

Acute non – variceal upper gastrointestinal haemorrhage

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Abstract

Upper gastrointestinal haemorrhage remains a common medical emergency with significant mortality. Management depends on appropriate and timely resuscitation, therapeutic endoscopy and surgery. This is made possible by a multidisciplinary approach incorporating protocols and scoring systems to aid risk stratification. Communication between members of the multidisciplinary team is important in determining the outcome for patients with high predicted mortality.

Keywords

Upper gastrointestinal haemorrhage, Peptic ulcer, Endoscopy, Management.

Introduction

Acute upper gastrointestinal haemorrhage (UGIH) remains a common cause of hospitalization despite advances in diagnosis and therapy. Incidence ranges from approximately 50 to 150 per 100,000 population per annum, leading to about 5000 deaths per annum in the UK.¹ The burden on health care resources is significant, with 125,000 to 150,000 admissions per annum in the USA at a cost of more than a billion dollars per year.² A recent audit by the British Society of Gastroenterology reported a mortality of 11% in patients admitted to hospital with UGIH and 33% in those who developed gastrointestinal haemorrhage while in hospital for other reasons.³ Most deaths occur in elderly patients and those with significant comorbidity.

Aetiology

The causes of UGIH are listed in Table 1. The commonest is peptic ulcer disease (Figure 1) accounting for up to half of such cases.⁴ In a proportion of cases no obvious cause is found. This could be accounted for by a missed lesion or bleeding from a more distal source.

Peptic ulcer disease (oesophageal, gastric and duodenal)

Helicobacter pylori (Hp) infection and non-steroidal anti-inflammatory drugs (NSAIDs) are major causes of gastric and duodenal ulceration. Gastro-oesophageal reflux disease is the primary cause of oesophageal ulceration, but NSAIDs and

Key Points

1. Upper GI haemorrhage is a common cause of acute medical admission with overall mortality in excess of 10%
2. Immediate fluid resuscitation should be initiated for patients who are haemodynamically compromised, with CVP monitoring where appropriate.
3. Following resuscitation, detailed clinical assessment, investigation and endoscopy should enable the clinician to confirm the diagnosis, assess the severity, identify the source of bleeding and predict outcome.

other drugs including bisphosphonates may also be implicated. NSAID-induced peptic ulcer disease is more common in the elderly. The effect of NSAIDs on the gastric mucosa is predominantly mediated by inhibition of the Cyclo-oxygenase (COX)-1 enzyme. Newer agents, which selectively inhibit COX-2 (e.g. Celecoxib, rofecoxib) are associated with a reduced risk of UGIH. Aspirin is another important risk factor, which is particularly relevant in view of the large numbers of prescriptions; use of enteric coated formulations does not reduce the risks.⁵

Inflammatory disease

Gastritis, duodenitis and oesophagitis are all common endoscopic findings, which may be asymptomatic and incidental to the presentation. Although bleeding may occur, this is generally small in quantity, and significant UGIH is unlikely. If the patient has presented with melaena or a haemodynamically compromising bleed, an alternative source should be sought if no other endoscopic cause is identified.

Oesophagus	Stomach	Duodenum / ileum
• Reflux oesophagitis • Oesophageal ulcer • Varices • Mallory-weiss tear • Carcinoma	• Gastritis • Gastric ulcer • Varices • Portal hypertensive gastropathy • Water-melon stomach • Dieulafoy's lesion • Angiodysplasia • Carcinoma • Lymphoma • Leiomyoma	• Duodenitis • Duodenal ulcer • Vascular malformation • Angiodysplasia • Aorto-enteric fistula • Polyps • Carcinoma (esp periampullary) • Meckels Diverticulum • Haemobilia

Table 1. Causes of upper gastrointestinal haemorrhage.

