Cardiovasc Intervent Radiol (2015) 38:329–335
DOI 10.1007/s00270-014-0928-8

CLINICAL INVESTIGATION ARTERIAL INTERVENTIONS

Outcome Following a Negative CT Angiogram for Gastrointestinal Hemorrhage

Victoria Chan · Donald Tse · Shaheen Dixon · Vivek Shrivastava · Mark Bratby · Suzie Anthony · Rafiuddin Patel · Charles Tapping · Raman Uberoi

Received: 15 January 2014 / Accepted: 21 April 2014 / Published online: 15 July 2014

Abstract
Objective This study was designed to evaluate the role of a negative computed tomography angiogram (CTA) in patients who present with gastrointestinal (GI) hemorrhage.
Methods A review of all patients who had CTAs for GI hemorrhage over an 8-year period from January 2005 to December 2012 was performed. Data for patient demographics, location of hemorrhage, hemodynamic stability, and details of angiograms and/or the embolization procedure were obtained from the CRIS/PACS database, interventional radiology database, secure electronic medical records, and patient's clinical notes.
Results A total of 180 patients had 202 CTAs during the 8-year period: 87 CTAs were performed for upper GI hemorrhage (18 positive for active bleeding, 69 negative) and 115 for lower GI hemorrhage (37 positive for active bleeding, 78 negative); 58.7 % (37/63) of patients with upper GI bleed and 77.4 % (48/62) of patients with lower GI bleed who had an initial negative CTA did not rebleed without the need for radiological or surgical intervention. This difference was statistically significant ($p = 0.04$). The relative risk of rebleeding, following a negative CTA, in lower GI bleeding versus upper GI bleeding patients is 0.55 (95 % confidence interval 0.32–0.95).
Conclusions Patients with upper GI bleed who had negative CTAs usually require further intervention to stop the bleeding. In contrast, most patients presenting with lower GI hemorrhage who had a negative first CTA were less likely to rebleed.

Keywords CT/CTA · Embolization · Gastrointestinal · Hemorrhage

V. Chan (✉) · D. Tse · S. Dixon · M. Bratby · S. Anthony · R. Patel · C. Tapping · R. Uberoi
Department of Radiology, Level 2, John Radcliffe Hospital, Headley Way, Oxford OX3 9DU, UK
e-mail: drvictoriac@gmail.com

D. Tse
e-mail: donald.tse@gmail.com

S. Dixon
e-mail: shaheen7noorani@gmail.com

M. Bratby
e-mail: mark.bratby@ouh.nhs.uk

S. Anthony
e-mail: suzie.anthony@ouh.nhs.uk

R. Patel
e-mail: rafiuddin.patel@ouh.nhs.uk

C. Tapping
e-mail: charles.tapping@ouh.nhs.uk

R. Uberoi
e-mail: raman.uberoi@orh.nhs.uk

V. Shrivastava
Department of Radiology, Hull Royal Infirmary, Anlaby Road, Hull HU3 2JZ, UK
e-mail: vivshriv@yahoo.com

Introduction

Acute gastrointestinal (GI) hemorrhage is a common medical emergency that is potentially life-threatening and challenging to manage. The incidence of acute upper GI hemorrhage in the United Kingdom ranges between 84 and 172 cases per 100,000 adults per year, whereas lower GI hemorrhage has an incidence of ~25 cases per 100,000 adult population per year; this increases significantly with increasing patient age [1, 2]. The majority of patients admitted to the hospital for acute GI bleeding settle with

fluid resuscitation, correction of coagulopathy, and/or upper GI endoscopic sclerotherapy. However, bleeding can recur in 25 % of cases, causing significant morbidity and mortality [3]. Hospital mortality for acute GI hemorrhage is 10 %, but this can reach up to 30 % with massive bleeding associated with hemodynamic instability or in patients who rebleed during hospitalization [3]. These patients require further intervention, imaging localization, and directed therapy to secure hemostasis.

