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Original Research

The Impact of Hepatitis C and Liver Disease on Risk of Complications After Total Hip and Knee Arthroplasty: Analysis of Administrative Data From Louisiana and Texas

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ABSTRACT

Background: Millions of Americans have hepatitis C and other liver diseases, many of whom have end-stage osteoarthritis requiring total joint arthroplasty (TJA). This study aimed to determine the extent to which hepatitis C and other liver diseases are independent risk factors for complications, including readmission and reoperation, in patients undergoing TJA.

Methods: Retrospective study of a REACHnet data set containing demographics, International Classification of Diseases (ICD) and Current Procedural Terminology (CPT) codes, and clinical and laboratory data for patients who underwent primary total knee or hip replacement from 2013 to 2017 at 3 hospital systems in Louisiana and Texas. Multivariable logistic regression analyses examined predictors of complications. Any complication was defined as a 90-day medical complication or readmission or reoperation within 1 year.

Results: Among 13,673 patients who met inclusion criteria, 14.9% (2044/13,673) had any complication, 11.7% (1600/13,673) were readmitted within 90 days, and 3.6% (497/13,673) had a reoperation within 1 year. Liver disease increased the odds for any complication (odds ratio [OR], 1.12; 95% confidence interval [CI], 1.08-1.18), 90-day medical complication (OR, 1.13; 95% CI, 1.04-1.22), and 90-day readmission (OR, 1.11; 95% CI, 1.06-1.17). Hepatitis C was not, by itself, associated with an increase in any type of complication but was usually associated with liver disease. Comorbidity severity was the strongest predictor of all types of complications after TJA.

Conclusion: Patients in Louisiana and Texas with liver disease were at increased risk for complications after TJA, corroborating findings of previous studies. Hepatitis C was not an independent predictor of complications because of its high association with liver disease.

Introduction

Total hip arthroplasty (THA) and total knee arthroplasty (TKA) are commonly performed procedures with over 520,000 and 750,000 operations, respectively, performed in the United States during 2014 [1]. These numbers are expected to rise, and each may eclipse 5 million procedures per year by 2040 [2]. Among approximately 50,300 Americans diagnosed with acute hepatitis C each year [3], 55%-85% eventually progress to chronic hepatitis C [4], such that about 2.4 million people live with chronic hepatitis C [5]. Approximately 3%-8% of orthopedic patients are infected with hepatitis C [6]. An estimated 1.8% of Americans or 4.5 million people have chronic liver disease including cirrhosis [7]. As medical therapy extends the life expectancy of patients with hepatitis C and liver disease, increasing demand for total joint replacement (TJR)

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among these patients is expected and is growing faster than that among the general population [8-10]; it is, therefore, increasingly important to understand the extent to which these conditions increase risk of complications after TJR.

Liver disease has been associated with worse outcomes and higher costs after TJR. A recent meta-analysis of 10 case-control studies found that hepatitis C (including acute infection, chronic infection, and unspecific infection) was associated with a longer hospital length of stay and a higher rate of complications and revision surgery in patients undergoing TJR [6]. A number of studies also have identified cirrhosis, the end stage of all liver diseases, as a risk factor for TJR complications, particularly periprosthetic joint infection (PJI); cirrhosis is associated with a longer length of stay, higher costs and rates of readmission, and increased mortality after TJR [6,8,10-17]. PJI results in hardware loosening and is a major cause of failure in TJR and revision surgery [15,18,19]. Most studies of liver disease and TJR have either examined patients with hepatitis C exclusive of other liver conditions or patients with cirrhosis. It is unclear to what extent hepatitis C infection alone and liver conditions defined more broadly predict risk for complications after TJR. The present study aims to analyze a large database of primary TJR patients treated in hospitals located in Louisiana and Texas to examine the potential risks associated with hepatitis C and liver disease. We predict that hepatitis C and other liver diseases are associated increased rates of complications.

Material and methods

Patients and design

We obtained a data set from the Research Action for Health Network (REACHnet) for patients who received a primary TKA or THA during 2013-2017 at one of the following hospitals or hospital systems in Louisiana and Texas: Ochsner Health System, Tulane University, Baylor Scott & White Health. All eligible patients were of black or white race and had a body mass index (BMI) recorded within 1 year of surgery of $\geq$20 mg/kg^2. The data set included demographics, International Classification of Diseases (ICD) 9 and 10 codes, Current Procedural Terminology (CPT) codes, medications, and laboratory data. For each patient, data were available 90 days before TJR and 1 year after surgery. The study was approved by the institutional review board at Louisiana State University Health Sciences Center.

