Accuracy of $^{99m}$Technetium-labeled RBC Scintigraphy and MDCT With Gastrointestinal Bleed Protocol for Detection and Localization of Source of Acute Lower Gastrointestinal Bleeding

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Background: Acute lower gastrointestinal bleeding (LGIB) is a major cause of morbidity and mortality. Multidetector row computed tomography (CT) with gastrointestinal (GI) bleed protocol is a novel diagnostic technique for detecting and localizing LGIB. Being rapid and noninvasive, it may be useful as a first-line modality to investigate cases of acute LGIB.

Goals: To assess and compare diagnostic accuracy of $^{99m}$Technetium (Tc)-labeled red blood cell (RBC) scintigraphy and multidetector row CT with GI bleed protocol for detection and localization of source of acute LGIB.

Study: Requirement of informed consent was waived for this retrospective study. Seventy-six patients had undergone either RBC scintigraphy, CT with GI bleed protocol, or both, followed by conventional angiography for evaluation of acute persistent LGIB between January 2010 and February 2014 at our institution. Accuracy of both modalities was assessed using conventional angiography as reference standard and compared using the 2-tailed, Fisher exact test. A $P$-value of <0.05 was considered statistically significant.

Results: Fifty-one, 20, and 5 patients had undergone RBC scintigraphy only, CT with GI bleed protocol only, and both modalities, respectively. Fourteen of 25 patients in the CT group had angiographic evidence of active bleeding as compared with 32 of 56 patients in the scintigraphy group. CT with GI bleed protocol had higher accuracy (96%) than $^{99m}$Tc-labeled RBC scintigraphy (55.4%, $P < 0.001$).

Conclusions: CT with GI bleed protocol was more accurate in detecting and localizing the source of acute LGIB as compared with $^{99m}$Tc-labeled RBC scintigraphy.

Key Words: diagnosis, gastrointestinal hemorrhage, multidetector computed tomography, radionuclide imaging, digital subtraction angiography

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protocol for detection and localization of the source of acute LGIB.

**MATERIALS AND METHODS**

This study was exempted from ethical approval by the institutional Ethics Review Committee, and requirement for informed consent was waived for this retrospective analysis.

**Study Participants**

LGIB was defined as GI bleeding distal to the ligament of Treitz. Patients presenting to the emergency department with hematochezia, and who had a negative nasogastric tube lavage, were presumed to have LGIB. Acute LGIB was defined as hematochezia with a negative nasogastric tube lavage that started <48 hours before presentation at the emergency department. For the purpose of this study, we only included patients with persistent LGIB i.e. on-going melena or hematochezia, which was not self-limiting. Patients who did not have hematochezia or melena for ≥24 hours were not considered to have persistent LGIB. Conversely, patients with unstable hemodynamics (tachycardia and hypotension) or those requiring transfusion of packed RBCs to maintain hemodynamics were considered to have persistent LGIB.

At our institution, patients with acute persistent LGIB are investigated either by endoscopy (when the rate of bleeding is slow) or radiologic imaging (either CT with GI bleed protocol or RBC scintigraphy). All patients with acute persistent LGIB, who do not undergo endoscopy, are evaluated with conventional angiography, irrespective of the results of preliminary radiologic imaging. Depending on the results of conventional angiography, angioembolization may be performed during the same setting. In rare cases, patients may undergo laparotomy, instead of, or in addition to, conventional angiography.

For the purpose of this study, patients presenting to our institution with acute persistent LGIB between January 2010 and February 2014, who underwent radiologic evaluation, were eligible for inclusion. Exclusion criteria included any contraindication to performance of conventional angiography, irrespective of the results of preliminary radiologic imaging. Depending on the results of conventional angiography, angioembolization may be performed during the same setting. In rare cases, patients may undergo laparotomy, instead of, or in addition to, conventional angiography.

