Arthroplasty Today 17 (2022) 107–113

Contents lists available at ScienceDirect

Arthroplasty Today

journal homepage: http://www.arthroplastytoday.org/

Original Research

Total Joint Arthroplasty Should Not Be Delayed in Hepatitis C Patients After Successful Treatment Achieving a Sustained Viral Load

Kyle H. Cichos, BS [a], Eric Jordan, BS [b, c], Kian Niknam, BS [d], Antonia F. Chen, MD, MBA [b, c], Erik N. Hansen, MD [d], Gerald McGwin Jr, PhD [e], Elie S. Ghanem, MD [a, *]

[a] Department of Orthopaedic Surgery, University of Alabama at Birmingham, Birmingham, AL, USA
[b] Department of Orthopaedic Surgery, Brigham and Women's Hospital, Boston, MA, USA
[c] Harvard Medical School, Boston, MA, USA
[d] Department of Orthopaedic Surgery, University of California San Francisco, San Francisco, CA, USA
[e] Department of Epidemiology, School of Public Health, University of Alabama at Birmingham, Birmingham, AL, USA

ARTICLE INFO

Article history:
Received 11 May 2022
Accepted 26 June 2022
Available online xxx

Keywords:
Hepatitis C
Outcomes
Total joint arthroplasty
Periprosthetic joint infection
Viral load level
Treatment

ABSTRACT

Background: Preoperative treatment recommendations and optimal time to perform total joint arthroplasty (TJA) in patients with hepatitis C virus after treatment completion for achieving best outcomes have not been elucidated. We aim to determine (1) if undetectable viral load (UVL) prior to TJA leads to decreased postoperative complication rates, specifically periprosthetic joint infection (PJI), and (2) if delaying TJA after treatment completion has benefit in decreasing PJI.

Methods: A retrospective review of all hepatitis C virus patients undergoing TJA at 3 academic tertiary care centers was conducted. A total of 270 TJAs performed from 2005 to 2019 were included, 125 with positive viral load at the time of surgery. The duration from completion of treatment regimen to TJA was recorded for the UVL cohort. The primary study outcome was PJI at 1-year follow-up. Secondary outcomes included in-hospital complications, mechanical revision TJA rates, and optimal time to TJA upon completion of treatment.

Results: Patients with positive viral load at the time of TJA had longer length of stay (3.9 vs 2.9 days, $P < .0001$) and a higher PJI rate at 1 year postoperatively (9% vs 2%, $P = .02$) than UVL patients. There was no difference of in-hospital complications or revision rates for mechanical etiologies. Delaying TJA after achieving a sustained virologic response did not impact PJI rates.

Conclusions: Sustained UVL prior to TJA is critical to minimize PJI irrespective of the treatment regimen utilized. Surgery can be performed with lower complication rates any time after achieving sustained virologic response.

Level of Evidence: Level III, prognostic retrospective cohort study.

Introduction

There are approximately 3 million people in the United States affected with hepatitis C virus (HCV) [1], many of which are asymptomatic with a variable spontaneous resolution rate where a patient's immune system clears the virus [2]. The overall rate of HCV in patients undergoing total joint arthroplasty (TJA) is extremely low, but these numbers are expected to continue rising with improved medical treatments and consequent increase in lifespan [3]. According to large national database studies, patients with HCV with or without cirrhosis undergoing total hip or knee arthroplasty are at an increased risk of medical and surgical complications, especially periprosthetic joint infection (PJI) [3–5]. A recent meta-analysis revealed that patients with HCV had higher complication rates, increased mechanical revision rates, and longer length of stay (LOS) after TJA [6].

Prior to 2011, the standard HCV treatment consisted of peginterferon alfa-2a (or 2b) and ribavirin administered for 24-48 weeks but had a suboptimal success rate in curing patients, was associated

* Corresponding author. Department of Orthopaedic Surgery, University of Alabama at Birmingham, 1313 13th Street South, Suite 207, Birmingham, AL 35205, USA. Tel.: +1 205 930 8543.
E-mail address: eghanem@uabmc.edu

https://doi.org/10.1016/j.artd.2022.06.014

with high treatment-related toxicity, and inevitably led to low patient compliance rates in treatment prior to elective TJA [7,8]. Direct acting antivirals (DAAs) have since been developed which are associated with fewer adverse side effects, shorter duration of treatment (approximately 12 weeks), and higher success rates (up to 99%) in achieving a sustained virologic response (SVR), defined as an undetectable RNA viral load (VL) 12 weeks after completing treatment [9,10]. A national focus and drive to treat patients with HCV using these novel DAAs ensued, including at the Veterans Affairs Hospitals where programs were developed to reduce HCV rates from 4.5% to 0.4% in the veteran population [11,12]. Consequently, a study conducted by Cancienne et al. determined that HCV patients who did not receive treatment prior to total knee arthroplasty had higher rates of both infection and aseptic revision 3 months following surgery, which renewed interest in optimizing this high-risk cohort prior to TJA [13].

