Original Article

Postoperative Risk of Hepatic Decompensation after Orthopedic Surgery in Patients with Cirrhosis

Eric M. Nyberg[1], Michael Batech[2], T. Craig Cheetham[2], Jose R. Pio[2], Susan L. Caparosa[2], Mary Alice Chocas[1] and Anshuman Singh*[1,3]

[1]*Department of Orthopaedics, Kaiser Permanente, San Diego, USA;* [2]*Department of Research & Evaluation, Kaiser Permanente, Pasadena, USA;* [3]*Department of Orthopaedics, University of California at San Diego, San Diego, USA*

Abstract

Background and Aims: Previous studies have shown increased hepatic decompensation in patients with cirrhosis undergoing surgery. However, there are little data available in cirrhotics undergoing orthopedic surgery compared to cirrhotics who did not undergo surgery. The aim of this study was to examine the demographics, comorbid conditions, and clinical factors associated with hepatic decompensation within 90 days in cirrhotics who underwent orthopedic surgery. ***Methods:*** This is a retrospective matched cohort study. Inclusion criteria were cirrhosis diagnosis, age > 18 years, ≥ 6 months continuous health plan membership, and a procedure code for orthopedic surgery. Up to five cirrhotic controls without orthopedic surgery were matched on age, gender, and cirrhosis diagnosis date. Data abstraction was performed for demographics, socioeconomics, clinical, and decompensation data. Chart review was performed for validation. Multivariable analysis estimated relative risk of decompensation. ***Results:*** Eight hundred fifty-three orthopedic surgery cases in cirrhotics were matched with 4,263 cirrhotic controls. Among the cases and matched controls, the mean age was 60.5 years, and 52.2% were female. Within 90 days after surgery, cases had more decompensation compared to matched controls (12.8% vs 4.9%). Using multivariable analysis, orthopedic surgery, a 0.5 g/dL decrease in serum albumin, and a 1-unit increase in Charlson Comorbidity Index were associated with a significant increase in decompensation within 90 days of surgery. Diabetes, chronic obstructive pulmonary disease, and chronic kidney disease were seen with increased frequency in cases vs. matched controls. ***Conclusions:*** Cirrhotics who underwent orthopedic surgery had a significant increase in hepatic decompensation within 90 days of surgery compared to matched controls. An incremental decrease in serum albumin and an incremental increase in the Charlson Comorbidity Index were significantly associated with hepatic decompensation after surgery.

Keywords: Cirrhosis; Orthopedic surgery.

Abbreviations: CCI, Charlson Comorbidity Index; CPT, Childs-Pugh-Turcotte; EMR, electronic medical record; ICD-9, International Statistical Classification of Diseases and Related Health Problems-9; IRB, Institutional Review Board; KPSC, Kaiser Permanente Southern California; MELD, Model for End-Stage Liver Disease; THA, total hit arthroplasty; TKA, total knee arthroplasty.

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***Correspondence to:** Anshuman Singh, Department of Orthopedics, The Garfield Specialty Center, 5893 Copley Drive, San Diego, CA 92111, USA. Tel: +1-213-359-2269, E-mail: Anshuman.X.Singh@kp.org

Introduction

Chronic liver disease is a leading cause of morbidity and mortality worldwide, and in 2011, cirrhosis was the 11th most common cause of death in the United States.[1] As the incidence of chronic liver disease and cirrhosis increases, more patients with cirrhosis are undergoing surgery of all types. Previous studies have demonstrated an elevated risk of perioperative morbidity and mortality in patients with cirrhosis who undergo nonhepatic surgery.[2–6] Additional studies have evaluated perioperative risks and complictions in cirrhotics undergoing orthopedic surgery and compared them to noncirrhotic controls.[7–14] A recent study by Kim et al. evaluated 609 patients with chronic liver disease who underwent surgery, including 246 patients who had cirrhosis and 363 patients without cirrhosis.[15] The cirrhotic group had markedly higher postoperative morbidity and mortality than those without cirrhosis.

