The role of computerized tomography in the evaluation of gastrointestinal bleeding following negative or failed endoscopy: A review of current status

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ABSTRACT

Gastrointestinal bleeding remains an important cause for emergency hospital admission with a significant related morbidity and mortality. Bleeding may relate to the upper or lower gastrointestinal tracts and clinical history and examination may guide investigations to the more likely source of bleeding. The now widespread availability of endoscopic equipment has made a huge impact on the rapid identification of the bleeding source. However, there remains a large group of patients with negative or failed endoscopy, in whom additional techniques are required to identify the source of bleeding. In the past, catheter angiography and radionuclide red cell labeling techniques were the preferred ‘next step’ modalities used to aid in identifying a bleeding source within the gastrointestinal tract. However, these techniques are time-consuming and of limited sensitivity and specificity. In addition, catheter angiography is a relatively invasive procedure. In recent years, computerized tomography (CT) has undergone major technological advances in its speed, resolution, multiplanar techniques and angiographic abilities. It has allowed excellent visualization of the both the small and large bowel allowing precise anatomical visualization of many causes of gastrointestinal tract (GIT) bleeding. In addition, recent advances in multiphasic imaging now allow direct visualization of bleeding into the bowel. In many centers CT has therefore become the ‘next step’ technique in identifying a bleeding source within the GIT following negative or failed endoscopy in the acute setting. In this review article, we review the current literature and discuss the current status of CT as a modality in investigating the patient with GIT bleeding.

KEY WORDS: Catheter angiography, computerized tomography, gastrointestinal tract, hematemesis
and these patients require additional techniques to identify a bleeding source. Other patients may have failed endoscopic examinations, this occurring more commonly in the colon where adequate bowel preparation may not be tolerated or feasible in some patient subgroups. In addition, colonoscopy may fail to visualize the entire bowel in some cases due to excessive looping and tortuosity. Patients who fail or have negative endoscopy will also require additional investigations in an attempt to identify a bleeding source.

While newer techniques for investigation of potential sources of small bowel blood loss, such as capsule endoscopy, have been developed, they are relatively labor-intensive and time-consuming for the clinician. In addition, the prolonged imaging time and patient preparation required for this technique, precludes the use of capsule endoscopy in cases of acute GI bleeding. Radiological imaging of the GIT therefore retains a crucial role in the evaluation of GI blood loss. In the past, catheter angiography and radionuclide red cell labeling techniques were the preferred ‘next step’ modalities used to aid in identifying the bleeding source. However, these techniques are also time-consuming and in case of catheter angiography, relatively invasive and of limited sensitivity and specificity when bleeding is not active or is intermittent in nature. In recent years, CT has undergone major technological advances making it faster and more sensitive. Multiplanar angiographic sequences allow three dimensional (3-D) demonstration of the mesenteric vessels and their branches [Figure 1] along with providing information on both the cause as well as anatomical location of GIT bleeding. Both the small and large bowel are well visualized on CT allowing for a ‘one stop’ investigative tool for both upper and lower GI bleeding. In many centers CT has therefore become the ‘next step’ technique in identifying the source of an acute GI bleed following negative or failed endoscopy. Its widespread availability and ease of use make it an ideal modality for these patients. In this review article we examine the current literature and discuss, with examples, the present role of CT in the investigation of patients with GI bleeding following negative or failed endoscopy in both the acute and more chronic clinical setting.

**Figure 1:** 3-D maximum intensity projection obtained during the arterial phase utilizing 64-slice CT nicely demonstrates the mesenteric vessels and their branches arising from the abdominal aorta

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**Etiology**

Gastrointestinal blood loss has a number of potential upper and lower tract sources. In the esophagus and stomach, potential causes of bleeding include reflux esophagitis, erosions within large hiatus herniae (Cameron’s erosions), erosive gastritis, peptic ulcer disease, esophageal and gastric varices as well as bleeding from focal abnormal gastric vessels such as Dieulafoy disease (gastric arteriolar bleeding). Other causes of bleeding include primary malignant tumors as well as mixed or benign tumors such as gastrointestinal stromal tumors (GIST). In the small bowel, bleeding may result from duodenitis, complications related to coeliac disease, a variety of benign and malignant tumors as well as rarer conditions such as a bleeding Meckel’s diverticulum. In the colon, common causes of bleeding include colon cancer, diverticular disease and ischemic or inflammatory colitis. Conditions such as angiodysplasia, vascular-enteric fistula and visceral artery aneurysms can be sources of both upper and lower GI bleeding.

