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Original research

The Impact of Hepatitis C on Complication Rates After Revision Total Knee Arthroplasty: A Matched Cohort Study

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ABSTRACT

Background: It is unclear if hepatitis C (HCV) negatively impacts outcomes of revision total knee arthroplasty (rTKA). The purpose of this study was to compare complication rates after rTKA for patients with HCV vs matched controls.

Methods: A retrospective cohort study was conducted using the PearlDiver database (PearlDiver Inc., Colorado Springs, CO). Patients with HCV who underwent rTKA (n = 1448) were matched 1:4 with controls (n = 5792) on age, sex, and several comorbidities. Rates of medical complications within 90 days and prothesis-related complications within 2 years postoperatively were compared with logistic regression for (1) patients with vs without HCV and (2) HCV patients who underwent aseptic vs septic rTKA.

Results: Relative to controls, patients with HCV exhibited significantly higher rates of medical complications (27.7% vs 20.9%; odds ratio [OR] 1.47), periprosthetic fractures (2.3% vs 1.1%; OR 2.20), all-cause repeat rTKA (11.7% vs 9.4%; OR 1.29), and repeat rTKA for prosthetic joint infection (PJI) (6.7% vs 3.6%; OR 1.92). Within the HCV cohort, HCV patients with initial septic rTKA exhibited significantly higher rates of medical complications (41.7% vs 22.7%; OR 2.39), all-cause subsequent rTKA (15.9% vs 10.2%; OR 1.67), and repeat rTKA for PJI (15.9% vs 3.4%; OR 5.39). Conversely, HCV patients with initial aseptic rTKA exhibited significantly higher rates of aseptic loosening (2.6% vs 7.4%; OR 0.33).

Conclusions: Patients with HCV exhibited significantly higher rates of medical and prosthesis-related complications after rTKA than controls. Among patients with HCV, initial septic rTKA was associated with significantly higher rates of medical complications, repeat rTKA, and PJI.

Introduction

Total knee arthroplasty (TKA) is a highly successful surgery performed in the United States (U.S.) [1]. More than 680,000 TKAs are performed each year in the U.S., and the annual TKA volume is projected to exceed 1.26 million by 2030 [2–4]. While TKA outcomes are predominantly excellent, the short-term risk of revision arthroplasty has remained relatively unchanged in recent years [5,6]. Consequently, the annual volume of revision TKA (rTKA) is also growing and is projected to surpass 128,000 procedures by 2030 [7]. Compared to primary TKA, rTKA is associated with a higher risk of complications and revision procedures [8–12]. Risk factors for poor outcomes after rTKA include the quality of the index primary TKA, indication for rTKA, and comorbidities such as obesity, diabetes, and tobacco use [13].

Hepatitis C (HCV) affects more than 3 million Americans and approximately 3.3% of the orthopaedic patient population [14,15]. Prior studies have demonstrated patients with HCV who undergo TKA exhibit higher rates of 90-day medical complications and surgical complications including rTKA than noninfected patients [16–20]. However, the impact of HCV on outcomes of rTKA has not been studied. As such, examination of HCV as a risk factor for postoperative complications following an rTKA is needed.

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The purpose of this study was to (1) analyze the impact of HCV on postoperative outcomes following an rTKA and (2) compare postoperative complication rates for HCV patients who underwent septic vs aseptic rTKAs. It was hypothesized that patients with HCV would exhibit significantly higher postoperative complication rates than matched controls and that HCV patients who underwent septic rTKAs would exhibit significantly higher rates of complications than HCV patients who underwent aseptic rTKAs.

Material and methods

Data source and study design

Patient records were queried from the PearlDiver Mariner Database (PearlDiver Inc., Colorado Springs, CO), a commercially available administrative claims database with deidentified patient data. The database contains the medical records of approximately 144 million patients across the U.S. from 2010 through Q3 of 2020 which are collected by an independent data aggregator. Researchers identify patients and outcomes using the Current Procedural Technology (CPT) and International Classification of Diseases, Ninth and Tenth Revision (ICD-9/ICD-10), codes on insurance claims. For this study, the "MKnee" data set was analyzed which contains records of a subset of patients with diagnoses and procedures localized to the knee. All health insurance payors are represented including commercial, private, and government plans. Institutional review board exemption was granted as provided data were deidentified and compliant with the Health Insurance Portability and Accountability Act. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

A retrospective cohort study was conducted to investigate the impact of HCV on complication rates following rTKA. Patients who underwent aseptic rTKA were identified by claims containing procedural codes for partial or total revision knee arthroplasty (eg, CPT-27486, CPT-27487) without associated diagnosis codes for prosthetic joint infection (PJI). One-stage septic rTKA (ie, revision for PJI) was defined by procedural codes for rTKA paired with diagnosis codes for PJI. For 2-stage septic revisions, the first stage of the procedure was defined by procedural codes for implant removal (eg, CPT-27488) with concomitant insertion of an antibiotic cement spacer (eg, CPT-11981). The second stage was defined by procedural codes for TKA (eg, CPT-27447) with concomitant removal of the antibiotic spacer (eg, CPT-11982) [21]. Patients who underwent 2-stage septic revisions were identified by a claim for each stage, with the claim for the second stage following the claim for the first stage. For these patients, postoperative complications were tracked from the date of the second stage. CPT, ICD-9, and ICD-10 procedural codes were used to define all procedures.