Any complication was defined as a medical complication within 90 days of surgery, readmission within 90 days, or reoperation within 1 year. Medical complications included anemia, thrombocytopenia, pneumonia, acute kidney failure, urinary tract infection, venous thrombotic events, serum reactions, transfusions, joint stiffness, neural deficit, vascular injury, hemorrhage, PJI, mechanical implant complication, implant loosening, wound infection, and wound complication. The ICD-9, ICD-10, and Current Procedural Terminology (CPT) codes used for patient selection and outcomes are shown in the Supplementary Appendix.

Statistical analysis

Univariable analysis examined complication rates by patient demographic and clinical characteristics. In addition, univariable analyses compared patients with and without liver disease. Chi-square tests were used to compare categorical variables and Wilcoxon signed-rank tests for continuous variables.

Logistic multiple regression analyses were performed to predict the likelihood of any complication, any medical complication within 90 days, hospital readmission within 90 days, and reoperation within 1 year. Variables entered into each mode included hepatitis C status, liver disease status, type of surgery (TKA vs THA), year of surgery, race, sex, age, BMI, and the Charlson Comorbidity Index. The Charlson Comorbidity Index was modified to exclude age and liver condition as these were already captured as covariates. Variables were standardized before performing regressions to ensure that odds ratios (ORs) were comparable. Standardized ORs quantify the effect of increasing each variable by one standardized unit. P values $< .05$ were considered statistically significant.

Results

Patient characteristics

A total of 13,673 met inclusion criteria. Among all patients, 15.0% (2044/13,673) had any complication, 11.7% (1600/13,373) were readmitted within 90 days, 3.6% (497/13,673) had a medical complication within 90 days, and 0.7% (94/13,673) had a reoperation within 1 year.

Table 1 presents the demographic and clinical characteristics of the overall sample and the univariable analyses for any complication. The majority of the sample was female (59.9%) and of white race (81%). The prevalence of hepatitis C and liver disease was 1.3% and 4.6%, respectively. Most patients with hepatitis C (80.2%) had concomitant liver disease, while most patients with liver disease (20.3%) did not have comorbid hepatitis C. Patients who experienced any complication had a significantly lower preoperative mean albumin (3.61 vs 3.71, $P < .001$) and platelet count (232.54 vs 237.03, $P = .037$) than patients who did not experience any complication. Only 6 of 182 patients with hepatitis C received treatment with a direct antiviral agent at any time before surgery. Among the 6 treated hepatitis C patients, 1 (16%) experienced a complication; in comparison, 42 of 176 (23.8%) untreated hepatitis C patients, many of which had concurrent liver disease, developed a complication.

Predictors of any complication (Fig. 1) and readmission within 90 days (Fig. 2) were liver disease (any complication: OR, 1.12; 95% confidence interval [CI], 1.08-1.18; 90-day readmission: OR, 1.11; 95% CI, 1.06-1.17), more severe comorbidity (any complication: OR, 1.30; 95% CI, 1.25-1.36; 90-day readmission: OR, 1.37; 95% CI, 1.30-1.43), black race (any complication: OR, 1.10; 95% CI, 1.05-1.15; 90-day readmission: OR, 1.13; 95% CI, 1.08-1.19), and BMI 30-40 mg/kg^2 (any complication: OR, 0.94; 95% CI, 0.89-0.996; 90-day readmission: OR, 0.94; 95% CI, 0.84-0.99). As shown in Figure 3, liver disease increased the risk of medical complication (OR, 1.13; 95% CI, 1.04-1.22), while patients with hepatitis C had a decreased risk of medical complication (OR, 0.76; 95% CI, 0.60-0.95). The latter result is likely due to the correlation between hepatitis C and liver conditions. THA (OR, 2.18; 95% CI, 1.75-2.71) and liver disease (OR, 1.17; 95% CI, 1.00-1.37) were predictors of reoperation within 1 year (Fig. 4). Removal of the 6 patients who were treated for hepatitis C from the multivariable analyses did not alter the findings.

