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***Retrospective Cohort Study***

**Hospital teaching status on the outcomes of patients with esophageal variceal bleeding in the United States**

Patel P *et al.* Outcomes of variceal bleeding

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**Abstract**

BACKGROUND

Acute variceal bleeding is a major complication of portal hypertension and is a leading cause of death in patients with cirrhosis. There is limited data on the outcomes of patients with esophageal variceal bleeding in teaching versus nonteaching hospitals. Because esophageal variceal bleeding requires complex management, it may be hypothesized that teaching hospitals have lower mortality.

AIM

To assess the differences in mortality, hospital length of stay (LOS) and cost of admission for patients admitted for variceal bleed in teaching versus nonteaching hospitals across the US.

METHODS

The National Inpatient Sample is the largest all-payer inpatient database consisting of approximately 20% of all inpatient admissions to nonfederal hospitals in the United States. We collected data from the years 2008 to 2014. Cases of variceal bleeding were identified using the International Classification of Diseases, Ninth Edition, Clinical Modification codes. Differences in mortality, LOS and cost were evaluated for patients with esophageal variceal bleed between teaching and nonteaching hospitals and adjusted for patient characteristics and comorbidities.

RESULTS

Between 2008 and 2014, there were 58362 cases of esophageal variceal bleeding identified. Compared with teaching hospitals, mortality was lower in non-teaching hospitals (8.0% *vs* 5.3%, *P* < 0.001). Median LOS was shorter in nonteaching hospitals as compared to teaching hospitals (4 d *vs* 5 d, *P* < 0.001). A higher proportion of non-white patients were managed in teaching hospitals. As far as procedures in nonteaching *vs* teaching hospitals, portosystemic shunt insertion (3.1% *vs* 6.9%, *P* < 0.001) and balloon tamponade (0.6% *vs* 1.2%) were done more often in teaching hospitals while blood transfusions (64.2% *vs* 59.9%, *P* = 0.001) were given more in nonteaching hospitals. Using binary logistic regression models and adjusting for baseline patient demographics and comorbid conditions the mortality, LOS and cost in teaching hospitals remained higher.

CONCLUSION

In patients admitted for esophageal variceal bleeding, mortality, length of stay and cost were higher in teaching hospitals versus nonteaching hospitals when controlling for other confounding factors.

**Key words:** Variceal bleeding; Teaching hospital; Mortality; National Inpatient Sample; Length of stay; Bleeding; Cirrhosis

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**Core tip:** This study assesses the outcomes of patients that present to the hospital with variceal bleeding amongst teaching and non-teaching hospitals. Patients that were managed at teaching facilities had higher mortality, length of stay and cost of hospitalization when compared to those at non-teaching facilities.

**Introduction**

Acute variceal bleeding (AVB) as a direct consequence of portal hypertension remains the most lethal complication amongst cirrhotic patients. Over the past three decades, mortality due to variceal bleeding has steadily decreased in concurrence with improved endoscopic and pharmacological therapies, including endoscopic sclerotherapy, banding ligation, vasoactive agents, and antibiotic prophylaxis[1–3]. In addition, a more efficient approach to improve hemodynamic stability, reduce portal pressure, and endoscopically treat variceal bleeding has now become the cornerstone of treatment in AVB[3]. Prompt endoscopic therapy (≤ 12 h) for AVB has also been associated with better outcomes in cirrhotic patients[4]. Early re-bleeding within 3-5 d of endoscopic therapy remains at approximately 20% for which aggressive treatment and early transjugular intrahepatic portosystemic shunt (TIPS) placement has shown increasing survival rates[5]. Despite this progression in treatment modalities, bleeding from gastroesophageal varices maintains a 6-wk mortality in approximately 15%-20% of patients with underlying cirrhosis[5]. Therefore, facilities to manage these cases require the necessary equipment and health-care personnel to initiate un-delayed treatment, prevent early re-bleeding, and decrease overall mortality.

It has been widely debated that certain disparities exist in delivery of medical care and patient safety outcomes when comparing teaching to nonteaching hospital[6]. While earlier studies have reported higher quality care and better patient outcomes in teaching hospitals, others have considered this evidence unsubstantial[6-10]. It has been further proposed that differences in patient outcomes within teaching versus nonteaching hospitals vary amongst multiple patient settings and specific diseases[10]. For instance, one study has demonstrated that among common medical conditions, such as acute myocardial infarction and congestive heart failure, teaching hospitals have lower mortality rates when compared to non-teaching hospitals[11]. Certain studies have shown that teaching hospitals may have higher rates of iatrogenic injury, though the underlying reasoning for this discrepancy has not been determined[12]. Furthermore, with the enactment of resident work hour regulations for teaching hospitals, trends in patient safety outcomes and mortality have been highly scrutinized[7,11]. Although duty hour limitations have been associated with a decrease in overall mortality, data for patients admitted for gastrointestinal bleeding remained equivocal between hospital settings[7].

