Journal of
AIDS & Clinical Research
ISSN: 2155-6113

Mekki et al., J AIDS Clin Res 2014,
DOI: 10.4172/2155-6113.1000351

Research Article Open Access

Abdominal Aortic Calcification in Patient's Infected by the Human Immunodeficiency Virus

Meriem Sarah Mekki[1,2#], Sophie Liabeuf[2,3,#,*], Julien Paccou[2,4], Thierry Izet[5], Cédric Renard[5], Ziad A Massy[2,6] and Jean Luc Schmit[1,2]

[1]*Department of Infectious Diseases, Amiens University Medical Center, Amiens, France*
[2] *INSERM U1088, Amiens, France*
[3]*Clinical Research Center, Division of Clinical Pharmacology, Amiens University Medical Center, Amiens, France, and Jules Verne University of Picardy, Amiens, France*
[4]*Rheumatology Department, Amiens University Medical Center, Amiens, France*
[5]*Radiology Department, Amiens University Medical Center, Amiens, France*
[6]*Division of Nephrology, AmbroiseParé Hospital, University of Versailles-Saint-Quentin-en-Yvelines, Boulogne-Billancourt, France*
[#]*These authors contributed equally to this work*

Abstract

In countries where highly active antiretroviral therapy (HAART) is available, cardiovascular disease is a major cause of morbidity and mortality in patients infected by the human immunodeficiency virus (HIV). Vascular calcification is used as subclinical marker of atherosclerosis. As vascular calcification is now considered to be an active, inflammatory process, its evaluation in HIV-infected patients may thus be clinically relevant. The primary objective of the present study was to determine and compare the prevalence of abdominal aortic calcification (using the multislice spiral computed tomography) in HIV-positive patients receiving HAART and in HIV-negative control subjects. The secondary objective was to determine the risk factors associated with the presence of abdominal aortic calcification in HIV-positive patients.

Seventy-seven HIV-positive patients and 77 HIV-negative controls were included in the study. We found that the prevalence of abdominal aortic calcification was similar in the two groups. Furthermore, the mean abdominal aortic calcification score was not significantly higher in HIV-positive patients than in controls. The following parameters were correlated with the aortic calcification score: age ($p<0.0001$), total cholesterol ($p=0.004$), low density lipoprotein cholesterol ($p=0.007$), estimated creatinine clearance ($p=0.039$), low viral load ($p=0.02$) and time since the diagnosis of HIV infection ($p=0.005$). However, in a multivariate analysis, only age was independently associated with the aortic calcification score ($p=0.007$).

In conclusion, abdominal aortic calcification is neither more frequent nor more severe in HIV-positive patients than in HIV-negative controls, and seems only to be affected by independent HIV factors (such as age) in the patients. It remains to be established whether the progression of abdominal aortic calcification is independent of HIV status (in contrast to what has been observed for coronary calcification).

Keywords: Aortic calcification; Human immunodeficiency virus infection; Multislice spiral computed tomography scan

Introduction

In countries where highly active antiretroviral therapy (HAART) is available, cardiovascular disease is a major cause of morbimortality in patients infected by the human immunodeficiency virus (HIV) [1].

Vascular calcification is used as subclinical marker of atherosclerosis. Indeed, vascular calcification is found to be associated with mortality and the occurrence of cardiovascular (CV) events in various patient populations. The coronary artery is the vascular calcification site that has been studied most extensively. However, atherosclerosis in vessels other than coronary or cerebral vessels may be predictive of CV mortality [2]. Indeed, abdominal aortic calcium deposits (detected by lateral lumbar radiography) are a marker of subclinical atherosclerotic disease and an independent predictor of subsequent CV morbidity and mortality in the general population [3].

Vascular calcification is now considered to be an active, inflammatory process [4]. It therefore makes sense to evaluate this process in HIV-infected patients, in view of their potential inflammatory status. However, the few (small) studies to have evaluated vascular calcification in this population focused solely on the coronary artery [5-8]. Indeed, to the best of our knowledge, there are no data regarding abdominal aortic calcification in this population.