Table 2 shows patient characteristics by liver disease status. Patients with liver disease were younger (62.7 vs 66.0 years, $P < .001$), more likely to undergo THA (38.5% vs 32.9%, $P < .001$), and more likely to have hepatitis C (23.0% vs 0.3%, $P < .001$), more likely to have higher BMI (32.8 vs 32.1, $P = .024$), and more likely to have severe comorbidity (1.5 vs 0.8, $P < .001$).

Discussion

In this study, multivariable analyses showed that patients who had liver disease were at increased risk for complications after TJR. Although others have shown that cirrhosis increases risk for complications after TJR [8,10-17], the present study indicates that liver disease more broadly defined also is a risk factor. Hepatitis C was

Table 1
Characteristics of the sample and results of univariable analyses for any complications.

Characteristic	All patients (n = 13,673), n (%)	Any complication (n = 2044), n (%)	No complication (n = 11,629), n (%)	*P* value
Total hip replacement	4530 (33.1)	712 (34.8)	3818 (32.8)	.08
Liver disease	634 (4.6)	161 (7.9)	473 (4.1)	<.001
Hepatitis C	182 (1.3)	43 (2.1)	139 (1.2)	.001
Black race	2561 (18.7)	470 (23)	2091 (18)	<.001
Male	5619 (41.1)	812 (39.7)	4807 (41.3)	.18
Year of surgery				<.001
2013-2014	4097 (30)	880 (43.1)	3217 (27.7)	
2015	4723 (34.5)	592 (29)	4131 (35.5)	
2016-2017	4853 (35.5)	572 (28)	4281 (36.8)	
	Mean (SD)	Mean (SD)	Mean (SD)	
Age, years	65.8 (10.7)	65.9 (11.8)	65.8 (10.5)	.254
CCI	0.9 (1.4)	1.3 (1.6)	0.8 (1.3)	<.001
Body mass index, kg/m^2	32.10 (6.7	32.31 (7.08)	32.11 (6.62)	.666
Laboratory values	Mean (SD, n)	Mean (SD, n)	Mean (SD, n)	
Albumin	3.70 (0.42, 3589)	3.61 (0.45, 57)	3.71 (0.42, 3018)	<.001
Sodium	139.62 (2.78, 6007)	139.60 (2.90, 870)	139.63 (2.77, 5137)	.998
Platelet count	236.35 (69.70, 5430)	232.54 (72.17, 827)	237.03 (69.23, 4603)	.037
INR	1.01 (0.16, 1257)	1.02 (0.16, 146)	1.01 (0.16, 1111)	.179
Creatinine	0.98 (0.63, 6463)	1.03 (0.71, 961)	0.97 (0.61, 5502)	.163
Bilirubin	0.58 (0.34, 3460)	0.57 (0.36, 560)	0.58 (0.34, 2900)	.108
TSH	2.22 (2.75, 265)	2.75 (6.07, 28)	2.15 (2.05, 237)	.185

CCI, Charlson Comorbidity Index; INR, International normalized ratio calibrated for cirrhosis values; SD, standard deviation; TSH, thyroid-stimulating hormone.