An increasing amount of studies have focused on evaluating the most cost-effective manner in which to practice medicine. There has been an association between teaching hospitals and high-quality care because of their ability to provide specialized health care, perform advanced procedures, act as leaders in medical education and research, and offer care for the underserved populations[7,8]. Within the current era of healthcare reform, most studies have shown higher costs in teaching hospitals compared with community facilities. This could be attributed to the utilization of more advanced, expensive diagnostic testing without any demonstrable improvement in outcomes[13-15]. In regards to AVB, recent studies have suggested the average cost of in-hospital treatment to be $6612 for those without any complications, and $23207 for those with complications[16]. After adjusting for geographic cost of living and patient factors, cost per case were similar across hospital type[17].

Due to the complexity in management of esophageal variceal bleeding, one can hypothesize that teaching hospitals have lower mortality. Given the limited data on outcomes of patients with variceal bleeding in teaching versus nonteaching hospitals, our study aims to assess the differences in mortality, length of stay (LOS), and hospital costs for patients admitted for AVB among different hospital settings within the United States.

**MATERIALS AND METHODS**

***Data source***

The National Inpatient Sample (NIS), maintained by the Healthcare Cost and Utilization Project (HCUP) of the Agency for Healthcare Research and Quality, is the largest database of inpatient hospital stays in the United States[18]. The NIS collects data from a 20% stratified sample of United States hospitals from 37 states and has been reliably used to estimate disease burden and outcomes. Each individual hospitalization is de-identified and maintained in the NIS as a unique entry with 1 primary discharge diagnosis and up to 29 secondary diagnoses during that hospitalization depending on the year of data collection. Each entry also carried information on patient demographics including age, sex, race, insurance status, primary and secondary procedures (up to 14), hospitalization outcome, total charges, and length of stay (LOS).

***Study sample***

The International Classification of Diseases 9th Version, Clinical Modification (ICD-9 CM) diagnosis codes (456.0 and 456.2) were used to identify patients (≥ 18 years) hospitalized with a primary diagnosis of esophageal variceal bleeding admitted between 2008 and 2014. If a patient had any other liver related diagnosis code (Supplementary Table 1) as their primary diagnosis they were also included. All patients that were admitted electively were excluded due to the inconsistency of elective admission and emergent nature of acute variceal bleeding. Only patients that had an EGD performed were included since endoscopy is necessary to diagnose a variceal bleed and also to exclude causes of nonvariceal upper GI bleeding. Cases that did not have mortality data or hospital teaching status were excluded. In total, 58362 cases were found using the above inclusion criteria. Secondary outcome variables were LOS and cost of hospitalization.

***Hospital teaching status***

Our primary exposure variable was the teaching status of the hospital each patient was treated at. In the NIS database, this data is divided into three separate categories: rural, urban-nonteaching and urban teaching. For our study, the rural and urban-nonteaching categories were combined into one category termed non-teaching while the urban teaching category was used to delineate all teaching hospitals.

***Predictive variables***

Other variables that were studied included age (divided into three groups; < 40 years, 40-59 years and > 60 years), gender, race, primary payer, hospital location, hospital bed size, and transfer status (in from another acute care hospital *vs* not a transfer).

In order to assess for comorbidities, the data was extracted to include the Elixhauser comorbidity Index[19]. This is a well-validated index based on ICD-9-CM codes that is meant to be used in large administrative data to predict mortality and hospital resource use[20]. The index has 30 comorbid categories that include both liver disease and coagulopathy. Due to the nature of our primary diagnosis, we excluded both of these variables from our index and therefore studied only 28 comorbidities. Since the NIS does not allow us to determine the severity of liver disease using either the Child-Pugh classification or Model for End Stage Liver Disease (MELD) score we assessed for separate conditions associated with liver decompensation. These included ascites (ICD-9-CM 789.5 and 789.59), hepatic encephalopathy (ICD-9-CM 572.2), spontaneous bacterial peritonitis (ICD-9-CM 567.23), hepatorenal syndrome (ICD-9-CM 572.4) and hepatocellular carcinoma (ICD-9-CM 155.0). Furthermore, we also separately analyzed data for patients with alcoholic cirrhosis (ICD-9-CM 571.2) as their underlying liver disease as this is one of the most common liver etiologies of variceal bleeding. Finally, common management options for esophageal variceal bleeding were also identified. These included blood transfusions (ICD-9-CM 99.00, 99.04, 99.05, 99.06, 99.07), balloon tamponade (ICD-9-CM 44.93 and 96.06), and portosystemic shunt (ICD-9-CM 39.1).

***Statistical analysis***

Hospital-level discharge weights provided by NIS were used to generate national estimates. Categorical variables were compared using the chi-square, whereas independent sample T test was used for continuous variables. Using binary logistic regression models mortality, LOS, and cost were examined after adjusting for baseline patient demographics, hospital details, procedures, and comorbid conditions. A *p*-value of < 0.05 was considered significant.

Inpatient cost of hospitalization was calculated by merging data from the NIS database with cost-to-charge ratios available from the Healthcare Cost and Utilization Project of the Agency for Healthcare Research and Quality. Given total charges for each inpatient stay available in the database, costs were then calculated by multiplying the total hospital charge with cost-to-charge ratios which were used to account for the inherent variability among hospitals and regions. All costs were adjusted for inflation according to the latest consumer price index data released by the United States government in December of 2017.

