JSES International 6 (2022) 910–916

Contents lists available at ScienceDirect

JSES International

journal homepage: www.jsesinternational.org

Does pre-arthroplasty antiviral treatment for hepatitis C reduce complication rates after total shoulder arthroplasty? A matched cohort study

Austin J. Ross, MD[a], Bailey J. Ross, MD[b], Olivia C. Lee, MD[a,c], Garrett H. Williams, MD[a], Felix H. Savoie III, MD[a], Michael J. O'Brien, MD[a], Fernando L. Sanchez, MD[a], William F. Sherman, MD, MBA[a,*]

[a]*Tulane University School of Medicine, Department of Orthopaedic Surgery, New Orleans, LA, USA*
[b]*Emory University School of Medicine, Department of Orthopaedics, Atlanta, GA, USA*
[c]*Louisiana State University School of Medicine, Department of Orthopaedic Surgery & Southeast Louisiana Veterans Health Care System, New Orleans, LA, USA*

ARTICLE INFO

Keywords:
Hepatitis C
Total shoulder arthroplasty
Reverse shoulder arthroplasty
Postoperative complications
Total joint arthroplasty
Antiviral treatment

Level of evidence: Level III; Retrospective Cohort Comparison using Large Database; Prognosis Study

Background: Hepatitis C virus (HCV) is associated with increased complications of risk after arthroplasty. The purpose of this study was to examine the impact of HCV and a pre-arthroplasty antiviral treatment on complications following total shoulder arthroplasty (TSA).

Methods: A retrospective matched cohort study was conducted using an administrative claims database. Patients who underwent TSA were identified with Current Procedural Terminology -23472 and International Classification of Diseases procedural codes. A total of 1244 HCV patients were matched 1:3 with 3732 noninfected controls across age, sex, diabetes mellitus, tobacco use, and obesity. The HCV patients with treatment before TSA were identified by claims containing antiviral drug codes. Multivariable logistic regression was used to compare rates of 90-day medical complications and prosthesis-related complications within 2 years postoperatively for (1) HCV patients vs. controls, (2) antiviral-treated HCV patients vs. controls, and (3) antiviral-treated HCV patients vs. untreated HCV patients.

Results: Patients with HCV exhibited significantly higher rates of blood transfusion (OR 2.12), acute kidney injuries (OR 1.86), inpatient readmission (OR 2.06), revision TSA (OR 1.48), dislocation (OR 1.92), mechanical complications (OR 1.39), and prosthetic joint infection (OR 1.53) compared to controls. Antiviral-treated HCV patients exhibited a significantly lower rate of myocardial infarction (OR 0.27) and comparable rates of all other complications relative to controls (all $P > .05$). Compared to untreated HCV patients, antiviral-treated HCV patients exhibited significantly lower rates of 90-day medical complications (OR 0.57) and prosthetic joint infection (OR 0.36).

Conclusions: HCV is associated with significantly increased complication rates after TSA. Antiviral treatment before TSA may reduce the risk of postoperative complications.

Total shoulder arthroplasty (TSA) is a highly successful treatment for traumatic and degenerative pathologies of the shoulder. Anatomic TSA and reverse TSA commonly yield excellent patient outcomes with improved joint function and significant pain reduction,[21,26,33] and both procedures are reported to have similar rates of postoperative complications.[17,22,28] Furthermore, annual TSA volume is growing exponentially at a rate that surpasses both total hip arthroplasty and total knee arthroplasty.[5,36] In order to minimize complications amidst the rising incidence of TSA, the preoperative optimization of arthroplasty candidates is critical.

Hepatitis C virus (HCV) is the cause for the most common bloodborne infection in the world and affects more than 3 million Americans.[16] Approximately 3.3% of the orthopedic patient population is infected with HCV, and anti-HCV antibody is present in more than 11% of veterans who undergo elective arthroplasty.[18,34] Currently, patients between the age of 50 and 75 exhibit the highest prevalence of chronic HCV and this demographic also

The Tulane University Human Research Protection Office Institutional Review Board determined that this study was exempt (Ref #: 2021-926).

*Corresponding author: William F. Sherman, MD, MBA, MFIN, FAAOS, Tulane University Department of Orthopaedic Surgery, 1430 Tulane Ave, New Orleans, LA 70112, USA.