Between 1995 and 2011, Deleuron et al. compared 363 cirrhosis patients with 109,159 noncirrhosis patients who had undergone total hip arthroplasty (THA) or total knee arthroplasty (TKA).[15] This Danish registry-based historical cohort study showed that cirrhosis patients who underwent THA or TKA for primary osteoarthritis had worse outcomes than reference patients undergoing the same procedures. Notably, cirrhotic patients had a high risk of readmission for infection, renal failure, and liver disease. These results indicated that the increased risk applied to all cirrhosis patients and was not restricted to severe cases. Orozco et al. compared hepatitis C and a nonhepatitis C groups who underwent orthopedic surgery and found that hepatitis C patients without significant fibrosis did not have an increased risk of complications. However, for TKA there was a correlation between greater fibrosis and higher infection rates. Liao et al. evaluated the complication rate after instrumental lumbar surgery between noncirrhotic patients and cirrhotic patients.[14] The rate of complications after instrumented lumbar surgery was significantly higher in patients with cirrhosis than in control patients, especially with subjects who had a Child-Turcotte-Pugh (CPT) score of 6 or more. The dominant postoperative complication in this study was deteriorated hepatic encephalopathy, which occurred even in patients with stable liver disease.

The risk of complications in cirrhotic patients after orthopedic surgery requires further evaluation. To date, the focus of research has been to compare individuals with cirrhosis to those without cirrhosis. The authors are not aware of any studies that have specifically evaluated the effect of orthopedic surgery on hepatic decompensation in cirrhotic patients compared to cirrhotic controls not undergoing orthopedic surgery. We feel that a cirrhotic control group is important since cirrhosis in itself is associated with a certain risk of decompensation due to the natural history of the disease. The aim of the present study was, therefore, to evaluate the risk of postoperative hepatic decompensation in patients with cirrhosis after undergoing orthopedic surgery compared to cirrhotic controls who did not undergo orthopedic surgery.

Methods

Study Population

This retrospective matched cohort study was conducted with Kaiser Permanente Southern California (KPSC). KPSC is an integrated health care delivery system comprising 14 hospitals, 214 outpatient clinics, and serving approximately 4 million members. All healthcare encounters were captured by a comprehensive electronic medical record (EMR) and by a thorough claims system. These data include information on patient demographics, socioeconomic status, coded diagnoses and procedures, laboratory test results, and other relevant information. The study was approved by the KPSC Institutional Review Board (IRB), and the IRB waived the requirement for patient informed consent as this was a database study without direct patient contact. The KPSC member population is varied and reflects that of the overall Southern California population.[16]

Inclusion criteria

Participants were included if they received a diagnosis of cirrhosis by International Statistical Classification of Diseases and Related Health Problems-9 (ICD-9) from 01 January 2003 to 31 December 2013, were ≥ 18 years old, and had ≥ 6 months continuous health plan membership (Fig. 1).

Cases and Controls

Cirrhotic cases and controls had the same inclusion criteria with the exception of cirrhotic cases having undergone orthopedic surgery based on Current Procedural Terminology procedure codes. Up to five cirrhotic controls not undergoing orthopedic surgery were matched to each case based on age, gender, cirrhosis diagnosis date, and surgery date. See Figure 1 for patient disposition.

Data collection

Data on baseline demographics, socioeconomics, comorbid conditions, lab values, Charlson Comorbidity Index (CCI), and Model for End-Stage Liver Disease (MELD) score were collected during the pre-index period, which was defined as 6 months prior to the index surgery date (primary index date). Baseline demographics included age, gender, race/ethnicity, and neighborhood household income. Household income was estimated on the basis of address using neighborhood income from the US Census. The Quan adaption of the CCI was calculated as an estimate of health status.[17,18] The cases undergoing surgery were matched with cirrhotic controls who did not undergo surgery using a second index date defined as the date of surgery for the case.

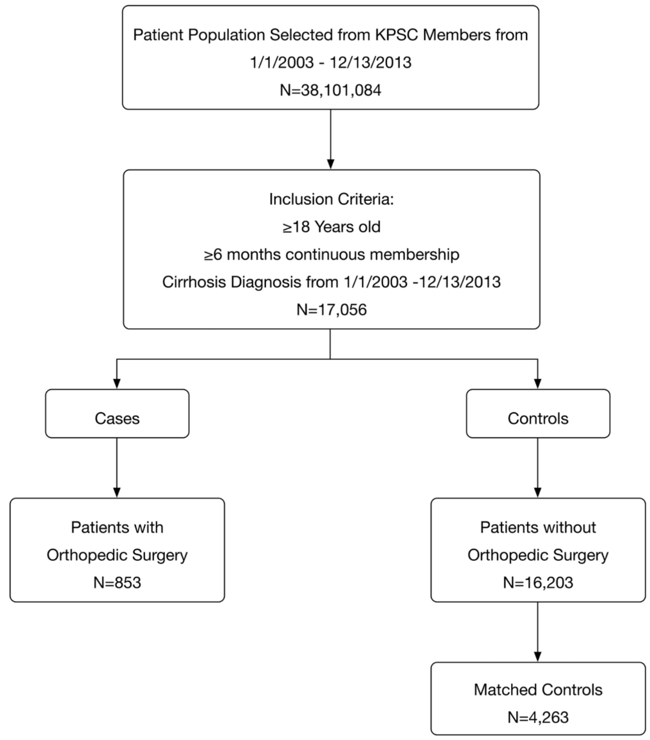

Fig. 1. Selection criteria for cases and controls.