**Workup of GI Bleeding**

Upper GI endoscopy and colonoscopy serve as the cornerstones of investigation of patients presenting with GIT bleeding. In patients older than 50 with occult bleeding, colonoscopy should be the first test performed. Colonic tumors, polyps >1 cm, colitis or vascular ectasias identified on colonoscopy can account for a lower GI source in patients with fecal occult blood (FOB) positive stool precluding the need for upper GI endoscopy. Initial investigation with upper endoscopy is warranted in patients with upper GI symptoms or those with risk factors for upper GI bleed e.g. high-dose aspirin or other non-steroidal medication. It should be noted that Warfarin therapy alone does not raise fecal blood levels sufficiently to account for FOB positive stool. Indeed, a prospective study evaluating the GIT in patients on anticoagulant therapy with FOB positive stool revealed that 15 out of 16 had new lesions, of which 20% were malignant, thus highlighting the need for formal GI evaluation in these patients. In approximately 5% of patients with chronic GI bleeding, upper endoscopy and colonoscopy fail to identify the exact site of bleeding and it is these patients in particular who need to be evaluated further by imaging.

**Diagnostic Difficulties**

The small bowel, especially distal to the duodenal bulb, is an uncommon but important site of bleeding. It is estimated that in only 3-5% of patients with GI bleeding is the source located between the second part of the duodenum and the ileocaecal valve. A number of endoscopic procedures have been developed in recent years in an attempt to adequately assess the small intestine. Nevertheless, identifying the source of bleeding in the small intestine can be difficult. A number of factors contribute to this, including small intestine length, its free-hanging course, inherent motility and overlying bowel loops. Push enteroscopy uses a long endoscope to view the small bowel beyond the reach of a standard scope. However, the enteroscope can go only 80-120 cm beyond the Ligament of Treitz.
In addition, the procedure is time-consuming, taking approximately 45 min, is uncomfortable for the patient, usually requiring sedation and analgesia. Sonde enteroscopy uses a longer endoscope inserted transnasally into the stomach and while this technique has the ability to examine the distal small bowel, in reality it fails to visualize the terminal ileum in up to 75% of patients.14 However, its major drawback is that it is extremely labor-intensive, taking an average of four hours to complete and has now been largely abandoned in favor of newer techniques such as wireless capsule endoscopy.12,13 Furthermore, bleeding from the small intestine is typically intermittent in nature, limiting the usefulness of many diagnostic tools. Due to the above factors, patients with obscure GI bleeding from small bowel sources often present recurrently with anemia and melaena, their symptoms chronic and intermittent in nature.11 Indeed patients with primary small bowel tumors are often at an advanced stage by the time a definitive diagnosis is reached15,16 and there has been no improvement in survival statistics in the last 40 years for patients with primary small bowel neoplasms,11 highlighting the delay in their diagnosis and in commencing treatment. One study reported that in patients with a small bowel tumor, the time between the onset of symptoms and tumor resection averaged 30.2 weeks.17 While tumors of the small bowel account for only 6% of all GI tumors,11 GI bleeding may be their only presenting feature, thus highlighting the importance of complete small intestine evaluation in cases of obscure GI bleeding.

