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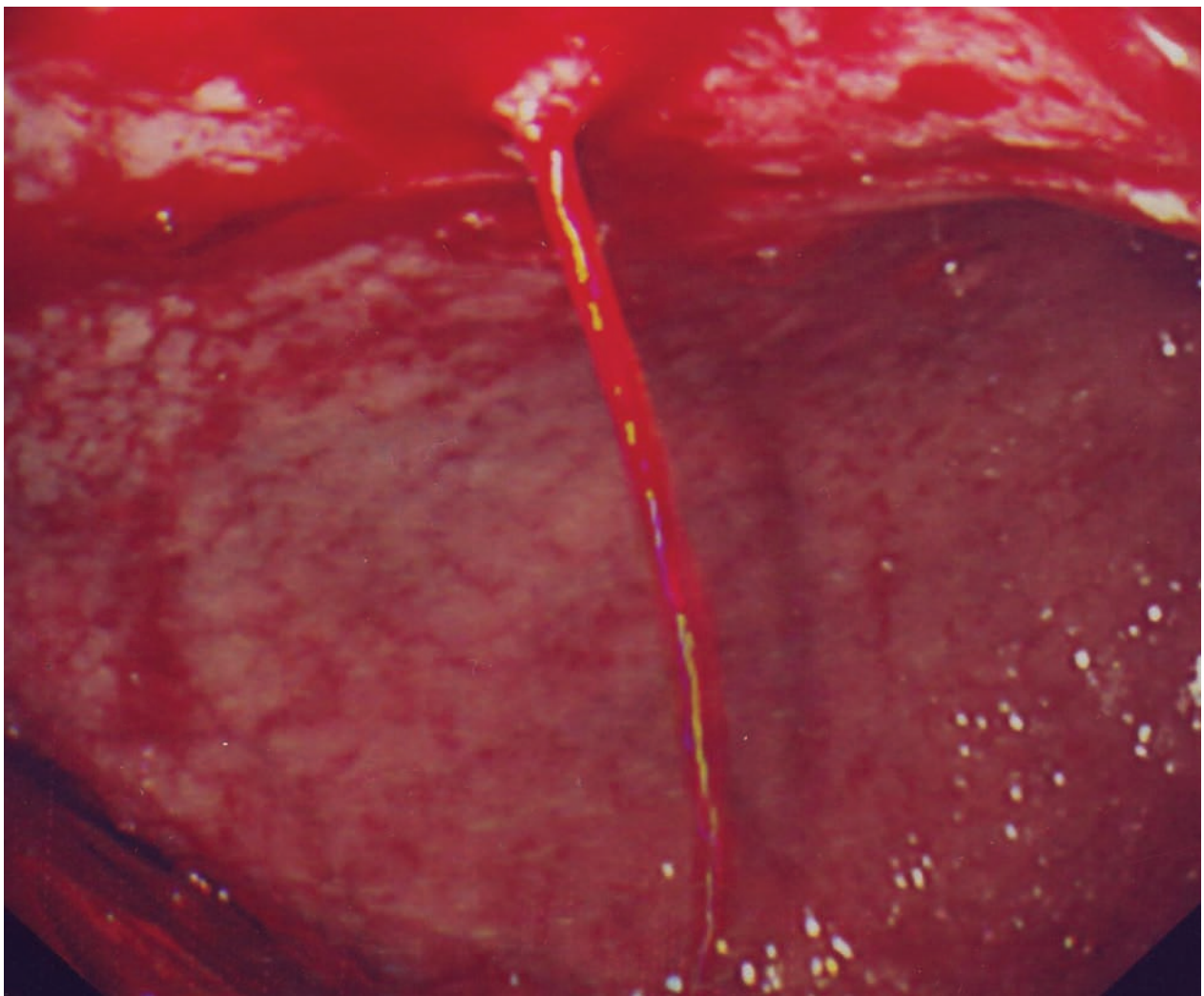


FIGURE 1
Arterial 'spurting' bleed from a vessel seen in a gastric ulcer. This was treated successfully endoscopically

What are the common causes?

