Upper Versus Lower Gastrointestinal Bleeding: A Direct Comparison of Clinical Presentation, Outcomes, and Resource Utilization

Chad T. Whelan, MD
Connie Chen, PharmD
Peter Kaboli, MD, MS
Juned Siddique, DrPH
Micah Prochaska, BA
David O. Meltzer, MD, PhD

1 Department of Internal Medicine, Loyola University Chicago Stritch School of Medicine, Maywood, Illinois.
2 Pfizer Pharmaceuticals, New York, New York.
3 Center for Research in the Implementation of Innovative Strategies in Practice (CRIISP) at the Iowa City Veterans Affairs (VA) Healthcare System, Iowa City, Iowa.
4 Division of General Internal Medicine, Department of Internal Medicine, University of Iowa Carver College of Medicine, Iowa City, Iowa.
5 Department of Preventive Medicine, Feinberg School of Medicine, Northwestern University, Chicago, Illinois.
6 Boonshoft School of Medicine, Wright State University, Dayton, Ohio.
7 Department of Internal Medicine, University of Chicago, Chicago, Illinois.

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PURPOSE: To compare prevalence, clinical outcomes, and resource utilization between subjects with lower gastrointestinal bleeding (LGIB) and upper gastrointestinal bleeding (UGIB).

METHODS: Using administrative data, patient surveys, and chart abstraction, comparisons between subjects admitted with LGIB and UGIB were made by employing bivariate and multivariate statistics.

RESULTS: A total of 367 subjects were identified, LGIB = 187 and UGIB = 180. Subjects with UGIB compared to LGIB had greater admission hemodynamic instability including tachycardia and orthostasis but clinical outcomes were similar. In multivariate analyses, no significant differences were observed for in-hospital mortality transfer to the intensive care unit (ICU) or 30-day readmission rate. Resource utilization was similar in UGIB and LGIB, including mean costs, length of stay, and number of endoscopic procedures.

CONCLUSIONS: Unlike prior studies, this direct comparison of LGIB to UGIB identified more similarities than differences with similar prevalence rates, clinical outcomes, and resource utilization, suggesting that the epidemiology of gastrointestinal bleeding may be changing. Journal of Hospital Medicine 2010;5:141–147. © 2010 Society of Hospital Medicine.

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Gastrointestinal bleeding (GB) is a frequent reason for acute hospitalization, with estimated rates of hospitalization at 375 per 100,000 per year in the United States.1 GIB is not a specific disease but rather a diverse set of conditions that lead to the clinical manifestations associated with bleeding into the gastrointestinal tract. One of the most commonly used organizing frameworks in gastrointestinal bleeding is the differentiation between upper gastrointestinal bleeding (UGIB) and lower gastrointestinal bleeding (LGIB). There are important differences in the etiologies between the 2 sources. For example, acid-related disease is a common etiology in UGIB but does not occur in LGIB. While some aspects of the acute management are shared between UGIB and LGIB, important differences exist in the management, including initial endoscopy and medication choice. There have been few direct comparisons of rates, resource use, and clinical outcomes between UGIB and LGIB.

Historically, rates of UGIB have been reported to exceed those of LGIB by 2-fold to 8-fold.2–5 Protocols, clinical practice guidelines, and policy decisions reflect this emphasis on UGIB.6–8 Among 9 guidelines hosted by National Guideline Clearinghouse addressing GIB, 6 were focused on UGIB, 2 on both UGIB and LGIB, and only 1 on LGIB.9 There are several reasons to believe that these relative incidence rates may not be accurate. First, recent advances in therapy and prevention of UGIB, such as the treatment of Helicobacter pylori infection; proton pump inhibitors (PPIs); and selective cyclooxygenase-2 (COX-2) inhibitors, may have affected the epidemiology of gastrointestinal bleeding.10–16 Among these therapies, only COX-2 inhibitors may also reduce the
incidence of LGIB. Therefore, these advances may result in a disproportionate drop in UGIB relative to LGIB. In addition, known risk factors for both LGIB and UGIB, including advancing age and renal failure, are increasing in the general population. Finally, given the recent increased recommendations for aspirin therapy and systemic anticoagulation, exposure to aspirin and warfarin have increased, both risk factors for LGIB and UGIB. Indeed, recent studies in the epidemiology of UGIB do suggest a changing pattern of etiologies of UGIB reflecting these advances. One study examining rates of both UGIB and LGIB demonstrate a decrease in hospitalizations overall for GIB driven by a reduction in UGIB while at the same time reporting an increase in the incidence of hospitalization for LGIB.

