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REVIEW

Lower GI bleeding: a review of current management, controversies and advances

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Abstract
Purpose Lower gastrointestinal (GI) bleeding is defined as bleeding distal to the ligament of Treitz. In the UK, it represents approximately 3 % of all surgical referrals to the hospital. This review aims to provide review of the current evidence regarding the management of this condition.
Methods Literature was searched using Medline, Pubmed, and Cochrane for relevant evidence by two researchers. This was conducted in a manner that enabled a narrative review of the evidence covering the aetiology, clinical assessment and management options of continuously bleeding patients.
Findings The majority of patients with acute lower GI bleeding can be treated conservatively. In cases where ongoing bleeding occurs, colonoscopy is still the first line of investigation and treatment. Failure of endoscopy and persistent instability warrant angiography, possibly preceded by CT angiography and proceeding to superselective embolisation. Failure of embolisation warrants surgical intervention.
Conclusions There are still many unanswered questions. In particular, the development of a more reliable predictive tool for mortality, rebleeding and requirement for surgery needs to be the ultimate priority. There are a small number of encouraging developments on combination therapy with regard to angiography, endoscopy and surgery. Additionally, the increasing use of haemostatic agents provides an additional tool for the management of bleeding endoscopically in difficult situations.

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Introduction

Lower gastrointestinal (GI) bleeding is defined as bleeding distal to the ligament of Treitz. The incidence is approximately 36 per 100,000 population [1] with a mortality of up to 3.9 % within 1 year [2, 3], although this may rise as high as 13 % by 5 years [4]. Lower GI bleeding in the UK represents approximately 3 % of all surgical referrals to hospital [5]. The mean age at presentation is in the range 63–77 years [6]. Up to 85 % of patients have self-limiting episodes [7], but rebleeding can occur with rates of up to 19 % within a year [4], with ongoing risks of rebleeding.

We conducted a narrative review of the evidence using online search tools (Medline, Pub Med) and previously published articles and Cochrane reviews.

This review aims to cover the aetiology, clinical assessment and the initial and advanced management options of continuously bleeding patients. It also covers all currently available and novel/ experimental interventions with the evidence available to support the controversial issues in an impartial way. We aim to empower the reader with a tool to have a broader understanding of the areas of controversy and highlight areas of further development.

Assessment and general management of lower gastrointestinal bleeding

The initial history and examination should be focussed on whether this is truly a lower GI bleed, the likely cause, and on the stability of the patient.

In general, lower gastrointestinal bleeding will present as haematochezia but bleeding from the small bowel may present as melaena, and bleeding from the proximal colon may present as darkened, maroon-coloured blood [8]. Additionally, in approximately 10 % of the cases, an upper GI source will present as haematochezia [9]. Pointers as to an upper GI source may be either a history of bleeding peptic ulcer or of chronic liver disease. Although insertion of an NG tube may help to identify an upper gastrointestinal source of bleeding, it is not routinely recommended for this purpose, since the sensitivity of the test is low and complications of this manoeuvre can occur [10, 11]. Other factors which suggest that haematochezia may be from the upper GI tract include a haemoglobin of less than 80 g/l, a rise in haematocrit, or a rise in blood urea/creatinine ratio; whilst per rectal passage of blood clots is more predictive of a colorectal or anal source [12, 13]. In all cases of massive haematochezia, oesophagogastroduodenoscopy should be performed as soon as possible to confirm or refute an upper gastrointestinal source [14].

The commonest cause of lower GI bleeding requiring hospital admission is diverticulosis, accounting for approximately 20–40 % of the cases [2, 9], as well as more than 50 % of rebleeding admission [15]. Right-sided diverticulitis is particularly likely to result in bleeding [16] After this, ischaemic colitis is the most common, at 12–16 % of total cases [16, 17] Common causes also include haemorrhoids and carcinomas of the colon and rectum [15]. Following these are bleeding after polypectomy, inflammatory bowel disease and infective colitis. A small number are a result of radiation proctitis. Angiodysplasias are less commonly the cause, but the source of these can be in the small bowel, and bleeding is often severe in such cases [9].

A history of severe abdominal pain with bloody diarrhoea could feature with ischaemic colitis or inflammatory bowel disease, depending on the age of the patient. Weight loss and intercurrent bleeding would suggest malignancy. A history of constipation and regular straining with recurrent preceding bleeding points towards haemorrhoids. In young patients with a history of diarrhoea, inflammatory or infective colitis would be suspected. With a recent history of broad-spectrum antibiotic use, bleeding, abdominal pain and diarrhoea in an elderly patient suggest *Clostridium difficile* colitis [18]. A history of recent radiotherapy or of colonoscopy with polyp removal should be attained. A drug history is paramount, particularly with reference to the use of anti-platelet agents, non-steroidals and anticoagulants.

Simple examination is unlikely to reveal the cause immediately. A rectal (PR) examination is necessary to reveal the nature of the bleeding and may also identify rectal carcinoma in 40 % of the cases [19]. The mainstay of examination otherwise should be tailored to assessing stability. Examination for pallor, capillary refill time, heart rate, and blood pressure should be acquired urgently. In cases where significant bleeding is suspected, urinary catheterisation is mandatory. Large bore access is required, with blood tests being taken for full blood count, urea and electrolytes, liver function, clotting and crossmatch.