Therefore, the goals of the present study were to (i) determine and compare the prevalence of abdominal aortic calcification (using multislice spiral computed tomography (MSCT)) in HIV-positive patients receiving HAART and in HIV-negative control subjects, and (ii) determine the putative risk factors associated with the presence of abdominal aortic calcification in these patients.

Patients and Methods

Study population

In the present study, HIV-positive patients attending the Division of Infectious Diseases at Amiens University Medical Center (Amiens, France) were compared with HIV-negative control subjects. The main inclusion criteria for HIV-positive patients were an HIV-positive blood sample and an MSCT scan performed between 2001 and 2011 (for any

***Corresponding author:** Sophie Liabeuf, Clinical Research Center, Division of Clinical Pharmacology, Amiens University Hospital, Avenue René Laennec, F-80054 Amiens, France, Tel: + 33 322 456085 ; E-mail: liabeuf.sophie@chu-amiens.fr

Received July 25, 2014; **Accepted** September 18, 2014; **Published** September 28, 2014

Citation: Mekki MS, Liabeuf S, Paccou J, Izet T, Renard C, et al. (2014) Abdominal Aortic Calcification in Patient's Infected by the Human Immunodeficiency Virus. J AIDS Clin Res 5: 351. doi:10.4172/2155-6113.1000351

of a variety of indications, including abdominal pain, peritonitis and biliary obstruction).

The HIV-negative control subjects were enrolled from a pool of healthy volunteers set up by the Clinical Research Center at Amiens University Medical Center. The study's objectives and protocol were approved by the local investigational review board, and all study participants accepted to be included in the present study.

The following data were collected for each enrolled case: demographic, clinical and biochemical data (including HIV history and CDC stage) were collected for the two months prior to or after the date of the MSCT scan. The CDC stage classification is as follows: A: primary infection, chronic lymphadenopathy, or no symptoms; B: no AIDS-defining clinical symptoms; C: AIDS-defining clinical event; CDC 1: $CD4^+$ T lymphocyte count equal to or above 500 cells/µl; CDC 2: count between 200 and 499 cells/µl; CDC 3: count below 200 cells/µl.

Quantification of aortic calcification

The presence and extent of aortic calcification were quantified with MSCT. All examinations were performed with a 64-detector scanner (Light speed VCT®, GE Healthcare, Milwaukee, WI, USA).

The volume acquisition started at the aortic hiatus of the diaphragm and ended at the third lumbar vertebra. The scanning parameters were as follows: collimation: 64×0.625 mm; slice thickness: 0.625 mm; pitch: 1; gantry rotation speed: 0.5 s/rotation; tube voltage: 120 kV; tube current: 300 mA.

The volume acquisition was analyzed with commercially available software (Volume Viewer® software, GE Healthcare). The abdominal aorta was segmented manually. In order to reduce errors due to noise, a threshold of 160 UH was applied. For all the MSCT scans, the total calcification volume was calculated (by the same person) as the sum of all voxels in the remaining volume. The abdominal aorta calcification score was calculated as follows: [(total calcification volume) / (aorta wall surface area)*100)]. The method for calculation of the calcification score has been described in detail elsewhere [9] and has been validated in different groups of patients [10,11].

Statistical analyses

Data are expressed as either the mean ± SD or the number (frequency), as appropriate. Intergroup comparisons were made using a χ^2 test for categorical variables and Student's t test or the Kruskal-Wallis test for continuous variables. Spearman correlations were used to identify parameters correlated with the aortic calcification score. Univariate linear regression was used to evaluate the association between the aortic calcification score and selected demographic, biochemical and clinical variables. Thereafter, a multiple linear regression analysis of the factors selected in the univariate analysis was used to identify those that were independently associated with the aortic calcification score. The threshold for statistical significance was set to $p \leq 0.05$. All statistical analyses were performed using SPSS software (version 13.0, SPSS Inc., Chicago, IL) for Windows (Microsoft Corp., Redmond, WA).

