Endothelial dysfunction in HIV-positive patients with acute coronary syndromes

Ahmed Vachiat, Therese Dix-Peek, Raquel Duarte, Pravin Manga

Abstract

Aim: This study investigated endothelial function in HIV-positive patients with acute coronary syndrome (ACS). Flow-mediated dilatation, pulse-wave velocity, carotid intima-media thickness and endothelial biomarkers were used to non-invasively investigate endothelial dysfunction.

Methods: Twenty HIV-positive patients with ACS (HIV+/ACS) were compared to 20 HIV-negative patients with ACS (HIV-/ACS) and 20 HIV-positive patients without ACS (HIV+/no ACS).

Results: Endothelial function measured by flow-mediated dilatation (FMD) was similar in both the HIV+/ACS (5.2; IQR 1.4–13.4%) and HIV-/ACS groups (3.7; IQR 2.3–4.4%) (p = 0.78). Arterial stiffness, measured by pulse-wave velocity (PWV) was low in all three cohorts. Carotid intima-media thickness (CIMT) was also low in all three cohorts. The vascular cellular adhesion molecule-1 (VCAM-1) levels in HIV-positive patients with and without ACS were significantly higher than in the HIV-/ACS cohort (p = 0.033 and 0.024, respectively).

Conclusion: Non-invasive investigations such as FMD, CIMT and PWV did not identify patients with HIV who were at high risk of ACS. Endothelial biomarkers may be more useful markers to identify HIV-positive patients who have endothelial dysfunction and increased risk of ACS.

Keywords: HIV, acute coronary syndromes, endothelial dysfunction, flow-mediated dilatation, pulse-wave velocity, carotid intima-media thickness

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There are approximately 37 million people living with human immunodeficiency virus (HIV) worldwide, of whom 70% live in sub-Saharan Africa. Increased life expectancy globally as a result of better access to combination antiretroviral therapy (cART) and high levels of traditional cardiovascular disease risk factors have increased the prevalence of ischaemic heart disease (IHD) in this population. Developed countries generally have an older HIV-positive population with a higher IHD risk profile compared to a younger HIV-positive population in the developing world with a lower IHD risk profile. Developed nations have substantial data on IHD in HIV-positive populations while there is a paucity of data from developing regions.

The endothelium lines the internal surface of blood vessels and is responsible for vascular homeostasis, such as maintenance of vascular tone and non-thrombotic vascular surfaces, as well as immunomodulation. With the onset of endothelial dysfunction, the vasculature is predisposed to vasconstriction, leukocyte adherence, platelet activation, pro-oxidation, thrombosis, impaired coagulation and vascular inflammation. Endothelial dysfunction has therefore been identified as a key step in promoting atherogenesis, and is well described to be an early predictor of future cardiovascular events in patients both with and without established cardiovascular disease.

Endothelial function can be measured in many different ways. The more common technique and one that is well validated is the non-invasive measurement of endothelial function, which relies on high-resolution ultrasound of the brachial artery. Another approach is by measuring endothelial biomarkers.

Endothelial biomarkers, such as cellular adhesion molecules, are either present on the surface of endothelial cells or are expressed on endothelial cells in response to certain stimuli. Endothelial biomarkers include the selectins (E-selectin, P-selectin, L-selectin), vascular adhesion molecule-1 (VCAM-1) and intercellular adhesion molecule-1 (ICAM-1), which are involved in leukocyte rolling, adhesion and trans-endothelial migration into sub-intimal spaces. There is evidence that these cellular adhesion molecules can be considered reliable biomarkers for the development and severity of atherosclerosis and could add to the predictive value of the classical risk factors for IHD in HIV-negative populations. There are insufficient data that this can be applied in HIV-positive patients, particularly those with acute coronary syndromes (ACS).

Endothelial function has been studied in HIV-positive patients since the onset of the epidemic. There appears to be an intricate interplay between endothelial function and inflammation, as markers such as VCAM-1 and ICAM-1 are elevated in patients early after HIV infection. The mechanism of endothelial
dysfunction and promotion of atherosclerosis in HIV-infected individuals is complex but is thought to be related to a number of factors including direct involvement of HIV, endothelial activation and vascular inflammation.17,18

Endothelial dysfunction is regarded as a link between infection, inflammation and atherosclerosis, and there are recent data suggesting the presence of endothelial dysfunction in untreated HIV-positive patients.19 Furthermore, following cART, it has been shown that there is a fall in markers of endothelial activation such as monocyte chemo-attractant protein, P-selectin and VCAM-1.20

Although endothelial function has been studied in numerous studies in the past, there is a paucity of data on endothelial function in HIV-positive patients presenting with ACS.21 Therefore we aimed, firstly, to assess the presence and degree of endothelial dysfunction in HIV-positive patients presenting with ACS by using flow-mediated dilatation (FMD) and endothelial biomarkers. Our secondary aim was to assess carotid intima–media thickness (CIMT) in these patients as a surrogate marker of atherosclerosis.