All analyses were performed using SPSS Statistics 23 (IBM Corp, Armonk, NY, United States).

**Results**

Between 2008 and 2014 there were 58362 admissions for esophageal variceal bleeding that fit our inclusion criteria (7295 annually based on study period).

***Teaching status of hospital***

Amongst hospital admissions for esophageal variceal bleeding, a total of 30382 took place in teaching hospitals while 27979 took place in non-teaching hospitals. Demographics and hospital characteristics are provided in Table 1. The average overall age of patients presenting with variceal bleeding was 55 (SD of 12) with a male predominance. More than half of the patients were Caucasian. The primary insurance payer was Medicare for a majority of the patients. A large portion of patients were treated in large hospitals (based on hospital region) and in the southern US. Though most patients were treated as initial admissions directly to the hospital under investigation, a small portion (7.4%) were transferred in from another acute care hospital.

In comparing teaching hospitals to non-teaching hospitals, the above characteristics remained true. Teaching hospitals had a higher percentage of minority patients compared to non-teaching hospitals. Teaching hospitals also had more Medicaid patients while non-teaching hospitals had more Medicare patients. A higher percentage of teaching hospitals with variceal bleeding was located in the Northeast and Midwest while a higher percentage of non-teaching hospitals was located in the South and the West. Furthermore, teaching hospitals had a greater percentage of transfers from outside acute care hospitals compared to non-teaching hospitals (11.5% *vs* 3.0% respectively).

Comorbid conditions as well as management for these patients can be seen in Table 2. Amongst all patients, more than half had greater than or equal to three comorbid conditions other than their underlying liver disease as determined by the Elixhauser comorbidity index. Between group differences were not statistically significant however.

More importantly, teaching hospitals were more likely to admit patients with alcoholic cirrhosis (53.0% *vs* 50.6%), features of hepatic decompensation (ascites, hepatic encephalopathy), hepatorenal syndrome (4.2% *vs* 2.2%), and hepatocellular carcinoma (4.6% *vs* 2.5%) when compared to non-teaching hospitals.

In terms of management, non-teaching hospitals had a higher rate of transfusion (64.2% *vs* 59.9%) as compared to teaching hospitals and a lower rate of balloon tamponade (0.6% *vs* 1.2%) and portosystemic shunt (3.1% *vs* 7.9%). The *P* value was < 0.001 for all comparisons.

***Mortality***

The overall mortality for all patients presenting with esophageal variceal bleeding was 6.7% in our study population. The unadjusted mortality was higher in teaching hospitals when compared to non-teaching hospitals (8.0% *vs* 5.3% respectively, *P* < 0.001). Mortality was higher amongst patients that were black males, older than 60 years, admitted to a large hospital, and transferred from another acute care hospital. These findings are outlined in Table 3.

Furthermore, there was also a significant difference amongst hospital teaching status and mortality when comparing comorbid conditions and management decisions (Table 4). There was a higher mortality in teaching hospitals in those patients with underlying alcoholic cirrhosis when compared to non-teaching hospitals (9.2% *vs* 6.3%) though this was not statistically different. The presence of liver decompensation (ascites and hepatic encephalopathy) was also associated with higher mortality in teaching hospitals compared to non-teaching hospitals. Hepatorenal syndrome and/or hepatocellular carcinoma also portended a higher risk for mortality in teaching hospitals. As far as management, mortality was higher in teaching hospitals when blood transfusions (8.7% *vs* 6.2%) or portosystemic shunts were performed (17.1% *vs* 9.9%) compared to non-teaching hospitals.

After adjustment for baseline patient characteristics including demographics, comorbid conditions, evidence of liver decompensation, management and transfer status the only significant factors that were associated with higher mortality were gender, race, transfer in from outside hospital and teaching status of hospital. Males had a higher rate of mortality when compared to females with adjusted OR 1.271 (95%CI: 1.075-1.503) as did Blacks when compared to Whites with adjusted OR 1.607 (95%CI: 1.246-2.074). Patients that were transferred in from an acute care hospital had a higher mortality than those that did not with an adjusted OR 1.490 (95%CI: 1.172-1.894). Overall, the adjusted OR of mortality in teaching hospitals compared to non-teaching hospitals was 1.249 (95%CI: 1.066-1.463) (Table 3).

***Length of stay and cost of hospitalization***

The median length of stay for all centers was 4 d with an interquartile range (IQR) of 3-7. Teaching hospitals had a median LOS of 5 d while non-teaching hospitals had a LOS of 4 d. The cost of hospitalization overall was $19049 in all centers. Teaching hospitals had a significantly higher cost of hospitalization of $22355 compared to non-teaching hospitals at $15535 (Table 5). Using linear regression analysis and controlling for baseline patient demographics, hospital characteristics, liver decompensation, associated conditions and management, the LOS and cost remained higher in teaching hospitals compared to non-teaching hospitals (Table 6).

