Trends in surgical volume and in-hospital mortality among United States cirrhosis hospitalizations

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Abstract

Background In the aging population of patients with cirrhosis in the United States, there is a potentially increased need for surgical procedures. However, individuals with cirrhosis have increased perioperative risk relative to patients without cirrhosis. We sought to quantify temporal trends in cirrhosis surgical procedures and in-hospital mortality in relation to surgical procedure type, elective admission status and compensated vs. decompensated status.

Methods We performed a retrospective cohort study of cirrhosis hospitalizations between 2005 and 2014 using the National Inpatient Sample. Surgical procedures of interest included cholecystectomy, hernia repair, and major abdominal, orthopedic and cardiovascular surgery. We plotted trends in volume and in-hospital mortality by procedure type, and used linear regression to test the significance of trends.

Results While the number of cirrhosis hospitalizations increased over time, the number of surgeries per 1000 admissions decreased (β=-1.454, P<0.001). When stratified by elective admission status, elective major orthopedic surgeries significantly increased over time (β=177.9; P<0.001). In-hospital mortality rates for most surgeries were significantly higher in the non-elective vs. elective setting (each P<0.001). In patients with compensated cirrhosis, there was a significant increase in the number of orthopedic (β=272.4; P<0.001) and hernia repair surgeries over time (β=191.1; P<0.001). Overall, there was significantly greater in-hospital mortality among patients with decompensated cirrhosis (each P<0.05). Q. Please mention the exact P-value unless <0.001

Conclusions Despite an increasing number of cirrhosis hospitalizations, the decreasing relative number of cirrhosis surgeries may indicate progressive surgical risk aversion. Future cirrhosis surgical risk scores should consider surgical procedure type, elective/non-elective status, and decompensation status.

Keywords Liver disease, procedures, outcomes, admission, elective, decompensation

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Introduction

The overall prevalence of cirrhosis in the United States (US) is estimated to be 0.27% of the general US population, or greater than 600,000 individuals [1]. A recent national study demonstrated a 25% increase in the number of hospitalizations of patients with cirrhosis from 2005-2014, with the majority of these patients being aged 51-69 years [2]. This reflects an aging population of patients with cirrhosis, who will presumably require higher rates of surgical procedures.

The data on national trends in surgical procedure volume and mortality among patients with cirrhosis are sparse. A study of national discharge data from 1998-2005 found stable surgical volumes among cirrhosis admissions, with

cholecystectomies performed much more commonly than major cardiovascular surgery, in contrast to non-cirrhosis admissions [3]. However, there have been no US national data published on cirrhosis surgical volume since that time. We recently demonstrated significant differences in in-hospital mortality by surgery type among cirrhosis admissions in the National Inpatient Sample database [4]. However, no recent studies have evaluated trends in volumes of major surgery in this population, which could serve to further contextualize these findings. In order to address these gaps, we sought to quantify temporal trends in surgical procedures among admissions with cirrhosis, as well as in-hospital mortality rates by surgical procedure type, elective or non-elective admission status, and by decompensation status.

Materials and methods

We performed a retrospective cohort study using complete data from the Nationwide Inpatient Sample (2005-2011) and National Inpatient Sample (2012-2014), collectively referred to here as the NIS. The NIS is the largest payer-independent database of US hospital discharges, and is maintained by the Agency for Healthcare Research and Quality (AHRQ) as part of the Healthcare Cost Utilization Project (HCUP) [5].

We combined the NIS datasets from 2005-2014, and identified all admission events with age ≥18 and an International Classification of Diseases (ICD)-9 diagnosis code for cirrhosis (571.2, 571.5). We classified admissions with decompensated cirrhosis using codes for variceal bleed (456.0, 456.2), hepatic encephalopathy (572.2), portal hypertension (572.3), hepatorenal syndrome (572.4) or ascites (789.5), consistent with prior NIS studies [3,6]. Demographic data (age, sex, race), primary insurance payer (Medicare, Medicaid, private, self-pay), hospital length of stay, hospital location/ teaching status (rural, urban nonteaching, urban teaching), hospital region (Northeast, Midwest, South, West), hospital size (small, medium, large) based on number of beds [7], elective vs. non-elective admission, and in-hospital death were collected for all admissions. Elixhauser comorbidity indices were also calculated for each admission [8]. This is a validated index for hospital-associated mortality that outperforms other comorbidity indices across a range of applications utilizing large administrative databases [9]. Finally, we classified the etiology of liver disease as hepatitis C, alcohol-related, fatty liver disease or unclassified/missing, based on prior methods [4].

