endoscopy and intervention

Non-variceal bleeding lesions are described with the Forrest classification, which is used to stratify the risk of rebleeding and mortality (Figure 1, Table 2). Dual therapy of adrenaline (epinephrine) (1:10,000) injection in combination with a mechanical method such as a Hemoclip® is the recognized standard for treatment of lesions with acute bleeding or signs of recent haemorrhage; this has been shown to be more effective than injection monotherapy alone (Figure 2).<sup>3</sup>

Patients in whom variceal bleeding is suspected should have i.v. antibiotics and i.v. terlipressin before endoscopy. Cirrhotic patients have a high chance of developing infections during their

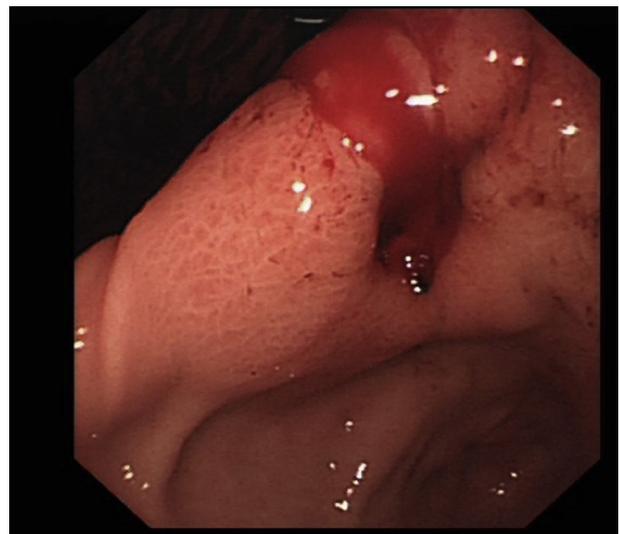


Figure 1 An ulcer (Forrest Ib) on the incisura.

**Forrest classification**

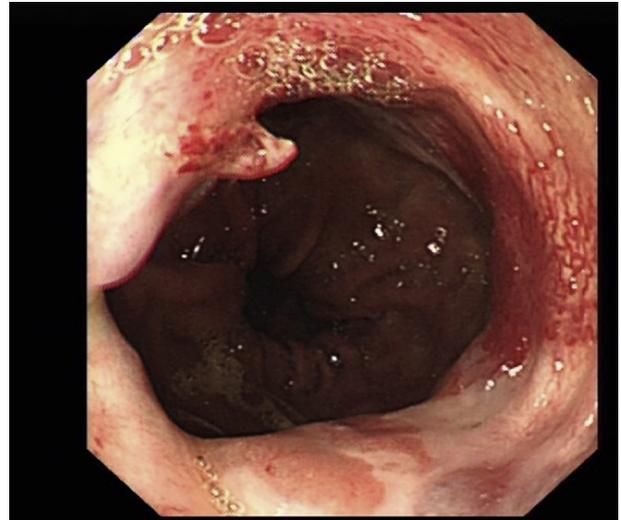
Forrest type	Appearance	Clinical implication
Ia	Spurting vessel	Acute haemorrhage
Ib	Oozing vessel	
IIa	Non-bleeding visible vessel	Signs of recent haemorrhage
IIb	Adherent clot	
IIc	Pigmented spot on ulcer	Lesions without active bleeding
III	Fibrin-covered base/no signs of recent haemorrhage	

**Table 2**

hospital admission, and the early administration of IV antibiotics has been shown to reduce mortality by 9%.<sup>2,4</sup> The choice of antibiotic will be advised by local protocols. The administration of terlipressin aims to reduce portal pressure and thereby bleeding risk; this medication can be stopped after definitive haemostasis has been achieved, or after 5 days.<sup>2</sup> Variceal band ligation is the preferred treatment for bleeding oesophageal varices, and repeated banding at 2–4-weekly intervals is required after initial treatment, aiming for eradication of varices (Figures 3 and 4).<sup>2</sup> Injection of cyanoacrylate glue or thrombin is recommended for bleeding gastric varices; the choice of agent will be guided by local practice and expertise.

If haemostasis cannot be achieved endoscopically in bleeding oesophageal varices, a Sengstaken–Blakemore tube can be inserted by a competent operator. This device consists of flexible plastic tubing with internal aspiration and balloon channels, and two inflatable balloons, one oesophageal and one gastric. The tube is passed into the stomach, and the gastric balloon inflated, traction then being applied to the tubing. This compression at the gastro-oesophageal junction stops portal blood flow through collateral vessels, thereby tamponading variceal bleeding.