A recent study by Bedair et al. concluded that HCV treatment irrespective of therapy modality (interferon or DAA) is essential prior to patients undergoing total hip arthroplasty as prevention for surgical complications, specifically PJI, despite the small cohort of only 42 total "treated" patients [14]. Of note, patients who completed their treatment but failed their therapy with persistent detectable VLs, many of which were treated with interferon, were included in the treated group, which skewed the results and underestimates the positive effect of treatment in preventing complications. A recent follow-up study concluded that patients with detectable VL at the time of TJA were prone to have longer operative time, extended LOS, and higher mechanical complications and infections than patients with undetectable VL (UVL) [15]. However, the previous study had some limitations and did not include relevant risk factors that play a confounding role in outcomes after surgery in HCV patients, particularly those related to the liver scores, fibrosis staging, and common comorbidities such as diabetes and inflammatory disease. We aim to determine if (1) UVL prior to TJA leads to decreased postoperative complication rates, specifically PJI, and (2) if delaying TJA after completion of treatment has a benefit in decreasing PJI rates.

Material and methods

We conducted a retrospective review, after obtaining institutional review board approval, of all patients diagnosed with HCV who underwent primary TJA between 2005 and 2019 at 3 academic tertiary care centers in the United States with specialized clinics dedicated for managing HCV patients. Revision TJA cases and primary simultaneous bilateral TJA were excluded from the cohort, while patients with multiple-staged primary TJAs were included, and the VL was noted prior to each TJA in such patients. Patients with a prior liver transplant history were included in our study. Only patients with available HCV VL prior to primary TJA were included. A minimum of 1-year follow-up was required, and mortality during follow-up was noted. After exclusion criteria, 270 primary TJAs performed on 226 patients were eligible for analysis. A total of 145 TJAs were performed with UVL prior to surgery, while 125 TJAs had a positive VL (PVL) at the time of surgery. Patient demographics, comorbidities including the presence of human immunodeficiency virus (HIV) and cirrhosis, HCV characteristics, perioperative variables, in-hospital outcomes, and postoperative outcomes including complications at 90 days and 1 year of follow-up were collected by medical record review. PJI was defined according to the Musculoskeletal Infection Society criteria [16]. HCV characteristics included VL (IU/mL), virus genotype, treatment medication (interferon and DAA), liver function tests, Model for End-Stage Liver Disease score [17,18], Child-Pugh Classification [19,20], liver fibrosis staging, and activity. The time duration (months) from a sustained UVL in patients who were successfully treated from the time of completion of treatment to TJA was recorded.

Interferon was utilized in 54 patients while 92 patients received DAAs, including 61 (66%) ledipasvir/sofosbuvir, 20 (22%) sofosbuvir/ribavirin, 7 (8%) sofosbuvir/velpatasvir, 2 (2%) sofosbuvir/velpatasvir/voxilaprevir, 1 (1%) glecaprevir/pibrentasvir, and 1 (1%) elbasvir/grazoprevir. An additional 3 patients cleared HCV without treatment and had UVL at the time of TJA, while 121 patients had PVL at the time of TJA. Patients who were not able to achieve a SVR, defined as UVL for at least 12 weeks after completion of treatment [21], were considered as failed treatment, and for patients not receiving further therapy, their persistent PVL was documented prior to TJA. There was no difference between groups in having a failed prior viral therapy, with 6 (4%) patients failing prior therapy before receiving therapy that eventually resulted in UVL and 4 (3%) patients failing prior therapy with persistent PVL at the time of TJA.

Patient demographics and comorbidities

Patients with UVL at the time of TJA were significantly older (mean age 59.6 [8] vs 54.9 [11], $P = .001$) with higher rates of hepatocellular carcinoma (6% vs 1%, $P = .02$) and a history of liver transplant (11% vs 4%, $P = .04$) compared to PVL patients. There was no significant difference between the 2 groups in HIV and cirrhosis rates (Table 1). There were more black patients in the PVL group (47% vs 19%, $P = .001$) along with a higher rate of hemophilia (10% vs 3%, $P = .02$) and a history of hemarthrosis (10% vs 4%, $P = .03$).

HCV-related variables

The majority of patients with PVL (97%) were untreated while 98% of the UVL group received treatment prior to TJA with interferon (37%) and DAA (61%) ($P < .001$). The average duration from recorded SVR to TJA was 51 months (range: 2-242 months) for the UVL group. Although liver function test scores were higher in the PVL group, the Child Pugh classification, Model for End-Stage Liver Disease score, and liver fibrosis and activity levels were similar to those of the UVL group (Table 2).

