

Research Article

Morbidity & Mortality in Patients with Human Immunodeficiency Virus Infection Undergoing Open Heart Surgery in an Integrated Healthcare System

Antonio Hernandez Conte, MD, MBA, FASA^{1,2*}; Sampreeti Chowdhuri, MD³; Alice R Pressman, PhD, MS^{2,4}; Su-Jau T Yang, MS⁵; Alexander A Argame, BS²; Chunyuan Qiu, MD⁶; Janet Hobbs⁷; Dhaval Trivedi, MD⁸; Blanding Jones, MD⁸

¹Department of Anesthesiology, Kaiser Permanente Los Angeles Medical Center, USA

²Department of Health Systems Science, Kaiser Permanente Bernard J. Tyson School of Medicine, USA

³Department of Anesthesiology, University of California, San Diego, USA

⁴Department of Epidemiology and Biostatistics, University of California, USA

⁵Kaiser Permanente Regional Research, USA

⁶Department of Anesthesiology, Kaiser Permanente Baldwin Park Medical Center, USA

⁷Kaiser Permanente Medical Library Services, USA

⁸Department of Cardiac Surgery, Kaiser Permanente Los Angeles Medical Center, Los Angeles, USA

***Corresponding author: Antonio Hernandez Conte, MD, MBA, FASA**

Kaiser Permanente Los Angeles Medical Center, Department of Anesthesiology, 4867 Sunset Blvd., 1st Floor, Los Angeles, California 90027, USA.

Tel: (323) 573-3900; Fax: (323) 783-8722

Email: Antonio.Conte@kp.org

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Abstract

Objective: This study sought to evaluate presurgical HIV-related immune characteristics and elucidate outcomes in HIV+ patients who underwent open heart cardiac surgery.

Design: Retrospective IRB-approved study utilizing hospital electronic medical records and Society of Thoracic Surgeons database. The study was conducted within a single integrated healthcare system where subjects underwent surgery at two hospitals.

Participants: Subjects were HIV+ patients who underwent open heart cardiac surgery from January 1, 2000 to December 31, 2021 and followed for a period of two years postoperatively. Data review with no active interventions; subjects had undergone open heart surgery.

Results: Patient characteristics, co-morbidities, and outcomes were compared in patients with HIV detectable viral load (HIV-DTL) versus undetectable (HIV-UDL) viral load at the time of surgery. 90.2% of patients with UDL viral load were being treated with ART at the time of surgery, versus only 9.8% of DTL patients ($p = 0.02$). However, there was no significant differences between CD4+ cell counts between patients with DTL vs UDL viral loads ($p = 0.83$). Additionally, both groups had a wide range of CD4+ counts with both groups having a wide range of CD4+ counts (137 – 1733 cells/mm³ in UDL patients vs 224 – 1467 cells/mm³ in DTL patients). Post-operatively, no patients had surgical site infections within 30 days of surgery or sternal wound infection within 90 days of surgery. 2-year mortality rate post-operatively was 9.7% overall with no differences between the two groups.

Conclusions: This study demonstrated differences in patient comorbidities between patients with HIV-DTL versus HIV-UDL viral load, including higher incidence of Type II diabetes and lower platelet count. This study found that HIV+ patients regardless of HIV viral load had positive outcomes overall including low 2-year mortality rates and low incidence of post-operative surgical site/sternal wound infections. Our findings indicate that well managed HIV+ patients on antiretroviral therapy within an integrated healthcare system can safely undergo cardiac surgery.

Keywords: Human immunodeficiency virus; Acquired immune deficiency syndrome; Cardiac surgery

Abbreviations: AIDS: Acquired Immune Deficiency Syndrome; ART: Anti-Retroviral Therapy; ASA: American Society of Anesthesiologists; CABG: Coronary Artery Bypass Graft; CPB: Cardio Pulmonary Bypass; HIV-DTL: HIV Detectable Viral Load; HIV: Human Immunodeficiency Virus; ICU: Intensive Care Unit; STS: Society of Thoracic Surgeons; HIV-UDL: HIV Undetectable viral load

Introduction

An estimated 39 million people are infected with the Human Immunodeficiency Virus-1 (HIV+) worldwide; among them, approximately 1.2 million live in the United States with 40,000 new infections annually [1]. Patients who are positive for HIV+ encompass a broad clinical spectrum of disease and a wide range of immunologic function compromises [2]. HIV antiretroviral therapy (ART) has dramatically improved long-term survival for HIV+ patients who adhere to therapy [3,4].

