

The Fat Attenuation Index in HIV-infected patients

Correspondence related to

Coronary atherosclerosis characteristics in HIV-infected patients on long-term antiretroviral therapy: Insights from coronary computed tomography-angiography.

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The recent article by Senoner et al ^[1] provides an interesting outline of coronary artery disease (CAD) characteristics as assessed by computed tomography angiography (CCTA) in HIV positive versus HIV negative patients.

We would like to congratulate the authors for their very interesting and innovative work. Specifically, the identification of HIV-positive individuals having a higher stenosis severity, and an increased number of high-risk plaque features when compared to HIV-negative individuals, is of note due to the advanced structural nature of these measures suggesting long standing differences between the two groups.

We have recently developed a new CCTA-derived imaging biomarker called Fat Attenuation Index (FAI), which is a sensitive index of vascular inflammation^[2]. This relies on the discovery that the inflamed coronary arteries release inflammatory molecules in the perivascular space, inducing lipolysis and preventing adipogenesis in the perivascular adipose tissue. As a result, there is a change in the composition of perivascular fat tissue, shifting the balance between the aqueous and lipid phases in favour of the former. By using a new image analysis method, we can visualise and quantify the 3D changes of perivascular fat composition by quantifying the gradient of perivascular attenuation in CCTA, and following a number of corrections for technical and biological/anatomical factors using the CaRi-HEART algorithm, we have generated FAI, which was tested in a large cohort (CRISP-CT study)^[3], demonstrating a striking prognostic value for future heart attacks. Given that HIV patients experience higher risk for cardiovascular events^[4], it is particularly interesting to understand whether FAI can be used for risk stratification of these patients, to guide prevention measures. Indeed, we have recently shown that in patients with the chronic inflammatory condition of psoriasis, biological therapy was associated with a reduced coronary artery inflammation assessed by perivascular FAI^[5].

The authors report that they used CCTA to study coronary inflammation, by measuring “FAI” in a population sample of 69 HIV positive patients and their matched controls. The assessment of FAI in HIV positive individuals, and its comparison between those without HIV in regards to cardiovascular disease risk is an exciting prospect. However, the authors report that they assessed “FAI” ‘within two ROI adjacent to non-calcified and high-risk lesions, and HU were recorded’^[1]. No methods for these ROI are given within the manuscript, and it is not clear how these ROI were generated and what they included in regards to tissues surrounding the coronary artery. This crude measurement of presumably mean attenuation in selected ROIs should not be defined as FAI, which is calculated by quantifying the 3D attenuation gradients around coronary vessels within a radial distance from the outer vessel wall equal to the diameter of the vessel, and it is followed by multiple corrections using the

CaRi-HEART algorithm, to generate a robust and reproducible value that is used to calculate the FAI-related residual inflammatory risk of the patient. Moreover, the application of FAI to specific coronary lesions, as was the case in the article in question, is possible, but it requires a rather complex analysis as we have described recently^[6].

The authors report that ‘a total of 27.8% of HIV-positive individuals displayed a positive perivascular “FAI” (more than -70HU)’. This is a peculiar approach to reporting the attenuation values for such a cohort, as no mention is made of how many control patients may also have had elevated attenuation values around coronary plaques. Moreover, it is not clear for which ROI that was segmented that these values are for. Further details in the methodology and comparison of the appropriately measured FAI between the HIV-positive patients and their matched controls is required to understand these data.

The authors also report that positive perivascular “FAI” was considered to be more than -70HU. In the original FAI validation paper, a cut point of -70.1HU for the fully weighted values was used to identify individuals with 6-9 times higher risk for fatal heart attacks, but that cut-off was specific for the proximal segment of the right coronary artery. The use of unadjusted perivascular attenuation measurements in ROIs around vessels is not a reliable measurement, while even for the fully weighted FAI measurements, each coronary segment has different cut-off to define inflamed vs non-inflamed vascular wall.

In conclusion, measuring coronary inflammation using the Fat Attenuation Index in HIV patients offers an exciting potential for deployment of personalized management of their cardiovascular risk, but further studies are needed before this test is introduced in the routine management of these patients.

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Conflicts:

C.A. is a founder and shareholder of Caristo Diagnostics, a CT image analysis company. The methods for analysis of the perivascular fat attenuation index and the calculations for the FAI-related risk are subject to patent EP 3 179 917 B1 and patent applications PCT/GB2015/052359, PCT/GB2017/053262, GB2018/1818049.9, GR 20180100490 and GR 20180100510 from the University of Oxford, and Caristo Diagnostics has the exclusive license of this IP.