Management and outcome of patients with blunt splenic injury and preexisting liver cirrhosis

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J Trauma Acute Care Surg Volume 76, Number 6 BACKGROUND: The response of liver cirrhosis (LC) patients to abdominal trauma, including blunt splenic injury (BSI) is unfavorable. To better

understand the response to BSI in LC patients, the present study reviewed a much larger group of such patients, derived from

the National Trauma Data Bank.

METHODS: The National Trauma Data Bank was queried for 2002 to 2010, and all adult BSI patients without severe brain trauma were

identified. LC and non-LC patients were compared using nonoperative management (NOM) failure and mortality as primary

outcomes. Predictors of these outcomes in LC patients were identified.

RESULTS: Of the 77,753 identified BSI patients, 289 (0.37%) had LC. Overall, 90% of the patients underwent initial NOM (86% in LC

and 90% in non-LC patients, p=0.091) with a global 90% success rate. Compared with non-LC patients, LC patients had a lower NOM success rate (83% vs. 90%, p=0.004) despite increased use of splenic artery angioembolization (13% vs. 8%, p=0.001). LC patients also had more complications per patient, an increased hospital and intensive care unit lengths of stay, and a higher mortality (22% vs. 6%, p<0.0001), which was independent of the treatment paradigm. In the LC group, mortality in those who underwent immediate surgery was 35% versus 46% in failed NOM (p=0.418) and 14% (p=0.019) in successful NOM patients. LC patients who did not require surgery were more likely to survive than those who had surgery alone (adjusted odds ratio [AOR], 0.30). Preexisting coagulopathy (AOR, 3.28) and Grade 4 to 5 BSI (AOR, 11.6) predicted NOM failure in LC patients, whereas male sex (AOR, 4.34), hypotension (AOR, 3.15), preexisting coagulopathy (AOR, 3.06), and Glasgow

Coma Scale (GCS) score of less than 13 (AOR, 6.33) predicted mortality.

CONCLUSION: LC patients have a higher rate of complications, mortality, and NOM failure compared with non-LC patients. Because LC patients

with failed NOM have a mortality rate similar to those undergoing immediate surgery, judgment must be exerted in selecting initial management options. (*J Trauma Acute Care Surg.* 2014;76: 1354–1361. Copyright © 2014 by Lippincott Williams & Wilkins)

LEVEL OF EVIDENCE: Prognostic/epidemiologic study, level III.

KEY WORDS: Blunt splenic injury; liver cirrhosis; nonoperative management; NTDB.

onoperative management (NOM) is currently used in approximately 65% of adult patients with blunt splenic injury (BSI)¹ with a failure rate of 4.2% to 13% in appropriately selected cases. 1-3 Recognized predictors of failed NOM include increasing age, higher Injury Severity Score (ISS), splenic injury grade (≥3), a high hemoperitoneum score, a "blush" on computed tomographic scan, and hypotension.^{4,5} Although liver cirrhosis (LC) induces many factors that could potentially lead to the exacerbation of BSI and failed NOM, such as portal hypertension, splenomegaly, coagulopathy, thrombocytopenia, malnutrition, and jaundice, its effect on the management and outcome of these patients has been poorly studied. Presently, there has been only one previous article, which directly addressed this issue.⁶ In that 2003 report of 12 cirrhotic patients with BSI, LC negatively affected the success rate of both NOM and survival. One other study, which focused on blunt abdominal trauma in general, concluded that LC in BSI patients (n = 20) leads to a high operative rate, low salvage rate of NOM, as well as high surgical morbidity and mortality rates. Lastly, a third investigation, focusing on laparotomy for trauma in general, reported that LC patients are at high risk for serious complications and death compared with a matched noncirrhotic group.8 Although these studies provided preliminary insight into the management of BSI in LC patients, they were all plagued with a small number of patients, which precluded definitive conclusions. The present study aimed to confirm the pilot observations of the previously cited reports and to identify predictors of failed NOM and mortality in LC patients with BSI, by reviewing a much larger cohort of patients derived from the National Trauma Data Bank (NTDB).

PATIENTS AND METHODS

Design

Data Abstraction

The American College of Surgeons (ACS) granted access to the research data set of the NTDB (The NTDB

remains the full and exclusive copyrighter property of the ACS) for the admission period of 2002 to 2010 (n = 3,523,486). All patients with splenic injuries were abstracted (n = 114,073) and narrowed down to 77,753 study subjects (Fig. 1). For these patients, the following information was collected: demographics, comorbidities, preexisting coagulopathy, admission systolic blood pressure (SBP) and Glasgow Coma Scale (GCS) score, ISS, grade of splenic injury, type and time to splenic surgery, angioembolization (AE) of the splenic artery, hospital and intensive care unit (ICU) length of stay (LOS), complications, and mortality. Demographic and clinical characteristics of the sample, along with completeness of data per category, are described in Table 1. Univariate comparisons between LC and non-LC patients were performed using failed NOM and mortality as primary outcomes, and predictors of failed NOM and mortality were discerned using multivariable logistic regression analysis.