We reviewed the 100 most common primary procedure codes from the annual data of all admissions in the cohort and created 5 surgical subcategories: cholecystectomy, hernia repair, major abdominal (including total/partial colectomy, nephrectomy, pancreatectomy, splenectomy, gastrectomy) [10], major orthopedic (including total/partial knee or hip replacement/revision, major open reduction procedure) [11], and major cardiovascular (including coronary artery bypass grafting, open cardiac valve replacement/repair, abdominal aortic aneurysm repair). ICD-9 Clinical Modification procedure codes are summarized in Supplementary Table 1.

We used NIS discharge weights, including adjusted trend weights for pre-2012 data, to produce national estimates of admissions with surgical procedures of interest [5]. Descriptive statistics were presented as medians and interquartile ranges for continuous variables and as percentages for categorical variables. Aggregate in-hospital mortality rates for each surgical procedure were calculated by dividing the number of hospitalizations ending in death by the total number of hospitalizations with a given surgical procedure. In order to assess trends, we tabulated and plotted the number of surgical procedures over time, stratified by procedure category. As trend lines appeared linear, we used univariable linear regression to estimate beta coefficients and test against a null hypothesis of beta=0, using a P-value threshold of <0.05 for statistical significance. To determine trends in surgical volume accounting for rising numbers of cirrhosis admissions, we repeated the above approach with all estimates divided by the number of national cirrhosis admissions (per 1000 admissions). In exploratory analyses, we produced plots of overall surgical volume and associated in-hospital mortality over time as stratified based on elective or non-elective admission status, as well as by compensated or decompensated cirrhosis status. For comparisons of beta coefficients between trend lines, we performed the Chow test.

Results

There were 221,296 surgical procedures of interest performed on patients admitted with cirrhosis from 2005-2014 (Table 1). Major abdominal and major cardiovascular surgeries had the highest elective admission rates (51.1% and 51.2%, respectively) and the highest median length of stay (9 and 10 days, respectively). Patients who underwent hernia repair or major orthopedic surgery were most likely to have alcohol-related liver disease (36.3% and 36.8%, respectively). The Elixhauser comorbidity index was highest in those undergoing major cardiovascular surgeries. In-hospital death rates were highest among those undergoing major abdominal (14.7%) and cardiovascular surgeries (9.9%), and lowest among those undergoing major orthopedic procedures (2.2%).

The estimated number of hospital admissions with cirrhosis increased significantly over time, from 380,246 in 2005 to 604,385 in 2014 (β=25,639, P<0.001; Table 2). Similarly, the absolute number of surgical procedures increased from 20,717 to 25,405 over the same period (β=499.05, P<0.001). While the most commonly performed procedure in each year was cholecystectomy, the highest rate of increase in overall surgical volume was observed in major orthopedic procedures, followed by hernia repairs, and then major cardiovascular surgeries (β=310.77, P<0.001; β=159.32, P<0.001; β=55.99, P=0.026; Fig. 1A, Table 2).

While the number of hospital admissions with cirrhosis increased over time, the number of surgeries per 1,000 cirrhosis admissions decreased from 2005 to 2014 (β=-1.454, P<0.001; Supplementary Table 2, Fig. 1B). The rates of cholecystectomy declined the most precipitously (22.3 per 1,000 in 2005 vs. 12.7 per 1,000 in 2014; β=-1.004, P<0.001), followed by