In order to limit potential transfer bias due to patients leaving or joining the data set during the study period, only patients with continuous database enrollment for at least 1 year prior and 2 years after the index rTKA were included. Pediatric patients and patients infected with hepatitis B or human immunodeficiency virus were excluded.

Patients with HCV were identified by claims containing ICD-9/ICD-10 diagnosis codes for acute, chronic, and/or unspecified HCV infection before or at the time of the index rTKA. Prior validation studies analyzing the accuracy of coding for the presence of HCV have reported a positive predictive value between 88% and 94%, while the negative predictive value for patients without documented HCV is 90% to 93% [22,23]. All codes used to define inclusion and exclusion criteria are provided in Appendix A.

Demographic data and clinical characteristics

Baseline demographic data including age, sex, body mass index (BMI), and U.S. region were obtained. Clinical characteristics queried included length of stay (LOS) during the initial rTKA and the prevalence of diabetes mellitus, tobacco use, chronic kidney disease, hypertension, and obesity. The distribution of indications for the initial rTKA (aseptic or septic) was also obtained.

Outcomes

Rates of medical complications during the index hospital encounter and within 90 days postoperatively were obtained. Medical complications queried included inpatient readmissions, deep vein thrombosis (DVT), pulmonary embolism, urinary tract infection (UTI), acute kidney injury (AKI), and blood transfusion. The diagnosis and procedural codes used to define these complications are provided in Appendix B.

Prosthesis-related complications were evaluated at 2 years postoperatively. Specific complications queried included manipulation under anesthesia and/or lysis of adhesions for knee stiffness, all-cause subsequent rTKA, PJI, aseptic loosening, and periprosthetic fracture. All-cause subsequent rTKA included revision of the femoral and/or tibial components, implant removal, and/or insertion of an antibiotic spacer. PJI was defined as repeat rTKA for infection (1-stage or 2-stage) using the same criteria for septic revisions as outlined above. Rates of all-cause repeat rTKA, revision for PJI, aseptic loosening, and periprosthetic fracture were queried after the 90-day global postoperative period in order to minimize the possibility that indications for initial rTKA were counted as complications during routine postoperative follow-ups. The codes used to define these complications are provided in Appendix A and Appendix B.

Statistical analysis

Statistical analyses were performed using the R statistical software (Version 4.1.0; R Project for Statistical Computing) integrated within the PearlDiver software with an α level set to 0.05. In order to reduce confounding bias, exact matching without replacement was performed to generate similar patient cohorts. HCV patients were matched at a 1:4 ratio with noninfected controls on the following parameters: age, sex, diabetes mellitus, tobacco use, obesity, chronic kidney disease, and hypertension.

Categorical variables were compared with a chi-square test, and continuous variables were compared with Welch's t test or the Mann-Whitney U test. Rates of postoperative complications were compared using multivariable logistic regression for (1) patients with HCV vs controls for all rTKA, (2) initial aseptic rTKA, and (3) initial septic rTKA and (4) for patients who underwent initial aseptic vs septic rTKA within the HCV cohort. Odds ratios (OR) with the corresponding 95% confidence intervals (CIs) were calculated for each outcome.

Results

Study population

A total of 51,548 patients who underwent rTKAs were identified, including 1462 (2.8%) patients with HV. After 1:4 matching, 1448 HCV patients were matched with 5792 noninfected controls (Table 1). Initial septic rTKA was significantly more common in the HCV cohort (26.5% vs 17.8%, $P < .001$). Patients with HCV had a significantly longer mean LOS (4.24 vs 3.29 days, $P < .001$). There were significant differences in region and BMI data between the

Table 1
Baseline demographic data and clinical characteristics of rTKA cohorts (matched 1:4).

Characteristics	HCV (n = 1448)	No HCV (n = 5792)	*P* value
Age (y), mean ± SD	59.03 ± 7.49	59.18 ± 7.56	.485
Female sex, n (%)	741 (51.2)	2955 (51.0)	.939
U.S. region, n (%)[a]			
Northeast	321 (22.2)	1038 (17.9)	**<.001**
South	590 (40.7)	2148 (37.1)	**.012**
Midwest	324 (22.4)	1871 (32.3)	**<.001**
West	208 (14.4)	705 (12.2)	**.028**
BMI, n (%)[b]			
<30	70 (18.0)	218 (11.7)	**.001**
30-35	93 (24.0)	381 (20.5)	.149
35-40	67 (17.3)	452 (24.4)	**.003**
>40	158 (40.7)	805 (43.4)	.366
Comorbidities, n (%)			
Diabetes mellitus	828 (57.2)	3305 (57.1)	.957
Obesity	946 (65.3)	3789 (65.4)	.975
Tobacco use	1101 (76.0)	4408 (76.1)	.984
Chronic kidney disease	443 (30.6)	1771 (30.6)	1
Hypertension	1338 (92.4)	5357 (92.5)	.956
Revision indication, n (%)			
Aseptic	1064 (73.5)	4761 (82.2)	**<.001**
Septic	384 (26.5)	1031 (17.8)	
LOS (d), Mean ± SD			
All rTKA	4.24 ± 3.51	3.29 ± 2.21	**<.001**
Aseptic	3.72 ± 2.85	3.09 ± 1.99	**<.001**
Septic	5.15 ± 4.45	3.79 ± 2.63	**<.001**

SD, standard deviation.
Bolded *P* values indicate statistically significant results.
[a] Region data available for 99% of included patients.
[b] BMI data available for 388 (26.8%) HCV patients and 1856 (32.0%) controls.

