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Analysis of Data From a French Nationwide Hospital Medical Information Database

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Background—We aimed to assess in-hospital case fatality and 1-year prognosis in HIV-infected patients with acute myocardial infarction.

Methods and Results—From the PMSI (Program de Medicalisation des Systèmes d'informatique) database, data from 277 303 consecutive acute myocardial infarction patients hospitalized from January 1, 2005, to December 31, 2009, were analyzed. Surviving patients were followed up for 1 year after discharge. HIV-infected patients were compared with uninfected patients. Among the cohort, HIV-infected patients (n=608) accounted for 0.22%. All-cause hospital and 1-year mortality rates were lower in the HIV-infected group than in uninfected patients (3.1% versus 8.1% [$P<0.001$] and 1.4% versus 5.5% [$P<0.001$], respectively). From the database, we then analyzed a cohort derived from a matching procedure, with 1 HIV patient matched with 2 patients without HIV, based on age and sex (n=1824). Ischemic cardiomyopathy was more frequent in the HIV group (7.6% versus 4.2%, $P=0.003$). Hospitalization and 1-year mortality rates were similar in the 2 groups (3.1% versus 2.1% [$P=0.168$] and 1.4% versus 1.7% [$P=0.642$], respectively). However, at 12 months, hospitalizations for episodes of heart failure were significantly more frequent in HIV-infected than in uninfected patients (3.3% versus 1.4%, respectively; $P=0.020$). HIV infection, diabetes mellitus, history of ischemic cardiomyopathy, and undergoing percutaneous coronary intervention were associated in univariate analysis with occurrence of heart failure. By multivariable analysis, HIV infection (odds ratio 2.82, 95% confidence interval 1.32–6.01), diabetes mellitus, and undergoing percutaneous coronary intervention remained independent predictors of heart failure.

Conclusions—The present study demonstrates that after acute myocardial infarction, HIV status influences long-term risk, although the short-term risk in HIV patients is comparable to that in uninfected patients. (***Circulation.*** **2013;127:1767-1774**.)

Key Words: epidemiology ■ HIV infections ■ myocardial infarction

Currently, ≈40 million people worldwide are infected with HIV, with 40 000 new cases each year in the United States.[1] Among European countries, France, along with Spain and Italy, is one of the most severely affected by HIV. Today in France, the number of people who discover their HIV infection per year is stable at between 6000 and 7000 cases. The number of patients living with HIV is increasing (from 106 000 in 1996 to 130 000 in 2005), in part because of the use of antiretroviral therapies.[2] Since 1996, highly active antiretroviral therapy (HAART) has been available in industrialized countries, making HIV a chronic infection rather than a fatal disease.[3] However, over the past 25 years, cardiovascular disease, especially coronary heart disease, has become the fourth-leading cause of death in these patients.[4] Recently, it has been shown that the incidence of myocardial infarction (MI) in HIV-positive patients was higher than that in the general population.[5] Chronic inflammation, immunosuppression, and antiretroviral treatment, particularly with protease inhibitors, as well as the high prevalence of certain risk factors such as smoking and dyslipidemia, are responsible for the early development of atherosclerosis in this sample.[6–10]

Clinical Perspective on p 1774

Previous studies have focused on the characteristics, management, and prognosis of HIV patients during an acute MI (AMI).[11–15] These studies demonstrated that HIV-infected patients had the same treatment at the acute phase, but that the rates of recurrent AMI and urgent percutaneous coronary intervention (PCI) during follow-up were higher

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than in HIV-uninfected patients. Unfortunately, in-hospital mortality could not be studied because there were too few patients (between 20 and 103).[11–17] The main objective of the present study was to determine the influence of HIV infection on in-hospital mortality within a large national cohort of patients with AMI. The second objective was to compare the 1-year prognosis in HIV-infected patients with that in HIV-uninfected patients.

Methods

Selection of Patients

The data for all patients admitted for AMI in France from January 2005 to December 2009 were collected from the national administrative database, the PMSI (Program de Medicalisation des Systèmes d'informatique), inspired by the US Medicare system. The reliability and validity of PMSI data have already been assessed.[18,19] Since 2004, each hospital's budget has depended on the medical activity described in this specific program, which compiles discharge abstracts related to all admissions in the 1546 French healthcare facilities, whether public or private. Information in these abstracts covers both medical and administrative data, including social security number, date of birth, and sex. These data are rendered anonymous, which makes it possible to link discharge abstracts related to a given patient, as usually done with Medicare data. Routinely collected medical information includes the principal diagnosis, secondary diagnoses, and procedures performed. Diagnoses identified during the hospital stay are coded according to the *International Classification of Diseases, Tenth Revision* (*ICD-10*). To avoid iatrogenic AMI, we selected patients in whom a diagnosis of MI was present as the primary discharge diagnosis. This approach was taken to specifically focus on patients who presented with acute myocardial ischemia and not those with AMI secondary to surgery, hypotension, or other events after admission.[20] In cases of multiple admissions of a patient for an AMI, only the first stay was included in our final analysis to avoid counting the same patient twice. MI was defined by an increase in serum troponin I (higher than the upper limit of the hospital's normal range) and clinical symptoms of ischemia or characteristic ECG signs. ST-segment–elevation MI (STEMI) was diagnosed when new ST-segment elevation of ≥1 mm was seen in any location or when new left bundle-branch block was found on the qualifying ECG. MI was selected with *ICD-10* codes I21 ("myocardial infarction") and codes I22 and I23. The present study population was dichotomized into patients with STEMI (codes I21.0, I21.1, I21.2, I21.3, and I21.9) and patients without STEMI (code I21.4). Transmural MI was classified as STEMI and subendocardial as non-STEMI. Among these cases, the HIV-infected group was identified with the HIV comorbidity codes reported in the PMSI database, based on the following codes: B20, HIV disease causing infectious and parasitic diseases; B21, HIV causing malignant tumors; B22, HIV disease resulting in other specified diseases; B23, HIV disease resulting in other conditions; B24, HIV without precision; B24-1, HIV infection in the AIDS stage; and Z21, asymptomatic HIV infection. Two subpopulations were then constituted: HIV-uninfected patients and HIV-infected patients.