E-mail address: Swilliam1@tulane.edu (W.F. Sherman).

https://doi.org/10.1016/j.jseint.2022.07.012

undergoes the majority of TSA procedures performed in the United States (U.S.).[6,19,20] HCV has been previously recognized as a risk factor for complications following elective arthroplasty.[11,15,18,29] Evidences in the lower-extremity arthroplasty literature suggests antiviral treatment before surgery mitigates the risk of postoperative complications conferred by HCV infection, possibly due to the restoration of immune function.[2,3,27,31]

However, there is a paucity of research on HCV as an independent risk factor for complications after TSA and previous studies have reported inconsistent findings.[7,35] Prior studies have also been limited by exclusive analyses of Veterans' Affairs[35] and Medicare-only populations,[7] which may have limited generalizability with respect to the total population of patients receiving TSA. Thus, the impact of HCV and preoperative antiviral treatment on complication rates following TSA at a national level remains unclear and further investigation is warranted.

The purpose of this study was to quantify the impact of HCV and preoperative antiviral treatment on complications following primary elective TSA. It was hypothesized that postoperative complication rates would be (1) significantly higher among HCV patients relative to controls, (2) comparable for HCV patients with preoperative antiviral treatment relative to controls, and (3) lower for antiviral-treated HCV patients compared to untreated HCV patients.

Materials and methods

Data source and study design

Patient records were queried from the PearlDiver Mariner Database (PearlDiver Technologies, Colorado Springs, CO, USA); an administrative claims database that contains de-identified inpatient and outpatient data. Researchers use International Classification of Diseases, Ninth and Tenth Revision (ICD-9/ICD-10) codes and Current Procedural Terminology (CPT) codes to identify patients and outcomes. The dataset analyzed ("MUExtr") contains the medical records of 7 million patients across the U.S. from 2010 through 2020 Q3 which are collected by an independent third-party data aggregator. All health insurance payers are represented. Institutional Review Board exemption was granted for this study as provided data was de-identified and compliant with the Health Insurance Portability and Accountability Act. No outside funding was received for this study.

A retrospective matched cohort study was conducted to compare complication rates following primary elective TSA for patients with HCV vs. controls, and to investigate the impact of preoperative antiviral treatment on postoperative complication rates. TSA included both anatomic and reverse shoulder arthroplasty and was defined with CPT-23472 and ICD-9/ICD-10 procedural codes. In order to limit potential transfer bias caused by patients joining or leaving the dataset during the study period, only patients with continuous database enrollment for at least 1 year before and 2 years after the index arthroplasty were included. Patients with a history of prior shoulder surgery including TSA, hemiarthroplasty, or fusion were excluded to isolate primary elective TSA cases. Additionally, patients undergoing TSA for proximal humerus fractures, pathologic fractures, fracture malunion or nonunion, shoulder infection, recurrent dislocation, or humeral head avascular necrosis were excluded. Patients with rheumatoid arthritis, hepatitis B, or human immunodeficiency virus were also excluded.

Patients infected with HCV were identified using ICD-9 and ICD-10 diagnosis codes for acute infection, chronic infection, and unspecified infection before or at the time of TSA. Prior validation studies on coding accuracy have reported a positive predictive value between 88% and 94% for patients with documented HCV and a negative predictive value between 90% and 93% for patients without documented HCV.[24,25] The complete list of codes used to define inclusion and exclusion criteria is available in Supplementary Appendix A.1.

Preoperative HCV treatment was defined as at least one pharmacologic claim for a common antiviral medication used for treating HCV before TSA. National drug codes, uniformed system of classification codes, and generic drug codes were used to identify antiviral medications on outpatient claims in the database (Supplementary Appendix A.2). Mean time between the last claim for antiviral medications and TSA was obtained.

Demographic data and clinical outcomes

Baseline demographic and clinical characteristics were obtained for all patients, including age, sex, the U.S. region, mean Charlson Comorbidity Index (CCI) score, and rates of the comorbidities of tobacco use, diabetes mellitus, and obesity. CCI is a metric that illustrates comorbidity burden as defined by a range of ICD diagnosis codes and is commonly used as a predictor of in-hospital mortality and resource utilization.[1] Additionally, for identified patients without documented HCV, rates of HCV screening at any time and within 1 year before TSA were queried using CPT codes (Supplementary Appendix A.3).

Rates of inpatient readmissions and medical complications within 90 days after TSA were obtained. Specific complications assessed included deep venous thrombosis, pulmonary embolism, acute kidney injury (AKI), blood transfusion, urinary tract infection (UTI), and myocardial infarction (MI) (Supplementary Appendix A.4).