**Discussion**

Given the advancements in pharmacologic and endoscopic interventions, mortality rates have improved[21]. Esophageal band ligation (EBL) has largely become standard of care due to its lower rate of complications, mortality and rebleeding[22]. Though the rates of mortality due to acute variceal bleeding are steadily declining, this complication of portal hypertension still remains one of the leading causes of death in cirrhotic patients[1]. Our study looked at 58362 cases of esophageal variceal bleeding in teaching and nonteaching hospitals between 2008 and 2014 and found that both mortality and length of stay was lower in non-teaching hospitals. In our hospitalized patient population, we found that a higher proportion of patients in teaching hospitals were of non-white race and underwent more rescue procedures (portosystemic shunt insertion). However, blood transfusions were more commonly given in nonteaching hospitals.

While upper gastrointestinal bleeding has previously been associated with a high mortality (up to 10%)[23,24], recent studies have shown that the mortality rate has decreased over the past 20 years to as low as 2.1%[21]. Additionally, rates of EGD performed early in the hospital stay have been steadily increasing over the same time period[21]. Interventions that are performed during EGD to limit bleeding, likely explain the reductions in mortality, transfusions and need for further supportive therapies such as vasopressors or ICU stays. Delays in EGD in nonteaching hospitals, may therefore, explain the higher rates of transfusions in those institutions but not the decreased mortality.

Our study revealed that hospital costs were higher in teaching hospitals. Prior studies have found that the overall cost during the hospitalization, including the cost of any procedures, were higher in patients who did not undergo early EGD[25].

A main strength of our study is that our sample size is representative of the inpatient population throughout the United States. It is unique in that it looks at the differences among teaching versus nonteaching hospitals in a study population that is nationally representative. Our study period was recent, from 2008 to 2014, and thus reflective of recent endoscopic management for esophageal variceal bleeds.

The current study has several limitations. First, the NIS is a database reliant on the delineation and coding of medical diagnoses, which if performed incorrectly can predispose to classification errors and inaccuracies. Second, a patient’s clinical acuity, preoperative and intraoperative performance status, and endoscopic procedure findings cannot be accessed within the NIS[26]. Third, the inherent features of the database do not allow us to fully assess a patient’s hospital course. This further limits our ability to distinguish temporal relationships between medical diagnoses and their causality with patient outcomes. Fourth, we did not include patients diagnosed with an AVB after admission to the hospital, which could have underestimated rates of mortality. Fifth, we were also unable to discern rates of re-bleeding post endoscopic intervention or if these AVB events were primary or recurrent, which if recurrent would place a patient at a higher risk of mortality[27,28]. Moreover, pertinent variables including lab values, endoscopic findings and therapies, vital signs were missing as these are not available using the NIS database. Lastly, pharmacological therapy such as octreotide as well as prophylaxis measures with nonselective beta-blockers is not included in the NIS, which are important confounders that may have affected patient outcome between hospital settings.

Despite this, the findings are intriguing. Further prospective studies may need to be completed in order to determine causality and delineate whether teaching status affects patient outcomes.

**ARTICLE HIGHLIGHTS**

***Research background***

Acute variceal bleeding is a major complication of portal hypertension and is a leading cause of death in patients with cirrhosis. There is limited data on the outcomes of patients with esophageal variceal bleeding in teaching versus nonteaching hospitals.

***Research motivation***

To understand if the teaching status of a hospital has better or poorer outcomes in management of patients with variceal bleeding.

***Research objectives***

Compare outcomes of mortality, length of stay and cost of hospitalization amongst patients presenting with acute variceal bleeding in cohorts of teaching *vs* nonteaching hospitals.

***Research methods***

We looked at retrospective data from a large national database of patients that presented with acute variceal bleeding

***Research results***

The mortality, length of stay and cost of hospitalization was higher amongst patients with acute variceal bleeding that presented to a teaching hospital. When controlling for comorbidities and hospital characteristics this remained statistically significant.

***Research conclusions***

Teaching hospitals did worse in outcomes for patients with variceal bleeding when compared to non-teaching hospitals. Further details may need to be deciphered as to what could contribute to these findings.

***Research perspectives***

Prospective studies at teaching and non-teaching institutions when controlling for severity of illness can shed light on whether teaching hospitals need to improve their delivery of care for patients with variceal bleeding.

**REFERENCES**

1 **Carbonell N**, Pauwels A, Serfaty L, Fourdan O, Lévy VG, Poupon R. Improved survival after variceal bleeding in patients with cirrhosis over the past two decades. *Hepatology* 2004; **40**: 652-659 [PMID: 15349904 DOI: 10.1002/hep.20339]

2 **El-Serag HB**, Everhart JE. Improved survival after variceal hemorrhage over an 11-year period in the Department of Veterans Affairs. *Am J Gastroenterol* 2000; **95**: 3566-3573 [PMID: 11151893 DOI: 10.1016/S0002-9270(00)02169-9]

3 **D'Amico G**, De Franchis R; Cooperative Study Group. Upper digestive bleeding in cirrhosis. Post-therapeutic outcome and prognostic indicators. *Hepatology* 2003; **38**: 599-612 [PMID: 12939586 DOI: 10.1053/jhep.2003.50385]

