Peripheral Arterial Disease in HIV Patients Older than 50 Years of Age

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Abstract

Our objective was to analyze the prevalence of peripheral arterial disease (PAD) in HIV patients at risk and to compare them with the general population. All HIV patients older than 50 years who attended our unit from October 2005–July 2006 and all persons attending for an annual medical checkup at an employees’ insurance association during the same period were invited to participate in the study. Of the latter (n = 407), a person of the same sex and age (±5 years) was included for each HIV patient. PAD was assessed by the ankle-brachial index (ABI) in all subjects, and all completed the Edinburgh questionnaire. Ninety-nine HIV patients and 99 persons from the general population of the same age and sex were included in the study. The HIV patients had a greater prevalence of dyslipidemia, diabetes, and PAD, which was symptomatic in five of them and in one subject from the general population. Patients with HIV infection older than 50 had a high prevalence of PAD, and as it was asymptomatic in half the cases, an ABI may be performed in this population to actively look for PAD. Control of cardiovascular risk factors and the use of such drugs as platelet antiaggregation agents should therefore be optimized in this population.

Introduction

Patients with HIV infection have a greater prevalence of cardiovascular risk factors and an increased incidence of cardiovascular events.1–5 Peripheral arterial disease (PAD) in these patients has received less attention, and, even when asymptomatic, it reflects the presence of premature atherosclerosis, which is associated with a greater risk for coronary heart disease and cerebrovascular disease.5–9 The ankle-brachial index (ABI), a noninvasive, low-cost, and useful test for detecting asymptomatic PAD, should be performed in patients older than 50 who have a high cardiovascular risk (>20% on the Framingham equation).10–12 We analyzed the prevalence of PAD in a cohort of HIV-infected patients aged 50 years or over and compared it with a group of subjects from the general population of similar sex and age.

Methods

We undertook a cross-sectional study of the prevalence of PAD in patients with HIV who were being followed in our unit (Virgen de la Victoria Hospital, Málaga, Spain) and in a group of healthy persons from the same geographical area. Subjects with unscheduled visits were not included. All HIV patients older than 50 years of age who attended our unit between October 2005 and July 2006 were invited to participate in the study. Additionally, all persons attending for an annual medical checkup at an employees’ insurance association during the same period were also invited to participate. Of these latter (n = 407), a person of the same sex and age (±5 years) was randomly chosen for each HIV patient. There was no specific condition making the subjects from this group pass through the medical checkup.

Blood was taken for laboratory analyses that included fasting glucose and the lipid profile. Subjects were diagnosed as having the metabolic syndrome if they met at least three of the following criteria13: waist circumference >102 cm in men or >88 cm in women, triglycerides ≥150 mg/dl, high-density lipoprotein cholesterol <40 mg/dl in men or <50 mg/dl in women, blood pressure ≥130/≥85 mm Hg or on antihypertensive medication, and fasting glucose >110 mg/dl. The Framingham risk score was calculated in all patients.13 Hypertension, hyperlipidemia, and diabetes mellitus were diagnosed according to international criteria.13–15 Measurement of the ABI was done with unidirectional Doppler (Hadeco ES-100X Mini Dop®, Kawasaki, Japan) and a mercury sphygmomanometer (Nova-Presameter, Stand-
Systolic blood pressure was measured in the posterior tibial and pedal arteries of both legs and in the brachial artery of both arms. The ABI for each leg was the result of dividing the higher of the two systolic blood pressure measurements in each leg, posterior tibial or pedal, by the higher of the two systolic blood pressure measurement in the arms. The value of the limb with the lowest ABI was used for each patient. A patient was considered to have PAD when the ABI was \( \leq 0.9 \). All patients completed the Edinburgh questionnaire in order to evaluate intermittent claudication. The study was approved by the Ethics and Research Committee of the Coordinating Centre. All the subjects included in the study were informed of the nature of the study and gave their consent to participate.

The data for each patient were entered into a database for later statistical analysis. The continuous variables were expressed as means (interquartile range [IQR]) and the categorical variables as number of cases (percentage). Contrast of the continuous variables was done with the Student \( t \)-test or the Mann-Whitney test for those variables that did not follow a normal distribution. Analysis of the degree of association of the categorical variables was done with the \( \chi^2 \)-square test and Yates correction or Fisher exact test. The data were analyzed with the statistical program SPSS, version 10.0 (SPSS software, Chicago, IL).