Prothesis-related complications assessed included periprosthetic fracture, prosthetic joint infection (PJI), prosthetic dislocation, all-cause revision TSA, prosthetic stiffness, and other mechanical complications at 1- and 2 years post-TSA. All-cause revision TSA included revision of the humeral and/or glenoid components, antibiotic cement spacer insertion (eg, for PJI), and removal of the prosthesis. PJI was defined with diagnosis and procedural codes representing revision surgeries for infectious processes affecting the shoulder prosthesis. Other mechanical complications included implant loosening or breakage, periprosthetic osteolysis, and wear of the articular surface.

Statistical analysis

Statistical analyses were performed using R statistical software (Version 4.1.0; R Project for Statistical Computing, Vienna, Austria) integrated within the PearlDiver software with an α level set to 0.05. In order to generate comparable cohorts, exact matching without replacement was performed to match HCV patients with controls in a 1:3 ratio on the following variables: age, sex, tobacco use, diabetes mellitus, and obesity.

Categorical variables were compared with chi-square analysis and continuous variables were compared with Welch's t-test or the Mann–Whitney U test. Postoperative complication rates among patients with HCV vs. controls without HCV were compared using multivariable logistic regression adjusting for age, sex, and CC. Subgroup analyses were also performed comparing complication rates for (A) HCV patients with antiviral treatment before TSA vs. controls and (B) HCV patients with vs. without antiviral treatment before TSA. Odds ratios (ORs) with corresponding 95% confidence intervals (CIs) were calculated for each outcome. For instances in which one cohort had no events for a certain complication, the Fisher Exact test was used to compare complication rates.

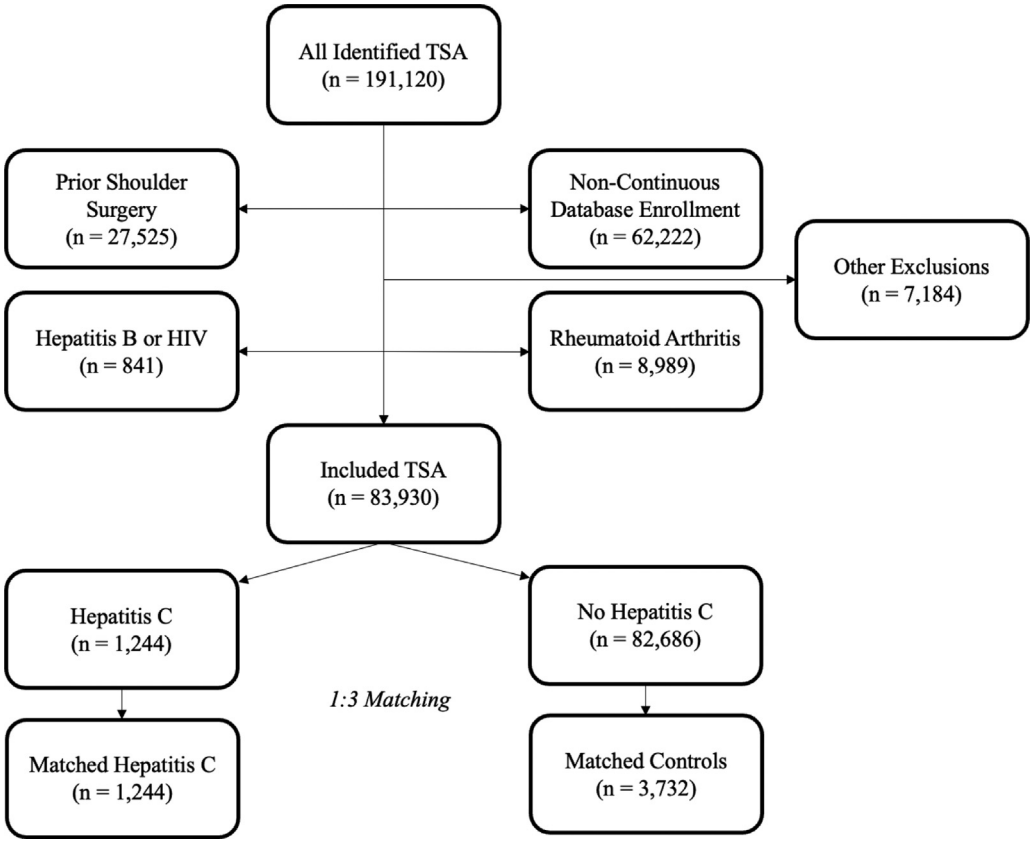

Figure 1 Flowchart outlining identification of study cohorts. *TSA*, total shoulder arthroplasty; *HIV*, human immunodeficiency virus.

