Assessment of cardiovascular risk in middle to older-age HIV-infected patients with coronary artery calcium CT scoring: preliminary results of a cross-sectional pilot study from the Montreal HIV and Aging cohort.

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Introduction

- Coronary heart disease (CHD) remains one of the main pathologies in the western hemisphere with its incidence rising with the age of the population. It is still accompanied by high morbidity and mortality rates, responsible globally of about one third of all deaths. The etiology of CHD is **multifactorial**.

- One of the causal factors more recently brought into attention, is supposedly an **HIV infection**, although there has been some controversy about this. HIV patients have a higher risk of developing cardiovascular disease and myocardial infarction than age-matched controls [1, 2]. The exact pathomechanisms leading to early CHD are not known in detail, and several studies attributed higher rates of CHD in HIV-positive patients to the infection itself and/or to antiretroviral treatment (ART), and/or life-style.

- **No conflicts of interest to disclose.**
Introduction

• For patients at risk for CHD, the major aim nowadays is to detect early subclinical CHD in order to install medical treatment which can potentially prevent disease progression, especially the formation of significant stenoses, occlusion and subsequent myocardial infarction.

• Coronary computed tomography (CT) is one of the imaging techniques which can evaluate and quantify the coronary plaque burden. The so-called calcium scoring CT (CSCT), without injection of intravenous contrast material, has some advantages over contrast-enhanced coronary CT, the major advantage being a significantly smaller radiation dose, the second being the complete absence of injected contrast and thus the impossibility to develop allergic adverse reactions and renal disease. So CSCT is still popular despite its known major disadvantage linked to the fact that the coronary vessel lumen is not directly visualized.
Introduction

- Direct coronary artery imaging techniques have been added to the classic exams to **stratify the individual risk** of a patient to develop symptomatic CHD. The identification of patients at risk for cardiovascular disease is undertaken by the aid of multivariate risk models such as the **Framingham risk score (FRS)** which estimates the individual risk of an asymptomatic patient for a cardiovascular event within 10 years [3]. Other models and modified versions exist [4]. Efforts were made to **improve such models** by adding newer techniques and other factors.

- The **CSCT** has an **added value** to models such as the FRS, helping to better stratify patients [5-7]. It has been shown that **medium risk patients** profit most from additional exams such as the CACS. CACS allows **reclassification** into higher or lower risk categories in as much as **25%** of these cases, so there are potential implications on patient therapy and outcome [5]. Implications on the high and risk categories are less important.
Objectives

• Thus, we wanted to test the hypothesis that an HIV infection leads to premature CHD as detected by an increased coronary artery calcium score (CACS) burden as compared to a matched non-HIV control group.

• We report preliminary results of CACS detection and quantification in an older HIV patient cohort.
Materials & Methods

- In this cross-sectional study, 39 medium risk HIV patients (35 male, 55.6 years (range 46-70)), without known CAD, were prospectively recruited, and underwent non-contrast ECG-gated CSCT. Agatston scores were coded in age/sex-specific percentiles. A subgroup of 31 HIV patients could be matched (age, sex, FRS 10-year risk) with non HIV controls from our local database, for comparison.

<table>
<thead>
<tr>
<th>Inclusion criteria for HIV patients</th>
<th>Exclusion criteria for controls</th>
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<tr>
<td>Extended medium risk FRS (4-25%)</td>
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<tr>
<td>No previous history for cardiac disease</td>
<td>Previous history for cardiac disease</td>
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Materials & Methods

- CSCT was carried out on Philips 256-slice CT hardware.
- Prospective ECG-gated incremental acquisition without injected intravenous contrast material, at 75% of the R-R-interval.
- A small field-of-view (FOV) of 250 mm was acquired, and the length of the scan in the z-axis was usually about 14 cm. Supplemental reconstruction using a FOV of 350 mm for the evaluation of adjacent structures.
- The scan was carried out with the following parameters: 120 kV, 80 mAs, collimation 32*0.625 mm, rotation time 0.33 s, cardiac standard filter, matrix 512. Images were reconstructed as 2.5 mm thick slices every 2.5 mm.
Results 1

- The matched groups of 31 HIV and 31 non HIV patients were similar (age, sex and FS).

