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Coinfection with Hepatitis C and HIV Is a Risk Factor for Poor Outcomes After Total Knee Arthroplasty

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Background: As medical management continues to improve, orthopaedic surgeons are likely to encounter a greater proportion of patients who have coinfection with human immunodeficiency virus (HIV) and hepatitis-C virus (HCV).

Methods: The New York Statewide Planning and Research Cooperative System (SPARCS) database was used to identify patients undergoing total knee arthroplasty between 2010 and 2014. Patients were stratified into 4 groups on the basis of HCV and HIV status. Differences regarding baseline demographics, length of stay, total charges, discharge disposition, in-hospital complications and mortality, and 90-day hospital readmission were calculated.

Results: Between 2010 and 2014, a total of 137,801 patients underwent total knee arthroplasty. Of those, 99.13% (136,604) of the population were not infected, 0.62% (851) had HCV monoinfection, 0.20% (278) had HIV monoinfection, and 0.05% (68) were coinfected with both HCV and HIV. Coinfected patients were more likely to be younger, female, a member of a minority group, homeless, and insured by Medicare or Medicaid, and to have a history of substance abuse. HCV and HIV coinfection was a significant independent risk factor for increased length of hospital stay (odds ratio [OR], 2.9; 95% confidence interval [CI], 1.75 to 4.81), total hospital charges in the 90th percentile (OR, 2.02; 95% CI, 1.12 to 3.67), ≥2 in-hospital complications (OR, 2.04; 95% CI, 1.04 to 3.97), and 90-day hospital readmission (OR, 3.53; 95% CI, 2.02 to 6.18).

Conclusions: Patients coinfected with both HCV and HIV represent a rare but increasing population of individuals undergoing total knee arthroplasty. Recognition of unique baseline demographics in these patients that may lead to suboptimal outcomes will allow appropriate preoperative management and multidisciplinary coordination to reduce morbidity and mortality while containing costs.

Level of Evidence: Prognostic Level III. See Instructions for Authors for a complete description of levels of evidence.

According to recent estimates by the U.S. Centers for Disease Control and Prevention, >1 million individuals are affected by the human immunodeficiency virus (HIV) in the United States, and the prevalence is expected to increase[1]. As the availability and efficacy of HIV medications such as highly active antiretroviral therapy (HAART) increase, patients with HIV are able to live longer with a higher quality of life than previously possible[2]. Consequently, a greater number of patients with an HIV diagnosis are undergoing orthopaedic procedures, with several reports on clinical outcomes in this specific patient population[1,3,4]. Similar to HIV, there has been increased focus in recent years on outcomes in patients with the hepatitis-C virus (HCV)[5,6]. Approximately 1.1% of people worldwide are affected by HCV[7]. In a trend similar to that of HIV, patients with HCV are also expected to live longer because of recent advances in antiviral therapy, with some authors predicting a 34% decrease in HCV liver pathology-associated deaths over the next decade[8].

As greater expenses, time, and research are expended to the treatment of these 2 different patient populations, focus is also increasing on a unique subset of patients: those with co-infection (infection with both HCV and HIV)[9-11]. Recent estimates have suggested that nearly one-fourth of all patients with HIV also carry a diagnosis of HCV[12], and in patients with a history of intravenous drug usage, coinfection rates can climb as high as 90%[11,13,14].

With the knowledge that patients with HCV and HIV are living longer and more likely to undergo orthopaedic procedures than before, it is not unreasonable to assume that there

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TABLE I Baseline Demographics on 137,801 Patients

