Early Predictors of Severity in Acute Lower Intestinal Tract Bleeding

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Background: Identification of high-risk patients with lower intestinal tract bleeding (LIB) is challenging, and prognostic factors have not been clearly defined. The aim of this study was to determine risk factors for severe acute LIB.

Methods: A total of 252 consecutive patients admitted with acute LIB were identified. Data were collected on 24 clinical factors available in the first 4 hours of evaluation. The outcome was severe bleeding, which was defined as continued bleeding within the first 24 hours of hospitalization (transfusion of ≥2 units of blood and/or hematocrit decrease of ≥20%) and/or recurrent bleeding after 24 hours of stability (additional transfusions, further hematocrit decrease of ≥20%, or readmission for LIB within 1 week of discharge).

Results: Severe LIB occurred in 123 patients (49%). Independent correlates of severe bleeding were as follows: heart rate, ≥100/min (odds ratio [OR], 3.67; 95% confidence interval [CI], 1.78-7.57); systolic blood pressure, ≤115 mm Hg (OR, 3.45; 95% CI, 1.54-7.72); syncope (OR, 2.82; 95% CI, 1.06-7.46); nontender abdominal examination (OR, 2.43; 95% CI, 1.22-4.85); bleeding per rectum during the first 4 hours of evaluation (OR, 2.32; 95% CI, 1.28-4.20); aspirin use (OR, 2.07; 95% CI, 1.12-3.82); and more than 2 active comorbid conditions (OR, 1.93; 95% CI, 1.08-3.44).

Conclusion: Clinical data available on initial evaluation can be used to identify patients at risk for severe LIB, who may benefit most from urgent intervention.

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and early intervention. To address this need, we collected clinical data from a cohort of consecutive patients admitted for acute LIB with the aim of determining risk factors for severe or recurrent bleeding.

**METHODS**

Patient Population and Study Location

All patients admitted to the Brigham and Women’s Hospital, Boston, Mass, from August 1, 1996, to June 30, 1999, were eligible for the study. The study protocol received approval from the hospital’s institutional review board. Patients were excluded from the study if any indication of a UGIB or a small bowel source of bleeding became evident during the admission. Such indications included hematemesis, coffee-ground emesis, or evidence of UGIB on endoscopy, nasogastric lavage, radionuclide scan, or angiography. In addition, patients described as having “melena” or “black” or “maroon” stools were required to have an upper gastrointestinal tract source excluded by either upper endoscopy or a nasogastric lavage. Other exclusion criteria included bleeding more than 3 days before presentation, low-grade bleeding (stool samples positive for occult blood or scant blood visible on toilet tissues only), patients transferred from inpatient units at other acute care hospitals, and patients already hospitalized for other indications.

Case Identification

A multistage case identification process was used to ensure that all patients hospitalized for LIB during the study period were ascertained. A total of 2323 candidate admissions were identified using a list of 69 International Classification of Diseases, Ninth Revision (ICD-9) codes representing LIB, as well as a wide range of diagnoses associated with LIB (eg, diverticulosis of colon). This set of diagnostic codes has been used previously to identify patients hospitalized with LIB and is intentionally broad.

The computerized discharge summaries from these 2323 hospitalizations were reviewed as a preliminary screen for study eligibility (L.L.S.). Patients were excluded at this stage if it was clear that they had no evidence of gastrointestinal bleeding or met any of the exclusion criteria. The most common reasons for exclusion at this stage were admission for a condition associated with LIB in the absence of bleeding (eg, colon cancer without overt bleeding), a history of an inflammatory condition (eg, inflammatory bowel disease), chronic or low-grade bleeding, and verified UGIB. Cases in which the presence, source, or acuity of bleeding was uncertain were not excluded at this point. This process narrowed the potential study candidates to 373. The medical records corresponding to these admissions were reviewed (L.L.S.). Patients were excluded because of unavailable medical records. Ultimately, 252 patients with acute LIB who satisfied all inclusion criteria were included in the study.

Data Collection

Data were collected using a standardized instrument. Potential predictors were collected from the record of the initial medical evaluation before ascertainment of outcomes from the subsequent entries in the hospital record. A comprehensive computerized hospital database was used to obtain laboratory values and blood product transfusion requirements. To assess interrater reliability, a separate reviewer independently reassessed a random sample (5%) of the records.

