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Disparities in Rates of Spine Surgery for Degenerative Spine Disease Between HIV Infected and Uninfected Veterans

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Abstract

Study Design—Retrospective analysis of nationwide Veterans Health Administration (VA) clinical and administrative data.

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IRB: This study was approved by the IRB of Yale University, and by the Human Subjects Subcommittee of the Research and Development Committee (i.e., IRB) of the VA Connecticut Healthcare System.

Objective—Examine the association between HIV infection and the rate of spine surgery for degenerative spine disease.

Summary of Background Data—Combination anti-retroviral therapy (cART) has prolonged survival in patients with HIV/AIDS, increasing the prevalence of chronic conditions such as degenerative spine disease that may require spine surgery.

Methods—We studied all HIV infected patients under care in the VA from 1996–2008 (n=40,038) and uninfected comparator patients (n=79,039) matched on age, gender, race, year, and geographic region. The primary outcome was spine surgery for degenerative spine disease defined by ICD-9 procedure and diagnosis codes. We used a multivariate Poisson regression to model spine surgery rates by HIV infection status, adjusting for factors that might affect suitability for surgery (demographics, year, comorbidities, body mass index, cART, and laboratory values).

Results—Two-hundred twenty eight HIV infected and 784 uninfected patients underwent spine surgery for degenerative spine disease during 700,731 patient-years of follow-up (1.44 surgeries per 1,000 patient-years). The most common procedures were spinal decompression (50%), and decompression and fusion (33%); the most common surgical sites were the lumbosacral (50%), and cervical (40%) spine. Adjusted rates of surgery were lower for HIV infected patients (0.86 per 1,000 patient-years of follow-up) than for uninfected patients (1.41 per 1,000 patient-years; IRR 0.61, 95% CI: 0.51, 0.74, P<0.001). Among HIV infected patients, there was a trend towards lower rates of spine surgery in patients with detectable viral loads levels (IRR 0.76, 95% CI: 0.55, 1.05, P=0.099).

Conclusion—In the VA, HIV infected patients experience significantly reduced rates of surgery for degenerative spine disease. Possible explanations include disease prevalence, emphasis on treatment of non-spine HIV-related symptoms, surgical referral patterns, impact of HIV on surgery risk-benefit ratio, patient preferences, and surgeon bias.

Keywords

disparities; HIV/AIDS; spine; surgery; outcomes

Introduction

In the era of combined antiretroviral treatment (cART), HIV/AIDS has been transformed into a chronic disease with survival measured in decades, and HIV infected patients survival long enough to develop chronic conditions that can require elective surgical intervention. Degenerative spine disease is a chronic progressive condition with a high prevalence in the general population, and the majority of adults will experience related symptoms such as low back pain at some time during their lives.[1] Most symptomatic episodes are self-limited and effectively treated with non-surgical modalities such as analgesics, physical therapy, and manipulation.[2] When these treatments fail, it is appropriate to consider surgical intervention in selected patients. Spine surgery for degenerative spine disease has become increasingly common in the United States[3;4] and is the subject of numerous academic publications, yet there are few publications describing outcomes of spine surgery for degenerative disease in HIV infected individuals.[5;6] The low United States population prevalence of HIV infection (estimated at 0.4%)[7] complicates the study of surgical procedures in HIV positive patients –

single institutions or even consortia may have insufficient numbers of HIV infected surgical patients to power meaningful analyses.

The Veterans Health Administration (VA) is the largest single provider of health care in the United States, with over 5 million veterans under care.[8] Between 1996 and 2008, the VA provided care to 40,594 HIV positive veterans, one of the largest cohorts of HIV infected patients under care in the world. The VA utilizes an electronic medical record and central data repositories containing nationwide clinical and administrative data, including diagnosis and procedure codes that permit the identification of surgical procedures and accompanying medical conditions. We used VA databases to perform a population-based study of the rate of spine surgery for degenerative spine disease in all HIV positive patients under care in the VA and in matched uninfected comparator patients.

Materials and Methods

The Veterans Aging Cohort Study Virtual Cohort (VACS-VC) uses VA administrative and clinical databases and a validated algorithm[9] to identify all HIV infected veterans that have received care within the VA from October 1, 1996 – September 30, 2008. VACS-VC contains detailed subject data from date of enrollment in the VA on 121,782 patients: 40,594 HIV infected Veterans, and on two uninfected comparator Veterans (n=81,188) matched to each HIV infected patient on age, gender, race, geographic region, and year of enrollment for care in the VA. VACS-VC data includes demographics, date of HIV diagnosis, combined anti-retroviral therapy (cART), survival, alcohol and drug use, comorbid conditions, body mass index (BMI), laboratory values, pharmacy data, hospital admissions and outpatient treatment encounters, and diagnosis and procedure codes.

The VA uses ICD-9 procedure codes to classify all inpatient procedures, and ICD-9 diagnosis codes to describe all inpatient and outpatient encounters.[10] VACS-VC utilizes ICD-9 codes dated from 12 months before until 6 months after starting care in the VA and validated algorithms to determine a broad spectrum of baseline comorbidities prevalent at study enrollment. Our analysis incorporated a subset of these comorbidities that might impact on surgical referral or selection for surgery, including significant cardiovascular, respiratory, hepatobiliary, renal, endocrine, rheumatologic, neoplastic, infectious, and psychiatric disease, alcohol use disorders, and drug abuse.