Definitions

1. LC. Patients with LC and/or gastric or esophageal varices were defined as LC. The identification of these patients was performed based on information retrieved from the comorbidities and diagnoses files ("preexisting LC" and/ or "gastric or esophageal varices"; DRG International Classification of Diseases—9th Rev. [ICD-9] codes 571.2, 571.5 for LC and 456.0, 456.1, 456.2 for gastric or esophageal varices). It should be noted that codes for esophageal or gastric varices were counted as LC, based on the fact that the vast majority of varices are caused by cirrhosis-induced portal hypertension. Only a small group of patients may have varices secondary to other uncommon causes such as Budd-Chiari Syndrome, extrahepatic portal vein obstruction, or portal vein thrombosis caused by pancreatitis, abdominal tumor, trauma, or inherent procoagulant disorders. 9 In addition, defining LC based on the presence of varices only has been previously used in other NTDB-based studies investigating cirrhosis in trauma

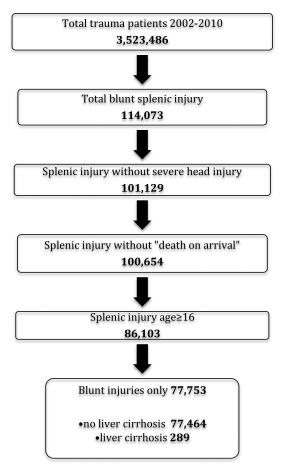


Figure 1. Study inclusion process.

- patients. ¹⁰ In our sample of 289 LC patients, 182 (63.0%) were identified by the specific code for LC, 103 (35.6%) were identified by the code for gastric/esophageal varices, and 4 patients (1.4%) had both comorbidities coded.
- BSI grade. The American Association for Surgery of Trauma Organ Injury Scale (AAST-OIS)¹¹ splenic injury grading was used based on the Association for the Advancement of Automotive Medicine Abbreviated Injury Scale (AIS) 98

- codes, ¹² as follows: Grades 1 and 2, 544212.2 and 544222.2; Grade 3, 544214.3 and 544224.3; Grade 4, 544226.4; Grade 5, 544228.5. Patients coded with nonspecified splenic injury severity (AIS 98 codes 544299.2, 544210.2, 544220.2) were retained in the regression analysis.
- Severe head injury. This is defined as head AIS score of 4 or greater.
- 4. Preexisting coagulopathy. This is an NTDB data element, defined as "any condition that places the patient at risk for excessive bleeding due to a deficiency of blood clotting elements (e.g., vitamin K deficiency, hemophilia, thrombocytopenia, chronic anticoagulation therapy with Coumadin, Plavix, or similar medications). Patients on chronic aspirin therapy are excluded."
- 5. Surgical procedures. These were identified based on ICD-9 procedure codes: total splenectomy (41.5), partial splenectomy (41.43), and splenorrhaphy (41.95).
- 6. AE. Because the ICD-9 does not have a specific code for AE of the splenic artery, ICD-9 codes for abdominal aortic angiography and embolization (38.86, 38.87, 39.79, 88.47) were used. Although this definition may be inaccurate because some patients may have had AE of other organs such as the liver or pelvis, it can still be used since this inaccuracy is likely distributed equally among all studied groups. Indeed, regression analyses with the sample restricted to patients who did not sustain concomitant liver injuries or pelvic fractures produced very similar results (data not shown). Therefore, the lack of specification of the reason for AE is unlikely to significantly bias the findings of the study.
- 7. Failed NOM. As most decisions for emergent surgery are taken within 2 hours from admission and in agreement with previous studies, ¹³ any splenic surgery (partial or total splenectomy, splenorrhaphy) performed after this time point was determined to be a failed NOM. In addition, failed NOM was defined as splenic surgery performed following AE, regardless of the time from admission. It should be noted that there is no universally accepted definition for NOM^{14,15} and that the above mentioned definitions were based on previous literature. ¹³
- 8. Complications. This is defined by the NTDB Data Dictionary.
- 9. Mortality. This refers to in-house mortality.

TABLE 1. Demographics (A) and Clinical Characteristics (B) of all Reviewed Patients

A. Demographics					
	Non-LC, $n = 77,464$	LC, $n = 289$	p	n (%) With Missing Values	
Age, median (IQR), y	35 (29)	51 (14)	< 0.0001	NA*	
Male, n (%)	51,054 (66)	205 (72)	0.060	516 (0.7)	
Comorbidities per patient, median (IQR)	1 (1)	2 (2)	< 0.0001	NA*	
Preexisting coagulopathy, n (%)	1,307 (2)	37 (13)	< 0.0001	NA*	
B. Clinical Characteristics					
Admission SBP < 90 mm Hg, n (%)	7,423 (10)	51 (18)	< 0.0001	1969 (2.5)	
ISS, median (IQR)	18 (17)	17 (16)	0.048	3418 (4.4)	
GCS score, median (IQR)	15 (0)	15 (1)	0.810	7390 (9.5)	
Spleen injury Grades 4-5, n (%)	23,113 (30)	110 (38)	0.003	18,536 (24)	

^{*}Nonparametric (Kruskal-Wallis) test used for continuous variables.