	Neither HCV nor HIV*	HCV without HIV	P Value	HIV without HCV	P Value	Both HCV and HIV	P Value
Percentage of total sample *(no.)*	99.13 (136,604)	0.62 (851)		0.20 (278)		0.05 (68)	
Percentage of 1,197 patients with HCV or HIV *(no.)*	NA	71.09 (851)		23.22 (278)		5.68 (68)	
Age† *(yr)*	66.2 (10.0)	59.9 (7.9)	<0.001	58.2 (9.1)	<0.001	55.5 (6.3)	<0.001
Sex *(% [no.])*							
Male	34.63 (47,312)	50.29 (428)	<0.001	49.28 (137)	<0.001	47.06 (32)	<0.001
Female	65.37 (89,292)	49.71 (423)	<0.001	50.72 (141)	<0.001	52.94 (36)	<0.001
Race *(% [no.])*							
White	74.42 (101,656)	48.77 (415)	<0.001	24.10 (67)	<0.001	22.06 (15)	<0.001
Black	9.73 (13,285)	21.27 (181)	<0.001	51.08 (142)	<0.001	41.18 (28)	<0.001
Hispanic	6.38 (8,715)	13.16 (112)	<0.001	11.51 (32)	<0.001	22.06 (15)	<0.001
Other	9.48 (12,948)	16.80 (143)	<0.001	13.31 (37)	<0.001	14.71 (10)	<0.001
Insurance *(% [no.])*							
Private	36.35 (49,658)	31.61 (269)	<0.001	29.86 (83)	<0.001	11.76 (8)	<0.001
Medicare	52.22 (71,334)	34.31 (292)	<0.001	40.29 (112)	<0.001	41.18 (28)	<0.001
Medicaid	5.37 (7,332)	26.67 (227)	<0.001	23.38 (65)	<0.001	44.12 (30)	<0.001
Other	6.06 (8,280)	7.40 (63)	<0.001	6.47 (18)	<0.001	2.94 (2)	<0.001
Not homeless *(% [no.])*	99.36 (135,734)	97.65 (831)	<0.001	93.53 (260)	<0.001	97.06 (66)	<0.001
Homeless *(% [no.])*	0.64 (870)	2.35 (20)	<0.001	6.47 (18)	<0.001	2.94 (2)	<0.001
Diagnosis *(% [no.])*							
Osteoarthritis	99.98 (136,573)	100.00 (851)	0.660	100.00 (278)	0.802	98.53 (67)	<0.001
Osteonecrosis	0.02 (31)	0.00 (0)	0.660	0.00 (0)	0.802	1.47 (1)	<0.001

*Patients without HIV and HCV served as reference for all statistical comparisons. For example, the mean age of patients with HCV monoinfection (59.9 years) was significantly younger than patients with neither HCV nor HIV (66.2 years) ($p < 0.001$). NA = not applicable. †The values are given as the mean, with the standard deviation in parentheses.

will also be a concomitant increase in coinfected patients seeking orthopaedic care. We sought to use a large, heterogeneous sample to identify prevalence rates of HCV and HIV coinfection in patients undergoing elective total knee arthroplasty, and to further determine how coinfection may affect in-hospital perioperative complications, length of stay (LOS), total hospital charges, discharge disposition, in-hospital mortality, and 90-day readmission rates.

Materials and Methods

The New York Statewide Planning and Research Cooperative System (SPARCS) database was searched to identify adult patients undergoing elective inpatient total knee arthroplasty. The SPARCS database has been used for numerous orthopaedic publications[15-20]. The time period of our study was between the years 2010 and 2014, as we thought that this would provide a large sample of patients reflective of both recent practice patterns in total knee arthroplasty and the availability of contemporary HCV-HIV therapy[21].

International Classification of Diseases, Ninth Revision (ICD-9) code 81.54 was used to identify patients undergoing total knee arthroplasty. Similar to prior methodology, patients with fracture-related diagnoses or evidence of malignancy and patients undergoing revision surgery were excluded[3]. We stratified patients into 2 groups on the basis of the primary diagnosis at the time of initial total knee arthroplasty: osteoarthritis or osteonecrosis. Patients with other diagnoses (rheumatoid arthritis or posttraumatic arthritis) were excluded.

Data on patient age, sex, race, and insurance at the time of initial total knee arthroplasty were collected. Patients were collapsed into 2 groups, "homeless" or "not homeless," to determine the impact this might have, given the association of HIV-HCV and socioeconomic status[22-24].

ICD-9 codes 070.41, 070.51, 070.44, 070.54, 070.70, and 070.71 were used to identify patients with HCV[6,25-27]. HIV diagnoses were identified using ICD-9 codes 042, 795.71, and V08[28-30]. The Elixhauser comorbidity criteria were used to identify concomitant medical comorbidities[31]. With the exception of HCV-HIV, all comorbidities were summed, and the overall comorbidity burden was stratified into 4 groups: 0, 1, 2, and ≥3 comorbidities. ICD-9 code 305.1 was used to