An association between HIV and cardiovascular disease, especially late-stage infection, was identified in the pre-ART era as early as the 1990s. Clinical and post-mortem reports from the pre-ART era have suggested that patients infected with HIV are at an increased risk for cardiovascular disease secondary to associated comorbidities, opportunistic infections, traditional cardiovascular risk factors, and infection with HIV itself [5-8]. While ART has significantly improved the long-term prognosis of patients with HIV, ART itself, has also been associated with numerous comorbidities [9]. Atherosclerosis, dyslipidemia, diabetes mellitus, lipodystrophy, renal function changes, osteopenia, and non-AIDS-defining cancers are increasingly described as occurring prematurely in multiple HIV cohorts [10-13].

Of particular interest is the phenomenon of premature atherosclerosis and associated cardiac disease in HIV patients [14-16]. Compounding the association of HIV and cardiovascular disease, the increased lifespan for HIV+ patients taking ART creates an increased opportunity for chronic degenerative diseases such as cardiovascular disease and accompanying variety of surgeries, including open heart surgeries, the risk of which is almost doubled in HIV+ patients [17,18].

In fact, the development of cardiovascular disease in HIV+ patients has become one of the most significant issues in HIV medicine [19-28]. The relative perioperative risk of HIV+ patients undergoing elective surgeries, including cardiac surgery, has become better understood in the last decade [29-31]. This study's primary goal was to evaluate the impact of HIV infection (detectable vs. undetectable viral load) on surgical site infection(s) development among individuals who are HIV+ and undergo cardiovascular surgery in an integrated health care system. Our secondary goal was to study the relationship between HIV infection/viral load upon short- and long-term mortality in this surgical population.

Methods

This study is a retrospective review of HIV+ patients aged 18 to 80 who have undergone cardiothoracic surgery from January 1, 2000, to December 31, 2021, at a single tertiary medical center within the Kaiser Permanente health system in southern California (KP SCAL). KP SCAL is a vertically and horizontally integrated health system actively managing 4.5 million patients who purchase health insurance to access health care within this closed system in south. Patients less than 18 years of age were excluded from the study. The KP SCAL's institutional Review Board approved this study, and subjects were not required to provide informed consent for this data-only study. Patients who underwent any cardiothoracic open-heart surgery requiring

cardiopulmonary bypass (i.e., coronary artery bypass grafting, valve(s) repair/replacement, and aortic surgery) were included in the study. This study did not include patients who had cardiologic percutaneous procedures such as transaortic valve replacement or assist devices.

Patient data points included assessment of general demographic information, past medical history, co-morbid conditions, detailed HIV history, all medications including ART history, baseline immunologic laboratory parameters, baseline laboratory data, postoperative intensive unit data, survival data, complications, and ICU length-of-stay.

The study subjects were categorized into two groups: 1) *HIV-infected with undetectable* (HIV-1RNA <100 copies/mL) viral load (HIV-UDL) or 2) *HIV-infected with detectable* (HIV-1RNA ≥100 copies/mL) viral load (HIV-DTL). We defined ART adherence based on pharmacy fill and refill data as receiving a multi-drug antiretroviral regimen within 30 days before surgery. Data was extracted from multiple sources, including hospital electronic medical records, institutional HIV Registry, and the *Society of Thoracic Surgeons (STS) Adult Cardiac Surgery Database* [32]. Due to the sensitive nature of HIV patient data, all data was protected to maintain patient confidentiality. Data was encoded, and patient names were anonymized and protected using the National Institutes of Health process for "highly confidential information," as well as Kaiser Permanente institutional HIV data protection guidelines.

Data Analysis

The resultant sample size was determined by the number of HIV+ patients having undergone cardiothoracic surgery within the study dates in our healthcare system (data from all eligible patients). Descriptive and inferential statistics were utilized to evaluate the study outcomes. All study patients were classified into one of two groups: HIV-DTL or HIV-UDL. All summary results are presented as mean and standard deviation for continuous variables; categorical variables are presented as numbers and percentages. Wilcoxon rank sum tests for continuous variables and Chi-square tests for categorical variables were used to compare the groups. All analyses were conducted using SAS EG version 8.2 (SAS INC, Cary, NC, USA), and $p < 0.05$ was considered statistically significant.

Results

Among the 65 HIV+ patients who met eligibility criteria, three patients were excluded due to unknown status of HIV-RNA1 viral load. The final study cohort included 53 HIV-UDL and 9 HIV-DTL patients.

Age, Sex, and BMI were similar between the two groups (Table 1). Racial differences were apparent between the two groups with a higher proportion of white individuals in the HIV-UDL than the HIV-DTL (49% vs 33%, $P=0.38$). All patients were classified as American Society of Anesthesiologists (ASA) Category IV as a result of their severe systemic disease related to cardiovascular disease. Case type (elective vs. urgent) was evenly split amongst patients in the HIV-UDL group, while

Table 1: Demographics.

