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Thirty-Day Postoperative Mortality Among Individuals With HIV Infection Receiving Antiretroviral Therapy and Procedure-Matched, Uninfected Comparators

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IMPORTANCE Antiretroviral therapy (ART) has converted human immunodeficiency virus (HIV) infection into a chronic condition, and patients now undergo a variety of surgical procedures, but current surgical outcomes are inadequately characterized.

OBJECTIVE To compare 30-day postoperative mortality in patients with HIV infection receiving ART with the rates in uninfected individuals.

DESIGN, SETTING, AND PARTICIPANTS Retrospective analysis of nationwide electronic medical record data from the US Veterans Health Administration Healthcare System, October 1, 1996, to September 30, 2010. Common inpatient surgical procedures were grouped using the Healthcare Cost and Utilization Project Clinical Classification System to match HIV-infected and uninfected patients in a 1:2 ratio. Data on 1641 patients with HIV infection receiving combination ART who were undergoing inpatient surgery were compared with data on 3282 procedure-matched, uninfected comparators. Poisson regression models of 30-day postoperative mortality were adjusted for procedure year, age, Charlson Comorbidity Index score, hemoglobin level, albumin level, HIV infection, CD4 cell count, and HIV-1 RNA level.

MAIN OUTCOMES AND MEASURES All-cause 30-day postoperative mortality.

RESULTS The most common procedures in both groups were cholecystectomy (10.5%), hip arthroplasty (10.5%), spine surgery (9.8%), herniorrhaphy (7.4%), and coronary artery bypass grafting (7.0%). In patients with HIV infection, CD4 cell distributions were 80.0% with 200/μL or more, 16.3% with 50/μL to 199/μL, and 3.7% with less than 50/μL; 74.1% of patients with HIV infection had undetectable HIV-1 RNA. Human immunodeficiency virus infection was associated with higher 30-day postoperative mortality compared with the mortality in uninfected patients (3.4% [56 patients]) vs 1.6% [53]); incidence rate ratio [IRR], 2.11; 95% CI, 1.41-3.17; $P < .001$). CD4 cell count was inversely associated with mortality, but HIV-1 RNA provided no additional information. After adjustment, patients with HIV infection had increased mortality compared with uninfected patients at all CD4 cell count strata (≥500/μL: IRR, 1.92; 95% CI, 1.02-3.60; $P = .04$; 200-499/μL: IRR, 1.89; 95% CI, 1.20-2.98; $P = .01$; 50-199/μL: IRR, 2.66; 95% CI, 1.29-5.47; $P = .01$; and <50/μL: IRR, 6.21; 95% CI, 3.55-10.85; $P < .001$). Hypoalbuminemia (IRR, 4.35; 95% CI, 2.78-6.81; $P < .001$) and age in decades (IRR, 1.47; 95% CI, 1.23-1.76; $P < .001$) were also strongly associated with mortality.

CONCLUSIONS AND RELEVANCE Current postoperative mortality rates among individuals with HIV infection who are receiving ART are low and are influenced as much by hypoalbuminemia and age as by CD4 cell status. Human immunodeficiency virus infection and CD4 cell count are only 2 of many factors associated with surgical outcomes that should be incorporated into surgical decision making.

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Antiretroviral therapy (ART) has transformed human immunodeficiency virus (HIV)/AIDS into a chronic disease with survival measured in decades,[1,2] and patients with HIV infection are now candidates for a range of surgical procedures; however, the relationship between improved overall survival and short-term surgical outcomes is unclear. Studies[3-9] published early in the HIV pandemic documented dramatically higher morbidity and mortality following surgical procedures in patients with HIV infection compared with uninfected individuals. More recent studies[10-15] in the ART era showed improved outcomes of selected surgical procedures. Indeed, successful solid-organ transplants in individuals with HIV infection are increasingly common, despite the challenges of managing organ rejection in immunocompromised patients.[16-19] The HIV-1 RNA and CD4 cell count may correlate with surgical outcomes and play a role in surgical decision making.[15,20-25]