4 **Chen PH**, Chen WC, Hou MC, Liu TT, Chang CJ, Liao WC, Su CW, Wang HM, Lin HC, Lee FY, Lee SD. Delayed endoscopy increases re-bleeding and mortality in patients with hematemesis and active esophageal variceal bleeding: a cohort study. *J Hepatol* 2012; **57**: 1207-1213 [PMID: 22885718 DOI: 10.1016/j.jhep.2012.07.038]

5 **Garcia-Tsao G**, Bosch J. Management of varices and variceal hemorrhage in cirrhosis. *N Engl J Med* 2010; **362**: 823-832 [PMID: 20200386 DOI: 10.1056/NEJMra0901512]

6 **International Working Party to Promote and Revitalise Academic Medicine**. Academic medicine: the evidence base. *BMJ* 2004; **329**: 789-792 [PMID: 15459055 DOI: 10.1136/bmj.329.7469.789]

7 **Shetty KD**, Bhattacharya J. Changes in hospital mortality associated with residency work-hour regulations. *Ann Intern Med* 2007; **147**: 73-80 [PMID: 17548403 DOI: 10.7326/0003-4819-147-2-200707170-00161]

8 **Shelton J**, Kummerow K, Phillips S, Arbogast PG, Griffin M, Holzman MD, Nealon W, Poulose BK. Patient safety in the era of the 80-hour workweek. *J Surg Educ* 2014; **71**: 551-559 [PMID: 24776874 DOI: 10.1016/j.jsurg.2013.12.011]

9 **Au AG**, Padwal RS, Majumdar SR, McAlister FA. Patient outcomes in teaching versus nonteaching general internal medicine services: a systematic review and meta-analysis. *Acad Med* 2014; **89**: 517-523 [PMID: 24448044 DOI: 10.1097/ACM.0000000000000154]

10 **Papanikolaou PN**, Christidi GD, Ioannidis JP. Patient outcomes with teaching versus nonteaching healthcare: a systematic review. *PLoS Med* 2006; **3**: e341 [PMID: 16968119 DOI: 10.1371/journal.pmed.0030341]

11 **Mueller SK**, Lipsitz S, Hicks LS. Impact of hospital teaching intensity on quality of care and patient outcomes. *Med Care* 2013; **51**: 567-574 [PMID: 23604017 DOI: 10.1097/MLR.0b013e3182902151]

12 **John J**, Seifi A. Incidence of iatrogenic pneumothorax in the United States in teaching vs. non-teaching hospitals from 2000 to 2012. *J Crit Care* 2016; **34**: 66-68 [PMID: 27288612 DOI: 10.1016/j.jcrc.2016.03.013]

13 **Singh S**, Purohit T, Aoun E, Patel Y, Carleton N, Mitre M, Morrissey S, Dhawan M, Thakkar S. Comparison of the outcomes of endoscopic ultrasound based on community hospital versus tertiary academic center settings. *Dig Dis Sci* 2014; **59**: 1925-1930 [PMID: 24573718 DOI: 10.1007/s10620-014-3075-9]

14 **Surgenor SD**, Corwin HL, Clerico T. Survival of patients transferred to tertiary intensive care from rural community hospitals. *Crit Care* 2001; **5**: 100-104 [PMID: 11299068 DOI: 10.1186/cc993]

15 **Caveney AF**, Silbergleit R, Frederiksen S, Meurer WJ, Hickenbottom SL, Smith RW, Scott PA. Resource utilization and outcome at a university versus a community teaching hospital in tPA treated stroke patients: a retrospective cohort study. *BMC Health Serv Res* 2010; **10**: 44 [PMID: 20170487 DOI: 10.1186/1472-6963-10-44]

16 **Adam V**, Barkun AN. Estimates of costs of hospital stay for variceal and nonvariceal upper gastrointestinal bleeding in the United States. *Value Health* 2008; **11**: 1-3 [PMID: 18237354 DOI: 10.1111/j.1524-4733.2007.00208.x]

17 **Shahian DM**, Nordberg P, Meyer GS, Blanchfield BB, Mort EA, Torchiana DF, Normand SL. Contemporary performance of U.S. teaching and nonteaching hospitals. *Acad Med* 2012; **87**: 701-708 [PMID: 22534588 DOI: 10.1097/ACM.0b013e318253676a]

18 **HCUP National Inpatient Sample (NIS)**. Healthcare Cost and Utilization Project (HCUP). 2012. [Internet]. Agency Healthc. Res. Qual. Rockville, MD. 2012. Available from: [www.hcup-us.ahrq.gov/nisoverview.jsp](http://www.hcup-us.ahrq.gov/nisoverview.jsp)

19 **Healthcare Cost and Utilization Project (HCUP)**. HCUP Elixhauser Comorbidity Software, Version 3.7 [Internet]. Agency Healthc. Res. Qual. 2017; Rockville, MD. 2017. Available from: [www.hcup-us.ahrq.gov/toolssoftware/comorbidity/comorbidity.jsp](http://www.hcup-us.ahrq.gov/toolssoftware/comorbidity/comorbidity.jsp)