Hepatic decompensation events that occurred 90 days after the surgery index date were accessed. Hepatic decompensation was defined as new onset or worsening of 1) ascites, 2) spontaneous bacterial peritonitis, 3) variceal bleeding, and/or 4) hepatic encephalopathy. Decompensation events were identified electronically using ICD-9 codes.

Validation of data

To validate the electronic algorithm and to verify decompensation events, chart review was performed on a 10% random sample of control subjects and with all surgery subjects included in the analysis. To increase algorithm accuracy for hepatic encephalopathy, codes for common medications used to treat this complication, including rifaximin and lactulose, were included in the electronic algorithm. Additionally, targeted chart review was performed to verify that lactulose and rifaximin were given for hepatic encephalopathy and not another medical reason. Further, in all cases with abdominal imaging, paracentesis, and/or upper endoscopy within 90 days after surgery, targeted chart review was performed to double-check specifically for ascites, spontaneous bacterial peritonitis, or variceal bleeding.

Statistical analyses

Descriptive statistics were presented as means and range for continuous variables and frequency (percentages) for categorical variables. Multivariable conditional robust Poisson regression was used to estimate relative risk of decompensation. SAS Enterprise Guide 4.3 (SAS Institute Inc., Cary, NC, USA) was used for all data analyses.

Results

Patient Characteristics

A total of 853 patients with cirrhosis who underwent orthopedic surgery (cases) were matched with 4,263 cirrhotic controls. Among the cases and matched controls, the mean age was 60 years, and 52% were female (Table 1). The distribution among ethnicities and neighborhood household income is shown in Table 1. The baseline CCI was similar overall between cases and controls, as shown in Table 1. Additionally, baseline comorbid conditions and selected laboratory parameters are shown in Table 2. The cases had less advanced liver disease by the selected laboratory parameters and had higher percentages of the selected comorbid conditions.

Rate of Complications

Within 90 days after surgery, patients with cirrhosis who underwent orthopedic surgery had more decompensation events compared to matched controls (12.8% vs 4.9%) (Fig. 2). Among the cases that had a decompensation event, 55% (60/109) underwent nonelective surgery and 78% (85/109) underwent a procedure associated with a higher volume of blood loss (78% moderate blood loss vs 22% low blood loss) (Table 3).

Using robust Poisson regression with a decompensation event as a binary outcome, the crude and multivariable adjusted relative risk estimates for decompensation events within 90 days after surgery were compared to that in a matched cohort (Table 4). Multivariable analysis showed a significant (2-fold) increase in the relative risk of developing a decompensation event within 90 days after surgery compared to matched cirrhotic controls. Multivariable analysis showed that the relative risk of decompensation was significantly increased for each 0.5 g/dL decrease in serum albumin (from 4.0 g/dL) and for each one point increase in the CCI.

Discussion

In this study of 853 patients with cirrhosis who underwent orthopedic surgery, the adjusted relative risk of decompensation within 90 days after surgery was 2-fold higher than that of 4,263 patients with cirrhosis (controls) matched by age, gender, and date of cirrhosis diagnosis. The rate of decompensation within 90 days after surgery in cases was 12.8% versus 4.9% in controls (Fig. 2). The baseline CCI was similar among cases vs. controls, however, individual laboratory parameters at baseline suggest that the cases were selected for as having a lower severity of liver disease compared to controls. This is implied by a baseline lower platelet count in cirrhotic controls than in cases. Lower platelet count is a commonly used surrogate marker for degree of portal hypertension in cirrhotics. Additionally, controls had lower baseline albumin compared to cases, while bilirubin was slightly higher among cases compared to controls. Despite this apparent selection for healthier patients, cases had a 2-fold increased rate of decompensation within 90 days after surgery. These findings support the suggestion of Rai et al. that the risk versus benefit of the procedure should be carefully assessed and discussed in patients with concurrent liver disease who are undergoing a surgical procedure.[19]