In addition to a changing epidemiology, a second reason for a potential underestimation of LGIB incidence is one of methodology. There are well-recognized limitations with using purely administrative data due to difficulties in accurately identifying patients with LGIB.

Studies using large administrative databases may not accurately identify LGIB because of the poor sensitivity and specificity of International Classification of Diseases, Ninth revision, Clinical Modification (ICD-9) codes for LGIB. While there are standard methods of identifying patients with UGIB using ICD-9 codes, there is no accepted standard for LGIB. Thus, estimates using only ICD-9 codes may overidentify or underidentify patients with LGIB. Prior studies that have most accurately identified patients with LGIB used a 2-step method to address this issue. The initial ICD-9 identification included a high sensitivity/low specificity approach. These identified patient charts undergo chart review to confirm the presence of an LGIB. This method is labor intensive and cannot be done using administrative databases. No direct comparison of UGIB to LGIB among hospitalized patients using this 2-step method has been done recently.

The current emphasis on UGIB as seen in the published guidelines could also be supported if patients with UGIB had greater resource utilization or worse clinical outcomes. Limited direct comparisons for these outcomes are available. However, 1 administrative database study reported similar mortality rates for UGIB (2.7%) and LGIB (2.9%) in 2006. No direct comparisons of other clinical outcomes or resource use outcomes are available. Therefore, the emphasis on UGIB in publications and guidelines is best supported by the incidence rates that are, as has already been discussed, problematic.

We conducted a retrospective cohort study to examine the incidences of UGIB and LGIB among patients admitted to an academic medical center over 2 years using methods designed to optimally identify patients with either UGIB or LGIB. Our study also examined differences in clinical outcomes and resource utilization between subjects with UGIB and LGIB to examine the relative severity of these 2 clinical entities. These results may be useful in determining the need to reconsider clinical approaches as well as protocols and guidelines among patients with gastrointestinal bleeding.

**Patients and Methods**

**Patients**

This retrospective cohort study evaluated all patients who were admitted with GIB to a large urban academic medical center from July 1, 2001 to June 30, 2003 and who consented to a larger study examining the effects of hospitalists on patient care. Subjects unable to provide consent due to death or lack of decisional capacity were consented via proxy. To identify patients with GIB, all patients were screened for a primary or secondary diagnosis of GIB using ICD 9 codes. These codes were selected for a very high sensitivity threshold to assure that all potential subjects with GIB were identified. All subjects identified using these codes underwent chart abstraction to determine if they met criteria for GIB. These inclusion criteria required documentation in any portion of the chart (including emergency department [ED] clinician documentation, admission note, nursing intake note, etc.) of signs or symptoms of GI hemorrhage upon admission, including: hematemesis, coffee ground emesis, gastrooccult-positive emesis, melena, hematochezia, maroon stools, and hemoccult-positive stools interpreted by the treating physician team as an acute GIB. Subjects identified using the ICD-9 codes and confirmed to have an acute GIB by chart review were included in the study and underwent additional chart abstraction and administrative data analysis.