Statistical analysis

Chi-squared tests were utilized to compare categorical variables, and 2-tailed Student's t-tests were used to compare continuous variables between the PVL and UVL groups. The in-hospital and postoperative outcomes of interest at 90 days and 1 year were compared between the 2 groups. A multivariable logistic regression analysis was attempted to determine the independent adjusted risk ratios of each significant variable from the initial analysis. P values $< .05$ were considered to be statistically significant.

Results

Perioperative characteristics

Patients with PVL were less likely to receive tranexamic acid (32% vs 64%, $P < .0001$) but more likely to have general anesthesia than the UVL group (81% vs 52%, $P < .0001$). Drains were used more frequently in PVL patients (71% vs 52%, $P = .002$). However, there was no difference in operative time, estimated blood loss, and intraoperative transfusion rates (Table 3).

Table 1
Patient demographics and comorbid conditions comparing undetectable viral load (UVL) to positive viral load (PVL) at the time of TJA.

Patient characteristics	All HCV TJA (n = 270)	Viral load undetectable (n = 145)	Viral load positive (n = 125)	*P* value
Sex, male, n (%)	161 (60)	81 (56)	80 (64)	.21
Race, n (%)[a]				
White	157 (57)	98 (77)	59 (50)	<.0001
Black	81 (30)	25 (19)	56 (47)	
Other	8 (3)	5 (4)	3 (3)	
Age, y, mean (SD)	57 (9)	59.6 (8)	54.9 (11)	<.01
BMI, kg/m^2, mean (SD)	29.0 (5)	29.5 (5)	28.4 (6)	.03
Comorbid conditions, n (%)				
Obesity	95 (35)	56 (39)	39 (31)	.25
Hemophilia	16 (6)	4 (3)	12 (10)	.02
Hemarthrosis	18 (7)	5 (4)	13 (10)	.03
Prior liver transplant	21 (8)	16 (11)	5 (4)	.04
Cirrhosis (total)	60 (22)	36 (25)	24 (19)	.38
Compensated	53 (20)	31 (21)	22 (18)	.26
Decompensated	7 (3)	5 (3)	2 (2)	
Hepatocellular carcinoma history	10 (4)	9 (6)	1 (1)	.02
DM	51 (19)	28 (19)	23 (18)	.88
Tobacco use	116 (43)	53 (37)	63 (50)	.03
HTN	178 (66)	100 (69)	78 (62)	.30
Hypothyroid	25 (9)	18 (12)	7 (6)	.06
PVD	23 (9)	14 (10)	9 (7)	.52
ESRD	48 (18)	25 (17)	23 (18)	.87
Iron-deficiency anemia	24 (9)	13 (9)	11 (9)	1.00
CVA/Stroke	21 (8)	15 (10)	6 (5)	.11
HIV	31 (11)	15 (10)	16 (13)	.57
CAD	27 (10)	15 (10)	12 (10)	1.00
HF	23 (9)	13 (9)	10 (8)	.83
COPD	38 (14)	21 (14)	17 (14)	.86
Depression	90 (33)	54 (37)	36 (29)	.16

BMI, body mass index; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; DM, diabetes mellitus; ESRD, end-stage renal disease; HF, heart failure; HTN, hypertension; PVD, peripheral vascular disease; SD, standard deviation.
[a] This variable was missing for 24 total patients (7 VL positive, 17 VL undetectable).

In-hospital postoperative outcomes

Patients with PVL had a longer hospital LOS, approximately 1 full day, than the UVL group (3.9 vs 2.9 days, $P < .0001$). However, patients with PVL had similar rates of discharge to skilled nursing or rehabilitation facilities (19% vs 19%, $P = 1.0$) and intensive care unit utilization (2% vs 3%, $P = 1.0$). Hospital-acquired complications including pulmonary embolus, sepsis, myocardial infarction, cerebrovascular accident, and postoperative anemia requiring transfusion were similar between the 2 groups ($P > .05$, Table 4).

Ninety-day and 1-year postoperative outcomes

The PJI rate was significantly higher in the PVL group at 90 days (6% vs 1%, $P = .04$), which persisted at 1 year (9% vs 2%, $P = .02$). The rate of superficial wound problems including cellulitis was 5 times higher in the PVL cohort (5% vs 1%, $P = .08$), but did not reach statistical significance. However, the number of revision TJAs for mechanical complications including fracture, dislocation, and loosening was similar between the 2 groups at 90 days ($P = 1.00$) and 1 year ($P = .58$) postoperatively (Table 5).