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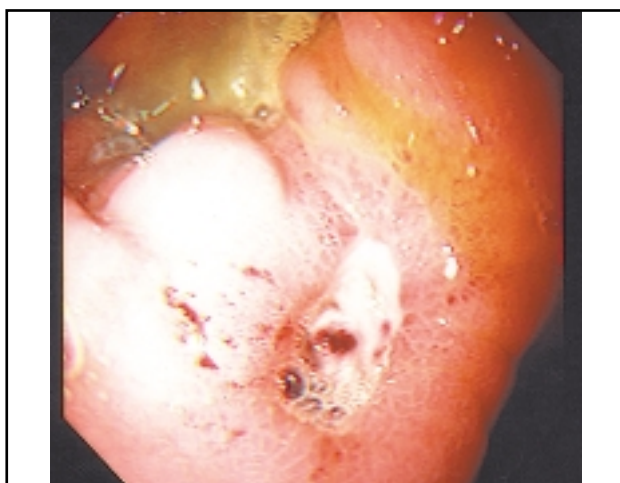


Figure 1. Gastric ulcer with visible vessel in base, indicating that this is a likely source of recent upper gastrointestinal haemorrhage.

Malignancy

This is not a common cause of UGIH but a tumour causing luminal obstruction or eroding into an adjacent vessel may present with haematemesis or melaena.

Vascular

Oesophageal varices are an important cause of significant UGIH in patients with portal hypertension. Although many similar principles apply, the management of variceal bleeding differs significantly enough from that of non-variceal haemorrhage to be the subject of a separate review. This will therefore not be discussed further here.

Vascular lesions may be difficult to detect and should be suspected when endoscopy is reported as normal in genuine UGIH. Dieulafoy's lesion is a small ectatic artery close to the gastric mucosa that can cause a large haemorrhage but is difficult to detect if not actively bleeding at the time of endoscopy. Angiodysplasia may be an isolated finding, or may be associated with Osler-Weber-Rendu syndrome, in which case multiple lesions may be identified. Water-melon stomach represents numerous gastric submucosal vessels and may be falsely interpreted as severe gastritis during endoscopy.

Aorto-enteric fistula should be suspected when UGIH occurs in a patient with an abdominal aortic graft or known aortic aneurysm.

Clinical assessment and initial management

Prioritising assessment and treatment is crucial in the management of gastrointestinal haemorrhage and is learnt with experience. A patient who is haemodynamically unstable requires a rapid initial assessment (volume of blood loss, pulse, BP and level of consciousness) together with resuscitation (oxygen, large bore cannulae and plasma expanders). A detailed clinical assessment can be deferred until the patient has been stabilised and should enable the clinician to:

1. Confirm the diagnosis of UGIH
2. Assess the severity
3. Identify the source
4. Assess the prognosis / relevant co-morbidity

Confirming the diagnosis and severity of bleeding

Patients may present with a clear history of blood loss from the upper gastrointestinal tract (fresh or altered blood in vomit / melaena). Very occasionally haemochaezia (fresh blood per rectum) occurs as a result of upper gastrointestinal haemorrhage in a patient with a large volume bleed. Other modes of presentation may include syncope, usually indicative of a large bleed, or symptomatic anaemia, which usually implies more chronic blood loss.

The severity of bleeding may be apparent from the history. Melaena and fresh haematemesis usually imply a larger bleed. Significant blood loss may result in tachycardia, followed by postural hypotension and ultimately systolic hypotension.

Identification of source

In many cases, the cause of bleeding is not evident after history and examination. However, a specific search for important clues should be made.

- Mallory Weiss tear: clear history of retching or vomiting prior to onset of haematemesis.
- Varices: signs of chronic liver disease with spider naevi, palmar erythema, jaundice or portal hypertension with ascites, splenomegaly and dilated abdominal veins.
- Peptic ulcer disease: past medical history of ulcers or use of NSAIDs / aspirin.
- Aorto-enteric fistula: history of abdominal aortic graft.
- Angiodysplasia and vascular malformations: elderly, Osler Rendu Weber syndrome or aortic stenosis.

