

CT Angiography For Overt Lower Gastrointestinal Bleeding: Is Time The Missing Link

Deepanshu Jain, Sujani Yadlapati, Ankit Chhoda, Akanksha Agrawal, Roshni Patel, Christopher Hibbard, Sameer Siddique

Deepanshu Jain, Christopher Hibbard, Sameer Siddique, Division of Gastroenterology, Department of Digestive Diseases and Transplantation, Einstein Healthcare Network, Philadelphia, PA, the United States

Sujani Yadlapati, Akanksha Agrawal, Roshni Patel, Department of Internal Medicine, Einstein Healthcare Network, Philadelphia, PA, the United States

Ankit Chhoda, Department of Internal Medicine, Yale-Waterbury Internal Medicine Program, Yale school of medicine, Waterbury, Connecticut, the United States

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Correspondence to: Deepanshu Jain, MD, Division of Gastroenterology, Department of Digestive Diseases and Transplantation, Einstein Healthcare Network, 5401 Old York Road, Philadelphia, PA 19141, the United States.

Email: deepanshu.jain.25@gmail.com

Telephone: +1-215-456-8210

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ABSTRACT

BACKGROUND: CT angiography (CTA) and interventional radiology angiogram (IRA) are used in work-up of acute lower

gastrointestinal bleed (LGIB).

METHOD: Retrospective study of patients with active LGIB who underwent CTA. Divided into CTA (+) and CTA (-) groups. CTA (+) was divided into IRA (+) or IRA (-).

RESULTS: 24.1% (49/203) had CTA(+) and 75.9% (154/203) had CTA (-). No statistical significant difference was noted for hemodynamic parameters, anti-platelets and anti-coagulants, thrombocytopenia, elevated INR or blood transfusion across CTA (+) and CTA (-) groups. Median decision to test (DTT) time for CTA (+) was 98 compared to 124.5 min for CTA(-) ($p = 0.039$). Univariate analysis revealed DTT time as the only factor with statistically significant effect on CTA outcome. LR ($p < 0.001$) and Phi coefficient ($p < 0.001$) suggested significant difference in distribution and association between number of positive risk factors and CTA (+) respectively. In CTA (+), 81.6% (40/49) had a follow-up IRA with 32.5% (13/40) being IRA (+) while 67.5% (27/40) were IRA (-). Overall, 6.4% (13/203) patients had positive IRA. Majority of CTA were ordered by ER- 39.9% (81/203) and IM- 42.9% (87/203). For emergency department (ER)- 23.5% had CTA (+) and 3.7% had IRA (+) compared to Internal Medicine(IM) category- 25.3% had CTA (+) ($p = 0.78$) and 5.7% had IRA(+ ($p = 0.53$)). 57.9% patients in CTA (+) had a follow-up IRA in ER category in contrast to 95.5% in IM ($p = 0.0038$).

CONCLUSION: One in sixteen patient benefits from CTA. IM did better than ER in selecting patients for CTA. Number of positive risk factors correlates with probability of CTA (+). Decreasing DTT time may be the key to improve diagnostic yield.

Key words: Lower gastrointestinal bleeding; Computed tomography angiography; Interventional radiology angiogram

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INTRODUCTION

Acute gastrointestinal bleeding (GIB) is a commonly encountered medical entity. It results in approximately 30,000 hospitalizations annually, accounting for 1 to 2% of all hospital admissions^[1,2]. In addition, GIB frequently complicates the clinical course of critically ill patients who have been admitted to hospital for alternative primary diagnoses^[2]. With advancement in technology, the tools available for the diagnosis and management of GIB have expanded. Despite this, the mortality rate, which ranges from 8 to 14% for these patients, has not changed^[3,4]. The evaluation and management of GIB often involves a multi-specialty approach involving gastroenterologists, radiologists, surgeons, and internists^[5].

Multiple modalities like radionuclide imaging, colonoscopy, endoscopy, catheter directed angiography, and CT angiography are available to manage patients with acute lower GI bleeding^[6]. Among these, multi-detector CT angiography (CTA) has emerged as a promising first line test due to its easy availability and high sensitivity for diagnosis and exclusion of active GIB^[7-8]. Based on recently published literature, the overall sensitivity and specificity of CTA for detecting GI bleeding was 85.2% and 92.1% respectively^[9,10]. CTA helps in localizing the site of bleeding and hence can help guide further therapeutic management as indicated including angiographic embolization, colonoscopy, surgery or conservative, expectant management. Due to poor efficacy of colonoscopy-directed hemostatic therapy in setting of active bleeding and high morbidity associated with surgery, angiographic embolization (with coil or glue) becomes the preferred treatment for patients with a positive CTA study. However, inappropriate use of CTA may expose the patient to unnecessary radiation, contrast-related renal injury, or allergic reactions, and can also squander available health resources.

