

Management of massive gastrointestinal haemorrhage

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Abstract

Acute gastrointestinal bleeding is a common medical emergency, accounting for approximately 85,000 admissions in the United Kingdom per annum. It is associated with significant morbidity and mortality. GI haemorrhage is commonly categorized according to source of blood loss; either upper GI (above the ligament of Treitz) or lower GI (below the ligament of Treitz). Rapid assessment, resuscitation and correction of coagulopathy should be undertaken to stabilize the haemodynamically compromised patient and definitive intervention should not be delayed. Clinicians may use of a range of treatment modalities, including endoscopic and interventional radiological techniques in order to get control of haemorrhage, which should be tailored to the site of bleeding and pathology. Where control is not achieved the clinician should consider either repeat intervention, use of alternative haemostatic techniques or different modalities to achieve haemostasis. Rarely is surgery the chosen treatment modality and surgical intervention should only be undertaken where all other measures to control haemorrhage have failed.

Keywords Emergency surgery; endoscopy; gastrointestinal haemorrhage; haematemesis; haematochezia; interventional radiology; lower GI bleed; management; melaena; upper GI bleed

Introduction

Gastrointestinal bleeding is a common medical emergency with an annual incidence of 1.33/1000 of the population which equates to approximately 85,000 cases per annum in the United Kingdom. It is the second most common reason for blood

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transfusion (after haematological malignancy), accounting for 14% of all transfusions.¹

Overall mortality from GI bleeding is estimated to be around 10%; however, the 2015 NCEPOD enquiry into massive GI haemorrhage concluded a mortality rate of 24% in patients who required a blood transfusion of four units or more.¹

The diagnosis and management of gastrointestinal haemorrhage differs depending on the origin of the bleeding and as such broadly falls into two categories:

- Upper GI – occurring proximal to the ligament of Treitz (a band of smooth muscle which extends from the duodenal-jejunal flexure to the left crus of the diaphragm). In practice this means any bleeding from the oesophagus, stomach or duodenum is classified as an upper GI bleed. Upper GI haemorrhage is often sub-classified to variceal bleeding (from oesophageal varices) and non-variceal bleeding to reflect differences in the management.
- Lower GI – occurring from any of the gastrointestinal tract beyond the ligament of Treitz. This includes jejunum, ileum as well as colon.

Presentation

The signs and symptoms of gastrointestinal bleeding vary depending on the site of pathology.

Upper GI bleeding typically manifests with symptoms of melaena, haematemesis, ‘coffee ground vomiting’ (caused by a reaction between blood and hydrochloric acid in the stomach, producing a characteristic appearance to vomitus) and Hb drop.²

Lower GI bleeding more commonly presents with symptoms of fresh red rectal bleeding (haematochezia) or passage of altered blood per rectum and Hb drop.

However, there is a degree of overlap and it is not uncommon in the event of significant haemorrhage for upper GI bleeds to present with fresh red rectal bleeding, with an estimated 11–15% of patients with a suspected lower GI bleed to have an upper GI pathology. Equally, patients with a caecal or distal small bowel bleed may present with melaena.³

It is important therefore, where possible, to obtain an accurate and thorough history from the patient or a collateral history from a relative or carer if required.

Focused history should include character, frequency and volume of blood loss, any associated symptoms such as pain, nausea, vomiting, acute change in bowel habit and presence of a febrile illness. A complete past medical history must be obtained, with focus on conditions which may indicate the patient is at increased risk of GI tract bleeding, for example, known liver disease, alcohol abuse, history of peptic or duodenal ulcer, malignancy or diverticular disease. It is also important to ascertain whether the patient is taking medication which may damage gastrointestinal mucosa, including non-steroidal anti-inflammatory medication and oral steroids, which predispose to ulceration and bleeding. Furthermore, it is important to identify if the patient is taking medications which increase the risk of bleeding, such as antiplatelets, warfarin, heparin and the new oral anti-coagulants such as rivaroxaban/apixaban.

It is essential to perform a full gastrointestinal examination of the patient. Be aware of any signs which may help to localize the source of the bleeding, such as the presence of an abdominal

Classification of shock

	Class of haemorrhagic shock			
	I	II	III	IV
Blood loss (mL)	Up to 750	750–1500	1500–2000	>2000
Blood loss (%blood volume)	Up to 15	15–30	30–40	>40
Pulse rate (per minute)	<100	100–200	120–140	>140
Blood pressure	Normal	Normal	Decreased	Decreased
Pulse pressure (mm Hg)	Normal or increased	Decreased	Decreased	Decreased
Respiratory rate (per minute)	14–20	20–30	30–40	>35
Urine output (mL/hour)	>30	20–30	5–15	Negligible
Central nervous system/mental status	Slightly anxious	Mildly anxious	Anxious, confused	Confused, lethargic

From 'ATLS - Advanced Trauma Life Support (2012). Chicago, Ill.: American College of Surgeons, Committee on Trauma.'

Table 1

mass. Examine for the presence of stigmata of chronic liver disease and for the signs of malignancy (such as palpable lymphadenopathy). You must perform a rectal examination (which allows accurate and objective assessment of melaena versus haematochezia) and consider proctoscopy in cases with symptoms of outlet bleeding.

Remember that while the source of bleeding may be inferred by symptoms and signs, it should never be assumed. Also consider that more than a third of acute GI haemorrhages occur in patients who are already hospital inpatients and as such clinicians need to be aware that the inpatient population is particularly at risk of GI haemorrhage, to prevent delay in diagnosis and management.¹

Initial management

Initial management of haemorrhage is common to any source and involves standard resuscitative measures. Assessment of the patient's airway and respiratory system is performed initially, with attention made to ensure adequacy of ventilation. Reduced conscious level and/or aspiration of either blood or gastric contents can result in airway obstruction. Oxygen saturations and respiratory rate are recorded and, in the event of inadequate ventilation, simple airway manoeuvres (head tilt, chin lift and jaw thrust) and adjuncts (Guedel and nasopharyngeal airway) attempted. In the event of a compromised airway or inadequate ventilation and perfusion, seek immediate anaesthetics support.^{2,4}

The patient's heart rate and blood pressure are recorded and wide bore peripheral venous access obtained (at least two 16–18 gauge intravenous cannulas). Blood tests including haemoglobin, haematocrit, urea, creatinine, electrolytes, liver function, prothrombin time (PT), activated partial thromboplastin time (APTT) and fibrinogen are performed and at least four units of blood cross-matched.

