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Decreasing Mortality Among Patients Hospitalized With Cirrhosis in the United States From 2002 Through 2010

Monica L. Schmidt,[1] A. Sidney Barritt,[2] Eric S. Orman,[3] and Paul H. Hayashi[2]

[1]University of North Carolina Liver Center and Gillings School of Global Public Health, [2]Division of Gastroenterology and Hepatology, University of North Carolina, Chapel Hill, North Carolina; [3]Division of Gastroenterology and Hepatology, Indiana University, Indianapolis, Indiana

This article has an accompanying continuing medical education activity on page e15. Learning Objective: Upon completion of this CME, successful learners will be able to identify temporal trends in inpatient cirrhosis outcomes in the US.

See editorial on page 897.

BACKGROUND & AIMS: It is not clear whether evidence-based recommendations for inpatient care of patients with cirrhosis are implemented widely or are effective in the community. We investigated changes in inpatient outcomes and associated features over time. **METHODS:** By using the Healthcare Cost and Utilization Project, National Inpatient Sample, we analyzed 781,515 hospitalizations of patients with cirrhosis from 2002 through 2010. We compared data with those from equal numbers of hospitalizations of patients without cirrhosis and patients with congestive heart failure (CHF), matched for age, sex, and year of discharge. The primary outcome was a change in discharge status over time. Factors associated with outcomes were analyzed by Poisson modeling. **RESULTS:** The mortality of patients with and without cirrhosis, and patients with CHF, decreased over time. The absolute decrease was significantly greater for patients with cirrhosis (from 9.1% to 5.4%) than for patients without cirrhosis (from 2.6% to 2.1%) or patients with CHF (from 2.5% to 1.4%) ($P < .01$). However, relative decreases were similar for patients with cirrhosis (41%) and patients with CHF (44%). For patients with cirrhosis, the independent mortality risk ratio decreased steadily to 0.50 by 2010 (95% confidence interval, 0.48–0.52), despite patients' increasing age and comorbidities. Hepatorenal syndrome, hepatocellular carcinoma, variceal bleeding, and spontaneous bacterial peritonitis were associated with a higher mortality rate, but the independent mortality risks for each decreased steadily. Sepsis was associated strongly with increased mortality, and the risk increased over time. **CONCLUSIONS:** Among patients with cirrhosis in the United States, inpatient mortality decreased steadily from 2002 through 2010, despite increases in patient age and medical complexity. Improvements in cirrhosis care may have contributed to increases in patient survival beyond those attributable to general improvements in inpatient care. Further improvements might require an increased use of proven therapies and the development of new treatments—particularly for sepsis.

Keywords: Liver Failure; Renal Failure; Decompensation; Predictors.

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Cirrhosis is the eighth leading cause of death and years of life lost in the United States.[1] The course of cirrhotic liver failure often requires hospitalizations for complications such as renal failure, variceal bleeding, ascites, hepatic encephalopathy, and hepatocellular carcinoma. In addition, cirrhosis affects the outcome of non–liver-related illnesses requiring hospitalization. Care of cirrhosis patients is complex and often is managed by a team of specialists including gastroenterologists, hepatologists, intensivists, and nephrologists. The risk of mortality can be high, but careful management can mitigate this risk.[2–5] Over the past 10 to 15 years, significant advancements have been made in the management of hepatorenal syndrome (HRS), variceal bleeding, spontaneous bacterial peritonitis (SBP), ascites, and hepatocellular carcinoma (HCC).[6–9] Such advances have led to the dissemination of several evidence-based practice guidelines by all 3 major hepatology associations.[10–12] Cirrhotic patients also may benefit from non–liver-specific guidelines such as sepsis care, particularly early identification of the systemic inflammatory response syndrome, and antibiotic administration.[13]

Studies have indicated that guideline dissemination and implementation are effective in changing practice behaviors and improving patient outcomes.[14,15] Therefore, we

Abbreviations used in this paper: CI, confidence interval; CHF, congestive heart failure; ED, emergency department; EGD, esophagogastroduodenoscopy; HCC, hepatocellular carcinoma; HCUP NIS, Healthcare Cost and Utilization Project, National Inpatient Sample; HRS, hepatorenal syndrome; ICD-9-CM, International Classification of Diseases, 9th revision, Clinical Modification; NC, noncirrhotic; RR, risk ratio; SBP, spontaneous bacterial peritonitis; TIPS, transvenous intrahepatic portosystemic shunt.

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hypothesized that guidelines for inpatient cirrhosis care have penetrated the wider medical community and have resulted in better outcomes. We analyzed a large, nationally representative sample of cirrhosis patients who were hospitalized from 2002 through 2010 across the United States. Our goal was to see if inpatient mortality of cirrhotic patients has improved over time and to evaluate clinical variables associated with mortality including specific cirrhosis-related diagnoses and interventions.