Determining surgical risk in cirrhotic patients is difficult, and multiple scoring systems have sought to quantify this risk. Kim et al. showed that the type of surgery, CPT score, and MELD score were independently associated with postoperative morbidity and mortality in patients with cirrhosis.[20]

Table 1. Demographic characteristics of patients with cirrhosis who had orthopedic surgery matched with patients with cirrhosis who did not have orthopedic surgery, by age, gender, and date of cirrhosis diagnosis, 2003–2013, n = 5116

	Orthopedic Surgery (Cases) n = 853 (16.7%)	No Orthopedic Surgery (Controls) n = 4,263 (83.3%)	*p*-value
Age (years, continuous)			0.8527
Mean (Range)	60.5 (18.0–91.0)	60.4 (18.0–93.0)	
Gender			0.9896
Female	445 (52.2%)	2225 (52.2%)	
Male	408 (47.8%)	2038 (47.8%)	
Race/Ethnicity			
White	485 (56.9%)	1888 (44.3%)	
Black	68 (8.0%)	421 (9.9%)	
Hispanic	236 (27.7%)	1444 (33.9%)	
Asian/Pacific Islander	53 (6.2%)	296 (6.9%)	
Other	11 (1.3%)	214 (5.0%)	
Neighborhood Household Income (Category)[1]			
< 45,000 USD	199 (23.6%)	1185 (28.3%)	
45,000 – 80,000 USD	429 (50.9%)	2017 (48.1%)	
> 80,000 USD	215 (25.5%)	990 (23.6%)	

[1] Neighborhood income is not reported income but is estimated on the basis of members' addresses using neighborhood income from US Census tract information.

Table 2. Comorbid conditions and laboratory parameters[1] of patients with cirrhosis who had orthopedic surgery matched with patients with cirrhosis who did not have orthopedic surgery, by age, gender, and date of cirrhosis diagnosis, 2003–2013, n = 5116

	Orthopedic Surgery (Cases)	No Orthopedic Surgery (Controls)	*p*-value
Charlson Comorbidity Index (categorical)			0.0966
≤ 1	92 (10.8%)	540 (12.8%)	
> 1	761 (89.2%)	3669 (87.2%)	
Chronic Heart Failure			0.2222
No	666 (78.1%)	3364 (79.9%)	
Yes	187 (21.9%)	845 (20.1%)	
Diabetes Mellitus			0.0083
No	483 (56.6%)	2587 (61.5%)	
Yes	370 (43.4%)	1622 (38.5%)	
COPD			0.0013
No	723 (84.8%)	3733 (88.7%)	
Yes	130 (15.2%)	476 (11.3%)	
Chronic Kidney Disease			0.0082
No	657 (77%)	3408 (81%)	
Yes	196 (23%)	801 (19%)	
MELD Score			0.0002
N	481	1427	
Mean (Range)	8.5 (6–31)	9.8 (6–44)	
INR			<0.0001
N	652	1666	
Mean (Range)	1.2 (0.9–3.2)	1.3 (0.9–5.2)	
Serum Creatinine (mg/dL) (categorical)			0.7464
≤ 1.5 mg/dL	675 (87.3%)	2037 (87.8%)	
> 1.5 mg/dL	98 (12.7%)	284 (12.2%)	
Total Bilirubin (mg/dL) (categorical)			0.0249
≤ 2.0 mg/dL	503 (87.5%)	1603 (83.6%)	
> 2.0 mg/dL	72 (12.5%)	314 (16.4%)	
Serum Albumin (g/dL) (categorical)			0.0001
> 3.5 g/dL	266 (56.2%)	683 (46.0%)	
< 3.5 g/dL	207 (43.8%)	802 (54.0%)	
Platelet Count (1000/μL) (categorical)			0.0005
≥ 75 × 1000/μL	727 (89.2%)	1901 (84.2%)	
< 75 × 1000/μL	88 (10.8%)	357 (15.8%)	

[1] The closest lab measured within 180 days of the cases' surgery date was used.

The present study shows that the MELD score and platelet count trend toward statistical significance as a predictor of the risk of decompensation within 90 days of orthopedic surgery. Due to the retrospective design of the present study, one or more parameters included in the MELD score were frequently missing, therefore, a trend toward significance is notable. Further, multivariable analysis showed that the relative risk of decompensation increased significantly with a corresponding incremental change in serum albumin and CCI (Table 4).