In this study, we aim to evaluate the usefulness of CT angiography in management of lower gastrointestinal bleeding.

MATERIALS AND METHODS

Study Location

The study was conducted at Einstein Medical Center, Philadelphia, USA, a 772 bedded tertiary care hospital.

Study duration

The study involved patients admitted to hospital over a span of 5 years (Jan, 2010 to Jan, 2016)

Inclusion Criteria: (1) Age \geq 18 years; (2) Inpatient hospitalization; (3) Patients who had CTA for presumed lower GIB.

Exclusion Criteria: (1) Patients transferred to other hospitals within 24 hours post CTA; (2) Patients with chronic kidney disease who were not dialysis dependent.

Data Collection

Medical charts of all patients who satisfied the inclusion and exclusion criteria were retrospectively reviewed for data collection to confirm indication for CTA (hematochezia), results of CTA (positive or negative), results of subsequent catheter directed angiogram, if performed (done by interventional radiologist, positive or negative). Data regarding the department of the physician ordering the CTA was also noted. Data for seven factors felt to influence the severity and acuity of blood loss and potentially the CTA outcome were also collected. These variables were collected at the time closest to the first diagnosis of hematochezia- hypotension (defined by SBP < 90 mm Hg or DBP < 60 mm Hg), tachycardia (heart rate > 100 beats

per minute), exposure to anti-platelet medications (aspirin, clopidogrel, ticagrelor) or anticoagulants (warfarin, rivaroxaban, apixaban, dabigatran), INR > 1.5, thrombocytopenia (platelet count < 150,000/mm³) and blood transfusion requirements. In addition, we also calculated the interval between the time when decision to get a CTA was made (when the order was placed in the electronic system) and the time when it actually happened (completion of study) for each patient in CTA (+) and CTA (-) groups. We have referred to this interval as decision to test time (DTT) for the rest of the manuscript.

Methodology

All patients received standard medical care with close monitoring of vital signs, blood tests (complete blood count, basic metabolic panel, coagulation parameters) and intravenous fluid resuscitation. Blood transfusion was considered if hemoglobin was noted to be less than 7 gm/dl (for patients without any known history of coronary artery disease) or 8 gm/dl (for patients with history of coronary artery disease). The study cohort was divided into two groups based on presence [CTA (+)] or absence [CTA (-)] of active bleed on CTA. Individual data for vital signs (BP and HR), medications (anti-platelets and anticoagulants), labs (platelet count, INR), blood transfusion requirement and DTT was collected for each patient across CTA (+) and CTA (-) groups. Interventional radiology angiogram (IRA) was followed for subjects with CTA (+). Based on the presence [IRA (+)] or absence [IRA (-)] of active bleeding on IRA, the CTA (+) group was further divided into two sub groups. The same has been represented in the Figure 1. We also categorized the results separately for each department who ordered the initial CTA: Emergency (ER), Internal Medicine (IM), and Surgery (Sr).

Statistical analysis

Descriptive data was presented with numbers and percentages for categorical and continuous variables (Table 1). Chi-square test (for categorical variables), unpaired t-test with Welch's correction (for mean DTT) and Mann-Whitney U test (for median DTT) was used to calculate p- value for determining statistical significance (Table 1). Uni-variate analysis was performed for all eight clinical, laboratory and systemic factors, which revealed only one statistical significant variable (Table 2) and hence obviating the need of multi-variate analysis. P value < 0.05 was used as a cut off to determine statistical significance. We also performed receiver operator curve (ROC) analysis to determine a cut off DTT associated with CTA (+) outcome (Figure 2). In last, we grouped patients with CTA (+) and CTA (-) outcome based on number of positive risk factors (seven clinical and laboratory variables, table 3 and calculate likelihood ratio (LR) to determine statistically significant distribution followed by Phi coefficient calculation to determine the effect-size association. SPSS 25 software was used for statistical analysis.