Results

Seventy-seven HIV-positive patients and 77 controls were included. Table 1 summarizes the characteristics of HIV negative and HIV-positive patients. HIV-positive patients had a mean age of 47 ± 12; 67.5% were males; mean time since diagnosis of HIV infection was

	HIV-negative control group	HIV-positive group			
			Aortic calcification score (%)		
	Total n=77	Total n=77	≤ 0.031 n=38	>0.031 n=39	p
Age (years)	61.1 ± 6.9	47.1 ± 12.1	41.1 ± 9.9	53.0 ± 11.3	<0.0001
Male gender, n (%)	44 (57)	52 (67.5)	20 (52.6)	32 (82.1)	0.006
BMI (kg/m²)	27.0 ± 5.9	22.8 ± 4.7	23.4 ± 4.8	22.2 ± 4.7	0.307
Smoking habit, n (%)	14 (18.2)	34 (44.1)	13 (34.2)	21 (56.4)	0.053
History of CV disease, n (%)	12 (15.5)	15 (19.5)	4 (10.5)	11 (28.2)	0.046
Lipodystrophy, n (%)	-	16 (20.8)	7 (18.4)	9 (23.0)	0.413
Diabetes, n (%)	3 (4)	3 (3.9)	2 (5.2)	1 (2.6)	0.500
Hypertension, n (%)	31 (41)	16 (20.8)	4 (10.5)	12 (30.8)	0.027
Systolic blood pressure (mmHg)	129.0 ± 18	125.0 ± 16.4	123.9 ± 18.7	125.9 ± 14.5	0.695
Diastolic blood pressure (mmHg)	81 ± 12	73.9 ± 10.3	71.4 ± 9.6	76.0 ± 10.6	0.131
Dyslipidemia, n (%)	26 (33.7)	26 (33.8)	8 (30.8)	18 (69.2)	0.018
Time since HIV diagnosis (years)	-	9.9 ± 7.6	7.6 ± 6.7	12.0 ± 7.9	0.011
Stage A1, n (%)	-	2 (2.6)	2 (5.2)	0 (0.0)	0.240
Stage A2, n (%)	-	14 (18.2)	8 (21.1)	6 (15.4)	0.364
Stage A3, n (%)	-	24 (31.2)	12 (31.6)	12 (30.8)	0.567
Stage B1, n (%)	-	1 (1.3)	0 (0.0)	1 (2.6)	0.506
Stage B2, n (%)	-	3 (3.9)	2 (5.3)	1 (2.6)	0.490
Stage B3, n (%)	-	6 (7.8)	3 (7.9)	3 (7.7)	0.650
Stage C1, n (%)	-	1 (1.3)	0 (0.0)	1 (2.6)	0.506
Stage C2, n (%)	-	6 (7.8)	5 (13.2)	1 (2.6)	0.094
Stage C3, n (%)	-	20 (26.0)	6 (15.8)	14 (35.9)	**0.039**

Data are expressed as mean ± SDor (for binary variables) the number (frequency).p: comparison within the HIV-positive group, as a function of the calcification score.

Abbreviations: BMI: body mass index; CV: cardioVascular.

Variables in bold type were found to be statistically significant.

Table 1: Clinical and demographic characteristics of the HIV-positiveand HIV-negative groups.

9.9 ± 7.6 years). Fifteen HIV patients had known CV disease and 44% were smokers; 26% had less than 200/mm^3 CD4 T lymphocytes at the visit immediately prior to the MSCT scan, and 33.7% had a viral load greater than 500 copies/ml. Ten of the 77 patients (13%) had not begun HAART.