Methods

This was a prospective study of 60 patients at a large urban public hospital in Johannesburg, South Africa, recruited over a three-year period (July 2012 to July 2015). Twenty HIV-positive patients presenting with ACS (HIV+/ACS) were compared to 20 HIV-negative patients with ACS (HIV-/ACS) and 20 HIV-positive patients without ACS (HIV+/no ACS).

Inclusion criteria included age ≥ 18 years and HIV-positive patients presenting with ACS. Risk factors for coronary artery disease (CAD) that were studied included age, smoking, hypertension, diabetes and family history of premature CAD (men ≥ 55 years, women ≥ 65 years of age). Exclusion criteria included prior myocardial infarction, life-threatening disease (men ≥ 55 years, women ≥ 65 years of age), hypertension, diabetes and family history of premature CAD (men ≥ 55 years, women ≥ 65 years of age). Ethical approval for the study was obtained from the local institutional body (M111143).

The HIV+/ACS and HIV-/ACS patients were matched for age and gender. The HIV+/no ACS patients could only be matched for gender as cART-naïve patients presenting at our HIV clinic were found to be much younger patients. CIMT thickness was measured in all three groups using an 11-Mhz transducer (Philips iE33 ultrasound machine) with the patient in the supine position with the head tilted 30 degrees to the left for the right carotid artery assessment and then 30 degrees to the right for the left carotid artery. The carotid artery bifurcation was visualised and the software automatically measured carotid artery intima thickness of the distal wall 10 mm from the bifurcation bulb.

Endothelial function was measured non-invasively using brachial FMD according to standardised guidelines.19 The maximum diameter of the brachial artery was measured at rest. A blood pressure cuff was then inflated to at least 50 mmHg above the systolic pressure to occlude arterial inflow for five minutes. The brachial artery diameter was again measured two minutes after cuff release when the maximum dilation of the vessel usually occurs.

Applanation tonometry of the radial artery converts the radial pulse wave into an aortic pulse wave. Pulse-wave velocity (PWV) was measured from sequential waveform measurements at the carotid and femoral sites. The distance that the pulse wave travelled was determined as the difference between the distance from the femoral sampling site to the suprasternal notch, and the distance from the carotid sampling site to the suprasternal notch.

Endothelial biomarkers were measured in all 60 patients and included interleukin (IL)-1β, IL-1Ra, IL-6, tumour necrosis factor alpha (TNF-α), monocyte chemotactic protein-1 (MCP-1), plasminogen activator inhibitor-1 (PAI-1), E-selectin, P-selectin, ICAM-1 and VCAM-1. Following blood collection in EDTA tubes, specimens were centrifuged for 20 minutes at 4°C and 1 000 × g. The plasma was decanted into 1.5-ml microcentrifuge tubes and stored at –70°C for later analysis.

IL-1β, IL-1Ra, IL-6, MCP-1 and TNF-α concentrations were quantified using the Bio-Plex Pro™ human cytokine standard 27 (Plex Bio-Rad Laboratories, Hercules, CA) as per manufacturer’s instructions. The plasma was diluted four-fold for these assays. E-selectin and P-selectin plasma levels were measured using the Human Magnetic Luminex assay (R&D Systems, Minneapolis, MN) as per manufacturer’s recommendations. Plasma was diluted two-fold to measure E-selectin and P-selectin levels. The serum concentrations for VCAM-1, ICAM-1 and PAI-1 were analysed in sera diluted 40-fold using the Milliplex human sepsis magnetic panel 1 (Merck Millipore, Billerica, MA) as per manufacturer’s instructions. Samples were analysed using the Bio-Plex 200 system (Bio-Rad) and concentrations were determined using the 5-PL method using Bio-Plex Manager 5.0 software.

Statistical analysis

The χ² test was used to assess the relationship between categorical variables and groups. The Fisher’s exact test was used where the requirements for the χ² test could not be met. The relationship between continuous variables and groups was assessed with one-way analysis of variance (ANOVA) for the three groups and the unpaired t-test for two groups. Post hoc tests for ANOVA were conducted using the Tukey–Kramer adjustment for multiple comparisons. Where the data did not meet the assumptions of these tests, a non-parametric alternative, the Kruskal–Wallis test was used for three groups, and the Wilcoxon rank sum test for two groups. Paired comparisons between continuous variables were carried out with the paired t-test or the Wilcoxon matched-pairs test. Data analyses were carried out using SAS version 9.4 for Windows. A 5% level of significance was used.