Capsule endoscopy is a new form of microtechnology,12 which uses a wireless video capsule, which is swallowed by the patient after a 10 h period of fasting and propelled through the small bowel by peristalsis, while the images captured are downloaded onto a computer for review after 8 h of transit time.13 While it allows examination of most of the small bowel and is noninvasive, it is relatively time-consuming and labor-intensive for the endoscopist, taking 50 to 100 min to review the images from one examination.12 The prolonged imaging time and patient preparation precludes the use of capsule endoscopy in cases of acute GI bleeding. Furthermore it is a costly technique when compared to other endoscopic procedures, the capsule itself costing $450 while physician time and other costs bring the overall average cost of capsule endoscopy to $850.12 In addition, complications such as impaction and small bowel stricture have been reported, with an estimated overall risk of 1%, this figure rising to an 8% risk of capsule impaction in patients with Crohn’s disease complicated by stricture formation which is a frequent occurrence in these patient subgroups.12,18 Indeed, patients in whom there is a clinical suspicion of an underlying small bowel stricture and those with history of previous abdominal surgery are recommended to have a patency test performed prior to a formal video capsule endoscopy examination.13 If the patency capsule becomes impacted, it is designed to dissolve and pass through the stricture, however, early studies indicate that the patency capsule can incompletely dissolve in such cases and may itself lead to impaction.13 Furthermore, while the role of capsule endoscopy in the visualization of mucosal lesions is well established, lesions beyond the mucosal lining cannot be diagnosed. Therefore extra-mucosal small bowel wall lesions, in particular GISTs, are indistinguishable from a true extrinsic lesion abutting the small bowel on capsule endoscopy, in comparison with CT which can clearly distinguish between these pathologies. It should also be noted that although no clinical cases have yet been reported in the literature, the presence of a cardiac pacemaker is considered a relative contraindication to capsule endoscopy due to concerns that the signals from the capsule might interfere with the function of the pacemaker12,13 which is not a concern with CT.

Moreover, a number of clinical conditions warrant special consideration when investigating potential underlying causes of GI bleeding. For example, HIV is associated with infection and neoplasm of the GIT, which can result in bleeding. The primary infectious etiology is cytomegalovirus (CMV) colitis while neoplastic etiologies include lymphoma and Kaposi’s sarcoma. Patients with coeliac disease, who present with occult or overt GI blood loss, should raise the suspicion of an underlying lymphoma and radiological imaging and in particular CT is a very valuable modality in the evaluation of these patient subsets.

Role of Radiology in Patients with GI Bleeding

Radiosotope scans

Radiological imaging of the GIT therefore retains a crucial role in the evaluation of occult and obscure GI blood loss. For patients with active GI bleeding in whom a source cannot be identified on OGD or colonoscopy, radionuclide scanning is still often performed. Technetium-99m labeled red blood cells or technetium sulphur colloid may be used for scintigraphic examinations.19 Labeled red blood cell scanning is superior to sulphur colloid scanning in detecting GI bleeding because the labeled red cells have a longer intravascular half-life than sulphur colloid, which permits delayed images to be obtained up to 24 h post administration, thus increasing the probability of identifying a bleeding site.11,20 In addition, the background activity of the liver and spleen is significantly less with labeled red cells and therefore the detection of bleeding points in small bowel or colon overlaying these organs is improved. Technetium-99m scanning is reported to be capable of detecting blood loss as low as 0.1 ml/min.12,21 It has several major drawbacks however. Even if bleeding is detected, it cannot specify an exact bleeding point, localizing only to a general area.22 In addition, it cannot identify the cause of bleeding such as a tumor due to its inability to give anatomical or structural information.

Mesenteric angiography

Mesenteric angiography may also be used in cases of active GI bleeding. In contrast with nuclear medicine scanning described above, mesenteric angiography is more likely to localize bleeding to a specific site, in reportedly between 50% and 72% of patients with massive GI bleeding.12,24 In addition, specific embolization therapy may be administered at the time of angiography if there is an amenable lesion. However, it is less sensitive, requiring a bleeding rate of at least 0.5 ml/min.13,21 thus limiting its use largely to cases of active bleeding. The diagnostic yield is improved when angiography is performed after a rapidly positive radiosotope scan is obtained11 and following the administration of anticoagulants, vasodilators or clot-lysing agents which can
precipitate or propagate bleeding. However, the potential risk of uncontrolled hemorrhage in the setting of a patient who is already actively bleeding, restricts the use of this latter technique to those without any significant comorbid illness, in whom all other diagnostic avenues have been exhausted.

Mesenteric angiography may be used in selected cases of chronic, occult GI blood loss where the endoscopic and other diagnostic workup is negative, in which case it may reveal an occult lesion such as angiodysplasia or small bowel tumor with a typical vascular pattern. However, it should be recognized that not all angiodysplastic lesions identified at the time of mesenteric angiography will be actively bleeding in which case prophylactic therapy is not recommended. The main disadvantages associated with angiography are that it is an invasive and time-consuming procedure, which in the absence of ongoing active bleeding is usually negative. It also gives little information about pathological processes such as diverticular disease and colonic tumors.