The low population prevalence of HIV infection in the United States (estimated at 0.4%)[26] makes it difficult to monitor changing patterns of surgical outcomes among patients with HIV infection. Data collected from single institutions or even multi-institutional collaborative studies may have insufficient numbers to power meaningful analyses of important adverse outcomes, such as death. Two large, multispecialty surgical studies[15,25] examined outcomes in patients with HIV infection since the advent of combination ART and included operations through 2002; only 1 of these studies contained uninfected comparator patients. The effectiveness of ART has improved dramatically since that time, with most patients receiving ART now achieving HIV-1 RNA suppression and significant immune system reconstitution.[27] To our knowledge, no study has compared surgical outcomes among patients with HIV infection receiving modern ART and uninfected individuals matched by surgical procedure.

The Veterans Health Administration (VA) is the largest single provider of health care in the United States, with more than 5 million veterans receiving care,[28] including more than 40 000 HIV-infected veterans; this is one of the largest cohorts of patients receiving treatment for HIV infection in the world. The VA uses an electronic medical record and central data repositories containing nationwide clinical and administrative data. We used VA databases to examine postoperative 30-day mortality following a variety of common surgical procedures in a nationwide cohort of HIV-infected veterans receiving ART from October 1, 1996, to September 30, 2010, and uninfected comparator patients matched by procedure. We explored the current relationship between perioperative mortality and indicators of immune function, anemia, and hypoalbuminemia among HIV-infected and uninfected individuals. We hypothesized that the 30-day postoperative mortality rate of patients with HIV infection is relatively low and that non-HIV biomarkers have a major influence on outcomes.

Methods

The Veterans Aging Cohort Study Virtual Cohort (VACS-VC) uses VA clinical and administrative databases and a validated algorithm[29] to identify all HIV-infected veterans who received care within the VA from October 1, 1996, to September 30, 2010. The VACS-VC contains detailed data from the date of enrollment in the VA on 132 540 patients, including 44 180 HIV-infected veterans, and 2 uninfected comparator patients (n = 88 360) matched to each HIV-infected patient on age, sex, race, geographic region, and year of enrollment for VA care. The VACS-VC data include demographics, comorbid conditions, survival, medications, laboratory values, hospital admissions, outpatient treatment encounters, and diagnosis and procedure codes.

We studied mortality after major inpatient surgical procedures on patients in the VACS-VC. This study was approved by the institutional review boards of the VA Connecticut Healthcare System and Yale University, with a waiver of informed consent. The VACS-VC determines vital status by combining VA, Social Security Administration, and Medicare death data.[30] Using all major surgeries in VACS-VC patients would have led to an imbalance of procedure types between HIV-infected and uninfected patients, possibly distorting outcomes. To avoid this imbalance, we employed a surgical procedure matching protocol using the Healthcare Cost and Utilization Project Clinical Classification System (CCS)[31] based on groupings of *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*), procedure codes.[32] We selected for analysis CCS groupings of common major surgical procedures representing multiple surgical specialties performed on patients in the VACS-VC database (eTable in the Supplement) and then matched patients without replacement within CCS procedure categories, randomly selecting 1 HIV-infected patient receiving ART for every 2 uninfected patients. Unmatched patients were excluded from the analysis. After the matching was complete, we combined some CCS categories for descriptive and analytic purposes (eTable in the Supplement). When patients had several dates of surgery, only the first surgery date was used in the analysis. Multiple *ICD-9-CM* procedure codes on the same day were considered part of the same procedure; when hernias, appendectomies, and lysis of adhesions were performed with other procedures, they were analyzed as part of the primary procedure CCS grouping. The year of surgery was analyzed as a continuous variable using cubic splines and 3 knots.[33]

To adjust for comorbid disease in our regression analyses, we used *ICD-9-CM* codes and a modification of the Charlson Comorbidity Index[34-36] that omitted symptomatic HIV infection, since HIV infection was coded as a separate variable (*ICD-9-CM* codes 042-044).[15] For descriptive purposes, we also used *ICD-9-CM* diagnosis codes to define selected common comorbid conditions: cancer, congestive heart failure, coronary artery disease, diabetes mellitus, hepatitis C infection, hypertension, and renal insufficiency. Each comorbid condition was defined by the presence of at least 2 outpatient codes or 1 inpatient code recorded within 2 years before the date of surgery.[37] Age was calculated at the date of surgery. Race was categorized as white, black, or other.