	HIV+ Viral Load Undetectable	HIV+ Viral Load Detectable	P-Value
	N=53	N=9	
Age	60.4 (10.4)	57.4 (11.6)	0.53
Sex (Male)	51 (96.2%)	9 (100%)	0.55
Race			0.38
Caucasian	26 (49.1%)	3 (33.3%)	
Non-Caucasian	27 (50.9%)	6 (66.7%)	
Body Mass Index	27.1 (5.8)	27.6 (5.1)	0.71
ASA Status			NA
I	0	0	
II	0	0	
III	0	0	
IV	53 (100%)	9 (100%)	
Case Type			0.28
Elective	28 (52.8%)	3 (33.3%)	
Urgent	25 (47.2%)	6 (66.7%)	
Type of Surgery			0.54
CABG	27 (50.9%)	3 (33.3%)	
Valve	17 (32.1%)	3 (33.3%)	
CABG+Valve	7 (13.2%)	2 (22.2%)	
Aorta	1 (1.9%)	0 (0%)	
Other	1 (1.9%)	1 (11.1%)	

HIV; Human Immunodeficiency Virus-1; ASA: American Society of Anesthesiologists; CABG: coronary artery bypass graft.

Data presented as mean (STD) for continuous variables.

Table 2: Human Immunodeficiency Virus History & Immune Characteristics.

	HIV+ Viral Load Undetectable	HIV+Viral Load Detectable	P-Value
	N=53	N=9	
HIV Risk Factor/Mode of HIV transmission			0.03
Men/Bisexual	34 (64.2%)	9 (100%)	
Other	19 (35.8%)	0 (0%)	
Hx of Previous AIDS	37 (69.8%)	4 (44.4%)	0.14
Years of HIV Infection	11.9 (7.6)	9.3 (8.6)	0.41
Years on Highly Active Antiretroviral Therapy	10.5 (6.6)	7.4 (7.5)	0.23
HAART at Time of Surgery	46 (86.8%)	5 (55.6%)	0.02
NRTI	36 (67.9%)	6 (66.7%)	0.94
NNRTI	19 (35.8%)	3 (33.3%)	0.88
PI	27 (50.9%)	5 (55.6%)	0.80
INSTI	19 (35.8%)	3 (33.3%)	0.88
Other	24 (45.3%)	3 (33.3%)	0.50
Other HAART	4 (7.5%)	1 (11.1%)	0.72
CD4+ Cell Count Prior to Surgery	615.9 (371.1)	620.9 (352.7)	0.83
CD8+ Cell Count	963.7 (541.6)	1231.3 (559.0)	0.12
CD4+/CD8+ Ratio	0.8 (0.6)	0.6 (0.4)	0.44
White Blood Cell Count	6.9 (2.3)	6.3 (2.2)	0.21
Hematocrit	38.9 (5.9)	37.6 (4.1)	0.44
Platelets	176757 (64723)	115000 (27404)	0.07
Creatinine	1.3 (1.5)	1.7 (1.9)	0.62

Data presented as mean (STD) for continuous variables. P-value<0.05 was considered statistically significant.

HIV: Human Immunodeficiency Virus-1; AIDS: Acquired Immune Deficiency Syndrome; HAART: Highly Active Antiretroviral Therapy; NRTI: Nucleoside Reverse Transcriptase Inhibitors; NNRTI: Nucleoside Reverse Transcriptase Inhibitors; PI: Protease Inhibitors; INSTI: Integrase Strand Transfer Inhibitors.

Data presented as mean (STD) for continuous variables.

P-value<0.05 was considered statistically significant.

two-thirds of the HIV-DTL patients were urgent cases. (53% vs. 66.7%, P=0.28). A minority of patients underwent a combined CABG/valve procedure (13% and 22% for HIV-UDL and HIV-DTL, respectively), while most had a single procedure.

Patients with detectable HIV viral load all acquired HIV from men having sex with men (MSM) transmission, while two-thirds of the HIV-UDL group had this mode of transmission (100% vs 64%, P=0.03) (Table 2). At the time of surgery, compared with HIV-DTL, a larger proportion of HIV-UDL were taking HAART (86.8% vs. 55.6%, p= 0.02). Although not statistically significantly different, compared with the HIV-DTL group, the HIV-UDL was more likely to have a history of Acquired Immune Deficiency Syndrome (AIDS) (69.8% vs. 44.4%, P=0.14), had lived with HIV for longer (11.9 vs. 9.3 years, P=0.41) and been on ART for a longer period of time (10.5 vs. 7.4 years, P=0.23). Patients in both groups were taking various ART therapies, with nucleoside reverse transcriptase inhibitors most commonly identified. Both patient groups had low normal CD4+ cell counts before surgery (615.9 and 620.9 cell/ml³ for HIV-UDL and HIV-DTL respectively). Notably, patients in HIV-UDL group had a higher platelet count than patients in the HIV-DTL (176,767 vs. 115,000, p = 0.07).