Computerized tomography

It is with the above limitations of conventional radiological investigations in mind that CT has emerged as a potential modality in the evaluation of these patients. Computerized tomography has undergone rapid improvements in recent years, enabling imaging of the whole abdomen and pelvis to be performed in seconds. The introduction of multislice CT with its angiographic capabilities has revolutionized imaging of the abdominal vasculature. The mesenteric arterial tree can now be visualized in multiple planes and 3-D formatting allows precise anatomical localization of conditions such as bleeding aneurysms. In addition, multiphasic contrast-enhanced techniques can now be utilized to detect extravasation of blood into the bowel (Figures 2 and 3). Unlike other techniques such as nuclear medicine studies and catheter angiography, CT has the advantage of being fast and noninvasive as well as facilitating precise anatomical delineation of pathological processes.

There is limited data in the literature reporting the use of CT in the evaluation of GI bleeds. Ettorre et al. published a series of 18 consecutive patients with acute GI bleeding who underwent catheterization of the abdominal aorta followed by single-detector helical CT angiography. All patients had an angiographic catheter placed at the origin of the coeliac trunk and received intra-arterial contrast injection. In their patients, helical CT showed the site of contrast extravasation in 13 out of 18 cases. While the authors demonstrated a positive influence of CT, the technique utilized was both time-consuming and invasive and not a practical proposition for many departments. Multislice CT has somewhat helped overcome these limitations by allowing rapid arterial phase imaging of the GI tract. In 2003, Kuhle et al. analyzed the ability of helical CT to depict active colonic hemorrhage. They did this by utilizing an animal model and showed that bleeding (extravasation) into the colon could be detected at a rate of 0.3 ml/min. This data suggests that helical CT may depict acute lower GI bleeding at a lower rate than the lower limit of 0.5 ml/min cited for mesenteric angiography and may approach the 0.2 ml/min limit cited for 99mTc RBC scanning. Ernst et al. studied a group of 19 patients with lower GI bleeding. They showed that contrast-enhanced helical CT located the bleeding site in 15 of their 19 patients. Another study by Tew et al. evaluated 13 patients with acute lower GI bleeding. All patients underwent multidetector CT (MDCT) angiography using a four-channel multidetector CT scanner. In their study seven of the 13 were shown to have bleeding into the bowel. In addition, the six patients in whom bleeding was not detected, all showed resolution of bleeding without further intervention. Therefore they obtained no false-positive or false-negative findings with MDCT. Computerized tomography has also been shown to be of use in cases of acute intermittent GI bleeding, where endoscopy has failed to localize a bleeding source and bleeding has stopped temporarily. Rajan et al. performed CT in seven patients who had clinically stopped bleeding temporarily and found that CT yielded a diagnosis in six of these patients (86%). In addition, they found CT to have a 100% specificity in the diagnosis of gastrointestinal stromal tumors (GISTs), a common underlying pathology in this subset of patients with intermittent GI hemorrhage.

Most of the studies in the literature focus on patients with acute bleeding and unfortunately there is little data reporting the utility of CT in chronic intermittent or occult GI bleeds. It is

![Figure 2](image1.png)  
**Figure 2**: A 73-year-old male on induction chemotherapy for acute lymphatic leukemia presented with massive bleeding per rectum. (A) Transverse arterial phase CT demonstrates high attenuation material within the left colon in keeping with active bleeding (arrow). (B) Coronal reformatted image shows anatomical location of active bleeding to better effect (arrow)

![Figure 3](image2.png)  
**Figure 3**: Delayed phase CT through the upper abdomen in a 55-year-old male alcoholic utilizing intravenous contrast but no oral contrast demonstrates high attenuation material in the stomach in keeping with active bleeding (arrow)
likely that it is in this second group of patients that CT may have its most important role. In this subgroup of patients, bleeding is slow or intermittent and therefore imaging with nuclear medicine studies and catheter angiography is likely to be negative. In our institution, it has been our experience that a significant proportion of patients with occult bleeding have had a diagnosis made by CT. Conditions such as GISTs [Figure 4], which are a relatively common cause of occult bleeding, are well visualized on CT. Nishida et al.\textsuperscript{[32]} reported their experience with MDCT scanning in patients with GISTs and its use in the detection of occult tumors in high-risk patients. They showed that tumors larger than 2 cm could be visualized and characterized. Most tumors measuring 1-2 cm in size could also be seen.

