High Rate of Asymptomatic Myocardial Ischemia in HIV Infected Population in Bobo-Dioulasso in Burkina Faso

TOUGOUMA SJB 1,6 *, ZOUNGRANA J 1,3, YAMEOGO AA 1,6, YAMEOGO NV 4,7, DIALLO I 4,5, HEMA A 3, HIEN H 2, SOME AS 3, TRAORE TI 3, MILLOGO GRC 4,7, KOLOGO KJ 4,7, SAWADOGO AB 3, OUEDRAOGO MS 1, ZABSONRE P 4,7

1. Polytechnic University of Bobo-Dioulasso, Higher Institute of Health Sciences, Bobo-Dioulasso, Burkina Faso
2. Centre Muraz of Bobo-Dioulasso, Burkina Faso
3. Department of Infectious Diseases and Day hospital CHU Souro Sanou, Bobo-Dioulasso, Burkina Faso
4. University of Ouagadougou, Training and Research Unit in Health Sciences (UFR / SDS)
5. Service of infectious diseases at Yalgado Ouedraogo Hospital, Ouagadougou, Burkina Faso
6. Service of Cardiology of the University Hospital Souro Sanou, Bobo-Dioulasso, Burkina Faso
7. Service of Cardiology at Yalgado Ouedraogo Hospital, Ouagadougou, Burkina Faso

Introduction
The cardiovascular complications have become the 3rd cause of death and the 4th reason for hospitalization of the patients infected by the HIV.

The objective of this work was to determine the frequency of asymptomatic myocardial ischemia among patients infected by the HIV receiving antiretroviral therapy.

Patients and Methods
It was a descriptive cross-sectional study which was conducted in November 2015. The patients infected by HIV1 receiving antiretroviral treatment, with asymptomatic myocardial ischemia were included in the study and they were followed up in the HIV clinic of the in Infectious diseases service of the University Hospital Souro Sanou of Bobo-Dioulasso (CHUSS)..

The includes patients benefited from a collection of cardiovascular risk factors, and of two measurements of the blood pressure in a sitting position after 10 minutes of rest and an electrocardiogram 12 derivations after rest.

Results
A total sample of 123 patients infected by HIV1 was selected, with a median age of 42 years (IQR: 36-50). It was composed of 79% of female. The cardiovascular risk factors found were distributed as follows: HTA (31.7%), obesity (33%), dyslipidemia (10.57%), active smoking (0.8%), diabetes (0.8%).

All the known hypertensive cases (5.7%) were insufficiently treated.

The median duration of exposure to the antiretroviral therapy was 5.3 years (IQR: 3-7.7).

The disorders of the repolarization were observed in 26 cases (21.13%). They were divided into under epicardic ischemia in 20 cases (16.26%), under endocardic lesion in 2 cases (1.63%) and after-effect of necrosis in 4 cases (3.25%). The Left ventricular hypertrophy was observed in 12 cases (9.76%) and all of them were hypertensive patients. QTc was lengthened among 7 patients (5.69%) independently of the class of antiretroviral therapy administrated.

Conclusion
Introduction:
The cardiovascular risk in patients infected by the Human Immunodeficiency Virus (HIV) will become in the future years, an increasingly significant concern for the doctors dealing with this infection because of the success of the antiretroviral treatment (ART). This concern involves a considerable lengthening of the survival of infected patients but also of the side effects of the ART. Since the appearance of the Highly Active Anti-Retroviral Treatment (HAART), the spectrum of the cardiologic attack during the infection by HIV was modified. It is now a question of facing the complications related to the antiretroviral treatment, in particular the acceleration of the atherosclerosis (coronary disease, arteriopathy of the lower limbs, cerebral vascular accident) [1-3]. EEEdemiologic studies showed that the incidence of the myocardial infarction is higher in HIV infected population than in the general population [4, 5]. In Africa the frequency of the coronary disease in patient infected by HIV is not well-known and some rare cases are reported in hospital series [6, 7]. The coronary disease is following the example of other metabolic diseases (Diabetes) which can be asymptomatic and of a fortuitously discovery. This study aimed at describing the frequency of asymptomatic myocardic ischemia in a population of patients infected by HIV under ART.

Patients and methods
The study was carried out in the HIV clinic of the department of medicine of the CHU Sanou Sourô (CHUSS) of Bobo-Dioulasso.