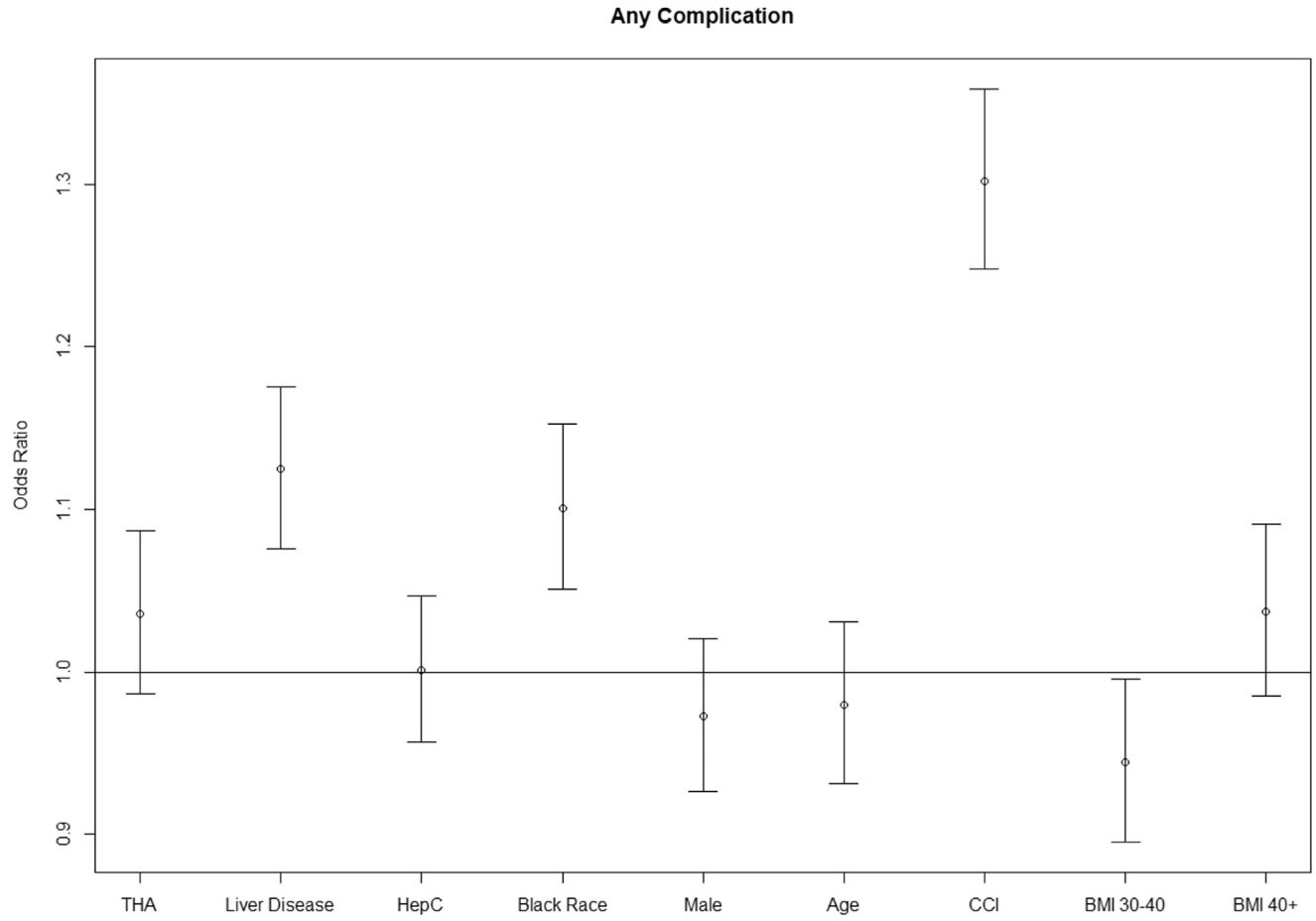

Figure 1. Predictors of any complication. Line bars indicate 95% confidence intervals. CCI, Charlson Comorbidity Index; HepC, hepatitis C.

