Is HIV Infection a Risk Factor for Complications of Surgery?

SIAN JONES, M.D.[1], CLYDE B. SCHECHTER, M.D.[2], CHERYL SMITH, M.D.[3], AND DAVID N. ROSE, M.D.[4]

Abstract

Background: The literature is inconsistent as to whether HIV-infected patients have higher rates of surgical complication than do HIV-uninfected patients. This inconsistency reflects the failure to control for confounding variables in many of the previous studies.

Methods: A retrospective cohort study of records of HIV-infected individuals who underwent surgical procedures between 1990 and 1995 was matched with the records of HIV-uninfected control patients. We performed a logistic regression analysis to determine the independent effects of HIVinfection and other potential risk factors for surgical complications.

Results: The crude rates of death and infectious and hematologic complications were higher among HIV-infected patients than among uninfected patients. Although the crude risk of having any complication was higher among the HIV-infected (odds ratio [OR]=2.47, p=0.015), the adjusted risk was not (OR=0.72 [p<0.613]). Variables significantly associated with complications were American Society of Anesthesiology (ASA) risk class (OR=2.7), age (OR=1.06 per year), and weight (OR=0.96 per kg).

Conclusions: HIV sero-status was not found to be an independent risk factor for complications of surgery. The most important risk factor for complication of surgery in HIV-infected patients is ASA risk class.

Key Words: AIDS, HIV, surgery, complication.

Introduction

DO HUMAN IMMUNODEFICIENCY VIRUS (HIV)-infected persons have higher surgical complication rates than do uninfected persons? The literature is remarkably inconsistent on this subject, with results of surgery reported as unacceptably poor (1–5) or remarkably favorable (6–11). A recent review found that the surgical literature consists mostly of descriptive, retrospective case series, with wide variability of the reported patient populations, surgical procedures, and methods for collecting and categorizing information on complications (12). Few studies used analytical methods to minimize confounding the comparison of groups with risk factors known to be associated with post-operative complications such as emergency procedures, malnutrition, contaminated wounds, uncontrolled diabetes and neutropenia. Of 114 reports of the outcome of surgery in HIV-infected and uninfected persons, only 10 studies matched groups by one or more variables, and only two of these found significant differences in complication rates (13, 14). We attempted to correct for these weaknesses in this retrospective cohort study by including relevant variables in the analysis. The purpose of the study was to determine if HIV infection is an independent risk factor for complications of surgery.

Methods

We reviewed the records of all HIV-infected patients who underwent a surgical procedure at Mount Sinai Medical Center, New York, from 1990 to 1995. Patients were identified through the hospital's discharge database and were included as cases if they had acquired immunodeficiency syndrome (AIDS) as defined by Centers for Disease Control and Prevention criteria (15) or if they had HIV infection, and a CD4

[1]Division of Infectious Diseases, Mount Sinai School of Medicine, New York, NY; [2]Department of Family Medicine and Community Health, Albert Einstein College of Medicine, Bronx, NY; [3]Department of Medicine, North General Hospital, Mount Sinai School of Medicine, New York, NY; and [4]Department of Medicine, Baystate Medical Center, Springfield, MA.

Address all correspondence to Sian Jones, M.D., Box 1009, Mount Sinai School of Medicine, 1 East 100th Street, New York, NY 10029; Email: joness01@doc.mssm.edu

Accepted for publication February 4, 2002.