This was This was a descriptive cross-sectional study which was conducted from November 2nd to November 30th, 2015. The target population were the patients followed in routine in the cohort of patients infected by HIV and are from the HIV clinic of CHUSS. It is a cohort progressively built since 1998, and now it includes 5000 patients.

The sampling was reasoned. It was a consecutive recruitment of patients infected by HIV over the period of study and who were meeting the inclusion criteria. The patients infected by HIV1 under ART, were included in the study and had given their consent.

Data-collection: The following data were collected in included patients:
- Cardiovascular risk factors (age, obesity, tobacco, oral contraception)
- Parameters related to HIV infection (date of seropositivity discovery, AIDS stage, nadir CD4, CD4 rate, viral load in the 3 previous months, the current ART)
- Two measurements in consultation of the blood pressure in sitting position after 10 minutes of rest,
- And of an electrocardiogram of surface of rest 12 derivations allowing the study of the rate/rhythm, conduction and the repolarization.

The following definitions were used:
- Hypertensive patients were defined by a Systolic Blood Pressure (SBP) 140 mmHg and/or Diastolic Blood Pressure (DBP) 90 mmHg in consultation and/or under antihypertensor treatment no matter the regularity of the treatment.
- Ischaemia under epicardic was defined by the presence of concordant negative T waves in a coronary territory.
- The under endocardic lesion was defined by significant under shift of the ST segment (> 1,5mm) concordant with a coronary territory.

In this study about patients infected by HIV1, it emerges that asymptomatic myocardial ischemia is frequent. It would be advisable to reinforce its tracking by using more powerful tests of ischemia, in order to better specify its gravity in this population with an increased cardiovascular risk.
The after-effect of necrosis was defined by an abrasion of the concordant waves R in a coronary territory and/or a wave Q broad (≥4/100 second) and deep (≥1/10 second).

Left ventricular hypertrophy (LVH) was defined by an index of Sokolov-Lyon ≥ 35mm

The lengthening of QT space was defined by a QT calculated according to the formula of Bazett of $0.44\text{s}$

Mode of data acquisition: We constituted a team of clinicians (infectiologists and cardiologists) involved in the follow-up of the cohort of these patients in order to collect data during the period of study.

The data were entered in Epidata, and were analyzed with STATA® 13. The sociodemographic, clinical, biological and electrocardiographic characteristics of the patients were described. The quantitative variables were described by the medians and their interquartile (IQR) and the qualitative variables were describe by their proportion (%). We used the exact test of Fisher for the comparison of the qualitative data and the Student T test for that of the quantitative information.

The data were collected with informed patients who gave their written consent. An information form was given to the participants and a consent form was filled out by them. Authorizations were obtained from the persons in charge of the cohort and from the department of medicine before the beginning of the data collection.

Results

One hundred and twenty three HIV1 infected patients were evaluated. The sociodemographic and clinical characteristics of the patients are reported in table I. The population was young with a median age of 42 years (IQR: 36-50), with a predominant female prevalence (79%). The cardiovascular risk factors found apart from HIV infection were the dyslipidemias in 13 cases (10.53%), the nicotinism in 1 case (0.8%), the obesity in 41 cases (33%), diabetes in 1 case (0.8%) and high blood pressure in 39 cases (31.7%). Lipodystrophy was present in 8 cases (6.5%). The HIV infection was old as testified by the median duration to the infection which was 6.9 years (IQR: 4.5-9.4). All the patients were under ART with a median duration of 5.3 years exposure (IQR: 3-7.7). The treatments were relatively effective with a median rate of CD4 with 578/mm3 (IQR: 443-758) and an undetectable viral load at 82.11% of the patients.

The data of the ECG of the 123 patients are reported in table II. The repolarization disorders were the most frequent anomalies with 26 cases i.e. 21.13%. They were divided into under epicardic ischemia in 20 cases (16.26%), in wave Q of old necroses in 4 cases (3.25%) and in under endocardic lesion in 2 cases (1.62%). The other anomalies observed were by order of frequency i) an isolated reversed wave T in D3 in 17 cases (13.82%), ii) a wave U in 15 cases (12.3%), iii) a sinusual tachycardia in 13 cases (10.57%), iv) a left ventricular hypertrophy (LVH) in 12 cases (9.76%) and the lengthening of QTc space in 7 cases (5.69%). The LVH was observed among hypertensive patients and five patients presenting the repolarization disorders had high blood pressure. The lengthening of QTc space was not statistically related to the anti-proteases treatment (p=1).