The endoscopy report should include the endoscopist's recommendation for next-line treatment, such as re-scoping, computed tomography angiogram or surgery, as well as advice

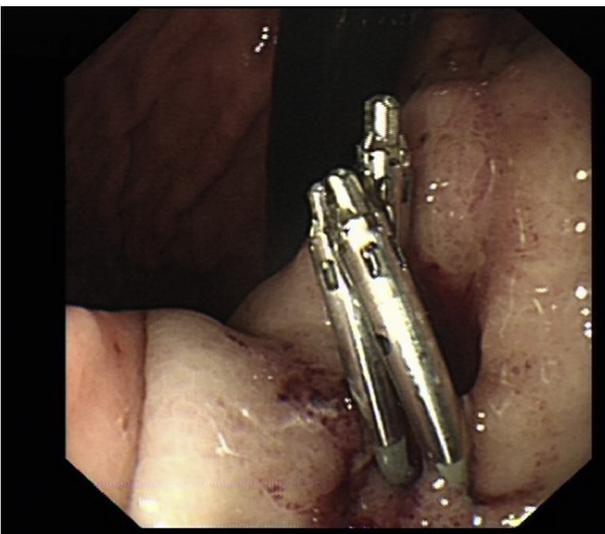
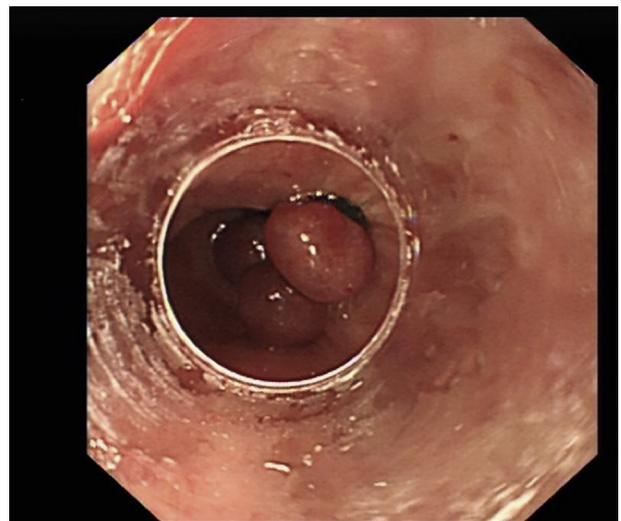
**Figure 3** A varix with the 'white nipple sign'.

on medications to be started, continued or stopped. Unfortunately, this information is often omitted, with 42% of non-variceal UGIB patients and 32% of variceal bleeders lacking a plan for re-bleeding.<sup>1</sup>

**Pharmacology**

With increasing multimorbidity of the general population, unwanted adverse effects related to pharmacotherapy are contributing to complex management decisions in patients presenting with acute UGIB. The risk of further haemorrhage must be balanced with the risk of thrombosis in individual indications.

**Antiplatelet therapy (aspirin and P2Y<sub>12</sub> inhibitors, e.g. clopidogrel):** it is now accepted practice to continue aspirin in suspected acute UGIB because of the benefit conferred on cardiovascular risk factors and long-term mortality.<sup>5</sup> There is no evidence that aspirin delays the healing of peptic ulcers when given with a proton pump inhibitor (PPI).

**Figure 2** The ulcer in Figure 1 after injection and clipping.**Figure 4** Varices after ligation.

If a patient is on both aspirin and a P2Y<sub>12</sub> inhibitor, at least one of these drugs should be continued, as this has been shown to reduce the risk of coronary stent thrombosis. If it is interrupted in these patients, a P2Y<sub>12</sub> inhibitor should not be stopped for more than 5 days.<sup>5</sup> The exception to this is patients who are at high risk of thrombosis (e.g. those with drug-eluting coronary stents) in whom a decision on discontinuation of antiplatelet therapy should be taken only after discussion with a cardiologist.