IQR, interquartile range; NA, not applicable (non-missing values were required for this variables).

Statistical Analysis General

Statistical analysis was performed using SAS 9.3 (SAS Institute, Cary, NC). Differences in demographic and clinical characteristics between patients with or without LC were determined by χ^2 tests for categorical variables and either t tests or Kruskal-Wallis tests for continuous variables, depending on the skewness of their distributions. All statistical testing was two sided with $\alpha = 0.05$.

The proportion of missing data for key variables was summarized, and the reliability of cirrhosis reporting was evaluated by comparing the prevalence of cirrhosis among trauma center levels and between early and later NTDB data set versions. Basic demographic and clinical characteristics of the sample were summarized, including the type of operative care and NOM in the LC and non-LC groups.

For the purposes of regression modeling, several variables were dichotomized as follows: SBP (<90 mm Hg and ≥90 mm Hg), age (<55 years and ≥55 years), early (2002–2006) and late (2007–2010) NTDB data sets, level of trauma center (ACS Levels 1–2 and all others). Grade of splenic injury was categorized as Grades 1 to 3 or Grades 4 to 5. For each of the regression models, generalized estimating equation methods were used to account for clustering within center. Patients missing the outcome of interest (i.e., mortality, failed NOM) were excluded from that model. Missing values for spleen injury severity and procedures were coded using missing indicators and retained the regression analyses.

Univariate Analysis

The associations between demographic and clinical variables with the outcomes of interest were examined via univariate analysis for the LC and non-LC groups separately. Among the LC patients, variables with at least a trend association (p < 0.1) with the outcome were chosen as candidates for the subsequent regression modeling of that outcome.

Multivariable Analysis of Failed NOM

Logistic regression analysis was used to identify predictors of failed NOM in LC patients controlling for a number of clinical and demographic variables and accounting for clustering of cases. Variables that were chosen for evaluation via forward selection in this model included: sex, SBP at arrival, preexisting coagulopathy, ACS trauma center level, NTDB data set period, and BSI grade. Adjusted odds ratios (AORs) and 95% confidence intervals (CIs) were computed for all predictor variables in the regression model, and model fit statistics, including receiver operating characteristic (ROC) curve and pseudo (Nagelkerke) R^2 statistics, were calculated.

Multivariable Analysis of Mortality

Logistic regression analysis was also used to identify predictors of mortality in patients with LC controlling for a number of clinical and demographic. Variables chosen to be evaluated via forward selection in this model included the following: age, sex, SBP at arrival, GCS, preexisting coagulopathy, grade of splenic injury, ACS trauma center level, NTDB data set period, and type of procedure as defined

previously (total or partial splenectomy, splenorrhaphy, AE. As previously mentioned, AOR and 95% CIs were computed for all predictor variables in the logistic model, as well as overall model fit statistics.

RESULTS

Demographics and Clinical Characteristics

While detailed results are provided in Table 1, several highlights emerged. First, the prevalence of cirrhosis in this group of BSI patients was 0.37%. Second, cirrhotic patients were older, had more comorbidities, and were more likely to have preexisting coagulopathy, admission hypotension (SBP < 90 mm Hg), and a higher BSI grade.

Treatment Strategy, Complications, and Outcomes

The majority (90%) of all patients with BSI underwent NOM, and only 10% had emergent splenic surgery (5,135 of 51,356) (Table 2A). There was no difference in the NOM attempt rate between LC and non-LC patients (86% vs. 90%, p = 0.091), and NOM's overall success rate was 90% (41,449) of 46,221). Compared with non-LC patients, LC patients had a lower NOM success rate (83% vs. 90%, p = 0.004) despite increased AE use (Table 2A). LC patients had more complications per patient, an increased hospital and ICU LOS, and a higher mortality rate (22% vs. 6%) (Table 2B). A detailed analysis of the mortality demonstrated a higher rate in LC patients regardless of the treatment paradigm, except for those who were successfully managed nonoperatively with AE (Table 3). Moreover, the mortality of failed NOM patients (46%) tended to be higher compared with those who underwent emergent surgery (35%); however, this difference did not reach statistical significance (p = 0.418). The management paradigms for LC patients are described in Figure 2.