We excluded from the analysis patients with zero follow-up time (n=2,705), i.e., whose only contact with the VA healthcare system was on their date of enrollment. We used ICD-9 procedure and diagnosis codes to identify all remaining patients in the database who underwent an inpatient surgical procedure for degenerative spine disease between October 1996 and September 2008 (Appendix). Dates of enrollment for care in the VA healthcare system were grouped into tertiles with similar number of patients: 1996–2000, 2001–2004, and 2005–2008. Inclusion criteria encompassed procedures on the vertebral bodies, intervertebral discs, and spinal ligaments and supporting structures. We excluded spinal diagnostic procedures, spine injections, procedures not directly related to treatment of degenerative spine disease (spinal pumps, spinal neurostimulators, spinal cerebrospinal fluid shunts or drains, spine biopsies, spine foreign body removals, spinal cord procedures), and procedures associated with a diagnosis of spinal tumor, congenital spine disorder, spine trauma, spine infection, inflammatory spinal condition, or spinal vascular disorder (Appendix). Eligible procedures were grouped using ICD-9 procedure codes and categorized as decompression, fusion, decompression and fusion, and motion preservation (Appendix). ICD-9 procedure and diagnostic codes were also used to classify the location of spine procedures (i.e., cervical, thoracic, lumbosacral, combined, or unspecified), and to identify spine diagnoses during the surgical admission.

Our analysis incorporated baseline cART, body mass index (BMI), and laboratory values for serum hemoglobin, serum albumin, CD4 cell count, and viral load. We defined cART as any multi-drug antiretroviral therapy administered between 90 days before and 1 year after enrollment into the VACS-VC. For laboratory results we used the value closest to the date of enrollment and collected from 12 months before until 6 months after enrollment. Laboratory and biometric data with non-normal distributions were categorized. Serum hemoglobin was trichotomized as normal (> 12 g/dl), mild anemia (10–12 g/dl), or severe anemia (< 10 g/dl). Serum albumin was dichotomized into normal (≥ 3.5 g/dl) or hypoalbuminemia (< 3.5 g/dl). CD4 cell count was stratified into five levels: ≥ 500, 350 – 499, 200 – 349, 50 – 199, and < 50 cells/mm^3. Viral load was categorized as undetectable (<500 copies/ml) or detectable (≥ 500 copies/ml). We used the closest BMI to the date of enrollment obtained within 12 months of enrollment. BMI was categorized as underweight (< 18.5 kg/m^2), normal (18.5 – 24.9 kg/m^2), overweight (25 – 29.9 kg/m^2) and obese (≥ 30 kg/m^2). The most recent BMI and preoperative laboratory values within 1 year of surgery and cART status at the time of surgery were also tabulated for all surgical patients. Excluding cases with missing values may bias results,[11] thus missing values for laboratory data and BMI were imputed using multiple imputation by chained equations implemented by the Stata v12.0 (Stata Corporation, College Station, Texas) ice command.[12–14] The imputation model included the outcome and all covariates, undertook 10 switching procedures, and generated five datasets. Imputed dataset results were combined using Rubin's rules.[15] No patient had more than five missing data values requiring imputation. Results, tables, and figures include imputed data.

Baseline demographics, comorbidities, cART, BMI, and laboratory values were tabulated and compared using the Wilcoxon sign-rank test for continuous variables and Chi squared or Fischer's exact test for categorical variables. A similar comparison on the subset of patients who underwent surgery for degenerative spine disease also incorporated surgical procedure and location, and spine diagnoses.

Simple and multivariate Poisson regressions were used to compare rates of surgery per 1,000 person-years of follow-up for HIV infected and uninfected patients. Poisson regression provides incidence rate ratios (IRR) showing the ratio of event rates (i.e., spine surgery) between different levels of a variable (e.g., HIV status). Patients were considered "at risk" for surgery from enrollment for care in the VA healthcare system (and thus enrollment into the VACS-VC) until death or the last known date of treatment within the VA through September 30, 2008. When patients had multiple dates of surgery for degenerative spine disease, only the first procedure was used in the analysis. Rates of surgery stratified by HIV status were calculated using simple Poisson regression. Kaplan-

Meier plots and the log rank test were used to examine rates of surgery stratified by HIV status. Multivariate Poisson regression was used to examine overall rates of surgery for HIV infected versus uninfected patients after adjusting for demographics, year of enrollment, co-morbid conditions, BMI, and serum hemoglobin and albumin values. A second multivariate Poisson model analyzing rates of surgery among HIV infected patients used a simple comorbidity score in lieu of individual comorbid disease variables because of power limitations, and also incorporated cART, CD4 cell count, and viral load. Simple Poisson regressions were used to identify individual comorbidities that were associated with surgery with a P value <0.200 (i.e., alcohol abuse, cancer, COPD, diabetes, drug abuse, hypertension, major depression, osteoarthritis, PTSD), and the number of these conditions was tabulated for each patient to generate the comorbidity score. The data met the assumptions of a Poisson model (goodness of fit Chi square = 9,489; P=1.000). Analyses were performed using Stata version 12, StataCorp, College Station, Texas.

Results

Study Population

After excluding 2,705 patients lacking follow up data, there were 119,077 eligible VACS-VC study patients eligible for analysis: 40,038 HIV infected, and 79,039 uninfected. The exclusions produced asymmetry in 2,679 matched patient triads, leading to slight differences in baseline demographics across the HIV infected and uninfected groups (Table 1). Among all 1,012 patients (0.85%) undergoing surgery for degenerative spine disease, there were no significant baseline differences between HIV infected and uninfected surgical patients in age, gender, race, or in the prevalence of most comorbid conditions (Table 2).