Variables

Demographic variables included age and sex. From the national administrative database, we included the following: (1) Risk factors for cardiovascular diseases and comorbidities such as smoking, high blood pressure (hypertension), diabetes mellitus, obesity, dyslipidemia, atrial fibrillation, peripheral artery disease, and renal failure, as well as type of MI; (2) revascularization procedures, including angioplasty (PCI: balloon angioplasty) and coronary artery bypass grafting; and (3) AIDS stage. In-hospital mortality was defined as deaths during the index hospitalization in the PMSI data set. By use of the unique hospital identifier, surviving patients were followed up during the 1-year period after the index hospitalization. Patients who were rehospitalized for a major cardiac event (nonfatal recurrent AMI, stroke, need for revascularization by PCI or coronary artery bypass grafting, hospitalization for heart failure, and in-hospital death) were tagged again in the PMSI database as a case and analyzed. Follow-up data were reported for most patients (73%).

Charlson Comorbidity Index

Given the importance of risk factors to prognosis and the difference in comorbidities between the 2 groups, we also calculated a modified Charlson Comorbidity Index (CCI) as a marker of comorbidity.[21] The genuine CCI assesses the number and severity of comorbid conditions. It is a numerically weighted score composed of 17 comorbid conditions (congestive heart failure, chronic pulmonary disease, cerebrovascular disease, dementia, diabetes mellitus without complications, liver disease, peptic ulcer disease, peripheral vascular disease, rheumatologic disease, hemiplegia or paraplegia, diabetes mellitus with complication, malignancy, renal disease, metastatic solid tumor, and HIV/AIDS). We used a modified CCI index that excluded HIV as a component of the score.

Statistical Analysis

The characteristics of the 2 groups (HIV-infected and HIV-uninfected patients) were first compared considering the overall population (n=277 303). Binary variables were compared with the χ^2 test or the Fisher exact test. The results for the different variables are expressed as percentages. Continuous variables were compared with the Student *t* test or the Mann-Whitney test. The results of the different variables are expressed as means and standard errors. Given the large difference in age and sex between the 2 groups and the major impact of such factors on the prognosis after AMI, we performed additional analyses by matching each patient from the HIV group with 2 HIV-uninfected patients for age and sex. The patients were matched by a simple random sampling without replacement because of the large number of controls. We formed 2 groups: 608 HIV-infected patients matched with 1216 HIV-uninfected patients on the 2 criteria. The characteristics of the 2 groups in this matched cohort were compared by a conditional logistic regression for binary variables and the Friedman test for continuous variables. A multivariable conditional logistic regression analysis was used to assess independent correlates of heart failure in the matched cohort (n=1824). All correlates of hospitalization for heart failure have been tested in univariate analysis. The variables that were significant with a 10% threshold (HIV infection, diabetes mellitus, history of ischemic cardiomyopathy, and undergoing PCI) were included in a multivariable analysis as the first model. A second model was performed with HIV infection, history of ischemic cardiomyopathy, the modified CCI index (ie, without HIV as a component of the index), and PCI as covariates in the model but without diabetes mellitus, to avoid multicollinearity (diabetes mellitus is a component of the CCI index). Odds ratios were calculated with their 95% confidence intervals. All tests were 2-sided. $P<0.05$ was considered statistically significant. All analyses were performed with SAS software (version 9.2, SAS Inc, Cary NC).

Results

Whole Cohort (n=277 303)

Over the 5 years studied, 277 303 patients hospitalized with AMI were included. The prevalence of HIV infection was 0.22% (608 patients). Of these, most 539 (89%) were men, compared with 183 533 (66%) in the uninfected group ($P<0.001$). The mean age was 50.0±10 years in HIV-infected patients compared with 68.3±14.9 years in HIV-uninfected patients ($P<0.001$). More than 90% of the HIV patients were <65 years old (Table 1). Patient demographics and coronary risk factors are given in Table 1. In-hospital mortality was significantly lower in the HIV-infected group than in the HIV-uninfected group (3.1% versus 8.1%, $P<0.001$). Surviving

Table 1. Baseline Characteristics in the Overall Cohort of HIV-Infected Patients and HIV-Uninfected Patients (n=277 303)

	HIV Infected (n=608)	HIV Uninfected (n=276 695)	*P* Value
Mean age, y	50.0±10	68.3±14.9	<0.001
18–55	459 (75.5)	63 380 (22.9)	
56–65	104 (17.1)	50 927 (18.4)	
66–75	33 (5.4)	56 679 (20.5)	
76–85	11 (1.8)	72 631 (26.2)	
>85	1 (0.1)	33 078 (11.9)	
Men	539 (88.6)	183 533 (66.3)	<0.001
Risk factors			
Current smoker	180 (29.6)	39 392 (14.2)	<0.001
Hypertension	106 (17.4)	99 244 (35.9)	<0.001
Diabetes mellitus	55 (9.1)	50 232 (18.2)	<0.001
Dyslipidemia	189 (31.1)	71 459 (25.8)	0.003
Obesity	19 (3.1)	25 621 (9.2)	<0.001
Modified CCI score			<0.001
0	342 (56.3)	140 404 (50.7)	
1	146 (24)	62 697 (22.7)	
2	68 (11.2)	34 856 (12.6)	
>3	52 (8.5)	38 838 (14)	
Ischemic cardiomyopathy	46 (7.6)	19 346 (7)	0.577
Atrial fibrillation	7 (1.1)	27 050 (9.77)	<0.001
Peripheral artery disease	14 (2.3)	10 995 (3.4)	0.035
Renal failure	13 (2.1)	12 732 (4.6)	0.003
Asymptomatic HIV infection	209 (34.4)	*	
Symptomatic HIV infection	399 (65.6)	*	
STEMI	550 (90.5)	233 689 (84.40)	<0.001
Revascularization			
Patients undergoing PCI	404 (66.4)	130 975 (47.3)	<0.001
Patients undergoing CABG	2 (0.3)	2161 (0.8)	0.347
In-hospital mortality	19 (3.1)	22 422 (8.1)	<0.001

Values are mean±SD or n (%).

