



## PRACTICE

## PRACTICE POINTER

## Acute upper gastrointestinal bleeding

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## What you need to know

- Acute upper gastrointestinal bleeding is a medical emergency, and appropriate initial resuscitation is crucial
- A normal haemoglobin value and blood pressure at presentation does not rule out substantial bleeding—increased heart rate is a more reliable measure of substantial blood loss
- The Glasgow-Blatchford score can help identify patients for whom outpatient care is suitable
- Aim for a haemoglobin level of 70-90 g/L for those without cardiac problems

Bleeding from the upper gastrointestinal tract (oesophagus, stomach, and duodenum) occurs in approximately 100 per 100 000 people annually.<sup>1 2</sup> It is a medical emergency associated with substantial mortality. A UK audit in 2007 found an overall mortality of 10%.<sup>3</sup> This practice pointer provides a guide to the initial management of upper gastrointestinal bleeding and subsequent management of bleeding that results from peptic ulceration, the most common cause (box 1).<sup>6</sup>

Box 1: Causes of upper gastrointestinal bleeding<sup>4 5</sup>

- Peptic ulcer (31%-67%)
- Gastritis or duodenitis (7%-31%)
- Variceal bleeding (4%-20%)
- Erosive oesophagitis (3%-12%)
- Mallory-Weiss tear (4%-8%)
- Tumours (2%-8%)
- Aorto-enteric fistulas, arteriovenous malformations, or Dieulafoy's lesions (2%-8%)

How might you manage patients initially?  
Assessment and resuscitation

Patients may present with melaena, vomiting fresh blood, or with “coffee ground” vomiting (vomit can take on the appearance of coffee grounds when blood reacts with hydrochloric acid in the stomach). Abdominal pain may also be present. Fresh per rectal bleeding (haematochezia) can occur in major brisk bleeding.<sup>7</sup>

Assess the patient's haemodynamic status. Look for visible signs of bleeding. Begin resuscitation in parallel with further clinical assessment. An approach to the initial management of patients with upper gastrointestinal bleeding is shown in the infographic. Early assessment by the intensive care team is recommended in the unstable patient, or where there is airway compromise (such as from haematemesis) or reduced level of consciousness.<sup>2</sup> Obtain a medical history alongside a physical examination. Monitor physiological observations including heart rate, blood pressure, respiratory rate, oxygen saturation, and level of consciousness. Large bore peripheral venous access is required, with at least two 16-18 gauge intravenous cannulas recommended.<sup>2</sup> Crystalloids are recommended for volume replacement.<sup>8</sup>

Blood tests should include haemoglobin level, haematocrit, platelet count, prothrombin time, international normalised ratio (INR), urea, creatinine, electrolytes, liver function, and blood cross-matching. When bleeding is acute, haemoglobin may be unchanged, even if the patient is haemodynamically unstable.<sup>9</sup> This is because the patient loses blood cells and also plasma. But within a few hours, interstitial fluid moves into the vascular space, and the haemoglobin level falls. Reassessing haemoglobin within a few hours can be clinically useful. Similarly, blood pressure may be normal, particularly in healthy individuals,

because of compensatory vasoconstriction, increased cardiac contractility, and tachycardia. A normal haemoglobin value and blood pressure in the acute setting does not exclude life threatening bleeding. An increased heart rate is a more sensitive early objective measure of haemodynamic status.<sup>10</sup>

In patients with anaemia, evidence from randomised trials and observational studies supports a restrictive blood transfusion strategy with a target haemoglobin level of 70-90 g/L.<sup>8 11 12</sup> This is to avoid counteracting the body's own haemostatic mechanisms of hypotension, vasoconstriction, and thrombus formation. For patients with ischaemic heart disease, aim for the higher haemoglobin level within this range to prevent myocardial infarction.<sup>13 14</sup>