**ICD-9 codes for GIB included:** esophageal varices with hemorrhage (456.0, 456.20), Mallory-Weiss syndrome (530.7), gastric ulcer with hemorrhage (531.00–531.61), duodenal ulcer with hemorrhage (532.00–532.61), peptic ulcer, site unspecified, with hemorrhage (533.00–533.61), gastrojejunal ulcer with hemorrhage (534.00–534.61), gastritis with hemorrhage (535.61), angiodysplasia of stomach/duodenum with hemorrhage (537.83), hematemesis (578.0–578.9), diverticular disease (562.00–562.9), other disorders of the intestine (569.00–569.9), congenital anomalies of the digestive system (751.00), proctocolitis (556.0), hemorrhoids (455.00–455.6), nong ASTERISK nontoxic colitis (006.2), noninfectious gastroenteritis and colitis (558.0–558.9), salmonella gastroenteritis (003.3), malignant neoplasm of colon (153), familial adenomatous polyposis (211.3), and gastric varices (456.8).

**Data**

Trained research assistants performed chart abstraction with validation by the principal investigators (PIs) of the first 15 charts to ensure accuracy. Subsequently, research assistants consulted with PIs with any questions during abstracting with final decisions being made by PIs. Detailed chart abstraction collected admission medication lists as obtained by the admitting physician team, including the use of PPIs, histamine-2 (H-2) blockers, COX-2 inhibitors, and...
medications known to increase the risk of GIB, such as nonselective NSAIDs (nsNSAIDs), aspirin, and other anticoagulants. Other clinical data including risk factors, comorbid illnesses, laboratory tests, and vital signs were also abstracted from subjects’ charts.

The source (UGIB vs. LGIB) and etiology (peptic ulcer disease [PUD], varices, diverticula, etc.) of bleeding were assessed using endoscopic reports as the primary source. When no clear source was identified on endoscopy or no endoscopy was done, the abstractor would review all progress notes, discharge summaries, and other diagnostic test results such as angiography in order to identify the source of bleeding (UGIB vs. LGIB). Endoscopic reports that identified a patient as having a UGIB or LGIB but no confirmed etiology were classified as undetermined etiology unless review of the other clinical documentation provided a specific etiology.

Tachycardia was defined as pulse greater than 100 beats per minute. Orthostasis was defined by either a drop in systolic blood pressure of 20 mmHg or an increase in pulse of 10 beats per minute. Hospital administrative databases were utilized to obtain resource utilization (ie, length of stay [LOS], total cost of care, intensive care transfers), Charlson comorbidity index,27 30-day readmission rate, and in-hospital mortality. Hospital costs were determined using TSI cost accounting software (Transition Systems Incorporated [now Eclipsys Corporation], Boston, MA), a validated system to assess actual direct and indirect costs of care.

### Statistical Analysis

Descriptive statistics (means and proportions) were calculated by location of GIB for all variables describing patient characteristics, clinical presentation, clinical outcomes, and resource utilization. Differences in age and Charlson comorbidity index by GIB location were evaluated using t tests. Differences in gender, race, and medication use were evaluated using chi-squared tests of independence.

We fit generalized linear models to investigate differences by location of bleed for those variables measuring clinical outcomes (inpatient mortality, intensive care unit [ICU] transfer, emergency surgery, 30-day readmission, change in hemoglobin) and those variables measuring resource outcomes (total cost, LOS, number of procedures, number of correct scopes, repeat scope indicator, incorrect scope indicator, number of red blood cell [RBC] transfusions). The repeat scope indicator was used to denote a repeat scope (either esophagogastroduodenoscopy [EGD] or colonoscopy) and the incorrect scope indicator was used to denote when the initial scope was negative and a follow-up scope from the other direction was positive (negative EGD followed by positive colonoscopy or negative colonoscopy followed by positive EGD). For each variable we fit 2 regression models, the first model (unadjusted effect) only included location of bleed as a covariate. The second model (adjusted effect) included location of bleed, age, gender, race (black/not black) and Charlson comorbidity index as covariates. Binary outcomes were modeled using logistic regressions. For continuous variables, we determined the distribution and link of the outcome variable using residual diagnostics and by comparing the log likelihood and information criteria of competing models. All analyses were performed using STATA SE Version 9.0 (StataCorp, College Station, TX)

This study was approved by the University of Chicago Institutional Review Board.