Table 1 Hospitalization characteristics for 2004-2014 cohort

Variable	Cholecystectomy (N=76,950)	Hernia repair (N=44,878)	Other major abdominal (N=34,158)	Major orthopedic (N=50,638)	Major cardiovascular (N=14,672)
Age (years; median, IQR)	60 (52-71)	58 (52-66)	61 (54-71)	62 (55-71)	64 (56-71)
Female (%)	43.7	31.3	41.8	50.2	26.0
Race (%)					
White	66.9	70.6	72.3	78.7	76.0
Black	8.8	8.6	8.5	6.5	6.8
Hispanic	17.0	16.1	13.2	10.2	11.0
Primary insurance (%)					
Medicare	46.4	41.6	46.9	56.5	54.1
Medicaid	14.4	19.6	13.5	13.6	12.9
Private	28.1	28.2	29.7	23.3	25.3
Self-pay	6.3	5.4	5.7	3.0	3.9
Elixhauser comorbidity index (median, IQR)	4 (2-5)	4 (3-5)	5 (3-6)	4 (2-5)	6 (5-8)
Etiology of liver disease (%)					
Hepatitis C	13.1	14.9	9.3	11.1	11.5
Alcohol	20.9	36.3	27.4	36.8	31.7
Fatty liver	10.9	7.7	12.6	7.3	8.4
Unclassified/missing	55.1	41.1	50.7	44.8	48.4
Decompensated cirrhosis (%)	19.7	37.4	25.7	17.8	17.9
Length of stay (days; median, IQR)	6 (3-9)	5 (3-10)	9 (5-16)	5 (3-8)	10 (6-17)
Elective admission (%)	29.5	33.2	51.1	41.8	51.2
Region (%)					
Northeast	14.4	17.1	17.3	17.7	18.5
Midwest	18.2	20.0	20.5	20.4	20.1
South	41.3	37.6	39.3	39.2	40.1
West	26.1	25.3	22.9	22.8	21.3
Hospital size					
Small	10.9	10.1	10.1	12.5	5.5
Medium	24.5	23.9	22.9	25.4	18.6
Large	64.6	66.0	66.8	62.0	75.9
Location/teaching status of hospital					
Rural	11.6	7.7	7.9	9.3	2.5
Urban nonteaching	41.8	35.5	34.5	41.9	28.5
Urban teaching	46.6	56.8	57.5	48.8	69.0
Inpatient death (%)	3.5	4.2	14.7	2.2	9.9
Hospital charges ($; median, IQR)	48,318 (28,045-92,271)	45,049 (24,897-93,337)	80,639 (45,651-152,326)	52,031 (35,013-82,672)	150,547 (94,492-258,331)

IQR, interquartile range

major abdominal surgery (8.9 vs. 6.3; β=-0.316; P<0.001) and hernia repair (8.9 vs. 6.3; β=-0.316; P<0.001). The only surgical subcategory volume to increase over time was major orthopedic surgeries, though this change was not statistically significant (from 9.9 to 11.4 per 1,000 cirrhosis admissions; β=0.083, P=0.078).

When surgical procedure volume was stratified by elective admission status (Fig. 2A), elective major orthopedic

Table 2 National estimates and trends in hospital surgical procedures among cirrhosis hospitalizations

Discharge year	Cholecystectomy (N=76,950)	Hernia repair (N=44,878)	Other major Abdominal (N=34,158)	Major orthopedic (N=50,638)	Major cardiovascular (N=14,672)	Total surgeries (N=221,296)	Total cirrhosis admissions (N=4,824,116)
2005	8394	3900	3383	3776	1265	20717	380246
2006	7812	3874	3596	4079	1458	20820	404908
2007	7526	4165	3270	4316	1257	20534	414285
2008	7803	4109	2989	4607	1200	20708	421855
2009	7328	4212	3314	4860	1665	21379	457917
2010	7860	4692	3326	4932	1223	22033	484560
2011	7841	4736	3434	5369	1509	22890	532159
2012	7640	4805	3430	5800	1480	23155	552525
2013	7080	5260	3625	6035	1655	23655	571275
2014	7665	5125	3790	6865	1960	25405	604385
Linear trend, (β, P-value)	-63.46 (P=0.101)	159.32* (P<0.001)	36.43 (P=0.142)	310.77* (P<0.001)	55.99* (P=0.026)	499.05* (P<0.001)	25639.80* (P<0.001)