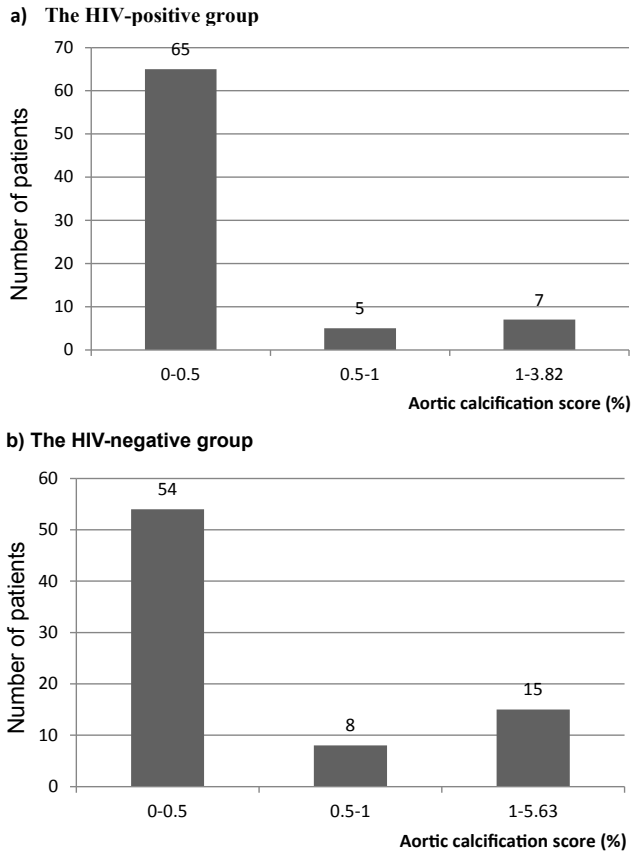

Figure 1: Distribution of aortic calcification scores.

Figure 1 presents the distribution of aortic calcification scores in the HIV-positive group (a) and in the HIV-negative group (b). In HIV-positive group, twenty-five percent of the patients had no detectable aortic calcification. Hence, a low prevalence of aortic calcification was evidenced by a low aortic calcification score; 91% of the study population displayed a calcification score below 1%. The mean and median aortic calcification scores were respectively 0.31 ± 0.7 and 0.031 for the HIV-positive group and 0.03 ± 0.04 and 0.01 ± 0.02 for the 10 patients who had not begun HAART; there was no significant difference between these two patient groups. Similarly, there was no significant difference between the HIV-positive group and the 77 HIV-negative control subjects in terms of the mean aortic calcification score (0.03 ± 0.04 and 0.7 ± 1.4, respectively; p=NS). The same results were found when we restricted the analysis to 30 HIV-positive patients and 30 control subjects matched for age (mean: 60.1 ± 6.1; range 48-83 years) and gender ratio (77% male) Again, the aortic calcification scores of HIV patients did not differ significantly when comparing the controls (mean: 0.66 ± 1.34; median: 0.18) and HIV patients (mean: 0.54 ± 0.84 (median=0.31).

When the HIV population was divided according to the median aortic calcification score (Tables 1 and 2), the patients with an above-median score were older, with a higher proportion of males, a higher proportion of smokers, a longer time since the diagnosis of HIV infection, higher total and low density lipoprotein (LDL) cholesterol levels and a greater likelihood of C3 stage disease, a history of CV disease and, lastly, ongoing treatment for hypertension and dyslipidemia (relative to patients with a below-median score). It is noteworthy that the above-median and below-median groups did not differ significantly in terms of HIV therapy modalities and the presence of concomitant infections (cytomegalovirus, hepatitis B and C, and Epstein Barr virus). The following parameters were correlated with the aortic calcification score: age (p<0.0001), total cholesterol (p=0.004), LDL cholesterol (p=0.007), estimated creatinine clearance (p=0.039), low viral load (p=0.02) and time elapsed since diagnosis of HIV infection (p=0.005) (Table 3). However, in multivariate analysis, only age was independently associated with the aortic calcification score (p=0.007).