UPPER GI BLEEDING IS A COMMON MEDICAL EMERGENCY WITH AN INCIDENCE IN THE UK OF 103 cases per 100,000 adults per year and is much more common in the elderly.[1]

A national audit by the British Society of Gastroenterology (BSG) on the management of upper GI bleeding in the UK, conducted between 1993 and 1994, showed 30-day mortality to be 14%.[2] Based on this audit several recommendations were made, including urgent endoscopy in high-risk patients and admission or early referral of patients with upper GI bleeding to gastroenterology teams. However, despite improvements in endoscopy, recognition of provoking factors and pharmacological interventions available when the audit was repeated in 2007 the mortality rate still remained significant at 10%.[3]

How should patients be assessed?

PRESENTATION

The most common presenting signs of acute upper GI bleeding are haematemesis, either bright red or 'coffee ground', and melaena. About 30% of patients with bleeding ulcers present with haematemesis, 20% with melaena, and 50% with both. »

What are the treatment options?

Table 1

Causes of acute upper gastrointestinal bleeding found at endoscopy in the UK [3]

Cause	Frequency (%)
Peptic ulcer	36
Varices	11
Mallory-Weiss tear	4.3
Oesophagitis	24
Erosive duodenitis or gastritis	35
Malignancy	3.7
Vascular malformations	2.7
No diagnosis found	19

Haematochezia usually suggests a lower GI source of bleeding, however, up to 5% of patients with bleeding ulcers have haematochezia and it indicates heavy bleeding into the upper GI tract.[4] An upper GI bleeding source should be considered when haematochezia presents with signs and symptoms of haemodynamic compromise such as syncope, postural hypotension, tachycardia, and shock should therefore direct one's attention to an upper GI source of bleeding.

More insidious presentations would include nausea, vomiting, epigastric pain, vasovagal phenomena, and syncope, however systemic symptoms such as these would be rare without a history of melaena.

COMMON CAUSES

Peptic ulcer disease, both gastric and duodenal, accounts for the majority of admissions for upper GI bleeding, see table 1, above. Significant bleeding can result from involvement of large vessels within the base of the ulcer see figure 1, p15.[3] The main risk factors for developing peptic ulcers are a history of NSAID use [5] or the presence of *Helicobacter pylori* infection.[6] Warfarin and clopidogrel use can potentiate bleeding, however clopidogrel can also induce bleeding independently in patients with previous peptic ulcer disease.[7]

Bleeding from oesophageal varices usually results in large volumes of bright red haematemesis, if a previous history of chronic liver disease (with or without varices) is known or signs of chronic liver disease are present then an upper GI bleed should be treated as a serious emergency regardless of cardiovascular stability.

Other causes of bleeding are listed in table 1, above, these include a mucosal (Mallory-Weiss) tear of the gastro-oesophageal junction secondary to vomiting, and multiple types of vascular abnormalities. Apart from variceal disease all other causes can vary in severity and with assessment and risk stratification appropriate initial management, early endoscopy or early discharge can be planned.

ASSESSMENT

Clinical risk factors for mortality in upper GI bleeding are: age; comorbidity; tachycardia and a low systolic blood pressure and should be assessed at presentation. The Rockall scoring system incorporates these clinical variables and can be used to predict mortality risk from an 'initial' pre-endoscopy score (see tables 2 and 3, opposite). This system is used widely in the UK. It was developed from a large prospective audit and has been validated numerous times.[8] If the endoscopy result is known then a 'full' score can also be used. As well as mortality the risk of re-bleeding can also be predicted which is usually used following endoscopy to aid more intensive therapy/observation decisions if high, see table 3, opposite. The benefits of this scoring system are not only that mortality can be predicted but also if initial scores are zero, patients suitable for early discharge with outpatient endoscopy can be identified, or admission avoided altogether.

When a delay in presentation of a haematemesis or melaena (over a number of days) occurs in a low-risk patient then a discussion with the local gastroenterology team to arrange urgent (within 24-48 hours) outpatient endoscopy can prevent hospital admission. In these cases access to up-to-date haemoglobin and urea results is especially useful,[9] however, nearly all patients with upper GI bleeding symptoms should be referred to secondary care for further assessment, endoscopy and intervention as required.