RESULTS

Over a time span of 5 years at our tertiary medical center, 203 adult patients underwent CTA for the evaluation of acute active lower gastrointestinal bleeding. 24.1% (49/203) had positive CTA and 75.9% (154/203) had negative CTA. For 202 patients (one patient excluded due to lack of data), no statistically significant difference was noted for hypotension, tachycardia, use of anti-platelets or anti-coagulants, thrombocytopenia, elevated INR or blood transfusion need across the CTA (+) and CTA (-) groups (Table 1). For 200 patients (three patients excluded due to lack of data), mean DTT time for CTA (+) group was 135 min (range, 34- 627 min) compared to 204 min for

CTA negative group (range, 11- 1293 min) ($p = 0.006$). Median DTT time for CTA (+) group was 98 min compared to 124.5 min for CTA (-) group ($p = 0.039$). Univariate analysis revealed DTT time as the only factor to have statistically significant effect on CTA outcome. Area under the curve for ROC analysis performed for DTT time was 0.594, thus limiting are ability to accurately predict a DTT time cut off associated with CTA (+) outcome. Table 3 depicts the proportion of patients with number of risk factors across CTA (+) and CTA (-) groups. Based on LR calculation (cells with absolute value of less than 5 were excluded), there was statistically significant difference in distribution of patients with different number of risk factors across CTA (+) and CTA (-) groups (value- 32.907 with p value < 0.001). The Phi coefficient value was 0.36 with a p value of < 0.001 suggesting statistically significant association between number of positive risk factors and probability of CTA (+) outcome. In CTA (+) group, 81.6% (40/49) had a follow up IRA. 32.5% (13/40) had a positive IRA and 67.5% (27/40) had a negative IRA. Overall, only 6.4% (13/203) patients had a positive IRA which required IR based therapeutic intervention (embolization) to stop ongoing bleeding. Majority of CTA were ordered by ER- 39.9% (81/203) and IM-

42.9% (87/203). Only 1.9% (4/203) were ordered by Sr and the rest (15.3% or 31/203) was ordered by a group of miscellaneous physicians. Within the ER category, 23.5% had CTA (+) and 3.7% had IRA (+) compared to the IM category where 25.3% had CTA (+) ($p = 0.78$) and 5.7% had IRA (+) ($p = 0.53$). 57.9% of patients in CTA (+) had a follow up IRA in the ER category in contrast to 95.5% in the IM category ($p = 0.0038$).

Table 1 Clinical variables for patients across CTA (+) and CTA (-) groups.

| S.No | Variable | CTA (+) | CTA (-) | P value |
|------|-----------------------------|-------------------|-------------------|---------|
| 1 | Decision to test time (min) | Mean: 135 + 116.2 | Mean: 204 + 224.1 | 0.006 |
| | | Range: 34-627 | Range: 11- 1293 | |
| | | Median: 98.0 | Median: 124.5 | 0.039 |
| 2 | Hypotension (+) | 17/49 (34.7%) | 43/153 (28.1%) | 0.379 |
| | Hypotension (-) | 32/49 | 110/153 | |
| 3 | Tachycardia (+) | 7/49 (14.3%) | 40/153 (26.1%) | 0.087 |
| | Tachycardia (-) | 42/49 | 113/153 | |
| 4 | Anti-platelets (+) | 24/49 (49.0%) | 76/153 (49.7%) | 0.932 |
| | Anti-platelets (-) | 25/49 | 77/153 | |
| 5 | Anti-coagulants (+) | 13/49 (26.5%) | 22/153 (14.1%) | 0.051 |
| | Anti-coagulants (-) | 36/49 | 131/153 | |
| 6 | INR > 1.5 (+) | 13/49 (26.5%) | 31/150 (20.7%) | 0.391 |
| | INR > 1.5 (-) | 36/49 | 119/150 | |
| 7 | Thrombocytopenia (+) | 12/49 (24.5%) | 40/151 (26.5%) | 0.782 |
| | Thrombocytopenia (-) | 37/49 | 111/151 | |
| 8 | Blood transfusion (+) | 6/49 (12.2%) | 19/153 (12.4%) | 0.974 |
| | Blood transfusion (-) | 43/49 | 134/153 | |

Table 2 Univariate analysis outcome.

| S. No | Variable | P-value | OR | 95% CI |
|-------|-----------------------|---------|-------|-------------|
| 1 | Decision to test time | 0.044 | 1.003 | 1.000-1.005 |
| 2 | Hypotension | 0.505 | 1.267 | 0.632-2.543 |
| 3 | Tachycardia | 0.117 | 0.495 | 0.205-1.193 |
| 4 | Anti-platelets | 0.964 | 1.015 | 0.534-1.931 |
| 5 | Anti-coagulants | 0.052 | 0.462 | 0.212-1.005 |
| 6 | INR > 1.5 | 0.999 | 0 | NA |
| 7 | Thrombocytopenia | 0.605 | 0.818 | 0.381-1.756 |
| 8 | Blood transfusion | 0.986 | 1.009 | 0.379-2.687 |