Resuscitation should be commenced with intravenous crystalloid fluid rather than colloid [20]. With regards to administration of blood, there is some evidence that restricting transfusion threshold to 7 days/dl may be associated with improved mortality in bleeding patients, even in high-risk groups [21, 22]. Clotting derangement should be corrected by the administration of suitable products.

Anti-fibrinolytic drugs have been demonstrated in upper GI bleeding to reduce mortality by approximately 5 % [23, 24]. However, there was a high dropout rate in the randomised studies analysed. More information is required to confirm the potentially beneficial effect of tranexamic acid on upper GI bleeding, and there is little information on lower GI bleeding per se. However, the large HALT-IT trial is currently recruiting patients to further assess the potentially beneficial effects of tranexamic acid [25]. One of the endpoints concerns effects on mortality from lower GI bleeding.

The mortality in lower GI bleeding is influenced by several factors, including being male, age greater than 70 years of age, the presence of intestinal ischaemia, hypovolaemia, requirement for transfusion of red cells, clotting deficiencies, or suffering bleeding whilst in hospital for another problem [2, 26, 27]. Correlates of severe bleeding include a low systolic blood pressure (<115 mmHg), increased heart rate (>100 bpm), bleeding PR during the first 4 h of evaluation, associated comorbidities and aspirin use [28]. The BLEED criteria have been used to aid the prediction of adverse outcome [29]. This model was developed and validated in US hospitals. Patient are categorised as high risk if they display any of the criteria of the following: ongoing bleeding, low systolic blood pressure, elevated prothrombin time, erratic mental status and unstable comorbid disease. However, Kollef et al.'s primary outcome refers to complications *after* 24 h of stabilisation of patients [29]. Alternatively, Camus et al. found the American Society of Anaesthesiologists (ASA) score to be 83.5 % accurate at predicting overall 30-day mortality in 235 patients [30]. However, it was not as useful at predicting rebleeding or surgical intervention requirement. In UK hospitals, some authors have argued that better predictors of adverse outcome are age >65 years; creatinine >150 μmol; abnormal haemodynamic parameters and continued bleeding in the first 24 h [5]. Some of these factors can be used to aid decision regarding intensive care unit (ITU) admission, since there is a great deal of inter-hospital variation in the proportion of patients admitted to ITU for management [29], with financial consequences for unnecessary admissions. One author predicted ongoing bleeding to be the most important factor for predicting complications within the first 24 h [31]. The aforementioned studies are relatively small, involving only several hundred patients each. However, ongoing bleeding is clearly an important factor in deciding admission to ITU [31].

On the other hand, there are likely to be patients who are admitted to hospital unnecessarily and who could be managed safely at home if there was a suitable evidence-based triage system in the emergency department. There is limited evidence on this. However, Patel et al. admitted patients with lower GI bleeding based on a pre-ascertained algorithm whereby patients who were not anticoagulated, had haemoglobin >13 g/dl, or systolic BP >115 mmHg were not admitted, managing to avoid 30 % of potential admissions. Patients were followed up for 6 weeks and had flexible sigmoidoscopy at this time [32]. The number of patients, however, was small; and more study is needed before a standard discharge algorithm could be applied to patients in the emergency department with lower GI bleeding.

Summary box 1: Assessment and general management of lower gastrointestinal bleeding

- The initial history and examination should be focussed on whether this is truly a lower GI bleed, the likely cause and on the stability of the patient.
- In all cases of massive haematochezia, OGD should be performed as soon as possible to assess for an upper GI source. Resuscitation should be commenced with intravenous crystalloid fluid rather than colloid.
- Restricting Hb to 7 g/dl may be associated with improved mortality in bleeding patients.
- The HALT-IT trial is currently recruiting patients to further assess the potentially beneficial effects of tranexamic acid.

Role of lower gastrointestinal endoscopy in the diagnosis and management of lower gastrointestinal bleeding

lThe use of colonoscopy is a valuable tool in the diagnosis of lower GI bleeding (LGIB). Estimates for the diagnostic yield in recent studies range from 42 to 100 % [33–37], with a recently pooled analysis of studies suggesting it to be nearer 90 % [38]. A clear advantage of colonoscopy over CT angiography and scintigraphy is that diagnosis and therapy for bleeding can be performed at the time of the procedure. Using angiography for diagnosis, this is also possible. There have been only a small number of studies comparing the two modalities of investigation. The results suggested a greater diagnostic yield from colonoscopy versus angiography, although only one study was a controlled trial, and it is interesting to note that the angiographic yields were lower in these studies than in numerous others [33, 39, 40], Furthermore, colonoscopy relies less on the presence of active bleeding for diagnosis, with the ability to observe lesions and stigmata of recent bleeding [41]. Additionally, follow-up colonoscopy will usually be required for full characterisation and definitive management of bleeding lesions treated angiographically [42]. Colonoscopy also appears quite safe, with complications in approximately 0.3 % of elective and 0.6 % of urgent procedures [38]. A clear disadvantage of colonoscopy versus radiological diagnostics is the inability to detect bleeding lesions from the small bowel. However, given the origin of the vast majority of lower GI bleeds from the colon, colonoscopy is generally agreed to be the first-line procedure of choice [9]. In the presence of very heavy bleeding, colonoscopic diagnosis may be difficult simply due to the volume of blood in the lumen. Secondary angiography would then be a useful option.