Causey et al. performed a single-center retrospective review of 64 cirrhotic patients who underwent nontransplant surgery under general anesthesia over a 6-year period of time to analyze outcomes on postoperative morbidity and mortality using CTP, MELD, and MELD-sodium (MELD-Na) scores.[21] Kim et al. utilized CTP and MELD-based indices to compare the abilities of liver indices to predict mortality for patients with liver cirrhosis who underwent elective surgery.[20] The authors concluded that a large-scale study is needed to validate how well liver indices that assess the severity of hepatic decompensation predict perioperative adverse events.[20] The present study strengthens the indication that these scoring systems are good predictors of perioperative risk. Further, this applies in cirrhotics undergoing orthopedic surgery compared to cirrhotics not undergoing orthopedic surgery, suggesting that events in the perioperative period precipitate

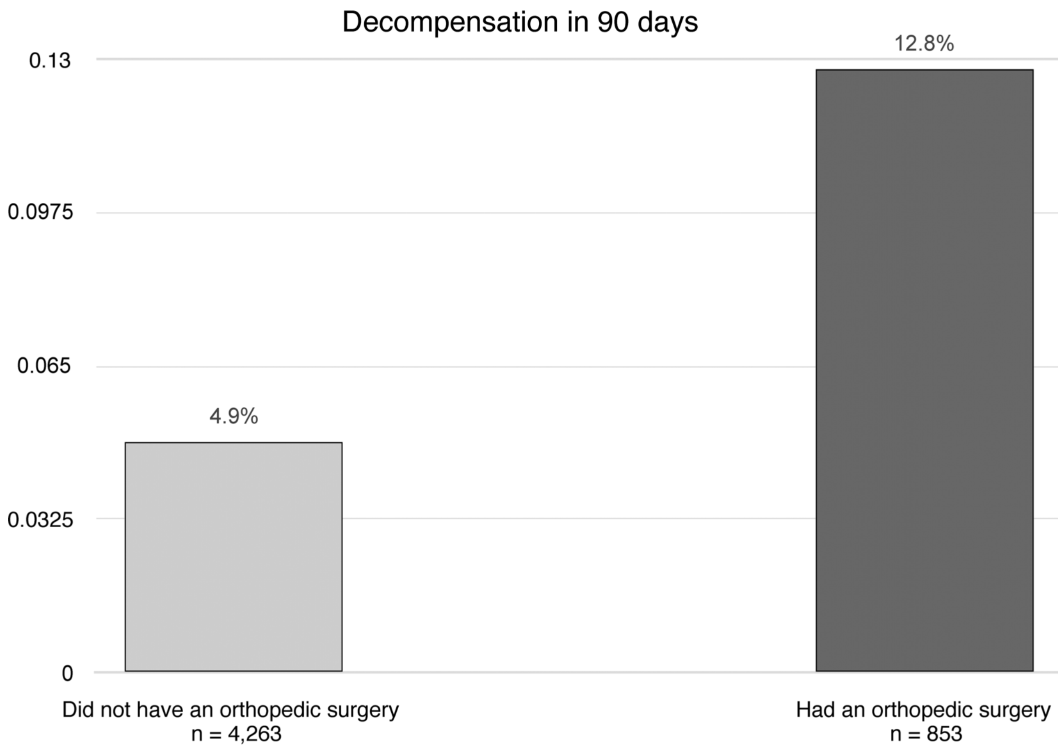

Fig. 2. Decompensation within 90 days after surgery among patients with cirrhosis who had orthopedic surgery matched with patients with cirrhosis who did not have orthopedic surgery, by age, gender, and date of cirrhosis diagnosis, 2003–2013.

hepatic decompensation at a significantly higher rate than that occurring due to the natural history of cirrhosis alone.

As the population in general is becoming more obese, it is expected that an increasing number of patients with obesity-related cirrhosis will undergo elective surgery. A study by Tiberi et al. compared 115 patients with cirrhosis and matched controls without cirrhosis who underwent THA or TKA from 2000 to 2012.[11] The authors concluded that patients with cirrhosis undergoing THA or TKA are at increased risk for medical and surgical complications. Patients with cirrhosis had longer hospital stays, more early post-operative hospital readmissions, and more frequent discharges to a skilled nursing or short-term rehabilitation facility compared with controls. Within 90 days of the procedure, the cirrhotic group had more hip dislocations, infections, and revision surgeries. In addition, the study found a correlation between increasing MELD scores and increased rates of complications; a MELD score of 10 or greater had the highest risk of complications. Using cirrhotics instead of healthy controls, our study demonstrates that exposure to orthopedic surgery is an independent risk factor for decompensation in this population.