Risk factors for PJI

A total of 14 patients were diagnosed with PJI at 1-year follow-up, 3 of which had UVL at the time of TJA. The multivariable regression analysis performed failed to converge due to the low rates of PJI present in our cohort. Hence age, hemarthrosis, and hemophilia were not independent predictors of 1-year PJI although the presence of UVL trended to significance (Table 6). Also, there was no difference in the time frame from treatment completion with SVR to TJA between the patients who developed PJI and those who did not (82 vs 50 months, $P = .54$).

Discussion

Patients with HCV undergoing TJA have significantly higher rates of surgical and postoperative complications following TJA, including hospital LOS, wound complications, revision surgery, and readmission than patients without HCV but can achieve similar functional activity levels and pain scores [22]. Historically, interferon treatment was administered but was found to be poorly tolerated, deterring patient access and limiting compliance in those who initiated treatment. Upon development, DAAs quickly gained favor due to their shorter 12-week treatment period and fewer side effects than interferon [23]. Although DAAs are safe and well tolerated, the high cost remains prohibitive, potentially limiting patient access [24]. We noted that nearly 45% of our patient cohort (125 TJA cases) did not receive treatment and had PVL when undergoing TJA, and many of them refused treatment due to the limitations and side effects of interferon. That being said, patients undergoing TJA treated with DAAs do not have lower medical or surgical complications, PJI, and revision TJA rates for mechanical causes than those treated with interferon [25]. In our study, patients receiving interferon or DAAs achieved high UVL rates, and the type of treatment was not a significant risk factor for developing PJI.

HCV patients who have been treated prior to TJA have PJI rates similar to those of patients without HCV at 90 days and 1 year postoperatively [26,27]. However, the effect of treatment on postoperative outcomes is complex since receiving treatment does not guarantee SVR—defined as a sustained UVL for at least 3 months after completion of treatment [9,27]. Renewed interest in

Table 2
HCV characteristics comparing undetectable viral load (UVL) to positive viral load (PVL) at the time of TJA.

Variable	All HCV TJA (n = 270)	Viral load undetectable (n = 145)	Viral load positive (n = 125)	*P* value
Viral load, IU/mL, mean (SD)	NA	0 (0)	2,531,173 (3905190)	NA
HCV QL10, Log IU/mL, mean (SD)	NA	0 (0)	5.92 (0.7)	NA
Genotype, n (%)				
1a	130 (48)	60 (41)	70 (56)	<.001
1b	32 (12)	18 (12)	14 (11)	
2b	37 (14)	19 (13)	18 (14)	
3a	18 (7)	6 (4)	12 (10)	
4	11 (4)	8 (6)	3 (2)	
Indeterminate	42 (15)	34 (23)	8 (6)	
Treatment group, n (%)				
Untreated	124 (46)	3 (2)	121 (97)	<.001
Interferon	54 (20)	53 (37)	1 (1)	
DAA[a]	92 (34)	89 (61)	3 (2)	
Failed prior viral therapy, n (%)	10 (3)	6 (4)	4 (3)	1.00
Time from SVR to surgery, mo, mean (range)	NA	51 (2-242)	NA	NA
AST, mean (SD)	34.5 (25)	26.6 (15)	43.6 (38)	<.0001
ALT, mean (SD)	34.3 (25)	25.9 (22)	44.1 (29)	<.0001
MELD level, n (%)				
1	222 (82)	121 (83)	101 (81)	.15
2	34 (13)	21 (15)	13 (10)	
3	14 (5)	3 (2)	11 (9)	
Childs Pugh Class, n (%)				
A	255 (94)	137 (94)	118 (94)	.84
B	14 (5)	7 (5)	7 (6)	
C	1 (1)	1 (1)	0 (0)	
Liver fibrosis stage, n (%)				
F0	44 (16)	21 (14)	23 (18)	.15
F1	32 (12)	15 (10)	17 (14)	
F2	28 (10)	15 (10)	13 (10)	
F3	33 (12)	15 (10)	18 (14)	
F4	55 (20)	35 (24)	20 (16)	
Not obtained/unknown	78 (29)	44 (30)	34 (27)	
Liver fibrosis activity, n (%)				
A0	75 (28)	41 (28)	34 (27)	.48
A1	77 (29)	35 (24)	42 (34)	
A2	31 (11)	20 (14)	11 (9)	
A3	9 (3)	5 (4)	4 (3)	
Not obtained/unknown	78 (29)	44 (30)	34 (27)	

QL10, quantitative log 10; NA, not applicable; AST, aspartate aminotransferase; ALT, alanine aminotransferase; MELD, Model for End-Stage Liver Disease; TJA, total joint arthroplasty; SD, standard deviation.
[a] DAA treatment group overall included: 66% ledipasvir/sofosbuvir, 22% sofosbuvir/ribavirin, 8% sofosbuvir/velpatasvir, 2% sofosbuvir/velpatasvir/voxilaprevir, 1% glecaprevir/pibrentasvir, 1% elbasvir/grazoprevir.