Preoperative infective endocarditis was present at twice the proportion in the HIV-DTL group compared with the HIV-UDL group, however, this was not statistically significant (22.2% vs. 11.3%, P=0.37), and there were no notable group differences for the presence of preoperative chronic lung disease, cancer, liver disease, cerebrovascular disease, illicit drug use, tobacco use, or alcohol use (Table 3).

Patients in the HIV-UDL group were more likely to have received a previous cardiac intervention (i.e. percutaneous coronary stent), although the difference was not statistically significant (18.9% vs 0%, P = 0.15) (Table 4). More than 60% of patients had an assigned diagnosis of heart failure prior to surgery. The majority of the study subjects were placed on preoperative angiotensin-converting enzyme inhibitors and preoperative β -blockers, indicating that their cardiac conditions were actively monitored and managed. During the perioperative course, blood products were administered less frequently for HIV-UDL patients than HIV-DTL patients (35.8% vs. 66.7%, P=0.08). Red blood cells were the blood product most commonly delivered to patients perioperatively.

Overall, postoperative complications were rare, including postoperative reintubation, readmission to the ICU, surgical site infections within 30 days of surgery, or sternal wound infections

Table 3: Co-Morbidities.

	HIV+ Viral Load Undetectable	HIV+ Viral Load Detectable	P-Value
	N=53	N=9	
Infective Endocarditis	6 (11.3%)	2 (22.2%)	0.37
Chronic Lung Disease	6 (11.3%)	1 (11.1%)	0.99
Illicit Drug Use within 1 year prior to Surgery	1 (1.9%)	0 (0%)	0.68
Liver Disease	6 (11.3%)	1 (11.1%)	0.99
Cancer	1 (1.9%)	0 (0%)	0.68
Cerebrovascular Disease	6 (11.3%)	1 (11.1%)	0.99
Cerebrovascular Accident in past	5 (9.4%)	1 (11.1%)	0.88
Tobacco Use	15 (28.3%)	2 (22.2%)	0.71
Alcohol Use	4 (7.5%)	1 (11.1%)	0.72

Table 4: Cardiac History, Status & Perioperative Course.

	HIV+ Viral Load Undetectable	HIV+ Viral Load Detectable	P-Value
	N=53	N=9	
Previous Cardiac Interventions	10 (18.9%)	0 (0%)	0.15
Previous CABG	1 (1.9%)	0 (0%)	0.68
Previous Percutaneous Coronary Intervention (stent)	6 (11.3%)	0 (0%)	0.29
Previous MI	15 (28.3%)	2 (22.2%)	0.71
Preoperative Cardiac Status	-	-	-
NYHA Heart Failure*	33 (62.3%)	6 (66.7%)	0.80
PreOP ACE-Inhibitor	21 (39.6%)	4 (44.4%)	0.79
PreOP Beta-Blocker	33 (62.3%)	4 (44.4%)	0.31
Mechanical Assist Devices			
Intra-Aortic Balloon Pump	3 (5.6%)	0 (0%)	0.46
ECMO	0 (0%)	0 (0%)	NA
Perioperative Course			
Blood Products Use Perioperatively (within 24 hours surgery)	19 (35.8%)	6 (66.7%)	0.08
Red Blood Cells			0.17
None	36 (67.9%)	4 (44.4%)	
1- 6 Unit	17 (32.1%)	5 (55.6%)	
Fresh Frozen Plasma			0.48
None	46 (86.8%)	7 (77.8%)	
1- 6 Unit	7 (13.2%)	2 (22.2%)	
Cryoprecipitate			0.72
None	49 (92.5%)	8 (88.9%)	
1- 6 Unit	4 (7.5%)	1 (11.1%)	
Platelets			0.75
None	45 (84.9%)	8 (88.9%)	
1- 6 Unit	8 (15.1%)	1 (11.1%)	

CABG: Coronary Artery Bypass Grafts; MI: Myocardial Infarction; ACE: Angiotensin Converting Enzyme
 *NYHA: New York Heart Association Classification standards.

within 90 days of surgery (Table 5). There were no statistically significant differences between groups for any perioperative complication. Seven patients were readmitted to the hospital, all in the HIV-UDL group. There were no cases of operative mortality, a single death at 30-day post-surgery (HIV-UDL group), two additional deaths 1-year post-surgery, and three additional deaths two years post-surgery, with no significant differences between groups.