Routine nasogastric tube placement is uncomfortable for patients and is no longer recommended. Previously it was thought to help distinguish between upper and lower gastrointestinal bleeding or obtain better visibility at endoscopy.<sup>15</sup> If emergency endoscopy is performed without fasting or if the stomach might contain much blood, a nasogastric tube is recommended.<sup>16</sup>

Pre-endoscopy scoring systems are useful for risk stratification. The Glasgow-Blatchford score (infographic) is especially useful to identify patients at low risk of extensive continued bleeding, who may be managed in the outpatient setting.<sup>12</sup>

## Pharmacological treatment

### Proton pump inhibitors

Intravenous high dose proton pump inhibitor, given as a bolus (eg, omeprazole 80 mg) followed by continuous infusion (eg, omeprazole 8 mg/hour), is recommended by the European Society of Gastrointestinal Endoscopy for patients who require admission.<sup>12</sup> For patients with ongoing bleeding or a visible vessel at endoscopy, the infusion can be continued for 72 hours. Although proton pump inhibitor treatment reduces bleeding stigmata and the need for endoscopic haemostatic intervention, a systematic review found no evidence that it reduces re-bleeding rates or mortality.<sup>17</sup> A systematic review of continuous intravenous versus intermittent oral proton pump inhibitor therapy for high risk bleeding ulcers found both approaches to be equally effective, so the use of continuous proton pump inhibitor infusion is controversial.<sup>18</sup> This specific component of the treatment may be tailored for each patient.

### Prokinetics

A single dose of intravenous erythromycin (250 mg) given 30 to 120 minutes before endoscopy is generally recommended to promote gastric emptying and improve endoscopic visualisation.<sup>2 15 19</sup>

### Suspected variceal bleeding

If variceal bleeding is suspected (for example, in patients with liver disease or alcohol abuse) administer a splanchnic vasoconstrictor, such as terlipressin or octreotide, intravenously. This is typically given with a broad spectrum antibiotic, such as a quinolone, cephalosporin, or piperacillin-tazobactam, because of the high risk of severe bacterial infections in these high risk patients.<sup>20</sup>

## Coagulopathy

National Institute for Health and Care Excellence (NICE) recommendations for managing coagulopathy in upper gastrointestinal bleeding are summarised in **box 2**. This and other guidance on coagulopathy in critically ill patients is mostly based on expert guidance as direct evidence is limited.<sup>12 21</sup> No

strong evidence exists to support the use of tranexamic acid.<sup>22 23</sup> Tranexamic acid increases the risk of cardiovascular and thromboembolic events, and many patients with upper gastrointestinal bleeding are already at increased risk of cardiovascular and thromboembolic events.<sup>4</sup>

### Box 2: NICE recommendations for managing coagulopathy in upper gastrointestinal bleeding

- Do not offer platelet transfusion to patients who are not actively bleeding and are haemodynamically stable
- Offer platelet transfusion to patients who are actively bleeding and have a platelet count of less than  $50 \times 10^9/L$
- Offer fresh frozen plasma to patients who have either a fibrinogen level of less than 1g/L or a prothrombin time (INR) or activated partial thromboplastin time greater than 1.5 times normal
- Offer prothrombin complex concentrate to patients who are taking warfarin and actively bleeding
- Treat patients who are taking warfarin and whose upper gastrointestinal bleeding has stopped in line with local warfarin protocols
- Do not use recombinant factor VIIa except when all other methods have failed

Whenever severe gastrointestinal bleeding occurs in patients taking novel oral anticoagulants (NOACs), seek further advice from a haematology specialist in coagulation.<sup>24 25</sup> If the patient is haemodynamically unstable, expert consultation should not be given priority over endoscopic intervention to stop the bleeding.