Our analysis included laboratory values for serum hemoglobin, serum albumin, HIV-1 RNA, and CD4 cells. We used the most recent available laboratory values collected within 1 year

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of surgery. All laboratory data had nonnormal distributions and were categorized using clinically meaningful cut points. Serum hemoglobin less than 10 g/dL (to convert to grams per liter, multiply by 10) was classified as anemia, and serum albumin less than 3.5 g/dL (to convert to grams per liter, multiply by 10) was classified as hypoalbuminemia.[38] We allocated patients to 1 of 6 CD4 count categories (uninfected or HIV-infected and a CD4 cell count of ≥500/μL, 350-499/μL, 200-349/μL, 50-199/μL, or <50/μL).[38-40] The categories of HIV-1 RNA were *uninfected or HIV-infected with undetectable* (<500 copies/mL) or *HIV-infected with detectable* (≥500 copies/mL) HIV-1 RNA[41] (some early laboratories did not quantify values <500 copies/mL). We defined ART based on pharmacy fill and refill data as receiving a multidrug antiretroviral regimen within 30 days before surgery.

Demographics, comorbidities, and laboratory values were tabulated and compared using the Wilcoxon signed rank test for continuous variables and the χ^2 test for categorical variables. There were missing laboratory values for serum hemoglobin (11.6%) and serum albumin (17.4%) across all patients, and HIV-1 RNA (3.1%) and CD4 cell count (3.2%) in patients with HIV infection. Excluding cases with missing values may bias results[42]; thus, we used multiple imputation to impute missing laboratory data and analyze results. The imputation model included the outcome and all covariates and generated 10 imputed data sets. Results from regressions performed on the imputed data sets were combined using Rubin's rules.[43]

The primary study outcome was all-cause mortality within 30 days of surgery. Univariate Poisson regressions were used to assess the relationships between 30-day mortality and HIV infection, demographics, comorbidities, year and type of procedure, and laboratory values. We excluded variables from the multivariate model that did not reach statistical significance in the univariate regressions, and we collapsed categorical variable strata with similar outcomes. The low numbers of deaths precluded analyses of specific surgical procedures. We used multivariate models adjusted for year of surgery, age, Charlson Comorbidity Index score, hemoglobin level, and albumin level to explore the association between HIV infection, CD4 cell count, HIV-1 RNA, and mortality. All regressions used clustering on CCS procedure grouping. The data met the assumptions of a Poisson regression model (goodness-of-fit χ^2 = 830 651; $P > .99$). Analyses were performed using Stata, version 13 (StataCorp).

Results

The CCS matching procedure yielded an analysis cohort of 4923 eligible matched surgical patients: 1641 HIV infected and 3282 uninfected (**Table 1**). Age, sex, race, and Charlson Comorbidity Index scores were similar between the cohorts. Patients with HIV infection were more likely to have surgery later in the study (61.4% vs 50.2%; $P < .001$) and anemia (10.0% vs 6.9%; $P < .001$); 80.0% of the HIV-infected group had a CD4 cell count of 200/μL or more, 16.3% of the HIV-infected group had a CD4 cell count between 50 and 199/μL, 3.7% had a CD4 cell count of less than 50/μL, and 74.1% had undetectable HIV-1 RNA. The most common CCS surgical procedure groupings were cholecystectomy (10.5% [519 patients]), hip arthroplasty (10.5% [516]), spine surgery (9.8% [480]), herniorrhaphy (7.4% [363]), and coronary artery bypass grafting (7.0% [345]) (**Table 2**). One hundred nine patients (2.2%) died within 30 days of surgery; among the deaths, 8 (7.3%) occurred on the day of surgery, 77 (70.6%) during surgical hospitalization, and 24 (22.0%) after acute care discharge. Infection was the cause of death in only 1 (1.8%) HIV-infected patient and in 3 (5.7%) uninfected comparator patients.