20 **Southern DA**, Quan H, Ghali WA. Comparison of the Elixhauser and Charlson/Deyo methods of comorbidity measurement in administrative data. *Med Care* 2004; **42**: 355-360 [PMID: 15076812 DOI: 10.1097/01.mlr.0000118861.56848.ee]

21 **Abougergi MS**, Travis AC, Saltzman JR. The in-hospital mortality rate for upper GI hemorrhage has decreased over 2 decades in the United States: a nationwide analysis. *Gastrointest Endosc* 2015; **81**: 882-888.e1 [PMID: 25484324 DOI: 10.1016/j.gie.2014.09.027]

22 **Laine L**, Cook D. Endoscopic ligation compared with sclerotherapy for treatment of esophageal variceal bleeding. A meta-analysis. *Ann Intern Med* 1995; **123**: 280-287 [PMID: 7611595 DOI: 10.7326/0003-4819-123-4-199508150-00007]

23 **Hwang JH**, Fisher DA, Ben-Menachem T, Chandrasekhara V, Chathadi K, Decker GA, Early DS, Evans JA, Fanelli RD, Foley K, Fukami N, Jain R, Jue TL, Khan KM, Lightdale J, Malpas PM, Maple JT, Pasha S, Saltzman J, Sharaf R, Shergill AK, Dominitz JA, Cash BD; Standards of Practice Committee of the American Society for Gastrointestinal Endoscopy. The role of endoscopy in the management of acute non-variceal upper GI bleeding. *Gastrointest Endosc* 2012; **75**: 1132-1138 [PMID: 22624808 DOI: 10.1016/j.gie.2012.02.033]

24 **Targownik LE**, Nabalamba A. Trends in management and outcomes of acute nonvariceal upper gastrointestinal bleeding: 1993-2003. *Clin Gastroenterol Hepatol* 2006; **4**: 1459-1466 [PMID: 17101296 DOI: 10.1016/j.cgh.2006.08.018]

25 **Garg SK**, Anugwom C, Campbell J, Wadhwa V, Gupta N, Lopez R, Shergill S, Sanaka MR. Early esophagogastroduodenoscopy is associated with better Outcomes in upper gastrointestinal bleeding: a nationwide study. *Endosc Int Open* 2017; **5**: E376-E386 [PMID: 28512647 DOI: 10.1055/s-0042-121665]

26 **Murphy M**, Alavi K, Maykel J. Working with existing databases. *Clin Colon Rectal Surg* 2013; **26**: 5-11 [PMID: 24436641 DOI: 10.1055/s-0033-1333627]

27 **D'Amico G**, Pagliaro L, Bosch J. Pharmacological treatment of portal hypertension: an evidence-based approach. *Semin Liver Dis* 1999; **19**: 475-505 [PMID: 10643630 DOI: 10.1055/s-2007-1007133]

28 **Bosch J**, García-Pagán JC. Prevention of variceal rebleeding. *Lancet* 2003; **361**: 952-954 [PMID: 12648985 DOI: 10.1016/S0140-6736(03)12778-X]

**Footnotes**

**Institutional review board statement**: This study did not require IRB approval due since the database is representative of nationally acquired data.

**Informed consent statement:** Due to the retrospective nature of this study as well as the using of a national database no human information was made available to authors. Therefore, informed consent was not needed to write this manuscript.

**Conflict-of-interest statement**: Authors declare no conflict of interest for this article.

**Data sharing statement**: No additional data are available.

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**Table 1 Patient demographics and hospital characteristics**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Variable** | **All (58362)** | **Teaching (30382)** | **Non-teaching (27979)** | ***P* value** |
| Patient age (yr) |  |  |  | < 0.001 |
| Median, (SD) | 55 (12.05) | 54 (11.83) | 55 (12.21) |  |
| Sex |  |  |  | 0.650 |
| Female | 18550 (31.8) | 9601 (31.6) | 8953 (32.0) |  |
| Male | 39803 (68.2) | 20781 (68.4) | 19026 (68.0) |  |
| Race |  |  |  | < 0.001 |
| White | 35192 (60.3) | 17166 (56.5) | 18018 (64.4) |  |
| Black | 4202 (7.2) | 2917 (9.6) | 1287 (4.6) |  |
| Hispanic | 11030 (18.9) | 5924 (19.5) | 5092 (18.2) |  |
| Asian or Pacific Islander | 1167 (2.0) | 668 (2.2) | 532 (1.90) |  |
| Native American | 875 (1.5) | 486 (1.6) | 392 (1.40) |  |
| Other | 1751 (3.0) | 1063 (3.5) | 699 (2.50) |  |
| Missing | 4144 (7.1) | 2188 (7.2) | 1959 (7.0) |  |
| Primary payer |  |  |  | < 0.001 |
| Medicare | 18442 (31.6) | 8720 (28.7) | 9709 (34.7) |  |
| Medicaid | 13540 (23.2) | 7869 (25.9) | 5680 (20.3) |  |
| Private and HMO | 14824 (25.4) | 7960 (26.2) | 6855 (24.5) |  |
| Self-pay | 7587 (13.0) | 3767 (12.4) | 3805 (13.6) |  |
| No charge | 700 (1.2) | 425 (1.4) | 308 (1.1) |  |
| Other | 3268 (5.6) | 1671 (5.5) | 1539 (5.5) |  |
| Hospital bed size |  |  |  | < 0.001 |
| Small | 6245 (10.7) | 4102 (13.5) | 2182 (7.8) |  |
| Medium | 15408 (26.4) | 8051 (26.5) | 7386 (26.4) |  |
| Large | 36710 (62.9) | 18229 (60.0) | 18410 (65.8) |  |
| Hospital region |  |  |  | < 0.001 |
| Northeast | 10564 (18.1) | 6988 (23.0) | 3581 (12.8) |  |
| Midwest | 9571 (16.4) | 5621 (18.5) | 3917 (14.0) |  |
| South | 23170 (39.7) | 11636 (38.3) | 11555 (41.3) |  |
| West | 15057 (25.8) | 6137 (20.2) | 8925 (31.9) |  |
| Transfer in from acute care hospital |  |  |  | < 0.001 |
| Yes | 4319 (7.4) | 3494 (11.5) | 839 (3.0) |  |
| No | 54043 (92.6) | 26888 (88.5) | 27140 (97.0) |  |

