Gastrointestinal Bleeding in Acute Ischemic Stroke: A Population-Based Analysis of Hospitalizations in the United States

Kavelin Rumalla, and Manoj K. Mittal, MD

Background and Objective: Over half of all patients admitted with acute ischemic stroke (AIS) suffer gastrointestinal complications. Our goal was to determine the burden of gastrointestinal bleeding (GIB) in hospitalized patients with AIS using the largest, all-payer, inpatient database in the United States. *Methods:* The Nationwide Inpatient Sample (2002-2011) was queried to identify all adult patients with a primary diagnosis of AIS with and without a secondary diagnosis of GIB. We used multivariable analyses, adjusting for pertinent confounders, to identify risk factors for GIB in AIS patients and to determine the effect of GIB on in-hospital complications and outcomes. *Results:* Of 3,988,667 patients hospitalized for AIS, there were 49,348 cases of GIB (1.24%). In multivariable analysis, patients with a history of peptic ulcer disease (odds ratio [OR]: 2.45, 95% confidence interval [CI]: 2.10-2.86) and liver disease (OR: 2.42, 95% CI: 2.26-2.59) were more likely to suffer GIB. Patients suffering from GIB were more likely to require intubation (OR: 2.04, 95% CI: 1.95-2.13) and blood transfusion (OR: 11.31, 95% CI: 11.00-11.63). The occurrence of GIB increased hospital length of stay by an average of 5.8 days and total costs by $14,120 per patient (all $P < .0001$). GIB was independently associated with a 46% increased likelihood of severe disability and 82% increased likelihood of in-hospital death (all $P < .0001$). *Conclusions:* GIB occurrence in patients with AIS is relatively rare but is associated with poor in-hospital outcomes, including mortality. We identified risk factors associated with GIB in AIS, which allows physicians to monitor patient populations at the highest risk. **Key Words:** Gastrointestinal bleed—gastrointestinal hemorrhage—stroke complications—stroke outcomes—nationwide inpatient sample.

Introduction

Hospitalized acute ischemic stroke (AIS) patients are at a high risk for various medical complications, which increase morbidity and mortality.[1] Gastrointestinal bleeding (GIB) may be associated with a poor prognosis in patients hospitalized for AIS.[1]

The association between GIB and AIS has been previously described in several countries.[2-7] However, due to the relatively rare nature of GIB in AIS, its epidemiology and impact on outcomes in patients hospitalized for AIS remains poorly characterized. An epidemiological population-based analysis of GIB in AIS has not been previously reported in the United States.

In the present study, we examined the incidence, risk factors, other hospital complications, and in-hospital outcomes associated with GIB in AIS using discharge data obtained from the Nationwide Inpatient Sample (NIS), Healthcare Cost and Utilization Project (HCUP), and Agency for Healthcare Research and Quality.

From the Department of Neurology, University of Kansas Medical Center, Kansas City, Kansas.

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Address correspondence to Manoj K. Mittal, MD, Department of Neurology, University of Kansas Medical Center, MS 2012, 3599 Rainbow Blvd, Kansas City, KS 66160. E-mail: mmittal2@kumc.edu.

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Methods

Data Source

The NIS is the largest and most widely used all-payer database of inpatient hospitalizations available in the United States. The NIS is a stratified sample of approximately 20% of all hospital discharges in the United States, which equates to approximately 8 million hospitalizations per year.[8] However, the application of HCUP discharge weights allows for national estimates and reliable results. Each unique deidentified discharge record consists of a number of patient-level, hospital-level, and outcome-level variables. The discharge records also contain 1 primary diagnosis field and 14 secondary diagnosis fields or less. Specific diagnoses and procedures can be identified in the NIS using International Classification of Diseases, Ninth Edition, Clinical Modification (ICD-9-CM) and Clinical Classification Software (CCS) codes. The CCS codes are provided by HCUP with the purpose of collapsing the multitude of ICD-9-CM diagnosis and procedure codes into clinically relevant categories.[8] As a data cleansing mechanism, discharge records with missing information for crucial variables such as age, gender, year, discharge quarter, or primary diagnosis were excluded.[9] According to the HCUP data agreement, authors are not allowed to disclose information in which the number of observations in any given cell is less than 11 cases. As the NIS is considered a publicly available deidentified database, our institution considered the present study exempt from institutional review board approval.