HIV-Infected Patients

Patients with HIV infection had higher rates of unadjusted 30-day mortality compared with uninfected patients (3.4% [56 patients] vs 1.6% [53]; incidence rate ratio [IRR], 2.11; 95% CI, 1.41-3.17; $P < .001$). Age, Charlson Comorbidity Index score, anemia, and hypoalbuminemia also had significant associations with postoperative mortality (all $P < .001$). There was no association of 30-day mortality with race, and with only 1 female death the study was underpowered to examine sex. In analyses confined to patients with HIV infection, a univariate model of HIV-1 RNA showed no association with mortality (IRR, 1.53; 95% CI, 0.88-2.65; $P = .13$). A forest plot of a multivariate model containing both HIV-1 RNA and CD4 cell count (**Figure**) illustrated the lack of association between HIV-1 RNA and mortality, as well as the nearly identical mortality of patients in the CD4 cell counts of 200/μL to 349/μL and 350/μL to 499/μL strata. Thus, in subsequent models, we dropped HIV-1 RNA and used a collapsed CD4 cell count stratum of 200 to 499/μL. After adjusting for procedure year, age, Charlson Comorbidity Index score, hemoglobin, and albumin, we found no mortality difference between patients with HIV infection with a CD4 cell count of 500/μL or more and those with a CD4 cell count of 200/μL to 499/μL (IRR, 0.97; 95% CI, 0.48-1.96; $P = .92$) or a CD4 cell count of 50/μL to 199/μL (IRR, 1.38; 95% CI, 0.85-2.25; $P = .19$), and a marked increase when the CD4 cell count dropped below 50/μL (IRR, 3.15; 95% CI, 1.56-6.35; $P = .01$) (**Table 3**).

Comparing the Cohorts

Broadening the analysis to include both uninfected individuals and patients with HIV infection, in the univariate analysis uninfected patients had a 1.6% 30-day postoperative mortality rate, there was little mortality difference in patients with HIV infection with a CD4 cell count of 500/μL or more (2.2%; IRR, 1.34; 95% CI, 0.72-2.51; $P = .36$), and mortality was inversely correlated with lower CD4 cell counts of 200/μL to 499/μL (3.1%; IRR, 1.91; 95% CI, 1.20-3.05; $P = .01$), 50/μL to 199/μL (5.2%; IRR, 3.24; 95% CI, 1.59-6.58; $P = .01$), and less than 50/μL (11.7%; IRR, 7.18; 95% CI, 4.24-12.16; $P < .001$). After adjustment, compared with uninfected patients, patients with HIV infection with CD4 counts greater than 200/μL had approximately twice the mortality of uninfected patients, those with a CD4 cell count from 50/μL to 199/μL had slightly greater mortality (IRR, 2.66; 95% CI, 1.31-5.43; $P = .01$), and patients with a CD4 cell count of less than 50/μL had markedly increased mortality (IRR, 6.26; 95% CI, 3.38-11.69; $P < .001$) (Table 3).