An elevated serum urea may be observed in the case of upper GI bleed as blood bound proteins (including haemoglobin, immunoglobulins etc.) are metabolized in the gut to blood urea nitrogen (BUN) which is then reabsorbed. Raised serum urea

may be a useful in the differentiation between upper and lower GI blood loss.

Measurement of lactate on either arterial or venous blood gas allows for a prompt assessment of tissue perfusion and allows for rapid assessment of the patient's blood volume status and has been demonstrated to be a sensitive predictor of mortality.⁵

Healthy patients, and in-particular young patients, have good compensatory mechanisms to ensure adequate circulatory pressure. Increases in myocardial contractility, heart rate and peripheral vasoconstriction maintain circulatory pressures at near normal levels and therefore a falling blood pressure is considered a late sign.

The ACS/ATLS guidelines on haemorrhage severity and class of hypovolaemic shock is a useful tool in the estimation of blood loss in patients with significant gastrointestinal bleeding (Table 1).

Crystalloid fluids are used initially for volume replacement; however, in the event of significant haemorrhage, blood products are more appropriate. Use of blood products should be judicious however, as over-transfusion can carry a significant risk and it may be prudent to adopt a policy of 'permissive hypotension' (maintaining blood pressure at a level required to maintain tissue perfusion and cognition) until definitive control of the source of bleeding can be established.^{6,7}

Hospitals will have a transfusion policy where, for stable patients, packed red blood cell transfusion is recommended below a threshold (typically Hb <70). However, in the event of acute haemorrhage this may not be so useful a guide: Hb may not fall immediately as the patient loses both red cells and plasma volume – therefore repeating Hb within a few hours will demonstrate the delayed drop as interstitial fluid moves from the extravascular to intravascular compartments.^{2,4}

All hospitals will have a 'major haemorrhage protocol', which should be activated in cases of major blood loss – particularly if bleeding is ongoing or the patient is haemodynamically unstable. Activation of the major haemorrhage protocol triggers the rapid and continuous issue of red cells and other blood products from

the blood bank in pre-agreed ratios – usually 1:1 packed red cells:fresh frozen plasma, with platelets and cryoprecipitate as directed by blood results. Key staff members in haematology, theatres and intensive care are also alerted when the protocol is activated.^{2,4,5}

Remember, a normal Hb and blood pressure does not exclude a potentially life-threatening haemorrhage.

Coagulopathy and clotting

Use of anticoagulants and antiplatelets has become commonplace and are often used for either primary or secondary thromboembolic prevention. Their widespread use has inevitably resulted in increased risk of bleeding and presents an extra challenge in the management of iatrogenic coagulopathy in the setting of acute haemorrhage.

In the setting of acute GI bleeding anticoagulants and antiplatelets are often held on admission while the primary haemorrhage is addressed.

However, there is a lack of evidence that stopping antiplatelets is beneficial in terms of reduced risk of re-bleeding, and there are concerns that doing so puts patients at risk of thrombotic complications. Some guidelines have suggested that patients taking dual-antiplatelet therapy and who are considered ‘very high risk’ of thromboembolic events (within 30 days of coronary stenting or within 90 days of acute coronary syndrome) should have dual-antiplatelet therapy continued to prevent stent occlusion or acute coronary syndrome. Patients taking dual antiplatelet therapy for longer than this period may stop their non-aspirin antiplatelet for up to 5–7 days before recommencing; however low dose aspirin should be continued.⁷

In those taking warfarin and other vitamin K antagonists who experience life-threatening haemorrhage, warfarin is reversed with 5 mg of intravenous vitamin K along with four-factor prothrombin complex concentrate (PCC). This contains human coagulation factors II, VII, IX and X, together with the endogenous inhibitor proteins S and C, and rapidly normalizes the INR. It is considered preferable to fresh frozen plasma (FFP) due to ease of administration, near normalization of INR and lower risk of volume overload.⁸

Factor Xa inhibitors (rivaroxaban, apixaban and edoxaban) have become more commonplace in clinical practice and offer the advantage over vitamin K antagonists in terms of predictability of dose-dependent plasma levels and anticoagulant effect, as well as offering a fixed-dose regimen and rapid onset of action. However, reversal of these drugs is more problematic. The first antidote to this class of drug has recently become available – Ondexxya, a recombinant inactive factor Xa molecule, which acts as a ‘decoy’, binding the Xa inhibitors to reduce their activity. The drug was granted a provisional marketing license in the European Union in March 2019; however, its implementation in clinical practice may be limited due to expense. In the absence of the direct antidote, four-factor PCC is often used to manage life-threatening bleeding in patients taking Xa inhibitors. The ASH guidelines suggest using *either* a direct antidote *or* four-factor PCC in this situation. However, in studies 32% of patients who received four-factor PCC for major haemorrhage while taking a factor Xa inhibitor found no benefit or experienced worsening bleeding.⁸

In the case of dabigatran (a direct thrombin inhibitor), a monoclonal antibody (idarucizumab) is available that specifically

binds to the anticoagulant and its metabolites, thereby reversing its action. When a patient has a massive haemorrhage while prescribed low molecular weight heparin (LMWH) or unfractionated heparin (UFH), protamine is used as a selective antidote to its anticoagulant mechanism of action.⁸ However, for LMWH reversal is usually incomplete.