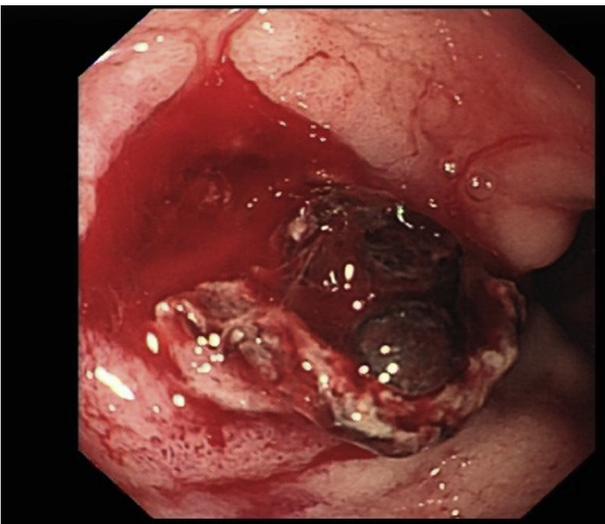
**Warfarin:** National Institute for Health and Care Excellence guidelines suggest administering prothrombin complex concentrate and vitamin K to patients on warfarin if they are actively bleeding. Fresh-frozen plasma is an alternative if prothrombin complex concentrate is unavailable.<sup>1</sup>

**Direct-acting anticoagulants:** the antithrombotic effects of DOACs last 1–2 days after administration. These medications can be restarted 1–2 days after haemostasis has been achieved in patients with a high cardiothrombotic risk.<sup>5</sup> Discussion between the endoscopist and cardiologist is recommended if there is clinical uncertainty.

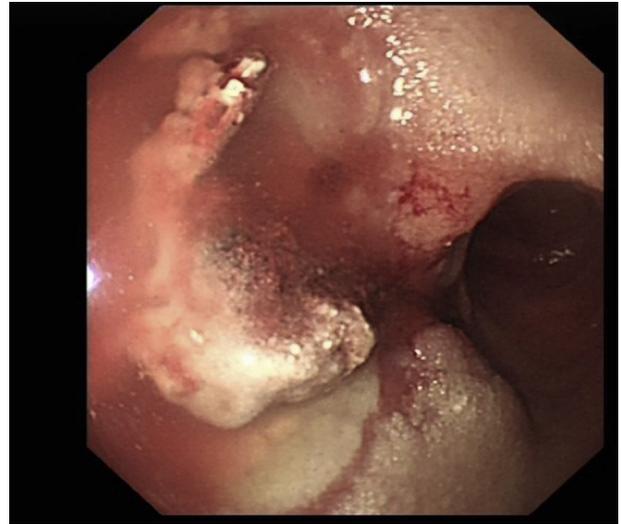
**Proton-pump inhibitors:** it is standard practice to use a 72-hour infusion of a PPI after endoscopic treatment for high-risk non-variceal UGIB; this is given as a bolus, followed by an infusion dose over the remaining hours. Guidelines published in 2018 suggest that the action of a high-dose oral PPI in peptic ulcer bleeding is comparable to that of an i.v. PPI, but there is no high-powered randomized controlled trial comparing the two.<sup>5</sup>

### New developments

Hemospray<sup>®</sup> is a haemostatic powder that can be applied directly to a site of bleeding (Figures 5 and 6). An initial study in 2011 confirmed the safety and efficacy of Hemospray<sup>®</sup> in peptic ulcer bleeding. These results are strengthened by the results of the Survey to Evaluate the Application of Hemospray<sup>®</sup> in the Luminal Tract (SEAL), which demonstrated effective management of both ulcer and non-ulcer bleeding with the use of Hemospray<sup>®</sup>. In this analysis, Hemospray<sup>®</sup> was also effective as



**Figure 5** Ulcer with adherent clot.



**Figure 6** The ulcer in Figure 5 after application of Hemospray<sup>®</sup>.

a rescue therapy after failure of conventional methods to achieve haemostasis.

Hemospray<sup>®</sup> has also shown efficacy in the management of gastric variceal bleeding. However, this has been limited to use as a bridging therapy to definitive treatment such as transjugular intrahepatic portosystemic shunt after the failure of Histoacryl<sup>®</sup> or thrombin, which are the recognized treatments for gastric variceal bleeding.

Use of over-the-scope clips (OTSCs) are increasingly used in situations where haemostasis has not been achieved by conventional endoscopic means. These larger clips are fitted to the end of the endoscope, rather than passing through the scope channel, as is the case with standard clips. This design allows a larger area of tissue to be compressed, with the aim of more effective haemostasis. One study demonstrated 97% primary haemostasis when OTSCs were used after failure of standard endoscopic treatment.