For upper GI hemorrhage, which is defined as bleeding proximal to the ligament of Treitz, oesophagogastroduodenoscopy (OGD) is well established as the primary procedure in the diagnosis and treatment of upper GI bleeding. It is known to identify the source of bleeding in $\sim$90 % of cases, with <10 % of patients requiring further treatment following an endoscopic therapeutic intervention [2]. In comparison, endoscopy is less reliable for the diagnosis and management of lower GI hemorrhage; hence, there is greater reliance on radiological imaging techniques to localize the source of bleeding as well as to plan and guide minimally invasive therapeutic procedures.

Multidetector CTA is a promising first-line modality for GI hemorrhage. It is time-efficient, sensitive, and allows accurate diagnosis or exclusion of active GI hemorrhage, thus having a profound impact on the evaluation and subsequent treatment of patients who present with acute GI bleeding [3]. We hypothesized that a negative CTA in patients with GI hemorrhage is a good indicator that further intervention is unlikely. The purpose of our study was to review the outcomes in all patients who presented with acute GI hemorrhage and had a negative CTA.

Materials and Methods

Ethics approval is not required by our institution for this retrospective study.

Patients

All patients who had acute GI hemorrhage and were referred to the radiology department of our institution for CTA and/or mesenteric angiography ± embolization from January 2005 to December 2012 were retrospectively reviewed. Patients with variceal or traumatic bleeding were excluded. The patients were identified from CRIS/PACS and our interventional radiology database. Data collection included patient demographics, site of hemorrhage, details of angiograms and the embolization procedure, comorbid conditions, clinical outcome, survival at 30 days, and incidence of rebleed at 30 days. The patients included 99 men and 81 women, with a median age of 74 (range 25–96) years.

Bleeding was considered upper or lower GI bleeding if its origin was located proximal or distal to the ligament of Treitz, respectively. All patients had clinical evidence of active GI bleeding, i.e., hematemesis, melaena, or hematochezia, with either: (1) transfusion requirements of at least 4 U during a 24-h period in hospital, or (2) evidence of a hemodynamic instability (systolic blood pressure <100 mmHg and tachycardia >100 beats/min). Refer to Fig. 1 for a summary of the management pathway.

CT Examination

CT examinations were performed with a 16- or 64-slice CT scanner (Lightspeed QX/I; GE Medical Systems, Milwaukee, WI) using a three-phase protocol: (1) a baseline 5-mm acquisition was performed from diaphragm to symphysis pubis without oral contrast preparation; (2) 100 ml of iodinated contrast medium (Niopam 370, Bracco UK Ltd, High Wycombe, UK) was administered by intravenous bolus injection via a 21-G cannula sited in the antecubital fossa, at 4 ml/s, using bolus-tracking software centered on the abdominal aorta at the level of the diaphragmatic hiatus (GE Healthcare, Milwaukee, WI). Helical acquisitions at 0.625 mm are reconstructed to 1.25 mm; and (3) a third series was acquired 90 s after the commencement of injection, giving a delayed (venous) phase of enhancement, with 5-mm acquisitions. A positive diagnosis of active bleeding was made if the extravasated contrast material measures more than 100 HU and if high density was seen within the lumen that was not present on the precontrast scan. If active bleeding was found, then the arterial phase images were reconstructed to identify the potential vessel responsible for the bleeding. The software used for these reconstructions is dependent on the CT machine; in our unit, a GE Advantage Workstation 4.4 (GE Medical Systems) was used. The arterial phase dataset was then reconstructed using the systems reformat algorithm.

Embolization Technique

At our institution, we perform selective catheterization of the mesenteric vessels with a selective 4/5-Fr catheter: SOS Omni catheter (Boston Scientific, France), Sidewinder catheter (Cordis, UK), or Cobra/Glide-Cobra catheter (Cook, Ireland). In some cases, particularly for patients with UGI bleed, we use the Progreat microcatheter (Terumo, Japan). Angiography is performed with selective 5- to 10-ml hand injections of the IMA, and 5- to 6-ml pump injections through the celiac and SMA, using Omnipaque 300 (GE Healthcare, Cork, Ireland). We routinely use Amplatzer plugs (St. Jude Medical, Plymouth, MN) for occluding larger vessels and the 0.035″ or 0.018″