*$P<0.05$
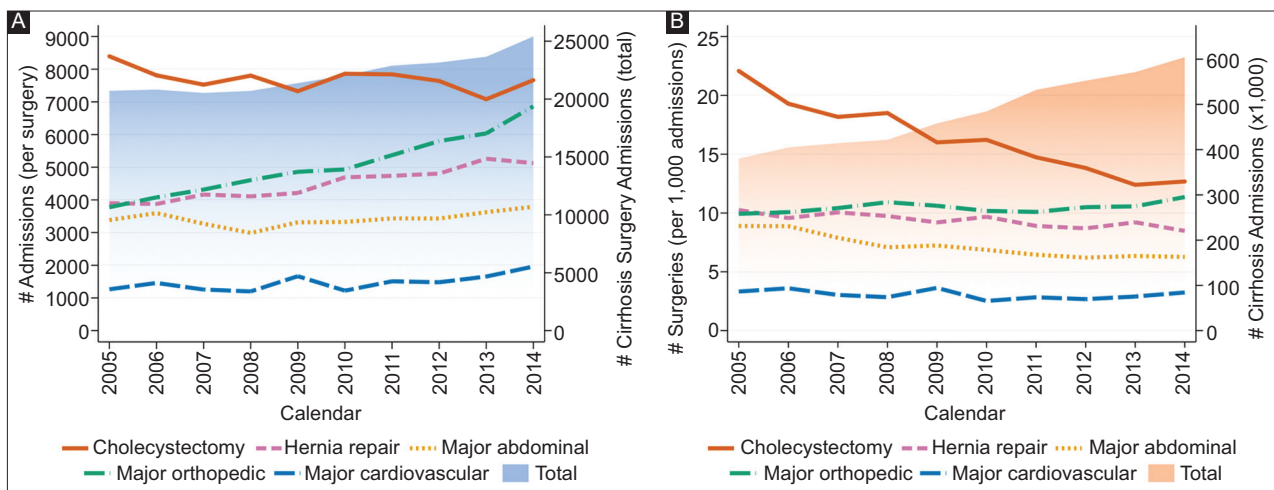
Figure 1 (A, B) National trends in cirrhosis surgery admissions by overall volume (A) and per 1000 cirrhosis admissions (B)

surgeries increased significantly over time (β=177.9; P<0.001), surpassing cholecystectomy as the most common procedure by 2011. Cholecystectomy, hernia repairs and major abdominal surgeries were performed significantly more often in the non-elective than in the elective setting (each P<0.001), with cholecystectomy being the most common non-elective procedure overall. Major orthopedic procedures and hernia repairs had significantly increasing annual volumes among non-elective admissions (β=131.4; P<0.001 and β=134.0; P<0.001).

In-hospital mortality rates for major abdominal, major cardiovascular, hernia repair and major orthopedic surgeries were significantly higher in the non-elective vs. elective setting (each P<0.001, Fig. 2B). For elective admissions, in-hospital mortality rates were ≤10% over the entire study period. Major abdominal surgeries had the overall highest in-hospital mortality rate among non-elective admissions, exceeding 20%

across all time points. Mortality rates of major abdominal surgeries declined significantly in the elective setting (β=-0.005; P=0.013) but not in the non-elective setting (β=-0.00; P=0.275). Major orthopedic surgeries generally maintained the lowest inpatient mortality rate amongst both groups.