Discussion

In this retrospective analysis of HIV+ patients undergoing cardiothoracic surgery at a single tertiary medical center within a large integrated healthcare system, we found that cardiovascular surgery is safe in HIV+ patients regardless of detectable HIV viral load. Both groups of HIV+ patients experienced overall positive outcomes, minimal rates of post-surgical infection, complications, and mortality. Patients with detectable viral loads tended to be more likely to undergo urgent surgery and less likely to have received previous cardiac interventions than those with undetectable viral loads.

Complication rates were very low in our cohort, with no surgical site infections within 30 days of surgery and no sternal wound infection within 90 days. There were also no incident cases of sepsis, and only one patient with an undetectable viral

Table 5: Surgical Infections, Complications, & Mortality.

	HIV+ Viral Load Undetectable	HIV+ Viral Load Detectable	P-Value
	N=53	N=9	
Reintubation postoperative	1 (1.9%)	0 (0%)	0.68
ICU Readmission	1 (1.9%)	1 (11.1%)	0.15
Surgical Site Infection within 30 days of Surgery	0	0	
Sternal Wound Infections within 90 Days of Surgery	0	0	
Reoperation for Bleeding	1 (1.9%)	1 (11.1%)	0.15
Reoperation for Any/All Reasons	2 (3.8%)	0 (0%)	0.55
Sepsis	0	0	
Stroke	0	0	
Pneumonia	1 (1.9%)	0 (0%)	0.68
Renal Failure	0	0	
New Rhythm Change Requiring Pacemaker	5 (9.4%)	1 (11.1%)	0.88
New Onset Atrial Fibrillation	11 (20.8%)	2 (22.2%)	0.92
Readmission to Hospital	7 (13.2%)	0 (0%)	0.46
Readmission Reason			
Arrhythmia	1 (1.9%)	0 (0%)	
CHF	2 (3.8%)	0 (0%)	
Respiratory/Pneumonia	2 (3.8%)	0 (0%)	
Other	2 (3.8%)	0 (0%)	
Mortality			
Operative Mortality	0	0	NA
30-day death post-surgery	1 (1.9%)	0 (0%)	0.68
1-year death post-surgery, cumulative	3 (5.7%)	0 (0%)	0.46
2-year death post-surgery, cumulative	5 (9.4%)	1 (11.1%)	0.88

load experienced post-surgical pneumonia (1.9%). Other studies have also previously evaluated post-surgical infection rates of HIV+ patients. One retrospective analysis by Wollner *et al.* of 16 HIV+ patients undergoing isolated CABG between 2005 and 2018 reported no sternal wound infection or mediastinitis [33]. In an older retrospective review by Trachiotis *et al.* evaluated 37 HIV+ patients undergoing CABG and valve replacement procedures, authors reported a 13.5% rate of post-surgical wound infection, 2.7% rate of deep sternal infection, and 5.4% rate of sepsis [34]. We evaluated patient mortality intraoperatively and postoperatively at 30 days, 60 days, 90 days, 1 year, and 2 years. There were no cases of operative mortality in our patient population and <10% cumulative postoperative mortality within 2 years of cardiovascular surgery. One rationale for improvements in mortality over time may be the decreased incidence of endocarditis in HIV+ patient populations. As a result, fewer patients are receiving surgery due to endocarditis, and more are receiving surgery due to the burden of chronic disease amongst HIV patients, which may impact the chances for survival in this patient population.

Our findings indicate that even patients with sub-optimal control of their HIV infection may safely undergo cardiac surgery. This may be due in part to advancements in surgical technique and perioperative management within an integrated healthcare system with active cross-communication between primary care providers and specialists. Another possible explanation for the positive outcomes in our patient population may be a result of model of care delivered within an integrated health system. The role of integrated health systems offers many advantages, however, this remains an area that warrants further research [35].

Caring for HIV+ patients undergoing cardiac surgery requires a multidisciplinary team of cardiologists, surgeons, primary care physicians, anesthesiologists, nurses, physical therapists and infectious disease specialists. An integrated health system allows for improved communication amongst highly specialized physicians and consistent team delivery, which may lead to improved care coordination. One recent study indicates that dyad familiarity between surgeon and anesthesiologist can reduce post-operative morbidities and mortalities for complicated surgeries [36]. In addition, our health plan model covers all patients similarly, removing significant financial barriers to care access. One study evaluating quality performance measures in the treatment of HIV+ patients in an extensive integrated health system found that the overall mortality rate of HIV+ patients is 50% of the national average for similar patients, indicating that an integrated health system model may be conducive to the higher quality of care in the treatment of HIV+ patients [37].