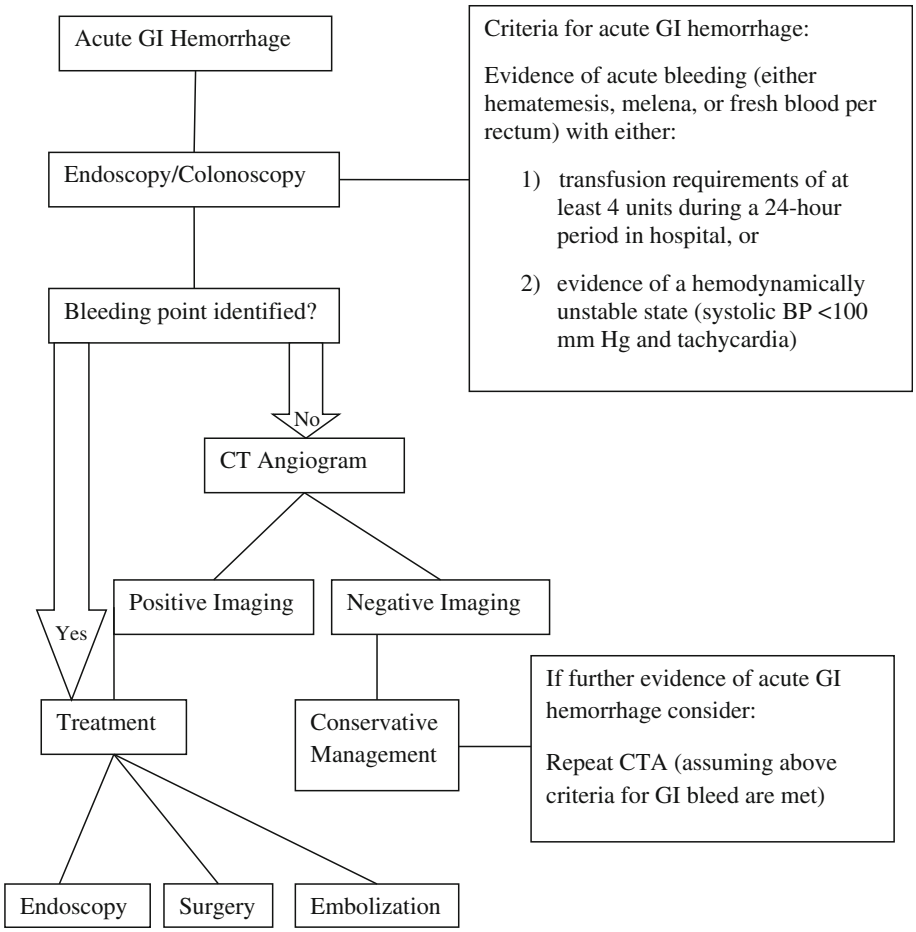

Fig. 1 Protocol for the management of patients presenting with acute GI hemorrhage at our institution

microcoils for more distal embolization (Nester and Tornado, Cook, UK; or Azur Hydrocoils, Terumo, Japan).

Data interpretation and Analysis

For both the UGI and LGI bleeding groups, the rates of rebleeding and subsequent intervention in CTA-negative patients were calculated. The χ^2 test was used to compare the observed rates between UGI bleeding patients and LGI bleeding patients. The relative risk for rebleeding following negative CTA of LGI vs UGI also was calculated. Statistical analysis was performed using SPSS 20 (SPSS, Chicago, IL).

Results

A total of 180 patients had 202 CTAs for acute GI bleeding during an 8-year period from January 2005 to December 2012. Of the 202 CTAs performed, 87 were for upper GI bleed and 115 for lower GI bleed. All patients had endoscopy before CTA, except for two patients who were deemed too unwell for an OGD. A summary of the results is shown in Fig. 2.

Patients in the Upper GI bleed Group

Of the 87 CTAs performed for upper GI bleed, 18 (20.7 %) were positive and 69 (79.3 %) were negative. The etiology of upper GI hemorrhage in this patient group include peptic ulcer disease (67 %), esophagitis or gastritis (14 %), gastric tumor (6 %), pancreatic tumor (6 %), dieulafoy lesion (4 %), Mallory–Weiss tear (2 %), and aorto-enteric fistula (1 %). A summary of the etiologies for upper GI bleed is shown in Table 1.