lymphocyte count had been performed within four months of surgery. Each HIV-infected patient was matched with two control patients for three variables: surgical procedure, age within 6 years and year of procedure within 5 years. Control patients were identified through the hospital's discharge database as having had the same procedure as HIV-infected cases, but not coded as having HIV infection or AIDS. When more than two control patients were available who matched with a particular case, selections were made randomly. Control patients were excluded if they had known risk factors for HIV transmission, if they had been treated with antineoplastic chemotherapy within one year of surgery, or if they had undergone organ transplantation. Each patient treated with high-dose corticosteroids within six months of surgery was matched with two controls similarly treated. Demographic and clinical information was entered into a database that included: indication for surgery, type of surgical procedure, emergent or elective surgery, anesthetic type, presence or absence of cardiopulmonary disease, pre-procedure antibiotics, CD4 count, serum albumin level, serum creatinine level, white blood cell (WBC) count, hematocrit, prothrombin time, serum alanine transaminase (ALT) level and American Society of Anesthesiology (ASA) risk class. Chemistry and hematologic laboratory values recorded were those obtained closest to the time of surgery. ASA risk class is a global rating based upon the anesthesiologist's assessment of the physical status of the patient: class I, normal healthy patient; class II, patient with mild systemic disease; class III, patient with severe systemic disease that limits activity but is not incapacitating; class IV, patient with incapacitating illness that is a constant threat to life; and class V, moribund patient not expected to survive 24 hours with or without operation (16).

Peri-operative and post-operative events were recorded as complications if they occurred within 30 days of surgery and if they were described in the medical record as a complication or an unexpected event. An event was classified as a complication if it met one of the following criteria: (a) death; (b) re-hospitalization or return to the operating room; (c) intra-operative complication (either surgical or anesthetic); (d) clinically apparent bleeding; (e) post-operative fever lasting more than 72 hours (all cases were ultimately found to have an infectious cause); (f) clinical diagnosis of infection requiring antibiotic treatment outside of routine prophylaxis; (g) extubation delayed by more than 24 hours or re-intubation; (h) post-operative bowel obstruction or ileus requiring placement of a naso-gastric tube; or (i) other clinically significant events such as post-operative deep vein thrombosis, cardiac arrhythmia or renal failure. All of the above information was obtained by direct review of the medical records and entered onto a standardized data collection form. Approval for this study was obtained from the Mount Sinai School of Medicine Institutional Review Board (IRB).

Statistical Analysis

Hypothesis testing was carried out using logistic regression to control for year of surgical procedure, ASA risk class, emergent versus elective surgery, age, gender, hematocrit, WBC count, platelet count, serum albumin, ALT, creatinine levels and body weight. The effect of clustering of patients by surgeons and type of surgery on standard errors was accounted for by using the Huber-White robust covariance estimator (17). Cases were dropped from analysis if data for any of the variables under analysis were missing.

Results

Study Population

Of the 52 HIV-infected patients identified and 104 HIV-uninfected controls, 26 were excluded from analysis due to missing variables. This resulted in 130 patients available for analysis: 43 with HIV infection and 87 without HIV infection. The demographic and clinical characteristics of the study population are outlined in Table 1. The HIV-infected and HIV-uninfected groups were well matched for age. A greater proportion of HIV-infected patients were males, compared to the uninfected patients. Similarly, a greater proportion of HIV-infected patients were non-white, compared to the uninfected patients. The majority of HIV-infected individuals (75%) were defined as having AIDS by virtue of a CD4 count <200 cells/μL. The mean CD4 count of the HIV-infected individuals was 177 cells/μL. The mean CD4 count of HIV-infected individuals excluded from the analysis was 152 cells/μL, which is not a statistically significant difference. Furthermore, the proportion of patients with a CD4 cell count less than 200 per μL was the same for patients included in the analysis as

TABLE 1
Demographics and Clinical Variables

	HIV-infected n=43	HIV-uninfected n=87	Normal values
Male, %	74	43	
Age, mean yrs	42 ± 9	43 ± 11	
Ethnicity			
African-American, %	35	10	
Asian, %	0	6	
White, %	40	68	
Hispanic, %	23	14	
Emergent surgery	58%	30%	
CD4 count, mean cells/μL	177 ± 226	—	480–1700
CD4 count<200 cells/μL, %	75	—	
Serum albumin, g/mL	3.4 ± 0.8	4.3 ± 0.5	3.5–4.9
ALT level, U/L	71 ± 74.6	30.3 ± 27.4	1–53
Serum creatinine, mg/mL	2.1 ± 4	1.1 ± 1.1	0.5–1.3
WBC, cells/mm^3	6.6 ± 3.8	8.9 ± 4.1	5–11
Hematocrit, %	32.8 ± 8.3	39.1 ± 4.8	34–48
Platelet count, cells/mm^3	201 ± 107	282 ± 97.7	150–450
Weight, kg	65.2 ± 11.1	71.3 ± 17.4	