Patient demographics and clinical characteristics in our study were somewhat comparable to those of other studies which evaluated HIV+ patients undergoing cardiothoracic surgery. However, in contrast to the Robich et al. study, in which HIV+ patients were more likely to have valve procedures, our study found that CABG procedures were the most common cardiac surgery performed [38]. While not statistically significant, our study revealed that within our healthcare system, HIV+ patients with detectable HIV viral loads had a higher incidence of urgent/emergent surgery compared to HIV+ patients with undetectable viral loads. This contrast between groups may indicate that preoperative characteristics of HIV+ patients, such as detectable viral load, may contribute to the likelihood of increased need or urgency for surgery. Our study suggests that there may be subtle differences in the urgency for cardiac surgery in HIV+ patients with detectable viral load, despite having low-normal CD4 cell counts.

A cohort study of the National Inpatient Sample (United States) observing rates of cardiac procedures found that patients with asymptomatic HIV infection received cardiac interventions at the same rate as uninfected adults hospitalized with the Acute Coronary Syndrome (ACS). Even over the past ten years, patients with symptomatic HIV/AIDS were less likely to undergo cardiac intervention (cardiac catheterization, percutaneous coronary intervention, and coronary artery bypass grafting) than uninfected adults hospitalized with ACS [39]. Therefore, in our study cohort, differences in cardiac intervention may partially be explained by differences in the history of prior AIDS since patients with detectable viral load had a higher percentage of previous AIDS history. Overall, our findings, in combination with previous research, indicate that patients with higher viral load tend to receive lower rates of cardiac intervention. Our findings also indicate that outcomes of cardiac intervention in HIV patients are generally positive irrespective of viral load. Further research is likely needed in this sector.

Despite differences in HIV viral load within our study cohort, both groups of HIV+ patients in our study had CD4 counts that averaged in the low normal range. HIV infection has a predilection and resultant cytotoxicity for CD4+ T-cells; persistent, untreated HIV infection leads to the eventual depletion of CD4+ T-cells over approximately ten to twelve years. Whereas non-HIV-infected patients have a CD4+ T-cell count of 500 to 1500 cells/ml³, HIV+ patients may manifest significantly compromised CD4+ T-cell counts well below the normal range at the initial diagnosis or presentation for cardiac surgery.

We offer two explanations for this noted similarity between the two groups. First, older recommendations for ART initiation did not advocate beginning anti-viral therapy until CD4+ T-cell counts diminished below 350 cells/ml³, while newer recommendations suggest that ART should be initiated before CD4+ cells decrease below 500 cells/ml³. Therefore, even HIV+ patients in the ART era can have a relatively large range of CD4+ T-cell counts. Second, HIV viral loads may sometimes become detectable despite compliance with ART, therefore, this may reflect the natural variation. Detectable HIV viral load and low CD4+ cell count are both important prognostic indicators of surgical outcomes in HIV+ patients undergoing a wide range of surgical procedures [40].

The main limitation of our study was a small sample size. As a result of the small sample size, some clinically meaningful differences between the two groups of patients were not statistically significant. The low incidence of HIV infection in the United States makes it difficult to study large cohorts of HIV+ patients who receive care within a closely coordinated system. Additionally, care provided in an integrated health system may not be generalizable to traditional non-integrated health systems in the United States. Further studies may be done to explore differences in mortality and outcomes between HIV+ patients and uninfected patients undergoing cardiovascular procedures within an integrated health system.

Overall, our study found that cardiovascular surgery is safe in HIV+ patients regardless of detectable HIV viral load; both groups of HIV+ patients experienced overall positive outcomes and minimal post-surgical infection, complications, and mortality rates.

Patients with detectable HIV viral loads tended to be more likely to undergo urgent surgery and less likely to have received previous cardiac interventions than patients with undetectable viral loads. However, despite patients with detectable viral load presenting more urgently for their surgeries, their post-surgical outcomes, infection rates, and mortality rates were low and not statistically significantly different from those of patients with detectable viral load.

Our findings indicate that even patients with sub-optimal control of their HIV infection may safely undergo cardiac surgery with proper perioperative management.