When cirrhosis surgery admissions were stratified by compensated or decompensated status, we observed significant increases in the absolute number of major orthopedic (β=272.4; P<0.001) and hernia repair (β=191.1; P<0.001) surgeries over time among patients with compensated cirrhosis (Fig. 3A). Trends in surgery volume were generally stable over time among patients with decompensated cirrhosis, and were numerically lower for each category as compared to patients with compensated cirrhosis. Regarding in-hospital mortality, decompensated cirrhosis conferred universally higher in-hospital mortality relative to compensated cirrhosis for each surgery type (Fig. 3B; each P<0.05 Q. Please mention the
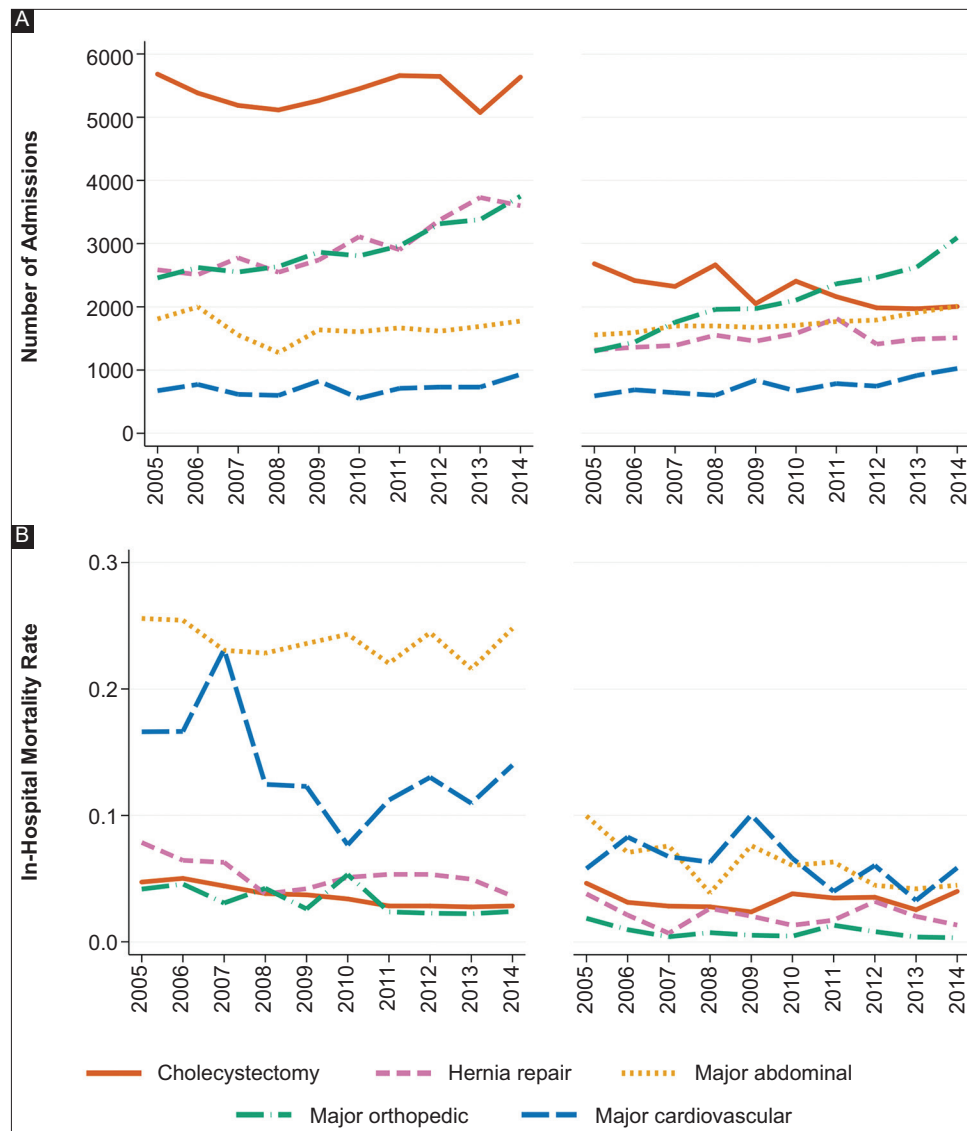
Figure 2 National trends in cirrhosis surgery admissions (A) and associated in-hospital mortality rates (B), each stratified by elective or non-elective admission status

exact P-value unless <0.001). In particular, although there was a trend towards decreasing in-hospital mortality for major abdominal surgery among patients with decompensated cirrhosis (β=-0.006, P=0.069), the in-hospital mortality rate remained significantly greater than that observed for patients with compensated cirrhosis (8.1% higher in 2014, P<0.001).

Discussion

In this large national study of data spanning more than one decade, we identified common surgical procedure categories for cirrhosis hospitalizations and revealed changes in overall national trends. We additionally performed analyses addressing differences by elective admission status,

compensated vs. decompensated status, as well as trends in in-hospital mortality.