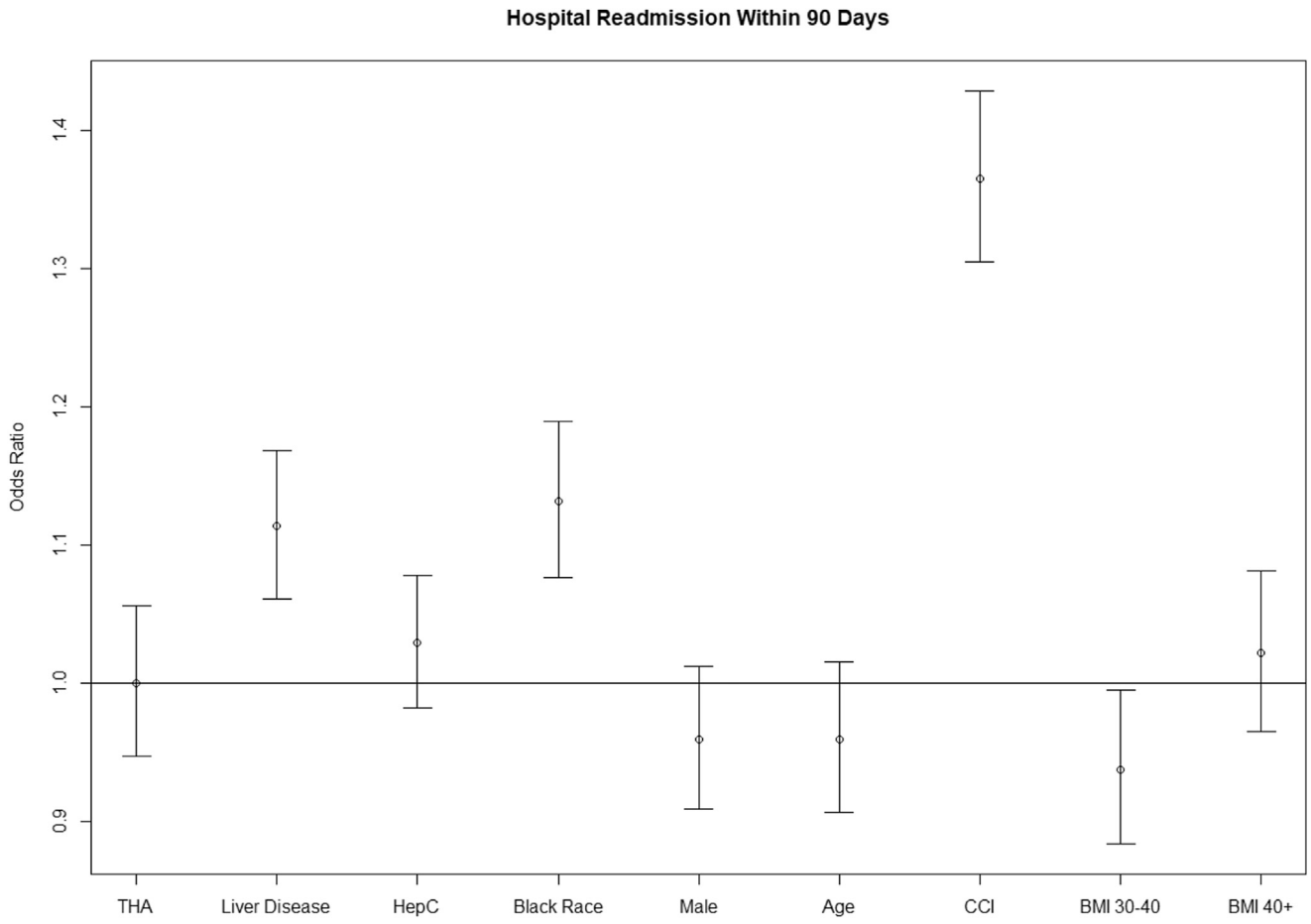

Figure 2. Predictors of hospital readmission within 90 days. Line bars indicate 95% confidence intervals. CCI, Charlson Comorbidity Index; HepC, hepatitis C.

associated with an increased risk of any complication in univariable analysis, but was not an independent predictor of any outcome in multivariable analyses, likely because 80% of patients with hepatitis C had comorbid liver disease which was strongly associated with outcomes. Our findings suggest that the sequalae from hepatitis C rather than hepatitis C itself may increase patients' risk for complications after TJR. Accordingly, it may be acceptable for surgeons not to delay TJR in patients with hepatitis C without concomitant liver disease but to be very wary of the risks associated with liver disease. To reduce potential risks presented by liver disease in patients undergoing TJR, patients with liver disease should be medically optimized before and after TJR. Preoperative optimization should include screening and intervention to address comorbidities associated with liver disease that may increase complication risk, such as anemia, thrombocytopenia, osteopenia, and osteoporosis [11,19].

Greater susceptibility for bacterial infection may be an important mechanism by which chronic liver disease increases risk of complications after TJR. Bacterial infections are a major contributing factor of morbidity and mortality in cirrhotic patients [20]. One study identified comorbid liver disease as the strongest predictor of deep PJI in patients undergoing TKA and THA [21], and 2 studies reported that infection was the most common complication and the major cause of prosthesis failure in cirrhotic patients undergoing THA [16,18]. There are other mechanisms by which chronic liver disease may contribute to postoperative complications as loss of liver function affects multiple organ systems and can produce coagulopathy, renal insufficiency, thrombocytopenia, encephalopathy, and multisystem organ failure [11,22-26].

Consistent with a growing body of literature showing that black race is a risk factor for poor outcomes after TJR [27-32], black race was a significant independent predictor of risk of complications after TJR in the present study. Potential modifiers of racial disparities in TJR outcomes include socioeconomic status and access to health care [28,31]. More severe comorbidity was also a significant predictor of risk of complications after TJR as has been reported in other studies [31-33]. Despite TJR being performed on an increasingly elderly and medically compromised patient population, the complication rates for TJR have continued to decrease over time [34-36], suggesting that steps can be taken to reduce risks of complications in patients with medical comorbidities.