lSome form of bowel preparation is recommended for colonoscopy in the setting of acute bleeding. This is aimed at improving visibility but is also necessary to reduce the chance of explosive gases building up which could be triggered by electrocautery [43]. The best methods of preparation are not established, but most authors favour the use of 4–6 l PEG with a preparation time of 3–4 h. Naturally, this may be difficult for patients, in which case, it is administered via nasogastric tube [44]. An alternative method for heavy bleeding patients described recently hydroflush colonoscopy. Here, three 1-l tap water enemas are delivered pre-procedure. During colonoscopy, high-flow water flushing and suctioning are used to clear clots and debris. It has been used for cases of massive bleeding (>6 U), where blood itself can act as a cathartic to clear the colon of hard stool. One of the potential advantages is the short preparation time required in a rapidly bleeding patient. However, there is limited data on its effectiveness, and future randomised studies are required to ascertain its usefulness in this subset of cases [45].

The timing of colonoscopy is still a matter of debate. Urgent colonoscopy within 24 h of admission is safe [36, 37]. Several studies have shown urgent colonoscopy to have a higher diagnostic yield than colonoscopy performed after 24 h [33, 46, 47]. However, in two randomised controlled trials and several other studies, this does not translate into improved patient's early or late rebleeding rates, rates of surgical intervention or survival [33, 34, 48, 49]. Several studies have suggested that urgent colonoscopy can reduce hospital costs, primarily by reducing patient stay [39, 50, 51]. However, the two randomised studies did not find this to be the case [33, 49]. Despite this, these studies do not end the matter because in one patient, stay and costs were not the primary endpoints [49] and in both sample sizes were small and may have been underpowered to truly detect the differences in these outcomes. Furthermore, in a recent very large cross-sectional study of 22,720 patients undergoing colonoscopy for acute LGIB, costs and patient stay were reduced *significantly* in those patients undergoing urgent (<24 h) colonoscopy [48]. Though an administrative set, it suggests larger, adequately powered randomised controlled trials are required to fully settle the issue on early colonoscopy. Currently, timing of colonoscopy is a matter for local departmental policy.

Several therapeutic modalities have been used to treat bleeding lesions or those with stigmata of recent haemorrhage. These include argon plasma coagulation, YAG laser, thermal coagulation, injection with adrenaline, band ligation and endoclips. The method of choice depends on the causative lesion. For

angiodysplasia, electro-cautery, argon or laser coagulation can all be applied. However, long-term rebleeding rates can be as high as 36 %, and patients often need several treatments to clear lesions completely [52, 53]. Haemorrhagic radiation telangiectasia can be treated successfully with several episodes of argon or radiofrequency ablation [54, 55]. Post-polypectomy bleeding responds to adrenaline with thermal therapy, endoclips, or endoscopic band ligation [9]. Recently, a multi-purpose over-the-scope clip (OTSC) has been used for the treatment of post-polypectomy bleeding refractory to conventional endoscopic therapy with success [56]. Clips are applied through a cap on the colonoscope after suctioning tissue into the cap. One of the advantages is that they are larger and can trap a greater amount of tissue, although one disadvantage is that once the bleeding site is found, the cap and clip are attached and colonoscopy must be repeated [57]. For diverticular bleeding, submucosal adrenaline injection, removal of clot to expose the underlying vessel and then thermal probe or haemoclips are effective therapy [16]. Thermal probes are not an option for vessels at the base of the diverticulum. Here, clips can be used. However, clips are less effective when applied across a diverticulum (reefing) rather than across a bleeding vessel per se [58]. Recurrent rates of bleeding following clipping vary from as little as 0 % up to 21 % [37, 59]. Notably, clip application seems to have higher rates of rebleeding when applied to bleeding diverticulae in the right colon [60]. Here, eversion of the diverticulum and endoscopic band ligation shows promise, with low rates of rebleeding using this method [61]. One advantage of this method over clip application is the ability to invert the diverticulum, thus more easily revealing the vessel at its base. This may explain its apparent superiority to clip application [62]. However, one significant disadvantage is the necessity to withdraw and reinsert the scope to apply the band once a bleeder is found, effectively meaning two colonoscopies.

Flexible sigmoidoscopy can also be a valuable diagnostic tool in bleeds caused by inflammatory, ischaemic, post-radiotherapy or infectious colitis. Limited therapy can also be performed, particularly for polypectomy bleeds and haemorrhoidal sources [16]. The latter can also be achieved through the proctoscope.

Summary box 2: Role of lower gastrointestinal endoscopy in the diagnosis and management of lower gastrointestinal bleeding

- The diagnostic yield of colonoscopy in a recent pooled analysis is near 90 %.
- A clear advantage of colonoscopy is that diagnosis and therapy for bleeding can be performed simultaneously.
- Colonoscopy is quite safe, with complications in approximately 0.3 % of elective and 0.6 % of urgent procedures.
- Some form of bowel preparation is recommended for colonoscopy in the setting of acute bleeding.
- Hydroflush colonoscopy is an alternative to usual bowel preparation, but more evidence is required to assess efficacy.
- The timing of colonoscopy is still a matter of debate.
- Flexible sigmoidoscopy can also be a valuable diagnostic tool in bleeds caused by inflammatory, ischaemic, post-radiotherapy or infectious colitis.

