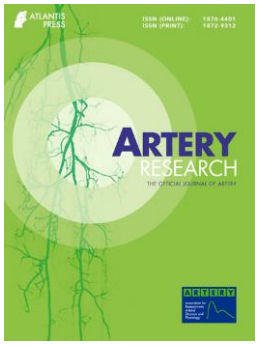

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LETTER TO THE EDITOR

HIV and atherosclerosis: Heterogeneity of studies results

Dear Editor,

We appreciated the article by Palios and colleagues published on your journal.[1] One notable point of the article is the detailed review of cardiovascular disease in HIV-infected subjects. While a certain degree of selection is necessary for such a kind of papers, we noticed some incompleteness on cited data on carotid atherosclerosis.

In recent years a large number of paper had focused on Intima-Media-Thickness (IMT) in HIV-positive subjects. Taking into consideration only studies of comparison with the general population, and among these, only the studies with at least 50 subjects enrolled (supposed as the minimum number needed to make a good IMT comparison study) results are not homogeneous. Some studies found an higher IMT value in HIV than in controls (and they were partially listed by Palios)[2–9] while others found the opposite result.[10–12]

One possible explanation of this difference is the heterogeneity in subjects selection between studies. Some studies have enrolled subjects treated with antiretroviral,[3,5,7,11] while others enrol only never treated subjects.[10] Some researcher excludes subjects with cardiovascular disease[3] while others do not.[4,7]

Methodological difference in acquisition of IMT is a second possible explanation of the not homogeneous results. Some protocols acquire IMT on several carotid artery (CA) segment (common, bulb and internal) and use both proximal and far wall.[2–4] Instead others measure IMT only at the far wall of the common CA.[5–12]

It is possible that these methodological differences alone, or together with the difference in inclusion criteria, lead to the different results obtained. As it is shown in Table 1, when measurements are acquired in different CA segments, results are in favour of a broader difference in IMT (more than 0.1 mm) between HIV+ and controls.[2–4] On the contrary, this difference is less broad (less than 0.1 mm)[5–9] or it does not appear at all[10–12] when only common CA is considered.

Notable Grunfeld et al.[13] measure IMT both in internal and in common CA. In the internal CA they found an higher value in HIV+ in comparison with controls, while data on common CA were similar in the two groups. It has to be noticed that in general population IMT has a higher reproducibility when acquired in the common CA.[14,15]

The inhomogeneity of data published extends also to endothelial function. Some studies show an impairment in Flow Mediated Dilation[16–19] and others do not.[20–22] When specific antiretroviral drugs were considered old generation protease inhibitors (PI) has determine endothelial dysfunction[23–26] while newer PI do not.[27–29]

Because of the increasing cardiovascular morbidity and mortality in HIV-subjects, the large interest of the scientific

Table 1 Results of the principal IMT comparison studies on HIV-positive subjects.

Reference	Number of patients	IMT measurement methods	IMT value
Studies with a broad (more than 0.1 MM) IMT difference			
Hsue PY,[2] Circulation 2004.	148 HIV+ (A) 63 controls (B).	Near and far wall of the common, bulb and internal carotid artery.	0.91 (A) and 0.74 (B).
Hsue PY,[3] AIDS 2006.	93 HIV+ on ART (A) 37 controls (B).	Near and far wall of the common, bulb and internal carotid artery.	0.95 (A) and 0.68 (B).
Ross AC,[4] Clin Infect Dis 2009.	73 HIV+ (A) 21 controls (B).	Near and far wall of the common, bulb and internal carotid artery.	1.25 (A) and 1.05 (B).
Studies with a less broad (less than 0.1 MM) IMT difference			
Papita A,[5] Med Ultrason 2011.	65 HIV+ on ART (A) 36 controls (B).	Far wall of the common carotid.	0.6 (A) and 0.51 (B).

(*continued on next page*)

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Table 1 (*continued*)

Reference	Number of patients	IMT measurement methods	IMT value
Charakida M,[6] Circulation 2005.	83 HIV+ (A) 59 controls (B).	Far wall of the common carotid.	0.6 (A) and 0.5 (B).
Johnsen S,[7] J Clin Endocrinol Metab 2006.	44 HIV+ on ART on PI (A) 40 HIV+ on ART not on PI (B) 86 controls (C).	Far wall of the common carotid.	0.65 (A), 0.61 (B) and 0.61 (C).
Lorenz MW,[8] Atherosclerosis 2008.	292 HIV+ (A) 1168 controls (B).	Far wall of the common carotid.	0.74 (A) and 0.72 (B).
Giuliano Ide C,[9] Coron Artery Dis 2008.	83 HIV+ (A) 83 controls (B).	Far wall of the common carotid.	0.48 (A) and 0.42 (B).
Studies with no difference in IMT measurements			
Bongiovanni M,[10] J Antimicrob Chemother 2008.	53 HIV+ naive (A) 133 HIV+ on ART (B) 54 controls (C).	Far wall of the common carotid.	0.58 (A), 0.64 (B) and 0.65 (C).
Currier JS,[11] AIDS 2005.	44 HIV+ on ART on PI (A) 44 HIV+ on ART not on PI (B) 44 controls (C).	Far wall of the common carotid.	0.69 (A), 0.71(B) and 0.69 (C).
Kaplan RC,[12] AIDS 2008.	Women: 1231 HIV+ (A) 496 controls (B) Men: 600 HIV+ (C) 325 controls (D).	Far wall of the common carotid.	0.72 (A), 0.71 (B), 0.75 (C) and 0.77 (D).

IMT = Intima Media Thickness.

community on early atherosclerosis in this framework do not surprise.

With this brief letter we want to underline that the issue is not completely defined and understood and there are still a lot of uncertainties. The article of Palios et al. has the merit to focus on the importance of IMT and endothelial function in understanding atherosclerosis progression in HIV.

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