The 1,012 surgical procedures for degenerative spine disease occurred during 700,731 person-years of follow-up, the equivalent of 1.44 procedures per 1,000 person-years. The most common surgical procedures were spinal decompression (50%) and decompression and fusion (33%), the most common surgery locations were the lumbosacral (50%) and cervical (40%) spine, and the most common spine diagnoses were ICD9 722.10 lumbar disc displacement (22%) and ICD9 724.02 lumbar spinal stenosis (17%) (Table 3). At the time of surgery, 68% of HIV positive patients were receiving cART, 25% had a CD4 cell count < 200 cells/mm^3, and 47% had a viral load > 500 copies/ml. Simple Poisson regression showed a significant difference in the unadjusted rate of surgery between HIV infected (1.13 per 1,000 person-years) and uninfected patients (1.57 per 1,000 person years; IRR 0.72, 95% CI: 0.62, 0.83, P<0.001) (Figure 1). After adjustment for demographics, year of enrollment, comorbidities, BMI, and serum hemoglobin and albumin, the multivariate Poisson model showed that HIV infected patients had significantly lower rates of surgery for degenerative spine disease (0.86 per 1,000 person years) compared to uninfected patients (1.41 per 1,000 person-years; IRR 0.61, 95% CI: 0.51, 0.74, P<0.001) (Table 4). Restricting the multivariate Poisson model to HIV infected patients, there was a trend towards less frequent surgery in patients with detectable viral load levels (IRR 0.76, 95% CI: 0.55, 1.05, P=0.099) (Table 5). Baseline cART and CD4 cell counts were not independent predictors of altered rates of spine surgery for degenerative disease in HIV infected patients (for all, P≥0.306).

Discussion

We studied rates of spine surgery for degenerative spine disease in patients selected from a cohort of all United States military Veterans with HIV infection under care from 1996 – 2008 (n=40,038) and matched uninfected controls (n=79,039). Our study focused on major procedures for degenerative spine disease intended to decompress neural structures (e.g., lumbar laminectomy) or stabilize spinal segments (e.g., cervical fusion), and we excluded minor procedures (e.g., injections), diagnostic procedures, procedures that did not address degenerative spine disease such as injections, percutaneous procedures, or surgeries performed for trauma, infection, tumors, and congenital defects. One thousand and twelve patients underwent spine surgery for degenerative spine disease, and after adjusting for demographics, an array of comorbidities spanning major organ systems and disease types, BMI, and laboratory values, HIV infected patients had a 39% lower rate of spine surgery for degenerative disease compared to uninfected patients.

In this study, we quantitate the end result of a process starting with degenerative spine symptoms and culminating in surgical intervention. Progression from symptoms to surgery is a multi-step process involving interactions between and decisions by patients, referring health care providers, and surgeons. Our data does not readily permit us to determine which of these steps is responsible for the disparity in rates of spine surgery for degenerative spine disease experienced by HIV positive patients. Perhaps our HIV infected population was less prone to develop symptomatic degenerative spine disease. The development of degenerative spine disease has been linked to increasing age,[16;17] male gender,[17] BMI,[17;18] physical stress,[19;20] height,[21] weight,[18;21] cigarette smoking,[22;23] inflammatory factors,[23;24] and genetics.[25;26] We adjusted for age, gender, and BMI in our analysis, but the remaining factors were unmeasured and may play some role in our findings. Our study cohort was selected from patients seeking care from the VA healthcare system, and the iatrotrophic stimulus likely differed by HIV status. Some HIV infected patients were initiating care for HIV-related symptoms, and a thus smaller proportion may have had degenerative spine disease symptoms at enrollment.

Symptoms related to degenerative spine disease may be obscured by the array of symptoms associated with HIV infection. In a 20-item HIV symptom index developed by Justice *et al.* based on symptom frequency, bother, and expert opinion, common manifestations of degenerative spine disease such as low back pain, neck pain, sciatica, or radiculopathy did not merit inclusion.[27] HIV infected patients and providers may be focusing on non-spine symptoms, with a corresponding reduction in attention to symptoms from spine disease. Specialty providers caring for HIV infected patients may be less effective at managing spine symptoms and less likely to refer patients for surgery. Many HIV infected patients are cared for in infectious disease clinics, and infectious disease specialists or physicians working in infectious disease clinics caring for HIV infected patients are not as comfortable as physicians in general medical clinics at treating common medical conditions like hypertension, diabetes, and hyperlipidemia.[28] A lack of physician comfort may lead to less effective or efficient management, and this phenomenon may extend to the management of spine diagnoses and symptoms.

The disparity in rates of surgery for degenerative spine disease may be grounded in the perception that HIV infection adversely affects the outcomes of spine surgery. The decreased rate of surgery among HIV positive patients may reflect an "appropriate" weighing of HIV infection in the surgical decision making process. Before the development of cART, reports on surgical procedures on HIV infected patients described increased complication rates and higher mortality, and worse outcomes were associated with factors such as active opportunistic infection, low serum albumin, concurrent organ failure, CD4 cell count, and viral load.[29–35] Since the adoption of cART in the developed world, declining rates of surgical complications and deaths in HIV infected patients may rival those experienced by uninfected individuals.[36–40] In the largest surgical series published to date, Horber and colleagues found only small differences in complications and outcomes when comparing 322 HIV infected patients to contemporaneous matched uninfected controls undergoing the same surgical procedures.[41] (None of the patients in the Horberg *et al*. report underwent spine surgery.) Indeed, despite the challenges of managing organ rejection in immunocompromised patients, successful solid organ transplants into HIV infected individuals are increasingly common.[42–44] The development and dissemination of cART has improved survival and doubtless contributed to improved modern surgical outcomes for HIV infected patients.[40] Referring providers and surgeons may also be selecting HIV infected patients for surgery that are likely to have better outcomes, accounting both for improved modern surgical outcomes and the disparity in rates of spine surgery seen in our study population.