Comments

Our work which describes the electrocardiographic anomalies among HIV infected patients with no cardiovascular symptom and followed-up in the hospital shows that these anomalies are frequent. In fact, the prevalence of deteriorations of the repolarization was high (21.13%). Of this prevalence 3.25% was old necrosis. These findings were already reported by Sani in Nigeria with a prevalence of 27% of deterioration of the repolarization [6]. Compared with the prevalence of 89% reported by Niakara in Ouagadougou [7], our prevalence seems low but this study took place in a hospitalization setting among HIV infected patients admitted in cardiology for cardiopathies of various nature.

Asymptomatic myocardic ischemia following as other metabolic diseases like type 2 diabetes, premonitory of occurrence of secondary cardiovascular events is a bad predictive factor [8].

Many retrospective studies and futurologies revealed a growing number of myocardial infarction among young HIV infected patients (less than 50 years) receiving ART [4, 9]. It seems that currently, according to the most recent studies [4, 5], the incidence of the myocardial infarction in the HIV infected is higher than that of the general population of the same age, especially, in patients treated by ART more especially...
### Table I. Socio-demographic and clinical characteristics of 123 HIV1 infected patients receiving ART and followed-up at HIV clinic of the Infectious diseases service of CHUSS of Bobo-Dioulasso, November 2015

| Characteristics                             | N= 123 |
|---------------------------------------------|--------|
| Female n(%)                                 | 97(78.86) |
| Age, median (IQR)                           | 42ans (36-50) |
| High Blood Pressure History n (%)           | 7(5.7) |
| Diabetes n (%)                              | 1(0.8) |
| Smokers n (%)                               | 1(0.8) |
| Obesity n (%)                               | 41(33) |
| Waist measurement, median(IQR)              | 82(75-92) |
| Hip measurement, median(IQR)                | 94(88-104) |
| Dyslipidemia n (%)                          | 13(10.57) |
| Lipodystrophy n (%)                         | 8 (6.5) |
| High Blood Pressure n (%)                   | 39(31.7%) |
| Profession Housewives n(%)                  | 46(37.4) |
| Hémoglobine, median (IIQ)                   | 12.2(10.5-14.7) |
| Lenght of HIV infection , median (IQR)      | 6.9(4.5-9.4) |
| Duration of receiving ART median (IQR)      | 5.3(3-7.7) |
| 1st line schemata n(%)                      | 102(83) |
| CD4 Count (/mm3), (n) median (IQR)          | 578(443-758) |
| Undetectable Viral Load n (%)               | 101(82.11) |

### Table II. Electrocardigraphic data of 123 HIV infected patients receiving ART and followed-up at HIV clinic of the Infectious diseases service of CHUSS of Bobo-Dioulasso, November 2015

| Data                                           | N=123  |
|------------------------------------------------|--------|
| Heart beat median (IQR)                        | 76(67-88) |
| Sinusal rythmic n (%)                          | 123(100) |
| Sinusal tachycardia s n (%)                    | 13(10.57) |
| Lengthened PR interval n (%)                   | 3(2.4) |
| Q wave of necrosis n (%)                       | 4(3.25) |
| Under shift ST n (%)                           | 2(1.63) |
| Ischemic T waves n (%)                         | 20(16.26) |
| Negative wave T isolated in D3 n (%)           | 17(13.82) |
| U waves n (%)                                 | 15(12.3%) |
| Left ventricular hypertrophy n (%)             | 12(9.76) |
| Right ventricular hypertrophy n (%)            | 3(2.44) |
| QTc, median (IIQ)                              | 0.38(0.37-0.41) |
| Lengthened QTc n (%)                           | 7(5.69) |
when the treatment includes an anti-protease. Vascular risks observed among HIV infected patients under ARV are explained by an acceleration of the process of atherosclerosis. This accelerated atherosclerosis is multifactorial associating traditional inflammatory factors and immunological factors, are still badly determined. Several traditional factors can increase this risk: 1) the presence of a dyslipidemia was reported in more than 13% of our HIV infected patients receiving ART, 2) a diabetes (0.8%), 3) the syndrome of lipodystrophy in 8% of the cases. However, the nicotinism found with a strong prevalence in the majority of the Western studies [1] was not found in our series. This difference could be explained on the one hand by the high proportion of women in our series who culturally do not smoke, and on the other hand, by weanings obtained from male smokers at the beginning of the care of the disease.