Other causes of GI bleeding such as diverticular disease [Figure 5] are also well depicted on CT. Computerized tomography has been shown to be the imaging modality of choice in evaluating diverticular disease and its complications.\textsuperscript{[33]} superseding barium studies and older imaging contrast studies. Computerized tomography is also excellent at depicting vascular anomalies causing GI bleeding such as aortoenteric fistulae. Aortoenteric fistula is often first suggested by CT with its ability to accurately visualize the relationship of the bowel to the adjacent aneurysm. In addition, pseudoaneurysms as well as other vascular anomalies may be precisely evaluated with CT [Figures 6 and 7]. Computerized tomography in such cases will also help triage the patient to the best treatment of the vascular lesion by either catheter-based techniques or open surgery. When CT is performed for the patient with the 'unknown' bleed, unexpected or unusual causes are often detected. In our institution we have detected a number of unexpected causes of chronic or obscure GI bleeds such as intussusception, Crohn’s disease, vasculitis and a variety of GI tumors [Figures 8-10].

\textbf{Figure 4:} Transverse CT through the upper abdomen following intravenous and oral contrast demonstrates a 5-cm necrotic gastrointestinal stromal tumor within the wall of the stomach (arrow). The lesion was missed on endoscopy because of its submucosal location.

\textbf{Figure 5:} Transverse CT with oral and intravenous contrast in an elderly patient with a lower GIT bleed demonstrates sigmoid diverticuli, bowel wall thickening and stranding of the mesentery in keeping with acute diverticulitis (arrow)

\textbf{Figure 6:} Transverse CT with intravenous and oral contrast in a young male patient with massive upper GIT bleed and negative endoscopy. There is a large pseudoaneurysm of the gastroduodenal artery (arrow). The patient had a history of chronic pancreatitis as an antecedent cause. The pseudoaneurysm was successfully treated by percutaneous thrombin injection under CT guidance.

\textbf{Figure 7:} Transverse CT through the upper abdomen in a 31-year-old unstable patient with a major upper GIT bleed and negative endoscopy. The patient had a recent history of endocarditis and was pyrexial on the present admission. (A) There is a large mycotic aneurysm in the liver with surrounding edema and abscess cavity formation (arrow). (B) The gallbladder is full of high-density material in keeping with blood (arrow) Further blood was seen within the common bile duct (not shown)
Computerized tomography technique

Imaging should be performed on a multidetector scanner and patients should be kept fasting prior to the procedure. Patients must also be kept well hydrated with intravenous (IV) fluids. When imaging is performed to detect acute GI bleeding, no oral contrast should be given, as this will obscure the visualization of intravenous contrast agent extravasation. Visualization of extravasation is a direct indicator of active bleeding. However, prior to giving intravenous contrast in cases of acute bleeding, it is useful to perform unenhanced imaging to detect preexisting hyperattenuating material in the bowel lumen which may result in a falsely positive scan. Objects such as metallic clips, suture material, bowel contrast or foreign bodies may all result in high attenuation material within the bowel. Following the unenhanced scan imaging should be performed in the arterial phase to detect active bleeding. We use 100-150 ml of non-ionic contrast material with an injector pump given at 4 ml/s. Imaging is then done from the diaphragm to the pubic symphysis. Typical multidetector parameters are 2.5 mm section thickness with a pitch of 1.5 with a reconstruction interval of 2 mm. The timing of the bolus is decided by using an automatic bolus triggering technique. Three-dimensional reconstruction is useful when a vascular anomaly is detected but it does not have to be performed routinely in every case. Additional imaging in the portal phase may be obtained, particularly when an underlying tumor or mass is suspected.

Computerized tomography findings

As described above, the purpose of the non-contrast scan is to identify hyperattenuating material involving the bowel, which may otherwise artificially give a false-positive reading on arterial phase imaging. Once these are excluded, arterial imaging is best performed when active acute bleeding is ongoing. Extravasated contrast is typically identified as a focal area of high attenuation within the bowel lumen, which represents a bleeding point [Figure 2]. The material within the bowel lumen should have an attenuation value of greater than 90 Hounsfield units (HU). Willmann et al. reported that the attenuation of active arterial extravasation should be greater than 90 HU while clotted blood should be below this value.