for those who were excluded. Analyzed and excluded patients had similar values for all variables (data not shown).

Procedures

The types of procedure performed are listed in Table 2. A majority of these procedures were major abdominal surgeries, either clean or contaminated. None of the major abdominal procedures were performed by laparoscopic surgery. The mixed category includes those patients who underwent combined procedures — most commonly abdominal and thoracic. Almost twice as many HIV-infected patients underwent procedures on an emergent basis as did patients who were not HIV-infected: 58% vs. 30%, p=0.001 (Table 1).

TABLE 2
Surgical Procedure Types

Procedure Type	HIV-infected n=43	HIV-uninfected n=87
Abdominal clean	18	38
Abdominal contaminated	7	9
Appendectomy clean	3	7
Appendectomy contaminated	4	6
Cardiothoracic	1	2
Bone	0	2
Head and neck	3	7
Mixed*	1	4
Pelvic clean	4	6
Pelvic contaminated	2	6

*Procedures involving both abdominal and thoracic cavity

Complications

Table 3 lists the types and corresponding numbers of complications that occurred in each group. Procedural complications were defined as those directly related to the procedure, such as technical complications occurring intraoperatively or bowel obstruction occurring postoperatively. Complications classified as organ dysfunction were those related to dysfunction of an organ system not directly related to the surgical procedure, such as renal failure, cardiac arrhythmia or respiratory failure. Infectious complications were the most common type of complication in each group, accounting for approximately half of all complications for both the HIV-infected and uninfected patients. Other types of complication, including death, were similarly distributed in both groups.

The crude rates of death, infectious and hematological complications were slightly higher among HIV-infected than the uninfected. The crude risk of having any complication was higher among the HIV-infected, OR=2.47 (p=0.015).

TABLE 3
Complications of Surgery

Type of Complication	HIV Status Infected n=43	Uninfected n=87
Death	3	2
Hematologic	3	0
Infectious	17	13
Organ dysfunction	3	3
Procedural*	4	7
Total	30	25

*Complications related directly to the procedure

TABLE 4
Logistic Regression Analysis of Risk Factors for Complications of Surgery
Number of Observations = 130

Risk Factor	Odds Ratio	(95% C.I.)
ASA risk class**	2.70	(1.50 ± 4.84)
Emergent surgery	1.13	(0.40 ± 3.18)
Procedure year	1.12	(0.85 ± 1.46)
WBC count	1.09	(0.96 ± 1.25)
Age*	1.06	(1.01 ± 1.11)
Hematocrit	1.01	(0.93 ± 1.11)
ALT level	1.00	(0.99 ± 1.01)
Platelet count	1.00	(0.99 ± 1.00)
Gender	0.97	(0.31 ± 3.06)
Weight*	0.96	(0.93 ± 1.00)
Creatinine level	0.87	(0.75 ± 1.02)
HIV infection	0.72	(0.20 ± 2.62)
Albumin level	0.62	(0.26 ± 1.51)

Robust standard errors in parentheses. * Significant at 5% level. **Significant at 1% level. Area under ROC curve=0.80. Hosmer-Lemeshow Goodness of Fit χ^2=6.69 (p=0.57).