### Results

Of the 750 patients with HIV infection being followed at our unit, 105 were older than 50 years of age, 99 of whom were included in the study together with another 99 persons from the general population of the same age and sex. Both groups contained 82.8% men, and the mean age was 58.2 years. Table 1 shows the contrast between the two groups. The HIV patients had a greater prevalence of dyslipidemia, diabetes, and PAD, which was symptomatic in five of them and in one subject from the general population (Edinburgh questionnaire). Although the prevalence of current smokers among HIV-infected patients was less than in the general population, the percentage of prior smokers in the HIV group was very high (55%). The HIV patients also used more platelet antiaggregation agents, antihypertensive drugs, lipid-lowering agents, and antidiabetic drugs. The mean follow-up period of the HIV patients was 109.7 months (IQR 69.3–150.6), the main route of transmission was sexual (52.5% homosexual and 36.4% heterosexual), and 42.4% of the patients had AIDS, with a CD4 lymphocyte count nadir of 146 cells/\( \mu l \) (IQR 52–228). Ninety-nine percent of the patients were receiving highly active antiretroviral therapy (HAART) for a mean period of 92.4 months (51.0–123.5) [protease inhibitors (PI) 49.9 months (IQR 24.0–67.0) and non–nucleoside reverse transcriptase inhibitors (NNRTI) 46.5 months (IQR 24.5–72.0)]. The viral load was undetectable in 91.9%, and the mean CD4 lymphocyte count was 482 (IQR 324–599) cells/\( \mu l \).

We assessed the risk factors associated with abnormal ABI values in the HIV-infected group, and no factor was found. Prevalence of PAD was similar among patients with and without metabolic syndrome and among those with and without a cardiovascular risk \( \geq 20\% \). Table 2 shows the features of the 10 HIV-infected patients with PAD.

**Table 1. Comparison of HIV-Infected Patients and Subjects from the General Population**

<table>
<thead>
<tr>
<th></th>
<th>HIV patients (n = 99)</th>
<th>Non-HIV subjects (n = 99)</th>
<th>RR (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex</td>
<td>82 (82.8)</td>
<td>82 (82.8)</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>58.6 (53.3–62.6)</td>
<td>57.8 (53.0–62.0)</td>
<td>0.37</td>
<td></td>
</tr>
<tr>
<td>Current smokers</td>
<td>30 (30.3)</td>
<td>46 (46.5)</td>
<td>0.69 (0.50–0.96)</td>
<td>0.02</td>
</tr>
<tr>
<td>BMI (kg/m(^2))</td>
<td>24.8 (22.6–26.4)</td>
<td>27.7 (25.6–29.6)</td>
<td>0.0001</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>36 (36.4)</td>
<td>39 (39.4)</td>
<td>0.77</td>
<td></td>
</tr>
<tr>
<td>Antihypertensive treatment</td>
<td>36 (100)</td>
<td>24 (61.5)</td>
<td>0.08</td>
<td></td>
</tr>
<tr>
<td>Hyperlipidaemia</td>
<td>68 (69.4)</td>
<td>36 (36.7)</td>
<td>2.00 (1.44–2.77)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Lipid lowering therapy</td>
<td>30 (44.1)</td>
<td>8 (22.2)</td>
<td>1.81 (1.42–2.31)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Current lipid profile</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total cholesterol (mg/dl)</td>
<td>196 (163–225)</td>
<td>215 (188–240)</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>HDL cholesterol (mg/dl)</td>
<td>50 (40–57)</td>
<td>52 (42–62)</td>
<td>0.29</td>
<td></td>
</tr>
<tr>
<td>LDL cholesterol (mg/dl)</td>
<td>109 (82–136)</td>
<td>136 (119–153)</td>
<td>0.0001</td>
<td></td>
</tr>
<tr>
<td>Triglycerides (mg/dl)</td>
<td>202 (101–236)</td>
<td>121 (71–143)</td>
<td>0.0001</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>31 (31.3)</td>
<td>12 (12.2)</td>
<td>1.63 (1.26–2.11)</td>
<td>0.002</td>
</tr>
<tr>
<td>Antidiabetic treatment</td>
<td>15 (48.3)</td>
<td>1 (8.3)</td>
<td>0.026</td>
<td></td>
</tr>
<tr>
<td>Current fasting glucose (mg/dl)</td>
<td>112 (91–117)</td>
<td>98</td>
<td>0.002</td>
<td></td>
</tr>
<tr>
<td>Family history of CHD</td>
<td>15 (15.2)</td>
<td>ND</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>Metabolic syndrome</td>
<td>39 (39.4)</td>
<td>33 (33.7)</td>
<td>0.46</td>
<td></td>
</tr>
<tr>
<td>CVR ( \geq 20% )</td>
<td>28 (29.5)</td>
<td>13 (13.4)</td>
<td>1.53 (1.17–20.2)</td>
<td>0.008</td>
</tr>
<tr>
<td>PAD(^a) (ABI &lt; 0.9)</td>
<td>10 (10.2)</td>
<td>1 (1.0)</td>
<td>1.91 (1.50–2.43)</td>
<td>0.01</td>
</tr>
<tr>
<td>Antiaggregation therapy</td>
<td>11 (11.1)</td>
<td>0 (—)</td>
<td>2.12 (1.82–2.47)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