Table 3 Proportion of patients with number of risk factors in CTA (+) and (-) groups.

| Outcome | Number of Risk Factors | | | | | | | |
|------------------|------------------------|------------|------------|------------|-----------|----------|-----|-----|
| | 0/7 | 1/7 | 2/7 | 3/7 | 4/7 | 5/7 | 6/7 | 7/7 |
| N = 195 | | | | | | | | |
| CTA (+) (N = 48) | 7 (14.6%) | 14 (29.2%) | 12 (25.0%) | 11 (23.0%) | 2 (4.7%) | 2 (4.7%) | 0 | 0 |
| CTA (-) (N =147) | 25 (17.0%) | 45 (30.6%) | 35 (23.9%) | 28 (19.1%) | 11 (7.5%) | 3 (2.0%) | 0 | 0 |

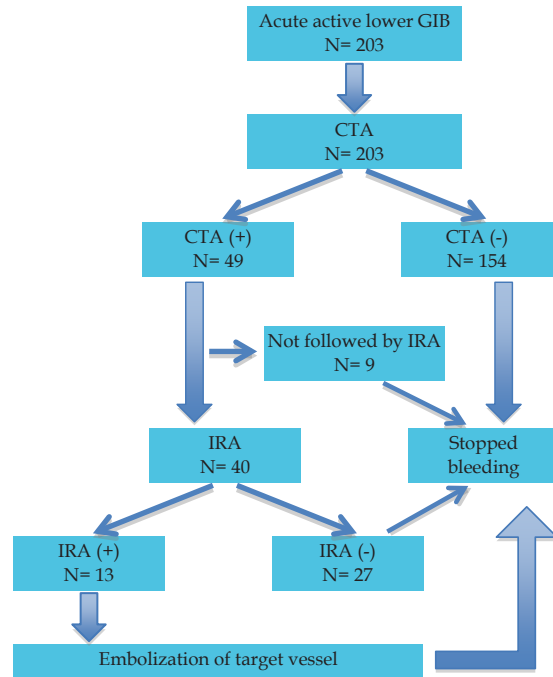


Figure 1 Study flowchart.

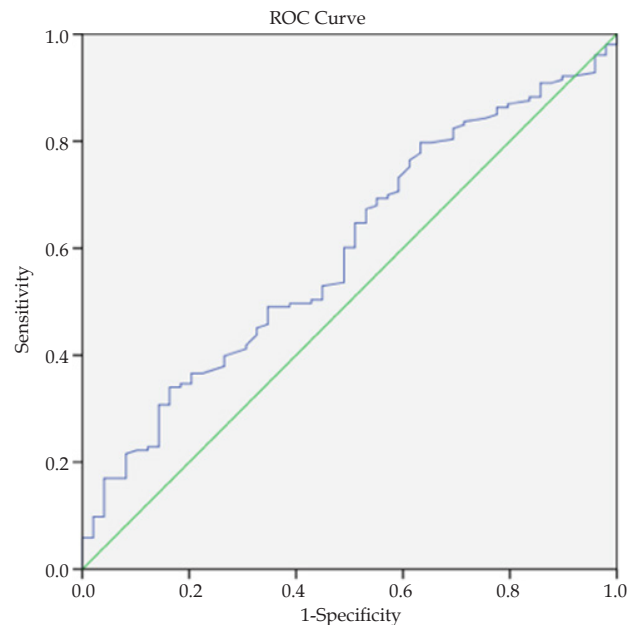


Figure 2 ROC for DTT time and CTA outcome.

DISCUSSION

Annual incidence of hospitalization is approximately 36/100,000 population for acute lower GIB^[11]. Acute lower GI bleeding is defined as blood loss that originated from the GI tract distal to the ligament of Treitz. The majority of patients present with either maroon colored stools or bright red blood or blood clots per rectum. Rarely, lower GIB can present as melena, and brisk upper GIB can present as bright red blood per rectum. Initial management of patients with active lower GIB remains supportive with aggressive resuscitation with intravenous fluids and blood transfusion as clinically indicated. Continued bleeding or brisk bleeding with hemodynamic instability warrants further work up with CTA or radionuclide imaging (Technetium-99m red blood cell scan) to determine the location of bleeding for subsequent catheter angiogram-based attempts at hemostasis. Tc-99m RBC scan, CTA, and catheter angiogram can pick up arterial or venous bleeds at rates of blood loss as slow as 0.2 ml/min, 0.3 ml/min and 0.5 ml/min respectively^[12].