Risk factors and comorbidity

Important factors that impact on morbidity and mortality include increasing age, coagulopathy and co-existing illness including organ failure and malignancy. Many of these factors form part of the Rockall scoring system (see below), which can only be calculated after endoscopy. However, evaluation of the 'pre-endoscopic' components of the score may give the clinician a clue to the likely outcome and help guide the urgency of endoscopy (Table 2).³

	Score 0	Score 1	Score 2	Score 3
Age	<60 yrs	60-79 yrs	>80yrs	
Shock	pulse <100/min Systolic BP >100 mmHg	pulse >100 Systolic BP >100 mmHg	pulse >100 Systolic BP <100 mmHg	
Comorbidity	None		CCF IHD	Renal failure Liver failure Cancer
Endoscopic Stigmata	None		Active bleeding Fresh adherent clot Visible Vessel	
Diagnosis	Mallory-weiss None	all others	Cancer of upper GI tract	

Table 2. Rockall scoring system.

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Initial investigations and treatment

Initial investigations should include the following:

- Haemoglobin, platelet count
- Clotting screen (not necessary following small bleeds unless taking anticoagulants)
- Group and save serum or cross match 2-6 units (depending on blood loss)
- Urea and electrolytes (urea:creatinine ratio of > 0.1 suggests upper, rather than lower gastrointestinal haemorrhage)
- Liver function tests
- Endoscopy (see below)

Two important aspects of the early management of gastrointestinal haemorrhage involve appropriate fluid resuscitation and correction of platelet or coagulation abnormalities. Fluid replacement with crystalloid (eg normal saline) or colloid (eg gelofusine) should be commenced while awaiting the arrival of cross-matched blood. In cases of severe haemorrhage, O-rhesus-negative or Group-only blood should be used to avoid further haemodilution. Insertion of a central venous cannula with monitoring of central venous pressure may be helpful to ensure adequate fluid replacement without risking fluid overload. This is particularly important for patients with cardiac or renal impairment, or for elderly patients who have experienced significant blood loss. Hourly measurement of urine output may be useful in the assessment of fluid status.

Platelet counts below 80 require a platelet transfusion. Clotting abnormalities may result from anticoagulant therapy, chronic liver disease or from the effect of large volume transfusion. Vitamin K and fresh frozen plasma may be used according to requirements. Anti-platelet agents (e.g. aspirin, clopidogrel) should be discontinued.

Endoscopy

1. Indications

Endoscopy is essential in the majority of patients. It is not only of diagnostic and prognostic value but serves as an important therapeutic tool. Upper gastrointestinal endoscopy can decrease hospitalisation costs by identifying patients who can be promptly discharged. However, there are situations where endoscopy can be avoided. Young, otherwise healthy patients who have had a single minor bleed, with a clear history of Mallory-Weiss tear can be discharged without undergoing endoscopy, following a period of observation. Similarly, patients with end-stage malignancy can often be managed without the need for endoscopy, when the overall prognosis and management plan is unlikely to be influenced.

2. Timing

The timing of endoscopy depends on the severity of bleeding and the need to provide therapy. An early endoscopy may provide a more rapid diagnosis, and may enable the provision of endoscopic therapy, but views may be compromised by blood and gastric contents. High-risk

patients with a significant UGIH, patients with suspected oesophageal varices and those with signs and symptoms of continuing bleeding require endoscopy as soon as possible after resuscitation is complete. All patients requiring endoscopy should undergo the investigation within 24 hours of admission.

3. Therapeutic endoscopy

The principle of endoscopic therapy is to terminate bleeding or reduce the risk of re-bleeding following endoscopy. Endoscopic therapy is indicated when active bleeding or stigmata of recent haemorrhage (e.g. visible vessel or fresh adherent clots) are seen.