Use of reversal agents and prothrombin complexes are only used in the event of life threatening haemorrhage and careful consideration given to the risks (thromboembolic events, difficulties in re-anticoagulation after cessation of bleeding and possible risk of propagation of bleeding) versus benefits of treatment and discussion with a haematologist is essential.⁸

Platelet transfusions are not to be offered to patients who are not actively bleeding and who are haemodynamically stable. Those who are actively bleeding and have a platelet count $<50 \times 10^9$ L should be given platelets. FFP is recommended for those patients with active bleeding who have a fibrinogen concentration <1.5 g/L or PT/INR/APTT >1.5 times the normal level.⁵ Cryoprecipitate – a more concentrated source of fibrinogen – should be considered if the fibrinogen remains <1.5 g/L despite FFP (Table 2).⁵

While an INR <2.5 prior to elective endoscopy is permissible, it is not appropriate to wait for correction of coagulopathy before embarking on intervention. Equally, there is no evidence to support ‘heparin bridging’ in the emergency setting.⁷

Following definitive management to control of haemorrhage and cessation of bleeding, careful consideration should be made as to whether to reinstate anticoagulant therapy.

NCEPOD data suggests that 23% of upper GI haemorrhages and 22–38% of diverticular haemorrhages subsequently re-bleed. Resuming anticoagulants following gastrointestinal bleed is associated with increased risk of major haemorrhage; however, there is no evidence that reinstating anticoagulants has an effect on the numbers of patients that re-bleed.^{1,7,8}

There is, however, increased risk of thromboembolic events following GI haemorrhage, likely resultant from shock and hypovolaemia leading to myocardial ischaemia, inflammation and oxidative stress leading to plaque rupture and a prothrombotic state. Resuming anti-coagulation reduces the risk of venous thrombo-embolus, pulmonary embolus and all-cause mortality. Therefore, where thromboembolic risk is high, anti-coagulants are reinstated as soon as the risks of thrombosis and embolism outweigh the risk of further significant bleeding.^{8,9}

NICE guidelines for correction of coagulopathy during acute upper GI bleed

Coagulopathy	Threshold	Management
Platelets	$<50 \times 10^9$ /L	Platelet transfusion
INR	>1.5	FFP
aPTT	>1.5	PCC (if on warfarin)
Fibrinogen	<1.5 g/L	FFP

INR, International Normalized Ratio; aPTT, activated partial thromboplastin time ratio; PCC, prothrombin complex concentrate; FFP, fresh frozen plasma.

Table 2

Any decisions regarding the reversal and re-instatement of anticoagulants and antiplatelets are best performed on a case-by-case basis and involve the assessment of the cause of bleeding, estimation of risk of re-bleeding for the individual patient, the anticoagulant used and risk factors for thromboembolic events. This is a multidisciplinary discussion involving liaison with cardiology/respiratory/stroke medicine, haematology as well as the managing medical or surgical team.

Tranexamic acid (a synthetic analogue of the amino acid lysine) acts by preventing plasminogen conversion to fibrin and preventing fibrin degradation. It is commonly used in the management of menorrhagia, epistaxis and in the prevention and treatment of significant haemorrhage following trauma. Its usefulness in the context of acute GI bleeding is yet to be fully established. However, the 'HALT-IT' trial, a multicentre, multinational double-blind, placebo, controlled trial aims to address this uncertainty. A previous Cochrane meta-analysis has demonstrated reduction in mortality; however, the studies to date are underpowered and of poor quality. Tranexamic acid does increase risk of cardiovascular and thromboembolic events and as such it is advisable to use it with caution, at least until the outcomes of the HALT-IT trial are published.^{2,4,10,11}

Upper GI haemorrhage

Upper GI bleeding occurs in approximately 100 patients per 100,000 annually. Considered a medical emergency, it has an overall mortality of 10%. Cases are typically admitted under the team that provide emergency upper GI endoscopy, as this is the diagnostic and treatment modality of choice, and in many trusts this is provided by medical teams rather than surgical teams.^{1,2}

Pathology

Peptic ulcers: Peptic ulcer disease is the most common cause for upper GI bleeding and accounts for approximately 31–67% of presentations.²

Ulceration beyond the mucosa into the submucosa results in inflammation, weakening and necrosis in arterial walls, leading to pseudoaneurysm formation, rupture and haemorrhage.¹²

Up to 90% of duodenal ulcers and 70% of gastric ulcers are associated with infection of *Helicobacter pylori*. This Gram-negative bacterium causes disruption of the mucosal barrier resulting in inflammation and ulceration of the gastric and duodenal mucosa. Incidence of peptic ulcer disease has declined significantly since the identification of *H. pylori* and the widespread use of proton pump inhibitors (PPIs).¹²

Use of non-steroidal anti-inflammatory drugs (NSAIDs) are also associated with peptic ulcer disease. These drugs inhibit cyclooxygenase and decrease mucosal prostaglandin synthesis, resulting in impaired mucosal defences and resulting in a 40-fold increased risk of gastric ulceration and eightfold increased risk of duodenal ulceration. Up to 20% of long-term NSAID users will have mucosal ulceration. For this reason, NICE recommends that all NSAIDs should be stopped during acute haemorrhage to prevent further mucosal damage. The decision to restart NSAIDs after GI haemorrhage should be considered carefully on a case-by-case basis. If the benefit of treatment appears to outweigh the potential risk of further bleeding then a prophylactic PPI

Forrest classification

The Forrest classification			
Class	Description	Endoscopic Intervention ¹⁴	Rebleeding Rate ⁴²
1A	Active spurting	Yes	55%
1B	Active oozing	Yes	55%
2A	Nonbleeding visible vessel	Yes	43%
2B	Adherent clot	Consider	22%
2C	Flat pigmented spot	No	10%
3	Clean ulcer base	No	5%

Adapted from: Nelms, D. W. & Pelaez, C. The Acute Upper Gastrointestinal Bleed. Surg. Clin. NA 98, 1047–e1057 (2018).