<table>
<thead>
<tr>
<th></th>
<th>HIV</th>
<th>non HIV</th>
<th>p</th>
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<tbody>
<tr>
<td>Age (mean)</td>
<td>56.8</td>
<td>56.5</td>
<td>0.58</td>
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<tr>
<td>Framingham FRS</td>
<td>10.7</td>
<td>10.3</td>
<td>0.23</td>
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</table>
Prevalence of coronary calcifications was 67.7% for both patient groups. Mean CAC score was lower for HIV (107±270) than for non HIV patients (176±316), and mean CAC percentile lower for HIV compared to non HIV patients (37±33, 42±37, respectively), but these differences are not significant.

<table>
<thead>
<tr>
<th></th>
<th>HIV</th>
<th>non HIV</th>
<th>p</th>
</tr>
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<tr>
<td>Agatston (mean)</td>
<td>107</td>
<td>176</td>
<td>0.39</td>
</tr>
<tr>
<td>Percentile (mean)</td>
<td>37</td>
<td>42</td>
<td>0.56</td>
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Results 3

HIV positive patients had a mean age/sex-specific percentile of 37 which is significantly lower (p=0.042) than a supposed mean percentile of 50 of a comparable standard population.
Discussion

• HIV patients under antiretroviral therapy nowadays have a longer life expectation and can develop concomitant diseases that can lead to a significant morbidity apart from complications due to the HIV infection itself. Atherosclerotic disease, especially when implicating the coronary vessels, can be such a condition which potentially leads to significant morbidity.

• Generally, a higher incidence in cardiac events has been reported for HIV patients versus uninfected controls [8, 9-12].
Discussion

• Unexpectedly, this could not be confirmed by our study which analyzed the presence of coronary artery calcifications in these two groups of patients by means of CSCT with the calculation of Agatston CACS. In fact, no significant difference could be shown between the main calcium scores in HIV patients versus a matched uninfected control group.

• This leads to the question whether the Agatston CACS is an adequate surrogate marker of cardiovascular disease.
Discussion

• In fact, there are direct correlations between the presence of coronary calcified plaques as detected by the CACS and the presence of plaques which are not necessarily calcified, as a sign of coronary artery disease. The correlation between the Agatston CACS and the presence of significant stenoses is good, but not perfect. Sensitivity and specificity values vary with the calcium score and especially with the age- and sex-specific percentiles [13, 14]. Still, the CACS is considered good enough in that it is actually used as an adjunct to standard exams in order to better stratify patients at medium cardiovascular risk [6].

• It is supposed to provide additional prognostic information as compared to risk models such as the FRS alone, so we considered CACS as an adequate marker for coronary artery disease.
**Limitations**

- The presence of a *selection bias* in the control group cannot be excluded with certainty. Although we chose controls who didn’t have a history of cardiac disease, there could be other parameters not taken into account that might have distorted our results.
- We matched both groups by the FRS which by itself means that controls had to present certain criteria which are not necessarily present in a «healthy» control population.
- The *number of participants* is still relatively limited.
Conclusion

• As expected, CAC prevalence is higher in middle to older-age HIV patients, as compared to previously reported younger historical HIV cohorts.

• Unexpectedly, mean CAC scores are similar in HIV patients and in non HIV controls.

• A prospective study using coronary CT angiography assessing both calcified and non calcified coronary artery plaques in HIV and non HIV individuals is underway.
Work in Progress & Outlook

- The study is being continued, but with the addition of a coronary CT angiography to assess possible non-calcified plaques.
- Example of a patient with a small calcification on the proximal LAD on CSCT (left). A significant stenosis is associated with this calcification (right, CT angiography, CPR).

<table>
<thead>
<tr>
<th>Scoring Results: Agatston Score Protocol</th>
<th>LAD</th>
<th>MLA</th>
<th>Total Coronaries</th>
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<tbody>
<tr>
<td>Score</td>
<td>16.64</td>
<td>3.44</td>
<td>25.08</td>
</tr>
<tr>
<td>#ROI (%)</td>
<td>2</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>AreaSg (sq.mm)</td>
<td>7.59</td>
<td>3.38</td>
<td>10.97</td>
</tr>
</tbody>
</table>
Work in Progress & Outlook

• The analysis of stenosing plaques will include an evaluation of their **volume** (outer wall volume – residual lumen = plaque volume («entre deux»)), their **density** (see included histogram) and of course the **degree of stenosis** (same patient).
References