TABLE II Baseline Comorbidities

	Neither HCV nor HIV* (N = 136,604)	HCV without HIV* (N = 851)	P Value	HIV without HCV* (N = 278)	P Value	Both HCV and HIV* (N = 68)	P Value
Alcohol abuse	0.90 (1,236)	6.70 (57)	<0.001	1.44 (4)	0.325	4.41 (3)	0.024
Arrhythmia	11.33 (15,472)	8.58 (73)	0.0106	7.55 (21)	0.046	5.88 (4)	0.180
Chronic deficiency anemia	9.37 (12,800)	10.46 (89)	0.2880	8.63 (24)	0.757	1.47 (1)	0.050
Chronic lung disease	16.85 (23,023)	28.67 (244)	<0.001	25.90 (72)	<0.001	42.65 (29)	<0.001
Coagulation deficiency	2.01 (2,747)	8.81 (75)	<0.001	4.32 (12)	0.015	5.88 (4)	0.048
Congestive heart failure	2.43 (3,317)	2.70 (23)	0.575	1.80 (5)	0.694	7.35 (5)	0.025
Depression	12.89 (17,604)	20.09 (171)	<0.001	19.06 (53)	<0.001	30.88 (21)	<0.001
Diabetes mellitus	21.83 (29,820)	24.21 (206)	0.096	15.47 (43)	<0.001	20.59 (14)	0.884
Drug abuse	0.86 (1,174)	15.86 (135)	<0.001	5.04 (14)	<0.001	25.00 (17)	<0.001
Fluid and electrolyte disorder	8.74 (11,945)	10.58 (90)	0.067	7.55 (21)	0.594	11.76 (8)	0.385
Hypertension	68.11 (93,035)	64.51 (549)	0.026	63.31 (176)	0.093	45.59 (31)	<0.001
Hypothyroidism	15.81 (21,596)	10.34 (88)	<0.001	4.32 (12)	<0.001	2.94 (2)	<0.001
Liver disease	0.87 (1,183)	54.76 (466)	<0.001	3.24 (9)	<0.001	55.88 (38)	<0.001
Neurologic disorder	1.94 (2,652)	1.29 (11)	0.210	2.52 (7)	0.507	1.47 (1)	0.788
Obesity	25.82 (35,265)	23.03 (196)	0.065	17.63 (49)	<0.001	22.06 (15)	0.579
Obstructive sleep apnea	7.92 (10,825)	7.17 (61)	0.445	5.40 (15)	0.148	1.47 (1)	0.042
Paralysis	0.10 (135)	0.12 (1)	0.570	0.00 (0)	0.759	0.00 (0)	0.935
Peripheral vascular disease	1.79 (2,450)	2.12 (18)	0.437	1.08 (3)	0.498	1.47 (1)	0.840
Psychiatric disorder	0.41 (557)	2.00 (17)	<0.001	0.72 (2)	0.314	1.47 (1)	0.168
Pulmonary circulatory disorder	1.24 (1,697)	1.41 (12)	0.693	1.08 (3)	0.210	4.41 (3)	0.018
Renal failure	3.69 (5,039)	5.29 (45)	0.017	4.68 (13)	0.348	2.94 (2)	0.743
Rheumatoid arthritis and/or collagen vascular disease	4.09 (5,583)	4.70 (40)	0.340	1.80 (5)	0.065	2.94 (2)	0.633
Valvular heart disease	4.58 (6,253)	2.59 (22)	0.003	2.52 (7)	0.112	0.00 (0)	0.071
Weight loss	0.10 (142)	0.12 (1)	0.588	0.00 (0)	0.591	0.00 (0)	0.791
Tobacco use	5.80 (7,926)	22.44 (191)	<0.001	15.83 (44)	<0.001	29.41 (20)	<0.001
No. of Elixhauser comorbidities			<0.001		<0.001		<0.001
0	10.73 (14,653)	4.47 (38)		11.15 (31)		4.41 (3)	
1	24.11 (32,937)	12.57 (107)		28.78 (80)		8.82 (6)	
2	26.93 (36,782)	22.09 (188)		22.66 (63)		13.24 (9)	
3	19.42 (26,522)	24.44 (208)		15.83 (44)		22.06 (15)	
≥4	18.82 (25,710)	36.43 (310)		21.58 (60)		51.47 (35)	

*The values are given as the percentage, with the numbers of patients in parentheses.

identify patients with a history of tobacco use[32-34]. To determine the incremental effect of HCV and/or HIV disease burden, patients were stratified into 4 groups: absence of both HCV and HIV, monoinfection with HIV, monoinfection with HCV, and coinfection with both HCV and HIV.

For purposes of statistical analysis, patients with neither HIV nor HCV served as our so-called healthy controls, and those with any combination of HCV and/or HIV were compared with this control group to determine differences in hospital LOS (days), total charges in U.S. dollars, discharge disposition (homebound versus skilled nursing facility), in-hospital complications, and in-hospital mortality. To account for inflation, total charges were adjusted to the year 2014. We used a unique encrypted patient identifier in the SPARCS database to longitudinally track all patients for 90-day all-cause hospital readmissions[18,20,35,36].