REFERRAL

Given the high mortality rate associated with upper GI bleeding nearly all patients with symptoms described above should be referred to secondary care for emergency admission and endoscopic assessment. This should also be the default position in borderline cases. Only young patients (<60 years) with no comorbidity, normal haemoglobin and normal urea can avoid inpatient hospitalisation if urgent outpatient endoscopy can be arranged with the local gastroenterology team.

Therapeutic endoscopy after upper GI bleeding has been clearly shown to reduce re-bleeding and the need for surgery and consequently there has been a push to provide timely endoscopy services for upper GI bleeding patients nationally.[10] A previous audit carried out in 1993 by the BSG found delays in undertaking endoscopy, leading the BSG guidelines to recommend that all medium- to high-risk patients with acute upper GI bleeding undergo endoscopy within 24 hours.[1] In a recent update of the audit 52% of hospitals provided a consultant-led out of hours endoscopy service. The risk adjusted mortality ratio was higher (1.51 versus 1.21) but not significant (p=0.1) in hospitals without such rotas. Individual reports have shown that out of hours endoscopy with a dedicated bleed unit may be able to reduce mortality significantly further.[11]

Early endoscopy in upper GI bleeding:

- allows early diagnosis
- provides the opportunity for endoscopic haemostasis
- enables complete risk stratification of non-variceal bleeding
- allows early discharge of patients with low-risk findings
- has resulted in a reduction in transfusion requirements and length of stay for all risk groups without cost shifting to the outpatient department.[12,13]

However, no study has been able to demonstrate that early endoscopy leads to a reduction in mortality, this is probably because the major determinant of survival is comorbidity rather than control of haemostasis.[8,14] Nevertheless the BSG guidelines along with others emphasise the importance of endoscopy within 24 hours of presentation particularly for high-risk patients.[15]

Patients failing to be controlled with endoscopy can have either interventional radiology with vessel embolisation or surgery. In the recent BSG audit this occurred in 1.7% and 2.2% of patients with upper GI bleeding respectively. The mortality rate in the patients who underwent

Table 2

Rockall score calculation [8]

Variable	Score 0	Score 1	Score 2	Score 3
Age (years)	<60	60–79	>80	
Shock	None	Pulse >100 beats/min & normal blood pressure	Pulse >100 beats/min; systolic blood pressure <100 mm Hg	–
Comorbidity	None	–	Cardiac; gastrointestinal cancer; other major comorbidity	Renal failure; liver failure; disseminated malignancy
Endoscopy diagnosis	Mallory-Weiss tear; no lesion; no stigmata of recent haemorrhage	All other diagnoses	Malignancy of the upper GI tract	–
Major stigmata of recent haemorrhage	None or dark spots	–	Blood in the upper GI tract; adherent blood clot; visible or spurting vessel	–

Table 3

Rockall score, re-bleeding, and mortality[8]

Risk score	Number	% Re-bleed	% Mortality
0	144	5	0
1	281	3	0
2	337	5	0.2
3	444	11	3
4	528	14	5
5	455	24	11
6	312	33	17
7	267	44	27
8	190	42	41

surgery with upper GI bleeding uncontrolled by endoscopy was 31%.

PHARMACOLOGICAL OPTIONS

Approximately one third of patients who present with a bleeding ulcer will develop recurrent bleeding within two years if left untreated after ulcer healing.[16] All patients should be discharged on an oral proton pump inhibitor (PPI), with dosage and duration dependent on the underlying aetiology, to decrease the risk of re-bleeding. All patients with a gastric ulcer should be considered for a repeat endoscopy at six weeks to check healing given the possible presentation of an early gastric cancer as a gastric ulcer. Subsequent secondary prevention for upper GI bleeding at discharge aims to prevent recurrence and management varies depending on the aetiology.

Helicobacter pylori eradication

The *H. pylori* infection rate in patients with bleeding peptic ulcers has been calculated as 80%.[17] Patients with peptic ulcer disease from *H. pylori* who are not using NSAIDs should undergo successful eradication and a further three weeks of PPI therapy.[18] In patients who have a history of NSAID or aspirin use continuation of PPI therapy after this period is discussed below.

Biopsy samples to test for the presence of *H. pylori* should be taken at initial endoscopy if possible before commencing PPI therapy. Eradication should be confirmed by breath test or biopsy to minimise the risk of re-bleeding from peptic ulcers. In the case of eradication failure, after compliance discussion, second-line treatment should be prescribed, see table 4, p18.