### Results

During the 2 years of observation, a total of 7741 subjects were admitted to the internal medicine service and enrolled in the hospitalist study. Of these, 1014 had a primary or secondary ICD-9 code that may be consistent with UGIB or LGIB and underwent chart review to determine if they had an acute GIB. Out of 1014 subjects, 647 were determined not to have an acute GI hemorrhage and were excluded from the remaining analyses; 367 of the 1104 subjects identified by ICD-9 codes were found to have a clinical presentation consistent with GIB and were included in this study. A total of 180 of these 367 had UGIB and 187 had LGIB. The mean age was 62.4 years, 56.7% were female, 82.6% were African American, 12.7% were Caucasian, and the mean Charlson index was 1.5 (Table 1). Among baseline characteristics, both gender and age were statistically associated with a difference in rates of upper vs. lower source bleeding, with LGIB patients more likely to be female (P = 0.01) and older (P < 0.001). Etiologies of UGIB include erosive disease, peptic ulcer disease, variceal bleeding, arteriovenous malformation, and malignancy. Etiologies of LGIB include: diverticulosis, colitis, arteriovenous malformation, cancer, ischemic colitis, polyph, hemorrhoidal bleed, ulcer, inflammatory bowel disease, other, and not determined (Table 2).

Baseline use of medications known to be associated with either increased or decreased risk of GIB was common. Approximately one-third of subjects with both LGIB and UGIB used aspirin and 10% used warfarin. LGIB subjects

| TABLE 1. Baseline Characteristics Among All Subjects Admitted for GI Hemorrhage |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|
|                                 | Upper and Lower | Upper GI Bleeding | Lower GI Bleeding | P Value         |
|                                 | GI Bleeding     | (n = 367)        | (n = 180)        | (n = 187)       |
| Age (years), mean (SD)          | 62.4 (18.0)     | 58.6 (18.2)      | 66.0 (17.1)      | <0.001          |
| Female gender (%)               | 56.7            | 50.0             | 61.1             | 0.01            |
| Race (%)                        |                 |                 |                 |                 |
| African American                | 82.6            | 85.3             | 80.1             | 0.43            |
| White                           | 12.7            | 10.7             | 14.5             | 0.001           |
| Other                           | 4.7             | 4.0              | 5.4              |                 |
| Charlson comorbidity index, mean (SD) | 1.5 (1.5) | 1.6 (1.6) | 1.4 (1.5) | 0.44 |

Abbreviations: GI, gastrointestinal; SD, standard deviation.
were less likely to use an nsNSAID ($P < 0.001$), but more likely to use a proton pump inhibitor (PPI) ($P = 0.06$) (Table 3).

Key initial clinical presentation findings included vital sign abnormalities and admission hemoglobin levels. While hypotension was not common (4.7%), resting tachycardia (37%) and orthostasis (16%) were seen frequently. Subjects with LGIB were significantly less likely than those with UGIB to present with orthostasis (8.8% vs. 21.0%, respectively; $P = 0.006$) and resting tachycardia (32.3% vs. 42.5%, respectively; $P = 0.04$). Subjects with LGIB had a higher admission hemoglobin than those with UGIB (10.7 vs. 9.7, respectively; $P < 0.001$) (Table 4).

We also examined several clinical outcomes. When comparing LGIB to UGIB patients for these clinical outcomes using bivariate and multivariate statistics, there was no difference for in-hospital mortality (1.1% vs. 1.1%), transfer to ICU (16.0% vs. 13.9%), 30-day readmission (5.9% vs. 7.8%), number of red blood cell (RBC) transfusions (2.7 vs. 2.4), or need for GI surgery (1.1% vs. 0.0%). The mean drop in hemoglobin was greater among subjects with LGIB compared to UGIB (1.2). Thirteen percent of subjects with LGIB required 2 colonoscopies while only 8% of subjects with UGIB required a second EGD while only 8% of subjects with LGIB received an EGD while only 8% of subjects with UGIB received a colonoscopy ($P = 0.001$) (Table 6).
Conclusions
This study represents one of the largest direct comparisons of LGIB to UGIB not based on administrative databases. The most striking finding was the nearly equal rates of LGIB and UGIB. There are 2 likely explanations for this surprising result. First, there may be methodological reasons that we identified a greater proportion of true LGIBs; our study used a highly sensitive search strategy of ICD-9 coding with confirmatory chart abstraction to ensure that as many LGIB and UGIB cases would be identified as possible while also excluding cases not meeting accepted criteria for GIB. The second possibility is that there is an actual change in epidemiology of GIB. Known risk factors for LGIB are increasing such as advancing age, increased use of chronic aspirin therapy, and renal disease. At the same time, significant advances in the treatment and prevention of UGIB have been made. Recent studies have demonstrated similar trends in admissions for upper and lower GI complications, suggesting that there may be a changing epidemiology due primarily to reductions in upper GI complications.1,16