In the logistic regression analysis, however, the adjusted OR of having any complication and having HIV infection was 0.72 (p<0.613) (Table 4). The greatest and most statistically significant association with surgical complication was ASA risk class, OR=2.70 (p=0.001). Both age and weight were also significantly associated with the risk of complication, with ORs of 1.06 per year and 0.96 per kilogram respectively. In addition to HIV infection, other potential risk factors found not to be significantly associated with complications of surgery were emergent surgery, procedure year, WBC count, hematocrit, serum ALT level, platelet count, gender, creatinine level, and albumin level.

A sub-analysis (data not shown) separating HIV-infected patients with CD4 counts of 200/μL or greater from those with counts of less than 200 cells/μL did not show a significant difference in association with surgical complications. However, the number of HIV-infected patients with CD4 counts of 200 cells/μL or greater was low, limiting the statistical power of this analysis.

Discussion

HIV sero-status was not found to be an independent risk factor for complications of surgery in our retrospective cohort study. Although the crude risk of HIV-infected patients having any complication was 2.47 times greater than for uninfected persons, a logistic regression analysis demonstrated that controlling for known risk factors eliminates the significant difference in complication rates between infected and uninfected patients. We found the most important risk factor for complications to be ASA risk class.

The discordance between the crude and adjusted odds ratios found in our study may explain the variability in complication rates found in the literature. A review of published studies documented inconsistent complication rates among HIV-infected patients for all fields of surgery (12). The field with the narrowest range of complication rates was dental surgery, and even here the reported rates ranged from 1– 20%. In the literature of major abdominal surgery, complication rates in HIV-infected patients ranged from zero to an average of 1.6 complications per patient, and mortality rates ranged from 0–60% (12).

Few published studies used analytical methods to minimize confounding for surgical complications by known risk factors (12). In a review of 114 reports describing complications in HIV-infected patients (12), only 3 reports, all cohort studies, were notable for their rigorous study designs (14, 18, 19). Only one of these studies found significantly greater complication rates in HIV-infected patients, and only for minor complications (14).

In several recent reports, surgical complication rates were found to be greater in HIV-infected patients than in uninfected patients (20–23). However, in each of the studies, the groups were matched only by age and gender, not by clinical variables or ASA risk class.

Our study matched patients by procedure type, age and year of procedure and then compared the effect of known risk factors on the complication rates between infected and uninfected patients. Nearly twice as many HIV-in-

fected patients had emergency operations as did uninfected patients, and although not statistically significant, HIV-infected patients tended to have lower weight, serum albumin levels, platelet and WBC counts, and higher serum ALT and creatinine levels.

Our study had several important limitations. First, we studied patients who contracted HIV infection in the years before the general use of highly active antiretroviral therapy (HAART). However, current standard therapies are known to decrease the risk for bacterial infections, improve nutritional status, and increase life expectancy (24), and one might reasonably expect that patients would tolerate surgery even better in the HAART era. Second, our sample size was not great enough to determine the contribution of more than a few known risk factors for surgical complications. As a result, the study's power to rule out the contribution of each of the examined variables was relatively low. Although we found a relative risk of 0.72 for the association of HIV infection and surgical complications, the 95% confidence intervals ranged from 0.20 to 2.62. Third, the retrospective study design resulted in the exclusion of many patients because of incomplete study variables. Finally, we did not document the seronegative status of control patients. We did, however, exclude from the control group all patients with risk factors for HIV infection.

Conclusion

We found no evidence to support an independent effect of HIV infection on the risk of surgical complications. We found instead that ASA risk class, a measure of general health status and preoperative risk, most closely correlates with complication rates. HAART has resulted in sharply diminished morbidity and mortality of HIV-infected patients. Still to be determined is the effect of HAART on the risks and outcomes of surgery.