The paucity of publications reporting on outcomes of surgery on HIV infected patients and their small sample sizes suggest that surgery on HIV infected individuals is still a relatively uncommon or unstudied event. Published reports of spine surgery on HIV infected patients are quite limited, and most do not deal with degenerative spine disease. [45–60] Only limited data are available on outcomes on HIV infected patients following spine surgery for degenerative spine disease. Eyenga and coworkers reported no complications after lumbar discectomy in nine HIV positive patients, improved sciatica symptoms in eight patients (89%) at three months follow-up, and no differences in outcomes when compared to a contemporaneous group of 68 uninfected patients undergoing the same procedure.[6] Young *et al.* described improvement in five patients after surgery for degenerative spine disease with two minor complications (superficial infection, spontaneously resolving postoperative fever).[5] Larger studies are required to accurately establish the outcomes of elective spine surgery for degenerative spine disease in HIV infected patients.

Patient preferences may be contributing to disparities in rates of spine surgery by HIV infection. In 2003 the Agency for Healthcare Research and Quality first issued a report documenting disparities in health outcomes and access to care across race, ethnicity, and socioeconomic status.[61] Differences in the rates of some procedures and treatments associated with race such as total knee replacement,[62;63] surgery for early stage lung cancer,[64;65] tooth extraction versus root canal therapy,[66] and end of life care,[67;68] can be explained in part by patient preferences. Our dataset does not contain data on patient preferences for spine surgery; however, it is possible that patient preferences may be contributing to reduced rates of spine surgery among HIV infected patients.

Concerns about personal safety may be influencing surgeons' decisions to offer surgery to HIV positive patients. The discussions that were prevalent early in the AIDS epidemic about the ethical responsibilities of caring for HIV infected patients in the face of personal risk of disease transmission have faded.[69;70] Subsequent epidemiologic studies showed extremely low rates of occupational HIV transmission to healthcare providers,[71] and there have been no documented occupation HIV infections in surgeons.[72] Additional evidence of occupational safety is provided by serosurveys showing very low rates of HIV seroconversion in the absence of non-occupational risk factors in orthopedic (0/3,267 = 0%) and general surgeons (1/740 = 0.14%).[73;74] Major medical organizations, including the American Medical Association[75] and the American College of Surgeons,[76] have released statements affirming the ethical obligations of physicians to treat patients with HIV infection.

Notwithstanding organized medicine's consensus about the ethical obligations of healthcare providers to care for HIV infected patients and the minimal personal risk involved, some physicians and dentists are reluctant to care for patients with HIV. The U.S. Department of Health and Human Services Office for Civil Rights reported a settlement in 2009 with a Texas orthopedic surgeon who declined to perform reconstructive knee surgery on an HIV infected Medicare beneficiary because blood spattering might expose them to the HIV virus, and referred the patient to another orthopedic surgeon 200 miles away.[77] Recent surveys of HIV infected patients have reported discrimination by dentists[78;79] and general practitioners.[79] A 2008 anonymous international web-based survey of refractive ophthalmological surgeons found that 33% of respondents considered HIV infected status without definite AIDS to be a relative contraindication to refractive surgery, and 16% considered HIV infection an absolute contraindication.[80] Follow-up surveys of respondents who declined to operate on HIV infected patients revealed that 51% were concerned with viral transmission to the surgeon or operating room staff. The data suggest that some Western healthcare providers limit care to HIV infected patients out of concern for personal safety. We do not know if these data generalize to spine surgeons and spine surgery in HIV infected patients.

Limitations

The selection, organization, and granularity of data within administrative and clinical databases are seldom designed to answer specific research questions and can limit analyses and conclusions; however, large databases provide significant advantages. VACS-VC uses multiple nationwide VA administrative and clinical databases, validated data extraction and cleaning algorithms, and a matched control population to assemble a rich database allowing for the investigation of complex research questions in the largest HIV infected cohort under treatment in the world. Non-VA surgical treatment options for degenerative spine disease are available, and some patients may have undergone surgery outside of the VA healthcare system, resulting in an underestimation of the rates of spine surgery. We have no *a priori* reason to suspect that HIV infected and uninfected patients would obtain surgery outside of the VA healthcare system at different rates, therefore the ratio of disparity in surgery rates between HIV infected and uninfected patients should be unaffected. We used baseline covariates in our multivariate regression models, and some of these values may have changed over time, affecting adjusted rates of surgery. There is conflicting evidence on the benefits of surgery for degenerative spine disease, and interpretation of our disparity findings is further complicated by the extensive regional and physician variation in rates of spine surgery. [81–84] It is impossible to say if either of the rates of surgery experienced by HIV infected or uninfected patients were appropriate.

Conclusion

HIV infected veterans experience significantly reduced rates of spine surgery for degenerative spine disease. Our data are insufficient to determine which step or steps in the progression from symptoms to surgery account for the disparity in surgical rates, and we can only speculate which patient, referring provider, surgeon, or system factors are contributing to the observed disparity. The incidence of spine disease, spine symptoms, referral patterns, the relationship between HIV infection and surgical outcomes, patient preferences, and surgeon bias may all play a role. There are no large studies on the impact of HIV infection on spine surgery outcomes. In the absence of reliable outcomes data and clear standards for undertaking spine surgery, we do not know whether the disparities in rates of spine surgery are affecting health outcomes in patients with HIV infection.