CABG indicates coronary artery bypass graft; CCI, Charlson Comorbidity Index; PCI, percutaneous coronary intervention; and STEMI, ST-segment–elevation myocardial infarction.

*No data available.

patients were followed up for 1 year after discharge for the occurrence of major cardiac events (Table 2). Recurrent AMI, stroke, and the need for revascularization in both infected and uninfected patients were similar. The rate of hospitalization at 1 year for heart failure and all-cause hospital mortality was lower in the HIV-infected group (3.3% versus 7.0%, *P*=0.002, respectively, and 1.4% versus 5.5%, respectively, *P*<0.001).

Matched Cohort (n=1824)

In this sample matched for age and sex, HIV infection was associated with a lower likelihood of hypertension and obesity (17.4% versus 22.1%, *P*=0.020, and 3.1% versus 11.0%, *P*<0.001, respectively; Table 3). The proportions of smokers and of those with diabetes mellitus and dyslipidemia were similar for the 2 groups. HIV patients presented an increased risk according to CCI score compared with non–HIV-infected patients (*P*<0.001). Ischemic cardiomyopathy was more frequent in the HIV group (7.6% versus 4.2%, *P*=0.003). A history of atrial fibrillation was less frequent in the HIV group (1.1% versus 3.0%, *P*=0.017). The proportions of patients with a history of peripheral artery disease and renal failure were no different in the HIV and non–HIV-infected group). Although the rate of STEMI was similar for both groups (90% versus 91%, *P*=0.752), the rate of revascularization by PCI was slightly higher in HIV-infected patients (66.4% versus 61.7%, *P*=0.047). In-hospital mortality, which was low, was similar for the 2 groups (3.1% versus 2.1%, *P*=0.168). Regarding symptomatic versus asymptomatic status in HIV-infected patients, in-hospital and 1-year outcomes were similar. Analysis of major cardiac events at 1 year after hospital discharge showed that the prognosis in HIV patients was very similar to that in noninfected patients for recurrent MI, stroke, the need for coronary artery bypass grafting, and all-cause mortality. However, patients with HIV infection were twice as likely as their matched noninfected patients to be rehospitalized for episodes of heart failure (3.3% versus 1.4%, *P*=0.020). HIV infection, diabetes mellitus, history of ischemic cardiomyopathy, and undergoing PCI were associated, in univariate analysis, with occurrence of heart failure. By multivariable analysis, HIV infection (odds ratio, 2.82; 95% confidence interval, 1.32–6.01), diabetes mellitus, and undergoing PCI remained independent predictors (Table 4). A second model that included the same variables but had diabetes mellitus replaced by the modified CCI score showed that HIV remained a predictor of risk for heart failure. This result was confirmed by Kaplan-Meier analysis (log rank=0.0203; Figure).

Discussion

Our study identified 277 303 patients admitted for AMI over a period of 5 years, which corresponds to ≈56 000 cases per year. Six studies were published between 2003 and 2010 on the topic, and in only 1 of these did the number of subjects included exceed 100 patients (103 HIV-infected patients, with 195 patients in the control group).[11,13,14,16,17] With 608 HIV patients with AMI, the sample in the present study is the largest to date on this subject. Therefore, we were able to compare the characteristics and mortality in AMI on a large scale; in addition, the present study is the only nationwide study on this subject.

Previous studies showed that HIV-infected patients were younger, more frequently male, and more likely to be smokers.[11–15,17] However, only 4 of those studies included a control group of uninfected patients,[12–14,17] and only 2 of the studies[12,14] matched the 2 groups for age, sex, and type of MI. In the present study, the prevalence of diabetes mellitus and hypertension was lower in HIV patients than in non–HIV-infected patients, and these results are in agreement with 2 other studies by Boccara et al[12] and Hsue et al,[13] who found similar values (20% and 10%, respectively). With regard to comorbidities, atrial fibrillation was less common among HIV-infected patients, probably because of their age and the lower prevalence of hypertension. It is clearly established that HIV infection and antiretroviral drugs may be responsible for lipid disturbances.[22] From the PMSI database, no data were available

Table 2. Prognosis at 1 Year in the Overall Population and in the Matched Cohort

	Overall Population			Matched Population		
	HIV Infected (n=435)	HIV Uninfected (n=201 176)	*P* Value	HIV Infected (n=435)	HIV Uninfected (n=945)	*P* Value
Recurrent MI	29 (6.7)	16 417 (8.2)	0.255	29 (6.7)	57 (6.0)	0.650
Stroke	4 (0.9)	2414 (1.1)	0.448	4 (0.9)	5 (0.5)	0.313
Episode of heart failure	15 (3.3)	15 384 (7.0)	0.002	15 (3.3)	14 (1.4)	0.020
Need for revascularization						
PCI	14 (3.2)	5409 (2.7)	0.593	14 (3.2)	15 (1.6)	0.078
CABG	0 (0)	596 (0.3)	0.487	0 (0)	3 (0.3)	0.579
Hospital death	6 (1.4)	11 993 (5.5)	<0.001	6 (1.4)	16 (1.7)	0.642

Values are n (%).