Either explanation would have implications for the care of patients with GIB. Clinical decision-making based on prior literature would support that in ambiguous clinical situations and initial evaluation for an UGIB is appropriate. Most risk stratification literature and clinical guidelines focus on UGIB. If rates of LGIB and UGIB are similar, then existing clinical decision protocols may need to be reevaluated to incorporate the higher likelihood of LGIB. This reevaluation would be less important if the clinical outcomes or resource utilization of UGIB was significantly greater than that for LGIB, but we did not find this was the case. Similarly, if the ability to distinguish between LGIB and UGIB were robust on clinical signs and symptoms, then a reevaluation would be less important. However, we found fairly similar numbers of patients initially receiving evaluation for UGIB then being evaluated for LGIB as we found patients initially receiving evaluation for LGIB then being evaluated for UGIB. This suggests the potential benefit of clinical decision protocols that could better distinguish between UGIB and LGIB and account for the potentially higher incidence of LGIB than previously thought.

In addition to affecting the attention paid to LGIB for acute management, a changed understanding of incidence could also affect the attention paid to prevention of LGIB. Of the recent nonendoscopic advances in the treatment and prevention of GIB, only the use of COX-2s (when used in place of traditional nsNSAIDs) reduces the risk of both LGIB and UGIB;14,16–18 H. pylori treatment and PPIs only prevent UGIB. Therefore, if the clinical and financial burdens of LGIB are similar to those seen in UGIB, more attention may need to be focused on preventing LGIB.

Baseline medication use was notable primarily for the similarities between UGIB and LGIB. Agents known to affect the rates of GIB were common in both groups. Over one-third of the population was using aspirin and 10% were taking warfarin. Over 20% of subjects were taking an nsNSAID or a COX-2 inhibitor. Almost one-quarter of subjects were taking an PPI, agents known to decrease rates of UGIB and potentially increase LGIB through the risk of C. difficile colitis. Notably, the only statistically significant difference in baseline medication use between subjects with UGIB and LGIB was the more than 3-fold higher use of nsNSAIDs in patients with UGIB as compared to LGIB. While current guidelines are not clear and consistent about which populations of at-risk patients should receive GI prophylaxis,28–30 these results suggest that patients admitted with GIB are very likely to be taking medications which impact the risk of GIB.

In terms of disease severity, the clinical presentation at admission suggests a greater degree of hemodynamic instability among subjects with UGIB. Rates of orthostatic hypotension and resting tachycardia are higher in UGIB subjects, as well as having a lower mean hemoglobin levels at presentation. However, despite the more severe clinical presentation, clinical outcomes did not differ significantly between the 2 bleeding sources. Thus, the most relevant clinical outcomes suggest that the severity of both LGIB and UGIB are similar. This similarity again suggest that the clinical burden of LGIB is not significantly different than UGIB.