Radiological applications in lower GI bleeding

Radiological methods can be extremely useful both for the diagnosis and management of bleeding. The principal methods of diagnosis involve red blood cell scintigraphy and CT angiography. Management requires the more invasive procedure of formal mesenteric angiography.

Scintigraphy

Red blood cells are labelled with technetium-99 before being returned to the patient. Labelling requires a short period and is relatively inexpensive [63]. Images are then taken sequentially, from 30 min to 24 h as required, to detect and localise the source of bleeding Theoretically, red blood cell scintigraphy is very sensitive, with the ability to detect as little as 0.1 ml/min of blood loss [64, 65]. Furthermore, imaging is taken initially and then can be continued for 24 h, potentially enhancing the sensitivity of detection of bleeding. Some authors have advocated that due to its less invasive nature and high sensitivity, it should be the *first* line of investigation for lower gastrointestinal bleeding [63, 66]. This may avoid further invasive tests or therapies in those who have a negative scintigram. Certainly there is evidence it can increase the likelihood of a positive subsequent arteriogram [67]. Whilst there are no studies comparing scintigraphy directly with endoscopic investigations, it is unlikely that scintigraphy will ever supersede the latter as the first-line investigation for lower GI bleeding. It is difficult to quantify the true sensitivity of scintigraphy in studies due to the often temporary, intermittent or settling nature of lower GI bleeding. However, per se scintigraphy can have a yield as low as 39 % in some studies [68]. The yield may be improved in patients who are less stable haemodynamically or who have required more than 2 units of blood transfusion [69, 70]. However, such patients may well be unsuitable to remain in the department of nuclear medicine for several hours. Furthermore, the specificity of the test can be reduced, at least in part a result of downstream transit of blood and therefore tracer from the bleeding point within the bowel lumen [71]. This can give a false positive or an apparent bleed at a different location than initially suspected from the films, with variability of accuracy of scintigraphy consequently from as high as 97 % in some studies to as low as 23 % [63, 67, 68, 72]. Additionally, there is no specific information about the nature of the bleeding lesion. Combination with single-photon emission computed tomography/computed tomography (SPECT/CT) images may improve this accuracy [73]. Furthermore, for this to be available as a service requires a 24-h nuclear medical technician to be available, in addition to a radiologist.

In fact, a particularly useful role for scintigraphy is likely to be as an accessory tool in lower GI bleeding, when initial endoscopy has failed to find a source and bleeding continues. In such cases the source, if found, and if the bleeding

continues intermittently, is often small bowel-related [74]. This can be picked up by scintigraphy when initial endoscopy has failed to locate the bleeding source [63, 72, 75]. Of particular relevance in this respect is the highly effective use of 99mTc-Pertechnetate scintigraphy to search for ectopic bleeding gastric mucosa in symptomatic Meckel's diverticulae [76, 77].

Summary box 3: Scintigraphy

- It is unlikely that scintigraphy will ever supersede endoscopic examination as the first-line investigation for lower GI bleeding.
- A particularly useful role for scintigraphy is likely to be as an accessory tool in lower GI bleeding, when initial endoscopy has failed to find a source and bleeding continues.

CT angiography

The use of triple-phase multi-detector CT angiography (Fig. 1) has increased in recent years. However, its exact role is still not fully defined in the management pathway of acute lower GI bleeding. Bleeding appears as extravasating contrast, which increases through arterial phase to portal venous phase [78]. Images are compared to an unenhanced background to avoid false-positive results from background pick-up. CT angiography has a baseline sensitivity to detect as little as 0.3 ml/min of blood loss, comparable to scintigraphy [79]. The sensitivity in human studies of acute GI bleeding for pick-up of active or recent bleeding varies from 79 to 100 %, with a high specificity of 85–100 % [80–85]. There is less information concerning lower GI bleeding exclusively. Marti and colleagues conducted a prospective study in 47 patients using CT angiography as first-line investigation. The sensitivity and accuracy of CT angiography for detecting active or recent haemorrhage were 100 and 93 % respectively in this study, with bleeding lesions being confirmed by standards of reference (colonoscopy, angiography or surgery). Obana et al. found the pick-up rate for bleeding less amongst patients presenting with lower GI bleeding secondary to diverticulosis [86]. However, colonoscopic pick-up rates were also less in this than in some studies, and there were delays between bleeding episodes and the performance of CT angiography which may have contributed to the overall low pick-up rates.

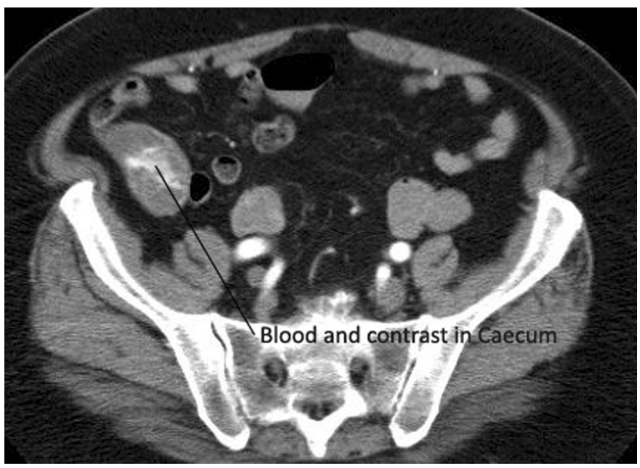

Fig. 1 CT angiogram demostrating blood in the caecum

One advantage of CT angiography is the ability to detect lesions in addition to active bleeding, which may be a contributing factor in its accuracy [81]. Though various studies do suggest accuracy rates of CT angiography to be greater than scintigraphy in lower GI bleeding, only one study compares scintigraphy directly with CT angiography [87]. This study suggested the findings of CT angiography to be slightly more accurate than red cell scintigraphy for the localisation of bleeding sites. However, the total sample size was small, with not all patients undergoing both CT angiography and scintigraphy, and only some of these with follow-up reference tests. More extensive study would be required for definitive information.