	The HIV-negative control group	The HIV-positive group			
			Aortic calcification score		
	Total n=77	Total n=77	≤ 0.031 n=38	>0.031 n=39	p
CD4 T lymphocyte count (/mm^3)	-	419.5 ± 256.0	410.6 ± 263.9	428.2 ± 251.2	0.766
HIV load (log_{10})	-	2.5 ± 1.5	2.7 ± 1.5	2.4 ± 1.4	0.336
HIV load greater than 500 copies/mln (%)	-	26 (33.7)	12 (31.6)	14 (35.9)	0.257
Serum calcium, mmol/L	2.3 ± 0.1	2.2 ± 0.4	2.2 ± 0.11	2.2 ± 0.5	0.596
Serum phosphate,mmol/L	0.9 ± 0.2	1.2 ± 0.3	1.1 ± 0.2	1.2 ± 0.4	0.613
Creatinine (mmol/L)	94.3 ± 11.6	90.5 ± 48.4	83.2 ± 27.5	97.6 ± 62.3	0.198
Creatinine clearance calculated with the MDRD formula (mL/mn/1.73 m^2)	98.2 ± 20.5	96.8 ± 79.5	108.6 ± 106.3	84.9 ± 34.6	0.196
Serum glucose	4.8 ± 1.2	5.2 ± 1.1	5.0 ± 0.7	5.3 ± 1.4	0.257
Serum total cholesterol (g/L)	2.2 ± 0.4	2.1 ± 0.7	1.8 ± 0.5	2.3 ± 0.8	0.002
Serum triglycerides (g/L)	1.1 ± 0.5	1.5 ± 1.1	1.4 ± 1.3	1.7 ± 0.9	0.343
Serum LDL cholesterol (g/L)	1.3 ± 0.3	1.4 ± 0.8	1.2 ± 0.8	1.6 ± 0.8	0.021
Serum HDL cholesterol (g/L)	0.6 ± 0.2	0.59 ± 0.28	0.53 ± 0.21	0.65 ± 0.34	0.07

Data are expressed as the mean ± SD or (for binary variables) the number (frequency). p: comparison within the HIV-positive group, as a function of the calcification score.
Abbreviations: LDL: low density lipoprotein; HDL: high density lipoprotein; MDRD: Modification of Diet in Renal Disease

Table 2: Clinical biochemistry data for the HIV-positiveand HIV-negative groups.

	r	p
Age	0.599	<0.0001
BMI	- 0.082	0.497
Systolic blood pressure	0.062	0.682
Diastolic blood pressure	0.178	0.236
CD4 T lymphocytes	0.120	0.299
HIV load	- 0.264	0.020
Time since HIV diagnosis	0.319	0.005
Creatinineclearance	- 0.237	0.039
Total cholesterol	0.328	0.004
LDL cholesterol	0.315	0.007
HDL cholesterol	0.162	0.175
Serum triglycerides	0.151	0.200
Serum calcium	0.034	0.773
Serum phosphate	- 0.072	0.538
Serum glucose	0.122	0.294

Abbreviations: r: Spearman's correlation coefficient; BMI: body mass index; LDL: low-density lipoprotein; HDL: high-density lipoprotein.

Table 3: Correlation between aortic calcification score and selected clinical or biochemical variables.

Discussion

In a cohort of 77 HIV-positive patients, we found that abdominal aortic calcification is neither more frequent nor more severe than in HIV-negative controls; in the patient group, only age was independently associated with the presence of abdominal aortic calcification.

To the best of our knowledge, this is the first study in which CT was used to study abdominal aortic calcification in HIV-positive patients. We found that HIV status was not correlated with basal vascular calcification. On the same lines, Talwani et al.'s study of the coronary artery failed to observe a difference in the respective proportions of HIV-infected patients (cases) and HIV-negative controls who had either clinically significant basal coronary artery calcification or detectable coronary artery calcification [6].

Similarly, Fitch et al. failed to detect a difference with respect to basal coronary artery calcification when comparing HIV-infected patients without metabolic syndrome on one hand and HIV-negative controls on the other. It is noteworthy that in Fitch et al.'s subgroup of HIV-infected patients with metabolic syndrome, the prevalence of coronary artery calcification was greater than in HIV-negative controls [5]. In the present study population, none of the HIV-infected patients had metabolic syndrome (according to the body mass index and blood lipid data). Moreover, the only factor independently associated with abdominal aortic calcification was age, which is one of the principal determinants of vascular calcification [12]. Taken as a whole, our present results suggest that HIV status is not correlated with basal vascular calcification; the effects of other factors (such as age and metabolic syndrome, as observed in the general population) appear to predominate.