2 cohorts although BMI data were only available for 26.8% of HCV patients and 32.0% of controls.

HCV vs controls, all rTKA

Within 90 days following rTKA, rates of at least 1 medical complication were significantly higher in the HCV cohort relative to controls (27.7% vs 20.9%; OR 1.47; 95% CI, 1.29-1.68). This included significantly higher rates of AKI, UTI, blood transfusions, and inpatient readmissions (all $P < .05$; Table 2).

Rates of at least 1 prosthesis-related complication were also significantly higher in the HCV cohort within 2 years after the rTKA (20.0% vs 17.2%; OR 1.21; 95% CI, 1.04-1.40), including significantly higher rates of periprosthetic fracture, all-cause repeat rTKA, and repeat rTKA for PJI (all $P < .05$). Among patients who underwent a repeat rTKA, PJI was significantly more common in the HCV cohort (57.4% vs 38.6%, $P < .001$) (Fig. 1a).

HCV vs controls, initial aseptic rTKA

Within 90 days after the initial aseptic rTKA, HCV patients exhibited significantly higher rates of medical complications than controls (22.7% vs 17.5%; OR 1.41; 95% CI, 1.19-1.65), including AKI, UTI, blood transfusions, and inpatient readmissions (all $P < .05$; Table 3).

Table 2
Postoperative complication rates after rTKA for patients with HCV vs controls.

Complication	HCV (n = 1448)		No HCV (n = 5792)		Statistical analysis (ref. group, HCV cohort)	
	n	%	n	%	OR (95% CI)	*P* value
90 D						
Any medical complication[a]	401	27.7%	1212	20.9%	**1.47 (1.29-1.68)**	**<.001**
DVT	5[b]	0.3%	43	0.7%	0.78 (0.34-1.59)	.539
PE	11	0.8%	49	0.8%	0.94 (0.46-1.76)	.867
AKI	92	6.4%	276	4.8%	**1.43 (1.11-1.82)**	**.005**
UTI	80	5.5%	235	4.1%	**1.42 (1.08-1.84)**	**.010**
Transfusion	146	10.1%	355	6.1%	**1.68 (1.37-2.06)**	**<.001**
Inpatient readmission	242	16.7%	703	12.1%	**1.47 (1.25-1.72)**	**<.001**
2 Y						
Any joint complication[a]	290	20.0%	994	17.2%	**1.21 (1.04-1.40)**	**.012**
MUA/LoA	66	4.6%	252	4.4%	1.03 (0.77-1.35)	.847
Subsequent rTKA	169	11.7%	542	9.4%	**1.29 (1.07-1.55)**	**.007**
PJI	97	6.7%	209	3.6%	**1.92 (1.49-2.50)**	**<.001**
Aseptic loosening	89	6.1%	330	5.7%	1.07 (0.83-1.36)	.603
Periprosthetic fracture	34	2.3%	63	1.1%	**2.20 (1.42-3.34)**	**<.001**

DVT, deep vein thrombosis; LoA, lysis of adhesions; MUA, manipulation under anesthesia; PE, pulmonary embolism; ref., reference.
Bolded OR/CI/*P* values indicate statistically significant results.
[a] The number of patients with at least 1 medical or joint complication.
[b] For the sake of protecting patients' identities, the PearlDiver software does not report exact patient counts when defined groups have <11 patients. In such instances, a cohort size of 5 (median between 1-10) was assigned although the software uses the real patient counts for the statistical analysis.

