

# Mortality and Morbidity in HIV-Infected Patients Undergoing Coronary Artery Bypass Surgery: a Case Control Study

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The use of highly active antiretroviral therapy (HAART) in patients with HIV infection has improved survival. This improvement combined with the metabolic effects of treatment has increased cardiovascular risk and the need for cardiac surgery in these patients.

We compared morbidity and mortality in HIV-infected patients (cases, n=7) and non-HIV-infected patients (controls, n=21) who underwent isolated coronary artery surgery between 1997 and 2004.

The durations of extracorporeal circulation and aortic cross-clamping were shorter in HIV-infected patients ( $P=.002$  and  $P=.014$ , respectively). The percentage of patients who experienced complications was similar, at 57.1% in both groups, but there was a slightly higher number of complications per patient in non-HIV-infected individuals. The mean length of total hospitalization was greater in HIV-infected patients (27.1 [13.3] vs 8.8 [5.3] days;  $P=.003$ ), as was that of postoperative hospitalization (18.2 [15.4] vs 7.9 [4.2] days;  $P=.08$ ).

No HIV-infected patient died or needed a repeat cardiac operation. No progression of the HIV infection was observed. Isolated coronary artery surgery in HIV-infected patients produces good results, and there is no increase in morbidity or mortality. Extracorporeal circulation did not influence disease progression.

**Key words:** *HIV infection. Coronary artery disease. Coronary artery surgery.*

## Morbimortalidad en pacientes con infección por el virus de la inmunodeficiencia humana que reciben cirugía de revascularización miocárdica: estudio de casos y controles

La mayor supervivencia y los efectos metabólicos del tratamiento antirretroviral han aumentado el riesgo cardiovascular y la necesidad de cirugía coronaria en individuos positivos para el virus de la inmunodeficiencia humana (VIH).

Comparamos la morbimortalidad entre pacientes VIH-positivos (casos, n = 7) y negativos (controles, n = 21) que recibieron cirugía de revascularización miocárdica (CRM) entre 1997 y 2004.

Los tiempos de circulación extracorpórea (CEC) y oclusión aórtica fueron inferiores en pacientes VIH-positivos ( $p = 0,002$  y  $p = 0,014$ , respectivamente). La incidencia de complicaciones fue similar (el 57,1% en ambos grupos), aunque el número de complicaciones por paciente fue ligeramente superior en los VIH-negativos. Los pacientes VIH-positivos precisaron mayor estancia hospitalaria total ( $27,1 \pm 13,3$  y  $8,8 \pm 5,3$  días;  $p = 0,003$ ) y postoperatoria ( $18,2 \pm 15,4$  y  $7,9 \pm 4,2$  días;  $p = 0,08$ ). Ningún paciente VIH-positivo falleció, precisó una nueva CRM ni mostró progresión de la enfermedad.

La CRM aislada obtiene buenos resultados en la infección por el VIH, sin incrementar la morbimortalidad. La CEC no influyó en la progresión de la infección.

**Palabras clave:** *Infección VIH. Enfermedad arterial coronaria. Cirugía de revascularización miocárdica.*

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The members of Endocarditis Study Group are listed in the Appendix.

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## INTRODUCTION

The sustained inhibition of viral replication and immune reconstitution<sup>1</sup> associated with highly active antiretroviral therapy (HAART) has greatly improved prognosis in patients with human immunodeficiency virus (HIV). Increased survival and the metabolic side effects associated with antiretroviral therapy<sup>2</sup> have, however, led to increased cardiovascular risk<sup>3-5</sup> in these patients and an increased need for cardiac surgery.

Although good surgical outcomes have been obtained in HIV-infected patients, there is a lack of outcomes data from large series and case-control studies.<sup>6-8</sup> In the present study, we analyze our experience of performing isolated coronary artery surgery (CAS) in HIV-infected and non-HIV-infected individuals to determine whether HIV infection increases the risk of complications after cardiac surgery.

## PATIENTS AND METHODS

Clinical records for patients who received an isolated CAS from June 1997 to January 2004 were reviewed retrospectively to identify all HIV-infected patients. No HIV-infected patient considered for surgery was rejected. As a control group, for each HIV-infected patient, 3 non-HIV-infected patients of the same age ( $\pm 10$  years) and sex were selected who had received the same type of intervention immediately prior to or after the corresponding HIV-infected patient. All patients received per-protocol antibiotic prophylaxis (intravenous glucopeptides/aminogluosides).

Preoperative, perioperative, and postoperative data were obtained from clinical records. For HIV-infected patients, data on duration, stage (CDC classification<sup>9</sup>), CD4 T-lymphocyte cell count, and viral load were also collected. Patients' were classified for preoperative surgical risk using the EuroSCORE system.<sup>10</sup>

The mean overall and postoperative length of hospital stay was calculated, together with morbidity and mortality. Postoperative complications assessed included fever requiring treatment with antibiotics, sepsis, surface infection of the surgical wound, mediastinitis, anemia requiring transfusion, use of additional surgical procedures, urinary infection, pneumonia, catheter related bacteremia, and stroke.