Predictors of Failed NOM and Mortality

Preexisting coagulopathy and splenic injury Grades 4 to 5 independently predicted failed NOM in LC patients (Table 4A), whereas male sex, admission hypotension, preexisting coagulopathy, and GCS score of less than 13 were predictors of mortality in this group (Table 4B). Patients who did not require surgery or AE were more likely to survive than those who received surgery alone (AOR, 0.32; 95% CI, 0.12-0.84). Compared with surgery alone, AE with or without surgery was not significantly associated with mortality. The model predicting failed NOM included data from 160 patients, with an ROC area of 0.819 (95% CI, 0.741–0.898) and a Nagelkerke R² value of 0.297. This model had 129 fewer patients than the mortality model because of missing information on the failed NOM outcome; no patients were excluded because of missing predictors as missing indicators were used for both missing splenic injury and missing procedure data. The model predicting mortality included data from 257 patients, with an ROC area of 0.839 (95% CI, 0.777-0.901) and a Nagelkerke R^2 value of 0.400. Thirty-two patients were dropped from this model because of missing information on hypotension (n = 12) and GCS score (n = 24).

TABLE 2. Treatment Strategy (A) and Complications and Outcomes (B) of all Reviewed Patients

A. Treatment Strategy				
		Non-LC, $n = 51,170*$	LC, $n = 186*$	p
Emergent surgery, n (%)		5,109 (10)	26 (14)	0.091
NOM, n (%)	Total	46,061 (90)	160 (86)	0.091
	AE	5,094 (10)	34 (18)	0.001
Successful NOM, n (%)	Total	41,317 (81)	132 (71)	0.001
	AE	4,085 (8)	25 (13)	0.009
Failed NOM, n (%)	Total	4,744 (9)	28 (15)	0.0097
	AE	1,009 (2)	9 (5)	0.0112
B. Complications and Outcomes				
	Non-LC, $n = 77,464$	LC, $n = 289$	<i>p</i> **	n (%) With Missing Values
Complications per patient, median (IQR)	1 (1)	1 (2)	< 0.0001	1485 (1.9)
Hospital LOS, median (IQR), d	6 (8)	7 (10)	0.010	21,840 (28)
ICU LOS, median (IQR), d	3 (5)	3 (12)	0.001	25,254 (32)
Mortality, n (%)	4,617 (6)	65 (23)	< 0.0001	1,598 (2.1)

^{*}Total number of patients with complete data on type and timing of surgical procedure.

Reliability of LC Reporting to NTDB Across Years

The reliability of LC reporting to the NTDB was evaluated by comparing the prevalence of LC in the early (2002-2006) versus late (2007-2010) data sets and by comparing the clinical characteristics of LC patients during these two periods. Analysis of the entire NTDB data sets for all patients across time showed that the prevalence of LC varied from 0.08% for the 2002 to 2006 data set to 0.2% for the later years, likely reflecting the greater amount of missing data in the early years. The clinical characteristics of BSI patients with LC between the early and later data sets showed some variations, none of which were statistically significant, and control of these factors was included the regression models. Specifically, the percentage of patients with SBP lower than 90 mm Hg in 2002 to 2006 and in 2007 to 1010 was 21 and 16, respectively. ISS of 10 of greater in the early period was 81% compared with 72% in the later period, and GCS score of 13 or greater was present in 81% and 88% of the patients, respectively. During the early years, BSI Grade 4 to 5 was present in 37% of the patients and in 39% of the patients in the later years. Lastly, 43% of the

participating hospitals in 2002 to 2006 were Level I to II trauma centers compared with 42% in 2007 to 2010.

DISCUSSION

As hypothesized, the present study demonstrated that BSI patients with LC have a higher risk of failed NOM (17% vs. 10%) and mortality (23% vs. 6%) compared with noncirrhotic patients. This supports preliminary observations from the only single previous study directly investigating the relationship between BSI and LC, which included only 12 LC patients. §6 In that study, LC patients had a 92% failure rate versus 19% in non-LC patients. Similarly, mortality in the LC group was 50%, whereas only 5.5% of non-LC patients died. Two other studies support the observation of increased NOM failure and mortality in LC patients. However, these reports provided indirect evidence only because they did not focus on the effect of LC on the outcome of BSI patients. Moreover, they also included only a small number of LC patients. In the first study, a review of 46 LC patients undergoing trauma laparotomy reported 45% mortality

TABLE 3. Analysis of Mortality of Reviewed Patients

		Non-LC, $n = 51,170*$		LC, $n = 186*$		
		Total No. Patients	Mortality, n (%)	Total No. Patients	Mortality, n (%)	p
Emergent surgery		5,109	818 (16)	26	9 (35)	0.027
NOM	Total	46,061	2,426 (5)	160	31 (19)	< 0.0001
	AE	5,094	414 (8)	34	11 (32)	< 0.0001
Successful NOM	Total	41,317	1,979 (5)	132	18 (14)	< 0.0001
	AE	4,085	191 (4.7)	25	5 (20)	0.01
Failed NOM	Total	4,744	447 (9)	28	13 (46)	< 0.0001
	AE	1009	223 (22)	9	6 (67)	0.006
Total		51,170	3,244 (6)	186	40 (22)	< 0.0001

^{*}Total number of patients with complete data on type and timing of surgical procedure.