Table 3

should be prescribed concurrently, which reduces the risk of new peptic ulcer formation by 50–80%.^{2,6,12}

Benign peptic ulcers are best assessed endoscopically where they are typically described as having smooth, rounded edges. The Forrest Classification (Table 3), categorizes ulcers into three classes, which helps guide management and risk-stratifies those patients at high risk of re-bleeding and mortality. Any ulcer other than a 2c or 3 are considered 'high risk'.⁴

Gastritis, duodenitis and oesophagitis: Stress gastritis is commonly seen in critically unwell inpatients and typically results from disruption to the mucosal defences (which are ordinarily maintained by mucus, bicarbonate and prostaglandins protecting the gastric mucosa from the acidic intra-luminal environment). NICE recommends routine use of PPIs for prophylaxis in critically ill patients admitted to ITU to prevent gastrointestinal haemorrhage.^{6,12}

Patients at risk of oesophagitis tend to have a history of gastro-oesophageal reflux disease and a hiatus hernia may be present. The stratified squamous epithelium that lines the oesophagus lacks many of the mucosal defences that protect to the caustic effects of gastric acid. Increased acid exposure and reflux of gastric contents into the distal oesophagus results in inflammation and erosions which can result in haemorrhage.

Mallory-Weiss tears are longitudinal lacerations in the gastric cardia or at the gastro-oesophageal junction. They account for 4–8% of upper GI bleeds and occur as a result of sudden increases in intragastric pressure, for example, after vomiting following an alcoholic binge.¹²

Spontaneous resolution of bleeding is common, and intervention is only required in 10% of cases. Lesions not actively bleeding can be managed with PPIs and anti-emetics alone and re-bleeding from these tears is rare (7%).⁷

Tumours/malignancy: Tumours of the upper GI tract rarely present with acute haemorrhage and only represent approximately 4–8% of acute upper GI bleeds. Often tumours are asymptomatic until a late stage, therefore at presentation the disease often advanced. Nevertheless, where ulcers and lesions which appear suspicious (elevated, irregular borders with

associated abnormal mucosal folds), biopsy should be undertaken as a matter of course, as approximately 6% of gastric ulcers have a malignant component. It is also necessary to repeat endoscopy in patients with gastric ulcers after 6 weeks to ensure healing – a non-healing ulcer is suspicious for an underlying malignant process. Duodenal ulcers are rarely malignant and as such routine biopsies are not recommended.

Dieulafoy lesions/vascular ectasia: Dieulafoy lesions are a rare cause of upper GI haemorrhage. These are large but histologically normal arterioles which protrude through the submucosa and mucosa and can occur anywhere in the GI tract, but typically are found on the lesser curve of the stomach and within 6cm of the gastro-oesophageal junction. Exposure to the acidic intraluminal environment, can result in necrosis and rupture of the affected arteriole resulting in sudden, brisk bleeding in a patient with no other significant symptoms.^{4,12}

Rare causes: Other rare causes of upper GI bleeding include aorto-enteric fistulae and haemobilia.

Aortoenteric fistulae occur following surgery to the aorta or GI tract. Often there is a 'herald bleed' followed by massive exsanguinous haemorrhage. An urgent CT/CTA should be undertaken in patients with suspected aortoenteric fistula (e.g. negative UGI endoscopy in patient with prior history of vascular surgery) and immediate life-saving reconstructive surgery is mandatory with extra-anatomic bypass reconstruction, removal of any infected synthetic material (e.g. aortic graft) and closure of any enterotomy. Perioperative mortality is inevitably extremely high.⁷

Haemobilia can result from instrumentation for the biliary system (e.g. following endoscopic retrograde cholangiopancreatography [ERCP]), from trauma or bleeding into the pancreatic ducts (hemosuccus pancreaticus). Endoscopic control of bleeding from the biliary system is difficult to establish, therefore interventional angiography is the most appropriate management.⁷

Variceal bleeding: Accounting for approximately 4–20% of upper GI bleeds, varices are abnormally dilated veins which occur as a result of portal hypertension and development of portosystemic shunts, commonly found in the distal oesophagus and upper stomach. Most cases are secondary to cirrhosis, but rarely varices may be caused by non-cirrhotic portal hypertension (veno-occlusive disease) or portal vein thrombosis. Gastric varices are further subdivided into gastro-oesophageal varices and isolated gastric varices depending upon their anatomical location.⁴

The management of patients who have suspected variceal bleeding differs from that of those with non-variceal bleeding which reflects the differences in the pathology in this cohort and associated high risk of mortality (20% within 6 weeks following first presentation of variceal bleeding).^{4,7}

On presentation, patients with suspected variceal bleeding should be commenced on a splanchnic vasoconstrictor which is continued until definitive haemostasis is achieved or until after 5 days following presentation. NICE guidelines currently recommend terlipressin; however, some authors recommend the somatostatin analogue octeotide which is licenced in North America.^{2,6}

Patients with variceal bleeds are at high risk of bacterial infection and antibiotics have been shown to reduce re-bleeding infections and mortality, and therefore prophylactic antibiotics are mandatory. Broad spectrum antibiotics (such as a quinolone, cephalosporin or piperacillin-tazobactam) are most appropriate, although local guidelines should be consulted.¹³

Pre-endoscopic care

Timing of endoscopy: Patients who are haemodynamically unstable and with evidence of active bleeding should undergo immediate endoscopy after initial resuscitative measures. All patients requiring admission should receive endoscopy within 24 hours. UK Hospitals should have access to 24 hour endoscopy services and an on-call endoscopy team, for this eventuality.^{2,6}

There is an association between endoscopies performed >24 hours after admission and increased mortality, evidencing the need for early intervention. Certainly, if after a period of stabilization the patient further deteriorates then intervention should not wait.²

While most 'in hours' endoscopy is performed in a dedicated endoscopy department, emergency 'out-of-hours' endoscopy is more commonly performed either in 'CEPOD' operative theatres or in an intensive care setting.