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Table 1. Characteristics of HIV-Infected and Uninfected Surgery Patients

Characteristic	No. (%) HIV-Infected (n = 1641)	No. (%) Uninfected (n = 3282)	*P* Value
Age, median (IQR), y	54.3 (48.4-60.1)	54.5 (49.2-60.2)	.23
Male sex	16 216 (98.5)	3213 (97.9)	.16
Race			
White	722 (44.0)	1462 (44.6)	.32
African American	758 (46.2)	1541 (47.0)	
Other	161 (9.8)	279 (8.5)	
Charlson Comorbidity Index score, mean (SD)	1.41 (1.76)	1.47 (1.76)	.28
0	645 (39.3)	1244 (37.9)	
1	351 (21.4)	721 (22.0)	
2	348 (21.2)	649 (19.8)	
3	165 (10.1)	356 (10.9)	
≥4	132 (8.0)	312 (9.5)	
Comorbid conditions			
CAD	194 (11.8)	560 (17.1)	<.001
Cancer	202 (12.3)	261 (8.0)	<.001
CHF	54 (3.3)	160 (4.9)	.01
Diabetes mellitus	242 (14.8)	799 (24.3)	<.001
Hepatitis C	338 (20.6)	304 (9.3)	<.001
Hypertension	632 (38.5)	1672 (50.9)	<.001
Renal insufficiency	132 (8.0)	198 (6.0)	.01
Procedure years[a]			<.001
1996-1997	45 (2.7)	168 (5.1)	
1998-2004	589 (35.9)	1465 (44.6)	
2005-2009	830 (50.6)	1435 (43.6)	
2010	177 (10.8)	214 (6.5)	
Hemoglobin, g/dL			<.001
≥10	1477 (90.0)	3055 (93.1)	
<10	164 (10.0)	227 (6.9)	
Albumin, g/dL			.31
≥3.5	1180 (71.9)	2409 (73.4)	
<3.5	461 (28.1)	873 (26.6)	
CD4 count, cells/μL			
≥500	600 (36.5)	NA	
350-499	358 (21.8)	NA	
200-349	355 (21.7)	NA	
50-199	268 (16.3)	NA	
<50	60 (3.7)	NA	
HIV-1 RNA, copies/mL			
<500	1217 (74.1)	NA	
≥500	424 (25.9)	NA	

Abbreviations: CAD, coronary artery disease; CHF, congestive heart failure; HIV, human immunodeficiency virus; IQR, interquartile range; NA, not available.

SI conversion factors: To convert albumin and hemoglobin to grams per liter, multiply by 10.

[a] Procedure year categories were derived from cubic spline knots used in Poisson regressions.

Relative Importance of Other Predictive Factors

Hypoalbuminemia was present in 28.1% of our patients and had a larger effect on mortality than all but the lowest CD4 cell count stratum of less than 50/μL (Table 3). Stratified mortality estimates of the combined effects of CD4 cell count, age, and hypoalbuminemia demonstrated their relative contributions to 30-day mortality (**Table 4**). Age was also a significant mortality risk predictor: the adjusted increased postoperative mortality risk associated with HIV infection and a CD4 cell count higher than 200/μL was equivalent to that of an uninfected patient 16 years older; for a CD4 cell count 50/μL to 199/μL, an uninfected patient 25 years older; and for a CD4 cell count of less than 50/μL, an uninfected patient 47 years older.

Discussion

We used a nationwide cohort of US military veterans to assess the association between HIV infection and 30-day postoperative mortality in the modern HIV treatment era. Our study

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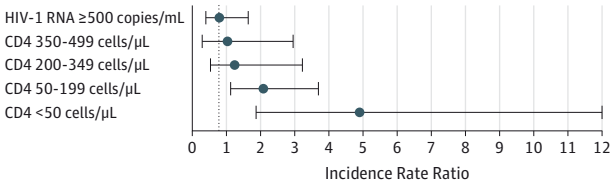
Table 2. CCS Groupings of Surgical Procedures[a]