Predictive Variables

Twenty-four potential predictors obtainable within 4 hours of presentation to the hospital were selected based on relevant literature and clinical experience. Variables recorded included the following: age; sex; ethnicity; comorbid conditions (according to the Charlson Comorbidity Index, a validated, weighted index of 19 comorbid conditions that predict mortality); history of diverticulosis and/or LIB; daily use of aspirin (any dosage) or use during the previous week of at least 2 doses of a nonsteroidal anti-inflammatory agent or anticoagulant medication; stool color and frequency; number of hours from onset of bleeding to presentation; bleeding per rectum during the first 4 hours of medical evaluation; history of syncope or lightheadedness; history of abdominal pain or cramping or recent change in bowel habit; initial heart rate and blood pressure; initial platelet count and prothrombin time; and presence on initial medical evaluation of abdominal tenderness, gross blood on rectal examination, or altered mental status.

Outcome Criteria

The principal outcome was severe LIB. In the absence of an accepted reference standard or definition for this entity, an operational definition based on clinical knowledge of markers of severe bleeding was adopted. Severe LIB encompassed both continued bleeding within the first 24 hours (defined by the requirement of at least 2 units of packed red blood cells and/or a decrease in hematocrit of ≥20%) and/or recurrent bleeding after 24 hours of clinical stability (defined by additional blood transfusion requirements and/or a further decrease in hematocrit of ≥20% and/or readmission to the hospital for LIB within 1 week of discharge). The initial change in hematocrit was calculated using the value obtained on presentation and the lowest value obtained during the first 24 hours of hospitalization. The change in hematocrit during the first 24 hours was used and not the admission value alone in an attempt to account for hematocrit equilibration. The change in hematocrit after rebleeding was based on the last value available before the rebleeding and the first hematocrit level obtained after rebleeding was recognized. The independent reviewer’s assessment of the outcome, severe LIB, was consistent in 88% of the records reviewed (κ, 0.78).

These outcome criteria for severe LIB were intended to capture a range of patients who require substantial inpatient support, independent of the process of care or underlying comorbid diseases. The purpose of delineating risk factors was to aid in risk stratification and, ultimately, in the triage of appropriate patients to early interventions such as urgent colonoscopy. Blood transfusions, though subject to variations in care practices, were included in the outcome criteria, because aggressive resuscitation can prevent a significant decrease in hematocrit even in the presence of severe bleeding. Death was not included as an outcome measure because the mortality rate in LIB is low (<5%) and death is rarely due to ongoing bleeding. Other data recorded included the origin of the bleeding, cause of mortality, if any, and information regarding diagnostic and therapeutic procedures (surgery, endoscopy, angiography, radionuclide scan).

Statistical Analysis

Statistical analysis was performed using the statistical software (SAS software package, version 7.1; SAS Institute Inc, Cary, NC). To simplify clinical application, all continuous data were
RESULTS

PATIENT CHARACTERISTICS

Fifty-seven percent of the patients were female, with an average age of 66 years (range, 20-97 years). Seventy-eight percent had at least one comorbid medical condition (Charlson Comorbidity Index score, ≥1). The mean initial hematocrit was 35%. A total of 103 patients (41%) required blood transfusions during the first 24 hours of hospitalization. Of these patients, 11 patients (11%) received only 1 unit of packed red blood cells, 52 patients (51%) received 2 units, and 40 (39%) received more than 2 units. Eleven patients (4%) underwent surgery for bleeding control. There were 6 deaths (2%), but none was due primarily to bleeding.

Inpatient colonoscopy was performed on 144 patients (57%). Sixty patients (24%) underwent flexible sigmoidoscopy. A total of 191 patients (76%) had either a flexible sigmoidoscopy or colonoscopy. Of the 47 patients who underwent only a flexible sigmoidoscopy, 41 (87%) had a documented left-sided source. Additional procedures included esophagogastroduodenoscopy in 40 patients (16%), a radionuclide scan in 34 (13%), and angiography in 22 (9%). Eighty-three patients (33%) were subjected to more than one procedure. Forty patients (16%) did not undergo any procedure during their hospital stay, primarily because of the availability of a presumed clinical diagnosis in the absence of persistent bleeding (27 patients). Twenty-three such patients had a prior diagnosis of gastrointestinal disease (eg, inflammatory bowel disease, colorectal cancer) and a compatible presentation. The clinical diagnosis of infectious colitis was made in 4 patients. Six patients refused intervention.