The clinical presentation of the coronary disease among HIV infected patients seems to be similar to that of the general population, starting from silent myocardic ischemia to the myocardial infarction with upper-shift of the segment ST. The incidence of silent myocardic ischemia in HIV infected subjects was evaluated by Duong et al. [10] using a simple effort electrocardiogram and have shown, among 100 infected subjects, an incidence of 11% of asymptomatic positive test. In the light of our data, and in spite of the absence of tests of ischemia under our working conditions, we can suggest that the risk of evolution towards the symptomatic coronary disease would be a reality for our HIV positive patients under ART (although currently the majority of our patients is under ART without anti-protease). The implementation of the tests of ischemia is thus essential for the detection of the silent myocardic ischemia which places the HIV infected patient under ART in a secondary logic of prevention by the implementation of anticipated and reinforced hygieno-dietetic and therapeutic recommendations with a strict control of the associated risk factors.

Conclusion

This study on the HIV infected patients under ART, highlighted that asymptomatic myocardic ischemia is frequent. It would be advisable to reinforce its diagnosis by more powerful tests of ischemia for a better specification of its seriousness in order to bring a response in terms of prevention and treatment in this target population with an increased cardiovascular risk.

Ethics

The data were collected with informed patients who gave their written consent. An information form was given to the participants and a consent form was filled out by them. Authorizations were obtained from the persons in charge of the cohort and from the department of medicine before the beginning of the data collection.

Abbreviations

AIDS: Acquired Immune Deficiency Syndrome
ARV: Antiretroviral Drugs
ARVT: Antiretroviral Drug treatment
BMI: Body Mass Index
CD4: Cluster+D6:D28 of Differentiation 4
CHUSS: University Teaching Hospital Souro Sanou.
HIV: Human Immunodeficiency Virus
IQR: Interquartile Range.
NNRTI: non-nucleotide reverse transcriptase inhibitor.
NRTI: nucleoside reverse transcriptase inverse.
SBP: Systolic Blood Pressure.
DBP: Diastolic Blood Pressure.

References

1. Grinspoon, S., Diabetes mellitus, cardiovascular risk, and HIV disease. Circulation, 2009; 119(6): 770-2.
2. Kaplan, R.C., et al. Ten-year predicted coronary heart disease risk in HIV-infected men and women. Clin Infect Dis, 2007; 45(8): 1074-81.
3. Friis-Moller N, et al. Combination antiretroviral therapy and the risk of myocardial infarction. N Engl J Med, 2003a; 349:1993-2003.
4. Mary-Krause M, Cotte L, Simon A, et al., and the 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: 2479-86.
5. Friis-Moller N, Sabin CA, Weber R, et al. Data Collection on Adverse Events of Anti-HIV Drugs (DAD) Study Group. Combination antiretroviral therapy and the risk of myocardial infarction. N Engl J Med 2003; 349: 1993-2003.
6. Sani M.U., Okeahialam B.N., Ukoli C. O.Electrocardiographic abnormalities in Nigéria AIDS.
patients. Cardiol Trop, 2004; 30, 117: 3-6.

7. Niakara A, Drabo YJ, Kambiré Y et al. Atteintes cardio-vasculaires et infection par le VIH : étude de 79 cas au CHN de Ouagadougou (Burkina Faso). Bull Soc Pathol Exot, 2002 ; 95(1) : 23-6.

8. Weiner DA, Ryan TJ, Parsons L et al. Significance of silent myocardial ischemia during exercise testing in patients with diabetes mellitus. A report from coronary artery surgery study (CASS) registry. Am J Cardiol 1991; 68: 729-34.

9. Klein D, Hurley LB, Quesenberry CPJ, Sidney S. Do protease inhibitors increase the risk for coronary heart disease in patients with HIV-1 infection? J Acquir Immune Defic Synd 2002 ; 30 : 471-7.

10. Duong M, Cottin Y, Piroth L, et al. Exercise stress testing for detection of silent myocardial ischemia in human immunodeficiency virus-infected patients receiving antiretroviral therapy. Clin Infect Dis 2002; 34: 523-8.