preoperative HCV VL as a main driver of postoperative outcomes after TJA has gained traction recently with an understanding of the limitations of these studies with respect to the availability of VL for analysis and smaller cohort sizes [15,27]. We determined that patients with a UVL had significantly lower PJI rates at 90-day and 1-year follow-up that approached those of the general population undergoing TJA [28,29]. The 1-year PJI rate of the PVL group in our study (9%) was similar to the 1-year deep infection rates (8.2%-9.5%) reported in previous studies [14,15,27]. We also noted that patients with UVL at the time of TJA had a significantly shorter LOS by approximately 1 full admission day similar to what Novikov et al. observed in their study assessing the effect of UVL on perioperative outcomes [15]. Contrary to their study, we did not find that a UVL was protective against mechanical complications or revision TJA in general or blood loss requiring transfusions. One potential explanation is that their patient population included a higher number of patients with PVL at the time of TJA, which explains their higher mechanical complication and PJI rates observed. Irrespective of the type of medication utilized for treatment, we concluded that once SVR is achieved, the patient can undergo TJA safely with lower PJI rates at any time frame after that with no improvement in complication rates when delaying surgery further.

Liver fibrosis due to HCV remains a concern especially given the effects it may have on medical and surgical outcomes after TJA with increase in rates of PJI and cellulitis compared to nonfibrotic patients [30]. Schwarzkopf et al. found that liver fibrosis is more prevalent in patients who received treatment for HCV than in those not treated, indicating that treatment was preferentially given to those patients with advanced disease [25]. We identified a similar trend in our cohort. Although both the PVL and UVL groups had similar liver fibrosis staging and activity levels, the rates of hepatocellular carcinoma and liver transplant were significantly higher in the UVL group, indicating either preferential treatment for patients with more advanced disease or patients with advanced disease were more likely to attempt treatment despite potential side effects (ie, interferon). Anecdotally, at least 18 additional patients not included in the failed viral therapy group declined to start/refused to continue treatment due to side effects and had this documented in their medical records. However, liver fibrosis staging and activity were not significant risk factors of PJI contrary to prior studies, possibly due to their small patient populations [22,30].

Coinfection with HIV and HCV has been shown to be associated with increased postoperative complications including PJI, with HCV driving the risk [31–33]. We did not appreciate in our study population any significant difference in HIV rates in patients with PVL and UVL, while HIV coinfection was not a risk factor for PJI. We attribute this to the fact that HCV as noted above is the main driver

Table 3
Perioperative characteristics comparing undetectable viral load (UVL) to positive viral load (PVL) at the time of TJA.

Variable	All HCV TJA (n = 270)	Viral load undetectable (n = 145)	Viral load positive (n = 125)	*P* value
TJA type, n (%)				
THA	138 (51)	75 (52)	63 (50)	.90
TKA	132 (49)	70 (48)	62 (50)	
Operative duration, min, mean (SD)	99 (31)	99 (30)	100 (34)	.94
Blood loss, mL, mean (SD)	263 (251)	232 (189)	300 (323)	.08
Implant details, n (%)				
Cemented	137 (51)	75 (52)	62 (50)	.80
Antibiotic cement	79 (58)	49 (65)	30 (48)	.04
ASA score, n (%)				.08
1	2 (1)	1 (1)	1 (1)	
2	59 (22)	37 (26)	22 (18)	
3	202 (75)	105 (72)	97 (78)	
4	7 (2)	2 (1)	5 (4)	
TXA use, n (%)	133 (49)	93 (64)	40 (32)	<.0001
Anesthesia type, general, n (%)	177 (66)	76 (52)	101 (81)	<.0001
Intraoperative blood transfusion, n (%) [mean units pRBCs]	1 (1)	0 (0)	1 (1) (2u pRBCs)	.46
Hemovac drain, n (%)	165 (61)	76 (52)	89 (71)	.002

ASA, American Society of Anesthesiologists; pRBCs, packed red blood cells; SD, standard deviation; THA, total hip arthroplasty; TKA, total knee arthroplasty; TXA, tranexamic acid.

Table 4
Acute postoperative outcomes comparing undetectable viral load (UVL) to positive viral load (PVL) at the time of TJA.