RISK FACTORS FOR SEVERE LIB

Univariate analysis (Table 2) revealed that patients with severe bleeding were more likely to present with signs of hemodynamic instability (initial systolic blood pressure, ≤115 mm Hg; initial heart rate, ≥100/min; history of syncope) and signs of persistent bleeding (gross blood on rectal examination, bleeding during the first 4 hours of evaluation). A nonender abdominal examination and a Charlson Comorbidity Index score of more than 2 were more common in patients with severe bleeding. Age, history of diverticulosis, history of LIB, and anticoagulation were notable among the variables that were not univariate predictors of severe bleeding.

Multivariable logistic regression analysis identified 7 independent risk factors for severe LIB: initial heart rate of 100/min or more, initial systolic blood pressure of 115 mm Hg or less, history of syncope, nonender abdominal examination, bleeding per rectum during the first 4 hours of evaluation, aspirin use, and Charlson Comorbidity Index score of more than 2 (Table 3). There were no confounders of this model. No significant interactions were found between the independent predictors and age (>66 years) or comorbid disease (Charlson Comorbidity Index score, >2).

BLEEDING EVENTS

One hundred twenty-three (49%) of the 252 patients experienced severe LIB. A total of 117 patients (46%) had continued bleeding, 18 (7%) had recurrent bleeding, and 13 (5%) had both. Of those patients with continued bleeding, 26 (22%) had a decrease in hematocrit of at least 20%, 69 (59%) received at least 2 units of packed red blood cells, and 22 (19%) had both. All 8 patients readmitted to the hospital for bleeding also met the criteria for continued bleeding during the initial bleeding episode. Five (83%) of the 6 deaths occurred in patients with severe bleeding. In the severe bleeding group, the mean initial and 24-hour nadir hematocrits were 31% and 26%, respectively, compared with 38% and 34% in the patients without severe bleeding.

The most common causes of bleeding included probable or definite diverticular hemorrhage, hemorrhoids, ischemic colitis, postpolypectomy, and malignancy (Table 1). Of the remaining diagnoses, the most prevalent were nonischemic forms of colitis. Definite diverticular hemorrhage was defined as colonoscopic visualization of a diverticulum with active bleeding, adherent clot, or visible vessel; evidence of bleeding on angiography or radionuclide scan corresponding to an area of diverticulosis on colonoscopy; or pathological confirmation in a resected specimen. Probable diverticular hemorrhage was defined as a complete colonoscopy that revealed only diverticulosis. No diagnosis was made in 22 patients (9%).
Lower intestinal tract bleeding is a unique disease process that differs substantially from UGIB in origin, presentation, and clinical course. In contrast to UGIB, prognostic factors important for risk stratification of patients with LIB have not been clearly defined. In our study, 7 independent risk factors for severe LIB were identified: tachycardia, low systolic blood pressure, syncope, nontender abdominal examination, bleeding per rec-
come in both UGIB and LIB. It is therefore possible that coagulopathy and change in mental status were risk factors in studies of UGIB, but not in our study, because they reflect underlying liver disease.

Unlike UGIB, the abdominal examination result in LIB varies with the underlying disease process. A nontender abdomen is commonly found in disorders associated with severe LIB (eg, diverticular hemorrhage, vascular malformations), whereas abdominal tenderness may accompany disorders with less severe LIB (eg, ischemic colitis, inflammatory bowel disease). This discrepancy seems to explain the significance of a nontender abdomen in our model.

Our study has several strengths. We used an encompassing list of ICD-9 codes to identify a comprehensive and heterogeneous cohort of consecutive patients with acute LIB. Data collection was conducted in a standardized and chronologic fashion and resulted in little missing information. In addition, an independent medical record review was undertaken to confirm the reliability of our review process. Potential risk factors were selected and formulated to be reliable and readily available during the initial evaluation of patients with LIB. The outcome measure was designed to reflect severe bleeding rather than hospital complications and mortality. Death is a rare complication of LIB in our study, death occurred in only 2% of patients.

Our study also has several limitations. Despite systematic attempts to minimize bias and missing data, retrospective investigation is often less complete and less accurate than prospective study. Importantly, the retrospective nature of the study did not permit standardization of the process of care, which can vary in this population. Moreover, this was a single institution study, and although the results were statistically cross-validated, their applicability to other populations requires further testing. In addition, the lack of a widely used definition or marker of severity of LIB complicates the identification of risk factors. Finally, the identified risk factors do not capture all patients at risk for severe bleeding. Other as-yet-unidentified factors are likely to be of prognostic importance in this complex entity.