H. pylori testing to confirm successful eradication should only be undertaken after PPI and antibiotic therapy has been completed and discontinued since testing within two weeks of these treatments (especially urease biopsy methods) may result in false-negative findings.[19] Repeat testing can of course be conveniently timed with the repeat endoscopy in cases of gastric ulcer disease.

There is no evidence to support empirical eradication of *H. pylori* in patients with bleeding peptic ulcers and this should only occur if exceptional circumstances prevent testing.

NSAIDs

Patients having experienced a bout of upper GI bleeding while on an NSAID should have their treatment discontinued or replaced by an NSAID with PPI cover.

Clinical factors reported to increase the risk of developing NSAID-associated upper GI complications include:

- a history of ulcer or GI bleeding
- increasing age
- concomitant anticoagulation
- concomitant corticosteroid therapy
- high-dose NSAID use.

The risk associated with the NSAID persists for approximately two months after the treatment is stopped, therefore PPI therapy of adequate duration should be considered.[20]

PPI and eradication of *H. pylori* infection are options to use in »

Table 4

Second-line therapy options for *Helicobacter pylori* treatment [40, 41, 42]

Regimen	Duration	Eradication rate	Comments
Standard first-line triple therapy			
proton pump inhibitor bd clarithromycin 500 mg bd amoxicillin 1,000 mg bd	7 days	70–80%	Clarithromycin resistance has lowered rates from 90%
proton pump inhibitor bd clarithromycin 500 mg bd metronidazole 500 mg bd	7 days	75–85%	Consider in patients allergic to penicillin
Second-line triple therapy			
levofloxacin 500 mg bd amoxicillin 1 g bd proton pump inhibitor bd	10 days	77%	
Second-line quadruple therapy			
proton pump inhibitor bd bismuth salicylate 525 mg bd metronidazole 250 mg qds tetracycline 500 mg qds	10 days	80%	Consider in patients allergic to penicillin

combination with NSAIDs in situations where it is necessary to continue the NSAIDs. Recurrent bleeding after six months among aspirin users has been shown in 1.9% of patients after *H. pylori* eradication therapy and 0.9% on long-term omeprazole (20 mg od). The aspirin dose used in the study ranged from 80 to 325 mg/day but was mainly low dose (mean 101 mg/day, n=250). Among naproxen users, respective figures are 18.8% after eradication therapy and 4.4% on long-term omeprazole (20 mg). Therefore PPIs should be used in preventing recurrent bleeding in patients who are taking non-aspirin NSAIDs but the risk (4.4%) should still be noted.[21]

Aspirin and clopidogrel

Aspirin therapy is associated with a dose-related risk. Aspirin doubles the risk of upper GI bleeding at daily doses of 75 mg and quadruples it at doses of 300 mg.[22] Enteric-coated formulations do not appear to reduce the risk.[23]

Patients requiring low-dose aspirin should resume taking aspirin as soon as the cardiovascular risks outweigh the risk of re-bleeding. This could be as early as five days after the onset of bleeding as the delay to a thrombotic event is generally reported as between seven and ten days.[24,25] A patient who has had an episode of non-variceal upper GI bleeding while taking aspirin and who still requires cardioprotection should take PPI prophylaxis with aspirin rather than clopidogrel alone.

The safety of clopidogrel compared with a combination of aspirin and esomeprazole has been evaluated in two randomised controlled trials involving patients with previous aspirin-induced peptic ulcer bleeding.[26,27] In one trial the cumulative incidence of recurrent bleeding during the 12-month period was 8.6% in the clopidogrel group and 0.7% in those taking aspirin 80 mg plus esomeprazole 20 mg twice daily.[27]

In patients who have bled on clopidogrel and are thus at a very high risk for re-bleeding, the benefits of PPI secondary prophylaxis can be used. Recent studies have shown that omeprazole decreases the antiplatelet effect of clopidogrel, possibly by inhibiting the CYP2C19 enzyme.[28] However, concomitant use of pantoprazole, lansoprazole, and esomeprazole did not have this effect, suggesting that the interaction between PPI and clopidogrel is not a class effect.[29,30]