CABG indicates coronary artery bypass graft; MI, myocardial infarction; and PCI, percutaneous coronary intervention.

on the HIV treatment; however, recent national data indicate that 85% of the infected subjects are currently under HIV treatment, which strongly suggests that in the HIV population in the present study, most patients had been prescribed HIV medications.[2] The proportions of dyslipidemic patients in the 2 groups in the present study were similar to those in the study by Hsue et al,[13] but the present study was unable to differentiate between hypercholesterolemia and hypertriglyceridemia. Nevertheless, Boccara et al[12] and Hsue et al[13] showed a higher frequency of hypertriglyceridemia in infected patients but similar cholesterol levels. In the present study, the percentage of STEMI was 90% in HIV-infected patients, and previous studies have reported similar rates.[12] The young age of people with HIV explains this trend, and Rosengren et al[23] demonstrated an inverse association between age and the likelihood of the AMI being an STEMI. The proportion of patients undergoing PCI during the acute phase was roughly similar (66.4% versus 61.7%, *P*=0.047) in the 2 groups in the matched cohort and was close to that reported by Boccara et al.[12] Moreover, there was no significant difference in the rate of overall revascularization (PCI or coronary artery bypass grafting; HIV 66.8% versus no HIV 62.7%, *P*=0.094). However, the study by Boccara et al[12] excluded patients with a previous history of cardiovascular disease (MI, angina, heart failure, and pulmonary hypertension), cardiogenic shock, and diseases that shortened life expectancy. In addition, Hsue et al[13] and Ambrose et al,[11] who did not exclude such patients, reported PCI rates of 43% and 50%, which are lower than in the present study. Finally, the European expanded GRACE registry (Global Registry of Acute Coronary Events) reported a PCI rate of 55% in 2009.[24]

Table 3. Baseline Characteristics in the Matched Cohort Between HIV-Infected Patients and HIV-Uninfected Patients (n=1824)

	HIV Infected (n=608)	HIV Uninfected (n=1216)	*P* Value
Risk factors			
Current smoker	180 (29.6)	367 (30.2)	0.793
Hypertension	106 (17.4)	268 (22.1)	0.020
Diabetes mellitus	55 (9.1)	130 (10.7)	0.262
Dyslipidemia	189 (31.1)	353 (29.0)	0.364
Obesity	19 (3.1)	134 (11.0)	<0.001
Modified CCI score			
0	342 (56.3)	819 (67.4)	<0.001
1	146 (24)	232 (19.1)	
2	68 (11.2)	85 (7)	
>3	52 (8.5)	80 (6.6)	
Ischemic cardiomyopathy	46 (7.6)	51 (4.2)	0.003
Atrial fibrillation	7 (1.1)	37 (3.0)	0.017
Peripheral arterial disease	14 (2.3)	32 (2.6)	0.666
Renal failure	13 (2.1)	22 (1.8)	0.617
Asymptomatic HIV infection	209 (34.4)	*	
Symptomatic HIV infection	399 (65.6)	*	
STEMI	550 (90)	1107 (91)	0.752
Revascularization			
Patients undergoing PCI	404 (66.4)	750 (61.7)	0.047
Patients undergoing CABG	2 (0.3)	12 (1)	0.150
In-hospital mortality	19 (3.1)	25 (2.1)	0.168

Values are n (%).

CABG indicates coronary artery bypass graft; CCI, Charlson Comorbidity Index; PCI, percutaneous coronary intervention; and STEMI, ST-segment–elevation myocardial infarction.

*No data available.

In-Hospital Mortality

Boccara et al, Hsue et al, and Matetzky et al had no mortality data among, respectively, 103, 68, and 24 HIV patients in their studies,[12–14] and only 1 death was recorded by Ambrose et al[11] among 51 subjects. Recently, Pearce et al[20] studied a large nationwide cohort collected from 1997 to 2006. In this cohort of 5984 HIV-patients, the authors reported a higher risk of in-hospital death after AMI in seropositive than in seronegative

Table 4. Multivariable Logistic Analysis for Heart Failure in the Matched Population (n=1380)

	Odds Ratio	95% CI	*P* Value
HIV infection	2.82	1.32–6.01	0.007
Diabetes mellitus	5.34	2.39–11.9	<0.001
Patients undergoing PCI	0.39	0.19–0.85	0.017

Adjustment covariables: history of ischemic cardiomyopathy.

CI indicates confidence interval; and PCI, percutaneous coronary intervention.

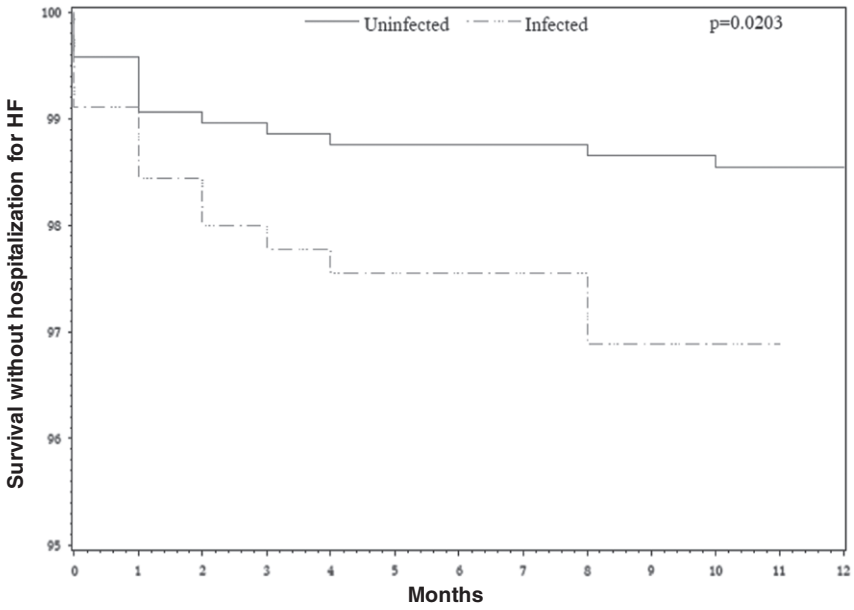

Figure. Time to heart failure (HF) hospitalization according to HIV status.