Outcome	All HCV TJA (n = 270)	Viral load undetectable (n = 145)	Viral load positive (n = 125)	*P* value
AMS/delirium	6 (2)	1 (1)	5 (4)	.10
ARF	1 (1)	0 (0)	1 (1)	.46
DVT	4 (2)	4 (3)	0 (0)	.13
PE	3 (1)	3 (2)	0 (0)	.25
MI	1 (1)	1 (1)	0 (0)	1.00
ARDS	2 (1)	1 (1)	1 (1)	1.00
CVA/stroke	2 (1)	2 (1)	0 (0)	.50
PNA	1 (1)	0 (0)	1 (1)	.46
UTI	0 (0)	0 (0)	0 (0)	NA
Sepsis	1 (1)	0 (0)	1 (1)	.46
Postoperative anemia requiring blood transfusion, n (%)	41 (15)	19 (13)	22 (18)	.31
Hospital blood transfusion, units pRBCs, mean (SD)	1.9 (0.9)	1.6 (0.7)	2.2 (1.0)	.17
ICU stay, n (%)	7 (3)	4 (3)	3 (2)	1.00
ICU d, mean (SD)	4.0 (3)	4.8 (5)	3.0 (2)	.86
LOS, d, mean (SD)	3.4 (1.9)	2.9 (1.7)	3.9 (2.2)	<.0001
Discharge disposition, n (%)				
Home	218 (81)	117 (81)	101 (81)	1.00
SNF/IPR	52 (19)	28 (19)	24 (19)	

AMS, altered mental status; ARDS, acute respiratory distress syndrome; ARF, acute renal failure; CVA, cerebrovascular accident; DVT, deep veinous thrombosis; ICU, intensive care unit; IPR, inpatient rehabilitation; MI, myocardial infarction; PE, pulmonary embolus; PNA, pneumonia; pRBCs, packed red blood cells; SNF, skilled nursing facility; UTI, urinary tract infection.

Table 5
Ninety-day and 1-year outcomes comparing undetectable viral load (UVL) to positive viral load (PVL) at the time of TJA.

Outcome, n (%)	All HCV TJA (n = 270)	Viral load undetectable (n = 145)	Viral load positive (n = 125)	*P* value
Ninety day				
Dislocation	3 (1)	2 (1)	1 (1)	1.00
PJI	10 (4)	2 (1)	8 (6)	.04
Periprosthetic fracture	2 (1)	1 (1)	1 (1)	1.00
Aseptic revision TJA	5 (2)	3 (2)	2 (2)	1.00
One year				
Dislocation	4 (2)	3 (2)	1 (1)	.63
PJI	14 (5)	3 (2)	11 (9)	.02
Periprosthetic fracture	4 (2)	2 (1)	2 (2)	1.00
Aseptic revision TJA	13 (5)	6 (4)	7 (6)	.58
Any-time postoperative				
Any-time PJI	20 (7)	5 (3)	15 (12)	.01
Cellulitis/wound dehiscence	8 (3)	2 (1)	6 (5)	.08
Hematoma	6 (2)	1 (1)	5 (4)	.10

Table 6
Multivariable regression analysis of risk factors for PJI in HCV patients undergoing elective TJA.

Variable	OR	95% CI	*P* value
PVL (vs UVL)	3.20	0.88-14.85	.09
Age, y	0.97	0.92-1.02	.23
Hemarthrosis	1.64	0.12-15.46	.69
Hemophilia	2.34	0.19-26.54	.50

CI, confidence interval; OR, odds ratio.

of complications rather than HIV and that the 3 academic medical centers participating in this study have dedicated clinics for both HIV and HCV patients that emphasize a holistic approach to patient care. On the contrary, we found that diagnoses of hemophilia and hemarthrosis were present in significantly higher rates in the PVL group and that both were significant risk factors for PJI after TJA in our HCV population. This is in concordance with current literature that highlights the increased complications rates in general with an emphasis on hematomas, wound dehiscence, postoperative bleeding, and surgical site infections [34,35].

Although our study has some limitations, we believe that they do not detract from the conclusions it supports. Our study is retrospective in nature, bringing with it the potential for missing data points which was minimized in our population given that the 3 academic centers have dedicated clinics to manage HCV patients that keep extensive medical records and laboratory profiles on their patients. Patients with UVL had higher rates of liver transplant and hepatocellular carcinoma, indicating that patients with advanced disease were more likely to undergo treatment which may underestimate the effect of treatment achieving SVR on complications and outcomes. We were unable to perform a multivariable analysis to determine if VL was an independent risk factor for infection among the extensive list of confounding variables tested. Contrary to the prior study by Novikov et al. [15], our study includes a much greater number of confounding patient- and HCV-related variables including liver scores and fibrosis staging, a higher number of treated patients with UVL who had low rates of complications, and a lower PJI rate possibly due to the rigorous PJI definition based on the Musculoskeletal Infection Society criteria that we utilized. All these inherent differences inevitably dilute our multivariable model, especially when the complication rates are so low. The VL variable was approaching significance ($P = .09$) in our statistical model, and we believe that with larger patient numbers, statistical significance can be achieved. However, this low rate of PJI is a testimony to the significant effect that VL has on lowering PJI and mechanical rates, highlighting the impetus of our study.

