Predicting mortality in patients with in-hospital nonvariceal upper GI bleeding: a prospective, multicenter database study

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Background: Nonvariceal upper GI bleeding (NVUGIB) that occurs in patients already hospitalized for another condition is associated with increased mortality, but outcome predictors have not been consistently identified.

Objective: To assess clinical outcomes of NVUGIB and identify predictors of mortality from NVUGIB in patients with in-hospital bleeding compared with outpatients.

Design: Secondary analysis of prospectively collected data from 2 nationwide multicenter databases. Descriptive, inferential, and multivariate logistic regression models were carried out in 338 inpatients (68.6 ± 16.4 years of age, 68% male patients) and 1979 outpatients (67.8 ± 17 years of age, 66% male patients). A predictive model was constructed using the risk factors identified at multivariate analysis, weighted according to the contribution of each factor.

Settings: A total of 23 Italian community and tertiary care centers.

Patients: Consecutive patients admitted for acute NVUGIB.

Interventions: Early endoscopy, medical and endoscopic treatment as appropriate.

Main Outcome Measurements: Recurrent bleeding, surgery, and 30-day mortality.

Results: The mortality rate in patients with in-hospital bleeding was significantly higher than that in outpatients (8.9% vs 3.8%; odds ratio [OR] 2.44; 95% confidence interval [CI], 1.57-3.79; $P < .0001$). Hemodynamic instability on presentation (OR 7.31; 95% CI, 2.71-19.65) and the presence of severe comorbidity (OR 6.72; 95% CI, 1.87-24.0) were the strongest predictors of death for in-hospital bleeders. Other independent predictors of mortality were a history of peptic ulcer disease and failed endoscopic treatment. Rebleeding was a strong predictor of death only for outpatients (OR 5.22; 95% CI, 2.45-11.10). Risk factors had a different prognostic impact on the 2 populations, resulting in a significantly different prognostic accuracy of the model (area under the receiver-operating characteristic curve = 0.83; 95% CI, 0.77-0-93 vs 0.74; 95% CI, 0.68-0.80; $P < .02$).

Limitations: Study design not experimental, no data on ward specialty, potential referral bias.

Conclusions: In-hospital bleeders have a significantly higher risk of death because they are sicker and more often hemodynamically unstable than outpatients. Predictors of death have a different impact in the 2 populations. (Gastrointest Endosc 2014;79:741-9.)

Abbreviations: ASA, American Society of Anesthesiologists; AUROC, area under the receiver-operating characteristic; CI, confidence interval; ICU, intensive care unit; IHB, in-hospital bleeders; IQR, interquartile range; NVUGIB, nonvariceal upper GI bleeding; OPB, outpatient bleeders; OR, odds ratio; PNED, Progetto Nazionale Emorragie Digestive; PPI, proton pump inhibitor; SD, standard deviation.

DISCLOSURE: *The authors disclosed no financial relationships relevant to this publication.*

0016-5107/$36.00
http://dx.doi.org/10.1016/j.gie.2013.10.009

Received June 25, 2013. Accepted October 2, 2013.

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Presented in part as an oral presentation, ASGE/AGA Topic Forum, Digestive Disease Week, May 18-21, 2013, Orlando, Florida.

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Acute nonvariceal upper GI bleeding (NVUGIB) remains a common medical problem that has significant associated morbidity, mortality, and health care resource use.[1-3] Mortality rates for NVUGIB have recently started to decrease,[4-6] mainly because of effective treatment of comorbidities, powerful antisecretory medications, and the use of urgent endoscopy for diagnosis and treatment of bleeding stigmata. Most studies have focused on the improvement of outcomes in patients presenting to the emergency department with NVUGIB, whereas only a few have focused on the development of hemorrhage that occurs after hospital admission for unrelated disorders (so-called in-hospital bleeding).[7-11] Recent data show that in-hospital bleeding is associated with poorer outcome,[5,12,13] but the reasons for increased mortality in this subgroup of patients have not been consistently identified.