First, our study demonstrated that while the number of cirrhosis admissions and absolute surgical volume is increasing over time, the number of surgeries per 1,000 cirrhosis admissions is decreasing. There are several possible explanations for this finding. First, as the population of patients with cirrhosis is aging, a similar need for surgery may result in excess hospitalization and hospital readmission for post-surgical complications. Second, the data may alternatively suggest an increasingly conservative approach to surgery that may potentially be explained by risk aversion attributable to a higher-risk patient population. A statewide population-based study found that new diagnoses of cirrhosis increased by 69% (from 620 to 1045) between 2004 and 2014 [12], with the greatest increase occurring in patients
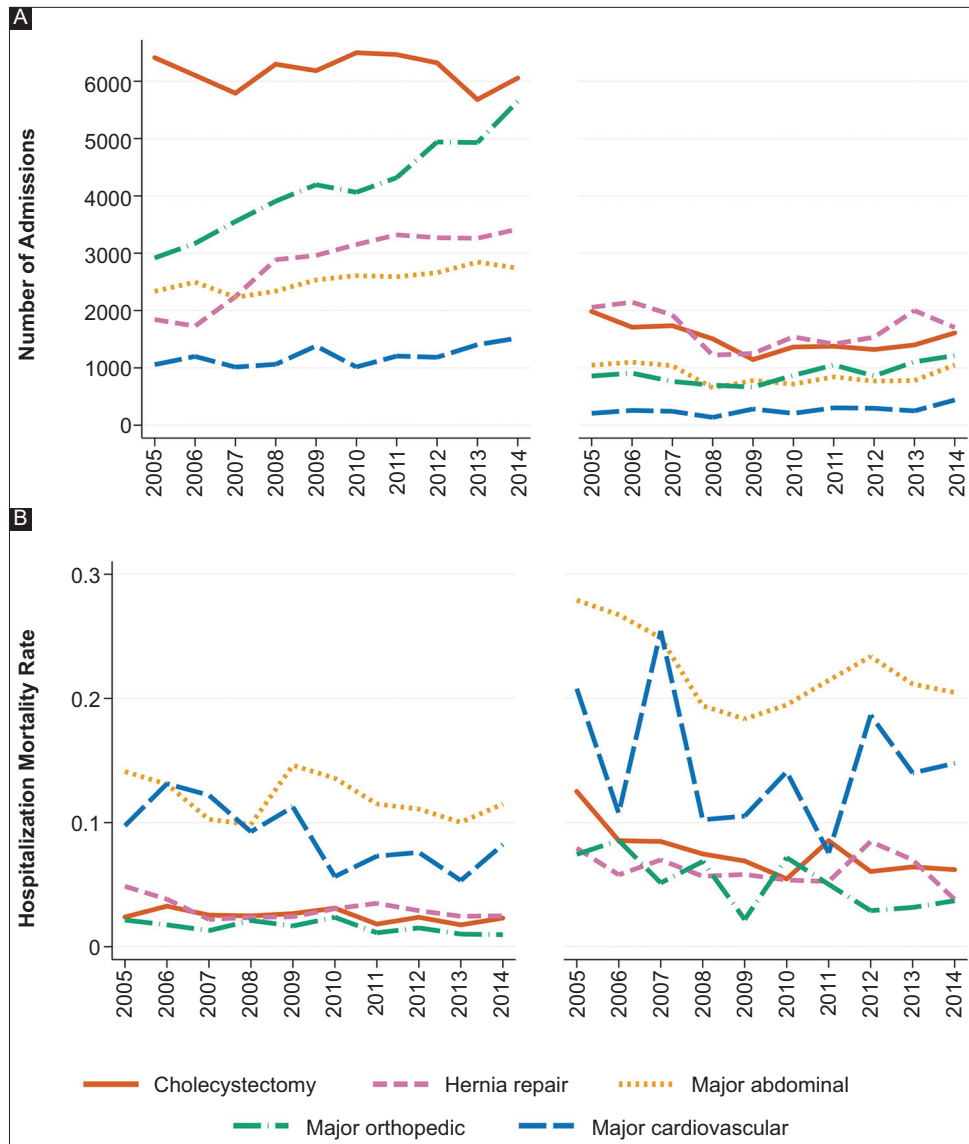
Figure 3 National trends in cirrhosis surgery admissions (A) and associated in-hospital mortality rates (B), each stratified by compensated or decompensated cirrhosis status

aged 65 years and older. Over the same time period, a study of 126 Veteran Administration hospitals showed that, while in-hospital mortality decreased from 11.4% to 7.6% among cirrhosis hospitalizations, 30-day post-discharge mortality increased from 9.3% to 10.1% [13]. Taken together, these data raise the question of whether an aging and frailer population of patients with cirrhosis could account for the relative decline in rates of invasive surgical procedures being offered to these individuals. Third, an additional explanation for risk aversion could be the expanded use of preoperative cirrhosis surgical risk scores such as the Mayo risk score [14], which has been demonstrated to overestimate surgical risk [15]. This is important, as risk aversion is apparently progressing despite relatively stable or potentially reduced in-hospital mortality among certain groups of patients (e.g., elective major abdominal surgery). This implies that preoperative

risk-stratification tools may need to be reassessed and/or recalibrated for the modern surgical era, as has been argued recently [16]. Future research is needed to distinguish between the above hypotheses.