^{**}Nonparametric (Kruskal-Wallis) test used for continuous variables.

IQR, interquartile range.

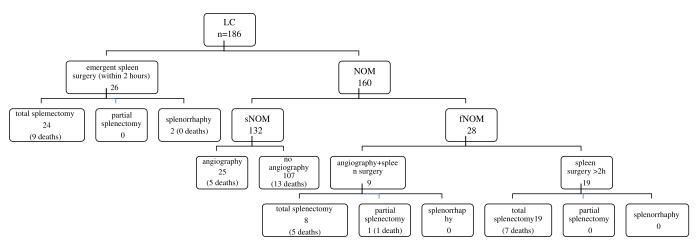


Figure 2. Treatment of LC patients. fNOM, failed NOM; sNOM, successful NOM. Please note that complete data was available for only 186 of the 289 LC patients.

in LC patients versus 24% in matched noncirrhotic patients.⁸ Likewise, evaluation of 30 cirrhotic blunt abdominal trauma patients who underwent emergent surgery showed 43% mortality, although no mortality or NOM failure rates were reported for the 20 BSI patients in that series.⁷ It should be noted that the increased NOM failure and mortality reported herein in LC patients with BSI are not surprising given similar reports previously published in LC trauma patients in general.^{16–22}

Several factors may contribute to the worse outcome observed in LC BSI patients. First, the spleens of cirrhotic patients undergo pathophysiologic changes that may promote NOM failure and mortality. These include splenomegaly from portal hypertension-induced venous engorgement, reticuloendothelial cell hyperplasia and fibrogenesis, and a higher blood flow through the spleen accompanied by an increased number of peripheral arterioles.²³ Second, most LC patients have thrombocytopenia (secondary to increased breakdown in the

TABLE 4. Final Multivariable Regression Models Predicting Failure of NOM (A) and Mortality (B)

A. Failure of NOM		
Predictor	P	AOR (95% CI)
Preexisting coagulopathy	0.028	3.45 (1.14–10.4)
Splenic injury		
Grades 4–5	< 0.0001	10.7 (3.44–33.4)
Unspecified	0.851	0.866 (0.194-3.87)
B. Mortality		
Male sex	0.001	4.32 (1.79–10.5)
SBP < 90 mm Hg	0.001	3.09 (1.57-6.11)
Procedures (reference, surgery alone)		
None	0.021	0.32 (0.12-0.84)
Angiography	0.444	0.58 (0.15-2.32)
Surgery + angiography	0.210	2.54 (0.59-10.9)
Missing	0.059	0.24 (0.05-1.05)
Coagulopathy	0.023	3.10 (1.17-8.25)
GCS score < 13	0.0004	6.16 (2.27–16.7)

pathologic spleen and decreased production in the bone marrow), which has been shown to promote bleeding in both surgical and medical conditions.²⁴ Third, many LC patients have coagulopathy caused by decreased production of coagulation factors.²⁵ Fourth, malnutrition (hypoalbuminemia) and hyperbilirubinemia, commonly seen in LC patients, were also demonstrated to negatively affect outcomes of LC patients in a variety of disease states. ^{26,27} Lastly, the presence of hepatic encephalopathy may also contribute to worse outcomes seen in LC patients. 28 It should be noted that although previous reports found that trauma center level impacts survival among cirrhotic patients, 10 it was not identified as a predictor of mortality in the present study. Unfortunately, because of the NTDB's limitations (lack of data), the present study could not directly evaluate the impact of each of these factors (except for preexisting coagulopathy) on the management and outcome of LC patients with BSI. Such knowledge could have aided tailoring the preferred initial treatment for LC patients. Furthermore, it could have also assisted in predicting prognosis and defining a potential role for interventions such as preoperative or postoperative transjugular intrahepatic portosystemic shunt placement in patients with portal hypertension. In addition, the NTDB does not contain the required data to determine Model for End-Stage Liver Disease (MELD) scores, which could potentially play a role in selecting operative versus NOM in cirrhotic patients with BSI.

In parallel to the increased NOM failure and mortality rates in the LC group, the present study also demonstrated that cirrhotic patients have an increased complication per patient ratio as well as prolonged hospital and ICU LOS. This is the first report of such correlations in BSI cirrhotic patients, although one previous study, which did not focus on cirrhotic BSI patients but instead on LC patients undergoing trauma laparotomy in general, reported similar observations. Specifically, it showed a complication rate of 45% in LC patients and 23% in the non-LC group. It also reported an ICU LOS of 11.5 days in LC patients versus 6.6 days in non-LC patients. The reasons for worse nonlethal outcome parameters in the LC group of BSI patients are likely similar to those discussed earlier for decreased NOM success rate and increased mortality.