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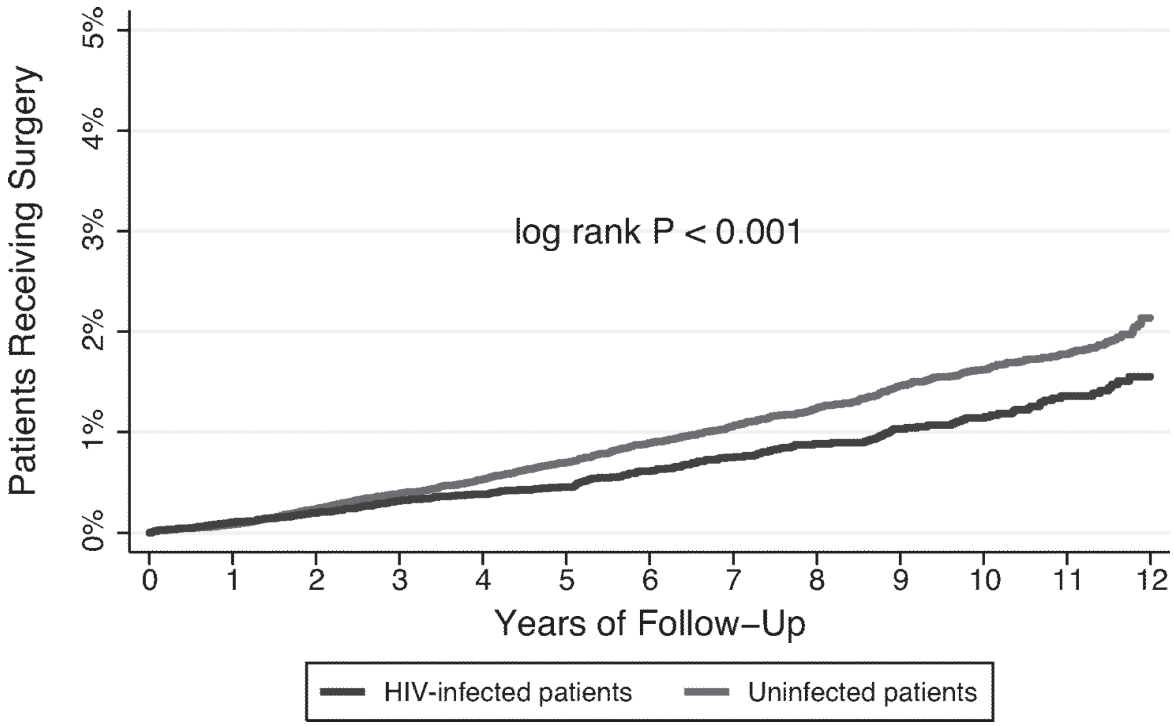

Figure 1.

Kaplan-Meier plot of surgery for degenerative spine disease in HIV-infected and uninfected patients. HIV-infected patients have significantly lower rates of surgery ($P < 0.001$).

Table 1

HIV Infected and Uninfected Study Patients at Baseline

		HIV Infected (n=40,038)	Uninfected (n=79,039)	P value
Age (years)	Mean (SD)	46.3 (10.2)	46.6(10.3)	<0.001
Gender	Male	39,102 (98%)	77,185 (98%)	0.951
Race	White	15,019 (38%)	30,927 (39%)	<0.001
	African American	19,340 (48%)	36,978 (47%)	
	Hispanic	2,985 (7.5%)	6,019 (7.6%)	
	Other	2,694 (6.7%)	5,115 (6.5%)	
Comorbidities	Alcohol abuse	6,456 (16%)	11,496 (15%)	<0.001
	Atrial fibrillation	308 (0.8%)	793 (1.0%)	<0.001
	CAD	1,422 (3.6%)	4,861 (6.2%)	<0.001
	Cancer	2,035 (5.1%)	2,554 (3.2%)	<0.001
	CHF	647 (1.6%)	1,299 (1.6%)	0.735
	Cirrhosis	418 (1.0%)	474 (0.6%)	<0.001
	COPD	1,733 (4.3%)	3,129 (4.0%)	0.003
	Depression, major	2,651 (6.6%)	4,625 (5.9%)	<0.001
	Diabetes	2,926 (7.3%)	9,640 (12%)	<0.001
	Drug abuse	7,484 (19%)	9,827 (12%)	<0.001
	Hepatitis B, chronic	1,191 (3.0%)	302 (0.4%)	<0.001
	Hepatitis C	3,716 (9.3%)	2,354 (3.0%)	<0.001
	Hypertension	7,020 (18%)	21,039 (27%)	<0.001
	Hyperlipidemia	2,306 (5.8%)	10,666 (13%)	<0.001
	Osteoarthritis	1,059 (2.6%)	5,380 (6.8%)	<0.001
	PTSD	1,896 (4.7%)	6,120 (7.7%)	<0.001
	PVD	412 (1.0%)	1,050 (1.3%)	<0.001
	Renal insufficiency	1,621 (4.1%)	1,325 (1.7%)	<0.001
	Schizophrenia	1,367 (3.4%)	4,880 (6.2%)	<0.001
	Stroke	628 (1.6%)	1,349 (1.7%)	0.080
	TIA	75 (0.2%)	181 (0.2%)	0.146
cART		20,997 (52%)	n/a	n/a
BMI, kg/m^2	<18.5	2,464 (5.0%)	1,052 (1.1%)	<0.001
	18.5–24.9	19,834(48%)	20,324 (22%)	
	25–29.9	12,590 (33%)	29,850 (37%)	
	≥30	5,150 (14%)	27,813 (40%)	
Hemoglobin, g/dl	>12	30,658 (77%)	72,920 (92%)	<0.001
	10–12	6,393 (16%)	4,660 (5.9%)	
	<10	2,987 (7.5%)	1,458 (1.9%)	
Albumin, g/dl	≥3.5	27,393 (68%)	69,499 (88%)	<0.001
	<3.5	12,645 (32%)	9,540 (12%)	
CD4 cell count, cells/mm^3	≥ 500	9,748 (24%)	n/a	n/a
	350 – 499	7,303 (18%)	n/a	

		HIV Infected (n=40,038)	Uninfected (n=79,039)	P value
	200 – 349	8,640 (22%)	n/a	
	50 – 199	8,807 (22%)	n/a	
	<50	5,540 (14%)	n/a	
Viral load, copies/ml	<500	11,154 (28%)	n/a	n/a
	≥ 500	28,884 (72%)	n/a	