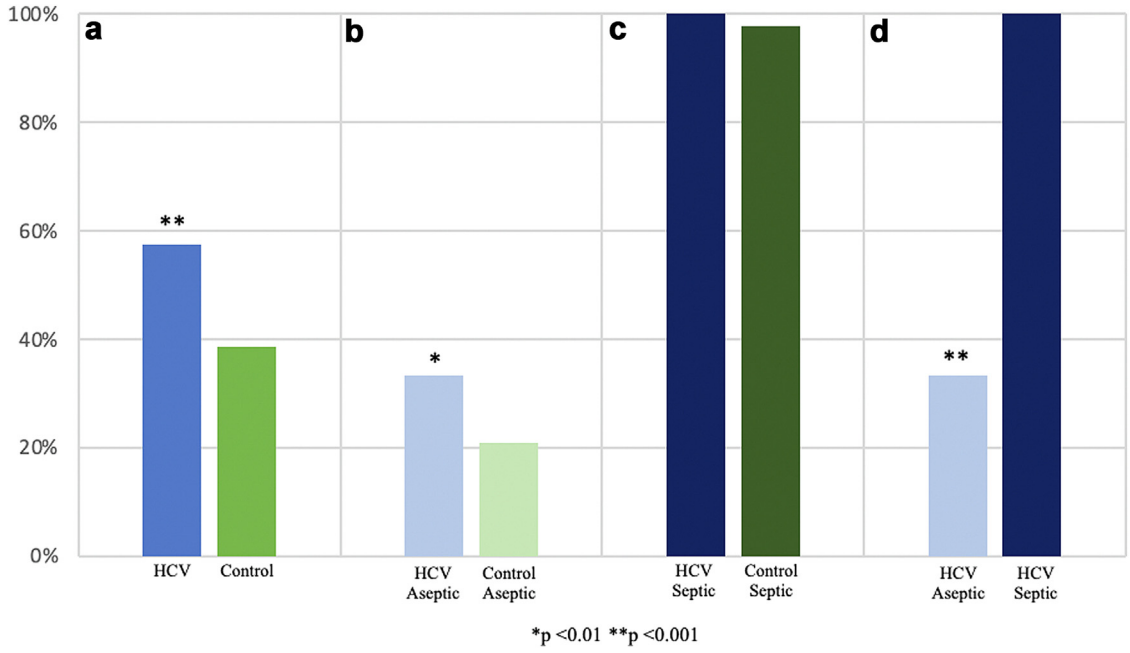

Figure 1. Among patients who underwent a subsequent rTKA, comparison of incidence of PJI (ie, subsequent septic rTKA) for (a) all HCV patients vs controls, (b) HCV patients with an initial aseptic rTKA vs controls with an initial aseptic rTKA, (c) HCV patients with an initial septic rTKA vs controls with an initial septic rTKA, and (d) HCV patients with an initial aseptic rTKA vs HCV patients with an initial septic rTKA.

Rates of periprosthetic fractures (2.4% vs 1.1% OR 2.28; 95% CI, 1.39-3.65) and repeat rTKA for incident PJI (3.4% vs 1.8%; OR 1.87; 95% CI, 1.24-2.75) were significantly higher in the HCV cohort within 2 years postoperatively. Among the identified patients with repeat revision procedures during the 2-year follow-up, PJI was a significantly more common indication for subsequent rTKA in the HCV cohort (33.3% vs 20.9%, $P = .009$) (Fig. 1b).

HCV vs controls, initial septic rTKA

Within the subgroup of included patients who underwent an initial septic rTKA (ie, revision for PJI), patients with HCV exhibited a significantly higher rate of blood transfusions than controls (18.8% vs 12.9%; OR 1.56; 95% CI, 1.12-2.17) (Table 4). Rates of all other medical complications were comparable (all $P > .05$).

At 2 years, patients with HCV exhibited significantly higher rates of all-cause repeat rTKA (15.9% vs 12.1%; OR 1.40; 95% CI, 1.01-1.96) and re-revisions for PJI (15.9% vs 11.8%; OR 1.41; 95% CI, 1.02-1.96). Notably, all 61 (100%) repeat rTKA procedures in the HCV cohort and 122 of 125 (97.6%) in the control cohort were performed for PJI ($P = .552$) (Fig. 1c).

HCV cohort, initial aseptic rTKA vs initial septic rTKA

Within the HCV cohort, patients who underwent an initial septic rTKA exhibited significantly higher rates of at least 1 medical

Table 3
Postoperative complication rates after aseptic primary rTKAs for patients with HCV vs controls.

Complication	HCV (n = 1064)		No HCV (n = 4761)		Statistical analysis (ref. group, HCV cohort)	
	n	%	n	%	OR (95% CI)	*P* value
90 D						
Any medical complication[a]	241	22.7%	832	17.5%	**1.41 (1.19-1.65)**	**<.001**
DVT	5[b]	0.5%	27	0.6%	0.74 (0.22-1.92)	.598
PE	5[b]	0.5%	39	0.8%	0.96 (0.41-1.97)	.926
AKI	56	5.3%	159	3.3%	**1.70 (1.23-2.32)**	**.001**
UTI	61	5.7%	177	3.7%	**1.62 (1.19-2.18)**	**.002**
Transfusion	74	7.0%	222	4.7%	**1.48 (1.12-1.94)**	**.005**
Inpatient readmission	137	12.9%	463	9.7%	**1.38 (1.12-1.69)**	**.002**
2 Y						
Any joint complication[a]	207	19.5%	799	16.8%	**1.18 (1.01-1.40)**	**.047**
MUA/LoA	53	5.0%	209	4.4%	1.12 (0.81-1.51)	.485
Subsequent rTKA	108	10.2%	417	8.8%	1.18 (0.93-1.47)	.157
PJI	36	3.4%	87	1.8%	**1.87 (1.24-2.75)**	**.002**
Aseptic loosening	79	7.4%	295	6.2%	1.20 (0.92-1.55)	.171
Periprosthetic fracture	26	2.4%	52	1.1%	**2.28 (1.39-3.65)**	**.001**

DVT, deep vein thrombosis; LoA, lysis of adhesions; MUA, manipulation under anesthesia; PE, pulmonary embolism; ref., reference.
Bolded OR/CI/*P* values indicate statistically significant results.
[a] The number of patients with at least 1 medical or joint complication.
[b] For the sake of protecting patients' identities, the PearlDiver software does not report exact patient counts when defined groups have <11 patients. In such instances, a cohort size of 5 (median between 1-10) was assigned although the software uses the real patient counts for the statistical analysis.

Table 4
Postoperative complication rates after a septic primary rTKA for patients with HCV vs controls.