TABLE III Total Knee Arthroplasty Complications

	Neither HCV nor HIV* (N = 136,604)	HCV without HIV (N = 851)	P Value	HIV without HCV† (N = 278)	P Value	Both HCV and HIV† (N = 68)	P Value
Acute renal failure†	1.30 (1,777)	2.47 (21)	0.005	2.16 (6)	0.182	2.94 (2)	0.221
Cardiac complications†	0.76 (1,042)	1.06 (9)	0.320	0.72 (2)	0.933	0.00 (0)	0.592
Neurologic complication†	0.08 (111)	0.00 (0)	0.401	0.00 (0)	0.634	0.00 (0)	0.814
Deep vein thrombosis†	0.45 (616)	0.00 (0)	0.080	0.72 (2)	0.357	0.00 (0)	0.735
Pulmonary embolus†	0.54 (740)	0.71 (6)	0.517	0.36 (1)	0.679	1.47 (1)	0.302
GI complication†	0.22 (302)	0.12 (1)	0.520	0.00 (0)	0.432	0.00 (0)	0.697
GU complication†	0.49 (670)	0.71 (6)	0.372	0.00 (0)	0.652	0.00 (0)	0.712
Hematoma and/or seroma†	0.38 (518)	1.29 (11)	0.002	0.36 (1)	0.975	2.94 (2)	0.027
Peripheral vascular complication†	0.16 (225)	0.24 (2)	0.614	0.36 (1)	0.423	0.00 (0)	0.737
ARDS†	0.21 (283)	0.35 (3)	0.264	0.00 (0)	0.442	1.47 (1)	0.023
Acute myocardial infarction†	0.21 (282)	0.24 (2)	0.854	0.00 (0)	0.448	0.00 (0)	0.701
Delirium†	1.63 (2,232)	2.94 (25)	0.002	2.52 (7)	0.230	1.47 (1)	0.915
Infection†	0.14 (195)	0.12 (1)	0.845	0.36 (1)	0.332	0.00 (0)	0.907
Required mechanical ventilation†	0.14 (195)	0.12 (1)	0.820	0.00 (0)	0.528	1.47 (1)	0.032
Postoperative shock†	0.01 (18)	0.00 (0)	0.737	0.00 (0)	0.8422	0.00 (0)	0.920
Transfusion†	17.60 (24,049)	16.92 (144)	0.651	18.35 (51)	0.752	19.12 (13)	0.922
Pulmonary complications†	0.40 (545)	0.47 (4)	0.743	0.00 (0)	0.653	2.94 (2)	0.002
No. of postoperative complications†			0.122		0.978		0.293
0	69.99 (95,605)	70.86 (603)		70.50 (196)		66.18 (45)	
1	19.61 (26,792)	17.27 (147)		19.42 (54)		17.65 (12)	
≥2	10.40 (14,207)	11.87 (101)		10.07 (28)		16.18 (11)	
Died in hospital†	0.05 (65)	0.12 (1)	0.353	0.00 (0)	0.716	0.00 (0)	0.857
Discharge†			0.548		0.018		0.643
Home	45.73 (62,474)	46.77 (398)		52.88 (147)		48.53 (33)	
Skilled nursing facility	54.27 (74,130)	53.23 (453)		47.12 (131)		51.47 (35)	
Readmitted in ≤90 days†	6.37 (8,701)	9.87 (84)	<0.001	12.95 (36)	<0.001	25.00 (17)	<0.001
Total charges† *(US$)*	42,000.81 ± 21,740.52	48,164.05 ± 27,511.38	<0.001	49,211.45 ± 21,843.76	<0.001	55,042.75 ± 27,956.90	<0.001
LOS† *(days)*	3.5 ± 1.7	4.0 ± 2.5	<0.001	4.1 ± 2.4	<0.001	5.0 ± 2.8	<0.001

*Patients without HIV and HCV served as reference for all statistical comparisons. †The values are given as the percentage, with the numbers of patients in parentheses. GI = gastrointestinal, GU = genitourinary, and ARDS = acute respiratory distress syndrome. ‡The values are given as the mean and the standard deviation. LOS = length of stay.