In contrast, the time since HIV diagnosis and the duration of HAART exposure appear to be important factors associated with the progression of vascular calcification [7,8].

In a recent study of 132 HIV-infected men receiving chronic antiretroviral therapy, it was found that coronary artery calcification progressed over the11-month follow-up period. This observation suggested that immune perturbations caused by HIV infection contribute to the progression of atherosclerosis and vascular calcification [8]. Similarly, it was reported that HIV infection, age and hypercholesterolemia were independently associated with coronary artery calcification progression in 25 HIV-infected men [7]. It remains to be seen whether the progression of abdominal aortic calcification is associated or not with HIV status, since our present study was not designed to collect data on this indicator.

The present study's limitations include the single-center design and the size of the cohort size (which may have been too small to detect a difference between HIV-positive and HIV-negative groups) and heterogeneity in clinical characteristics (including medication use) in the HIV-positive group. In contrast, the present study's major strength is the presence of a control population. This study is also the first to have evaluated abdominal aortic calcification in HIV-positive patients.

In conclusion, abdominal aortic calcification score is rare in HIV-positive patients and is no more frequent that in HIV-negative controls. Abdominal aortic calcification appears to be associated only with HIV-independent factors, such as age. It remains to be established whether the progression of abdominal aortic calcification is independent of HIV status (in contrast to what has been observed for coronary calcification).

References

1. Friis-Møller N, Sabin CA, Weber R, d'Arminio Monforte A, El-Sadr WM, et al. (2003) Combination antiretroviral therapy and the risk of myocardial infarction. N Engl J Med 349: 1993-2003.
2. Witteman JC, Kok FJ, van Saase JL, Valkenburg HA (1986) Aortic calcification as a predictor of cardiovascular mortality. Lancet 2: 1120-1122.
3. Wilson PW, Kauppila LI, O'Donnell CJ, Kiel DP, Hannan M, et al. (2001) Abdominal aortic calcific deposits are an important predictor of vascular morbidity and mortality. Circulation 103: 1529-1534.
4. Six I, Massy ZA (2010) [Inflammation and vascular calcifications]. Nephrol Ther 6 Suppl 1: S13-18.
5. Fitch KV, Lo J, Abbara S, Ghoshhajra B, Shturman L, et al. (2010) Increased coronary artery calcium score and noncalcified plaque among HIV-infected men: relationship to metabolic syndrome and cardiac risk parameters. J Acquir Immune Defic Syndr 55: 495-499.
6. Talwani R, Falusi OM, Mendes de Leon CF, Nerad JL, Rich S, et al. (2002) Electron beam computed tomography for assessment of coronary artery disease in HIV-infected men receiving antiretroviral therapy. J Acquir Immune Defic Syndr 30: 191-195.
7. Guaraldi G, Zona S, Orlando G, Carli F, Ligabue G, et al. (2011) Human immunodeficiency virus infection is associated with accelerated atherosclerosis. J Antimicrob Chemother 66: 1857-1860.
8. Guaraldi G, Zona S, Orlando G, Carli F, Ligabue G, et al. (2012) Progression of coronary artery calcium in men affected by human immunodeficiency virus infection. Int J Cardiovasc Imaging 28: 935-941.
9. Temmar M, Liabeuf S, Renard C, Czernichow S, Esper NE, et al. (2010) Pulse wave velocity and vascular calcification at different stages of chronic kidney disease. J Hypertens 28: 163-169.
10. Flipon E, Liabeuf S, Fardellone P, Mentaverri R, Ryckelynck T, et al. (2012) Is vascular calcification associated with bone mineral density and osteoporotic fractures in ambulatory, elderly women? Osteoporos Int 23: 1533-1539.
11. Paccou J, Boudot C, Renard C, Liabeuf S, Kamel S, et al. (2014) Total calcium-sensing receptor expression in circulating monocytes is increased in rheumatoid arthritis patients with severe coronary artery calcification. Arthritis Res Ther 16: 412.
12. Leopold JA (2013) Vascular calcification: an age-old problem of old age. Circulation 127: 2380-2382.