COX-2 inhibitors

The safety of a COX-2 inhibitor compared with a combination of a non-selective NSAID and a PPI has been evaluated with similar rates of re-bleeding ulcers found at six months.[31] One randomised controlled trial demonstrated a significantly lower rate of recurrent upper GI bleeding with a COX-2 inhibitor plus a PPI (0%) compared with a COX-2 inhibitor alone (8.9%) over one year.[32] However two meta-analyses have demonstrated an excess risk of serious cardiovascular events associated with COX-2 inhibitors compared with placebo.[33,34] Recent guidelines endorsed by the BSG suggest COX-2 inhibitors are not recommended in patients with cardiovascular risk. If cardiovascular risk is a concern, naproxen with a PPI is recommended when alternative analgesic therapies fail.[15]

Oesophageal varices

The mainstay of pharmacological treatment of portal hypertension is nonselective beta-blockade with propanolol. This improves mortality and re-bleeding risk in oesophageal varices.[35] Nitrates can be added or substituted if required.[36,37] Most centres should offer repeat endoscopy with further banding to help eradicate the varices as well. Patients with varices should also be on PPI therapy to help prevent oesophagitis which can lead to re-bleeding. The one-year mortality of variceal bleeding is up to 80% mostly due to the underlying liver disease so most management is directed towards maintaining liver function.[38,39]

CONCLUSION

Upper GI bleeding is a common medical emergency with significant mortality and remains a considerable challenge. Rapid appropriate assessment and referral for early endoscopy can prevent morbidity and possibly reduce mortality. The use of reliable scoring systems has enabled early discharge and an evidence-based approach to subsequent secondary prevention can avoid recurrence.

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key points

SELECTED BY

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Upper GI bleeding is a common medical emergency with an incidence in the UK of 103 cases per 100,000 adults per year and is much more common in the elderly. The most common presenting signs are haematemesis (bright red or 'coffee ground') and melaena. About 30% of patients with bleeding ulcers present with haematemesis, 20% with melaena, and 50% with both. Up to 5% of patients with bleeding ulcers have haematochezia and this indicates heavy bleeding into the upper GI tract. An upper GI bleeding source should be considered when haematochezia presents with signs and symptoms of haemodynamic compromise.

Peptic ulcer disease, both gastric and duodenal, accounts for the majority of admissions for upper GI bleeding. The main risk factors for developing peptic ulcers are a history of NSAID use or the presence of *H. pylori* infection. Bleeding from oesophageal varices usually results in large volumes of bright red haematemesis. Other causes of bleeding include mucosal (Mallory-Weiss) tear of the gastro-oesophageal junction secondary to vomiting, and multiple types of vascular abnormalities.

Clinical risk factors for mortality in upper GI bleeding are age, comorbidity, tachycardia and a low systolic blood pressure. Given the high mortality rate associated with upper GI bleeding nearly all patients with symptoms described above should be referred to secondary care for emergency admission and endoscopic assessment. This should also be the default position in borderline cases.

Early endoscopy in upper GI bleeding: allows early diagnosis; provides the opportunity for endoscopic haemostasis; enables complete risk stratification of non-variceal bleeding and allows early discharge of patients with low-risk findings. Around a third of patients who present with a bleeding ulcer will develop recurrent bleeding within two years if left untreated after ulcer healing. All patients should be discharged on an oral proton pump inhibitor (PPI) with dosage and duration dependent on the underlying aetiology to decrease the risk of re-bleeding.

Patients with peptic ulcer disease from *H. pylori* who are not using NSAIDs should undergo successful eradication and a further three weeks of PPI therapy. Patients having experienced a bout of upper GI bleeding while on an NSAID should have their treatment discontinued or replaced by an NSAID with PPI cover. Aspirin doubles the risk of upper GI bleeding at daily doses of 75 mg and quadruples it at doses of 300 mg. Patients requiring low-dose aspirin should resume taking aspirin as soon as the cardiovascular risks outweigh the risk of re-bleeding.

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Useful information

Current guidelines endorsed by the British Society of Gastroenterology: *SIGN 105. Management of acute upper and lower gastrointestinal bleeding.* **www.sign.ac.uk**

Digestive Disorders Foundation (CORE) **www.corecharity.org.uk/Helicobacter-pylori.html**

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