Some authors have suggested the potential use of CT angiography as the first-line investigation in lower GI bleeding [81, 82]. As well as its accuracy, it is generally more rapid than scintigraphy, does not require specialist nuclear medical technicians on-site and, unlike colonoscopy, does not require the considerable time for bowel preparation. One additional obvious advantage over endoscopy is the ability to pick-up bleeding sites in the small bowel, though these are less common than colonic bleeding sites [17]. The obvious principal disadvantage is the inability to perform therapy directly. However, CT angiography can be used as a suitable selection agent for angiographic intervention [82, 88], allowing avoidance of the extra risks associated with this invasive technique [89]. It can allow for pre-assessment of differences in a patient's particular vascular anatomy and make subsequent vessel selection easier for embolisation during formal angiography [90]. This line of investigation and management would likely be advantageous as first line in an unstable patient who could not easily undergo the bowel preparation time required for colonoscopy and may not be stable enough to withstand the haemodynamic shifts associated with this approach. An additional potential downside to CT angiography in this situation is the requirement to tolerate the nephrotoxic effects of intravenous contrast, as well as subsequent contrast during formal angiography. It is likely that such patients would need to be candidates for high-dependency management. An additional benefit of a CT angiography as a first choice for unstable patients is that some evidence suggests that those with a negative scan have a good chance of bleeding settling spontaneously [82, 91]. Those with a positive scan could be directed to angiographic or surgical intervention at that time.

CT angiography could also be used as an additional investigation after endoscopic options have failed to find a source for bleeding. Several authors have noted its use here [88, 92]. There may be a disadvantage here compared to scintigraphy in that the

screening time would be relatively short. However, the role for CT angiography would be expected for patients with clear signs of ongoing bleeding with source not found on colonoscopy, rather than intermittent or occult bleeding.

Summary box 4: CT angiography

- The exact role is still not fully defined in the management pathway of acute lower GI bleeding.
- It has a baseline sensitivity to detect as little as 0.3 ml/min of blood loss.
- The sensitivity in human studies of acute GI bleeding for pick-up of active or recent bleeding varies from 79 to 100 %, with a high specificity of 85–100 %.
- It can be used as a suitable selection agent for angiographic intervention.
- When performing CT angiography as a first choice for unstable patients, some evidence suggests that those with a negative scan have a good chance of bleeding settling spontaneously.
- CT angiography can be used as an additional investigation after endoscopic options have failed to find a source for bleeding.

Angiography and embolisation

Angiography can detect bleeding rates as low as approximately 0.5 ml/min and may be even more sensitive when using digital subtraction angiography [93] (Fig. 2). The major advantage of this method is that embolisation can be used to control bleeding sites observed on imaging. Access is usually via the common femoral artery, with the use of selective catheters to analyse contrast extravasation, in the superior mesenteric, inferior mesenteric and, if necessary, internal iliac distribution [94]. When a bleeding site is identified, the aim is 'superselective embolisation', i.e., of a target vessel as close as possible to the site of bleeding. This is particularly important because occlusion of a distal supply should only be of vessels supplying a small segment of bowel to minimise the risk of bowel ischaemia [95, 96] A larger 4–5 Fr catheter is introduced into the parent artery supplying the artery of choice. This enables coaxial introduction of a smaller 3 Fr catheter over a small 0.014 in. guide wire to reach as close as possible the target vessel responsible for the site of bleeding, preferably the vasa recta [97]. A variety of agents can then be used to embolise the bleeding artery. These range from coils to polyvinyl alcohol particles and the relatively new liquid agents, *N*-butyl 2-cyanoacrylate glue and Onyx [98].