CCS Grouping	No. (%) HIV-Infected	No. (%) Uninfected
Cholecystectomy	173 (10.5)	346 (10.5)
Open	58 (3.5)	116 (3.5)
Laparoscopic	115 (7.0)	230 (7.0)
Hip arthroplasty	172 (10.5)	344 (10.5)
Spine surgery	160 (9.8)	320 (9.8)
Herniorrhaphy	121 (7.4)	242 (7.4)
CABG	115 (7.0)	230 (7.0)
Colon, sigmoid, rectum resection	114 (7.0)	228 (7.0)
Vascular access	109 (6.6)	218 (6.6)
Lower extremity amputation	107 (6.5)	214 (6.5)
Appendectomy	90 (5.5)	180 (5.5)
Lobectomy or pneumonectomy	89 (5.4)	178 (5.4)
Peripheral vascular bypass	68 (4.1)	136 (4.1)
Heart valve surgery	53 (3.2)	106 (3.2)
Knee arthroplasty	40 (2.4)	80 (2.4)
Prostatectomy	39 (2.4)	78 (2.4)
Nephrectomy	38 (2.3)	76 (2.3)
Intracranial surgery	33 (2.0)	66 (2.0)
Endarterectomy	31 (1.9)	62 (1.9)
Radical lymph node dissection	31 (1.9)	62 (1.9)
Lysis of adhesions	30 (1.8)	60 (1.8)
Thyroidectomy	21 (1.3)	42 (1.3)
CABG plus heart valve surgery	7 (0.4)	14 (0.4)
Total	**1641** (100)	**3282** (100)

Abbreviations: CABG, coronary artery bypass graft; CCS, Clinical Classification System; HIV, human immunodeficiency virus.

[a] Based on groupings of *International Classification of Diseases, Ninth Revision, Clinical Modification*, procedure codes. See eTable in the Supplement for details of the groupings.

Figure. Relationship Between HIV-1 RNA, CD4 Cell Count, and 30-Day Postoperative Mortality in Patients With Human Immunodeficiency Virus (HIV) Receiving Antiretroviral Therapy



Limit lines indicate 95% CIs. The reference group was patients with HIV infection with a CD4 cell count of 500/μL or more and an undetectable HIV-1 RNA of less than 500 copies/mL (indicated by the vertical line).

Table 3. 30-Day Postoperative Mortality: Adjusted Multivariate Poisson Regressions[a]

Characterisic	IRR (95% CI)	*P* Value
HIV-Infected Patients		
CD4 count, cells/μL		
>500	1 [Reference]	
200-499	0.97 (0.48-1.96)	.92
50-199	1.38 (0.85-2.25)	.19
<50	3.15 (1.56-6.35)	.01
Age, per 10-y increase	1.60 (1.22-2.03)	.01
Charlson Comorbidity Index score	1.16 (1.06-1.28)	.01
Hemoglobin <10 g/dL	1.66 (0.82-3.37)	.16
Albumin <3.5 g/dL	4.30 (2.53-7.31)	<.001
All Patients		
HIV infection status and CD4 count, cells/μL		
Uninfected	1 [Reference]	
Infected		
≥500	1.92 (1.02-3.60)	.04
200-499	1.89 (1.20-2.98)	.01
50-199	2.66 (1.29-5.47)	.01
<50	6.21 (3.55-10.85)	<.001
Age, per 10-y increase	1.47 (1.23-1.76)	<.001
Charlson Comorbidity Index score	1.18 (1.09-1.27)	<.001
Hemoglobin <10 g/dL	1.37 (0.77-2.42)	.28
Albumin <3.5 g/dL	4.35 (2.78-6.81)	<.001

Abbreviations: HIV, human immunodeficiency virus; IRR, incidence rate ratio.

SI conversion factors: To convert albumin and hemoglobin to grams per liter, multiply by 10.