Results

The HIV+/ACS patients had a mean age of 51.1 years (± 8.1) and 13 were male (65%). The mean age of 36.0 years (± 6.8) in the HIV+/no ACS group was significantly lower than that of the HIV+/ACS group [51.1 years (± 8.1)] and the HIV-/ACS group [52.3 years (± 9.0)] (p < 0.0001). The proportion of males in each group ranged between 50 and 80%, but the differences were not statistically significant (p = 0.14) (Table 1).

Ten (50%) of the HIV+/ACS group were on cART and none was on protease inhibitors. Seven (35%) of the patients in the HIV+/ACS group were newly diagnosed with HIV. There were 15 (75%) hospital admissions with ST-segment elevation myocardial infarction (STEMI) (eight anterior, seven inferior), three (15%) with non-ST segment elevation myocardial infarction and two patients with unstable angina (10%). The typical presentation...
in the HIV+/ACS group was a young patient with STEMI involving the left anterior descending artery, which was the most common artery involved (60%), followed by the right coronary artery (35%) and the left circumflex artery (20%).

Risk factors in the HIV+/ACS group included smoking in 11 (55%), hypertension in six (30%), diabetes in two (10%), dyslipidaemia in two (10%), and one (5%) patient had a family history of IHD. The prevalence of diabetes and dyslipidaemia was higher in the HIV-/ACS group compared to the HIV+/ACS and the HIV+/no ACS groups ($p = 0.0006$ and $p = 0.0002$, respectively). The prevalence of smoking and hypertension was lower in the HIV+/no ACS group compared to the other HIV+/ACS and the HIV-/ACS groups ($p = 0.0012$ and $p = 0.0006$, respectively). Low-density lipoprotein (LDL) levels were no different in ACS patients whether they were HIV positive or negative. HIV-positive patients without ACS had significantly lower LDL levels.

Endothelial function was measured using FMD in all three groups. The median percentage difference in FMD between baseline (before blood pressure cuff inflation) and post blood pressure cuff deflation was significantly higher for the HIV+/no ACS group (14.3; IQR 6.7–20.6%) compared to the HIV+/ACS group (5.2; IQR 1.4–13.4%) and the HIV-/ACS group (3.7; IQR 2.3–4.4%) ($p = 0.044$ and $p = 0.0016$, respectively).

### Table 1. Patient demographics, risk factors and clinical investigations

<table>
<thead>
<tr>
<th></th>
<th>HIV+/ACS $n=20$</th>
<th>HIV-/ACS $n=20$</th>
<th>HIV+/no ACS $n=20$</th>
<th>$p$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)$^*$</td>
<td>51.1 (8.1)</td>
<td>52.3 (9)</td>
<td>36 (6.8)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Race (black), n (%)</td>
<td>17 (75)</td>
<td>7 (35)</td>
<td>20 (100)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>13 (65)</td>
<td>16 (80)</td>
<td>10 (50)</td>
<td>0.14</td>
</tr>
<tr>
<td>Smoking</td>
<td>11 (55)</td>
<td>10 (50)</td>
<td>1 (5)</td>
<td>0.0012</td>
</tr>
<tr>
<td>Hypertension</td>
<td>6 (30)</td>
<td>7 (35)</td>
<td>0</td>
<td>0.0006</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2 (10)</td>
<td>9 (45)</td>
<td>0</td>
<td>0.0006</td>
</tr>
<tr>
<td>Dyslipidaemia</td>
<td>2 (10)</td>
<td>10 (50)</td>
<td>0</td>
<td>0.0002</td>
</tr>
<tr>
<td>Family history</td>
<td>1 (5)</td>
<td>2 (10)</td>
<td>0</td>
<td>0.31</td>
</tr>
<tr>
<td>CIMT (mm)</td>
<td>0.66 (0.16)</td>
<td>0.70 (0.06)</td>
<td>0.50 (0.00)</td>
<td>0.0005$^*$</td>
</tr>
<tr>
<td>PWV (m/s)</td>
<td>4.1 (1.1)</td>
<td>4.6 (1.0)</td>
<td>3.6 (0.6)</td>
<td>0.12</td>
</tr>
</tbody>
</table>