Follow-up data (status [alive/dead] and the need for a further CAS) were obtained via personal interview during periodic check-ups.

Statistical analyses were performed in SPSS (version 12.0, SPSS Inc., Chicago). Quantitative variables were expressed as means  $\pm$  standard deviation and qualitative variables as percentages. Descriptive analysis was followed by between group comparisons using the  $\chi^2$  test or Fisher's exact test for qualitative variables, and non-parametric tests for numerical data. *P* values  $<.05$  were considered statistically significant.

## RESULTS

### Characteristics of HIV-Infected Patients

Seven HIV-infected patients who received CAS were identified (0.5% of all CAS performed in the center during the study period). Risk factors for infection were injecting drug use in 1 (14.3%) patient, homosexual risk behaviors in 1 (14.3%), and heterosexual risk behaviors

in 5 (71.4%). Mean time with the infection was 8.6 years (range, 2-15 years). Mean preoperative CD4+ T cell count was 340.5 cells/ $\mu$ L (range, 61-959). Four (80%) of the 5 patients for which data on viral load were available had values of  $<200$  copies/mL. Six (85.7%) patients were receiving antiretroviral therapy and in 4 (66.6%), the treatment regime included protease inhibitors (PI). Two (28%) patients were co-infected with the hepatitis C virus.

All patients received a left internal mammary artery graft to the anterior descending coronary artery; saphenous vein grafts were used in the remaining vessels. One patient (14.3%) received a quadruple derivation, 2 (28.6%) a triple anastomosis, 3 (42.8%) a double anastomosis, and 1 (14.3%) a single anastomosis. Median sternotomy was the most commonly used approach, although in the patient who received the single anastomosis a left anterior minithoracotomy was used. Extracorporeal circulation (ECC) was employed in five (71.4%) of the 7 procedures.

HIV infection stage remained the same in all patients during follow-up. An increase in the CD4+ T cell count was observed in 4 patients for whom pre- and postoperative data were available ( $142.2 \pm 68.3$  and  $266 \pm 147.9$  cells/ $\mu$ L, respectively). Viral load remained undetectable ( $<200$  copies/mL) 1-3 months after the intervention. HAART was reintroduced when the patient recommenced taking food orally.

### Comparison of HIV-Infected and Non-HIV-Infected Patients

All patients were male, and the mean age was lower in the group of HIV-infected patients ( $P<.05$ ). The preoperative characteristics of both groups are shown in table 1 and intervention characteristics by study group in table 2.

Table 3 provides a summary of morbidity and mortality and the mean length of stay by study group. The overall index of postoperative complications was similar in both groups, although the number of complications per individual was slightly higher in non-HIV-infected patients. Four (57.1%) HIV-infected patients had postoperative complications: 2 had fever of unclear origin with negative blood cultures; 2 had persistent mediastinic hemorrhage with re-intervention required in 1 case; 1 had pneumonia caused by *Haemophilus influenzae* which resolved with antibiotic treatment, although mechanical ventilation was required, and; 1 had a urinary infection caused by *Escherichia coli*. The surgical wound did not become infected in any of the HIV-infected patients.

Twelve (57.1%) patients in the control group had postoperative complications: 3 had mediastinic hemorrhage which required re-intervention in 1 case; 2 had pneumothorax; 1 had hospital-acquired pneumonia, with no germ isolated; 1 had respiratory infection; 4 had fever of unknown origin requiring treatment with

**TABLE 1. Baseline Patient Characteristics for the 2 Study Groups\***

	HIV-Infected (n=7)	Non-HIV-Infected (n=21)	P
Age, mean±SD, years	49.6±8.1	59.9±10.3	.05
Cardiovascular risk factors, n (%)			
Smoking habit	6 (86)	14 (67)	.33
Hypertension	3 (43)	18 (86)	.04
Dyslipidemia	5 (71)	14 (67)	.6
Diabetes	2 (28)	9 (43)	.42
Heart disease, n (%)			
Prior AMI	3 (43)	10 (48)	.83
Prior angioplasty	–	–	–
EuroScore, mean±SD	1.3±1.3	2.7±2.2	.12

\*SD indicates standard deviation; AMI, acute myocardial infarction; HIV, human immunodeficiency virus.

antibiotics, and which was probably catheter-related in 2 individuals; 3 had urinary infection; 1 had self-limited diarrhea; and 2 had surface infection of the surgical wound caused by *Staphylococcus aureus* which was sensitive to treatment with meticillin and coagulase-negative staphylococcus; 1 patient had sternal instability with no germ isolated and with no need for re-intervention, and 1 had stroke.

Only 1 patient in the control group died from a ventricular arrhythmia which was unrelated to the infectious process.

During follow-up, which was completed in 100% of cases (mean, 30.1 months; range, 10-70 months), all of the HIV-infected patients were in good clinical condition and did not require a further CAS.