patients after adjustment for age, sex, ethnicity, medical comorbidities, hospital type, and number of in-hospital procedures (hazard ratio, 1.38; 95% confidence interval, 1.01–1.87; *P*=0.04). In the present study, the in-hospital mortality rate (8.1%) in patients without HIV (overall population) was slightly higher than that in the French Registry of Acute Coronary Syndrome With or Without ST Elevation (FAST MI; 6.9%) published in 2010.[25] Moreover, the European GRACE Registry reported an in-hospital mortality of 6.8% in 2005 (4.6% and 2.2% for STEMI and non-STEMI, respectively).[26] A Danish team studied mortality after a first MI in 44 HIV patients compared with a matched control group of uninfected patients (1:4 ratio)[27]; the authors compared mortality at 90 days and at 5 years and found no significant differences throughout the follow-up. Finally, a recent study by Martin-Reyes,[17] which included 23 HIV patients with AMI, all of whom had PCI, showed no significant difference for in-hospital mortality (8.7% versus 1.7%), even though 2 patients died in the HIV group.

One-Year Prognosis

The study of the prognosis at 1 year showed a similar risk of major adverse cardiac events, including recurrent AMI, among those with and without HIV infection. Boccara and colleagues[12] found no differences between the 2 groups (10% versus 9%, hazard ratio = 1.4, 0.6–3.0, 95%) for a combined criterion (cardiovascular mortality, recurrent acute coronary syndrome, new coronary revascularization, or stroke). The results of the present study are in agreement with these findings. However, Boccara et al[12] reported a higher rate of recurrent acute coronary syndrome in HIV patients during the first year of follow-up (9% versus 3%; hazard ratio, 6.5; 95% confidence interval, 1.7–23.9). These discrepancies regarding late recurrent events may be explained by the following: (1) The authors included as an outcome recurrent acute coronary syndrome, including unstable angina, which is a heterogenous and less well-defined clinical entity with only a small number of events in both the HIV and non–HIV-infected groups (n=9 and n=5, respectively). (2) Our database, which included a more contemporary cohort, may reflect improved current acute management of MI, including the increased use of drug-eluting stents. Recent data have shown that drug-eluting stent use in HIV patients is safe and efficacious and reduces the impact of drug compliance in the long term.[27] However, this conclusion remains purely speculative, because no data were available on the use of drug-eluting stents in the database in the present study. Interestingly, we found a trend toward a greater need for revascularization by PCI in the HIV-infected group, which is in line with the trend toward a higher rate of target-lesion revascularization in such patients.

In addition, we found an increased risk of hospitalization for heart failure in the year after the acute event in the HIV group. There are several hypotheses regarding this increased risk of heart failure. One is that HIV infection itself, which increases the inflammatory burden and stent thrombosis, as well as compliance with treatment in HIV patients, may affect the prognosis. This difference in prognosis was also reflected by the slightly higher proportion of PCI revascularization procedures among HIV patients, even though the difference was not significant. However, angiographic data and information about compliance with cardiovascular drugs were not available in the present study. Because more patients in the HIV cohort had primary PCI, and there was no difference in the rate of stent thrombosis, as reflected by recurrent MI after discharge, HIV-related inflammation or stent thrombosis may have not accounted for or only weakly accounted for the increase in heart failure in the present study. An interesting study using data from a contemporary US medical center database analyzed the outcomes from HIV-infected patients with coronary artery disease who had undergone PCI between 2000 and 2007 and who received bare-metal stents or drug-eluting stents. The authors concluded that the rate of major adverse cardiac events, including coronary revascularization, nonfatal MI, and cardiovascular death, was similar for HIV-infected and non–HIV-infected patients and that treatment with drug-eluting stents in the HIV population was safe and

efficacious. Moreover, the authors showed that in the HIV-infected patients, the impact of compliance with cardiovascular drugs on major adverse cardiac events in the long term (3.1 years) appeared to be reduced.[28]

Another hypothesis concerns the fact that asymptomatic systolic and diastolic ventricular dysfunction remains frequent in HIV-infected patients, even in the HAART era,[29] and is only partially understood. The influence of antiretroviral drugs on the cardiovascular system is still a matter of debate, and accurate single-drug effect analyses remain challenging. Cardiomyopathy is still the most frequent cardiac manifestation, and the occurrence of AMI often marks a turning point in these patients, who often present with asymptomatic left ventricular dysfunction. In the present study, prior ischemic cardiomyopathy was more common in HIV patients, which may explain, at least in part, the higher risk of heart failure after AMI; however, the impact of cardiac dysfunction on prognosis remains to be explored. Therefore, further follow-up data are necessary to confirm these findings even in the HAART era. Additional studies are needed to evaluate the impact of these dysfunctions on long-term survival and quality of life. Whether these patients require more intensive management at follow-up with drugs used for heart failure (eg, angiotensin-converting enzyme inhibitors, β-blockers, and mineral corticoid receptor antagonists) remains to be demonstrated.[30] In the present study, it seems likely that most HIV patients were undergoing therapy with HAART, as shown in the Boccara study, because HAART is available and free in France; however, this conclusion remains purely speculative, because no data were available on the use of HAART in our database.

Smoking cessation and goals for low-density lipoprotein cholesterol are potential target to optimize the follow-up after AMI; however, full control of the risk factors for cardiovascular diseases remains challenging. Boccara et al12 showed that during follow-up, only 50% of HIV patients were weaned off smoking versus 80% in the control group (P=0.002); however, the impact of secondary prevention remains to be explored, given that the risk of recurrent MI and cardiovascular death was similar for the 2 groups.