Initial Positive CTA (18/87)

In the group of 18 patients who had positive scans, 16 proceeded to have mesenteric angiography and embolization; all remained stable and did not rebleed. One patient also had a partial gastric resection, and one patient died shortly after the scan due to a massive UGI bleed.

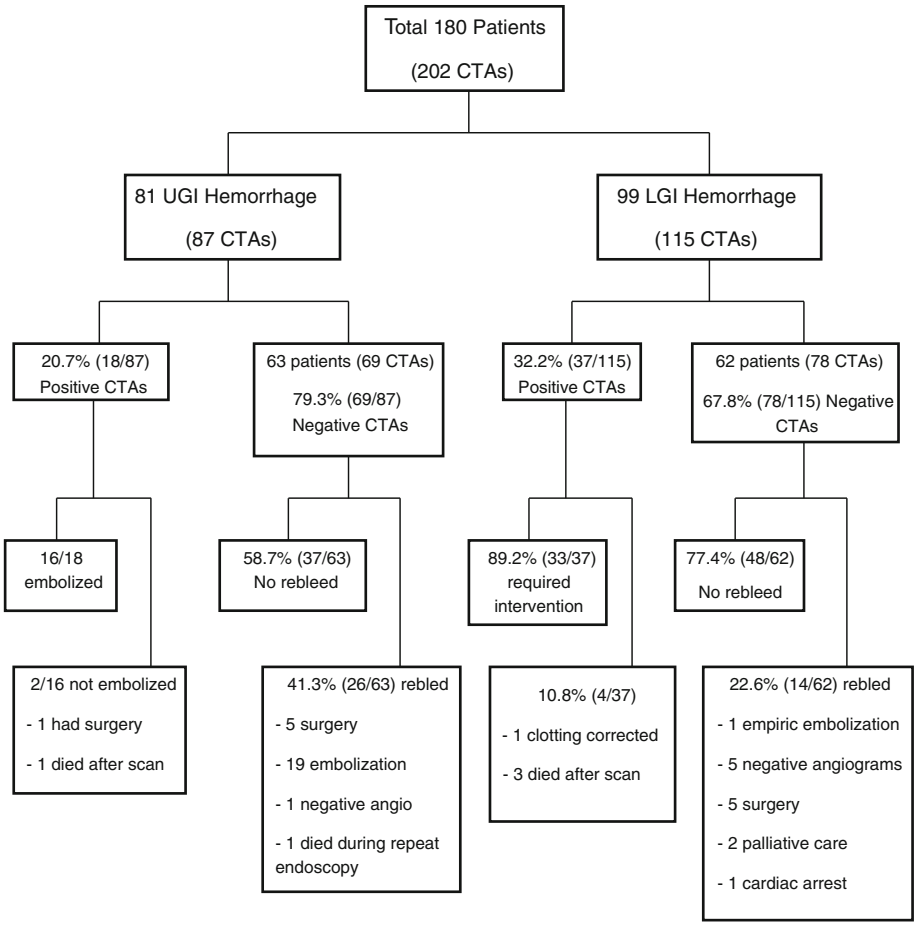

Fig. 2 Results summary

Table 1 Etiology of UGI hemorrhage ($n = 81$)

Etiology of UGI hemorrhage	Frequency %
Peptic ulcer disease	67
Esophagitis/gastritis	14
Esophageal/gastric tumor	6
Pancreatic tumor	6
Dieulafoy lesion	4
Mallory–Weiss tear	2
Aortoenteric fistula	1

Initial Negative CTA (69/87)

A total of 63 patients with upper GI bleed had 69 negative CTAs. Six patients had two scans each in this group, all of which rebled after a first negative CTA; four patients also had empiric gastroduodenal artery embolization and had no further bleeding episodes. Two patients did not have embolization and continued to bleed despite a second negative CTA; one required two laparotomies to stem hemorrhage, whilst one patient had a laparotomy and Billroth II operation.

Of patients who had a first negative CTA, 58.7 % (37/63) had no further bleeding episodes and remained stable, whereas 41.3 % (26/63) of patients who had negative CTAs rebled. Five of these went on to have surgical intervention, 1 had a repeat endoscopy but died during the procedure due to exsanguination from what was thought to be an aorto-enteric fistula, 20 patients had mesenteric angiography of which 10 had successful targeted embolizations, 9 had empiric gastroduodenal artery embolizations, and 1 patient with a negative angiogram All 20 patients did not rebleed.