\(^a\)Symptomatic PAD in 5 HIV patients and in one non-HIV subject.

BMI: body mass index. CHD: coronary heart disease. ND: No data. CVR: cardiovascular risk. PAD: peripheral arterial disease. Quantitative variables are expressed as mean (IQR). Qualitative variables are expressed in absolute values and percentages.
Discussion

This cohort of patients with HIV infection, almost all on HAART and with a long follow-up period, had excellent immunovirological control despite a very low CD4 lymphocyte nadir and a high percentage of cases with AIDS. In comparison with the group of general persons, this group of HIV patients had a high prevalence of cardiovascular risk factors, with an important percentage having a cardiovascular risk >20% and PAD, in half the cases asymptomatic.

Interestingly, the HIV patients were less often smokers than the general persons, whereas all the series of HIV patients that have analyzed this factor have found the opposite.1-3 On the other hand, the HIV patients were more likely to use platelet antiaggregation agents, antihypertensive drugs, lipid-lowering agents, and antidiabetic drugs than the other subjects. Thus, although almost 70% of the HIV group had dyslipidemia, the lipid profile of these patients was more favorable than in the general group. This may reflect the regular follow-up in a group of patients with a chronic disease, who were very probably receiving preventive measures with treatment for cardiovascular risk factors,4,5 unlike the general population, in whom the control and management of these factors was probably deficient. Nevertheless, although the HIV patients were receiving a better follow-up, deficiencies were detected in the management of their cardiovascular risk, for example in relation with the use of platelet antiaggregation agents, which should at least have been indicated for the 31% of the patients who were diabetic,11,20 although they were only prescribed for just 11% of the whole group.

The best predictors of a pathological ABI are age, diabetes, and smoking, followed by plasma lipids and hypertension.21-26 A greater prevalence of a low ABI has also been found in patients with a high cardiovascular risk as estimated by the Framingham equation26,27 and in patients with the metabolic syndrome, although this latter does not add much to many of the traditional risk factors to predict asymptomatic PAD.21,22 Many of these factors are very common in HIV patients receiving antiretroviral therapy,4,5 and therefore a high prevalence of PAD may be expected in these patients in the long term. However, a low prevalence of PAD in HIV-infected patients with multiple cardiovascular risk factors has been recently reported,28 but the authors suggest that it would have been higher in an older population. In line with this comment, we did find a higher prevalence of PAD in HIV patients older than 50 years, and a similar prevalence in younger subjects has been recently reported in the Swiss HIV Cohort Study.27 Although we found no factor related to the presence of PAD in HIV patients, it may be due to the high prevalence of traditional risk factors among this older than 50 years population.

In summary, patients with HIV infection who were older than 50 years of age had a high prevalence of PAD, and as it was asymptomatic in half the cases, an ABI may be performed in this population to actively look for PAD. Control of cardiovascular risk factors and the use of such drugs as platelet antiaggregation agents should therefore be optimized in this population.

References


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