Defining risk factors for severity in acute LIB is a first step in understanding this disorder and improving its management. Beyond prognostic information, the availability of risk factors for severe bleeding should help to identify patients who are most likely to benefit from aggressive care. Technologic advancements in endoscopy have greatly improved the utility of colonoscopy in LIB. Traditionally, colonoscopic evaluation was delayed due to the need for bowel cleansing, the fear of increased procedural risks, and the lack of proven therapeutic efficacy. In recent years, several studies suggest that emergent colonoscopy (within 12 to 24 hours of admission) for acute lower intestinal tract hemorrhage is safe and effective. Endoscopic therapy using a variety of techniques, including epinephrine injection and thermal contact, can be used in 15% to 50% of patients and provides effective hemostasis in 70% to 100%. Early colonoscopic intervention, particularly for severe diverticular bleeding, in addition to improving diagnostic and therapeutic yield, may decrease rebleeding and surgical intervention rates, length of hospital stay, and cost of treatment. However, this procedure is logistically complicated and resource intensive, and it may not be appropriate or feasible for patients without severe

tum during the first 4 hours of medical evaluation, aspirin use, and more than 2 active comorbid conditions (Charlson Comorbidity Index score, >2). The likelihood of severe bleeding increased with the number of risk factors present. The identified risk factors are easy to obtain during the initial evaluation and may aid in the triage of patients to timely and appropriate diagnostic and therapeutic interventions.

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Previously designed to evaluate prognostic factors for gastrointestinal bleeding have focused largely on patients with UGIB and LIB. A prediction rule has been developed for a mixed population of patients with either UGIB or LIB. Principal risk factors for poor outcomes identified in these studies include hypotension, hematemesis, anemia, ongoing bleeding, endoscopic stigmata of recent hemorrhage, evidence of cirrhosis, comorbid disease, advanced age, change in mental status, elevated blood urea nitrogen level, and coagulopathy. Some of the risk factors identified in our study parallel those derived for patients with UGIB and LIB. Markers of hemodynamic instability (tachycardia, hypotension, syncope), as well as bleeding soon after presentation, reflect blood volume loss and bleeding rate; as such, it is not surprising that these factors are predictive of outcome in both UGIB and LIB.

There are notable differences between our findings and those derived from populations with UGIB, emphasizing the importance of defining LIB-specific risk factors. Several points of divergence may be ascribed to differing origins of bleeding in UGIB and LIB. Variceal bleeding is a significant source of UGIB but not LIB. It is therefore possible that coagulopathy and change in mental status were risk factors in studies of UGIB, but not in our study, because they reflect underlying liver disease.

Unlike UGIB, the abdominal examination result in LIB varies with the underlying disease process. A nontender abdomen is commonly found in disorders associated with severe LIB (eg, diverticular hemorrhage, vascular malformations), whereas abdominal tenderness may accompany disorders with less severe LIB (eg, ischemic colitis, inflammatory bowel disease). This discrepancy seems to explain the significance of a nontender abdomen in our model.

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Our study also has several limitations. Despite systematic attempts to minimize bias and missing data, retrospective investigation is often less complete and less accurate than prospective study. Importantly, the retrospective nature of the study did not permit standardization of the process of care, which can vary in this population. Moreover, this was a single institution study, and though the results were statistically cross-validated, their applicability to other populations requires further testing. In addition, the lack of a widely used definition or marker of severity of LIB complicates the identification of risk factors. Finally, the identified risk factors do not capture all patients at risk for severe bleeding. Other as-yet-unidentified factors are likely to be of prognostic importance in this complex entity.

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bleeding. Therefore, the ability to target high-risk patients for emergent colonoscopy should significantly improve the utility of this procedure in practice.

In conclusion, our study reveals that simple, objective clinical criteria available on initial presentation can be used to identify patients at risk for severe or recurrent LIB. These criteria seem to be additive to routine clinical judgment, and their systematic application may aid in the triage of LIB patients to appropriate care and timely interventions. Further studies are planned to validate these findings prospectively in other populations and to develop a prediction rule for use in the initial care of patients with acute LIB.

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