References

1. Burack JH, Mandel MS, Bizer LS. Emergency abdominal operations in the patient with acquired immunodeficiency syndrome. Arch Surg 1989; 124:285–286.
2. Carroll BJ, Rosenthal RJ, Philips EH, Bonet H. Complications of laparoscopic cholecystectomy in HIV and AIDS patients. Surg Endosc 1995; 9:874–878.
3. Potter DA, Danforth DN, Jr, Macher AM, et al. Evaluation of abdominal pain in the AIDS patient. Ann Surg 1984; 199:332–339.
4. Robinson G, Wilson SE, Williams RA. Surgery in patients with acquired immunodeficiency syndrome. Arch Surg 1987; 122:170–175.
5. Wexner SD, Smithy WB, Milsom JW. The surgical management of anorectal diseases in AIDS and pre-AIDS patients. Dis Colon Rectum 1986; 29:719–723.
6. Adolph MD, Bass SN, Lee SK, et al. Cytomegaloviral acalculous cholecystitis in acquired immunodeficiency syndrome patients. Am Surg 1993; 59:679– 684.
7. Binderow SR, Shaked AA. Acute appendicitis in patients with AIDS/HIV infection. Am J Surg 1991; 162:9–12.
8. Carillo EH, Carillo LE, Byers PM, et al. Penetrating trauma and emergency surgery in patients with AIDS. Am J Surg 1995; 170:341–344.
9. Heary RF, Hunt CD, Krieger AJ, Vaid C. HIV status does not affect microbiologic spectrum of neurologic outcome in spinal infections. Surg Neurol 1994; 42:417–423.
10. Whitney TM, Macho JR, Russell TR, et al. Appendicitis in acquired immunodeficiency syndrome. Am J Surg 1992; 164:467–471.
11. Wilson SE, Robinson G, Williams RA, et al. Acquired immune deficiency syndrome (AIDS). Indications for abdominal surgery, pathology and outcome. Ann Surg 1989; 210:428–434.
12. Rose DN, Collins M, Kleban R. Complications of surgery in HIV-infected patients. AIDS 1998; 12:2243– 2251.
13. Capelli MS, Godil A. Amulticenter case-controlled study of percutaneous endoscopic gastrostomy in HIV seropositive patients. Am J Gastroenterol 1993; 88:2059–2066.
14. Semprini AE, Castagna C, Ravizza M, et al. The incidence of complications after caesarian section in 156 HIV-positive women. AIDS 1995; 9:913– 917.
15. Centers for Disease Control and Prevention. 1993 revised classification system for HIV infection and expanded surveillance of definition for AIDS among adolescents and adults. MMWR Morb Mortal Wkly Rep 1992; 41(No. RR-17).
16. Dripps RD, Lamont A, Eckenhoff JE. The role of anesthesia in surgical mortality. JAMA1961; 178:261–266.
17. White H. A heterosketasticity-consistent covariance matrix estimator and a direct test for heterosketasticity. Econometrica 1980; 48:817–830.
18. Ayers J, Howton MJ, Layon AJ. Postoperative complications in patients with human immunodeficiency virus disease: clinical data and a literature review. Chest 1993; 103: 1800–1807.
19. Dodson TB. HIV status and the risk of postextraction complications. J Dent Res 1997; 76:1644–1652.
20. Bova R, Meagher A. Appendicitis in HIV-positive patients. Aust N Z J Surg 1998; 68(5):337–339.
21. Davis PA, Corless DJ, Gazzard BG, Wastell C. Increased risk of wound complications and poor healing following laparotomy in HIV-seropositive and AIDS patients. Dig Surg 1999; 16(1):60–67.
22. Maiques-Montesinos V, Cervera-Sanchez J, Bellver-Pradas J, et al. Post-cesarean section morbidity in HIV-positive women. Acta Obstet Gynecol Scand 1999; 78(9):789–792.
23. Morandi E, Merlini D, Salvaggio A, et al. Prospective study of healing time after hemorrhoidectomy: influence of HIV infection, acquired immunodeficiency syndrome, and anal wound infection. Dis Colon Rectum 1999; 42(9): 1140–1144.
24. Palella FJ, Delaney KM, Moorman, AC, et al. Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. N Engl J Med 1998; 338(13):853–860.