For the purpose of this study, patients presenting to our institution with acute persistent LGIB between January 2010 and February 2014, who underwent radiologic evaluation, were eligible for inclusion. Exclusion criteria included any contraindication to performance of conventional angiography, irrespective of the results of preliminary radiologic imaging. Data for all patients were extracted using the institutional Radiology Information System. Etiology of LGIB was calculated to be 35.4 mSv (ie, unenhanced, tube voltage of 120 kV, and tube current of 400 mA. At 0.8 second per rotation, reconstruction interval of 2 mm, table speed of 1.5 cm per rotation, gantry rotation speed of 60 and 180 seconds after contrast administration, respectively. This was different from previously used protocols in the literature, which typically obtain delayed phase images at 300 seconds after contrast administration. A volume of 100 mL of nonionic contrast medium (ioxehol, Omnipaque 350; Nycomed-Amersham, Princeton, NJ) was injected at a rate of 3 to 6 mL/s using an automated injector by peripheral intravenous cannulae of at least 18 gauge bore. Scan delay was automatically determined by bolus-triggering software (SmartPrep; GE Healthcare, Milwaukee, WI) using a circular region of interest placed within the abdominal aorta and a trigger threshold of 100 HV for starting image acquisition. All scans covered an area starting from xiphisternum up to pubic symphysis. Scans were performed with a slice thickness of 3 mm, pitch of 1.5, table speed of 1.5 cm per rotation, gantry rotation speed of 0.8 second per rotation, reconstruction interval of 2 mm, tube voltage of 120 kV, and tube current of 400 mA. At these settings, the median effective radiation dose for our patients was calculated to be 35.4 mSv (ie, unenhanced, arterial, porto-venous, and delayed phases combined).

A single consultant radiologist having >10 years of experience in CT body imaging reviewed the films of MDCT examination (Z.H.). MDCT scan was considered positive when the unenhanced scan did not show any hyperdense material within the bowel lumen, whereas subsequent phases revealed hyperdense material within the lumen. If there was hyperdense material within bowel loops on unenhanced scan, which increased in amount on subsequent scanning, this also constituted a positive scan. At

**Reference Standard**

Conventional arteriography was considered as the reference standard for diagnosis of LGIB as previously established in the literature. Digital subtraction angiography (DSA) was performed in all patients using Angiostar (Siemens Medical Systems, Erlangen, Germany). All procedures were performed by consultant interventional radiologists having at least 5 years of experience in catheter-based angiography. Vascular access was established using the femoral artery in all patients. Selective cannulation of celiac, superior mesenteric, and inferior mesenteric arteries was performed serially. The average fluoroscopy time for patients included in this study was 32 minutes. On the basis of previously published literature, the effective radiation dose was likely in the range of 18 to 22 mSv. Angiography scans were reviewed by a single interventional radiologist having >5 years of experience in interventional radiology (T.U.H.). All studies were reviewed for the presence of active extravasation of contrast material in the distribution of these arteries. The presence or absence of LGIB and the site of GI bleeding was recorded for each study. At the time of interpretation of conventional angiography, the consultant radiologist was blinded to the results of CT with GI bleed protocol and 99mTc-labeled RBC scintigraphy.

**99mTc-labeled RBC Scintigraphy**

99mTc-labeled RBC scintigraphy was performed according to standard departmental protocol (Supplemental Methods, Supplemental Digital Content 1, http://links.lww.com/JCG/A211). At a typical dose of 700 MBq, the effective radiation dose for RBC scintigraphy scans was estimated to be 7.8 mSv. These scans were then reviewed by a single consultant radiologist having >10 years of experience in nuclear medicine reporting (M.U.Z.). The presence or absence of LGIB and the site of LGIB (if present) was noted for each scan. At the time of interpretation of scintigraphy scans, the consultant radiologist was blinded to the results of conventional angiography.