Referral for consideration of interventional radiology and embolization should be part of the management of cases refractory to endoscopic treatment. In a recently published NCE-POD report, 70% of hospitals that admitted patients with acute gastrointestinal bleeds had an interventional radiology service. However, only half of these centres had an on-call rota, and only 27% could provide on-site embolization regardless of the day of admission.<sup>1</sup> This highlights the need for further development of this bleeding-related service. ◆

### KEY REFERENCES

- 1 National Confidential Enquiry in to Patient Outcome and Death (NCEPOD). Time to Get Control? A review of the care received by patients who had a severe gastrointestinal haemorrhage. July 2015, <https://www.ncepod.org.uk/2015gih.html>.
- 2 Tripathi D, Stanley AJ, Hayes PC, et al. UK guidelines on the management of variceal haemorrhage in cirrhotic patients. *Gut* 2015; **64**: 1680–704.
- 3 Galnek I, Dumonceau J, Kuipers E, et al. Diagnosis and management of nonvariceal upper gastrointestinal hemorrhage: European Society of Gastrointestinal Endoscopy (ESGE) guideline. *Endoscopy* 2015; **47**: a1–46.

- 4 Bernard B, Grangé J, Khac E, Amiot X, Opolon P, Poynard T. Antibiotic prophylaxis for the prevention of bacterial infections in cirrhotic patients with gastrointestinal bleeding: a meta-analysis. *Hepatology* 1999; **29**: 1655–61.
- 5 Sung J, Chiu P, Chan F, et al. Asia-Pacific working group consensus on non-variceal upper gastrointestinal bleeding: an update 2018. *Gut* 2018; **67**: 1757–68.

**FURTHER READING**

- Bryant R, Kuo P, Williamson K, et al. Performance of the Glasgow-Blatchford score in predicting clinical outcomes and intervention in hospitalized patients with upper GI bleeding. *Gastrointest Endosc* 2013; **78**: 576–83.
- Tang Y, Shen J, Zhang F, Zhou X, Tang Z, You T. Scoring systems used to predict mortality in patients with acute upper gastrointestinal bleeding in the ED. *Am J Emerg Med* 2018; **36**: 27–32.

**TEST YOURSELF**

To test your knowledge based on the article you have just read, please complete the questions below. The answers can be found at the end of the issue or online [here](#).

**Question 1**

A 23-year-old man presented with repeated vomiting over 24 hours. The most recent vomit was described as 'bright red'. He had been drinking heavily for the previous 3 days. On clinical examination, he looked well, his heart rate was 90 beats/minute, and blood pressure was 115/70 mmHg. Blood results were awaited.

**What is the most likely diagnosis?**

- A Peptic ulcer bleed
- B Mallory–Weiss tear
- C Gastritis
- D Variceal bleed
- E Upper gastrointestinal malignancy

**Question 2**

A 56-year-old woman presented having been vomiting dark red blood for the previous 4 hours. She had not opened her bowels that day. She had previously been found to have cirrhosis related to excess alcohol ingestion. On clinical examination, her heart rate was 110 beats/minute, and blood pressure was 65/50 mmHg. Oxygen saturations were 96% on air.

**Investigations**

- Haemoglobin 70 g/litre (115–165)
- Urea 12.5 mmol/litre (2.5–7.0)

**What is the most appropriate next step in her management?**

- A Crystalloid IV
- B Antibiotics IV
- C Terlipressin IV
- D Insert urinary catheter
- E Blood transfusion

**Question 3**

A 70-year-old man presented with a urinary tract infection but started passing 'black' stools. He had a history of myocardial infarction, hypertension and arthritis. He was taking aspirin, ramipril, simvastatin, lansoprazole and ibuprofen. On clinical examination, his heart rate was 88 beats/minute, and blood pressure was 110/80 mmHg. Oxygen saturations were 99% on air. There was mild tenderness in the epigastrium on palpation.

**Investigations**

- An ulcer was found in the antrum at endoscopy

**What is the most appropriate action to take about his medication?**

- A Continue the ibuprofen
- B Give vitamin K
- C Continue the aspirin
- D Change the aspirin to clopidogrel
- E Change the lansoprazole to omeprazole