Second, we found an increasing volume of major orthopedic surgeries among patients with cirrhosis, regardless of elective admission status, although the rates per 1000 cirrhosis admissions have remained generally stable over time. Other studies have demonstrated that the volume of both total knee (TKR) and total hip (THR) replacements has been increasing annually among the general population. Cram *et al* reported a 161.5% overall increase in TKR from 1991-2010 in a Medicare population [17]. Nwachukwu *et al* found a 1.5% annual increase in THR from 2005-2011 [18]. These trends probably reflect the demonstrated improvements in quality of life and mobility in concert with the acceptable safety profile

of these procedures [19,20]. In our study, the increase in major orthopedic procedures among elective cirrhosis admissions was more than 200% from 2005-2014. This notable trend may correspond to the expanding awareness that frailty and poor functional status increase mortality for patients with cirrhosis, in addition to the lower perceived risk of these procedures [21,22]. As such, elective procedures to improve mobility and decrease pain may be beneficial in selected patients.

Third, in an exploratory analysis of surgery-specific mortality trends, we first noted significantly higher in-hospital mortality rates when procedures were performed in the non-elective setting. The notable exception, however, was in the case of cholecystectomy, where in-hospital mortality rates were similar for elective and non-elective hospitalizations. This is a surprising finding, as the prevailing literature suggests a uniformly higher mortality rate with cholecystectomies performed under emergent circumstances. Our analysis also showed wide variation in in-hospital mortality rates by procedure type, primarily among non-elective cases. This is consistent with recently published literature demonstrating differences in short-term mortality by surgery type in adjusted models [4,23]. In particular, we found extremely high in-hospital mortality among patients undergoing non-elective major abdominal surgery, and among decompensated patients undergoing major abdominal surgery. The grave prognosis in these circumstances should be incorporated into clinical practice when considering surgical management, and in prognostic discussions with patients and healthcare proxies. Stated more broadly, the data presented herein suggest that future efforts to risk stratify patients with cirrhosis preoperatively should take account of the surgical procedure type, as well as the elective or non-elective surgical indication.

Finally, in a subgroup analysis of surgery admissions and in-hospital mortality stratified by compensated vs. decompensated cirrhosis status, we noted a significant increase in the absolute number of major orthopedic surgeries over time among patients with compensated cirrhosis. The current literature suggests higher rates of complications and mortality, and a longer length of hospital stay for orthopedic procedures compared with non-cirrhotic patients; however, these studies to do not stratify by compensated or decompensated status [24,25]. We also noted an increase in the total volume of hernia repair surgeries among patients with compensated cirrhosis over time, in line with current findings in the literature. In a recent retrospective review the mortality rate in patients with cirrhosis undergoing umbilical hernia repair was 1.3% for a model for end-stage liver disease (MELD) score <15 and 11.1% in patients with MELD 15 or greater [26]. Cholecystectomy remained the most common procedure performed over time in the compensated group. This can be attributed to the low complication rates and reduced hospital length of stay associated with laparoscopic cholecystectomy in patients with cirrhosis [27,28]. We also noted significantly higher rates of in-hospital mortality among patients with decompensated cirrhosis as compared to patients with compensated cirrhosis undergoing surgical procedures. These findings are consistent with the established literature that patients with decompensated cirrhosis are at higher risk of infection, bleeding, hepatic encephalopathy, poor nutritional status, and hemodynamic, renal and cardiopulmonary complications compared to individuals with compensated cirrhosis. In a 2006 systematic review of 118 studies, median survival time in patients with compensated vs. decompensated cirrhosis was greater than 12 years and around 2 years, respectively [29]. A recently published review of 87 studies found that, generally for elective procedures, patients with compensated cirrhosis had a minimal increase in perioperative mortality and that patients with decompensated cirrhosis had higher rates of mortality [30]. Therefore, compensated vs. decompensated status should be factored into preoperative risk assessment when evaluating patients with cirrhosis for surgery.