Patients in the Lower GI Bleed Group

Ninety-nine patients with lower GI bleed had 115 CTAs, 37 of which were positive and 78 negative. The etiology of lower GI bleed in this patient group included diverticular disease (59 %), enterocolitis or inflammatory bowel disease (14 %), angiodysplasia (13 %), colonic polyp (8 %), colonic tumor (5 %), and vasculitis (1 %). A summary of the etiologies for lower GI bleed is shown in Table 2.

Initial Positive CTA (37/115)

In the group of patients who had positive CTAs, 89.2 % (33/37) had intervention to secure hemostasis: 17 were

Table 2 Etiology of LGI hemorrhage ($n = 99$)

Etiology of LGI hemorrhage	Frequency %
Diverticular disease	59
Enterocolitis/inflammatory bowel disease	14
Angiodysplasia	13
Colonic polyp	8
Colonic tumor	5
Vasculitis	1

embolized successfully; 3 had empiric embolizations; 3 patients had negative angiograms, of which 2 remained stable and 1 rebled 21 days later but had no rebleed after empiric embolization of the superior rectal artery and internal iliac artery; 2 had unsuccessful embolization procedures and proceeded to have hemicolectomies; 6 patients went straight to surgery; and 2 patients were treated endoscopically—colonic ulcers sutured and injected.

For the four patients who had positive CTA but no intervention, one patient who was on warfarin for atrial fibrillation stopped bleeding after clotting derangement was corrected, whilst three patients died soon after the CTA due to cardiac arrest.

Initial Negative CTA (78/115)

Sixty-two patients with lower GI bleed had 78 negative CTAs. Three patients had three CTAs each and ten patients had two CTAs each. Forty-eight of 62 patients (77.4 %) who had a first negative CTA had no further clinical or radiological evidence of bleeding and settled spontaneously on conservative management, hence avoiding endoscopic, radiological, or surgical intervention.

Fourteen of 62 patients (22.6 %) with negative CTA had further episodes of bleeding. Eleven patients had further intervention: one had an empiric distal rectal artery embolization, five had negative angiograms with no rebleed, one had a negative angiogram but continued to bleed hence was taken to theatre, four patients went straight to surgery (3 had colectomies and 1 had enterolysis and excision of Meckel's diverticulum). The decision was made for palliation due to terminal cancer in two patients with negative CTA but had recurrent bleeding, and one patient died of a cardiac arrest after a second positive CTA. This patient was on warfarin and had an INR of 5 on the day of the scan. Of the 14 patients with lower GI hemorrhage who rebled after an initial negative CTA, all had hemodynamic instability, 4 were on warfarin, and 2 had cancer-related bleeding, one patient with colonic lymphoma and the other had radiation proctitis postradiotherapy for metastatic prostate carcinoma).

Comparison Between UGI and LGI Bleed Patients with an Initial Negative CTA

Among patients with a first negative CTA, no rebleeding was observed in 37 of 63 patients (58.7 %) with UGI bleeding; in LGI patients this proportion was significantly higher, in 48 of 62 patients (77.4 %; $p = 0.04$). The relative risk (RR) for rebleeding after a negative CTA is significantly lower for LGI patients compared with UGI patients [RR = 0.55, 95 % confidence interval (CI) 0.32–0.95].

The proportion of patients with a first negative CTA who required surgery or embolization, including prophylactic embolization following rebleeding, also is significantly lower for LGI patients than for UGI patients (6/62 vs. 24/63 patients, $p = 0.0004$). The RR for requiring surgery or embolization following negative CTA in LGI patients compared with CTA-negative UGI patients is 0.25 (95 % CI 0.11–0.58).