[a] Model was also adjusted by procedure year modeled using cubic splines.

offers significant advantages over the 2 other published ART-era multispecialty surgical outcomes studies[15,25] of patients with HIV infection. Horberg et al[15] studied 332 HIV-infected and HIV-noninfected patient pairs matched on surgical procedure in Northern California, but their study size was modest and the trial ended in 2002. Wiseman et al[25] studied 1322 HIV-infected surgery patients in British Columbia, but their study also ended in 2002 and they had no uninfected comparator group. The present study used a nationwide sample containing more patients with HIV infection who were receiving ART, an uninfected comparator group matched on surgical procedure, and data through 2010. Unlike earlier reports of high surgical mortality in HIV-infected individuals, the patients receiving ART in our study had a relatively low 3.4% rate of 30-day postoperative mortality. Furthermore, postoperative mortality in HIV-infected individuals is influenced as much by hypoalbuminemia and age as by HIV status. For example, after adjustment, HIV-infected individuals with a CD4 cell count higher than 200/μL can be expected to have a postoperative mortality rate similar to that in an uninfected individual 16 years older: surgery on a 50-year-old patient with HIV infection who is receiving ART has a 30-day mortality risk similar to that of a 66-year-old individual without the infection.

Surgery on patients with HIV infection in the early years of the HIV pandemic was accompanied by substantial complications and mortality. Worse outcomes were associated with active opportunistic infections, concurrent organ failure, low serum albumin, and low CD4 cell count.[3-9] Most of these surgical series were relatively small, from a single institution, and lacked a control group, instead using historical comparators to interpret the findings. Because the death and complication rates decreased with the development and dissemination of drugs used in ART in the mid-1990s, many studies were underpowered to examine fatalities, instead focusing on nonfatal complications, or longer follow-up intervals. Those few

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Table 4. Stratified, Adjusted 30-Day Postoperative Mortality Rates Estimated From Multivariate Poisson Regression[a]

Characteristic	Age, y	Albumin, g/dL	30-d Mortality, % (95% CI)
Uninfected	45	≥3.5	0.2 (0.0-0.4)
	65	≥3.5	0.4 (0.1-0.8)
	45	<3.5	0.9 (0.1-1.7)
	65	<3.5	1.9 (0.5-3.4)
HIV-infected, CD4, cells/μL			
≥500	45	≥3.5	0.4 (0.1-0.7)
	65	≥3.5	0.9 (0.3-1.4)
	45	<3.5	1.7 (0.4-3.0)
	65	<3.5	3.7 (1.3-6.2)
200-499	45	≥3.5	0.4 (0.1-0.7)
	65	≥3.5	0.8 (0.2-1.5)
	45	<3.5	1.7 (0.5-2.9)
	65	<3.5	3.7 (1.3-6.1)
50-199	45	≥3.5	0.5 (0.2-0.9)
	65	≥3.5	1.2 (0.3-2.1)
	45	<3.5	2.4 (0.9-3.9)
	65	<3.5	5.2 (1.7-8.6)
<50	45	≥3.5	1.3 (0.1-2.4)
	65	≥3.5	2.8 (0.4-5.1)
	45	<3.5	5.6 (3.9-10.7)
	65	<3.5	12.0 (16.9-22.4)

Abbreviations: HIV, human immunodeficiency virus; IRR, incidence rate ratio.

SI conversion factors: To convert albumin to grams per liter, multiply by 10.

[a] Mortality rates were adjusted using procedure year 2010 and mean values for Charlson Comorbidity Index score and hemoglobin level.

studies that examined death often were underpowered to perform multivariate analyses. Some reports continued to show increased complications[22,23,44-50] and death[44,46,49] in patients with HIV infection, but others documented declining rates of surgical complications and deaths in the HIV infection group that rivaled those experienced by uninfected individuals across many surgical specialties including orthopedics,[51-57] cardiovascular surgery,[13,58-61] bariatric surgery,[62] transplant surgery,[16,24,63] obstetrics,[10,11,64] urologic surgery,[65] neurosurgery,[66] and general surgery.[12,14,15]

Not all patients with HIV infection have the same prognosis. Patients receiving ART, especially those who maintain or regain immune function, are likely to have more favorable health outcomes. CD4 cell count is an indicator of immune system function.[67] The most common CD4 cell count threshold used in surgical decision making in patients with HIV infection has been 200/μL since the Centers for Disease Control and Prevention began classifying the CD4 cell count into 3 categories: 500/μL or more, 200/μL to 499/μL, and less than 200/μL.[39] Some reports[3,6,20,46,49,68-71] have shown worse outcomes associated with a CD4 cell count of less than 200/μL, whereas others[15,48,72,73] have not. The CD4 threshold of 200/μL has also been used as a criterion for inclusion in studies[24,74] of solid-organ transplantation in patients with HIV infection.