SD = Standard deviation; CAD = Coronary artery disease; CHF = Congestive heart failure; COPD = chronic obstructive pulmonary disease; PTSD = post-traumatic stress disorder; PVD = peripheral vascular disease; TIA = Transient ischemic attack

cART = Combination anti-retroviral therapy

BMI = Body mass index

Table 2

Surgical and Non-Surgical Patients at Baseline

		Patients Undergoing Degenerative Spine Surgery (n=1,102)			Non-Surgery Patients (n=118,065)		
		HIV Infected (n=228)	Uninfected (n=784)	P value	HIV Infected (n=39,810)	Uninfected (n=78,255)	P value
Age (years)	Mean (SD)	45.3 (8.4)	45.4 (8.2)	0.694	46.3 (10.2)	46.6 (10.3)	<0.001
Gender	Male	222 (97%)	767 (98%)	0.621	38,880 (98%)	76,418 (98%)	0.919
Race	White	104 (46%)	370 (47%)	0.823	14,915 (37%)	30,57 (39%)	<0.001
	African American	110 (48%)	357 (46%)		19,230 (48%)	36,621 (47%)	
	Hispanic	12 (5.3%)	44 (5.6%)		2,973 (7.5%)	5,975 (7.6%)	
	Other	2 (0.9%)	13 (1.7%)		2,692 (6.8%)	5,102 (6.5%)	
Comorbidities	Alcohol abuse	48 (21%)	130 (17%)	0.138	6,408 (16%)	11,366 (15%)	<0.001
	Atrial fibrillation	1 (0.4%)	5 (0.6%)	1.000	307 (0.8%)	788 (1.0%)	<0.001
	CAD	6 (2.6%)	55 (7.0%)	0.011	1,416 (3.6%)	4,806 (6.1%)	<0.001
	Cancer	12 (5.3%)	17 (2.2%)	0.022	2,023 (5.1%)	2,537 (3.2%)	<0.001
	CHF	0 (0%)	7 (0.9%)	0.360	647 (1.6%)	1,292 (1.7%)	0.753
	Cirrhosis	0 (0%)	2 (0.3%)	1.000	418 (1.1%)	472 (0.6%)	<0.001
	COPD	11 (4.8%)	33 (4.2%)	0.712	1,722 (4.3%)	3,096 (4.0%)	0.003
	Depression, major	28 (12%)	85 (11%)	0.551	2,623 (6.6%)	4,540 (5.8%)	<0.001
	Diabetes	21 (9.2%)	85 (11%)	0.540	2,905 (7.3%)	9,555 (12%)	<0.001
	Drug abuse	53 (23%)	114 (15%)	0.003	7,431 (19%)	9,713 (12%)	<0.001
	Hepatitis B, chronic	6(2.6%)	4 (0.5%)	0.011	1,185 (3.0%)	298 (0.4%)	<0.001
	Hepatitis C	14 (6.1%)	24 (3.1%)	0.045	3,702 (9.3%)	2,330 (3.0%)	<0.001
	Hypertension	37 (16%))	209 (27%)	0.001	6,983 (18%)	20,830 (27%)	<0.001
	Hyperlipidemia	8 (3.5%)	85 (11%)	<0.001	2,298 (5.8%)	10,581 (14%)	<0.001
	Osteoarthritis	15 (6.6%)	109 (14%)	0.003	1,044 (2.6%)	5,271 (6.7%)	<0.001
	PTSD	16 (7.0%)	96 (12%)	0.030	1,880 (4.7%)	6,024 (7.7%)	<0.001
	PVD	2 (0.9%)	9 (1.2%)	1.000	410 (10%)	1,041 (1.3%)	<0.001
	Renal insufficiency	5 (2.2%)	4 (0.5%)	0.032	1,616 (4.1%)	1,321 (1.7%)	<0.001
	Schizophrenia	6 (2.6%)	26 (3.3%)	0.830	1,361 (3.4%)	4,854 (6.2%)	<0.001
	Stroke	2 (0.9%)	18 (2.3%)	0.277	626 (1.6%)	1,331 (1.7%)	0.106
	TIA	0 (0%)	8 (1.0%)	0.210	75 (0.2%)	173 (0.2%)	0.254

		Patients Undergoing Degenerative Spine Surgery (n=1,102)			Non-Surgery Patients (n=118,065)		
		HIV Infected (n=228)	Uninfected (n=784)	P value	HIV Infected (n=39,810)	Uninfected (n=78,255)	P value
cART		113 (50%)	n/a	n/a	20,884 (52%)	n/a	n/a
BMI, kg/m^2	<18.5	14 (6.1%)	10 (1.3%)	<0.001	2,450 (6.2%)	1,042 (1.3%)	<0.001
	18.5 – 24.9	122 (54%)	244 (31%)		19,712 (50%)	20,080 (26%)	
	25 – 29.9	62 (27%)	302 (38%)		12,528 (31%)	29,548 (38%)	
	>30	29 (13%)	228 (29%)		5,120 (13%)	27,585 (35%)	
Hemoglobin, g/dl	>12	183 (80%)	720 (92%)	<0.001	30,475 (77%)	72,200 (92%)	<0.001
	10 – 12	33 (15%)	44 (5.7%)		6,359 (16%)	4,616 (6.0%)	
	<10	12 (5.1%)	20 (2.5%)		2,975 (7.5%)	1,439 (1.8%)	
Albumin, g/dl	≥3.5	154 (668%)	663 (85%)	<0.001	27,239 (68%)	68,835 (88%)	<0.001
	<3.5	74 (32%)	121 (15%)		12,571 (32%)	9,420 (12%)	
CD4 cell count, cells/mm^3	≥ 500	74 (32%)	n/a	n/a	9,675 (24%)	n/a	n/a
	350 – 499	47 (21%)	n/a		7,256 (18%)	n/a	
	200 – 349	50 (22%)	n/a		8,591 (22%)	n/a	
	50 – 199	35 (15%)	n/a		8,772 (22%)	n/a	
	<50	23 (10%)	n/a		5,517 (14%)	n/a	
Viral load, copies/ml	<500	81 (36%)	n/a	n/a	11,073 (28%)	n/a	n/a
	≥ 500	147 (64%)	n/a		28,737 (72%)	n/a	