**Table 2 Patient comorbidities and management**

|  |  |  |  |
| --- | --- | --- | --- |
| **Variable** | **All (58362)** | **Teaching (30382)** | **Non-teaching (27979)** |
|
| Elixhauser comorbiditiesa |  |  |  |
| 0 | 2568 (4.4) | 1398 (4.6) | 1175 (4.2) |
| 1 | 8929 (15.3) | 4679 (15.4) | 4281 (15.3) |
| 2 | 14707 (25.2) | 7565 (24.9) | 7135 (25.5) |
| ≥ 3 | 32157 (55.1) | 16740 (55.1) | 15388 (55.0) |
| Liver comorbidities |  |  |  |
| Alcoholic cirrhosis | 30232 (51.8) | 16102 (53.0) | 14157 (50.6) |
| Ascites | 19551 (33.5) | 10998 (36.2) | 8534 (30.5) |
| Hepatic encephalopathy | 9280 (15.9) | 5286 (17.4) | 4001 (14.3) |
| SBP | 1109 (1.9) | 760 (2.5) | 336 (1.2) |
| Hepatorenal syndrome | 1868 (3.2) | 1276 (4.2) | 616 (2.2) |
| Coagulopathya | 27255 (46.7) | 14340 (47.2) | 12870 (46.0) |
| Hepatocellular carcinoma | 2101 (3.6) | 1398 (4.6) | 699 (2.5) |
| Management |  |  |  |
| Blood transfusion | 36184 (62.0) | 18199 (59.9) | 17963 (64.2) |
| Balloon tamponade | 525 (0.9) | 365 (1.2) | 168 (0.6) |
| Portosystemic shunt | 3268 (5.6) | 2400 (7.9) | 867 (3.1) |

a*P* > 0.05 in comparison between groups. All data are proportions [*n* (%)]. Comparisons between groups made with *χ2* test. All comparisons had *P* < 0.001 between groups unless otherwise stated.

**Table 3 Mortality associated with patient demographics and hospital characteristics**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Variable** | **Mortality (%)a** | **Unadjusted OR (95%CI)** | **Adjusted OR (95%CI)1** | ***P* value** |
|
| Patient age (yr) |  |  |  | 0.226 |
| Age < 40 | 5.5% | 1.0 | 1.0 |  |
| Age 40-59 | 6.7% | 1.226 (0.900-1.669) | 1.182 (0.858-1.628) | 0.196 |
| Age > 60 | 7.1% | 1.312 (0.955-1.801) | 1.397 (0.989-1.974) | 0.094 |
| Sex |  |  |  | 0.001 |
| Female | 5.6% | 1.0 | 1.0 |  |
| Male | 7.3% | 1.323 (1.126-1.555) | 1.271 (1.075-1.503) | 0.005 |
| Race |  |  |  | 0.001 |
| White | 6.4% | 1.0 | 1.0 |  |
| Black | 10.2% | 1.664 (1.308-2.118) | 1.607 (1.246-2.074) | < 0.001 |
| Hispanic | 6.1% | 0.948 (0.778-1.155) | 0.942 (0.766-1.157) | 0.567 |
| Asian or Pacific Islander | 6.6% | 1.040 (0.621-1.742) | 1.046 (0.619-1.768) | 0.867 |
| Native American | 6.7% | 1.062 (0.587-1.922) | 1.071 (0.572-2.002) | 0.831 |
| Other | 7.6% | 1.214 (0.971-1.518) | 1.131 (0.895-1.429) | 0.304 |
| Primary payer |  |  |  | 0.001 |
| Medicare | 6.7% | 1.0 | 1.0 |  |
| Medicaid | 7.9% | 1.180 (0.978-1.423) | 1.027 (0.844-1.250) | 0.789 |
| Private and HMO | 6.0% | 0.887 (0.729-1.078) | 0.837 (0.683-1.026) | 0.087 |
| Self-pay | 7.2% | 1.069 (0.849-1.346) | 1.098 (0.864-1.395) | 0.445 |
| No charge | 4.0% | 0.580 (0.254-1.326) | 0.517 (0.214-1.247) | 0.142 |
| Other | 4.9% | 0.706 (0.487-1.025) | 0.671 (0.456-0.988) | 0.043 |
| Hospital bed size |  |  |  | 0.001 |
| Small | 5.2% | 1.0 | 1.0 |  |
| Medium | 5.8% | 1.115 (0.836-1.486) | 1.094 (0.814-1.470) | 0.551 |
| Large | 7.4% | 1.458 (1.123-1.892) | 1.272 (0.970-1.668) | 0.082 |
| Hospital region |  |  |  | 0.143 |
| Northeast | 7.4% | 1.0 | 1.0 |  |
| Midwest | 7.1% | 0.961 (0.760-1.216) | 0.960 (0.744-1.238) | 0.752 |
| South | 6.1% | 0.814 (0.667-0.994) | 0.914 (0.740-1.129) | 0.403 |
| West | 7.0% | 0.946 (0.766-1.169) | 1.110 (0.882-1.397) | 0.372 |
| Transfer in from acute care hospital |  |  |  | < 0.001 |
| No | 6.2% | 1.0 | 1.0 |  |
| Yes | 11.9% | 2.041 (1.643-2.536) | 1.490 (1.172-1.894) | 0.001 |
| Hospital teaching status |  |  |  | < 0.001 |
| Teaching | 8.0% | 1.557 (1.345-1.803) | 1.249 (1.066-1.463) | 0.006 |
| Non-teaching | 5.3% | 1.0 | 1.0 |  |