In our study, we retrospectively studied patients (N=202) who received CTA for presumed active lower GIB. On an average, every fourth patient (24.1%) had a positive result from CTA while only every sixteenth patient had a positive IRA and consequent angiographic hemostasis performed. The majority of CTA studies were initiated by physicians in IM (42.9%) or the ER (39.9%). The proportion of patients with positive CTA were similar for these two groups of physicians (25.3% for IM and 23.5% for ER; $p = 0.78$) suggesting that there was no difference in the clinical decision making among physicians regarding the need of CTA. The majority of the patients had a negative CTA (75.9%), which could be attributed to one of the following reasons: (1) the initial presumptive diagnosis of active lower GIB was inaccurate (unlikely) or (2) the test failed to detect the active GIB because the rate of bleeding was lower than the minimal cut off for the test (< 0.3 mL/minute) or (3) the bleeding had stopped by the time patient got the scheduled CTA study. Many patients may have bleeding that is intermittent in nature. To detect a bleeding lesion, the diagnostic test has to be performed when it is clinically active and it is of utmost importance that the diagnostic tests are done in a time sensitive manner. Other than DTT time, no statistically significant difference was noted for any of the clinical or laboratory parameter across CTA (+) and CTA (-) group. The mean and median DTT time for CTA (+) group was significantly lower when compared to CTA (-) group. This brings us to an essential question- do we need time sensitive protocols for GIB like for other entities like acute cerebrovascular accident (CVA) or acute coronary syndrome (ACS). We did try to determine a cut off value for DTT time interval to aim for in real world clinical setting, but our ROC analysis was underpowered for such calculation.

In an ideal scenario, every patient with a positive CTA should be followed by a therapeutic IRA. In our study, majority of the patients with active bleed on CTA had IRA (81.6%). Patients who did not have a follow up IRA (after a positive CTA) either had stopped bleeding by the time they were scheduled for IRA, were too hemodynamically unstable to undergo it, or had expired. We did find a statistically significant difference ($p = 0.0038$) in the proportion of patients who underwent IRA after a positive CTA across IM (95.5%) and ER (57.95) groups. This observed trend may be suggestive of better patient selection by IM physicians when compared to ER physicians in deciding the appropriateness of the need of CTA. Of the patients who did undergo IRA, only a third of the patients (32.5%) had a positive study and underwent therapeutic embolization. The remaining 67.5% had spontaneously stopped bleeding by the time of the IRA to allow

detection and therapy.

To date, there is no single objective (clinical or laboratory) parameter, which reliably distinguishes between patients with active bleeding versus non-active other than visual proof of blood per rectum. Similarly, in our study, we failed to find any statistically significant difference for any of the potential clinical variables (vital signs, blood thinners, coagulopathy or transfusion requirements) associated with bleeding or which potentially could worsen the severity or duration of bleeding across the CTA (+) and CTA (-) groups. We did find a statistically significant association between number of positive risk factors and the probability of positive CTA outcome. Approximately one in every sixteen patients (6.4%) undergoing CTA for presumed active lower GIB underwent definitive treatment by IR embolization. This number was higher when IM physicians ordered the test (5.7%) than the ER physician group (3.7%), but the results did not reach statistical significance. The results from our study do question the real world utility of CTA.

As physicians, we need to better risk-stratify patients to identify those who will benefit from CTA and those who will just do fine with conservative management. Involving gastroenterologists early may streamline decision making to improve the diagnostic yield of CTA and IRA and possibly divert a select percentage of patients to undergo urgent colonoscopy after rapid bowel preparation as well as select patients in whom supportive care and observation alone may be appropriate.

Limitations of our study include- retrospective design, small sample size and inability to appraise the decision making process of physicians taking care of these patients.

CONCLUSION AND FUTURE DIRECTIONS

The findings in our study are unique and are representative of real world outcomes from a community tertiary hospital. Only, one in sixteen patient benefits from CTA in work up of presumed overt lower gastrointestinal bleeding. The probability of a positive CTA increases with number of positive risk factors. Shorter time interval between the decision (to obtain a CTA) and actual study was the only statistically significant parameter across patients with positive versus negative CTA. GIB has long been known to be predominantly intermittent in nature and thus, time sensitive protocols for lower GIB work up (like for CVA and ACS) may help improve patient outcomes, balance side effects and decrease overall healthcare cost. Future prospective studies should be directed at time sensitive CTA protocols for patients with lower GI bleeding and for determining which patients would benefit from this approach and compare these results to historical control cohort to validate these findings.

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