Statistical Analysis

A 1-way analysis of variance (ANOVA) was used for continuous variables in order to determine if a difference among cohorts existed, with subsequent utilization of pairwise comparisons to determine specific differences between paired groups. Categorical variables were analyzed with the chi-square and/or the Fisher exact test, and multivariate logistic regression was performed to provide odds ratios (ORs) within a 95% confidence interval. As in previous studies that used large registries, only variables present in at least 2% of the population were utilized for the multivariate analysis[37-39].

SAS version 9.3 (SAS Institute) was used for statistical analyses, with p values of <0.05 considered significant. Institutional review board approval was not required as human subject research was not performed.

Results

Between 2010 and 2014, 163,348 patients underwent total knee arthroplasty. Eight percent (13,067) were excluded because the indication for surgery was the need for revision or involved a fracture or malignancy diagnosis. An additional 7.6% (12,480 patients) were excluded because of

TABLE IV Multivariate Analysis for Major Outcomes After Total Knee Arthroplasty*

	Both HCV and HIV Versus Neither HCV or HIV			Both HCV and HIV Versus HIV without HCV			Both HCV and HIV Versus HCV without HIV		
	OR	95% CI	P Value	OR	95% CI	P Value	OR	95% CI	P Value
Non-homebound discharge	0.96	0.58-1.58	0.890	1.14	0.65-2.00	0.280	0.79	0.47-1.34	0.190
Extended LOS	2.91	1.75-4.81	<0.001	1.84	1.12-3.28	<0.001	1.89	1.11-3.21	<0.001
Extended charges	2.02	1.12-3.67	<0.001	1.51	0.77-2.94	0.950	1.43	0.76-2.66	0.790
≥2 postop. complications	2.04	1.14-3.97	<0.001	1.79	0.82-3.91	0.388	1.54	0.76-3.1	0.391
Readmitted	3.53	2.02-6.18	<0.001	1.85	0.95-3.59	0.566	2.58	1.41-4.71	<0.001

*Patients without HIV and HCV served as reference for all statistical comparisons. CI = confidence interval, LOS = length of stay.

incomplete data. A total of 137,801 patients met the final inclusion criteria. Of those, 99.13% of the patients had neither HCV nor HIV, 0.62% had HCV monoinfection, 0.20% had HIV monoinfection, and 0.05% were documented as coinfected with both HCV and HIV.

Baseline Demographics

Of the patients having a total knee arthroplasty, those with HCV monoinfection (mean age [and standard deviation], 59.9 ± 7.9 years; $p < 0.001$), those with HIV monoinfection (mean age, 58.2 ± 9.1 years; $p < 0.001$), and those with coinfection (mean age, 55.5 ± 6.3 years; $p < 0.001$) were significantly younger than patients without either disease (mean age, 66.2 ± 10.0 years). Females made up a substantial majority of patients undergoing total knee arthroplasty without any disease (65.37%), and they also were more likely to be coinfected (52.94%; $p < 0.001$) than males. Minimal differences between the sexes were observed for patients who had monoinfection with HCV or HIV (Table I). White patients made up 74.42% of patients without any disease, while an increasing proportion of minority patients were observed as disease burden increased (Table I). Similar trends were observed regarding insurance, as Medicare and privately insured patients represented the majority of healthy patients, while patients with any combination of HCV and HIV were most often insured by Medicare or Medicaid ($p < 0.001$). Only 0.64% of patients without HCV or HIV were documented as "homeless," compared with 2.9% of coinfected patients ($p < 0.001$). The diagnosis of osteonecrosis was extremely rare in healthy patients, patients with monoinfection with HCV, and those with monoinfection with HIV (0.02%, 0%, and 0%, respectively), whereas 1.47% of coinfected patients had the diagnosis.

Concomitant Medical Comorbidities

Several notable trends were observed regarding concomitant comorbidities in patients with HCV and/or HIV (Table II). The prevalence of alcohol, drug, and tobacco abuse was notably higher in patients with HCV or HIV monoinfection and in those with coinfection than in patients without disease ($p < 0.001$). The prevalence of liver disease was <1% in healthy control patients and 3.24% in HIV-monoinfected patients, but >50% in HCV-monoinfected or coinfected cohorts ($p < 0.001$), with coagulation disorders paralleling this pattern of increasing liver-disease burden and coagulopathy. Depression and psychiatric comorbidities also followed the trend of being more prevalent in monoinfected or coinfected patients compared with healthy controls. The majority of major medical comorbidities were significantly more prevalent in patients with monoinfection or coinfection than in healthy patients ($p < 0.001$). Exceptions to this included arrhythmia, obesity, obstructive sleep apnea, hypertension, and hypothyroidism, which were significantly more prevalent in healthy patients than in those with HCV and/or HIV (Table II).