a*P* < 0.001 for all comparisons of crude mortality between groups in bivariate *χ2* analyses. 1Adjusted for age, sex, race, primary insurance, hospital bed size, region, transfer status, features of hepatic decompensation, and management.

**Table 4 Patient comorbidities and management with associated mortality**

|  |  |  |  |
| --- | --- | --- | --- |
| **Variable** | **Mortality overall (*n* = 58362)** | **Mortality teaching (*n* = 30382)** | **Mortality non-teaching (*n* = 27979)** |
|
| Elixhauser comorbidities |  |  |  |
| 0 | 4202 (7.2) | 3008 (9.9) | 1455 (5.2) |
| 1 | 4085 (7.0) | 2734 (9.0) | 1287 (4.6) |
| 2 | 4144 (7.1) | 2886 (9.5) | 1371 (4.9) |
| ≥ 3 | 3794 (6.5) | 2157 (7.1) | 1567 (5.6) |
| Liver comorbidities |  |  |  |
| Alcoholic cirrhosisa | 4494 (7.7) | 2795 (9.2) | 1763 (6.3) |
| Ascites | 5953 (10.2) | 3585 (11.8) | 2266 (8.1) |
| Hepatic encephalopathy | 9338 (16.0) | 5165 (17.0) | 3973 (14.2) |
| SBP | 11322 (19.4) | 8294 (27.3) | 1567 (5.6) |
| Hepatorenal syndrome | 23695 (40.6) | 12335 (40.6) | 11415 (40.8) |
| Coagulopathy | 4844 (8.3) | 2917 (9.6) | 1931 (6.9) |
| Hepatocellular carcinoma | 7821 (13.4) | 4770 (15.7) | 2266 (8.1) |
| Management |  |  |  |
| Blood transfusion | 4319 (7.4) | 2643 (8.7) | 1735 (6.2) |
| Balloon tamponade | 30290 (51.9) | 15616 (51.4) | 14857 (53.1) |
| Portosystemic shunt | 8871 (15.2) | 5195 (17.1) | 2770 (9.9) |

a*P* > 0.05 in comparison between groups. All data are proportions [*n* (%)]. Comparisons between groups made with *χ2* test. All comparisons had *P* < 0.001 between groups unless otherwise stated.

**Table 5 Length of stay and cost of hospitalization**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Variable** | **All (58362)** | **Teaching (30382)** | **Non-teaching (27979)** | ***P* value** |
|
| Length of stay |  |  |  | < 0.001 |
| Median (IQR) in days | 4 (3-7) | 5 (3-8) | 4 (3-6) |  |
| Cost of hospitalization |  |  |  | < 0.001 |
| Mean in US dollars (SD) | $19049 (11880) | $22355 (12996) | $15535 (10935) |   |

IQR: Interquartile range.

**Table 6 Mortality, length of stay and cost in teaching *vs* nonteaching logistic regression**

|  |  |  |  |
| --- | --- | --- | --- |
| **Variable** | **OR/coefficient** | **95%CI** | ***P* value** |
| Mortality | 1.249 | 1.066-1.463 | 0.006 |
| LOS | 1.72 | 1.46-1.97 | < 0.001 |
| Cost | 6651 | 5646-7656 | < 0.001 |

LOS: Length of stay; OR: Odds ratio.