## Endoscopic intervention

The timing of endoscopic intervention is the subject of debate and requires clinical judgment.<sup>26 27</sup> Definitive endoscopic treatment should not be unduly delayed if the patient remains haemodynamically unstable despite adequate resuscitation measures.<sup>28 29</sup> However, where the patient is stable, or becomes so after resuscitation, the optimal timing of the initial endoscopy is debatable.<sup>26 30</sup> A recent large cohort study among stable patients with severe comorbidity showed an association between those who underwent endoscopy within 6-36 hours and reduced in-hospital mortality, compared with those who had endoscopy later.<sup>26</sup> Among patients who were haemodynamically unstable there was an association between those who underwent endoscopy within 6-24 hours and reduced in-hospital mortality, compared with patients undergoing endoscopy within 0-6 hours or after >24 hours.<sup>26</sup> The European Society of Gastrointestinal Endoscopy recommends endoscopy within 24 hours for haemodynamically stable patients, and within 12 hours for patients with haemodynamic instability that persists despite resuscitation.<sup>12</sup> Endotracheal intubation before endoscopy does not appear to influence in-hospital mortality or length of hospital stay in patients with upper gastrointestinal bleeding, but the published studies are few, small, and mostly of questionable methodological quality.<sup>12 31 32</sup> In the absence of more robust evidence, the decision whether to intubate or not must be individualised for each patient, accounting for haemodynamic instability, but also risk of aspiration and the need for airway protection.

Ninety percent of patients do not bleed again after endoscopic haemostatic intervention for a bleeding peptic ulcer.<sup>33</sup> Routine second look endoscopy is therefore not recommended unless the patient develops clinical signs of re-bleeding.<sup>34</sup> Gastric ulcers should be biopsied to exclude malignancy. Repeat endoscopy with biopsies in the outpatient clinic is indicated for gastric ulcers until they are completely healed, usually within 6-8 weeks.

Historically, surgery was the standard treatment when endoscopic intervention failed to achieve haemostasis, or following re-bleeding despite such intervention. However, surgery for bleeding peptic ulcers is associated with 8%-33% risk of postoperative mortality.<sup>35</sup> Transcatheter arterial embolisation was introduced in the 1970s, and has since gradually gained acceptance as an alternative to surgery in these patients. This technique is widely used in clinical practice, and studies have shown that, although it has a higher re-bleeding risk compared with surgery, this is outweighed by fewer complications and shorter hospital stay, as well as a lower all-cause mortality.<sup>36</sup> If haemostasis cannot be achieved at endoscopy in the case of variceal bleeding, there is evidence to support the early (within 72 hours of endoscopy) use of a transjugular intrahepatic porto-systemic shunt.<sup>37</sup>

## How to manage patients after the acute bleeding episode

### Anti-acid medication and eradication of *Helicobacter pylori*

Where patients have bleeding ulcers associated with *Helicobacter pylori*, eradication therapy reduces the re-bleed rate from 20% to 3%.<sup>38-40</sup> All patients who have had a bleeding peptic ulcer should be tested for *H pylori* as soon as possible, preferably at the first endoscopy. Acute bleeding increases the risk of a false negative test, so if the initial test is negative the patient should be offered re-testing, preferably within a month.<sup>39,41,42</sup> A stool antigen test (sensitivity 94%, specificity 97%) or urea breath test (sensitivity 95%, specificity 98%) can be offered.<sup>43</sup> Proton pump inhibitor therapy needs to be withheld for two weeks before a stool test to avoid a false negative result. Where this is undesirable (eg, because of concerns about re-bleeding), a serology test is an alternative. The drawback of serology testing is that *H pylori* antibodies usually remain after treatment, lowering the test's specificity.