There are several limitations that we acknowledge in this study. First, as with any administrative database study, there is possible misclassification due to coding errors. This could cause over- or underestimation of observed trends; however, in aggregate we would expect this impact to be minimal [4]. Second, the use of in-hospital mortality as a metric does not capture patients who die shortly after discharge. This limitation of the NIS dataset warrants caution in interpreting the findings of this study with regard to short-term mortality after surgery in patients with cirrhosis. Third, by the nature of the NIS database, this analysis does not incorporate outpatient surgeries that do not involve hospitalization, expected to have a different risk profile. This may impact the external validity of this study, and it is important to highlight that the observed data reflect major surgical procedures requiring hospitalization. Fourth, the NIS database does not include laboratory data that would allow us to evaluate the impact of MELD score on surgical risk. It is additionally challenging to classify chronic comorbidities not directly related to hospitalization, as administrative codes are only supplied for individual admissions. Finally, we intentionally did not compare surgical trends or outcomes to patients without cirrhosis, as it is well-established that cirrhosis confers a greater surgical risk relative to patients without cirrhosis. Furthermore, the goal of this work was to focus on salient differences in surgical procedure types among patients with cirrhosis.

In conclusion, in this large analysis of national hospitalization data, we identified notable changes in surgical procedure trends among cirrhosis hospitalizations between 2005 and 2014. In-hospital mortality was higher among patients admitted non-electively, and varied substantially based on the type of surgery performed. Additional studies are needed to confirm and elucidate the underlying mechanism of these findings. However, our study highlights the need for risk prediction models that take account of surgical procedure type, elective/non-elective surgical indication, and decompensation status.

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Supplementary material

Supplementary Table 1 Classification of surgical procedures by ICD-9 clinical modification (CM) procedure codes*

Surgery classification	Subcategorization	ICD-9-CM procedure codes
Cholecystectomy		5123, 5122, 5121, 5124
Hernia repair		1711, 1712, 1713, 1721, 1722, 1723, 1724, 4642, 5300, 5301, 5302, 5303, 5304, 5305, 5310, 5311, 5312, 5313, 5314, 5315, 5316, 5317, 5321, 5329, 5331, 5339, 5341, 5342, 5343, 5349, 5351, 5359, 5361, 5362, 5363, 5369
Major abdominal	Total/partial colectomy	4572, 4573, 4574, 4575, 4576, 4579, 4581, 4582, 4583, 4604, 4850, 4851, 4852, 4859, 4862, 4863
	Total/partial nephrectomy	554, 5551, 5552, 5553, 5554
	Total/partial pancreatectomy	5251, 5252, 5253, 5259, 526, 527
	Total/partial splenectomy	4142, 4143, 415
	Total/partial gastrectomy	435, 436, 437, 4381, 4382, 4389, 4391, 4399
Major orthopedic	Total/partial knee, hip replacement or revision	8151, 8152, 8153, 8154, 8155
	Open reduction procedures (tibia/fibula, femur, radius/ulna, humerus)	7921, 7922, 7925, 7926, 7931, 7932, 7935, 7936
Major cardiovascular	Coronary artery bypass graft	3610, 3611, 3612, 3613, 3614, 3615, 3616, 3617, 3619
	Open cardiac valve repair or replacement	3510, 3511, 3512, 3513, 3514, 3520, 3521, 3522, 3523, 3524, 3525, 3526, 3527, 3528
	Abdominal aortic aneurysm repair	3834, 3844, 3864, 3971

*The presence of these procedure codes in any position was sufficient to classify a surgery during a hospital admission

Supplementary Table 2 National estimates and trends in surgical procedure rates per 1,000 cirrhosis hospitalizations

Discharge year	Cholecystectomy	Hernia repair	Other major abdominal	Major orthopedic	Major cardiovascular	Total
2005	22.1	10.3	8.9	9.9	3.3	54.5
2006	19.3	9.6	8.9	10.1	3.6	51.4
2007	18.2	10.1	7.9	10.4	3.0	49.6
2008	18.5	9.7	7.1	10.9	2.8	49.1
2009	16.0	9.2	7.2	10.6	3.6	46.7
2010	16.2	9.7	6.9	10.2	2.5	45.5
2011	14.7	8.9	6.5	10.1	2.8	43.0
2012	13.8	8.7	6.2	10.5	2.7	41.9
2013	12.4	9.2	6.3	10.6	2.9	41.4
2014	12.7	8.5	6.3	11.4	3.2	42.0
Linear Trend, (β, P-value)	-1.004* (P<0.001)	-0.166* (P=0.001)	-0.316* (P<0.001)	0.083 (P=0.078)	-0.052 (P=0.231)	-1.454* (P<0.001)

*P<0.05