Another finding of the present study is the identification of preexisting coagulopathy and higher splenic injury grades (Grades 4–5) as predictors of failed NOM in LC patients. This finding is important because it may assist the surgeon in deciding whether to pursue emergent surgery or NOM in LC patients, especially given the high mortality rate in this group when NOM fails. Although no data are available for direct comparison, this observation is supported by a previous report that LC patients who failed NOM had higher ISS and splenic injury severity grades, required more blood transfusions, and had a higher mortality rate when compared with non-LC patients.⁶

The present study also identified predictors for mortality, which included the male sex, admission hypotension, preexisting coagulopathy, and GCS score of less than 13. This finding complements an earlier report that a higher ISS, a severely elevated prothrombin time, a larger transfusion requirement, and a lower serum albumin predict mortality in LC patients.⁶ Shock on admission and higher MELD scores were identified as risk factors for mortality in another study, which focused on blunt trauma rather than BSI cirrhotic patients.⁷ In the general population, Grade 4 to 5 splenic injury, moderate or large hemoperitoneum, and increased ISS and age have all been associated with failed NOM.⁴ Moreover, a recently published review of general patients⁵ found that age greater than 40 years, ISS greater than 25, and splenic injury grade of 3 or higher correlated with mortality. Similar to the identification of NOM predictors, the delineation of these mortality predictors could potentially help in the selection process of BSI LC patients to NOM or immediate surgery.

The mortality analysis performed in the present study showed that LC patients with failed NOM had a higher but not statistically different mortality compared with those undergoing immediate surgery. The lack of statistical significance between these two treatment approaches may reflect insufficient number of patients. If, however, this trend could be verified in the future, it would support emergent surgery rather than NOM in LC patients.

The present study demonstrated that the attempt rate of NOM in BSI patients with or without LC was similar. Because LC patients had a higher rate of admission hypotension, this finding could reflect reluctance by many surgeons to perform surgery on LC patients with BSI. Given the differences outlined earlier between LC and non-LC patients, the need for clear management guidelines is emphasized. Analysis of the treatment strategies showed that LC patients had a lower NOM success rate despite increased AE use (13% vs. 8%, p = 0.010). It also revealed that LC patients with BSI who were successfully treated with NOM had a higher use of AE. However, this was not associated with improved survival, and these patients had a higher mortality rate compared with non-LC patients who successfully underwent NOM. This is in contrast to previous studies showing a beneficial effect of AE on the success rate of NOM in BSI patients. For example, a recent retrospective review of 1,039 patients, of whom 19% underwent AE, found that the addition of AE to NOM significantly decreased the failure rate of this approach in patients with splenic injury Grades 4 to 5.²⁹ Although the reason(s) for this difference is obscure, it is conceivable that the significant comorbidities of LC, which have been shown to negatively affect outcome in surgical patients, ^{7,8,17,30,31} account for this disparity.

According to the NTDB data reviewed herein, the prevalence of LC in BSI patients is 0.37%. In contrast, other studies reported 0.08% to 0.21% prevalence in the hospital population in general.^{32–34} The reasons for this difference are unknown. However, given that alcoholism is a common etiology for LC, it is possible that LC patients are more exposed to trauma (vehicular crashes, falls, strike by a car, and assaults) compared with non-LC patients. It should be noted that the analysis of the entire NTDB data sets across periods varied from 0.08% for the 2002 to 2006 data set to approximately 0.2% for the later years, likely reflecting the greater amount of missing data in the early years. The underrepresentation of cirrhotic BSI patients from that period reduced the sample size and is a limitation of the present study. However, this limitation, while reducing the statistical power of the analyses, is unlikely to have biased the results, particularly since the clinical profile of BSI patients with LC across periods is comparable.

The present study has several limitations. First, this is a retrospective review, which is inherently inferior to prospective evaluations. Second, the analyzed data were derived from the NTDB, an aggregate of multiple registries, which has wellrecognized drawbacks.³⁵ For example, it is not a populationbased data bank but rather a collection of "convenience samples" submitted by participating institutions with varying quality of data collection and entry. Moreover, the accuracy of reporting LC to NTDB is unknown, and there is great variability in complication and comorbidities data that may introduce bias and challenge data interpretation.³⁶ Furthermore, LC as used in this study is not a well-defined disease entity but rather a "catch-all" diagnosis that covers a wide range of actual disease processes and severity. In addition, each NTDB entry is coded as an "incident key," assumed to be a single patient, whereas, in fact, it represents an admission to the emergency department. Thus, a patient can be entered, theoretically, several times into the NTDB if he or she was admitted to different hospitals with the same injury diagnosis. Lastly, the definition of NOM and failed NOM may have been compromised because it is not based on concrete clinical scenarios or standardized criteria. Despite the previously mentioned shortcomings, this article is valuable, in that it reviewed a large number of patients, which could not have been assembled otherwise, as well as performed a detailed statistical analysis of national data. A third limitation of the present study is the size difference between the compared groups; the small study cohort of LC patients was compared with the much larger non-LC patient group. This however was unavoidable, given the very low rate of LC patients in the BSI patient population in general (0.37%).