A variety of techniques are employed. Injection of dilute adrenaline (1:10,000) into the tissues around a bleeding or visible vessel may induce vasoconstriction along with a local tamponade effect of the vessel. Alternatively, sclerosants (eg ethanolamine) may be injected directly into a bleeding vessel to induce local thrombus formation. Thermocoagulation of a vessel is equally effective, and particularly useful for the management of angiodysplastic and Dieulafoy lesions. Mechanical clips and bands may be also applied to vascular lesions, particularly oesophageal varices. These techniques can be used alone or in combination.⁶

Post-endoscopy management

Patients with upper gastrointestinal haemorrhage are primarily admitted by general physicians. Previous studies have shown a favourable cost-benefit ratio⁷ and a reduced mortality⁸ for patients admitted under the care of a gastroenterologist, compared to a general physician. Another study has shown that introduction of a clinical care protocol can substantially reduce the length of hospital stay.⁹ Some hospitals admit all patients with upper gastrointestinal haemorrhage into a high-dependency area designed specifically for the treatment of gastrointestinal bleeding. Such 'bleeding units' are often managed jointly by medical and surgical staff. Mortality is reported to be lower in these specialist units,¹⁰ with better adherence to guidelines.

Patients who are haemodynamically stable with no evidence of ongoing bleeding 4-6 hours after endoscopy may be allowed oral fluids. There is no evidence to support prolonged fasting in this group of patients. Normal gastroscopy, Mallory-weiss tear or the finding of an ulcer with a clean base in a young patient is associated with a very low risk of rebleed and mortality. Such patients can be discharged early. In contrast, active bleeding from a peptic ulcer in a shocked patient carries an 80% risk of continuing bleed or of death. A non-bleeding visible vessel is associated with 50% risk of rebleed. These patients will need very close monitoring to identify early signs of rebleeding. There is emerging evidence to suggest that patients who rebleed may benefit from repeat therapeutic endoscopy before considering surgery.¹¹ This should be considered on an individual basis, and in discussion with a senior member of the surgical team.

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Medical treatment

Acid suppressing drugs

Use of acid suppressants is based on the observation that when pH falls below 6 platelet aggregation is disrupted and fibrinolytic activity increases allowing clot lysis. There is no convincing data to support the use of Histamine-2 receptor antagonists (H2RAs, e.g. ranitidine), which do not reliably increase gastric pH to 6. Similarly proton pump inhibitors (PPIs), when used in standard doses, are no better than placebo in influencing the clinical course of upper gastrointestinal haemorrhage. H2RAs and standard dose PPIs are therefore unlikely to be helpful.^{12,13} A recent study from Hong Kong reported a significant reduction in ulcer re-bleed rate when an intravenous bolus of omeprazole was followed by an infusion of 8 mg / hr for 72 hours, in patients with endoscopic stigmata of haemorrhage.¹⁴ The mortality rate and need for surgery was also lower with omeprazole compared to placebo, but these differences were not statistically significant. Many hospitals have now incorporated this into their management protocols for patients felt to be at high risk of peptic ulcer re-bleeding following endoscopy. There is no evidence to support the routine use of intravenous PPI for unselected patients or prior to endoscopy.

Antifibrinolytic drugs

These drugs prevent clot lysis, thereby potentially reducing the rebleed rate once clot has formed. Intravenous Tranexamic acid can be considered for patients likely to re-bleed although the evidence for its efficacy is not convincing.¹⁵

Prognosis

The most commonly used prognostic tool in the UK is the Rockall score (Table 2, Figure 2),³ which is based on clinical examination and endoscopic findings. Calculation of the score is particularly useful in the identification and management of low-risk patients (score 0 or 1), who can be discharged soon after recovery from endoscopy. It may also help to guide the management of more unstable patients providing, for example, an objective criterion (eg score 5 or more) on which to base a decision to move a patient to a high dependency area.