References

1. <https://www.who.int/data/gho/data/themes/hiv-aids/hiv-aids#:~:text=Since%20the%20beginning%20of%20the,at%20the%20end%20of%202022>
2. Farizo KM, Buehler JW, Chamberland ME, White BM, Froelicher ES, Hopkins SG, et al. Spectrum of disease in persons with Human Immunodeficiency Virus infection in the United States. *JAMA*. 1992; 267: 1798-805.

3. Lohse N, Hansen AB, Pedersen G, Kronborg G, Gerstoft J, Sorensen HT, et al. Survival of persons with and without HIV infection in Denmark, 1995-2005. *Annals of Internal Medicine*. 2007; 146: 87-95.
4. Palella FJ, Baker RK, Moorman AC, Chmiel JS, Wood KC, Brooks JT, et al. Mortality in the highly active antiretroviral therapy era, changing causes of death and disease in the HIV outpatient study. *J Acquir Immune Defic Syndr*. 2006; 43: 27-34.
5. Currie PF, Jacob AG, Foreman AR, Elton RA, Brettell RP, Boon NA. Heart muscle disease related to HIV infection: prognostic implications. *BMJ*. 1994; 309: 1605-1607.
6. Anderson DW, Virmani R, Reilly JM, Leary TO, Cunnion RE, Robinowitz M, et al. Prevalent myocarditis at necropsy in acquired immunodeficiency syndrome. *J Am Coll Cardiol*. 1988; 11: 792-9.
7. Herskowitz A, Choou Wu T, Willoughby SB, Vlahov D, Ansari AA, Beschoner WE, et al. Myocarditis and cardiotoxic viral infection associated with human immunodeficiency virus. *J Am Coll Cardiol*. 1994; 24: 1025-32.
8. Jacob AJ, Sutherland GR, Bird AG, Brettell RP, Ludlam CA, McMillan A, et al. Myocardial dysfunction in patients infected with HIV: prevalence and risk factors. *Br Heart J*. 1992; 68: 549-553.
9. Torriani FJ, Komarow L, Parker RA, Cotter BR, Currier JS, Dube MP, et al. Endothelial function in Human Immunodeficiency Virus-infected antiretroviral-naive subjects before and after starting potent antiretroviral therapy. *J Am Coll Cardiol*. 2008; 52: 569-76.
10. Wanke CA. Epidemiological and clinical aspects of the metabolic complications of HIV infection the fat redistribution syndrome (editorial). *AIDS*. 1999; 13: 1287-93.
11. Carr A, Samaras K, Chisholm DJ, Cooper DA. Pathogenesis of HIV-1-protease inhibitor-associated peripheral lipodystrophy, hyperlipidaemia, and insulin resistance. *Lancet*. 1998; 351: 1881-3.
12. Carr A, Samaras K, Thorisdottir A, Kaufman GR, Chisholm DJ, Cooper DA. Diagnosis, prediction, and natural course of HIV-1 protease-inhibitor-associated lipodystrophy, hyperlipidaemia, and diabetes mellitus: a cohort study. *Lancet*. 1999; 353: 2093-9.
13. Biviji AA, Paiement GD, Steinbach LS. Musculoskeletal manifestations of Human Immunodeficiency Virus infection. *J Am Acad Orthop Surgery*. 2002; 10: 312-20.
14. Periard D, Telenti A, Sudre P, Cheseaux JJ, Halfon P, Raymond MJ, Marcovina SM, et al. Atherogenic dyslipidemia in HIV-infected individuals treated with protease inhibitors. The Swiss HIV cohort study. *Circulation*. 1999; 100: 700-5.
15. Henry K, Melroe H, Huebsch J, Hermundson J, Levine C, Swensen L, et al. Severe premature coronary artery disease with protease inhibitors (letter, see comments). *Lancet*. 1998; 351: 1328.
16. Flynn TE, Bricker LA. Myocardial infarction in HIV-infected men receiving protease inhibitors (letter). *Annals of Internal Medicine*. 1999; 131: 548.
17. Shah AS, Stelzle D, Lee KK, Beck EJ, Alam S, Clifford S, et al. Global burden of atherosclerotic cardiovascular disease in people living with HIV: systematic review and meta-analysis. *Circulation*. 2018; 138: 1100-12.
18. Shah AS, Stelzle D, Lee KK, Beck EJ, Alam S, Clifford S, et al. Global Burden of Atherosclerotic Cardiovascular Disease in People Living With HIV: Systematic Review and Meta-Analysis. *Circulation*. 2018; 138: 1100-12.
19. Prendergast BD. HIV and cardiovascular medicine. *Heart*. 2003; 89: 793-800.
20. Vittecoq D, Escaut L, Chironi G, Teicher E, Monsuez JJ, Andrejak M, et al. Coronary heart disease in HIV-infected patients in the highly active antiretroviral treatment era. *AIDS*. 2003; 17: S70-S6.