Materials and Methods

Data Source

Data were extracted from discharges in the Nationwide Inpatient Sample (NIS), Healthcare Cost and Utilization Project (HCUP), Agency for Healthcare Research and Quality for the years 2002–2010.[16] The HCUP NIS is a 20% stratified sample of hospitals in the United States. It is the largest all-payer inpatient care database with hospitals spread across 46 states, and these states comprise more than 97% of the US population. The HCUP NIS contains more than 8 million hospital stays per year from more than 1000 hospitals. A full range of hospitals is sampled including community and academic centers. Data are entered as individual discharge records. Each record has a unique identifier, demographic data, hospital type, admission type, transfer status, hospitalized inpatient mortality indicator, discharge to palliative care, primary diagnosis, secondary diagnoses (up to 15), and procedure codes (up to 15). Admission diagnoses are not included in this data set. Time from admission to various primary procedures (eg, endoscopy and paracentesis) is provided as well as a diagnosis and procedure groups and patient comorbidity elements. Third-party payer status is included in the data set, however, “self-pay” is not defined further (ie, paid out of pocket vs inability to pay).

Cohort selection. The HCUP NIS contains 71,718,458 individual discharge records from 2002 through 2010. By using the International Classification of Diseases, 9th revision, Clinical Modification (ICD-9-CM) diagnostic and procedural codes, we extracted the subpopulation of patient admissions with cirrhosis (n = 781,678) from the HCUP NIS database (Supplementary Table 1). We included hospital discharges from 2002 through 2010 that had one or more of the following diagnoses: alcoholic cirrhosis of liver (571.2), biliary cirrhosis (571.6), or cirrhosis without mention of alcohol (571.5). Identification of cirrhotic patients using these codes in administrative data from the Veterans Affairs had a positive predictive value of 90% and a negative predictive value of 87%.[17] We included elective admissions (n = 57,960).

To determine whether changes in mortality were specific to cirrhosis care, we compared mortality data between the cirrhotic cohort and a noncirrhotic (NC) cohort matched 1:1 on age, sex, and year of discharge. Inpatient care of congestive heart failure also has advanced. Therefore, we compared mortality data between the cirrhotic cohort and a noncirrhotic cohort with congestive heart failure (CHF), matched 1:1 on age, sex, and year of discharge. After matching, each cohort contained 781,515 hospitalizations. These cohorts became the focus of our analyses.

Outcomes, primary variables, and covariates. Our primary outcome was “died while hospitalized,” as labeled in the HCUP NIS. The secondary outcome was discharge to palliative care. Our primary independent variable was year of discharge. Primary covariates of interest were 5 cirrhosis-related diagnoses, which can be fatal and require specific interventions: HRS, HCC, variceal bleeding, sepsis, and SBP. We also examined 3 procedures: esophagogastroduodenoscopy (EGD) within 1 day of admission, paracentesis within 1 day of admission, and transvenous intrahepatic portosystemic shunt (TIPS) at any time during the stay. These are captured readily in the HCUP NIS. Unfortunately, many other important cirrhosis-related interventions and diagnostic tests (eg, albumin use for SBP) are not captured and therefore were not available for analysis. Twenty-eight of the Agency for Healthcare Research and Quality comorbidity measures contained in the HCUP NIS were combined to generate the Elixhauser Comorbidity Index.[18,19] Use of this index to adjust for comorbidities in administrative databases was supported by Austin et al[19] using mathematic proofs. Major diagnoses and predictive covariates were defined using ICD-9-CM codes and are shown in Supplementary Table 1. To define the time to paracentesis or EGD, the HCUP NIS data element indicating the day on which the procedure was performed was used in conjunction with the primary procedure. If EGD or paracentesis was performed within 1 day after admission, we captured it using a combination of a time-to-procedure code and our primary diagnosis codes.[16] We also adjusted for a length of stay less than 2 days because many of these hospitalizations may represent the extremes of mortality risk that are less influenced by inpatient care (eg, moribund status, false alarm admissions for spurious laboratory results, and overnight observations after minor procedures). Patient demographic (eg, age, sex) and hospital characteristics (eg, academic, community based) were extracted from the HCUP NIS and included in the analysis.

Statistical analyses. Data were analyzed using the Stata 12.0 software package (Stata Corp LP, College Station, TX). HCUP NIS data are provided in a 2-stage cluster design incorporating clustering at the hospital level and discharge level. HCUP provides weighting of discharges based on the hospital type and volume of discharges relative to their sampling region. Two-way chi-square analyses were performed on categoric variables and t tests were performed for continuous variables. Poisson regression with robust (Huber–White) standard errors was used to determine incident risk ratios (RR) for predictors of in-hospital mortality.[20] We tested the Poisson models for overdispersion using a Pearson goodness-of-fit test. Models were not overdispersed ($P = 1.00$) and were appropriate for our analyses. Regression analyses controlled for several variables including calendar year of admission, major diagnostic and procedures covariates, age, sex, race, primary payer, Elixhauser comorbidity index, admission source, length of stay, and weekend admission. Referent categories were admission year 2002, age younger than 40 years, male sex, white, a routine admission, and self-pay listed as the primary payer.

We also hypothesized that an increased uptake of specific guidelines for the care of HRS, SBP, sepsis, variceal bleed, and HCC may have improved survival and would be reflected in decreasing mortality risk ratios from year to year. Therefore, we created interaction terms between each diagnosis and year of discharge (eg, HRS $\times$ 2002, HRS $\times$ 2003, and so forth). A more appropriate use of EGD within 1 day of admission, paracentesis within 1 day of admission, and TIPS may have led to similar decreasing risk ratios for inpatient mortality over time. To investigate this possibility,