Conclusions

In conclusion, achieving SVR prior to TJA is an important driver for improved outcomes including decreased hospital LOS and PJI rates. Fibrosis staging and activity levels were not significant factors although hepatocellular carcinoma and liver transplant were more prevalent in patients who received treatment and achieved a UVL. Although HIV coinfection was present in similar rates in patients with UVL and PVL and did not affect the rate of PJI. There is no clinical benefit or reduction in complication rates with delaying elective TJA after SVR has been achieved.

Conflicts of interest

Dr. A. F. Chen receives royalties from Stryker; is a paid consultant for 3M, Avanos, BICMD, bOne, Convatec, Ethicon, GLG, Guidepoint, Heraeus, IrriMax, Pfizer, PhagoMed, and Stryker; has stock or stock options in bOne, Graftworx, Hyalex, IrriMax, Joint Purification Systems, and Sonoran; receives financial or material support from publishers like SLACK Incorporated and UpToDate; is in the editorial or governing board of Journal of Arthroplasty, Annals of Joint, Clinical Orthopaedics and Related Research, Journal of Bone and Joint Infection, Knee Surgery, Sports Traumatology, Arthroscopy, Journal of Bone and Joint Surgery, and Journal of Orthopaedic Research; and is a board member in the American Academy of Orthopaedic Surgeons, American Joint Replacement Registry, American Association of Hip and Knee Surgeons, and the European Knee Association. Kyle Cichos is a paid consultant for Symcel. Dr. Ghanem is a paid consultant for Symcel, Heraeus Medical, and Tissue Tech Inc. Dr. Erik Hansen receives royalties from and is a paid consultant for Corin U.S.A. All other authors declare no potential conflicts of interest.

For full disclosure statements refer to https://doi.org/10.1016/j.artd.2022.06.014.

References

[1] Chak E, Talal AH, Sherman KE, Schiff ER, Saab S. Hepatitis C virus infection in USA: an estimate of true prevalence. Liver Int 2011;31:1090–101.
[2] Davis GL, Alter MJ, El-Serag H, Poynard T, Jennings LW. Aging of hepatitis C virus (HCV)-infected persons in the United States: a multiple cohort model of HCV prevalence and disease progression. Gastroenterology 2010;138:513–21.
[3] Issa K, Boylan MR, Naziri Q, Perfetti DC, Maheshwari AV, Mont MA. The impact of hepatitis C on short-term outcomes of total joint arthroplasty. J Bone Joint Surg Am 2015;97:1952–7.
[4] Best MJ, Buller LT, Klika AK, Barsoum WK. Increase in perioperative complications following primary total hip and knee arthroplasty in patients with hepatitis C without cirrhosis. J Arthroplasty 2015;30:663–8.
[5] Salomon B, Krause PC, Dasa V, Shi L, Jones D, Chapple AG. 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. Arthroplast Today 2021;7:200–7.
[6] Wei W, Liu T, Zhao J, Li B, Li S, Liu J. Does the hepatitis C virus affect the outcomes of total joint arthroplasty? A meta-analysis of ten studies. J Orthop Sci 2019;24:822–9.
[7] Aghemo A, De Francesco R. New horizons in hepatitis C antiviral therapy with direct-acting antivirals. Hepatology 2013;58:428–38.
[8] Jaeckel E, Cornberg M, Wedemeyer H, et al. Treatment of acute hepatitis C with interferon alfa-2b. N Engl J Med 2001;345:1452–7.
[9] Ghany MG, Morgan TR. Hepatitis C guidance 2019 update: American association for the study of liver diseases-infectious diseases society of America recommendations for testing, managing, and treating hepatitis C virus infection. Hepatology 2020;71:686–721.
[10] Smith-Palmer J, Cerri K, Valentine W. Achieving sustained virologic response in hepatitis C: a systematic review of the clinical, economic and quality of life benefits. BMC Infect Dis 2015;15:1–19.
[11] Calore BL, Cheung RC, Giori NJ. Prevalence of hepatitis C virus infection in the veteran population undergoing total joint arthroplasty. J Arthroplasty 2012;27:1772–6.
[12] Shapiro CBH, Cheung RC, Giori NJ. Prevalence of hepatitis C virus infection in the veteran population undergoing total joint arthroplasty: an update. J Arthroplasty 2021;36:467–70.
[13] Cancienne JM, Kandahari AM, Casp A, et al. Complication rates after total hip and knee arthroplasty in patients with hepatitis C compared with matched control patients. J Am Acad Orthop Surg 2017;25:e275–81.
[14] Bedair HS, Schurko BM, Dwyer MK, Novikov D, Anoushiravani AA, Schwarzkopf R. Treatment for chronic hepatitis C prior to total hip arthroplasty significantly reduces periprosthetic joint infection. J Arthroplasty 2019;34:132–5.
[15] Novikov D, Feng JE, Anoushiravani AA, et al. Undetectable hepatitis C viral load is associated with improved outcomes following total joint arthroplasty. J Arthroplasty 2019;34:2890–7.
[16] Parvizi J, Gehrke T. Definition of periprosthetic joint infection. J Arthroplasty 2014;29:1331. 1331.
[17] Kamath PS, Wiesner RH, Malinchoc M, et al. A model to predict survival in patients with end-stage liver disease. Hepatology 2001;33:464–70.
[18] Malinchoc M, Kamath PS, Gordon FD, Peine CJ, Rank J, ter Borg PCJ. A model to predict poor survival in patients undergoing transjugular intrahepatic portosystemic shunts. Hepatology 2000;31:864–71.
[19] Child CG, Turcotte JG. Surgery and portal hypertension. Major Probl Clin Surg 1964;1:1–85.
[20] Pugh RN, Murray-Lyon IM, Dawson JL, Pietroni MC, Williams R. Transection of the oesophagus for bleeding oesophageal varices. Br J Surg 1973;60:646–9.
[21] Jacobson IM, Lim JK, Fried MW. American gastroenterological association institute clinical practice update-expert review: care of patients who have achieved a sustained virologic response after antiviral therapy for chronic hepatitis C infection. Gastroenterology 2017;152:1578–87.