In-Hospital Complications

After total knee arthroplasty, the rate of postoperative complications varied widely among the study groups (Table III). Healthy patients had nearly half the rate of acute renal failure as HCV and HIV-monoinfected and coinfected patients. Hematoma and/or seroma complications were significantly higher in HCV-monoinfected and coinfected patients than in healthy controls. The rate of postoperative acute respiratory distress syndrome and mechanical ventilation was significantly higher ($p = 0.023$) in coinfected patients (1.47%) than in the other cohorts. Healthy patients and patients with HIV monoinfection had higher rates of in-hospital deep vein thrombosis than did patients with HCV monoinfection and patients with coinfection, although this difference did not reach significance. Postoperative delirium was significantly higher ($p = 0.002$) in patients with HCV monoinfection (2.94%) compared with the other groups. Transfusions were required in 19.12% of coinfected patients and 18.35% of patients with HIV monoinfection compared with 16.92% of patients with HCV monoinfection ($p = 0.922$) and 17.60% of healthy controls.

Overall in-hospital mortality was highest for HCV-monoinfected patients (0.12%), but this difference did not reach significance. HIV-monoinfected patients demonstrated a higher rate of home discharge (53%; $p = 0.018$) than healthy controls, with no differences observed in other cohorts. Mean LOS and charges after total knee arthroplasty

TABLE V Etiology for Total Knee Arthroplasty Readmission in ≤90 Days*

Etiology	Neither HCV or HIV† (N = 8,701)	HCV without HIV† (N = 84)	HIV without HCV† (N = 36)	Both HCV and HIV† (N = 17)	P Value
Acute myocardial infarction	1.82 (158)	0.00 (0)	0.00 (0)	5.88 (1)	0.283
Alcohol and/or drug related	1.30 (113)	3.57 (3)	0.00 (0)	5.88 (1)	0.075
Cellulitis	7.80 (679)	9.52 (8)	2.78 (1)	11.76 (2)	0.576
DVT or PE‡	6.59 (573)	2.38 (2)	2.78 (1)	0.00 (0)	0.336
Fluid or electrolyte abnormality	4.65 (405)	4.76 (4)	8.33 (3)	5.88 (1)	0.502
Gastrointestinal	10.60 (922)	4.76 (4)	8.33 (3)	5.88 (1)	0.335
Cardiac	8.10 (705)	4.76 (4)	0.00 (0)	0.00 (0)	0.142
Hepatobiliary	1.01 (88)	1.19 (1)	0.00 (0)	0.00 (0)	0.753
Infection§	13.94 (1,213)	22.62 (19)	16.67 (6)	11.76 (2)	0.14
Misc. medical#	13.92 (1,211)	10.71 (9)	8.33 (3)	11.76 (2)	0.719
Misc. orthopaedic**	5.59 (486)	2.38 (2)	5.56 (2)	11.76 (2)	0.318
Procedure-related complications††	7.01 (610)	9.52 (8)	8.33 (3)	5.88 (1)	0.682
Pain	2.06 (179)	8.33 (7)	5.56 (2)	11.76 (2)	<0.001
Psychiatric	1.23 (107)	4.76 (4)	0.00 (0)	5.88 (1)	0.008
Renal	1.95 (170)	3.57 (3)	13.89 (5)	0.00 (0)	<0.001
Respiratory	6.67 (580)	4.76 (4)	11.11 (4)	5.88 (1)	0.568
Sepsis	3.52 (306)	1.19 (1)	0.00 (0)	0.00 (0)	0.634
Urinary tract infection	2.25 (196)	1.19 (1)	8.33 (3)	0.00 (0)	0.144

*Patients without HIV and HCV served as reference for all statistical comparisons. †The values are given as the percentage, with the number of patients in parentheses. ‡DVT = deep vein thrombosis, and PE = pulmonary embolism. §Infection refers to prosthesis-related infection. #Miscellaneous medical indicates etiologies such as diabetes-related complications or thyroid disorders. **Miscellaneous orthopaedic indicates etiologies such as lumbago, ankle sprain, or shoulder injuries. ††Procedure-related complications indicate occurrences such as dislocation or revision.

followed an incremental trend in our cohort: the lowest values were observed for healthy controls, with steady increases in LOS and charges as the disease burden increased: healthy controls (3.5 ± 1.7 days), HCV monoinfection (4.0 ± 2.5 days; $p < 0.001$), HIV monoinfection (4.1 ± 2.4 days; $p < 0.001$), and coinfection (5.0 ± 2.8 days; $p < 0.001$). The mean inflation-adjusted charge was $42,000.81 ± $21,740.52 for healthy controls compared with $48,164.05 ± $27,511.38 ($p < 0.001$) for patients with HCV monoinfection, $49,211.45 ± $21,843.76 ($p < 0.001$) for those with HIV monoinfection, and highest at $55,042.75 ± $27,956.90 for those with coinfection ($p < 0.001$).