Results

Study population

A total of 83,390 patients who received primary elective TSA were identified (Fig. 1), including 1244 (1.5%) patients with documented HCV infection. Within the HCV cohort, 186 (15.0%) patients had a record of previous antiviral treatment at a mean time of 2.39 ± 1.89 years before TSA. Among the identified patients without documented HCV infection, 4.3% (3558/82,686) had a record of HCV screening at any time before TSA and 1.5% (1224/82,686) were screened within 1 year before TSA.

All 1244 HCV patients were successfully matched with 3732 controls without HCV (Table I). The 2 cohorts were statistically comparable across all matched variables. The mean CCI score was significantly higher in the HCV cohort (3.07 vs. 1.72, $P < .001$). The U.S. regional distribution also differed between the cohorts.

Table I
Demographic data and clinical characteristics of matched patient cohorts.

Characteristics	HCV (n = 1244)	No HCV (n = 3732)	*P* value
Age (y), Mean ± SD	62.30 ± 7.17	62.43 ± 7.33	.565
Female Sex, n (%)	556 (44.7)	1668 (44.7)	1
U.S. Region (%)*			
Northeast	221 (17.8)	632 (16.9)	.523
South	457 (36.7)	1374 (36.8)	.987
Midwest	308 (24.8)	1235 (33.1)	< **.001**
West	255 (20.5)	484 (13.0)	< **.001**
CCI, Mean ± SD	3.07 ± 2.68	1.72 ± 2.11	< **.001**
Comorbidities, n (%)			
Diabetes Mellitus	573 (46.1)	1719 (46.0)	1
Tobacco Use	861 (69.2)	2583 (69.2)	1
Obesity	552 (44.4)	1656 (44.4)	1

HCV, hepatitis C virus; *SD*, standard deviation; *CCI*, Charlson comorbidity index.
Bolded *P*-values indicate statistically significant results.
*Region data was available for 99% of each study cohort.

HCV patients vs. controls

Within 90 days postoperatively (Table II), patients with HCV exhibited a significantly higher rate of at least one medical complication (12.9% vs. 9.1%; OR, 1.26; 95% CI, 1.02-1.54). Specifically, patients with HCV exhibited significantly higher rates of blood transfusion (2.2% vs. 1.0%; OR, 2.12; 95% CI, 1.25-3.54), AKI (3.0% vs. 1.3%; OR, 1.86; 95% CI, 1.18-2.92), and inpatient readmission (4.6% vs. 2.5%; OR, 2.06; 95% CI, 1.47-2.85). Rates of MI (2.2% vs. 2.7%; OR, 0.59; 95% CI, 0.37-0.91) and UTI (1.8% vs. 2.6%; OR, 0.60; 95% CI, 0.36-0.95) were significantly lower in the HCV cohort.

At 1 year following TSA, patients with HCV exhibited significantly higher rates of all-cause revision (4.4% vs. 2.8%; OR, 1.49; 95% CI, 1.05-2.09), prosthetic dislocation (2.8% vs. 1.6%; OR, 1.66; 95% CI, 1.07-2.55), PJI (3.5% vs. 1.8%; OR, 1.76; 95% CI, 1.17-2.61), and other mechanical complications (3.2% vs. 2.1%; OR, 1.55; 95% CI, 1.03-2.29). The rate of at least one prosthesis-related complication at 1 year postoperatively was statistically comparable between the cohorts (14.6% vs. 13.0%; OR, 1.11; 95% CI, 0.92-1.34).

At 2-year follow-up, the HCV cohort exhibited significantly higher rates of all-cause revision (5.7% vs. 3.7%; OR, 1.48; 95% CI, 1.09-1.99), prosthetic dislocation (3.6% vs. 1.9%; OR, 1.92; 95% CI, 1.33-2.87), PJI (4.4% vs. 2.7%; OR, 1.53; 95% CI, 1.08-2.15), and other mechanical complications (4.6% vs. 3.3%; OR, 1.39; 95% CI, 1.01-1.92). Rates of periprosthetic fracture and prosthetic stiffness were comparable between the cohorts at both 1- and 2-year follow-ups (all $P > .05$).

Table II
Complication rates at 90 days, 1 year, and 2 years after TSA for patients with HCV vs. controls.