Hsieh et al. have demonstrated an association between volume of blood loss and urgency of surgery and postoperative morbidity and mortality.[7] Similarly, we showed that a higher percentage of cases with a decompensation event had urgent surgery and underwent a procedure associated with higher blood loss (Table 3).

To our knowledge, this is the first matched cohort study to evaluate the rate of hepatic decompensation in cirrhotic patients undergoing orthopedic surgery compared to cirrhotic patients not undergoing surgery. A strength of this study is that it reflects a "real world" population including a large number of patients matched with up to five controls. The ethnic and socioeconomic distribution of the study population

Table 3. Association of surgical urgency and procedural blood loss with decompensation in 90 days (n = 863)

	No decompensation in 90 days, n = 744 (87.2%)	Decompensation in 90 days, n = 109 (12.8%)
Elective procedure status		
Non-elective	230 (30.9%)	60 (55.0%)
Elective	514 (69.1%)	49 (45.0%)
Procedure blood loss		
Low loss	349 (46.9%)	24 (22.0%)
Moderate loss	395 (53.1%)	85 (78.0%)

Table 4. Crude and multivariable adjusted relative risk estimates for decompensation within 90 days of surgery (using robust Poisson regression with decompensation event as a binary outcome)

	Crude	Multivariable adjusted
Orthopedic surgery		
No surgery	Reference	Reference
Had a surgery	2.57 (2.05, 3.21)	**2.05 (1.60, 2.62)**
Age (5-year increase)		
	1.08 (1.03, 1.13)	0.98 (0.93, 1.04)
Gender		
Female	Reference	Reference
Male	1.30 (1.02, 1.65)	1.02 (0.78, 1.32)
Race/Ethnicity		
White	Reference	Reference
Black	0.98 (0.67, 1.44)	0.76 (0.46, 1.24)
Hispanic	0.96 (0.75, 1.23)	1.01 (0.76, 1.34)
Asian/Pacific Islander	1.07 (0.72, 1.61)	1.23 (0.82, 1.85)
Neighborhood household income		
< 45,000 USD	1.07 (0.82, 1.38)	0.92 (0.68, 1.25)
45,000 – 80,000 USD	Reference	Reference
≥ 80,000 USD	1.03 (0.78, 1.36)	1.08 (0.80, 1.47)
MELD score (5-unit increase)		
	1.28 (1.21, 1.35)	1.06 (0.99, 1.14)
Serum albumin albumin (0.5-g/dL decrease)		
	1.59 (1.49, 1.70)	**1.49 (1.37, 1.62)**
Platelet count (25-unit decrease)		
	1.14 (1.09, 1.19)	1.03 (0.99, 1.07)
Charlson Comorbidity Index (1-unit increase)		
	1.22 (1.17, 1.27)	**1.11 (1.06, 1.17)**

is consistent with that of the general population of Southern California.[16] Further, the study was conducted within a large healthcare delivery system with an EMR allowing comprehensive evaluation of the medical care provided to patients, minimal ingress and egress, and thorough manual chart review was performed to validate the electronic algorithm and to confirm decompensation.

We matched cases with controls by age, gender, and cirrhosis diagnosis date; however, a limitation of the study is that we were not able to match cases and controls by markers of severity of liver disease. This was not possible due to incomplete clinical data for matching all criteria within an appropriate time period defined as 180 days. Additionally, we were unable to determine baseline CPT score and ASA score due to the nature of the study. Further limitations include drawbacks that are characteristic of retrospective studies, and those limitations inherent in using an electronic algorithm for data abstraction. These limitations include a risk of not identifying certain factors due to deficiencies in coding although an extensive chart review was performed, as noted above.

Conclusions

In summary, this study demonstrates a significant (2-fold) increase in the risk of hepatic decompensation in patients with cirrhosis within 90 days of undergoing orthopedic surgery compared to cirrhotics not undergoing orthopedic surgery. This finding reinforces the need for perioperative optimization of patients with cirrhosis and supports close monitoring of cirrhotic patients in the months following orthopedic surgery.

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Conflict of interest

None

Author contributions

Conception and design, interpretation of data, write-up, and preparation of manuscript (EMN), study design, analysis and interpretation of data, write-up, and critical review of manuscript (MB), conception and design, interpretation of data, write-up, and critical review of manuscript (TCC), data collection, write-up, and critical review of manuscript (JRP), data collection, write-up, and critical review of manuscript (MAC), data collection, write-up, and critical review of manuscript (SLC), conception and design, interpretation of data, write-up, and critical review of manuscript (AS).

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