In conclusion, the present study established that LC patients with BSI have a higher rate of NOM failure, morbidity, and mortality compared with non-LC patients. It also showed that preexisting coagulopathy and Grade 4 to 5 BSI predicted NOM failure in LC patients, whereas male sex, hypotension, preexisting coagulopathy, and GCS score less than 13 predicted mortality in this group of patients. Because LC patients with failed NOM have a mortality rate similar to those undergoing immediate surgery, careful selection of NOM versus operative intervention must be executed. The possibility that LC patients with BSI Grade 4 to 5 or preexisting coagulopathy may benefit from emergent surgery should be investigated in the future.

AUTHORSHIP

N.B. conceived the project and designed the protocols with R.R., collected the data, analyzed the data together with R.R. and J.L.B., and drafted the manuscript. J.B. performed all statistical analysis, analyzed the data with N.B. and R.R., and critically edited the manuscript. V.D. assisted with data management and drafting of the manuscript. S.S.A. assisted with data management and editing of the manuscript. R.R. conceived the project, designed the protocols, analyzed the data together with N.B. and J.L.B., and critically revised the manuscript.

DISCLOSURE

The authors declare no conflicts of interest.

REFERENCES

- Banerjee A, Duane TM, Wilson SP, Haney S, O'Neill PJ, Evans HL, Como JJ, Claridge JA. Trauma center variation in splenic artery embolization and spleen salvage: a multicenter analysis. *J Trauma Acute Care Surg*. 2013;75:69–74; discussion 74–75.
- Clancy AA, Tiruta C, Ashman D, Ball CG, Kirkpatrick AW. The song remains the same although the instruments are changing: complications following selective non-operative management of blunt spleen trauma: a retrospective review of patients at a level I trauma centre from 1996 to 2007. J Trauma Manag Outcomes. 2012;6:4.
- Bhullar IS, Frykberg ER, Siragusa D, Chesire D, Paul J, Tepas JJ 3rd, Kerwin AJ. Age does not affect outcomes of nonoperative management of blunt splenic trauma. J Am Coll Surg. 2012;214(6):958–964.
- Bhangu A, Nepogodiev D, Bowley DM. Meta-analysis of predictive factors and outcomes for failure of non-operative management of blunt splenic trauma. *Injury.* 2012;43:1337–1346.
- Olthof DC, Joosse P, Van der Vlies CH, De Haan RJ, Goslings JC. Prognostic factors for failure of nonoperative management in adults with blunt splenic injury: a systematic review. *J Trauma Acute Care Surg*. 2013;74:546–557.
- Fang JF, Chen RJ, Lin BC, Hsu YB, Kao JL, Chen MF. Liver cirrhosis; an unfavorable factor for nonoperative management of blunt splenic injury. *J Trauma*. 2003;54:1131–1136; discussion 1136.
- Lin BC, Fang JF, Wong YC, Hwang TL, Hsu YP. Management of cirrhotic patients with blunt abdominal trauma: analysis of risk factor of postoperative death with the Model for End-Stage Liver Disease score. *Injury*. 2011;43:1457–1461.
- Demetriades D, Constantinou C, Salim A, Velmahos G, Rhee P, Chan L. Liver cirrhosis in patients undergoing laparotomy for trauma: effect on outcomes. *J Am Coll Surg*. 2004;199:538–542.
- 9. de Franchis R. Evolving consensus in portal hypertension. Report of the Baveno IV consensus workshop on methodology of diagnosis and therapy in portal hypertension. *J Hepatol*. 2005;43:167–176.
- Bukur M, Felder SI, Singer MB, Ley EJ, Malinoski DJ, Margulies DR, Salim A. Trauma center level impacts survival for cirrhotic trauma patients. *J Trauma Acute Care Surg.* 2013;74:1133–1137.
- Injury Scoring Scale. The American Association for the Surgery of Trauma. Published 1994. Available at: http://www.aast.org/library/traumatools/ injuryscoringscales.aspx#spleen. Accessed March 2012.
- The Association for the Advancement of Automotive Medicine. AIS 2005 Update 2008. Barrington, IL: Association for the Advancement of Automotive Medicine; 2008.
- 13. Smith J, Armen S, Cook CH, Martin LC. Blunt splenic injuries: have we watched long enough? *J Trauma*. 2008;64:656–665.
- 14. Jeremitsky E, Kao A, Carlton C, Rodriguez A. Does splenic embolization and grade of splenic injury impact nonoperative management in patients sustaining blunt splenic trauma? *Am Surg.* 2011;77:215–220.
- McIntyre LK, Schiff M, Jurkovich GJ. Failure of nonoperative management of splenic injuries: causes and consequences. *Arch Surg.* 2005;140: 563–568; discussion 568–569.