Complication	HCV (n = 1244)	Controls (n = 3732)	Logistic regression analyses	
	n (%)	n (%)	OR (95% CI)[†]	*P* value
90 Days				
Medical Complications[*]	161 (12.9)	343 (9.2)	**1.26 (1.02-1.54)**	**.028**
DVT	5 (0.4)[‡]	20 (0.5)	1.09 (0.44-2.45)	.855
Transfusion	27 (2.2)	36 (1.0)	**2.12 (1.25-3.54)**	**.005**
PE	5 (0.4)[‡]	16 (0.4)	0.89 (0.29-2.34)	.838
UTI	22 (1.8)	97 (2.6)	**0.60 (0.36-0.95)**	**.039**
AKI	37 (3.0)	47 (1.3)	**1.86 (1.18-2.92)**	**.007**
MI	27 (2.2)	102 (2.7)	**0.59 (0.37-0.91)**	**.021**
Inpatient Readmission	67 (5.4)	93 (2.5)	**2.06 (1.47-2.85)**	**< .001**
1 Year				
Prosthesis Complications[*]	182 (14.6)	485 (13.0)	1.11 (0.92-1.34)	.280
Periprosthetic Fracture	5 (0.4)[‡]	14 (0.4)	1.79 (0.70-4.28)	.209
All-Cause Revision	55 (4.4)	103 (2.8)	**1.49 (1.05-2.09)**	**.023**
Mechanical Complication	40 (3.2)	77 (2.1)	**1.55 (1.03-2.29)**	**.031**
Dislocation	35 (2.8)	60 (1.6)	**1.66 (1.07-2.55)**	**.022**
Stiffness	89 (7.2)	300 (8.0)	0.88 (0.68-1.13)	.329
Prosthetic Joint Infection	43 (3.5)	68 (1.8)	**1.76 (1.17-2.61)**	**.006**
2 Years				
Prosthesis Complications[*]	226 (18.2)	591 (15.8)	1.15 (0.96-1.36)	.116
Periprosthetic Fracture	13 (1.0)	28 (0.8)	1.40 (0.69-2.70)	.339
All-Cause Revision	71 (5.7)	138 (3.7)	**1.48 (1.09-1.99)**	**.011**
Mechanical Complication	57 (4.6)	122 (3.3)	**1.39 (1.01-1.92)**	**.044**
Dislocation	45 (3.6)	70 (1.9)	**1.92 (1.29-2.82)**	**.001**
Stiffness	105 (8.4)	346 (9.3)	0.91 (0.72-1.14)	.429
Prosthetic Joint Infection	55 (4.4)	101 (2.7)	**1.53 (1.08-2.15)**	**.015**

HCV, hepatitis C virus; *CI*, confidence interval, *DVT*, deep venous thrombosis; *PE*, pulmonary embolism; *UTI*, urinary tract infection; *AKI*, acute kidney injury; *MI*, myocardial infarction; *TSA*, total shoulder arthroplasty.
Bolded OR (95% CI) and *P*-values indicate statistically significant results.
[*]The number of patients with at least one medical or prosthesis-related complication at each follow-up.
[†]Reference group, HCV, cohort.
[‡]PearlDiver does not report patient counts for defined cohorts that contain < 11 patients. When this occurred, a cohort size of 5 (median between 1 and 10) was assigned. The true rates of these complications cannot be quantified, though the PearlDiver software uses the real patient counts during statistical analysis.

Independent of HCV status, several significant associations were also found between demographics variables and postoperative complications (Supplementary Appendix B.1 and Supplementary Appendix B.2). Notably, CCI > 3 was associated with significantly higher rates of medical complications within 90 days of TSA (OR, 2.16; 95% CI 1.76-2.65), all-cause revision at 1-year postoperatively (OR, 1.54; 95% CI 1.74-2.20), and PJI at 1 year (OR, 1.60; 95% CI 1.03-2.43) and 2 years postoperatively (OR, 1.52; 95% CI 1.04-2.18).

Antiviral-treated HCV patients vs. controls

Compared to non-infected controls (Table III), HCV patients with antiviral treatment before TSA exhibited slightly lower and statistically comparable rates of at least one medical complication (8.6% vs. 9.1%; OR, 0.71; 95% CI, 0.40-1.17) within 90 days postoperatively. The rate of MI was significantly lower in the HCV cohort (1.1% vs. 2.4%; OR, 0.27; 95% CI, 0.07-0.90). Rates of all other medical complications were comparable (all $P > .05$).

Antiviral-treated HCV patients exhibited comparable rates of at least one prosthesis-related complication at both 1 year (13.4% vs. 13.0%; OR, 0.97; 95% CI, 0.62-1.48) and 2 years postoperatively (16.1% vs. 15.8%; OR, 0.95; 95% CI, 0.62-1.41). Rates of each individual prosthesis-related complication were also statistically comparable at both 1 and 2 years postoperatively (all $P > .05$).