Multivariate logistic regression (Table IV) indicated that, compared with patients without HCV or HIV, those with coinfection were at increased odds for having an extended LOS, ≥2 in-hospital complications, being readmitted to the hospital within 90 days ($p < 0.001$), and increased hospital charges. The odds of 90-day readmission for coinfected patients compared with healthy controls were significant (OR, 3.53; $p < 0.001$).

Hospital Readmissions

The readmission rate for the 90-day period after surgery was 6.37% for healthy controls, with higher rates observed in patients with HCV monoinfection (9.87%), HIV monoinfection (12.95%), and coinfection (25.0%), which was the highest ($p < 0.001$). In general, patients with HCV or HIV monoinfection or coinfection were readmitted at much higher rates for alcohol or drug-related issues and for psychiatric disorders. However, pain ($p < 0.001$), psychiatric conditions ($p = 0.008$), and renal disorders ($p < 0.001$) were the only reasons for readmission demonstrating significantly different rates among the groups. The complete etiology for readmission after total knee arthroplasty can be found in Table V.

Discussion

A total of 137,801 patients undergoing elective total knee arthroplasty between 2010 and 2014 were analyzed for differences in the following surgical outcomes on the basis of the HCV and HIV status: hospital perioperative complications, LOS, total charges, discharge disposition, in-hospital mortality, and 90-day readmissions.

Analysis found that, compared with healthy controls, patients undergoing total knee arthroplasty with HCV or HIV monoinfection or coinfection were likely to be younger, female, a member of a minority race, and insured by either Medicare or Medicaid. Previous authors have reported similar demographic findings[1,4,5,40], and have attributed these data to socioeconomic risk factors and greater participation in at-risk activities. Our

finding that monoinfected or coinfected patients were more likely to be homeless most likely reflects our socioeconomic findings, and represents an area where appropriate preoperative planning, patient selection, and awareness of residency status could reduce prolonged LOS and hospital readmissions.

Interestingly, we did not note a significantly greater rate of osteonecrosis in patients with monoinfection undergoing total knee arthroplasty (Table I), and only 1.47% of coinfected patients had osteonecrosis. Compared with the hip, osteonecrosis of the knee is an exceedingly rare condition, and the literature is often limited to case series[41,42]. Variations in vascular supply between the hip and knee could account for some of these pathophysiologic findings, but continued research is still warranted.

Potentially some of the most concerning findings in our data were the inordinately higher rates of alcohol, drug, and tobacco abuse along with depression in monoinfected and coinfected patients compared with healthy controls (Table II). Furthermore, we noted a stepwise increase in prevalence rates of these comorbidities as HIV and/or HCV disease burden increased, with coinfected patients having highest rates of drug abuse and depression. The awareness that these patients may continue to participate in at-risk activities highlights an opportunity for orthopaedic surgeons and their teams to offer counseling, needle-exchange programs, and smoking cessation interventions[43,44]. Involvement of a psychiatrist as part of the care team could allow for appropriate management of depression, which has previously been linked to suboptimal outcomes in orthopaedics[45,46]. In summary, a thorough preoperative evaluation regarding individual and group social support systems in place for high-risk patients on discharge could identify actionable areas for intervention that could reduce postoperative complications and hospital readmissions.

Monoinfected and coinfected patients had approximately 2 and 3 times, respectively, the rates of chronic lung disease compared with healthy controls—findings that could be attributed to previously mentioned rates of tobacco use along with recurrent respiratory infections found in HIV[47-49], and higher than average rates of obstructive lung disease in HCV[50-52].

HCV is a known etiologic cause of liver cirrhosis and/or dysfunction, with HIV rarely being implicated[5,37,53,54]. Furthermore, the liver is responsible for producing a majority of clotting factors, providing credence to our results that HCV-monoinfected and coinfected patients were more likely to have coagulopathy compared with healthy controls and HIV-monoinfected patients. Notably, these baseline findings did not translate into a greater rate of postoperative transfusion in monoinfected or coinfected patients, which could potentially be due to existing preoperative awareness of risk factors and perioperative optimization of blood and volume status.