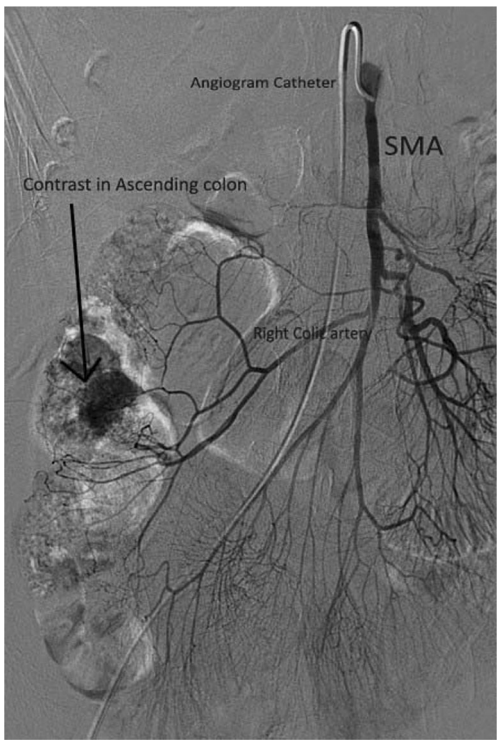

Fig. 2 Mesenteric angiogram demonstrating bleeding in the ascending colon

There is a wide range of literature, with over 1000 patients reported having undergone angiography and superselective embolisation for lower GI bleeding in more than 30 studies. Most are small retrospective studies, differing their timing, selection and methods of embolisation (coils, particles or liquids). Consequently, it is difficult to gauge accurately the success of embolisation, its precise and most definitive role in lower GI bleeding, and which agents should be selected. Angiography can detect extravasation in 22–61 % of the cases [99–104]. Transfusion of above 5 units of blood or 4 units of fresh frozen plasma in the preceding 24 h, haemodynamic instability at the time of angiography, older age and being an ITU patient all correlate with increasing positivity of mesenteric angiography [69, 100]. Performance of CT angiography before invasive mesenteric angiography does not convincingly alter this pick-up rate, although the earlier the patient proceeds from CT to invasive angiography does increase the sensitivity of the latter [105, 106].

Most studies support mesenteric embolisation to be a useful tool in lower GI bleeding. All studies, however, are retrospective analyses. Technical success rates in most studies range from 85 to 100 % [106–115]. Rebleeding rates are variable but range from 0 to 20 % in most studies [97, 103, 107, 110, 111, 116–118], although a small number of studies have reported higher rates of clinical failure of up to 50 % [112]. There is little data on the effectiveness of mesenteric embolisation in different bleeding aetiologies, though Khanna et al. performed a meta-analysis of 26 studies—6 of which met the inclusion criteria—of the use of mesenteric embolisation as the primary intervention in diverticular bleeding. Rates of rebleeding were 15 % in diverticular aetiology versus 40 % for non-diverticular aetiology [119].

The main risks include ischaemic complications to bowel supplied by the embolised vessels. Though Silver et al. reported serious ischaemic complications in 64 % of patients undergoing superselective embolisation [120], this study was based on data gathered during the earlier days of this procedure. In fact the vast majority of studies reveal superselective embolisation to have a small number of ischaemic complications, ranging from 0 to 7 % [99, 108–110, 114, 116]. Other complications include contrast

acute kidney injury, which is particularly important if a patient is undergoing CT angiography followed by invasive angiography, haematoma, and femoral artery thrombosis with limb ischaemia [38]. Complication rates are high with empiric embolisation which should be avoided [109].

The question of the appropriate embolic agent to use depends partly on operator preference. However, embolisation to occlude vessels just proximal to the vasa recta is preferable to avoid interfering with the collateral circulation to the segment of bowel concerned and thus minimising risk of ischaemia. An advantage of coils is their ability to be picked up radiologically, and a size can be chosen to 'fit' the required vessel [94, 98]. *N*-butyl 2-cyanoacrylate glue (NBCA) is a more recently developed liquid agent which has been tested successfully in several studies of lower GI bleeding [121, 122]. It is expensive and its use can be a technical challenge for those learning [98], but rate success seems to be high and bowel ischaemic complications low [123]. There is an additional advantage of the set glue being easily visible fluoroscopically [94].

The invasive nature and potential risks of mesenteric angiography and embolisation render it second line in investigation and treatment to endoscopy in most cases. Certainly it would be a useful alternative to surgery. In some cases colonoscopy can be used to localise a bleeding area with clips. This technique allows successful embolisation in cases with ongoing bleeding resistant to endoscopic management, which are also negative on angiography [124]. In upper GI bleeding, this strategy has been shown in some studies to be preferable to surgery [125]. However, surgery may be preferable to repeating embolisation after failure [102].

Summary box 5: Angiography and embolisation

- Angiography can detect bleeding rates as low as approximately 0.5 ml/min and may be even more sensitive when using digital subtraction angiography.
- Embolisation can be used to control bleeding sites observed on imaging.
- CT angiography before invasive mesenteric angiography can improve the pick-up rate if performed in quick succession.
- Technical success rates in most studies range from 85 to 100 %; rebleeding can occur up to 20 %.
- Rates of rebleeding were 15 % in diverticular aetiology versus 40 % for non-diverticular aetiology.
- The invasive nature and potential risks of mesenteric angiography and embolisation render it second line in investigation and treatment to endoscopy in most cases.

Surgery for lower gastrointestinal bleeding

Only a small number of patients require surgery overall. The most recent prospective data suggests that this is approximately 6 % of the total lower GI bleeds [30]. The number has been estimated at 18–25 % of patients who require transfusion [9]. Absolute indications are failure of non-surgical management for bleeding and complications of non-surgical interventions, such as clinically significant intestinal ischaemia [126]. Relative indications include persistent haemodynamic instability despite aggressive resuscitation and a transfusion requirement of greater than 6 units of blood [9]. If surgery is performed, preoperative localisation of the bleeding site is ideal, since this allows guidance for segmental intestinal resection [127]. In particular, identification of small intestinal bleeding lesions preoperatively can allow arterial injection of methylene blue which has been demonstrated to be successful for aiding intra-operative localisation of the lesion [128, 129]. If a source has not been identified preoperatively, intra-operative enteroscopy or colonoscopy on-table can be valuable on localisation [130, 131]. If localisation is not possible, but the suspected cause is colonic, total or subtotal colectomy is the indicated therapy rather than blind segmental resection of the colon. In the latter case, rebleeding rates are substantially higher [132–134]. The overall mortality from surgery for lower GI bleeding in the most recent case series is approximately 15.9–17 %[135, 136]. There is no evidence that early performance of total or subtotal colectomy to avoid the time spent attempting to localise bleeding preoperatively improves survival. That a significant portion of surgical mortality arises from anastomotic leak questions tantalisingly as to whether stoma formation without primary anastomosis might improve this [135].