Pre-endoscopic nasogastric tube (Ryles tube) insertion is no longer considered to offer any benefits and should be avoided.^{1,2}

Risk stratification: Given the high morbidity and mortality associated with acute upper GI haemorrhage and reported re-bleed rate of approximately 5–20% after successful endoscopic intervention, it is essential to appropriately risk stratify patients to identify those at high risk of serious adverse events, to predict

Glasgow-Blatchford criteria

Criteria (on admission)	Score
Hb - Male (g/L)	
120–130	1
100–120	3
<100	6
Hb - Female (g/L)	
100–120	
<100	6
Urea (mmol/L)	
6.5–8	2
8–10	3
10–25	4
≥25	6
Systolic blood pressure (mmHg)	
100–109	1
90–99	2
<90	3
Others	
Pulse ≥100	1
Melaena	1
Syncope	2
Hepatic disease	2
Cardiac failure	2

From: Blatchford O, Murray W, Blatchford M. A risk score to predict need for treatment for upper gastrointestinal haemorrhage. *Lancet* 2000; 356: 1318–21.

Table 4

Post endoscopy Rockall score

Criteria (on admission)	Score
Age*	
<60	0
60–79	1
≥80	2
Shock*	
Pulse >100	1
Systolic BP <100 mmHg	2
Co-morbidity*	
Cardiac, other major	2
Renal/liver failure, cancer	3
Endoscopic Diagnosis	
Normal, Mallory-Weiss	0
Ulcer, erosion, oesophagitis	1
Cancer	2
Endoscopic SRH	
Clean base ulcer, flat pigmented spot	0
Active bleeding, clot, vessel, blood	2

*Denotes components of pre-endoscopy Rockall Score. From: Rockall T, Logan R, Devlin H et al. Risk assessment after acute upper gastrointestinal haemorrhage. *Gut* 1996; 38: 316–21.

Table 5

endoscopic and clinical outcomes and to aid appropriate triage of patients.^{1,2}

Current NICE guidelines advocate a two-step risk assessment for the assessment of acute upper GI haemorrhage.

Prior to endoscopy and within 24 hours of admission, the Glasgow-Blatchford score (Table 4) is used to risk-stratify patients. Low-risk patients (i.e. with a Blatchford score 0–1) may be appropriately discharged for example with suitable outpatient endoscopic investigations. The higher the Blatchford score, the higher the risk of adverse clinical outcome and the more urgently endoscopy should be considered.^{2,6}

NICE recommends use of the full (post endoscopy) Rockall scoring system (Table 5) to predict risk of re-bleeding or death following endoscopic intervention, with those who score >2 considered at increased risk.⁶

The 2015 NCEPOD enquiry into GI haemorrhage suggests that all patients who have had GI bleeding should have an agreed re-bleed plan which should be based on individual risk and pathology. This second stage risk stratification guides clinicians in terms of planning for further treatments and interventions.¹

Proton pump inhibitors (PPIs) act by irreversibly blocking that H⁺/K⁺ gastric proton pump in gastric parietal cells, preventing the luminal secretion of H⁺ ions and reducing gastric acid production by up to 99%.

The use of PPIs in acute upper GI haemorrhage prior to endoscopy remains a controversial topic. The European Society of Gastrointestinal Endoscopy (ESGE) recommends intravenous high dose proton pump inhibitor (omeprazole 80 mg) be given as a bolus on presentation followed by continuous infusion (omeprazole 8 mg/hr) for all patients requiring admission.

This recommendation is, however, refuted by NICE guidelines which advise against offering PPIs prior to emergency endoscopy, citing that there is no evidence that PPIs reduce re-bleeding rates or mortality in this cohort may ‘downgrade’ the underlying pathology at the time of endoscopy and may be used as a ‘holding measure’ which may lead to delay in definitive management in the form of endoscopy.^{1,2,6}

It is the authors’ experience that use in the pre-endoscopic cohort is widespread and indeed a recent NCEPOD audit found that 73% of patients with acute bleeding received PPI contradictory from guidance, indicating a clear disparity between national standards and common practice.¹

Prokinetics: ESGE recommends intravenous erythromycin (250 mg) 30–120 minutes prior to gastroscopy to improve mucosal visualization.² There is no evidence to support the use of metoclopramide.⁴

Endoscopic management

Endoscopic therapy – non-variceal UGIH: In the case of non-variceal upper GI bleeding, NICE guidelines recommend one of the following methods to achieve haemostasis.^{4,6}

- **Mechanical treatment** – direct compression of a bleeding vessel using a purpose designed haemostasis device such as an endoclip or haemoclip.
- **Thermal Coagulation (with or without adrenaline injection)** – may be achieved using either contact thermal haemostasis (monopolar diathermy) or through non-contact thermal haemostasis (such as argon plasma coagulation, which is especially useful in the management of angiodysplastic lesions)
- **Fibrin or Thrombin treatment (with or without adrenaline injection)** – specifically designed compounds which may be applied over a large area. These substances mechanically adhere to bleeding points while activating coagulation factors. They are considered useful when managing large areas of oozing such as in gastritis, malignancy or portal hypertensive gastropathy.

Injection of adrenaline alone has been demonstrated to be inferior to the above methods; however, it can be utilized as an adjunct to the above treatment modalities.⁶

Several novel modalities have been proposed as either an adjunct or a therapeutic alternative to treat non-variceal GI bleeding. Products such as Hemospray (a haemostatic powder spray) have been advocated, particularly in areas difficult to access endoscopically using traditional techniques (such as the lesser curve of the stomach, posterior bulb of the duodenum and gastric cardia). However, large randomized, prospective studies are lacking and as yet such techniques are not recommended in national guidelines.¹⁴

Endoscopic therapy – variceal UGIH: NICE and the British Society of Gastroenterology recommend variceal band ligation (VBL) for oesophageal varices. This involves deployment of a small rubber band from the endoscope around the varices to induce strangulation and thrombosis of the vessel. Following the procedure some patients may develop ulceration at the site of deployment, but this can be improved with PPI use.^{4,6}

Gastric varices should be offered N-butyl-2-cyanoacrylate injection as first-line therapy. Commonly referred to as ‘glue’, this

strongly adhesive substance is injected into bleeding varices resulting in haemostasis and has been found to be superior to VBL in achieving haemostasis and reducing re-bleed rates in the sub-cohort of patients. Thrombin injection may also be used for this purpose and this has a reported haemostasis of 94% with a re-bleed rate of 18%.^{4,6}