Our results concerning resource utilization demonstrate a similar pattern. While the point estimates for costs and LOS suggest that UGIB may be associated with higher resource utilization, these differences were not significant in either bivariate or multivariate analyses. Those subjects with UGIB did receive more total endoscopic procedures than subjects with LGIB. More interesting though was that 24% of all subjects received an endoscopy of the “opposite” site (LGIB with EGD and UGIB with colonoscopy). These results suggest that the site of bleeding is not clear in a significant

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| TABLE 6. Comparison of Resource Utilization Among All Subjects Admitted for GI Hemorrhage Using Bivariate and Multivariate Analyses |
|----------------|----------------|----------------|----------------|----------------|----------------|
|                | Upper GI Bleeding | Lower GI Bleeding | Bivariate Value | Multivariate Value |
| (n = 180)     | (n = 187)        |                  |                |                 |
| Cost ($), median | 14,301 (17,196) | 11,892 (13,100) | 0.13           | 0.21            |
| Cost ($), mean (SD)* | 9,548 | 7,890 | — | — |
| Length of stay (days), mean (SD)* | 5.7 (7.0) | 5.1 (5.3) | 0.37 | 0.72 |
| Number of endoscopies/patient, mean (SD)* | 1.3 (0.5) | 1.2 (0.9) | 0.18 | 0.20 |

NOTE: Multivariate analyses control for age, gender, race (black/not black), and Charlson index.

Abbreviations: GI, gastrointestinal; GLM, generalized linear model; OLS, ordinary least squares; SD, standard deviation.

*Modeled using a GLM with a gamma distribution and log link.

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proportion of patients who present with GIB. These additional endoscopies are associated with increased risk, costs, LOS, and discomfort to patients. Improving our ability to accurately predict the source (upper vs. lower) of bleeding would allow us to reduce the number of these excess endoscopies. Additionally, it is interesting that despite the almost universal use of endoscopies, 20% of LGIB and 14% of UGIB subjects could not have a specific etiology identified during endoscopy or subsequent workup.

There are some important limitations to this study. While the sample size is among the largest of its type involving chart abstraction, it may be underpowered to detect some differences. Additionally, our results are from a single urban academic medical center with a patient population that is predominantly African American, which may limit generalizability. This study required consent and therefore only examines a subset of patients admitted to the medical center with GIB, which could potentially introduce bias into the sample. However, it is not clear why there would be systematic differences in subjects who choose to consent vs. those who decide not to consent that would affect the results of this study in substantive ways.

Despite significant efforts at identifying all subjects with GIB admitted during this time period, there were potential methodological reasons that may have resulted in some cases being missed. Only subjects admitted to a medicine service were approached for consent. All subjects in this medical center with GIB are admitted to a medicine service. We captured all subjects who were initially admitted to a medicine service as well as those admitted initially to an ICU and then transferred to the floor at any point prior to discharge. It is possible, though, that a subject would be admitted to an ICU for GIB and die prior to being transferred to the floor. While it is the impression of the director of the ICU that this would be a very unusual event, as most of the patients would be discharged to the floor prior to death (personal communication), given the very low mortality rate seen in this study, small numbers of missed events could have a significant impact on the interpretation of in-hospital mortality results. It is also important to note that this medical center did not have the ability to perform endoscopy prior to admission for patients with GIB at the time of the study; all patients who presented with GIB would have been admitted and identified for this study. Finally, we were unable to routinely identify the rationale for obtaining an endoscopic exam. We assumed that all endoscopic exams were done for the purpose of evaluating and/or treating the GIB for which the subject was admitted. It is possible that some subjects had additional endoscopies for other reasons, which would have led to our overestimating the rates of additional endoscopies for GIB.

This study highlights the similarities between LGIB and UGIB rather than the differences. There were few significant differences between the 2 bleeding sources in terms of incidence, clinical outcomes, and resource utilization. In fact, the study also suggests that determining the source of bleeding may not be clear, given the high rates of “opposite” site endoscopies. While this study did reveal several similarities between UGIB and LGIB, it also highlights the need to identify improved strategies to improve the sensitivity and specificity of identification of LGIB compared to UGIB, both for clinical purposes and for research. The value of such improved clinical algorithms have the potential to improve both the cost and outcomes of care, while better algorithms for separating UGIB and LGIB using administrative data might help produce more precise estimates of costs and clinical outcomes, and aid in the development of risk stratification models.

References