[22] Pour AE, Matar WY, Jafari SM, Purtill JJ, Austin MS, Parvizi J. Total joint arthroplasty in patients with hepatitis C. J Bone Joint Surg Am 2011;93:1448–54.
[23] Belperio PS, Chartier M, Ross DB, Alaigh P, Shulkin D. Curing hepatitis C virus infection: best practices from the U.S. Department of veterans Affairs. Ann Intern Med 2017;167:499–504.
[24] Hayes CN, Chayama K. Why highly effective drugs are not enough: the need for an affordable solution to eliminating HCV. Expert Rev Clin Pharmacol 2017;10:583–94.
[25] Schwarzkopf R, Novikov D, Anoushiravani AA, et al. The preoperative management of Hepatitis C may improve the outcome after total knee arthroplasty. Bone Joint J 2019;101-b:667–74.
[26] Bendich I, Takemoto S, Patterson JT, Monto A, Barber TC, Kuo AC. Preoperative treatment of hepatitis C is associated with lower prosthetic joint infection rates in US veterans. J Arthroplasty 2019;34:S319–326.e1.
[27] Cornell E, Novikov D, Niu R, Staatz K, Schwarzkopf R, Smith EL. Hepatitis C antiviral treatment decreases all-cause complications after total joint arthroplasty regardless of the presence of fibrosis. J Arthroplasty 2021;36:1551–5.
[28] Kurtz SM, Lau EC, Son MS, Chang ET, Zimmerli W, Parvizi J. Are we winning or losing the battle with periprosthetic joint infection: trends in periprosthetic joint infection and mortality risk for the medicare population. J Arthroplasty 2018;33:3238–45.
[29] Pulido L, Ghanem E, Joshi A, Purtill JJ, Parvizi J. Periprosthetic joint infection: the incidence, timing, and predisposing factors. Clin Orthop Relat Res 2008;466:1710–5.
[30] Orozco F, Post ZD, Baxi O, Miller A, Ong A. Fibrosis in hepatitis C patients predicts complications after elective total joint arthroplasty. J Arthroplasty 2014;29:7–10.
[31] Kildow BJ, Politzer CS, DiLallo M, Bolognesi MP, Seyler TM. Short and long-term postoperative complications following total joint arthroplasty in patients with human immunodeficiency virus, hepatitis B, or hepatitis C. J Arthroplasty 2018;33:S86–92.e1.
[32] Fang C, Cornell E, Dicken Q, Freccero D, Mattingly D, Smith EL. Coinfection of HIV and hepatitis C increases complication rates after total joint arthroplasty. SICOT J 2020;6:37.
[33] Mahure SA, Bosco JA, Slover JD, Vigdorchik J, Iorio R, Schwarzkopf R. Risk of complications after THA increases among patients who are coinfected with HIV and hepatitis C. Clin Orthop Relat Res 2018;476:356–69.
[34] Chiasakul T, Buckner TW, Li M, Vega R, Gimotty PA, Cuker A. In-hospital complications and readmission in patients with hemophilia undergoing hip or knee arthroplasty. JB JS Open Access 2020;5:e0085.
[35] Li Z, Feng B, Du Y, Wang Y, Bian Y, Weng X. Complications of total knee arthroplasty in patients with haemophilia compared with osteoarthritis and rheumatoid arthritis: a 20-year single-surgeon cohort. Haemophilia 2020;26:861–6.