Where these methods fail adequately to achieve haemostasis it may be necessary to consider a second-line endoscopic technique to control haemorrhage. Balloon tamponade (e.g. Sengstaken-Blakemore tube) may be undertaken in most cases of oesophageal and junctional variceal haemorrhage. These are successful in controlling haemorrhage in 91% of cases but re-bleed rates are high (approximately 50%), which means they are often utilized in a temporizing manner and should be removed after 2 days. The tubes are often poorly tolerated and may result in pressure necrosis, aspiration pneumonia and rarely oesophageal perforation. Therefore, patients should be intubated and carefully monitored in an intensive care setting. More recently self-expanding metal stents have been used for the same purpose and can remain in place for 14 days.⁴

Use of Hemospray and other novel haemostatic techniques have been trialled in the management of variceal bleeding and while early results are encouraging more studies are required before such techniques are implemented routinely.¹⁵

Management - interventional radiology is now considered standard second-line care when endoscopic control of upper GI haemorrhage has failed, where there is evidence of re-bleeding after initial control or where the bleeding source could not be identified during initial endoscopy.⁶

CT angiography has a sensitivity of 86% and specificity of 95% for obscure GI blood loss and may be used to help identify vascular malformations, neoplasms as well as excluding potential small and large bowel sources of bleeding. However, in order accurately to identify a source of blood loss patients must be bleeding at a rate of 0.5 ml/min.⁴

If a bleeding source is identified, then the interventional radiologist may attempt selective angiography of the mesenteric vessels and radiological embolization where appropriate. The most common source of bleeding and target for embolization is the gastroduodenal artery. Haemostasis is largely achieved using coils, however several other products including polyvinyl alcohol particles and gelfoam are available for this purpose.⁴

Embolization of vessels may result in abdominal pain, ischaemia, arterial injury and contrast induced nephropathy, but is considerably much less morbid than traditional surgical salvage.

In the case of bleeding varices, where endoscopic control has failed, a trans-jugular intrahepatic portosystemic shunt (TIPSS) procedure can be undertaken. This procedure involves the radiologically guided deployment of a stent bridging the portal and hepatic veins, essentially creating a portosystemic shunt across the liver parenchyma and resulting in rapid reduction in portal pressure. These procedures are performed only in specialist centres and there are several contra-indications and considerations that should be addressed prior to treatment. Therefore, early liaison with a specialist liver centre with interventional radiology services is essential where standard endoscopic management has failed.^{4,6}

Management – surgery: Once considered to be the default option for patients with uncontrolled upper GI haemorrhage, surgery is now considered the treatment modality of last resort when all other means to control haemorrhage have failed. Indeed improvements in endoscopic management and increased availability of interventional radiology have seen a fall in surgery for all GI bleeding of 50% over 10 years and the 2007 BSG audit suggests that only 2.3% of patients underwent surgical management of uncontrolled haemorrhage.¹

Surgery depends upon the origin and pathology resulting in haemorrhage (see Table 6). The most common surgical procedure being under-running or over-sewing of bleeding duodenal or gastric ulcers.

Mortality from surgery is high (29%) and compares poorly to interventional radiology (10%) and despite overall improvements in mortality figures, deaths occurring after surgery have remained static for the past 10 years.^{4,12}

Follow-up/ongoing care: IV PPI is recommended for 72 hours after successful haemostasis or where there is stigmata of recent haemorrhage with no active bleeding observed.^{1,6}

Long-term primary and secondary PPI prophylaxis can be used; however, side effects include increased risk of hip fracture, *Clostridium difficile* infection, pneumonia and possibly gastric cancer. For this reason one must consider carefully the risks and benefits and as lower dose as possible should be employed.^{4,6}

It is essential that during endoscopy that a *Campylobacter*-like organism (CLO) test is performed and that if positive that the

Surgical options for upper GI bleeding

Disease process	Surgical option
Peptic ulcer	Oversew
	3-point ligation of gastroduodenal artery
	Vagotomy and pyloroplasty
	Vagotomy and antrectomy
	Highly selective vagotomy
Mallory-Weiss tear	Oversew
Dieulafoy lesion	Oversew
	Wedge resection
Varices	Portacaval shunt
	Mesocaval shunt
	Distal splenorenal shunt
Gastric cancer	Distal gastrectomy
	Total gastrectomy
	D2 lymphadenectomy
Hemobilia	Selective ligation
	Resection of aneurysm
	Nonselective ligation
	Liver resection
Aortoduodenal fistula	Angiography and stent (if hemodynamically stable)
	Open repair
	Extra-anatomic bypass

From Feinman, M. & Haut, E. R. Upper gastrointestinal Bleeding. Surg. Clin. NA 94, 43–53 (2014).

Table 6

patient has *H. pylori* eradication treatment (currently recommended to be PPI for 4 weeks and dual antibiotic therapy [amoxicillin or clarithromycin and metronidazole] for 7 days) as soon as enteral nutrition is recommenced. *H. pylori* eradication is linked to improved outcomes, reduced rates of re-bleed and if commenced immediately loss to follow-up is prevented and improved compliance is observed. *H. pylori* eradication prevents the need for long-term PPI use and eliminates any potential side effects of ongoing treatment. Patients should be re-tested for *H. pylori* at least 6 weeks after initial positive CLO test, and 2 weeks after completing the 4-week course of PPI. Testing for the presence of *H. pylori* while taking PPI treatment may result in a false negative result. Retesting can be performed via urease breath test or increasingly via a stool antigen test.⁴

Following variceal bleeding, repeat endoscopy is recommended at 2–4 week intervals, as recurrent varices may warrant further band ligation. A non-selective β -blocker such as propranolol or carvedilol may be used to reduce portal pressure by splanchnic vasoconstriction and reduced cardiac output. These have no role in prevention of varices development but may be useful in prevention of bleeding in patients with established cirrhosis and varices.¹³

All patients with portal hypertension should be referred to a hepatology services for full work up; where appropriate screening (including for hepatocellular carcinoma) and surveillance can be established.⁴