Complication	HCV (n = 384)		No HCV (n = 1031)		Statistical analysis (ref. group, HCV cohort)	
	n	%	n	%	OR (95% CI)	*P* value
90 D						
Any medical complication[a]	160	41.7%	380	36.9%	1.27 (0.99-1.62)	.057
DVT	5[b]	1.3%	16	1.6%	0.65 (0.18-1.84)	.477
PE	5[b]	1.3%	5[b]	0.5%	1.03 (0.22-3.68)	.970
AKI	36	9.4%	117	11.3%	0.87 (0.57-1.29)	.514
UTI	19	4.9%	58	5.6%	0.97 (0.55-1.64)	.920
Transfusion	72	18.8%	133	12.9%	**1.56 (1.12-2.17)**	**.008**
Inpatient readmission	105	27.3%	240	23.3%	1.28 (0.98-1.69)	.075
2 Y						
Any joint complication[a]	83	21.6%	195	18.9%	1.18 (0.88-1.58)	.271
MUA/LoA	13	3.4%	43	4.2%	0.73 (0.36-1.37)	.362
Subsequent rTKA	61	15.9%	125	12.1%	**1.40 (1.01-1.96)**	**.046**
PJI	61	15.9%	122	11.8%	**1.41 (1.02-1.96)**	**.039**
Aseptic loosening	10	2.6%	35	3.4%	0.76 (0.35-1.51)	.471
Periprosthetic fracture	5[b]	1.3%	11	1.1%	2.08 (0.78-5.41)	.138

DVT, deep vein thrombosis; LoA, lysis of adhesions; MUA, manipulation under anesthesia; PE, pulmonary embolism; ref., reference.
Bolded OR/CI/*P* values indicate statistically significant results.
[a] The number of patients with at least 1 medical or joint complication.
[b] For the sake of protecting patients' identities, the PearlDiver software does not report exact patient counts when defined groups have <11 patients. In such instances, a cohort size of 5 (median between 1-10) was assigned although the software uses the real patient counts for the statistical analysis.

complication (41.7% vs 22.7%; OR 2.39; 95% CI, 1.86-3.06), including AKI, blood transfusions, and inpatient readmissions (all $P < .05$; Table 5).

Rates of all-cause repeat rTKA (15.9% vs 10.2%; OR 1.67; 95% CI, 1.19-2.34) and re-revisions for PJI (15.9% vs 3.4%; OR 5.39; 95% CI, 3.53-8.36) at 2-year follow-up were significantly higher among HCV patients who underwent an initial septic rTKA. PJI was a significantly more common indication for a repeat rTKA in patients who underwent an initial septic rTKA (100% vs 33.3%, $P < .001$) (Fig. 1d). Patients with HCV who underwent an initial aseptic rTKA exhibited a significantly higher rate of aseptic loosening (2.6% vs 7.4%; OR 0.33; 95% CI, 0.17-0.65).

Discussion

The present study provides novel data illustrating significantly higher postoperative complication rates after an rTKA in patients with HCV than those in age-, sex-, and comorbidity-matched controls. Patients with HCV exhibited a significantly longer mean LOS during the index rTKA, as well as significantly higher rates of 90-day medical complications and joint complications within 2 years postoperatively. These results align with data from prior studies analyzing HCV in primary arthroplasty [16–20]. The increased complication risk in this population is multifactorial and driven by factors such as viral-mediated immune dysfunction and thrombocytopenia [20,24]. Given that an rTKA is associated with higher complication rates than a primary TKA, these data add to existing literature by suggesting HCV exacerbates this increased complication risk relative to noninfected controls.

Recent epidemiologic analyses have identified PJI as the most common indication for rTKA (20.4%-25.2%) [6,25]. In this study, 19.5% of initial rTKA procedures were performed for PJI, illustrating that infection remains a major cause of failure after a primary TKA. Previous studies have reported higher rates of complications

Table 5
Postoperative complication rates after aseptic vs septic primary rTKAs among patients with HCV.

Complication	HCV aseptic rTKA (n = 1064)		HCV septic rTKA (n = 384)		Statistical analysis (ref. group, septic rTKA)	
	n	%	n	%	OR (95% CI)	*P* value
90 D						
Any medical complication[a]	241	22.7%	160	41.7%	**2.39 (1.86-3.06)**	**<.001**
DVT	5[b]	0.5%	5[b]	1.3%	2.79 (0.66-11.85)	.164
PE	5[b]	0.5%	5[b]	1.3%	1.04 (0.23-3.61)	.960
AKI	56	5.3%	36	9.4%	**1.81 (1.15-2.79)**	**.009**
UTI	61	5.7%	19	4.9%	0.86 (0.49-1.42)	.590
Transfusion	74	7.0%	72	18.8%	**2.93 (2.06-4.17)**	**<.001**
Inpatient readmission	137	12.9%	105	27.3%	**2.55 (1.91-3.39)**	**<.001**
2 Y						
Any joint complication[a]	207	19.5%	83	21.6%	1.12 (0.85-1.52)	.453
MUA/LoA	53	5.0%	13	3.4%	0.62 (0.31-1.12)	.145
Subsequent rTKA	108	10.2%	61	15.9%	**1.67 (1.19-2.34)**	**.003**
PJI	36	3.4%	61	15.9%	**5.39 (3.53-8.36)**	**<.001**
Aseptic loosening	79	7.4%	10	2.6%	**0.33 (0.17-0.65)**	**.001**
Periprosthetic fracture	26	2.4%	5[b]	1.3%	0.85 (0.36-1.81)	.706

DVT, deep vein thrombosis; LoA, lysis of adhesions; MUA, manipulation under anesthesia; PE, pulmonary embolism; ref., reference.
Bolded OR/CI/*P* values indicate statistically significant results.
[a] The number of patients with at least 1 medical or joint complication.
[b] For the sake of protecting patients' identities, the PearlDiver software does not report exact patient counts when defined groups have <11 patients. In such instances, a cohort size of 5 (median between 1-10) was assigned although the software uses the real patient counts for the statistical analysis.

including subsequent revisions after an initial septic rTKA [26–28]. Belt et al. reported a 16% rate of all-cause repeat rTKA at 1 year after a septic rTKA, while lower re-revision rates were observed after an aseptic rTKA for indications such as loosening (3%) [26]. In this study, initial septic revisions were significantly more common in the HCV cohort. Furthermore, among patients with HCV, PJI was a significantly more common indication for a repeat rTKA. These data suggest that patients with HCV are at an increased risk of septic failure after both primary TKAs and rTKAs.