Summary box 6: Surgery for lower gastrointestinal bleeding

- Six percent of the total lower GI bleeds eventually require surgery.
- Preoperative localisation of the bleeding site is ideal.
- Intra-operative enteroscopy or colonoscopy on-table can be valuable on localisation.
- If localisation is not possible, but the suspected cause is colonic, total or subtotal colectomy is the indicated therapy.
- The overall mortality from surgery for lower GI bleeding in the most recent case series is approximately 15.9–17 %.
- That a significant portion of surgical mortality arises from anastomotic leak, questions as to whether stoma formation without primary anastomosis might improve this.

Novel approaches to intervention in lower GI bleeding

Haemostatic agents

Recently, there has been interest in the use of topical haemostatic agents as endoscopic haemostatic agents. The two most used in lower GI bleeding are the Ankaferd Blood Stopper and Hemospray. Ankaferd Blood Stopper is a mixture

of plant extracts, including 5 mg *Thymus vulgaris* (dried grass extract), 9 mg *Glycyrrhiza glaba* (dried leaf extract), 8 mg *Vitis vinifera* (dried leaf extract), 7 mg *Alpinia officinarum* (dried leaf extract), and 6 mg *Urtica dioica* (dried root extract) [137]. Its mechanism of action is thought to involve the generation of a meshwork protein scaffold, which then aggregates erythrocytes and leucocytes into a plug [138]. Hemospray is a synthetic product which absorbs water from blood and tissue, allowing it to become firmly adherent to them. Thus, it rapidly forms an adherent layer preventing bleeding. This layer sloughs off after 2–3 days [139]. Hemospray also has a direct action to enhance clot formation [140].

There is data on the use of Ankaferd Blood Stopper in lower GI bleeding after polypectomy [141, 142], during bleeding from radiation colitis [143] and malignant lesions [144].This is a mixture of its use as a primary agent or after the failure of other endoscopic techniques. With the obvious limitations of these small-case series, success rates were encouraging.

Most of the work on Hemospray has come from studies of upper GI bleeding. In the SEAL (Survey to Evaluate the Application of Hemospray in the Luminal Tract), Hemospray was used prospectively on 63 patients with acute upper GI bleeding in ten European centres as either monotherapy or rescue therapy after initial failure of other endoscopic treatments (and would have otherwise required surgery or interventional radiology). Primary success rate was 76 % with 15 % rebleeding rate at 7 days. Interestingly, all patients who had failure of other endoscopic interventions received successful Hemospray treatment [145]. Sulz et al. found a 93 % success rate in the use of Hemospray after the failure of other endoscopic methods, with 7.5 % rebleeding rates [146]. Work is emerging in acute lower GI bleeding, with several small-case series demonstrating its feasibility as primary endoscopic treatment [147–150]. Arterial spurters are likely to require additional treatment to avoid rebleeding [147].

Haemostatic applications have the potential advantage of not requiring particular accuracy. They can be applied easily to a technically difficult area to reach, for example, with endoscopic clips or needles. Additionally, they could be useful in massive haemorrhage, in an attempt to gain control of a bleeding field. They may also be suitable for the general oozing that is typical of some tumour bleeds. One of the potential disadvantages of these powders could be a potential tendency to block endoscope delivery lumens, if any moisture is present in them [151]. Though they are promising, more controlled