One minor result demonstrated by our results was increased reoperation within 1 year for patients undergoing THA compared to TKA. This result is supported by George et al. who examined THA vs TKA outcomes [37]. They retrospectively examined THA vs TKA using procedural coding and found increased 30-day readmission and reoperation for patients undergoing THA compared to TKA [37]. Increased reoperation rate seems to be an inherent aspect of THA that we have demonstrated with our results.

This study had several limitations which should be noted. Laboratory data were not consistently available for all patients although it is standard of care to acquire a complete blood count and comprehensive metabolic panel before surgery. It is unclear whether missing laboratory data were due to irregular recording of

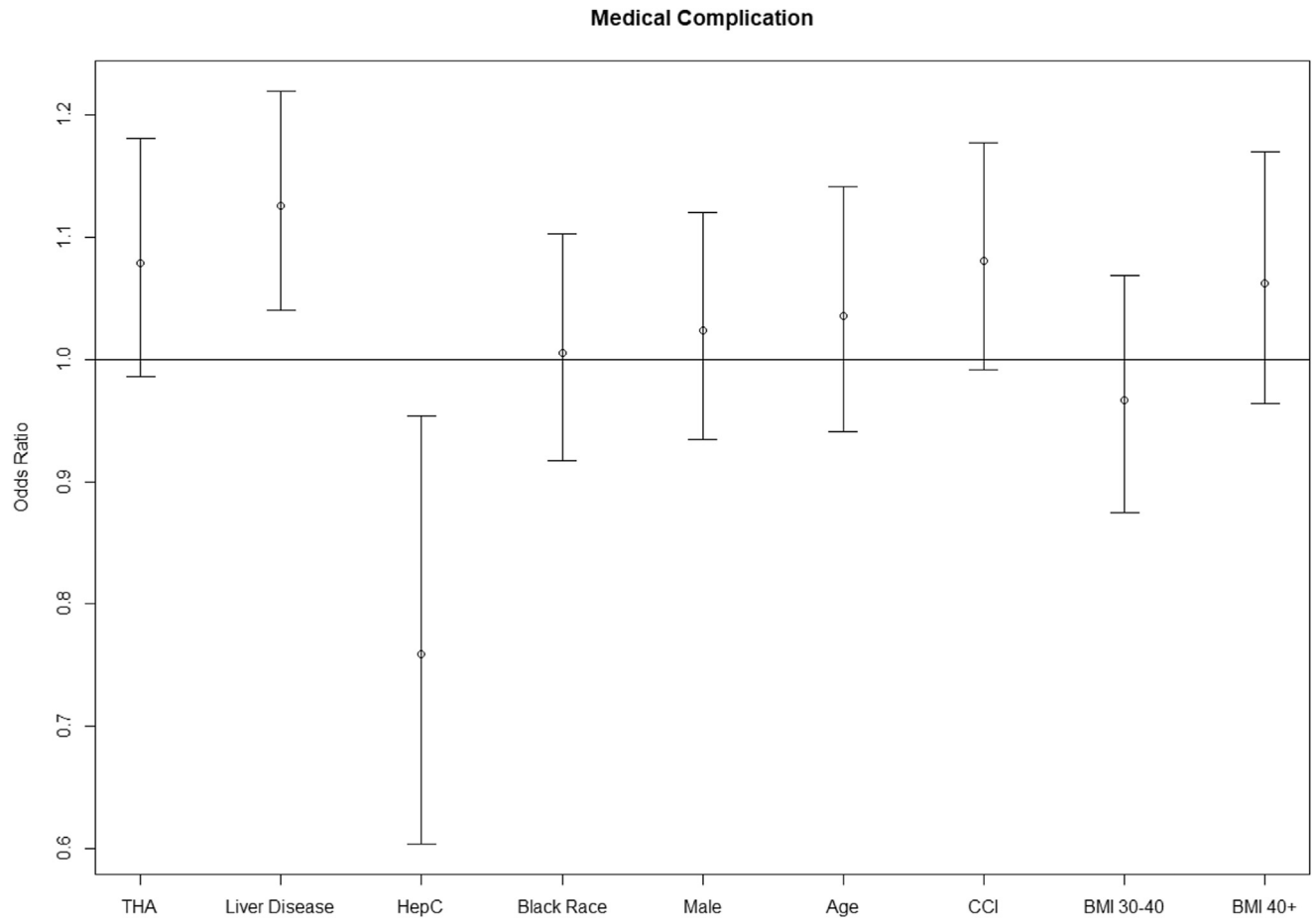

Figure 3. Predictors of any medical or surgical complication within 90 days. Line bars indicate 95% confidence intervals. CCI, Charlson Comorbidity Index; HepC, hepatitis C.