### Laboratory

#### Normal values

- Haemoglobin (g/dl) 14.3–18.3
- Creatinine (µmol/l) < 1.7
- Total cholesterol (mmol/l) < 4.5
- Triglycerides (mmol/l) < 1.7
- HDL (mmol/l) > 1.0 male
- LDL (mmol/l) < 2.5
- CD4 (cells/mm³) 301 (205–417)

#### Median change in FMD (%)

<table>
<thead>
<tr>
<th></th>
<th>HIV+/ACS</th>
<th>HIV-/ACS</th>
<th>HIV+/no ACS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline to BP cuff inflation</td>
<td>30.0</td>
<td>22.5</td>
<td>15.0</td>
</tr>
<tr>
<td>Baseline to nitrate</td>
<td>7.5</td>
<td>5.0</td>
<td>7.5</td>
</tr>
</tbody>
</table>

*Mean ± SD, $^*$median (IQR).

CIMT = carotid intima-media thickness, PWV = pulse-wave velocity, LDL = low-density lipoprotein, HDL = high-density lipoprotein, CD4 = cluster of differentiation.
Patients without ACS had the most vasoreactivity compared to the patients with ACS.

The mean PWV in the HIV+/ACS group was 4.1 m/s (SD 1.1), 4.6 m/s (SD 1.1) in the HIV-/ACS group and 3.9 m/s (SD 1.1) in the HIV+/no ACS group. These values were all low with no significant differences between the three groups ($p = 0.12$) (Table 1).

CIMT was measured in all three groups. The mean CIMT of the two groups with ACS was not different. The CIMT in the group without ACS (0.50; ± 0.08 mm) was marginally but significantly lower than the CIMT of both the HIV+/ACS group (0.66; ± 0.16 mm) and the HIV-/ACS group (0.70; ± 0.06 mm) ($p = 0.0005$ and $p < 0.0001$, respectively) (Table 1).

There were significant differences in the endothelial biomarkers VCAM-1, ICAM-1, IL-6 and E-selectin in the three groups (Table 2). The median VCAM-1 levels in HIV-positive patients with and without ACS were significantly higher than in the HIV-/ACS cohort. However, median ICAM-1 levels were significantly higher in HIV-positive patients without ACS than in the HIV+/ACS and HIV-/ACS cohorts. The HIV+/no ACS group had significantly lower median levels of IL-6 than both the HIV+/ACS and the HIV-/ACS groups. The median E-selectin levels in the HIV+/ACS patients and HIV-/ACS patients were significantly lower than that of the HIV+/no ACS group. There was no significant difference in median IL-1β, IL-1Ra, MCP-1, TNF-α, P-selectin and PAI-1 levels between the groups.

<table>
<thead>
<tr>
<th>Table 2. Endothelial biomarkers</th>
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<tbody>
<tr>
<td>Medium levels (interquartile ranges)</td>
</tr>
<tr>
<td>VCAM-1 (ng/ml)</td>
</tr>
<tr>
<td>ICAM-1 (ng/ml)</td>
</tr>
<tr>
<td>IL-6 (pg/ml)</td>
</tr>
<tr>
<td>E-selectin (ng/ml)</td>
</tr>
<tr>
<td>IL-1β (pg/ml)</td>
</tr>
<tr>
<td>IL-1Ra (pg/ml)</td>
</tr>
<tr>
<td>MCP-1 (pg/ml)</td>
</tr>
<tr>
<td>TNF-α (pg/ml)</td>
</tr>
<tr>
<td>P-selectin (ng/ml)</td>
</tr>
<tr>
<td>PAI-1 (ng/ml)</td>
</tr>
</tbody>
</table>

There were significant differences in the following endothelial biomarkers; VCAM-1, ICAM-1, IL-6 and E-selectin. The median VCAM-1 levels in HIV-positive patients with and without ACS were significantly higher than in the HIV-/ACS cohort. However, median ICAM-1 levels were significantly higher in HIV-positive patients without ACS than in the HIV+/ACS and HIV-/ACS cohorts. The HIV+/no ACS group had significantly lower median levels of IL-6 than both the HIV+/ACS and the HIV-/ACS groups. The median E-selectin levels in the HIV+/ACS patients and HIV-/ACS patients were significantly lower than that of the HIV+/no ACS group. There was no significant difference in median IL-1β, IL-1Ra, MCP-1, TNF-α, P-selectin and PAI-1 levels between the groups.

**Discussion**

Studies suggest that an overall 1.5–2.0-fold increased risk of acute myocardial infarction is conferred by HIV infection. Common to most studies is that the mean age at presentation of ACS in HIV-infected patients is a decade younger than the general population, with a mean age of 50 years. This is similar to our cohort where the mean age was 51 years.