Lower GI haemorrhage

Lower GI haemorrhage significant enough to warrant hospital admission is less common than upper GI haemorrhage at approximately 33–77 cases per 100,000 of the population per annum. It forms approximately 3% of all acute surgical admissions; however, it is important to note that small volume lower GI bleed, not warranting hospital admission, is much more common and likely to be under-reported.³

Unlike upper GI haemorrhage, 80% of lower GI bleeds stop spontaneously after initial resuscitation and correction of coagulopathy with only a small proportion of patients requiring intervention. In most hospitals lower GI haemorrhage is managed by the on-call general surgical team and for the majority of patient's general ward-based care is sufficient with few patients requiring level 2 or 3 care.¹⁶

Overall mortality from lower GI bleeding is much less than upper GI bleeding at approximately 3.4%, and mortality is generally related to co-morbidities rather than gross exsanguination. This means that elderly, frail, comorbid patients and those admitted to hospital due to other reasons are most at risk.³

It is essential therefore to exclude an upper GI source of blood loss and where there is any doubt about origin of haemorrhage, particularly in the haemodynamically compromised patient, rapid assessment for an upper GI bleeding source should be undertaken as described above.

Pathology

Diverticular bleeding is the most common cause for lower GI bleeding accounting for approximately 30–65% of cases in a Westernized population. Diverticular disease (development of small pockets within the wall of the bowel) is common in the UK population, and occurs with increasing frequency with age – the majority individuals in their eighth and ninth decades of life will

have developed some diverticulae, but it is possible to see patients in their 20s and 30s with the condition. It is thought to be related to dietary (lack of fibre) and lifestyle components (smoking and obesity) but may involve some heritability.⁸

Bleeding occurs as a complication of the condition when small vessels in the wall of a diverticulum are eroded and are most prevalent in the sigmoid and descending colon. Incidence of re-bleeding after a single diverticular bleed is low (approximately 15%), but is much higher after subsequent bleeds (approximately 50% of patients with two episodes of bleeding will have a further bleed).¹⁶

Vascular abnormalities: Angiodysplasias are responsible for approximately 5–10% of acute lower GI bleeds. Mainly affecting the caecum and ascending colon (but may affect the small bowel in 15% of patients), these lesions result from abnormally dilated mucosal capillaries communicating with tortuous and dilated submucosal veins and have a typical 2–5 mm flat, red, regular bordered appearance at endoscopy. As with diverticular disease, incidence of angiodysplastic lesions increases with age.^{8,16}

Although spontaneous resolution of bleeding is high (90%), there is a relatively high re-bleed rate with 26% of patients having re-bled at 1 year and 45% at 3 years post index bleed.¹⁶

Other vascular abnormalities including varices and Dieulafoy lesions may also be observed in the lower GI tract; however, their incidence is rare (<3%).⁸

Neoplasms and polyps: Colorectal cancer is the fourth most common cancer in the UK, with 42,000 new diagnoses per year. Rectal bleeding is one of the 'red flag symptoms' that warrants urgent referral and investigation and sometimes this can manifest as an acute bleed, although it is important to note that benign polyps may also present with haemorrhage.

Fresh red rectal bleeding is most commonly associated with left-sided tumours (accounting for >60% of cancers). Neoplasms and polyps are responsible for 2–15% of acute lower GI bleeds.

Ischaemic colitis and other colitides: Ischaemic colitis accounts for approximately 5–20% of presentations. It may affect any part of the colon but typically affects the 'vascular watershed' area of the splenic flexure supplied by the marginal artery of Drummond; bridging the middle colic (supplied by the superior mesenteric artery) and left colic (supplied by the inferior mesenteric artery) arteries. The condition is brought about by inadequate blood supply to the affected colonic wall leading to erosive lesions and secondary bleeding.⁸

There are numerous causes for the development of ischaemic colitis (which may result from either arterial or venous hypoxia); however, the condition is broadly divided into occlusive and non-occlusive disease and may be thrombotic or embolic in origin.

Management is dependent on the degree of ischaemia with full thickness necrosis and gangrene indicating the need for surgical resection; however, in most cases the condition will be transient, and resolution of symptoms observed with appropriate non-operative management.

Inflammatory colitis (encompassing inflammatory bowel disease) and infective colitis may also result in GI haemorrhage although less common.

Where the pelvic organs have previously been irradiated (e.g. in prostate cancer treatment) one should suspect radiation proctitis and colitis and this can occur months after completing treatment.

Meckel's diverticulum: Often referred to by the 'rule of 2s' (under two inches in length, within two feet from the ileocaecal valve, affecting 2% of the population, typically presenting under the age of two and containing two types of heterotrophic mucosa), Meckel's diverticulum is the most common congenital malformation in the GI tract. They may present with lower GI haemorrhage originating from the distal small bowel as a result of acidic secretions from ectopic gastric mucosa causing ulceration.¹⁶

Anal lesions and post-polypectomy bleeding: The management of anal lesions (most commonly haemorrhoids – accounting for 5–20% of lower GI bleeds) and post-polypectomy bleeding (accounting for 2–7% of presentations) may be thought of as different from other sources of lower GI haemorrhage as the source of blood loss can be identified from an adequate history and examination.⁸

As with other causes of lower GI bleeding, lesions within the anal canal will often spontaneously stop haemorrhaging; however, where active bleeding is observed during examination (including through the use of proctoscope or rigid sigmoidoscopy), attempts can be made at haemostasis through direct application of pressure, cautery or through application of sutures. This may need to be done under general anaesthesia for patient comfort and to improve visualization.

Where control of bleeding in this manner fails or where another source of bleeding is suspected, then anal lesions should be managed as per higher lesions and outlined below.