data at various sites or differences in physician preoperative laboratory ordering practices. Owing to the lack of consistent laboratory data, we were not able to stratify patients based on their Model for End-stage Liver Disease (MELD) scores. The small number of patients with hepatitis C who did not have concomitant liver disease may have limited the study's power to determine the risks associated with hepatitis C alone. We note that Best et al. found noncirrhotic hepatitis C to be associated with increased risk for perioperative complications after TJR [38]. A larger sample is needed to determine whether hepatitis C in the absence of any other liver conditions is an important predictor of complications after TJR. Finally, the number of patients with treated hepatitis C was surprisingly small. Many of the new treatments for hepatitis C started becoming available during this time period which could contribute to the low number of patients receiving treatment. Patients with Medicaid also may not have qualified for treatment because Louisiana and Texas had strict guidelines for qualifying for treatment during this time period. It was not until 2019 that Medicaid in Louisiana expanded to include hepatitis C treatment for all patients [39]. Recent studies demonstrate the possible benefits associated with treatment of hepatitis C [11,40,41]. Future studies should examine the effects of treated vs untreated hepatitis C patients using a very large patient population examining complications using clinical and ICD coding data. Our project is not equipped to make a recommendation on this issue; however, treatment of hepatitis C leads to decreased severity of liver disease which could potentially increase success after TJA.

Conclusion

This study expands upon the findings of previous studies by showing that liver disease more broadly defined than cirrhosis is associated with an increased risk of complications in patients undergoing TJR. Although hepatitis C did not appear to predict complications after TJR, conclusions regarding the risks presented by hepatitis C alone are not definitive given the small number of patients with hepatitis C and no other liver conditions in the study sample. Despite the increased risk of complications, TJR usage in the chronic liver disease population has increased over the last decade [35]. Surgeons should be aware of the risk presented by liver disease, order pertinent laboratory tests to determine the severity of liver disease, and medically optimize this population before surgery. Future studies should examine both the presence of liver disease and the severity of disease using the MELD score [9] as well as features of hepatitis C (eg, acute vs chronic, treated vs untreated, alone vs with concomitant liver disease) to more comprehensively determine the relationship between liver disease and risk in patients undergoing TJR.

Conflict of interests

P. C. Krause is a OTA EBQVS Committee member. V. Dasa is in the speakers bureau of/gave paid presentations for Bioventus, Swiftpath, and Pacira; is a paid consultant for Bioventus and Pacira; has stock or stock options in SIGHT Medical, My Medical Images, and