In subgroup analyses based on the indication for an initial rTKA, patients with HCV who underwent an initial aseptic rTKA exhibited significantly higher rates of medical complications relative to controls. Among patients who underwent an initial septic rTKA, however, only rates of transfusions were significantly higher for patients with HCV. These data suggest that HCV is an important risk factor for medical complications after a aseptic rTKA. Conversely, given that a septic rTKA itself is a strong risk factor for poor short-term outcomes [26–28], HCV may only marginally increase the risk of medical complications after a septic rTKA relative to controls who are also at high risk. At 2-year follow-up, patients with HCV also exhibited significantly higher rates of re-revisions for PJI and periprosthetic fracture, which are both common modes of failure after an rTKA [26,29,30]. As such, these findings suggest patients with HCV have an increased risk of both aseptic and septic failure after rTKAs.

Within the HCV cohort, patients who underwent an initial septic rTKA exhibited significantly higher rates of 90-day medical complications, all-cause repeat rTKAs, and re-revisions for PJI than patients with an initial aseptic rTKA. This result is consistent with prior literature reporting higher complication rates after a septic rTKA [26]. Interestingly, patients with HCV who underwent an initial aseptic rTKA exhibited a significantly higher rate of aseptic loosening. In addition to recurrent infection, aseptic loosening is a major etiology of failure after rTKAs. Kienzle et al. reported high rates of aseptic loosening (22%) after a septic rTKA at 7.3-year follow-up [31] although rates were <5% at 2 years which is comparable to the rate of 2.6% found in this study. Belt et al. demonstrated that indications for subsequent revisions are most commonly recurrences of the initial rTKA indication [26]. Therefore, our data showing higher rates aseptic loosening among patients with HCV who underwent an initial aseptic rTKA may simply reflect higher rates of loosening at the time of the index rTKA.

Limitations

There are several limitations to this study. First, by only evaluating complications within 2 years, this analysis is limited to short-term outcomes. Furthermore, because continuous database enrollment for 2 years after an rTKA was required for inclusion, patients who died within 2 years after the surgery were excluded. Therefore, these results may not be applicable to patients with a high perioperative mortality risk. This limitation is notable given that the mortality risk after an rTKA is not insignificant, especially for patients undergoing a septic rTKA and those with a greater comorbidity burden, both of which are more common in patients with HCV [27,32,33]. Additionally, the possibility of coding errors is inherent with any analysis of administrative claims data. Such instances are rare and made up only 0.7% of Medicare and Medicaid payments in 2021 [34]. However, in a recent validation study comparing billing records against operative reports, Roof et al. found that ICD-10 procedural coding for rTKA is often imprecise [35]. Therefore, it must be acknowledged that including ICD-10 procedural codes in this study consequently introduced coding bias. The impact of this limitation was mitigated through nuanced definitions of aseptic and septic rTKAs (Appendix A), as well as the concomitant use of both CPT and ICD-9 procedural codes which have demonstrated high accuracy in validation studies [36,37]. With respect to aseptic loosening, it is possible that some patients who underwent a septic rTKA had clinically significant implant loosening attributed to infection. It is also possible that some patients who underwent an aseptic rTKA had occult infections during the initial and/or subsequent revision that were undiagnosed. Given that loosening is common in the setting of PJI [38–40], such cases may have influenced the results.

It is possible that some patients had HCV but were never diagnosed and, therefore, could have been included in the control cohort. An additional limitation is that the database does not contain information regarding the viral load which prevents comprehensive characterization of HCV patients' clinical status at the time of rTKAs. It was also not possible to identify HCV genotypes or the degree of liver damage (eg, Child-Pugh score). The HCV and control cohorts also differed significantly with respect to U.S. regional distribution, which may reflect geographic differences in HCV prevalence. Region was controlled for in the logistic regression analyses to mitigate the impact of this possible confounder. Lastly, although exact matching and multivariable regression were used, other confounders could have influenced the results. For example, there are certain confounding variables that may be more common in the HCV cohort such as intravenous drug and alcohol abuse, homelessness, and low socioeconomic status, all of which are only partially available or entirely inaccessible in the database. BMI data were also not universally available for all included patients, and therefore, the adjustment for BMI was incomplete.

To the authors' knowledge, this is the first analysis of complications after rTKAs in patients with HCV. As these patients often have more comorbidities than most patients undergoing an rTKA and higher comorbidity burdens are associated with an increased complication risk [41–44], medical optimization before an rTKA is critical in this population. Recent analyses have reported improved outcomes after a primary arthroplasty in patients with HCV who received preoperative antiviral treatment [16,45–47]. It is likely that similar interventions before an rTKA also decrease the complication risk in this population. Future studies are needed to investigate this hypothesis.