Antiviral-treated HCV patients vs. untreated HCV patients

Antiviral-treated HCV patients exhibited a significantly lower rate of at least one medical complication within 90 days compared to untreated HCV patients (8.6% vs. 13.7%; OR, 0.57; 95% CI, 0.32-0.96). Rates of PJI at 2 years postoperatively were also significantly lower for antiviral-treated patients (1.6% vs. 4.9%; OR, 0.36; 95% CI, 0.14-0.98). All other complications within 2 years postoperatively were statistically comparable (all $P > .05$).

Discussions

Patients with HCV in the present study demonstrated significantly higher rates of medical and prosthesis-related complications following TSA relative to matched controls. Only 1.4% of patients without documented HCV infection were screened for HCV within the year preceding TSA, and only 15% of identified HCV patients received antiviral treatment before TSA. Postoperative complication rates among antiviral-treated HCV patients were statistically comparable compared to noninfected controls and lower compared to untreated HCV patients. These results highlight the importance of recognizing HCV as a risk factor for poor outcomes following TSA and suggest that it may be modifiable with targeted preoperative optimization via antiviral treatment.

In this study, 15% of patients in the HCV cohort received antiviral treatment before TSA. Previous studies using the U.S. Department of Veterans' Affairs dataset have reported slightly higher treatment rates of 17.3%-23.4% among HCV patients seeking elective arthroplasty.[3,35] These findings illustrate ongoing low treatment rates in the HCV population despite the increased availability of direct-acting antivirals (DAA) over the past decade. Prior studies have estimated half of all patients infected with HCV in the U.S. receive a diagnosis, and less than half of diagnosed patients receive treatment.[14,39] The CDC currently recommends one-time HCV screening for all adults older than 18 years, living in an area where the

Table III
Complication rates at 90 days, 1 year, and 2 years after TSA for subgroup analyses of (A) treated HCV patients vs. controls and (B) antiviral-treated vs. untreated HCV patients.

Complication	Controls (n = 3732)	Antiviral-treated HCV (n = 186)	Untreated HCV (n = 1058)	Treated HCV vs. Controls		Antiviral-treated HCV vs. Untreated HCV	
	n (%)	n (%)	n (%)	OR (95% CI)†	*P* value	OR (95% CI)†	*P* value
90 Days							
Medical Complications*	343 (9.2)	16 (8.6)	145 (13.7)	0.71 (0.40-1.17)	.213	**0.57 (0.32-0.96)**	**.045**
DVT	20 (0.5)	0 (0.0)	5 (0.5)§	N/A	.622‡	N/A	.613‡
Transfusion	36 (1.0)	3 (1.6)	24 (2.3)	1.30 (0.31-3.76)	.693	0.70 (0.17-2.04)	.586
PE	16 (0.4)	0 (0.0)	5 (0.5)§	N/A	1‡	N/A	.756‡
UTI	97 (2.6)	3 (1.6)	19 (1.8)	0.47 (0.11-1.29)	.231	0.74 (0.17-2.25)	.661
AKI	47 (1.3)	4 (2.2)	33 (3.1)	1.26 (0.37-3.20)	.688	0.58 (0.17-1.51)	.333
MI	102 (2.7)	2 (1.1)	25 (2.4)	**0.27 (0.07-0.90)**	**.044**	0.46 (0.07-1.59)	.335
Inpatient Readmission	93 (2.5)	6 (3.2)	61 (5.8)	1.13 (0.43-2.43)	.794	0.56 (0.21-1.23)	.200
1 Year							
Prosthesis Complications*	485 (13.0)	23 (12.4)	159 (15.0)	0.97 (0.62-1.48)	.899	0.92 (0.57-1.43)	.735
Periprosthetic Fracture	14 (0.4)	1 (0.5)	5 (0.5)§	1.66 (0.09-8.57)	.676	0.70 (0.04-4.05)	.775
All-Cause Revision	103 (2.8)	6 (3.2)	49 (4.6)	1.02 (0.39-2.19)	.967	0.69 (0.26-1.53)	.420
Mechanical Complication	77 (2.1)	5 (2.7)	35 (3.3)	1.28 (0.44-2.94)	.623	0.79 (0.27-1.89)	.648
Dislocation	60 (1.6)	6 (3.2)	29 (2.7)	1.59 (0.55-3.72)	.347	1.02 (0.34-2.47)	.972
Stiffness	300 (8.0)	15 (8.1)	74 (7.0)	0.99 (0.55-1.65)	.974	1.18 (0.64-2.05)	.589
Prosthetic Joint Infection	68 (1.8)	3 (1.6)	40 (3.8)	0.75 (0.18-2.06)	.657	0.49 (0.12-1.39)	.257
2 Years							
Prosthesis Complications*	591 (15.8)	30 (16.1)	196 (18.5)	0.95 (0.62-1.41)	.818	0.86 (0.55-1.29)	.498
Periprosthetic Fracture	28 (0.8)	1 (0.5)	12 (1.1)	0.78 (0.04-3.74)	.841	0.40 (0.02-2.04)	.446
All-Cause Revision	138 (3.7)	8 (4.3)	63 (6.0)	1.03 (0.45-2.02)	.944	0.72 (0.31-1.45)	.411
Mechanical Complication	122 (3.3)	7 (3.8)	50 (4.7)	1.11 (0.50-2.44)	.808	0.78 (0.32-1.66)	.566
Dislocation	70 (1.9)	8 (4.3)	37 (3.5)	2.01 (0.82-4.21)	.094	1.12 (0.45-2.43)	.804
Stiffness	346 (9.3)	17 (9.1)	88 (8.3)	0.97 (0.58-1.63)	.915	1.09 (0.61-1.84)	.772
Prosthetic Joint Infection	101 (2.7)	3 (1.6)	52 (4.9)	0.51 (0.12-1.39)	.285	**0.36 (0.14-0.98)**	**.039**