Eradication regimens vary depending on local antibiotic resistance patterns, but typically combine a proton pump inhibitor with amoxicillin and clarithromycin, or (in the case of penicillin hypersensitivity) metronidazole and clarithromycin, for one week.<sup>21</sup> Duodenal ulcers associated with *H pylori* do not routinely require further proton pump inhibitor treatment outside the eradication period. For gastric ulcers associated with *H pylori*, proton pump inhibitor therapy should continue until the control endoscopy is performed, 6-8 weeks later.<sup>44</sup>

In peptic ulcers not associated with *H pylori* or non-steroidal anti-inflammatory drugs (NSAIDs), the risk of recurrent bleeding appears to be higher. An observational study showed that 42% of these patients had another bleeding episode within seven years.<sup>45</sup> This supports the use of long term maintenance therapy with a proton pump inhibitor in this group of patients. Explain to patients the close link between smoking and peptic ulcer disease.<sup>46</sup>

### Discontinuation of antiplatelet and anti-inflammatory drugs

When to restart aspirin for secondary prevention of cardiovascular disease depends on the endoscopic findings. Aspirin can be continued the same day in patients with peptic ulcer bleeding defined as Forrest grade IIc (adherent clot) or III (flat haematin spot or clean base). Patients with Forrest grade Ia-IIb (spurting bleed or oozing bleed) can resume aspirin three days after endoscopic haemostasis has been achieved<sup>12,47</sup> in combination with continuous (lifelong) treatment with a proton

pump inhibitor to prevent recurrent bleeding. Maintain a low prophylaxis dose, to minimise the risk of long term adverse effects (increased risk of hip fracture, *Clostridium difficile* infection, pneumonia, and possibly gastric cancer).<sup>48</sup>

Advise patients who use NSAIDs other than aspirin to avoid these if possible. If not feasible, changing to a cyclo-oxygenase-2 inhibitor can be as effective in avoiding recurrent peptic ulcer bleeding as combining a regular NSAID with a proton pump inhibitor.<sup>49</sup> In patients at higher risk of re-bleeding (eg, older patients or those with multiple comorbidities) combining a cyclooxygenase-2 inhibitor and a proton pump inhibitor is recommended.<sup>50</sup> Prescribing a proton pump inhibitor to people who take NSAIDs reduces the risk of new peptic ulcer bleeding by 50%-80%.<sup>50</sup> Histamine 2 receptor inhibitors (eg, ranitidine) have no advantage over proton pump inhibitors in terms of re-bleeding risk, but can be considered as an alternative for long term treatment.<sup>51</sup>

#### Questions for further research

- Does prophylactic embolisation after successful endoscopic haemostasis in patients with ulcers and a high re-bleeding risk reduce re-bleeding, readmission, and mortality?
- Are histamine 2 blockers an effective and acceptable alternative to proton pump inhibitors where long term peptic ulcer bleeding prophylaxis is needed?

#### Education into practice

- How does your workplace identify low risk patients who can be managed in an outpatient setting?
- How many of your patients with peptic ulcer bleeding leave with clear written advice on the use of ulcer promoting drugs and proton pump inhibitors?

#### Additional educational resources

- The European Society of Gastrointestinal Endoscopy (ESGE) guidelines: [https://www.esge.com/assets/downloads/pdfs/guidelines/2015\\_s\\_0034\\_1393172.pdf](https://www.esge.com/assets/downloads/pdfs/guidelines/2015_s_0034_1393172.pdf)
- The National Institute for Health and Care Excellence (NICE) guidelines: <https://www.nice.org.uk/guidance/cg141>
- The American College of Gastroenterology (ACG) guidelines: <https://gi.org/guideline/management-of-patients-with-ulcer-bleeding/>

#### Information resources for patients

- The National Institute for Health and Care Excellence (NICE) public information. (Free resource, no registration needed): <https://www.nice.org.uk/guidance/cg141/ifp/chapter/About-this-information>

#### How patients were involved in the creation of this article

We asked patients who were hospitalised for peptic ulcer bleeding about their experience and for comments. Their experience of discomfort caused by a nasogastric tube was often mentioned. We included this in the article, stressing current guidance that a nasogastric tube is not usually clinically necessary.

#### How this article was created

We based the article mainly on current guidelines and on systematic reviews. We searched PubMed to identify recent original studies on upper gastrointestinal or peptic ulcer bleeding and reviewed relevant articles, with a focus on those published during the last five years.

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