Conclusions

Patients with HCV exhibited significantly higher rates of postoperative medical complications, subsequent rTKA, PJI, and periprosthetic fracture relative to matched controls. Within the HCV cohort, patients who underwent an initial septic rTKA exhibited significantly higher rates of medical complications, all-cause repeat rTKAs, and re-revisions for PJI than patients with an initial aseptic rTKA. These data suggest that, similar to primary TKAs, HCV is a risk factor for poor outcomes following an rTKA.

Conflicts of interest

Dr. G. N. Guild is a paid consultant for and receives research support from Smith & Nephew and has stock or stock options in Total Joint Orthopaedics. All other authors declare no potential conflicts of interest.

For full disclosure statements refer to https://doi.org/10.1016/j.artd.2022.09.010.

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Appendix A
Codes used to define inclusion and exclusion criteria.

Criteria	Code(s)
Hepatitis C	ICD-9-D-07051, ICD-9-D-07054, ICD-9-D-07070, ICD-10-D-B1710, ICD-10-D-B182, ICD-10-D-B1920
Aseptic rTKA	
rTKA	CPT-27486, CPT-27487, ICD-9-P-0080, ICD-9-P-0081, ICD-9-P-0082, ICD-9-P-0083, ICD-9-P-0084, ICD-10-P-0SWC0JZ, ICD-10-P-0SWD0JZ, ICD-10-P-0SWC0JC, ICD-10-P-0SWCXJZ, ICD-10-P-0SWD0JC, ICD-10-P-0SWV0JZ, ICD-10-P-0SWDXJZ, ICD-10-P-0SWW0JZ, ICD-10-P-0SWC09Z, ICD-10-P-0SWT0JZ, ICD-10-P-0SWD09Z, ICD-10-P-0SWU0JZ
PJI (excluded)	ICD-9-D-99666, ICD-10-D-M01X61, ICD-10-D-M01X62, ICD-10-D-M01X69, ICD-10-D-T8453XA, ICD-10-D-T8453XD, ICD-10-D-T8453XS, ICD-10-D-T8454XA, ICD-10-D-T8454XD, ICD-10-D-T8454XS
1-Stage septic rTKA	
rTKA	CPT-27487, ICD-9-P-0080, ICD-10-P-0SWC0JZ, ICD-10-P-0SWCXJZ, ICD-10-P-0SWD0JZ, ICD-10-P-0SWDXJZ
PJI	ICD-9-D-99666, ICD-10-D-M01X61, ICD-10-D-M01X62, ICD-10-D-M01X69, ICD-10-D-T8453XA, ICD-10-D-T8453XD, ICD-10-D-T8453XS, ICD-10-D-T8454XA, ICD-10-D-T8454XD, ICD-10-D-T8454XS
2-Stage septic rTKA	
First stage	
Hardware removal	CPT-27488, ICD-9-P-8006, ICD-10-P-0SPC0JZ, ICD-10-P-0SPD0JZ
Spacer insertion	CPT-11981, ICD-9-P-8456, ICD-10-P-0SHC08Z, ICD-10-P-0SHD08Z, ICD-10-P-0SRC0EZ, ICD-10-P-0SRD0EZ
Second stage	
TKA	CPT-27447, ICD-9-P-8154, ICD-10-P-0SRC0J9, ICD-10-P-0SRC0JA, ICD-10-P-0SRC0JZ, ICD-10-P-0SRD0J9, ICD-10-P-0SRD0JA, ICD-10-P-0SRD0JZ
Spacer removal	CPT-11982, ICD-9-P-8457, ICD-10-P-0SPC08Z, ICD-10-P-0SPC0EZ, ICD-10-P-0SPD08Z, ICD-10-P-0SPD0EZ
Exclusion criteria	
Hepatitis B	ICD-9-D-07020, ICD-9-D-07021, ICD-9-D-07022, ICD-9-D-07023, ICD-9-D-07030, ICD-9-D-07031, ICD-9-D-07032, ICD-9-D-07033, ICD-9-D-V0261, ICD-10-D-B160, ICD-10-D-B161, ICD-10-D-B162, ICD-10-D-B169, ICD-10-D-B180, ICD-10-D-B181, ICD-10-D-B1910, ICD-10-D-B1911, ICD-10-D-Z2251
HIV	ICD-9-D-042, ICD-9-D-07953, ICD-10-D-B20, ICD-10-D-Z21, ICD-10-D-B9735
Comorbidities	
Tobacco use	ICD-9-D-3051, ICD-9-D-V1582, ICD-10-D-F17220, ICD-10-D-F17221, ICD-10-D-F17223, ICD-10-D-F17228, ICD-10-D-F17229, ICD-10-D-F17290, ICD-10-D-F17291, ICD-10-D-F17293, ICD-10-D-F17298, ICD-10-D-F17299, ICD-10-D-Z720
Diabetes mellitus	ICD-9-D-24900:ICD-9-D-25099, ICD-9-D-7902, ICD-9-D-79021, ICD-9-D-79022, ICD-9-D-79029, ICD-9-D-7915, ICD-9-D-7916, ICD-10-D-E090:ICD-10-D-E139
Obesity	ICD-9-D-2780, ICD-9-D-27800, ICD-9-D-27801, ICD-9-D-27802, ICD-9-D-27803, ICD-10-D-E660:ICD-10-D-E669
Chronic kidney disease	ICD-9-D-585, ICD-9-D-5851, ICD-9-D-5852, ICD-9-D-5853, ICD-9-D-5854, ICD-9-D-5855, ICD-9-D-5856, ICD-9-D-5859, ICD-9-D-7925, ICD-10-D-N18:ICD-10-D-N189
Hypertension	ICD-9-D-4010:ICD-9-D-4059, ICD-10-D-I10:ICD-10-D-I159

Appendix B
Codes used to define complications.