**MDCT With “GI Bleed Protocol”**

MDCT was performed using either a 64-row (Aquilion 64, Toshiba, Japan) or 320-row (Aquilion ONE, Toshiba) detector CT scanner with a “GI Bleed protocol” that was slightly different from protocols reported previously in the literature. The “GI Bleed protocol” included an unenhanced CT scan followed by an arterial phase imaging, starting approximately 15 seconds after the administration of the intravenous contrast medium. Portovenous and delayed phase imaging was then performed sequentially at 60 and 180 seconds after contrast administration, respectively. This was different from previously used protocols in the literature, which typically obtain delayed phase images at 300 seconds after contrast administration. A volume of 100 mL of nonionic contrast medium (ioxehol, Omnipaque 350; Nycomed-Amersham, Princeton, NJ) was injected at a rate of 3 to 6 mL/s using an automated injector by peripheral intravenous cannulae of at least 18 gauge bore. Scan delay was automatically determined by bolus-triggering software (SmartPrep; GE Healthcare, Milwaukee, WI) using a circular region of interest placed within the abdominal aorta and a trigger threshold of 100 HV for starting image acquisition. All scans covered an area starting from xiphisternum up to pubic symphysis. Scans were performed with a slice thickness of 3 mm, pitch of 1.5, table speed of 1.5 cm per rotation, gantry rotation speed of 0.8 second per rotation, reconstruction interval of 2 mm, tube voltage of 120 kV, and tube current of 400 mA. At these settings, the median effective radiation dose for our patients was calculated to be 35.4 mSv (ie, unenhanced, arterial, porto-venous, and delayed phases combined).

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the time of interpretation of MDCT scans, the consultant radiologist was blinded to the results of conventional angiography.

**Statistical Methods**

Statistical analysis was performed on Statistical Analysis Software (SAS) version 9.1.3 and GraphPad InStat version 3.0. A true positive was defined as the presence of LGIB on both conventional angiography and scintigraphy or MDCT (Fig. 1). A true negative was defined as the absence of LGIB on both conventional angiography and scintigraphy or MDCT. A false positive was taken if either scintigraphy or MDCT showed active extravasation of blood, while subsequent arteriography was normal. Likewise, a false negative was considered if scintigraphy or MDCT showed no evidence of hemorrhage, while arteriography demonstrated active GI bleeding. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated along with 95% confidence intervals (CI) for diagnosis of LGIB using conventional angiography as gold standard. Overall accuracies of RBC scintigraphy and CT with GI bleed protocol were also calculated. For this calculation, the number of patients for whom the site of GI bleeding was incorrectly localized was subtracted from the total number of true positives. The 2-tailed, Fisher exact test was used to compare sensitivity, specificity, and overall accuracy of the 2 modalities. A P-value of < 0.05 was considered as statistically significant.

**RESULTS**

**Study Participants**

A total of 78 patients underwent radiologic evaluation for acute persistent LGIB at our institution between January 2010 and February 2014. Of these, 2 patients died before radiologic evaluation could be completed and were excluded from the study. These patients were 83 and 88 years old, respectively, and respective causes of death were ventricular fibrillation and respiratory failure. As autopsies were not performed in these patients, the etiologies of LGIB remained unknown. The remaining 76 patients were included in our study cohort (Fig. 2). Further characteristics of these patients are provided in Supplementary Results (Supplemental Digital Content 1, http://links.lww.com/JCG/A211) and Supplementary Tables 1 and 2 (Supplemental Digital Content 2, http://links.lww.com/JCG/A212).