Another hypothesis concerns the lack of compliance with treatments, which is estimated at only ≈60% in HIV patients.[31,32] Treatment compliance with β-blockers, an association of platelet aggregation inhibitors, statins, angiotensin-converting enzyme inhibitors, and the correction of cardiovascular risk factors (known as BASIC) is crucial in postinfarction patients, because these drugs have proved to be effective against mortality and the risk of recurrence.[33–36] Characterization of the risk associated with the HIV group is indeed crucial for management and prevention strategies in such patients. Whether the risk is driven by different risk factors may be addressed in the matched cohort, which showed either similar rates of smoking, diabetes mellitus, and dyslipidemia or even a favorable risk profile (less hypertension and obesity) in the HIV group. Therefore, these findings strongly suggest the lack or weak impact of such variables on the reported risk found in the HIV group. Moreover, multivariable analysis showed that HIV conferred a strong 240% (P=0.007) increased risk, which further strengthens the hypothesis of an independent impact of HIV or HAART on the occurrence of heart failure. However, we cannot exclude the possibility of other unmeasured confounding that would drive the prognosis. No data are available regarding HIV status in relation to mortality, but the discrepancy in the context of increased risk of heart failure reported in HIV patients emphasizes the fact that physicians need to be aware of the risks in such patients and be particularly aware of secondary prevention after an acute coronary event. In addition, the present study included patients with documented AMI, and the cohort included a wide spectrum of patients with AMI, thereby offering a real-life perspective of the presentation, management, and outcomes of AMI.

Study Limitations

Given the reliance on *ICD-10* codes for the selection of patients and the ascertainment of outcomes, there was a potential for misclassification- or underdetection-related biases. However, the demographic characteristics, risk factors, and outcomes of the present study population were very similar to previous French epidemiological studies of AMI or MI registries that used validated standardized data collection and data quality checks.[12,37] Even though we cannot exclude the bias of misclassification or underdiagnosis, they may have only a minor impact on the findings. Because testing for HIV was not mandatory in the present study cohort, we must assume that a very few (0.09%)[38] patients in the control group (HIV uninfected) may have been infected with HIV but undeclared, corresponding to only 1 or 2 undiagnosed HIV patients in the control group of the matched cohort. This rate is too weak to have a major impact on the findings. Only a limited amount of quantitative information is available, and we could not differentiate between subjects treated with antiretroviral drugs and those without such treatment. It is now recognized that protease inhibitors in particular increase the risk of MI.[6] In addition, the CD4 count and viral load could have been listed, because they are known to be prognostic factors in these patients. However, rates of acute procedures such as PCI were found to be slightly higher in the HIV group (66% versus 62%), which suggests that HIV patients were not undertreated in the acute phase. Moreover, recent data from the literature on smaller samples also suggested that initial management in HIV patients and control subjects was similar, which further reinforces the hypothesis that there are no differences in acute treatments. The same could be said for left ventricular ejection fraction and coronary artery disease.

The retrospective design of the present study and the incomplete data drive its limitations. However, the retrospective nature of the present study was similar to most previous works on this topic, and the present findings are consistent with the conclusions of a major prospective study[12] that suggested the key role of secondary prevention in HIV patients after AMI. There are no contemporary data in either our data set or the literature on long-term medications taken by HIV patients in the secondary prevention of AMI. Moreover, in HIV patients, although adherence to medications may be particularly difficult, it is a primary determinant of the clinical course.[39] One shortfall of the design of the present study is obviously the lack of data regarding adherence to treatments during the follow-up period, as well as discharge treatment, or important

predictors of prognosis after MI (time to reperfusion, left ventricular ejection fraction, creatine kinase or troponin peak), which may have negatively influenced the prognosis. The rate of loss to follow-up in the study was high (27%). Differential attrition can lead to significant selection bias and distortion of the outcomes of interest. To determine whether the high rate of loss to follow-up may have significantly affected the prognosis, we further compared baseline characteristics of those who were lost to follow-up with the characteristics of the tagged hospitalized patients, including age, sex, and HIV status. We found no significant difference for the 2 populations (with versus without hospitalization), which strongly suggests that the subgroup of patients without tagged hospitalization may not profoundly impact our findings.

Despite these limitations, the strength of our results is related to the large size of our sample (608 patients with HIV in a total of 277 303 patients with AMI), with a national recruitment. Finally, the results of the present study may be specific to the French healthcare system and its financial resources and cannot be generalized a priori to other countries with different healthcare systems or different levels of funding.

Conclusions

The present study confirmed that in HIV patients, although traditional risk factors are no worse, infarct occurs at a younger age. In our nationwide study, short- and long-term mortality in HIV-infected patients was similar to that in uninfected patients. However, we observed a higher rate of heart failure in infected patients, which emphasizes the importance of secondary prevention in these patients. Prospective studies are needed to specifically address the levels of treatment adherence and management of risk factors in such populations and their impact on the prognosis.

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Disclosures

None.