Despite the overall higher comorbidity burden, monoinfected and coinfected patients did not demonstrate a significantly higher number of postoperative complications. As alluded to previously, this could be due to the relatively low rate of complications after total knee arthroplasty in parallel with greater resource allocation for these high-risk patients[55-57]. This greater resource allocation could be reflected in the longer mean LOS and total charges found for monoinfected and coinfected patients compared with healthy controls. We believe that, given the relatively low rate of observed postoperative complications in infected patients, the longer LOS is most closely related to socioeconomic factors that precluded expeditious home discharge. Similarly, the comparatively low rate of discharge to skilled nursing facilities seen in monoinfected and coinfected patients could be due to insurance-related factors that prevented higher levels of care. Finally, it is worth noting that while many of these high-risk coinfected patients may have had higher rates of complications after discharge (such as infection or pneumonia) warranting readmission, many of them may have delayed seeking timely medical care within our 90-day window because of socioeconomic status and/or access to care—again highlighting the importance of establishing a viable "medical home" for this cohort.

Despite these findings, we still noted that coinfected patients were significantly more likely to have an extended LOS, higher total charges, and multiple in-hospital complications and to be readmitted to the hospital within 90 days compared with healthy controls (Table IV). Readmissions data indicated that 25% of coinfected patients were readmitted within 90 days of discharge, a rate 4 times higher than that for patients without any disease and twice as much as that for monoinfected patients. The 3 most common etiologies for readmission in coinfected patients were pain, a psychiatric condition, and alcohol and/or drug abuse related (Table V). Pain has been widely implicated as an etiology for readmission after total knee arthroplasty[58,59], and it is possible that these high-risk patients could have preexisting opioid tolerance due to the observed high rates of abuse. Physician-directed counseling and appropriate pain management consultation could potentially decrease hospital readmissions for pain-related issues.

Our study has limitations inherent to large database studies[60]. Most notably, due to the current ICD-9 system, we were unable to comment on disease burden in patients affected by HCV and/or HIV. Similarly, we were unable to determine if patients were receiving HAART or HCV antiretroviral therapy. Additionally, it is possible that there was a subset of patients within the HCV cohort who had received antiviral treatment and been "cured" but were still documented and/or coded as having HCV. These patients could be represented by those with residual cirrhosis but no actual disease burden. Future smaller-scale studies with detailed patient characteristics could shed light on this unique cohort. Despite our relatively large sample size, the overall low prevalence of monoinfected and coinfected patients may be the reason it was not possible to reach significance in certain calculations. We encourage future validation against an independent sample of data to determine whether the same predictors are identified and whether the magnitude of their predictive contribution remains consistent. To our knowledge, however, we provide the first analysis of patients coinfected with HCV and HIV in a large sample drawn from a heterogeneous population from 2010 to 2014, reflecting the most recent trends in both orthopaedics and medical management.

We wish to draw notice to the potentially high rate of underdiagnosis for HIV, HCV, and subsequently coinfection[61-63]. Prior literature is robust surrounding HCV[5,64] and HIV-associated complications[1,3,4]. The awareness, however, that there may exist a large population of undiagnosed and undertreated patients because of a lack of access to care should continue to promote awareness among the medical community to have a high index of suspicion for potential cases.

To that effect, the New York State Department of Health implemented the Hepatitis C Testing Law in 2014, becoming the first state in the country to do so[65]. This law stipulates that health-care providers must offer HCV screening to any patient born between 1945 and 1965. Furthermore, for patients in whom HCV screening is positive, providers are required to offer further testing and medical guidance. Continued implementation of this law should help to improve HCV detection rates, thus allowing patients and providers an earlier ability to seek appropriate medical care. As HCV and HIV therapy becomes more widely available, it may become possible for appropriately selected patients to undergo therapy to be "cured" or achieve "clinical remission" prior to receiving a total knee arthroplasty, thus reducing complication rates and containing costs.

In conclusion, patients coinfected with both HCV and HIV represent a rare but increasing population of individuals undergoing total knee arthroplasty. Recognition of unique baseline demographics in this patient population that may lead to suboptimal outcomes will allow appropriate preoperative management and multidisciplinary coordination. Continued efforts to minimize underdiagnoses while simultaneously increasing access to care are warranted to reduce morbidity and mortality while containing costs. ■

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