HCV, hepatitis C virus; *CI*, confidence interval, *DVT*, deep venous thrombosis; *PE*, pulmonary embolism; *UTI*, urinary tract infection; *AKI*, acute kidney injury; *MI*, myocardial infarction; *TSA*, total shoulder arthroplasty.
Bolded OR (95% CI) and *P*-values indicate statistically significant results.
*The number of patients with at least one medical or prosthesis-related complication at each follow-up.
†Reference group, Antiviral-Treated HCV cohort.
‡Fischer-Exact test used to compare complication rates.
§PearlDiver does not report patient counts for defined cohorts that contain <11 patients. In this situation, when it was not possible to derive the actual patient counts by using counts in Table II, for the HCV cohort and subtracting counts for the subgroups of treated/untreated HCV, patients, a cohort size of 5 (median between 1 and 10) was assigned. The true rates of these complications cannot be quantified, though the PearlDiver software uses the real patient counts during statistical analysis.

prevalence of HCV is 0.1% or greater.[32] Only 1.4% of patients without documented HCV infection in this study were screened for HCV within a year before TSA, which suggests that HCV screening has not been routinely performed before TSA. This data highlights a potential area of improvement given that HCV is a known risk factor for poor postoperative outcomes and preoperative treatment may decrease complications of risk. Arthroplasty surgeons should consider adding HCV screening to routine pre-TSA lab work when HCV status is uncertain, especially in areas where HCV is endemic.[6]

HCV has been previously recognized as a risk factor for prosthesis-related complications following elective arthroplasty.[18] Prior research has associated HCV infection with a greater risk of PJI,[11,31] mechanical complications,[8,38] and revision surgery[23,31] after both total knee arthroplasty and total hip arthroplasty. At 1- and 2 years postoperatively, HCV patients in this study exhibited significantly higher rates of revision TSA, PJI, dislocation, and other mechanical complications compared to matched controls. These findings align with data from a prior Medicare database study in which rates of PJI, revision TSA, dislocation, and postoperative fractures were significantly higher among TSA patients infected with HCV.[7] Rates of transfusion, AKI, and inpatient readmission within 90 days postoperatively were also significantly higher in the HCV cohort. These results corroborate prior reports of increased 90-day medical complications amongst HCV patients following both lower extremity arthroplasty[4,12,18] and TSA.[7] The etiology of this increased perioperative complication risk is multifactorial and may be secondary to extrahepatic manifestations of HCV infection including thrombocytopenia, glomerulonephritis, and leukocytoclastic vasculitis.[13,37,40] Impaired physiologic responses to surgery, delayed wound healing, and lower rates of resource access and follow-up may also contribute.[7,29] Furthermore, significantly higher complication rates were found in the HCV cohort while controlling for comorbidity burden via CCI, which also demonstrated significant associations with many complications. This result suggests that the risk of postoperative complications associated with HCV is not solely mediated by a higher comorbidity burden. Our data illustrating higher complication rates in this population highlights the importance of preoperative risk stratification and medical optimization before TSA.