Inclusion Criteria

The NIS was queried from 2002 to 2011 and all hospitalizations for ischemic stroke were accessed using primary ICD-9-CM codes (433.01, 433.10, 433.11, 433.21, 433.31, 433.81, 433.91, 434.00, 434.01, 434.11, 434.91, and 436).[10,11] Patients suffering from GIB during hospitalization were identified by searching all secondary diagnosis fields for the CCS code 153. Patients admitted electively and those below the age of 18 were excluded from this analysis.

Variables of Interest

The patient-level variables were age (18-44, 45-59, 60-74, 75+), sex (male or female), race (white, black, Hispanic, Asian or Pacific Islander, Native American, other), and payer status (Medicare, Medicaid, private," or other). Hospital-level variables included hospital location (rural or urban), bed size (small, medium, or large), teaching status (nonteaching or teaching), and admission day (weekday or weekend). HCUP defined the names for all of these variables. The Elixhauser comorbidity groupings identify 31 pre-existing comorbidities that are known to influence in-hospital outcomes.[12] The Elixhauser comorbidity "blood loss anemia" was excluded from analyses due to its strong overlap and potentially confounding effect with gastrointestinal hemorrhage. We used ICD-9-CM procedure codes to identify the in-hospital interventions of cerebral angiography (88.41), intravenous thrombolytic therapy (99.10), and mechanical thrombectomy (39.74). In-hospital complications included intracerebral hemorrhage (431), pneumonia (486, 481, 482.8, and 482.3), deep vein thrombosis (DVT; 451.1, 451.2, 451.81, 451.9, 453.1, 453.2, 453.8, and 453.9), pulmonary embolism (PE; 415.1), urinary tract infection (UTI; 599.0 and 590.9), septicemia (995.91, 996.64, 038.0, 995.92, and 999.3), acute kidney injury (AKI; 584.5-584.9), intubation (96.04), tracheostomy (31.10, 31.20, 31.21, and 31.29), mechanical ventilation (96.72), gastrostomy (43.11-43.19), and blood transfusion (99.04).[13-15] We assessed the in-hospital outcomes of length of stay (LOS), total hospital costs, discharge disposition, and in-hospital mortality. Total hospital costs were calculated using the NIS total charge variable and the HCUP cost-to-charge ratio files.[16] To adjust costs from each year to the 2011 U.S. dollar, we used an Internet-based inflation calculator from the Bureau of Labor Statistics for conversion rates.[17] To allow certain continuous variables to serve as outcome variables in binary logistic regression models, these variables were dichotomized based on standard deviation and percentiles. The variables "LOS" and "total hospital costs" were recoded into dichotomous outcome variables of "prolonged LOS" (at or above the 90th percentile for costs) and "increased costs" (at or above the 90th percentile for costs). The NIS-defined variable "discharge disposition" was recoded into categories of "none or minimal disability" (routine discharge) or "moderate to several disability" (transfer to short-term hospital, home health care, transfer to long-term facility, or mortality).[18]

Statistical Analysis

We used the SPSS v.23 statistical software for all statistical analyses (SPSS, Inc., Chicago, IL) and an alpha level or a P value less than .0001 determined the statistical significance. In a bivariate analysis utilizing the chi-square test, patient demographics, pre-existing comorbidity, hospital type, in-hospital procedures, in-hospital complications, and in-hospital outcomes were compared among AIS patients with and without GIB. Factors with a P level less than .05 in the bivariate analysis and at least 10 cases were included in subsequent multivariable logistic regression models and only statistically significant variables were retained in the model. This model was used to identify the factors that were independently associated with the development of GIB in patients with AIS. We included other concomitant in-hospital complications as predictor covariates in all multivariable models to adjust for the potential confounding effect on in-hospital outcomes. In additional multivariable models, we examined the independent effect of GIB occurrence on prolonged