Survival at 30 days

The overall 30-day mortality rate was 13.9 % (25/180 patients). Patients with lower GI hemorrhage had a slightly higher mortality rate at 14.8 % (12/81) compared with 13.1 % (13/99) in patients with upper GI hemorrhage. Of the 25 patients who were dead at 30 days, 7 died due to continuous/significant GI hemorrhage (6 were upper GI bleeds and 1 lower GI bleed; all patients had negative CTA scans except for 1 UGI bleed patient who had a positive scan, continued active hemorrhage, and died soon after the scan), 6 in which decision was made for palliation, and the remaining 12 patients had deaths attributed to other medical causes or comorbidities: 3 with myocardial infarction, 2 with cardiac failure, 4 with bronchopneumonia, 1 with metastatic renal cancer, 1 with metastatic prostate cancer, and 1 with ventriculitis/brain tumour.A summary of the overview of co-morbidities related to GI hemorrhage is shown in Table 3.

Discussion

Traditionally, radionuclide imaging and conventional catheter angiography with intra-arterial digital subtraction angiography (DSA) were used to detect the source of upper and lower GI bleeding when endoscopic measures have failed. However, anatomical localization with radionuclide imaging can be insensitive with variable accuracy rates whilst mesenteric angiography is invasive and requires highly skilled angiographers [2]. Currently, multislice detector CTA allows non-invasive and accurate assessment of the arterial tree, allowing for planning of therapeutic interventions, such as

Table 3 Overview of comorbidities related to GI hemorrhage

Comorbidity	Frequency (total number)
GI malignancy (esophageal, gastric, pancreatic, colonic, lymphoma)	18
Non-GI malignancy (renal, adrenal, prostate, non-Hodgkin's lymphoma, chronic myeloid leukemia, ventricular tumor)	14
Peptic ulcer disease	54
Inflammatory bowel disease	14
Diverticular disease	58
Cardiovascular disease (ischemic heart disease, hypertension, atrial fibrillation, congestive cardiac failure)	50
Chronic obstructive pulmonary disease/ bronchopneumonia	15

embolization or surgery. CTA therefore has become the first-line radiological imaging modality in the assessment of patients presenting with acute GI hemorrhage.

An increasing number of studies advocate the use of CTA in acute GI hemorrhage, because it is recognized as a useful diagnostic tool for fast and accurate detection and localization of acute GI hemorrhage. A study first published by Ettore et al. in 1997 found that helical CT angiography revealed the site of hemorrhage in 72 % (13/18) of patients and the diagnosis of bleeding site was confirmed at surgery in 11 of these 13 patients. Despite the small sample size, this study proved that helical CT angiography is an easier and faster technique than conventional angiography for localizing GI bleeding and is useful as a guide for subsequent selective angiography [4]. Subsequently, Yoon et al. [5] demonstrated an accuracy of 88.5 % (22/26) for the detection of acute GI bleeding using multidetector row CT. Wu et al. [3] and Anthony et al. [2] proposed that CT angiography should be used routinely for the investigation of patients who meet the criteria for acute GI hemorrhage due to its high accuracy and the ability to show the precise location and etiology of bleeding, thereby directing management.

Most published studies have demonstrated the accuracy and usefulness of CTA in the management of acute GI hemorrhage but not many have looked into the value of a negative CTA. Foley et al. [6] recommended CTA as a primary imaging modality in unstable patients with GI hemorrhage as a positive CTA can guide a patient's subsequent intervention, whereas patients with a negative CTA are more likely to settle spontaneously.

Our study focuses on the outcome of the group of patients with acute lower GI bleed who had a negative CT scan. Lower GI hemorrhage is a common presenting symptom, especially in elderly patients, due to the higher prevalence of colonic diverticulosis and vascular disease [7]. 22.6 % of patients in our study who had acute lower GI bleed with a negative CTA required further radiological or surgical intervention to stem hemorrhage. All patients in this group had hemodynamic instability—29 % were on warfarin and 14 % had cancer-related bleeding—all of which are factors associated with higher risk of rebleeding and these patients therefore would require more intense monitoring. For the other 77.4 %, this group of patients had no further episodes of bleeding after a first negative CTA and only supportive measures were required. We therefore conclude that a negative CTA is a good prognostic indicator and may obviate the need for angiographic examination, hence reducing the rate of negative angiographies. Supportive management and adopting a "wait-and-see" strategy with the possibility of repeating the CTA in cases of rebleeding is recommended for this group of patients. In comparison, the proportion of patients with upper GI hemorrhage who rebled after an initial negative CTA was higher at 41.3 %. This group of patients also is more likely to require further intervention to stem hemorrhage. A study by Dixon et al. [8] showed that in upper GI hemorrhage cases refractory to endoscopic treatment, empiric embolization may be attempted.