21. Ambrose JA, Gould RB, Kurian DC, DeVoe MC, Pearlstein NB, Coppola JT, et al. Frequency of and outcome of acute coronary syndromes in patients with human immunodeficiency virus infection. *Am J Cardiol*. 2003; 92: 301-3.
22. Matetzky S, Domingo M, Kar S, Noc M, Shah PK, Kaul S, et al. Acute myocardial infarction in Human Immunodeficiency Virus-infected patients. *Ach Intern Med*. 2003; 163: 457-60.
23. Varriale P, Saravi G, Hernandez E, Carbon F. Acute myocardial infarction in patients infected with human immunodeficiency virus. *Am Heart J*. 2004; 147: 55-9.
24. Barbaro G, Barabarini G, Pellicelli AM. HIV-associated coronary arteritis in a patient with fatal myocardial infarction. *N Engl J Med*. 2001; 344: 1799-800.
25. Barbaro G. Cardiovascular manifestations of HIV infection. *JR Soc Med*. 2001; 94: 384-90.
26. Escaut L, Monsuez JJ, Chironi G, Merad M, Teicher E, Smadja D, et al. Coronary artery disease in HIV infected patients. *Intensive Care Med*. 2003; 29: 969-73.
27. Khunnawat C, Mukerji S, Havlicek D, Touma R, Abela GS. Cardiovascular manifestation in Human Immunodeficiency Virus-infected patients. *Am J Cardiol*. 2008; 102: 635-42.
28. Guaraldi G. Cardiovascular complications in HIV-infected individuals. *Current Opinion in HIV and AIDS*. 2006; 1: 507-13.
29. Yanagawa B, Verma S, Dwivedi G, Ruel M. Cardiac surgery in HIV patients: state of the art. *Canadian Journal of Cardiology*. 2019; 35: 320-5.
30. Rose DN, Collins M, Kleban R. Complications of surgery in HIV-infected patients. *AIDS*. 1998; 12: 2243-51.
31. Dominici C, Chello M. Impact of human immunodeficiency virus (HIV) infection in patients undergoing cardiac surgery: a systematic review. *Reviews in Cardiovascular Medicine*. 2020; 21: 411-8.
32. Kim KM, Arghami A, Habib R, Daneshmand MA, Parsons N, Elhalabi Z, et al. The Society of Thoracic Surgeons Adult Cardiac Surgery Database: 2022 Update on Outcomes and Research. *The Annals of Thoracic Surgery*. 2023; 115: 566-74.
33. Wollner G, Zimpfer D, Manduric M, Laufer G, Rieger A, Sandner SE. Outcomes of coronary artery bypass grafting in patients with human immunodeficiency virus infection. *Journal of Cardiac Surgery*. 2020; 35: 2543-9.
34. Trachiotis GD, Alexander EP, Benator D, Gharagozloo F. Cardiac surgery in patients infected with the human immunodeficiency virus. *The Annals of thoracic surgery*. 2003; 76: 1114-8.
35. Heeringa J, Mutti A, Furukawa MF, Lechner A, Maurer KA, Rich E. Horizontal and vertical integration of health care providers: a framework for understanding various provider organizational structures. *International Journal of Integrated Care*. 2020; 20: 2.
36. Togioka BM, Mayo SC. Surgeon-Anesthesiologist Dyad Familiarity—What Are the Unintended Consequences? *JAMA Surgery*. 2023; 158: 473-474.
37. Horberg M, Hurley L, Towner W, Gambatese R, Klein D, Antoniskis D, et al. HIV quality performance measures in a large integrated health care system. *AIDS patient care and STDs*. 2011; 25: 21-8.

38. Robich MP, Schiltz N, Johnston DR, Mick S, Tse W, Koch C, et al. Outcomes of patients with human immunodeficiency virus infection undergoing cardiovascular surgery in the United States. *The Journal of Thoracic and Cardiovascular Surgery*. 2014; 148: 3066-75.
39. Clement ME, Lin L, Navar AM, Okeke NL, Naggie S, Douglas PS. Lower likelihood of cardiac procedures after acute coronary syndrome in patients with human immunodeficiency virus/acquired immunodeficiency syndrome. *Medicine*. 2018; 97: e9849.
40. King JT, Perkal MF, Rosenthal RA, Gordon AJ, Crystal S, Rodriguez-Barradas MC, et al. Thirty-day postoperative mortality among individuals with HIV infection receiving antiretroviral therapy and procedure-matched, uninfected comparators. *JAMA surgery*. 2015; 150: 343-51.