Only 99mTc-labeled RBC scintigraphy was performed in 51 (67.1%) patients, whereas 20 (26.3%) had undergone only MDCT with GI bleed protocol. Another 5 patients (6.6%) had undergone both 99mTc-labeled RBC scintigraphy and MDCT with GI bleed protocol. The mean time interval between 99mTc-labeled RBC scintigraphy and conventional angiography was 6 hours and 40 minutes (SD: 5h and 1min), whereas the average interval between MDCT with GI bleed protocol and conventional angiography was 6 hours and 3 minutes (SD: 4h and 16min). Etiologies of LGIB and other characteristics of patients who underwent 99mTc-labeled RBC scintigraphy alone, MDCT with GI bleed protocol alone, or both modalities were comparable (Supplementary Table 2, http://links.lww.com/JCG/A212). No contrast or angiography-related complications occurred in our patient cohort.

**Findings on 99mTc-labeled RBC Scintigraphy**

Of 56 (73.7%) patients who underwent 99mTc-labeled RBC scintigraphy, 42 (75% of 56) had evidence of LGIB on scintigraphy. Of these, 26 (61.9% of 42) also had LGIB on conventional angiography, whereas 16 (38.1% of 42) patients had a negative angiography. Of the 26 (61.9% of 42) patients who had positive findings on both studies, the site of bleeding was misdiagnosed by 99mTc-labeled RBC scintigraphy in 3 (11.5% of 26) patients. Among the 14 (25% of 56) patients who showed no evidence of bleeding on scintigraphy, conventional angiography revealed active LGIB in 6 (42.9% of 14) patients. These results are summarized in Table 1.

**Findings on MDCT With GI Bleed Protocol**

A total of 25 (32.9%) patients underwent MDCT with GI bleed protocol among whom 15 (56% of 25) had evidence of LGIB. Of these 25 scans, 19 (76% of 25) and 6 (24% of 25) were performed on 64-row and 320-row CT scanners, respectively. Of the 15 patients with evidence of LGIB on CT scans, 10 (67% of 15) and 5 (33% of 15) were diagnosed on arterial and delayed phase scans, respectively. Conventional angiography revealed active LGIB in 14 (93.3% of 15) patients. In the only patient with a false-positive scan, the time interval between MDCT and conventional angiography was 17 hours and 40 minutes. Moreover, among the 10 (40% of 25) patients with a negative CT scan, none had evidence of LGIB on subsequent angiography. The site of bleeding was accurately identified by MDCT for all patients with evidence of LGIB. These results are summarized in Table 2.

**Estimates of Accuracy**

Using conventional arteriography as gold standard, sensitivity and specificity of 99mTc-tagged RBC scintigraphy was 81.2% (95% CI: 62.9%, 92.1%) and 33.3% (95% CI: 16.4%, 55.3%) with PPV and NPV of 61.9% (95% CI: 45.6%, 76%) and 57.1% (95% CI: 29.7%, 81.2%), respectively. In contrast, sensitivity and specificity of MDCT with GI bleed protocol was 100% (95% CI: 65.6%, 100%) and 90.9% (95% CI: 57.1%, 99.5%) with PPV and NPV of 93.3% (95% CI: 66%, 99.6%) and 100% (95% CI: 65.5%, 100%), respectively. Overall accuracy of RBC scintigraphy was 55.4% (95% CI: 42.3%, 68.4%), whereas that of MDCT was 96% (95% CI: 88.3%, 100%) (Table 3). CT with GI bleed protocol had a higher specificity (90.9%) than 99mTc-labeled RBC scintigraphy (33.3%) for detection and localization of source of LGIB (P < 0.01). However, no statistically significant difference (P > 0.05) was noted between the sensitivity of CT with GI bleed protocol (100%) and 99mTc-labeled RBC scintigraphy (81.2%). Overall accuracy of CT with GI bleed protocol (96%) was significantly higher (P < 0.001) than that of 99mTc-labeled RBC scintigraphy (55.4%).