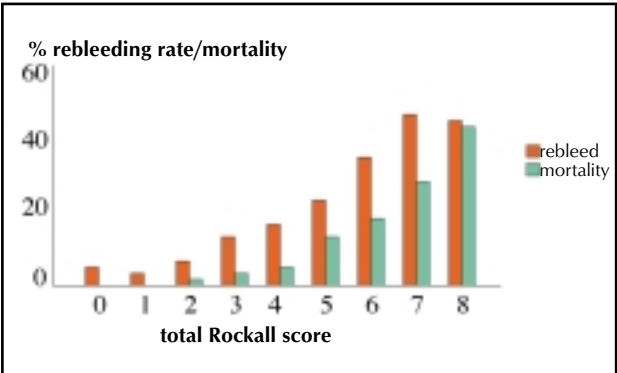


Figure 2. Rebleeding and mortality as predicted by Rockall scoring.

Surgery

Early involvement of the surgical team is essential in the management of high risk patients as follows:

- Severe non-variceal bleeding
- High Rockall score (score 5 or more)
- Stigmata of recent haemorrhage on endoscopy
- Failure to control haemorrhage by endoscopic therapy
- Rebleed or continued bleeding

Despite advances in resuscitation, medical and endoscopic therapy, bleeding may continue requiring surgical treatment. Torrential bleeding may obscure endoscopic therapy, the site of lesion may not allow endoscopic therapy or the endoscopic therapy may have failed to stop bleeding. Success of surgical intervention is dependent on appropriate timing, before the onset of organ failure (due to prolonged hypotension) or coagulopathy (due to gross blood transfusion, >8 units). It is preferable to carry out a planned urgent operation rather than a rushed emergency procedure in a poorly resuscitated patient. The indications for surgery are complex and dependent on a variety of factors including the site and nature of the lesion. Vascular lesions may be more appropriately managed by radiological shunting or embolisation when endoscopic fails, while proximal gastric and oesophageal ulcers may be difficult to access surgically and require radical and complex resections. The indications for surgery summarised in Figure 3 imply a surgically remediable lesion (eg duodenal ulcer) and should be applied in the context of the patient’s overall clinical condition in discussion with a senior member of the surgical team.

Patient under 60:	2 documented ‘rebleeds’ in hospital or 8 units of blood required for volume replacement
Patient over 60:	1 documented ‘rebleed’ in hospital or 4 units of blood required for volume replacement

Figure 3. Indications for surgery in peptic ulcer bleeding.

Further Investigations

Gastroscopy should be repeated if no cause is found, with consideration of push enteroscopy if a small bowel source is considered possible. If colonic bleeding is suspected (eg fresh pr blood loss, no haematemesis, urea: creatinine ratio <0.1) then colonoscopy should be arranged. Small bowel radiology is commonly employed when gastroscopy and colonoscopy are normal, but is rarely useful. Occasionally a meckel’s scan may be useful. If there is still no diagnosis and bleeding continues a labelled red blood cell scan should be considered. This technique can detect a rate of blood loss as low as 0.1 ml/min. Angiography is another investigation which can help localise a bleeding point but is only useful when patients are bleeding at a rate of >1 ml/min. This technique may allow therapeutic intervention in patients where

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endoscopic therapy cannot be provided and for those not fit for surgery.

Follow up management

Patients with Hp infection will require eradication therapy as soon as oral intake is allowed and Hp status should be checked after 8 weeks with a urea breath test (UBT). Proton pump inhibitors may cause false negative UBT and should be stopped at least 2 weeks prior to the investigation. Patients with NSAID-related ulcers should

stop NSAIDs and take PPIs for 6 to 8 weeks. Any future use of NSAIDs should be considered only after healing of the ulcer has been verified endoscopically. If on-going treatment with NSAIDs is required after healing, the safest approach is to use the least gastro-toxic NSAID (eg ibuprofen), in combination with a gastro-protective agent such as misoprostol or PPI. Use of a COX-2-specific inhibitor may be an alternative. Patients who have bled from gastric ulcers should undergo repeat endoscopy in six weeks to confirm ulcer healing and exclude malignancy.

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