SD = Standard deviation; CAD = Coronary artery disease; CHF = Congestive heart failure; COPD = chronic obstructive pulmonary disease; PTSD = post-traumatic stress disorder; PVD = peripheral vascular disease; TIA = Transient ischemic attack

cART = Combination anti-retroviral therapy

BMI = Body mass index

Table 3

HIV Infected and Uninfected Patients at Surgery

		HIV Infected (n=228)	Uninfected (n=784)	P value
Procedure*	Decompression	134 (59%)	377 (48%)	0.060
	Fusion	32 (14%)	122 (16%)	
	Decompression and Fusion	60 (26%)	277 (35%)	
	Motion preservation	2 (0.88%)	8 (1.0%)	
Location*	Cervical	87 (38%)	320 (41%)	<0.001
	Thoracic	3 (1.3%)	7 (0.90%)	
	Lumbosacral	104 (46%)	404 (52%)	
	Combined	7 (3.1%)	23 (2.9%)	
	Unspecified	27 (12%)	30 (3.8%)	
Spine Diagnoses**	722.10 Lumbar disc displacement	56 (25%)	169 (23%)	0.366
	724.02 Lumbar spinal stenosis	34 (15%)	138 (18%)	0.369
	721.1 Cervical spondylosis with myelopathy	29 (13%)	93 (12%)	0.729
	722.71 Cervical disc displacement without myelopathy	19 (8.3%)	6 (8.4%)	1.000
	722.0 Cervical disc displacement	17 (7.5%)	69 (8.8%)	0.890
	723.0 Cervical spinal stenosis	11 (5.3%)	77 (9.8%)	0.016
	721.0 Cervical spondylosis	7 (3.1%)	38 (4.8%)	0.360
	721.3 Lumbosacral spondylosis	7 (3.1%)	34 (4.3%)	0.451
cART		155 (68%)	n/a	n/a
BMI, kg/m^2	<18.5	7 (3.0%)	14 (1.8%)	<0.001
	18.5 – 24.9	104 (45%)	200 (26%)	
	25 – 29.9	85 (37%)	303 (39%)	
	>30	32 (14%)	267 (34%)	
Hemoglobin, g/dl	>12	196 (86%)	743 (95%)	<0.001
	10 – 12	24 (11%)	37 (4.7%)	
	<10	8 (3.6%)	5 (0.59%)	
Albumin, g/dl	≥3.5	178 (78%)	721 (92%)	<0.001
	<3.5	50 (22%)	63 (8.1%)	
CD4 cell count, cells/mm^3	≥ 500	86 (38%)	n/a	n/a
	350 – 499	47 (21%)	n/a	
	200 – 349	39 (17%)	n/a	
	50 – 199	28 (12%)	n/a	
	<50	29 (13%)	n/a	
Viral load, copies/ml	<500	120 (53%)	n/a	n/a
	≥ 500	108 (47%)	n/a	

* Based on ICD9 procedure and diagnosis codes from surgical admission

** ICD9 diagnosis codes from surgical admission

cART = Combination anti-retroviral therapy

BMI = Body mass index

Table 4

Multivariate Poisson Regression Model of 1,012 Spine Surgeries in 111,047 HIV Infected and Uninfected Patients

Variable		IRR	95% CI	P value
HIV infected		0.61	0.51, 0.74	<0.001
Age				
	< 40	1.00	n/a	n/a
	40 – 49	1.25	1.06, 1.47	0.007
	50 – 59	1.06	0.89, 1.29	0.567
	60 – 69	0.69	0.49, 0.97	0.034
	≥ 70	0.15	0.06, 0.42	<0.001
Race				
	White	1.00	n/a	n/a
	Black	0.74	0.64, 0.85	<0.001
	Hispanic	0.56	0.42, 0.73	<0.001
	Other	0.31	0.19, 0.53	<0.001
Selected Comorbidities	Alcohol abuse	1.00	0.81, 1.24	0.998
	CHF	0.54	0.25, 1.18	0.121
	Diabetes	1.17	0.93, 1.46	0.176
	Drug abuse	1.03	0.83, 1.28	0.795
	Hepatitis C	0.94	0.63, 1.33	0.716
	Hypertension	1.25	1.06, 1.48	0.009
	Osteoarthritis	2.28	1.96, 2.90	<0.001

Note: Regression also adjusted for gender, year, additional baseline comorbidities (atrial fibrillation, cancer, chronic obstructive pulmonary disease, cirrhosis, coronary artery disease, hepatitis B, hyperlipidemia, major depression, peripheral vascular disease, post-traumatic stress disorder, renal insufficiency, schizophrenia, stroke, transient ischemic attack), baseline BMI, and baseline serum albumin and serum hemoglobin.