**DISCUSSION**

Annual incidence of hospitalization for acute LGIB is approximately 36 per 100,000 people and acute LGIB accounts for about 20% of cases of acute GI bleeding. In our study cohort, the prevalence of acute LGIB was 51.3% (39/76), which is comparable to that of other similar studies. Massive LGIB can have a mortality of approximately 15% and patients with 2 or more comorbidities, or those aged 70 years or above, are at a higher risk of mortality. In our study cohort, 39.5% (30/76) of...
patients had 2 or more comorbid conditions, whereas 21% (16/76) of patients were aged 70 years or above (Supplementary Results, Supplemental Digital Content 1, http://links.lww.com/JCG/A211 and Supplementary Table 1, Supplemental Digital Content 2, http://links.lww.com/JCG/A212.

FIGURE 1. Images obtained in a 50-year-old man with melena and hematochezia for 2 days. A, No source of active bleeding noted on ⁹⁹ᵐTechnetium-labeled tagged-red cell scintigraphy. B, Unenhanced and (C) arterial phase (axial plane) images of computed tomography with gastrointestinal bleed protocol demonstrating the appearance of hyperdense material within small bowel loops. D, Digital subtraction angiography performed subsequently confirms active bleeding from a branch of the superior mesenteric artery in the region of ileum.
These statistics indicate that our study cohort fairly represented the population of patients who are likely to undergo radiologic evaluation of acute LGIB in actual practice. Characteristics of patients and etiologies of LGIB in our study cohort were also comparable to those of previously published studies.\textsuperscript{1,2,4,10,11,16,17}

DSA has been traditionally considered to be the radiologic reference standard for evaluation of GI bleeding,\textsuperscript{13} as was the case in our study. However, over the years, validity of DSA as a reference standard has been questioned.\textsuperscript{18} RBC scintigraphy was initially thought to be an attractive option for evaluation of LGIB as it was highly sensitive and could detect bleeding as slow as 0.3 mL/min—in contrast to the lower limit of 0.5 mL/min quoted for conventional angiography.\textsuperscript{19,20} However, many studies over time have demonstrated the high false-positive rate of this modality, which has curtailed its use to a limited group of patients with intermittent bleeding.\textsuperscript{5} The results of our study further substantiate these notions as \textsuperscript{99mTc}-labeled RBC scintigraphy had a low specificity of 33.3%.

With the advent of multidetector row CT scanners, CT has emerged as a promising modality for detection of GI bleeding. Intravenous contrast-enhanced MDCT has been shown to reveal GI bleeding as slow as 0.35 mL/min in animal studies,\textsuperscript{21} which is nearly the same as that reported previously for tagged RBC scintigraphy.\textsuperscript{12} Clinical studies that have evaluated the accuracy of MDCT in the past have also shown encouraging results.\textsuperscript{1,2,4,10,11,22–32} However, most of these studies did not provide comparative analysis between MDCT with GI bleed protocol and RBC scintigraphy. Our study showed that CT with GI bleed protocol was more accurate in detecting and localizing the source of acute LGIB than \textsuperscript{99mTc}-labeled RBC scintigraphy. The high accuracy (96%) of MDCT with GI bleed protocol that we report is comparable to the results reported by Yamaguchi and Yoshikawa,\textsuperscript{10} Jaeckle et al,\textsuperscript{23} and Yoon et al.\textsuperscript{1} In our study, there were no false-negative cases of MDCT implying that not even a single case of LGIB was missed by MDCT. Moreover, there was only 1 false-positive case in which LGIB was detected on MDCT, whereas no bleeding was demonstrable on subsequent DSA. This may be attributed to the spontaneous cessation of bleeding from the initial source of hemorrhage, or vasoconstriction of the implicated vessels, as the time delay between MDCT scan and DSA, in this case, was >17 hours. All CT scans in our study were performed using 64-row or 320-row CT scanners. The higher number of rows and slices in modern scanners has improved the precision with which digital

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\textbf{Positive} & 23 & 16 & 42 \\
\textbf{Accurately localized} & 23 & 16 & 42 \\
\textbf{Inaccurately localized} & 3 & 13 & 16 \\
\textbf{Negative} & 6 & 8 & 14 \\
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\textbf{Total} & 32 & 24 & 56 \\
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\caption{Results of \textsuperscript{99mTc}-labeled Red Blood Cell (RBC) Scintigraphy Used for the Diagnosis of Gastrointestinal Bleeding in Our Study Subjects}
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\caption{Results of Multidetector row Computed Tomography With Gastrointestinal (GI) Bleed Protocol for the Diagnosis of Lower GI Bleeding in Our Study Subjects}
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images are acquired. This may account for the higher sensitivity and specificity of MDCT observed in our study.