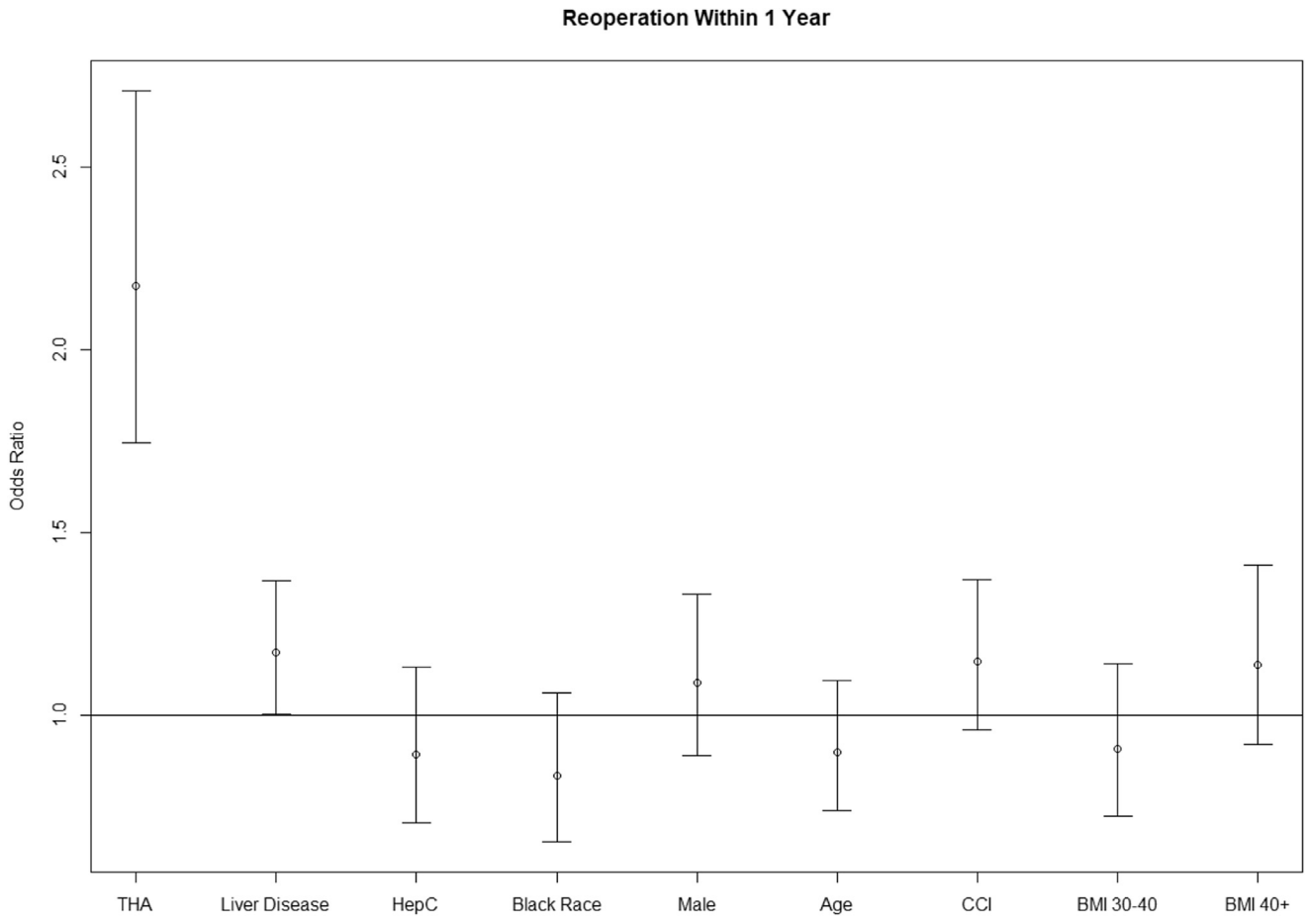

Figure 4. Predictors of reoperation within 1 year. Line bars indicate 95% confidence intervals. CCI, Charlson Comorbidity Index; HepC, hepatitis C.

Table 2
Characteristics of patients with and without liver disease.

Characteristic	Liver disease (n = 634), n (%)	No liver disease (n = 13,039), n (%)	*P* value
Total hip replacement	244 (38.5)	4286 (32.9)	.004
Hepatitis C	146 (23.0)	36 (0.3)	<.001
Black race	134 (21.1)	2427 (18.6)	.124
Male	260 (41)	5359 (41.1)	.997
Year of surgery			.257
2013-2014	202 (31.9)	3895 (29.9)	
2015	226 (35.6)	4497 (34.5)	
2016-2017	206 (32.5)	4647 (35.6)	
	Mean (SD)	Mean (SD)	
Age, years	62.7 (9.6)	66.0 (10.7)	<.001
Charlson Comorbidity Index	1.5 (1.7)	0.8 (1.3)	<.001
Body mass index, kg/m^2	32.8 (7.1)	32.1 (6.7)	.024
Laboratory values	Mean (SD, n)	Mean (SD, n)	
Albumin	3.58 (0.49, 283)	3.71 (0.42, 3306)	<.001
Sodium	139.50 (2.84, 375)	139.63 (2.78, 5632)	.344
Platelet count	217.20 (83.19, 336)	237.61 (68.54, 5094)	<.001
INR	1.05 (0.20, 74)	1.01 (0.15, 1183)	.008
Creatinine	1.05 (0.91, 398)	0.97 (0.60, 6065)	.893
Bilirubin	0.73 (0.62, 278)	0.56 (0.30, 3182)	<.001
TSH	3.56 (7.94, 16)	2.13 (2.03, 249)	.618

INR, International normalized ratio calibrated for cirrhosis values; SD, standard deviation; TSH, thyroid-stimulating hormone.

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Supplementary data

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