In the patient who has had recent polypectomy, there is no need for radiological investigation before proceeding to colonoscopy, which is the diagnostic and therapeutic modality of choice in BSG guidelines. Haemoclips and endoclips with or without adrenaline are recommended to control bleeding. Heater probe and bipolar diathermy anywhere other than in the rectum (below the peritoneal reflection) should be used with caution as the bowel wall is thinner and at increased risk of perforation following polypectomy.³

Risk stratification: British Society of Gastroenterology (BSG) guidelines recommend a two-staged approach to the assessment of the patient with lower GI bleeding. Initially patient should be assessed for signs of haemodynamic instability and shock (calculated using the shock index [SI = heart rate/systolic blood pressure]) and if the patient is haemodynamically unstable or has an SI > 1 then the patient should undergo emergent investigation with or without definitive management.

Haemodynamically stable patients or those with an SI of ≤ 1, should be assessed using the Oakland score (Table 7).

This scoring system allows identification of those patients who are unlikely to suffer serious adverse event (Oakland score < 8) defined as a 95% chance of safe discharge and those who warrant expedited/inpatient but not emergent investigation (Oakland score > 8).

The Oakland score is specific to lower GI bleeds and has been validated in the United Kingdom and has been found to be superior to other risk assessment tools in predicting safe discharge, transfusion requirements and re-bleeds, but is inferior to other scoring systems in predicting mortality.³

Management – CT angiography and interventional radiology: Where there is haemodynamic instability or where active

bleeding is suspected, BSG guidelines suggest that CT angiography should be performed. Where a bleeding source is identified through extravasation of contrast appearing as a 'blush', and where local facilities allow, patients may then undergo targeted intervention by way of embolization. Where interventional radiology is unavailable, such findings would at least give an indication to an endoscopist of the likely origin of bleeding and help guide endoscopic intervention.

There are no direct comparisons in the literature between embolization and endoscopic intervention in the management of lower GI bleeding; however, targeted embolization is reported to be 93–100% successful. Empirical arterial embolization may also be beneficial, even where no active bleeding is seen, and this may be particularly useful when dealing with bleeding from a tumour with a reported clinical success rate of 68%.

Oakland score

Predictor	Score component value
Age	
<40	0
40–69	1
≥70	2
Gender	
Female	0
Male	1
Previous LGIB admission	
No	0
Yes	1
DRE findings	
No blood	0
Blood	1
Heart rate	
<70	0
70–89	1
90–109	2
≥110	3
Systolic blood pressure	
<90	5
90–119	4
120–129	3
130–159	2
≥160	0
Haemoglobin (g/L)	
<70	22
70–89	17
90–109	13
110–129	8
130–159	4
≥160	0

Patients scoring ≤ 8, with no other indications for hospital admission are suitable for immediate discharge from Accident and Emergency and outpatient investigation.

DRE, digital rectal examination; LGIB, lower gastrointestinal bleeding.

From Oakland, K. et al. Diagnosis and management of acute lower gastrointestinal bleeding: guidelines from the British Society of Gastroenterology. *Gut*; 0: 1–14 (2019).

Table 7

There are, however, risks associated with embolization including bowel ischaemia (7–24%) and re-bleeding (10–50%). Empirical embolization is associated with a higher 30-day mortality (31%) compared to targeted treatment (9%). BSG guidelines therefore conclude that the decision to proceed to embolization or primary therapeutic colonoscopy following CTA should be based on local expertise and patient factors.³

Management – flexible sigmoidoscopy/colonoscopy: Identification of bleeding point and ability to achieve haemostasis is often more challenging due to limitation of view (presence of faecal matter and blood ‘coming towards’ the scope), particularly in the unprepared bowel. It may be possible to give the patient a rapid purge through the use of polyethylene glycol electrolyte-based solution (4–6 litres over 3–4 hours for NG tube) or through the use of enema to improve visualization; however, views may still be unsatisfactory, with reports of diagnostic yield ranging widely from 48 to 100%.^{3,16}

The timing of endoscopic intervention remains controversial with many conflicting studies; however, BSG guidelines suggest that patients with evidence of major bleeding, this should take place on the ‘next available list’ and within 24 hours.³

The endoscopic management of lower GI bleeding includes using the same haemostatic techniques as used in acute upper GI haemorrhage, namely mechanical treatment, use of thermal coagulation and fibrin/thrombin products. No one technique appears superior to another; however, the BSG recommend the use of mechanical clips as first-line modality in diverticular bleeding due to low risk, wide availability and ease of use. Angiodysplastic lesions may, on the other hand, be more amenable to thermal coagulation.^{3,16}

CO₂ and gas exchange should be used and use of diathermy and argon plasma coagulation limited in this setting due to the risk of gas explosion and while sub-mucosal infiltration of adrenaline may be useful in obtaining initial haemostasis, its use should be limited in the rectum and anal canal due to the risk of migration into the systemic circulation.³

Management – other options: In approximately 10% of patients with lower GI bleed the source of the bleeding is never identified. Where patients remain haemodynamically stable there is option to repeat investigations or to progress to more specialized investigations including Tc99m scintigraphy, CT or MR enterography, video capsule endoscopy, push enteroscopy or double-balloon enteroscopy. These investigations are of more use where obscure small bowel bleeding is suspected but their availability and use in clinical practice is limited.^{3,16}

Management – surgery: In extremely limited circumstances (e.g. in aorto-enteric fistula) surgery would be classed as the treatment modality of choice, otherwise, it should be considered a salvage option, only to be used when all other means to control haemorrhage have failed. Where there is an identified bleeding source but haemorrhage control has failed, a segmental colectomy may be performed. Where no identifiable bleeding source is identified, a subtotal colectomy may be undertaken. However both of these procedures are associated with significant morbidity and mortality.^{3,16}

Recent guidelines suggest that immediately prior to skin incision, a further attempt should be made using on-table colonoscopy to identify bleeding source and where possible control haemorrhage. It is suggested that only subspecialist colorectal surgeons should undertake such procedures due to the high risk profile.³

Summary

GI haemorrhage is a relatively common presentation to acute hospitals and may be associated with significant morbidity and mortality.

Outcomes can be improved by rapid assessment and appropriate, targeted resuscitation, correction of coagulopathy together with early intervention.

Interventional endoscopy and radiology should now be considered the therapeutic intervention of choice, with salvage surgery only considered where other modalities have failed. ♦

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