The aim of this study was to define the frequency of recurrent bleeding, the need for surgery, and death in patients with NVUGIB occurring while already hospitalized for another condition (in-hospital bleeders [IHBs]) and patients who start NVUGIB as outpatients (outpatient bleeders [OPBs]) and to better define the risk factors for mortality.

Take-home Message

- There are substantial differences between in-hospital and outpatient upper GI bleeders in terms of both clinical risk profile and treatment patterns.
- The mortality rate for nonvariceal upper GI bleeding in patients with in-hospital bleeding is more than doubled compared with outpatient bleeding and is essentially related to hemodynamic impairment and comorbid illnesses, but independent risk factors have a different impact on the 2 populations. Future studies should take these differences into account when assessing outcomes.

METHODS

Two nationwide prospective, multicenter databases (Progetto Nazionale Emorragie Digestive [PNED 1 and PNED 2] studies) containing data on consecutive patients admitted to participating hospitals for acute NVUGIB were analyzed.[4,5] The PNED1 study was carried out between March 2003 and March 2004, whereas the PNED2 study included patients observed between April 2007 and May 2008 (Appendix 1, available online at www.giejournal.org). In each study, a project-specific research database was developed that collected data from participating sites across Italy.

A patient was categorized in the study population as an OPB if he or she presented to a medical facility because of a new-onset of NVUGIB (clinical evidence of overt upper GI bleeding on admission or a history of hematemesis/coffee ground vomiting, melena, hematochezia, or a combination of any of these within 24 hours preceding admission); an IHB was defined as a patient in whom NVUGIB developed while the patient was already hospitalized for an unrelated illness. Bleeding was confirmed only if the presence of hematemesis, melena, or dark, tarry materials on rectal examination was documented and witnessed by nursing or medical staff. Patients were entered in the registry only if an upper GI endoscopy was performed. Patients were excluded if they were younger than 18 years of age, had chronic anemia or obscure GI hemorrhage without clinical evidence of acute hemorrhage, had a portal hypertensive-related etiology of acute upper GI bleeding such as varices, or were transferred from another institution.

Upper GI endoscopy was performed within 24 hours to confirm the source of bleeding. Endoscopic therapy of high-risk ulcer stigmata included injection of diluted epinephrine, thermal coaptive coagulation or argon plasma coagulation, application of hemoclips, or a combination thereof. The choice of the specific modality of endotherapy was left to the discretion of the operator according to the individual site's protocol.

Comorbidity was defined as the presence of any one of the following diseases: (1) cardiac diseases including ischemic heart disease and congestive heart failure and hypertension; (2) chronic pulmonary diseases; (3) acute and chronic liver disease including liver failure and cirrhosis; (4) GI diseases including a history of or surgery for peptic ulcer; (5) acute and chronic renal diseases; (6) vascular disorders including peripheral and central vascular diseases; (7) cerebrovascular disease; (8) diabetes mellitus and endocrine diseases; (9) hematologic disorders including leukemia and lymphoma; and (10) the presence of any malignancy.

Outcomes

In these 2 studies, mortality was defined as any death occurring within 30 days of the index bleeding episode. A bleeding-related death was defined as any death occurring (1) after uncontrolled bleeding; (2) occurring within 48 hours after endoscopy, without any other causes; (3) occurring during surgery for uncontrolled bleeding; (4) because of surgical adverse events or within 1 month after surgery; and (5) because of endoscopy-related mortality. Under nonbleeding-related death were considered patients with comorbidity dying without hemorrhagic shock at presentation.[6,14]

Continued or persistent bleeding was defined as (1) failure to control arterial bleeding endoscopically; (2) the presence of bloody nasogastric aspirate after endoscopic treatment; (3) hemodynamic instability, with a systolic blood pressure less than 100 mm Hg and a pulse greater than 100 beats per minute, or both; and/or (4) the need for continuous replacement of blood or fluid volume. Persistent hemorrhage was usually considered an indication for emergency surgery or percutaneous embolization. Recurrent bleeding was defined as recurrent vomiting of