References

1. Centers for Disease Control and Prevention. Basic statistics from the Divisions of HIV/AIDS Prevention. http://www.cdc.gov/hiv/topics/surveillance/basic.htm. 2010. Accessed April 9, 2013.
2. Yéni P. Rapport 2010 sur la prise en charge médicale des personnes infectées par le VIH. http://www.sante.gouv.fr/rapport-2010-sur-la-prise-en-charge-medicale-des-personnes-infectees-par-le-vih-sous-la-direction-du-pr-patrick-yeni.html. 2010. Accessed April 9, 2013.
3. Palella FJ Jr, Delaney KM, Moorman AC, Loveless MO, Fuhrer J, Satten GA, Aschman DJ, Holmberg SD; HIV Outpatient Study Investigators. Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. *N Engl J Med*. 1998;338:853–860.
4. Lewden C, May T, Rosenthal E, Burty C, Bonnet F, Costagliola D, Jougla E, Semaille C, Morlat P, Salmon D, Cacoub P, Chêne G. Changes in causes of death among adults infected by HIV between 2000 and 2005: the "Mortalite 2000 and 2005" surveys (ANRS EN19 and Mortavic). *J Acquir Immune Defic Syndr*. 2008;48:590–598.
5. Lang S, Mary-Krause M, Cotte L, Gilquin J, Partisani M, Simon A, Boccara F, Bingham A, Costagliola D; French Hospital Database on HIV-ANRS CO4. Increased risk of myocardial infarction in HIV-infected patients in France, relative to the general population. *AIDS*. 2010;24:1228–1230.
6. Friis-Moller N, Reiss P, Sabin CA, Weber R, Monforte A, El-Sadr W, Thiébaut R, De Wit S, Kirk O, Fontas E, Law MG, Phillips A, Lundgren JD. Class of antiretroviral drugs and the risk of myocardial infarction. *N Engl J Med*. 2007;356:1723–1735.
7. Mary-Krause M, Cotte L, Simon A, Partisani M, Costagliola D; Clinical Epidemiology Group from the French Hospital Database. Increased risk of myocardial infarction with duration of protease inhibitor therapy in HIV-infected men. *AIDS*. 2003;17:2479–2486.
8. Obel N, Thomsen HF, Kronborg G, Larsen CS, Hildebrandt PR, Sørensen HT, Gerstoft J. Ischemic heart disease in HIV-infected and HIV-uninfected individuals: a population-based cohort study. *Clin Infect Dis*. 2007;44:1625–1631.
9. Triant VA, Lee H, Hadigan C, Grinspoon SK. Increased acute myocardial infarction rates and cardiovascular risk factors among patients with human immunodeficiency virus disease. *J Clin Endocrinol Metab*. 2007;92:2506–2512.
10. Savès M, Chêne G, Ducimetière P, Leport C, Le Moal G, Amouyel P, Arveiler D, Ruidavets JB, Reynes J, Bingham A, Raffi F; French WHO MONICA Project and the APROCO (ANRS EP11) Study Group. Risk factors for coronary heart disease in patients treated for human immunodeficiency virus infection compared with the general population. *Clin Infect Dis*. 2003;37:292–298.
11. Ambrose JA, Gould RB, Kurian DC, DeVoe MC, Pearlstein NB, Coppola JT, Siegal FP. Frequency of and outcome of acute coronary syndromes in patients with human immunodeficiency virus infection. *Am J Cardiol*. 2003;92:301–303.
12. Boccara F, Mary-Krause M, Teiger E, Lang S, Lim P, Wahbi K, Beygui F, Milleron O, Gabriel Steg P, Funck-Brentano C, Slama M, Girard PM, Costagliola D, Cohen A; Prognosis of Acute Coronary Syndrome in HIV-infected patients (PACS) Investigators. Acute coronary syndrome in human immunodeficiency virus-infected patients: characteristics and 1 year prognosis. *Eur Heart J*. 2011;32:41–50.
13. Hsue PY, Giri K, Erickson S, MacGregor JS, Younes N, Shergill A, Waters DD. Clinical features of acute coronary syndromes in patients with human immunodeficiency virus infection. *Circulation*. 2004;109:316–319.
14. Matetzky S, Domingo M, Kar S, Noc M, Shah PK, Kaul S, Daar E, Cercek B. Acute myocardial infarction in human immunodeficiency virus-infected patients. *Arch Intern Med*. 2003;163:457–460.
15. Varriale P, Saravi G, Hernandez E, Carbon F. Acute myocardial infarction in patients infected with human immunodeficiency virus. *Am Heart J*. 2004;147:55–59.
16. Boccara F, Ederhy S, Janower S, Benyounes N, Odi G, Cohen A. Clinical characteristics and mid-term prognosis of acute coronary syndrome in HIV-infected patients on antiretroviral therapy. *HIV Med*. 2005;6:240–244.
17. Martín-Reyes R, Galeote G, Moreno R, Sánchez-Recalde A, López De Sá E, López-Sendón JL. Percutaneous coronary intervention in HIV infected patients with human immunodeficiency virus admitted with acute coronary syndrome: case-control study [in Spanish]. *Med Clin (Barc)*. 2010;135:691–694.
18. Couris CM, Polazzi S, Olive F, Remontet L, Bossard N, Gomez F, Schott AM, Mitton N, Colonna M, Trombert B. Breast cancer incidence using administrative data: correction with sensitivity and specificity. *J Clin Epidemiol*. 2009;62:660–666.
19. Chantry AA, Deneux-Tharaux C, Cans C, Ego A, Quantin C, Bouvier-Colle MH; GRACE study group. Hospital discharge data can be used for monitoring procedures and intensive care related to severe maternal morbidity. *J Clin Epidemiol*. 2011;64:1014–1022.
20. Pearce D, Ani C, Espinosa-Silva Y, Clark R, Fatima K, Rahman M, Diebolt E, Ovbiagele B. Comparison of in-hospital mortality from acute myocardial infarction in HIV sero-positive versus sero-negative individuals. *Am J Cardiol*. 2012;110:1078–1084.
21. Charlson M, Szatrowski TP, Peterson J, Gold J. Validation of a combined comorbidity index. *J Clin Epidemiol*. 1994;47:1245–1251.
22. Périard D, Telenti A, Sudre P, Cheseaux JJ, Halfon P, Reymond MJ, Marcovina SM, Glauser MP, Nicod P, Darioli R, Mooser V. Atherogenic dyslipidemia in HIV-infected individuals treated with protease inhibitors: the Swiss HIV Cohort Study. *Circulation*. 1999;100:700–705.