IRR = Incidence rate ratio

CI = Confidence interval

CHF = Congestive heart failure

Table 5

Multivariate Poisson Regression Model of 228 Spine Surgeries in 40,038 HIV Infected Patients

Variable		IRR	95% CI	P value
Age				
	< 40	1.00	n/a	n/a
	40 – 49	1.16	0.82, 1.61	0.394
	50 – 59	1.13	0.76, 1.68	0.540
	60 – 69	0.74	0.37, 1.48	0.395
	≥ 70	0.42	0.10, 1.74	0.231
Race				
	White	1.00	n/a	n/a
	Black	0.72	0.54, 0.96	0.025
	Hispanic	0.53	0.29, 0.97	0.041
	Other	0.16	0.04, 0.67	0.012
Comorbidity Score		1.27	1.14, 1.41	<0.001
cART		0.90	0.68, 1.20	0.488
CD4 cell count ≥ 200 cells/mm^3		1.26	0.80, 1.98	0.306
Viral load ≥ 500 copies/ml		0.76	0.55, 1.05	0.099

*Regression also adjusted for gender, year, baseline BMI, and baseline serum albumin and serum hemoglobin.

IRR = incidence rate ratio

CI = Confidence interval

cART = Combination anti-retroviral therapy

Appendix

<u>**Inclusion Criteria**</u>	
ICD-9 Procedure Codes	**Description**
Decompression	
03.02	Reopening of laminectomy site
03.09	Other exploration and decompression of spinal canal
80.5x	Excision, destruction of intervertebral disc, unspecified
Fusion	
81.0x	Spinal fusion
81.3x	Refusion of spine
81.62	Fusion or refusion of 2–3 vertebrae
81.63	Fusion or refusion of 4–8 vertebrae
81.64	Fusion or refusion of 9 or more vertebrae
84.51	Insertion of interbody spinal fusion device
Motion preservation	
84.59	Insertion of other spinal devices
84.6x	Replacement of spinal disc
84.8x	Insertion, replacement, and revision of posterior spinal motion preservation device(s)
<u>**Exclusion Criteria**</u>	
ICD-9 Procedure Codes	**Description**
03	**Operations on spinal cord and spinal canal structures**
03.01	Removal of foreign body from spinal canal
03.1	Division of intraspinal nerve root
03.2x	Cordotomy
03.3x	Diagnostic procedures on spinal cord and spinal canal structures
03.4	Excision or destruction of lesion of spinal cord or spinal meninges
03.5x	Plastic operations on spinal cord structures
03.6x	Lysis of adhesions of spinal cord and nerve roots
03.7x	Shunt of spinal theca
03.8	Injection of destructive agent into spinal canal
03.9x	Other operations on spinal cord and spinal canal structures
81.6	**Other procedures on spine**
81.65	Percutaneous vertebroplasty
81.66	Percutaneous vertebral augmentation
ICD-9 Diagnosis Codes	**Description**
013	**Tuberculosis of meninges and central nervous system**
013.4x	Tuberculoma of spinal cord
013.5x	Tuberculous abscess of spinal cord
015	**Tuberculosis of the bones and joints**
015.0	Vertebral column
324	**Intracranial and intraspinal abscess**
324.1	Intraspinal abscess

Inclusion Criteria

ICD-9 Procedure Codes	Description
192	**Malignant neoplasm of other and unspecified parts of nervous system**
192.2	Spinal cord
192.3	Spinal meninges
198	**Secondary malignant neoplasm of other unspecified sites**
198.3	Brain and spinal cord
198.4	Meninges (cerebral) (spinal)
198.5	Bone and bone marrow
225	**Benign neoplasm of brain and other parts of nervous system**
225.3	Spinal cord
225.4	Spinal meninges
336	**Other diseases of spinal cord**
336.1	Vascular myelopathies
720	**Ankylosing spondylitis and other inflammatory spondylopathiess**
720.0	Ankylosing spondylitis
720.1	Spinal enthesopathy
720.2	Sacroiliitis, not elsewhere classified
720.8x	Other inflammatory spondylopathies
720.9	Unspecified inflammatory spondylopathy
721	**Spondylosis and allied disorders**
721.6	Ankylosing vertebral hyperostosis
721.7	Traumatic spondylopathy
722	**Intervertebral disc disorders**
722.9	Other and unspecified disc disorder (calcification of intervertebral cartilage or disc, discitis)
733	**Other disorders of bone and cartilage**
733.13	Pathologic fracture of vertebrae */
741	**Spina bifida**
741.0x	With hydrocephalus
741.9x	Without mention of hydrocephalus
742	**Other congenital anomalies of the nervous system**
742.5x	Other specified anomalies of spinal cord
747	**Other congenital anomalies of circulatory system**
747.82	Spinal vessel anomaly
756	**Other congenital musculoskeletal anomalies**
756.1x	Anomalies of spine
805	**Fracture of vertebral column without mention of spinal cord injury**
805.0x	Cervical, closed
805.1x	Cervical, open
805.2	Dorsal [thoracic], closed
805.3	Dorsal [thoracic], open
805.4	Lumbar, closed
805.5	Lumbar, open

Inclusion Criteria	
ICD-9 Procedure Codes	**Description**
805.6	Sacrum and coccyx, closed
805.7	Sacrum and coccyx, open
805.8	Unspecified, closed
805.9	Unspecified, open
806	**Fracture of vertebral column with spinal cord injury**
806.0x	Cervical, closed
806.1x	Cervical, open
806.2	Dorsal [thoracic], closed
806.3	Dorsal [thoracic], open
806.4	Lumbar, closed
806.5	Lumbar, open
806.6	Sacrum and coccyx, closed
806.7	Sacrum and coccyx, open
806.8	Unspecified, closed
806.9	Unspecified, open
839	**Other, multiple, and ill-defined dislocations**
839.0x	Cervical vertebra, closed
839.1x	Cervical vertebra, open
839.2x	Thoracic and lumbar vertebra, closed
839.3x	Thoracic and lumbar vertebra, open
839.4x	Other vertebra, closed
839.5x	Other vertebra, open
905	**Late effects of musculoskeletal and connective tissue injuries**
905.1	Late effect of fracture of spine and trunk without mention of spinal cord lesion
952.9	Unspecified site of spinal cord