Other findings on CT are largely related to the particular underlying cause of the bleeding. Masses such as small and large bowel tumors are generally well visualized. Inflammatory bowel disease, ischemic colitis and vascular abnormalities can also be identified and characterized [Figures 11 and 12]. In cases of chronic or occult bleeding, active bleeding will not be seen and the purpose of imaging is to diagnose the cause of bleeding rather than identify the actual bleed.

Limitations of computerized tomography

While CT is an excellent modality in identifying the underlying cause of GI bleeding, it has some limitations. It utilizes ionizing radiation and the use of intravenous contrast agents is contraindicated in patients with moderate to severe renal impairment and a history of anaphylaxis to contrast media. While large colonic tumors and most small bowel tumors are
well visualized, bleeding polyps and small colonic tumors may easily be missed. However, it is anticipated that such lesions will be detected during colonoscopy, which is the more appropriate test in such circumstances. Angiodysplasia of the bowel is also difficult to image on CT. While active bleeding may be seen and is a good indirect sign, visualization of the actual angiodysplastic segment is rarely possible. Another limitation of CT compared to catheter angiography is its inability to treat the bleed at the same sitting. Patients will need to be transferred to the angiographic laboratory for transcatheter embolization or to the operating theatre as is appropriate in each case. However, it is anticipated that CT will facilitate precise preoperative localization and characterization of the bleeding source, making either surgery or catheter-directed therapy significantly easier.

Figure 11: CT of the abdomen following oral and intravenous contrast demonstrates marked bowel wall thickening and enhancement of the colon (arrows). A diagnosis of colitis was suspected. Final diagnosis was pseudomembranous colitis.

Figure 12: CT of the upper abdomen in a 30-year-old alcoholic patient with a history of pancreatitis and prior splenic vein thrombosis. The patient had persistent upper GIT bleeding. The spleen is enlarged in keeping with the patient’s history of splenic vein thrombosis. There are markedly enlarged gastric varices identified which were felt to account for the upper GIT bleed (arrow). The patient was successfully treated by transcatheter embolization.

Both upper and lower GI bleeds present a significant challenge for clinicians. In the acute phase, patients may be hemodynamically unstable, requiring rapid assessment and treatment [Figures 13 and 14]. With more chronic GI bleeds, there is less urgency; however, it is equally important to find the underlying cause of bleeding [Figure 15]. Endoscopy still plays the primary role in the initial investigation of GI bleeding and the type of endoscopy (upper or lower) will largely be dictated by the clinical presentation. However, endoscopy may be negative or impractical in some patients. It is this subgroup of patients in whom CT may make the largest impact. There is increasing data to suggest that CT should be the ‘next step’ investigative procedure in cases of active GI hemorrhage and should supersede more invasive and time-consuming procedures such as catheter angiography and red cell scintigraphy respectively. Indeed in many centers, CT angiography is now being performed as the next step in patients without a definitive source of active GI bleeding, conventional mesenteric angiography not being performed unless active extravasation of contrast is demonstrated on CT except in cases of hemodynamic instability due to massive hemorrhage. Not only has CT proven to be a cost-effective alternative to catheter-directed mesenteric angiography in the detection of active GI bleeding, but may also

Conclusion
Chronic GI bleeding
OGD and Colonoscopy
OGD positive
Treat as appropriate
OGD negative
CT
CT positive
Bleeding stopped
CT negative
Bleeding stopped
Occult GI bleeding
CT
CT positive
OGD and Colonoscopy
OGD positive
Treat as appropriate
OGD negative
CT
CT positive
Bleeding stopped
Refer as appropriate
CT negative
Bleeding stopped
CT
CT positive
Treat as appropriate
CT negative
Observe
If stable, prep for Colonoscopy
Observe +/- Colonoscopy +/- treat as appropriate

Figure 15: Management algorithm incorporating CT in the evaluation of the patient with chronic, occult GI bleeding

References

Stunell, et al.: Computerized tomography in gastrointestinal bleeding