23. Rosengren A, Wallentin L, K Gitt A, Behar S, Battler A, Hasdai D. Sex, age, and clinical presentation of acute coronary syndromes. *Eur Heart J*. 2004;25:663–670.
24. Goodman SG, Huang W, Yan AT, Budaj A, Kennelly BM, Gore JM, Fox KA, Goldberg RJ, Anderson FA Jr; Expanded Global Registry of Acute Coronary Events (GRACE2) Investigators. The expanded Global Registry of Acute Coronary Events: baseline characteristics, management practices, and hospital outcomes of patients with acute coronary syndromes. *Am Heart J*. 2009;158:193–201.e1.
25. Danchin N, Puymirat E, Aissaoui N, Adavane S, Durand E. Epidemiology of acute coronary syndromes in France and in Europe [in French]. *Ann Cardiol Angeiol (Paris)*. 2010;59(suppl 2):S37–S41.
26. Fox KA, Steg PG, Eagle KA, Goodman SG, Anderson FA Jr, Granger CB, Flather MD, Budaj A, Quill A, Gore JM; GRACE Investigators. Decline in rates of death and heart failure in acute coronary syndromes, 1999-2006. *JAMA*. 2007;297:1892–1900.
27. Rasmussen LD, Gerstoft J, Kronborg G, Larsen CS, Pedersen G, Obel N. Mortality after myocardial infarction in HIV-infected patients who have initiated HAART. *AIDS*. 2007;21:873–875.
28. Ren X, Trilesskaya M, Kwan DM, Nguyen K, Shaw RE, Hui PY. Comparison of outcomes using bare metal versus drug-eluting stents in coronary artery disease patients with and without human immunodeficiency virus infection. *Am J Cardiol*. 2009;104:216–222.
29. Cerrato E, D'Ascenzo F, Biondi-Zoccai G, Calcagno A, Frea S, Grosso Marra W, Castagno D, Omedè P, Quadri G, Sciuto F, Presutti D, Frati G, Bonora S, Moretti C, Gaita F. Cardiac dysfunction in pauci symptomatic human immunodeficiency virus patients: a meta-analysis in the highly active antiretroviral therapy era. *Eur Heart J*. January18, 2013. doi:10.1093/eurheartj/ehs471. http://eurheartj.oxfordjournals.org/content/early/2013/01/17/eurheartj.ehs471.long Accessed January 1, 2013.
30. Lipshultz SE, Mas CM, Henkel JM, Franco VI, Fisher SD, Miller TL. HAART to heart: highly active antiretroviral therapy and the risk of cardiovascular disease in HIV-infected or exposed children and adults. *Expert Rev Anti Infect Ther*. 2012;10:661–674.
31. Andréo C, Bouhnik AD, Soletti J, Bertholon DR, Moatti JP, Rossert H, Spire B. Non-compliance in HIV-infected patients, supported by a community association [in French]. *Santé Publique*. 2001;13:249–262.
32. Singh N, Squier C, Sivek C, Wagener M, Nguyen MH, Yu VL. Determinants of compliance with antiretroviral therapy in patients with human immunodeficiency virus: prospective assessment with implications for enhancing compliance. *AIDS Care*. 1996;8:261–269.
33. Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S). *Lancet*. 1994;344:1383–1389.
34. Freemantle N, Cleland J, Young P, Mason J, Harrison J. β Blockade after myocardial infarction: systematic review and meta regression analysis. *BMJ*. 1999;318:1730–1737.
35. Yusuf S, Sleight P, Pogue J, Bosch J, Davies R, Dagenais G; The Heart Outcomes Prevention Evaluation Study Investigators. Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. *N Engl J Med*. 2000;342:145–153.
36. Yusuf S, Zhao F, Mehta SR, Chrolavicius S, Tognoni G, Fox KK; Clopidogrel in Unstable Angina to Prevent Recurrent Events Trial Investigators. Effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST-segment elevation. *N Engl J Med*. 2001;345:494–502.
37. Puymirat E, Simon T, Steg PG, Schiele F, Guéret P, Blanchard D, Khalife K, Goldstein P, Cattan S, Vaur L, Cambou JP, Ferrières J, Danchin N; USIK USIC 2000 Investigators; FAST MI Investigators. Association of changes in clinical characteristics and management with improvement in survival among patients with ST-elevation myocardial infarction. *JAMA*. 2012;308:998–1006.
38. Crémieux AC, D'Almeida KW, de Truchis P, Simon F, le Strat Y, Bousquet V, Semaille C, le Vu S, Lert F. Undiagnosed HIV prevalence based on nontargeted screening in emergency departments. *AIDS*. 2012;26:1445–1448.
39. Mark J. Atkinson, Jeffrey J. Petrozzino. An evidence-based review of treatment-related determinants of patients' nonadherence to HIV medications. *AIDS Patient Care STDS*. 2009;11: 903–914.

CLINICAL PERSPECTIVE

After more than 2 decades of the AIDS epidemic, the spectrum of HIV-associated vascular diseases has evolved considerably. Now that patients have better life expectancy, it has been found that they are more likely than the population at large to experience premature cardiovascular diseases such as acute myocardial infarction. This excess risk may be the consequence of HIV infection, antiretroviral therapies, or other factors. The pathophysiology of this accelerated process is complex and multifactorial and may potentiate the impact of traditional cardiovascular risk factors. The analysis of this large nationwide hospital database, using a matching method, confirmed in a population of acute myocardial infarction patients receiving antiretroviral therapies in a developed country that HIV-infected patients share the same short-term and 1-year mortality as uninfected patients. However, in the year after acute myocardial infarction, HIV-infected patients experience an increased risk of hospitalization for heart failure (odds ratio, 2.82; 95% confidence interval, 1.32–6.01). Despite several study limitations, our study showed that the occurrence of acute myocardial infarction in a population infected with HIV was often associated with asymptomatic cardiac dysfunction and increased incidence of symptomatic heart failure after acute myocardial infarction. Prospective studies are needed to better understand the potential impact of treatment adherence, as well as management of risk factors in secondary cardiovascular prevention.