Our study showed that tagged red cell scintigraphy had lower sensitivity, specificity, and overall accuracy as compared with MDCT with GI bleed protocol. The sensitivity (81.2%) and specificity (33.3%) of RBC scintigraphy that we report is in line with multiple previous reports including that of Hunter and Pezim and Voeller et al. Some studies reported a high sensitivity of tagged RBC scintigraphy when used in conjunction with DSA. However, even in these studies, specificity and localization rate of tagged RBC scintigraphy remained low. Specifically, Hunter and Pezim reported a very high false-localization rate of 42% when surgical procedures were performed solely on the basis of the results of tagged RBC scintigraphy.

One major advantage of MDCT over 99mTc-tagged RBC scintigraphy is that it allows precise localization of the site of bleeding within the GI tract. As observed in our study, all cases of LGIB were accurately localized by MDCT with GI bleed protocol, whereas 99mTc-tagged RBC scintigraphy inaccurately localized bleeding in 3 cases. This information can be used by the interventional radiologist to selectively cannulate the implicated vascular territory and angiembolize culprit vessels, which may potentially reduce fluoroscopy times and limit radiation exposure to patients.

LGIB presents a clinical conundrum for the emergency physician when endoscopy is not possible or is inconclusive. On the basis of the results of several previous studies and the present study, we strongly feel that an algorithm incorporating MDCT with GI bleed (as an initial diagnostic modality) be followed in such cases. Patients with a positive scan may then be subjected to an invasive DSA, which will allow angioembolization to be done during the same setting. In contrast, patients with a negative scan can be admitted to an in-patient unit for close monitoring and, or elective colonoscopy.

Before drawing any conclusions, one must keep in mind the limitations that are inherent to this study. First and foremost, we did not quantify the rate of bleeding in patients included in our study. Rapid and profuse bleeding is detectable on all radiologic modalities, whereas slow and intermittent bleeding can be missed on certain modalities. However, we did measure nadir hemoglobin levels and number of packed RBC transfused in our patients (Supplementary Results, Supplemental Digital Content 1, http://links.lww.com/JCG/A211 and Supplementary Table 1, Supplemental Digital Content 2, http://links.lww.com/JCG/A212), which correlate directly with the rate and amount of blood lost. Second, our study included only 5 patients who underwent both tagged RBC scintigraphy and MDCT, which may make a head-to-head comparison difficult. But, no significant differences were noted between patients who underwent RBC scintigraphy and those who underwent MDCT with GI bleed protocol in our study (Supplementary Table 2, Supplemental Digital Content 2, http://links.lww.com/JCG/A212). Therefore, a comparison of diagnostic accuracies between these 2 groups in this study was valid and reliable. Another limitation worth mentioning is the small sample size of our study, which barred us from performing any subgroup analysis. Despite this, the number of patients included in our study (n = 76) were more than that of Jaekle et al (n = 36), Al-Saeed et al (n = 27), Yoon et al (n = 26), Zink et al (n = 20), and Yamaguchi and Yoshikawa (n = 10).

CONCLUSIONS
CT with GI bleed protocol was more accurate in detecting and localizing the source of acute LGIB than 99mTc-labeled RBC scintigraphy. Patients with LGIB should undergo CT with GI bleed protocol rather than RBC scintigraphy for detecting and localizing the source of LGIB.

REFERENCES