## DISCUSSION

The number of HIV-infected patients who receive an isolated CAS is small, so that there is a lack of data for this population. The characteristics of this population differ from those of HIV-infected patients receiving valve replacement surgery due to infectious endocarditis in our center, as they have a higher mean age, a lower number of injecting drug users, lower surgical risk,<sup>11</sup> and a EuroSCORE of <6 which places these patients in a low risk group with an expected mortality of 1.39%. The low surgical risk cannot be attributed to careful patient selection as all HIV-infected patients evaluated for surgery were included. There were few differences between HIV-infected and non-HIV-infected individuals receiving CAS, though HIV-infected patients were significantly younger.

HIV-infected individuals have traditionally been considered poor candidates for surgery because of poor prognosis, the risk of disease progression, and the risk of transmission to health-care personnel. Surgical outcomes in the patients analyzed in this study contradict this view,

**TABLE 2. Intervention Characteristics by Study Group\***

	HIV-Infected (n=7)	Non-HIV-Infected (n=21)	P
Interventions with ECC, n (%)	5 (71.4)	21 (100)	
Type of intervention, n (%)			
Elective	7 (100)	17 (80.9)	.29
Urgent	–	4 (19.1)	–
Number of anastomosis, mean±SD	2.4±0.9	3.2±0.8	.08
Duration of aortic clamping, mean±SD, min	21.1±23.3	44.7±15.2	.014
Duration of ECC, mean±SD, min	41.3±29.9	76.1±23.5	.002

\*ECC indicates extracorporeal circulation; SD, standard deviation; HIV, human immunodeficiency virus.

**TABLE 3. Morbidity, Mortality, and Length of Hospital Stay in the 2 Study Groups\***

	HIV-Infected (n=7)	Non-HIV-Infected (n=21)	P
Mortality, n (%)			
Early	–	1 (4.7)	–
Late	–	–	–
Morbidity, n (%)	4 (57.1)	12 (57.1)	.6
Fever	2 (28.6)	4 (19.1)	
Sepsis	–	–	
Infection of surgical wound	–	2 (9.5)	
Mediastinitis	–	–	
Pneumonia/respiratory infection	1 (14.3)	1 (4.8)	
Urinary tract infection	1 (14.3)	3 (14.3)	
Catheter related bacteremia	–	2 (9.5)	
Diarrhea	2 (28.6)	1 (4.8)	
Bleeding/reintervention	–	3 (14.3)	
Pneumothorax	–	2 (9.5)	
Stroke	–	1 (4.8)	
Atrial fibrillation	–	–	
Hospital stay, mean±SD, days			
Post-intervention	18.2±15.4	7.9±4.2	.08
Total	27.1±13.3	8.8±5.3	.003

\*SD indicates standard deviation; HIV, human immunodeficiency virus.

although the majority of studies report a slightly higher number of postoperative complications, even after minor surgical procedures, than that observed here in non-HIV-infected patients.<sup>12-14</sup>

Previous experience in valve replacement surgery showed surgical responses to be adequate in HIV-infected individuals, independently of disease staging,<sup>11</sup> which is considered by some authors to be a contraindication for surgery. Outcomes with CAS in the present study were equally favorable.<sup>6-8,11</sup> We found that duration of ECC and aortic clamping were significantly lower in HIV-infected patients, although this did not produce

differences in the levels of hospital morbidity and mortality and was due to a technical issue unconnected with the presence of HIV infection. The incidence, characteristics and severity of infectious complications were similar in both groups, and were independent of disease staging in the HIV-infected patients. Mortality was higher in non-HIV-infected patients, although as there was only one death, this finding lacks significance. The greater length of hospital stay observed in HIV-infected patients could be explained by the fact the diagnosing and treating complications in these patients is more complex.

It has been suggested that the negative impact of protease inhibitors on the short- and medium-term results of CAS in HIV-infected patients<sup>7</sup> limit indications for surgery. In this study, there was no recurrence of angina, nor an increased need for angioplasty or revascularization in any of the HIV-infected patients during follow-up, although these results require confirmation in a larger sample with a longer follow-up period.

Cardiac surgery in general, and particularly ECC, have been associated with the progression of HIV infection,<sup>15</sup> although more recent data, especially since the introduction of HAART, do not support this idea.<sup>16,17</sup> In this study, none of the HIV-infected patients showed disease progression, immunological deterioration, or increased viral replication after the intervention. However, the small sample size makes it difficult to determine whether there are advantages to employing ECC.

Limitations of the current study include the retrospective design, the small sample size and the fact that some patients were operated on without ECC. There were also significant differences in mean age between the 2 groups, principally because the age range for the control group was increased by  $\pm 10$  years to account for the fact that HIV-infected patients develop ischemic heart disease earlier than the general population.

In conclusion, these results indicate that outcomes associated with isolated CAS in HIV-infected patients can be acceptable, and that there is no concomitant increase in morbidity or mortality, or disease progression.

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## APPENDIX. Members of the Hospital Clínic-Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS) de Barcelona Endocarditis Study Group

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