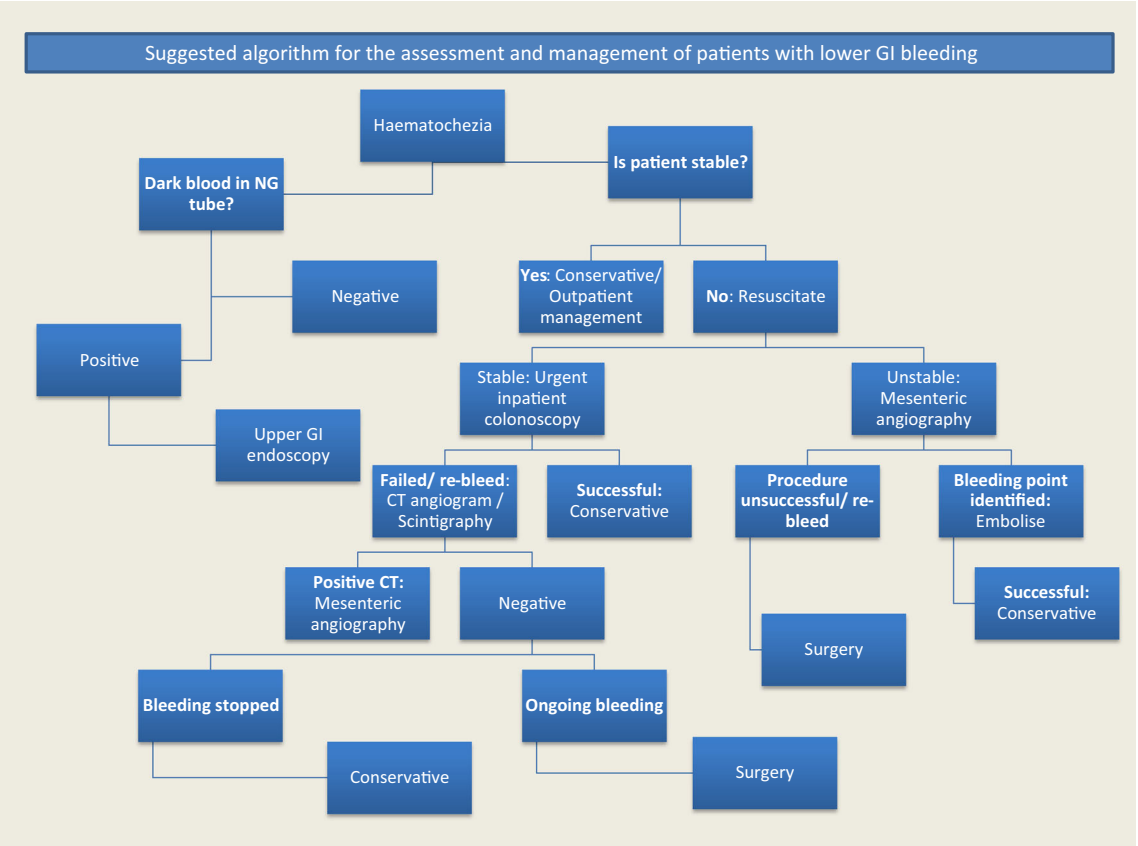

Fig. 3 Suggested algorithm for the assessment and management of patients with lower GI bleeding

studies are required in the applications of haemostatic agents before they can be thoroughly evaluated.

Therapeutic barium enema for diverticular bleeding

High-dose barium impaction therapy for diverticular bleeding is not a new phenomenon and has been described as early as 1970 [152]. There are several case reports and series describing the successful use of barium for the termination of diverticular bleeding in patients where the next resort was surgery [153–157]. A concentrated (200 %) barium sulphate solution is used, at a volume of approximately 400 mls. In all cases barium used terminated bleeding. Furthermore, some authors have noted that the barium can remain impacted in diverticulae for some months [158]. This has been postulated to reduce recurrence in diverticular bleeding. In one study barium impaction was suggested to be as effective as endoscopic therapy in reducing recurrence of diverticular bleeding [155]. Whilst these studies are not controlled and likely subject to publication bias, Nagata et al. demonstrated barium impaction therapy to be superior to conservative management for the prevention of hospitalisation for recurrent bleeding in diverticulosis [159]. Certainly a potential advantage of barium impaction therapy is that it seems to be tolerated well by comorbid and elderly patients [154]. Naturally, if such a patient were subsequently to require colonic resection, however, this might prove more difficult in the presence of luminal barium.

Summary box 7: Haemostatic agents

- The two most used in lower GI bleeding are the Ankaferd Blood Stopper and Hemospray.
- Haemostatic applications have the potential advantage of not requiring particular accuracy.
- Could be useful in massive haemorrhage, in an attempt to gain control of a bleeding field.
- They may also be suitable for the general oozing that is typical of some tumour bleeds.

Therapeutic barium enema for diverticular bleeding

- The barium can remain impacted in diverticulae for some month, thus reducing recurrence in diverticular bleeding.
- A potential advantage of barium impaction therapy is that it seems to be tolerated well by co-morbid and elderly patients.

Conclusions

The majority of patients with acute lower GI bleeding can be treated conservatively in the first instance, with subsequent colonoscopy as the first line of investigation, after excluding an upper GI source. In cases where ongoing bleeding occurs, colonoscopy is still the first line of investigation and treatment. However, failure of endoscopy, persistent instability of the patient or a cause above the caecum warrants angiography, possibly preceded by CT angiography and proceeding to superselective embolisation. Failure of embolisation warrants surgical intervention. In cases of diverticular bleeding, therapeutic barium enema is worth consideration, especially in high-risk patients. Patients with higher ASA scores and ongoing bleeding should be admitted to ITU. A suggested algorithm for the management of lower GI bleeding is shown in Fig. 3.

There are still many unanswered questions. In particular, the development of a more reliable predictive tool for mortality, rebleeding and requirement for surgery needs to be the ultimate priority. The questions regarding the use of tranexamic acid should have an answer after the completion of the HALT-IT trial. The precise role for CT angiography requires more clarity. The debate surrounding the possible economic benefit of early colonoscopy requires further, adequately powered randomised trials focussing on the endpoints of hospital stay and total cost. The extensive data on the safety and efficacy of superselective embolisation needs pooling, in attempt to offer a more reliable estimate, as well as to help to define better the clinical situations where it might be used as first-line therapy. Additionally, the most effective embolisation agents are not clear.

There are a small number of encouraging developments on combination therapy with regard to angiography, endoscopy and surgery. Additionally, the increasing use of haemostatic agents provides an additional tool for the management of bleeding endoscopically in difficult situations. Further work is required to define their efficacy.

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