Despite the increased availability of effective antiviral pharmacotherapy with demonstrated curative potential over the last decade, there is minimal data on its impact on complication rates in HCV patients undergoing TSA.[9,30] In an analysis of a Veterans' Affairs database, Su et al identified 548 patients with HCV who underwent TSA and found 128 (23.4%) with a record of DAA treatment before TSA. Compared to untreated HCV patients, DAA-treated HCV patients in their study exhibited lower but statistically comparable rates of all complications assessed, including medical complications, infection, and mechanical complications.[35] In the present study, antiviral-treated HCV patients exhibited a significantly lower rate of MI and comparable rates of all other medical and prosthesis-related complications compared to non-infected controls. Within the HCV cohort, antiviral-treated patients exhibited significantly lower rates of medical complications and PJI than untreated patients. Rates of several other complications were also notably lower for

antiviral-treated patients but did not reach statistical significance, likely due to inadequate power. These results illustrate a strong association between preoperative antiviral treatment and reduced complication rates after TSA in patients with HCV. As such, this data provides evidence to support recommending preoperative antiviral treatment before TSA in patients with HCV, though further larger-scale research is needed to strengthen this recommendation.

Limitations

Several limitations must be acknowledged. First, since the PearlDiver database only provides data on a particular group of patients during a specific time period, sampling bias is present, and the results may not be applicable to patients undergoing TSA outside of the U.S. By only evaluating prosthesis-related complications at 2 years following TSA, this analysis is limited to short-term clinical outcomes. Furthermore, because continuous database enrollment for 2 years after TSA was required for inclusion, patients who died within 2 years after surgery were excluded and therefore this data may not be representative of patients with high perioperative mortality risk. An additional limitation concerns the complex nature of medical billing, wherein there is a possibility of coding bias through manual entry of codes for billing. Coding errors are inherent in any analysis of administrative claims data; however, such instances are rare and comprise only 0.7% of Medicare and Medicaid payments in 2020.[10] Similar to prior studies, the present study analyzed anatomic and reverse shoulder arthroplasty together.[7,35] Although subgroup analyses for each individual procedure would be worthwhile, most patients in both cohorts (64.6%) received TSA billed with CPT-23472 which is used for both anatomic and reverse TSA. Consequently, the exact distribution of anatomic and reverse shoulder arthroplasty in each cohort is unknown and it is unclear if HCV and pre-arthroplasty antiviral treatment impacts outcomes of either procedure disproportionately. Additionally, granular data such as implant type, surgeon experience, surgical approach, and operative time were not available in the database which may have influenced outcomes.

It is possible that some patients with undiagnosed HCV infections could have been included in the control cohort. Similarly, antiviral treatment could only be identified via outpatient prescription claims filed in the years included in the dataset. Consequently, patients with antiviral treatment before 2010 could not be identified and may have been excluded from the treated HCV cohort. The database also does not contain data regarding viral load which prevents analysis of viral load as an independent variable with respect to complication rates and the efficacy of preoperative antiviral treatment. Therefore, it is possible that the reported complication rates for the treated cohort are higher than the rates observed in patients with preoperative antiviral treatment who achieve sustained virologic response before TSA. Based on the small number of identified HCV patients with antiviral treatment before TSA, it is also possible that the subgroup analyses were underpowered. For example, rates of several complications were much lower for treated HCV patients than for untreated HCV patients, but did not reach statistical significance. As this limitation is similar to prior analyses, future larger-scale studies of nationally representative populations are needed to further investigate the impact of pre-arthroplasty antiviral treatment on complication rates after TSA. Rates of HCV screening were evaluated within 1 year before TSA to determine its utilization as an element of pre-arthroplasty laboratory workup. However, it is possible that some patients had a more distant history of screening and negative results would have obviated the need for further testing. It is also possible that some patients were screened for HCV but were not identified by our screening criteria. Lastly, although matching and multivariable regression were used, other unknown or known confounders which are unavailable in the database such as socioeconomic status, illicit drug abuse, and resource access could have influenced the results.

There are several strengths of this analysis. This study analyzes contemporary data (2010-2020 Q3) and, to the authors' knowledge, is the first study to analyze the impact of HCV on outcomes of primary elective TSA in a nationally-representative sample inclusive of all health insurers. Additionally, this is the first study to report data suggesting an association between preoperative antiviral treatments and reduced short-term complications after TSA. This data can be a useful resource to surgeons treating patients with HCV and to researchers seeking to conduct future investigations in this area.

Conclusions

Patients with HCV exhibited significantly increased rates of complications after primary elective TSA compared to matched controls. However, HCV patients with antiviral treatment before TSA exhibited comparable complication rates compared to non-infected controls, and significantly lower rates of medical complications and PJI than untreated HCV patients. These findings suggest antiviral treatment before TSA may reduce complication risk in HCV patients.

Disclaimers:

Funding: No funding was disclosed by the authors.
Conflicts of interest: The authors, their immediate families, and any research foundation with which they are affiliated have not received any financial payments or other benefits from any commercial entity related to the subject of this article.

Supplementary Data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jseint.2022.07.012.

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