Our study also reviewed the overall 30-day mortality rate, which was 13.9 % in this cohort of patients (14.8 % in lower GI bleed and 13.1 % in upper GI bleed). This is comparable to the results from a large systematic review by Straube et al. [9] and a study by Holster and Kuipers [10]; the mortality rates for patients with upper GI bleed were estimated at 12 and 6–13 % respectively. A study by Anthony et al. [11] documented a 30-day mortality rate of 18 % in patients with acute lower GI bleed. These patients often have many other comorbid conditions, and similar to Anthony et al., our study found that only approximately one third of patients die as a direct consequence of GI hemorrhage. Forty-eight percent of patients had deaths attributed to other medical causes or comorbidities, such as myocardial infarction, cardiac failure, bronchopneumonia, and ventriculitis, whereas 24 % of patients died of preexisting metastatic cancer. Although there was no clear association of a certain comorbidity with the risk of rebleeding or increased mortality, patients with multiple comorbidities tend to fare worse, are less likely to survive a massive GI hemorrhage or rebleed, and most patients with terminal cancer were deemed more suitable for palliation versus active treatment to stem hemorrhage.

Conclusions

Computed tomography angiography (CTA) should be the standard of care for assessment of patients presenting with acute lower GI bleed and in patients following failed

endoscopic treatment for upper GI hemorrhage where the bleeding site remains obscure. A negative CTA is a good indicator that patients presenting with lower GI hemorrhage with a negative first CTA are much more likely to settle spontaneously without the need for intervention compared with patients with upper GI hemorrhage.

Conflict of interest Victoria Chan, Donald Tse, Shaheen Dixon, Vivek Shrivastava, Mark Bratby, Suzie Anthony, Rafiuddin Patel, Charles Tapping, and Raman Uberoi declare that they have no conflict of interest.

References

1. Acute upper gastrointestinal bleeding, NICE Clinical Guidelines (CG141), Issued June 2012
2. Anthony S, Milburn S, Uberoi R (2007) Multi-detector CT: review of its use in acute GI haemorrhage. Clin Radiol 62:938–949
3. Wu LM, Xu JR, Yin Y, Qu XH (2010) Usefulness of CT angiography in diagnosing acute gastrointestinal bleeding: a meta-analysis. World J Gastroenterol 16(31):3957–3963
4. Ettore GC, Francioso G, Garribba AP, Fracella MR, Greco A, Farchi G (1997) Helical CT angiography in gastrointestinal bleeding of obscure origin. Am J Roentgenol 168(3):727–731
5. Yoon W, Jeong YY, Shin SS, Lim HS (2006) Acute massive gastrointestinal bleeding: detection and localization with arterial phase multi-detector row helical CT. Radiology 239(1):160–167
6. Foley PT, Ganeshan A, Anthony S, Uberoi R (2010) Multi-detector CT angiography for lower GI bleeding: can it select patients for endovascular intervention? J Med Imaging Radiat Oncol 54(1):9–16
7. Martí M, Artigas JM, Garzón G, Álvarez-Sala R, Soto JA (2012) Acute lower intestinal bleeding: feasibility and diagnostic performance of CT angiography. Radiology 262(1):109–116
8. Dixon S, Chan V, Shrivastava V, Anthony S, Uberoi R, Bratby M (2013) Is there a role for empiric gastroduodenal artery embolization in the management of patients with active upper GI hemorrhage? Cardiovasc Interv Radiol 36(4):970–977
9. Straube S, Tramèr MR, Moore RA, Derry S, McQuay HJ (2009) Mortality with upper gastrointestinal bleeding and perforation: effects of time and NSAID use. BMC Gastroenterol 9:41
10. Holster IL, Kuipers EJ (2012) Management of acute non-variceal upper gastrointestinal bleeding: current policies and future perspectives. World J Gastroenterol 18(11):1202–1207
11. Anthony T, Penta P, Todd RD, Sarosi GA, Nwariaku F, Rege RV (2004) Rebleeding and survival after acute lower gastrointestinal bleeding. Am J Surg 188(5):485–490