Complication	Code(s)
DVT	ICD-9-D-4532, ICD-9-D-4533, ICD-9-D-4534, ICD-9-D-45382, ICD-9-D-45384, ICD-9-D-45385, ICD-9-D-45386, ICD-10-D-I26:ICD-10-D-I2699
PE	ICD-9-D-4151:ICD-9-D-4159, ICD-10-D-I26:ICD-10-D-I269
Blood transfusion	ICD-9-P-9904, ICD-10-P-3023, ICD-10-P-30230AZ, ICD-10-P-30230G0, ICD-10-P- 30230G2, ICD-10-P-30230G3, ICD-10-P-30230G4, ICD-10-P-30230H0, ICD-10-P-30230H1, ICD-10-P- 30230J0, ICD-10-P-30230J1, ICD-10-P-30230K0, ICD-10-P-30230K1, ICD-10-P-30230L0, ICD-10-P-30230L1, ICD- 10-P-30230M0, ICD-10-P-30230M1, ICD-10-P-30230N0, ICD-10-P-30230N1, ICD-10-P-30230P0, ICD-10-P- 30230P1, ICD-10-P-30230Q0, ICD-10-P-30230Q1, ICD-10-P-30230R0, ICD-10-P-30230R1, ICD-10-P- 30230S0, ICD-10-P-30230S1, ICD-10-P-30230T0, ICD-10-P-30230T1, ICD-10-P-30230V0, ICD-10-P- 30230V1, ICD-10-P-30230W0, ICD-10-P-30230W1, ICD-10-P-30230X0, ICD-10-P-30230X2, ICD-10-P-30230X3, ICD-10-P-30230X4, ICD-10-P-30230Y0, ICD-10-P-30230Y2, ICD-10-P-30230Y3, ICD-10-P- 30230Y4, ICD-10-P-30233AZ, ICD-10-P-30233G0, ICD-10-P-30233G2, ICD-10-P-30233G3, ICD-10-P- 30233G4, ICD-10-P-30233H0, ICD-10-P-30233H1, ICD-10-P-30233J0, ICD-10-P-30233J1, ICD-10-P- 30233K0, ICD-10-P-30233K1, ICD-10-P-30233L0, ICD-10-P-30233L1, ICD-10-P-30233M0, ICD-10-P- 30233M1, ICD-10-P-30233N0, ICD-10-P-30233N1, ICD-10-P-30233P0, ICD-10-P-30233P1, ICD-10-P- 30233Q0, ICD-10-P-30233Q1, ICD-10-P-30233R0, ICD-10-P-30233R1, ICD-10-P-30233S0, ICD-10-P- 30233S1, ICD-10-P-30233T0, ICD-10-P-30233T1, ICD-10-P-30233V0, ICD-10-P-30233V1, ICD-10-P-30233W0, ICD-10-P-30233W1, ICD-10-P-30233X0, ICD-10-P-30233X2, ICD-10-P-30233X3, ICD-10-P- 30233X4, ICD-10-P-30233Y0, ICD-10-P-30233Y2, ICD-10-P-30233Y3, ICD-10-P-30233Y4, ICD-10-P- 30240AZ, ICD-10-P-30240G0, ICD-10-P-30240G2, ICD-10-P-30240G3, ICD-10-P-30240G4, ICD-10-P- 30240H0, ICD-10-P-30240H1, ICD-10-P-30240J0, ICD-10-P-30240J1, ICD-10-P-30240K0, ICD-10-P- 30240K1, ICD-10-P-30240L0, ICD-10-P-30240L1, ICD-10-P-30240M0, ICD-10-P-30240M1, ICD-10-P- 30240N0, ICD-10-P-30240N1, ICD-10-P-30240P0, ICD-10-P-30240P1, ICD-10-P-30240Q0, ICD-10-P- 30240Q1, ICD-10-P-30240R0, ICD-10-P-30240R1, ICD-10-P-30240S0, ICD-10-P-30240S1, ICD-10-P-30240T0, ICD-10-P-30240T1, ICD-10-P-30240V0, ICD-10-P-30240V1, 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Urinary tract infection	ICD-9-D-5990, ICD-10-D-N390
Acute kidney injury	ICD-9-D-5845, ICD-9-D-5846, ICD-9-D-5847, ICD-9-D-5848, ICD-9-D-5849, ICD-10-D-N17:ICD-10-D-N179
MUA/LoA	CPT-27570, CPT-29884
Periprosthetic fracture	ICD-9-D-99644, ICD-10-D-M9712XA, ICD-10-D-T84042A, ICD-10-D-T84043A, ICD-10-D-M9711XA
Aseptic loosening	ICD-9-D-99641, ICD-10-D-T84032A, ICD-10-D-T84032D, ICD-10-D-T84032S, ICD-10-D-T84033A, ICD-10-D-T84033D, ICD-10-D-T84033S
Secondary rTKA	Any codes for rTKA (aseptic or septic) as outlined in Table S1
PJI	Same criteria outlined in Table S1 for septic rTKA

DVT, deep vein thrombosis; LoA, lysis of adhesions; MUA, manipulation under anesthesia; PE, pulmonary embolism.