- Talving P, Lustenberger T, Okoye OT, Lam L, Smith JA, Inaba K, Mohseni S, Chan L, Demetriades D. The impact of liver cirrhosis on outcomes in trauma patients: a prospective study. *J Trauma Acute Care Surg.* 2013;75: 699–703
- Nau C, Wutzler S, Dörr H, Lehnert M, Lefering R, Laurer H, Wyen H, Marzi I, , Trauma Registry of DGU. Liver cirrhosis but not alcohol abuse is associated with impaired outcome in trauma patients - a retrospective, multicentre study. *Injury*. 2013;44:661–666.
- Christmas AB, Wilson AK, Franklin GA, Miller FB, Richardson JD, Rodriguez JL. Cirrhosis and trauma: a deadly duo. Am Surg. 2005;71: 996–1000.
- Dangleben DA, Jazaeri O, Wasser T, Cipolle M, Pasquale M. Impact of cirrhosis on outcomes in trauma. J Am Coll Surg. 2006;203:908–913.
- Tinkoff G, Rhodes M, Diamond D, Lucke J. Cirrhosis in the trauma victim. Effect on mortality rates. Ann Surg. 1990;211:172–177.
- Wahlstrom K, Ney AL, Jacobson S, Odland MD, Van Camp JM, Rodriguez JL, West MA. Trauma in cirrhotics: survival and hospital sequelae in patients requiring abdominal exploration. *Am Surg.* 2000;66: 1071–1076.
- de Goede B, Klitsie PJ, Lange JF, Metselaar HJ, Kazemier G. Morbidity and mortality related to non-hepatic surgery in patients with liver cirrhosis: a systematic review. *Best Pract Res Clin Gastroenterol*. 2012;26:47–59.
- Tarantino G, Savastano S, Capone D, Colao A. Spleen: a new role for an old player? World J Gastroenterol. 2011;17:3776–3784.
- 24. Hugenholtz GG, Porte RJ, Lisman T. The platelet and platelet function testing in liver disease. *Clin Liver Dis.* 2009;13:11–20.
- Caldwell SH, Sanyal AJ. Coagulation disorders and bleeding in liver disease: future directions. Clin Liver Dis. 2009;13:155–157.
- Periyalwar P, Dasarathy S. Malnutrition in cirrhosis: contribution and consequences of sarcopenia on metabolic and clinical responses. *Clin Liver Dis*. 2012;16:95–131.
- Saliba F, Ichal P, Levesque E, Samuel D. Cirrhotic patients in the ICU: prognostic markers and outcome. Curr Opin Crit Care. 2013;19:154–160.
- Wlodzimirov KA, Eslami S, Abu-Hanna A, Nieuwoudt M, Chamuleau RA. A systematic review on prognostic indicators of acute on chronic liver failure and their predictive value for mortality. *Liver Int.* 2003;33:40–52.
- Bhullar IS, Frykberg ER, Siragusa D, Chesire D, Paul J, Tepas JJ, Kerwin AJ. Selective angiographic embolization of blunt splenic traumatic injuries in adults decreases failure rate of nonoperative management. *J Trauma Acute Care Surg.* 2012;72:1127–1134.
- Patel MS, Malinoski DJ, Nguyen XM, Hoyt DB. The impact of select chronic diseases on outcomes after trauma: a study from the National Trauma Data Bank. J Am Coll Surg. 2011;212:96–104.
- Georgiou C, Inaba K, Teixeira PG, Hadjizacharia P, Chan LS, Brown C, Salim A, Rhee P, Demetriades D. Cirrhosis and trauma are a lethal combination. World J Surg. 2009;33:1087–1092.
- National Hospital Discharge Survey: 2010 Detailed diagnosis and procedure tables, Number of first-listed diagnoses. Available at: http://www.cdc.gov/nchs/data/nhds/10Detaileddiagnosesprocedures/2010det10_numberfirstdiagnoses.pdf.
- 33. Digestive Diseases in the United States: Epidemiology and Impact. Bethesda, MD: NIDDK; 1994. NIH Publication No. 94-1447.
- Fleming KM, Aithal GP, Solaymani-Dodaran M, Card TR, West J. Incidence and prevalence of cirrhosis in the United Kingdom, 1992–2001: a general population-based study. 2009;51:233–234.
- 35. Haider AH, Saleem T, Leow JJ, Villegas CV, Kisat M, Schneider EB, Haut ER, Stevens KA, Cornwell EE 3rd, MacKenzie EJ, et al. Influence of the National Trauma Data Bank on the study of trauma outcomes: is it time to set research best practices to further enhance its impact? *J Am Coll Surg*. 2012;214:756–768.
- Kardooni S, Haut ER, Chang DC, Pierce CA, Efron DT, Haider AH, Pronovost PJ, Cornwell EE 3rd. Hazards of benchmarking complications with the National Trauma Data Bank: numerators in search of denominators. *J Trauma*. 2008;64:273–277; discussion 277–279.