In our study, HIV infection was associated with a postoperative mortality rate approximately twice that of uninfected individuals, and among patients with HIV infection, a CD4 cell count of less than 50/μL was associated with a substantially higher rate of mortality (Table 3). These findings are similar to those of the 2 large ART era multispecialty surgical case series that identified a CD4 threshold of 50/μL as the best predictor of morbidity[15] or mortality,[25] with other CD4 count values not providing meaningful mortality discrimination. Our larger number of patients and case matching methods may explain why we were able to document an additional CD4 cell count mortality threshold of 200/μL. Only 3.7% of our patients had a CD4 cell count of less than 50/μL, which is consistent with data indicating that nearly all patients with HIV infection receiving ART are currently maintaining CD4 cell counts of more than 50/μL.[27] The markedly elevated 30-day postoperative mortality rate associated with a CD4 cell count of less than 50/μL is thus relevant for only a small portion of modern surgical patients with HIV infection receiving ART.

We did not find an independent effect of HIV-1 RNA on perioperative mortality. Some studies have shown an association between HIV-1 RNA and postoperative complications,[15,63] but others failed to show an independent association between HIV-1 RNA and postoperative mortality[25,44,46] or complications.[9,44,64] A total of 74.1% of our patients had undetectable HIV-1 RNA at the time of surgery; this is a proportion similar to estimates based on US Department of Health and Human Services data indicating that 78% of patients receiving ART have HIV-1 RNA of less than 200 copies/mL.[75] In our study, CD4 cell count was highly predictive of mortality, but HIV-1 RNA provided no additional information. All of our HIV-infected study population was receiving ART, thereby lowering HIV-1 RNA levels and reducing variation and predictive power.

The association between HIV infection, CD4 cell count, and mortality must be viewed in the context of other factors associated with perioperative mortality. Many uninfected patients have postoperative risks that exceed those of HIV-

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infected patients with CD4 cell counts above 200/μL. For example, a 45-year-old HIV-infected patient with a CD4 cell count of 200/μL or more had a lower rate of 30-day postoperative mortality than did any 65-year-old uninfected patient or a 45-year-old uninfected patient with hypoalbuminemia (Table 4).

Limitations

The low mortality rate required us to pool results across surgical procedures, and we cannot say whether the mortality differential was uniform across various types of surgery. We studied a veteran population consisting primarily of men. Despite procedure matching and multivariate adjustment, there may be factors associated with postoperative mortality not captured in the VACS-VC database and unevenly distributed by HIV status or among patients with HIV infection with different HIV-1 RNA levels or CD4 cell counts. Our analysis was limited to 30-day postoperative mortality. Although analyses about 30-day postoperative mortality are valuable and mortality correlates with complications, clinicians and patients will be interested in future studies about the relationship between HIV infection and postoperative complications (eg, infection, myocardial infarction), disease-specific outcomes (eg, spinal fusion rates, vascular graft patency), and patient-oriented outcomes (eg, health-related quality of life, functional status, and pain).

Conclusions

Among HIV-infected patients receiving ART, modern postoperative mortality rates are low and lower CD4 cell counts are associated with increased mortality, but characteristics other than HIV status, such as age and hypoalbuminemia, are also important determinants of outcome. Clinicians and patients should consider HIV infection and CD4 cell count as just 2 of many factors associated with surgical outcomes that should be incorporated into surgical decision making.

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Study concept and design: King, Perkal, Rosenthal, Gordon, Crystal, Rodriguez-Barradas, Gibert, Rimland, Justice.
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