IHD in HIV-positive patients presenting with ACS have different risk-factor profiles in developing and developed regions. Traditional risk factors such as hypertension, diabetes and dyslipidaemia are more common in developed regions. The current study had fewer patients with hypertension, diabetes, dyslipidaemia and family history of IHD in HIV-positive patients with ACS.

In developing countries smoking appears to be the dominant risk factor with prevalence rates of 24.4% in HIV-positive males. More than half of the HIV+/ACS patients in our cohort were smokers with fewer other traditional risk factors. Furthermore, there is evidence that smoking contributes to endothelial dysfunction. These findings make smoking cessation an important modifiable risk factor for the prevention of IHD in HIV-positive patients.

Mechanisms for the development of atherosclerosis in HIV are multifactorial and include chronic inflammation and immune activation. These in turn may also lead to endothelial dysfunction, further contributing to the pathogenesis of atherosclerosis. Endothelial dysfunction is associated with increased levels of reactive oxygen species and decreased nitric oxide levels and hence decreased vascular reactivity. HIV itself has been linked to endothelial dysfunction. This is supported by findings of a significant improvement in FMD in patients in the first 24 weeks after initiation of cART, suggesting that suppression of HIV viraemia leads to improved endothelial function.

The HIV-1 envelope protein gp120 and the regulatory protein Tat are associated with endothelial cell apoptosis and increased cellular adhesion molecules (ICAM-1, E-selectin). Furthermore, a prothrombotic state [increase of von Willebrand factor, PAI-1, cellular adhesion molecules (ICAM-1, E-selectin)]. Furthermore, a prothrombotic state [increase of von Willebrand factor, PAI-1, tissue plasminogen activator (t-PA)] have been implicated in the pathogenesis of atherosclerosis in HIV-positive patients. Telomere length and CDKN2A expression were both consistent with increased biological ageing in HIV-infected individuals. Anti-retroviral therapies may be linked to CAD, specifically protase inhibitors, however the risk of CAD associated with anti-retroviral therapy is small compared with the impressive reductions in all-cause mortality with cART.
Endothelial dysfunction is well known to be associated with atherosclerosis in HIV-negative populations. It has also been described in HIV-positive patients without ACS. In our study, HIV+/ACS patients had almost the same degree of endothelial dysfunction as the control group of ACS patients without HIV. Although it would appear that endothelial dysfunction was not more prevalent in the HIV-positive group with ACS, it must be borne in mind that the latter group had significantly fewer coronary risk factors such as hypertension, diabetes, dyslipidaemia and family history of IHD compared to the HIV-negative patients with ACS, suggesting that HIV infection itself contributed to endothelial dysfunction. HIV-positive patients without ACS had the highest brachial artery vasoreactivity compared to the patients with ACS. This is an interesting finding but is most likely a reflection of the much younger age of this group compared to the other two groups.

In HIV-positive patients, endothelial activation may lead to structural and functional vascular changes. Exposure to long-term sub-clinical inflammation is related to accelerated stiffening of large arteries. Peripheral waveform analysis using PWV has been shown to provide a non-invasive method of measuring 'global' endothelial function. Increasing levels of arterial stiffness are correlated with higher PWV. The value for stiff vessels is a PWV > 10 m/s and this value has been found to be an independent marker of end-organ damage. In our study we found uniformly low values (< 5 m/s) for PWV. This finding, we believe, is largely an age-related effect. This is supported by Fourie et al. who recently reported increasing PWV velocities only after the age of 50 years in HIV-positive, cART-naive patients.

By studying ACS patients who were HIV positive and comparing them to ACS patients who were HIV negative, we were able to assess endothelial activation in both groups of patients. In developing countries, high levels of endothelial markers such as IL-6, TNF-α, PAI-1 and sCD14 have been reported in HIV-positive compared with HIV-negative patients. Studies of endothelial function from developing nations have demonstrated that in recently seroconverted Kenyan women, endothelial biomarkers (VCAM-1 and ICAM-1) were significantly elevated in these patients early after HIV infection.

In a recent study from South Africa, HIV-positive patients were found to have higher levels of adhesion molecules compared to HIV-negative patients, with an odds ratio of 3.9 (2.2–7.0) for ICAM-1 and 16.2 (7.5–35) for VCAM-1. Furthermore, the same investigators reported that ICAM-1 and VCAM-1 were elevated in both treated and cART-naive patients, with the odds being greater for the never-treated group.

Another study from South Africa, which assessed endothelial biomarkers in ACS patients who were HIV positive, also found significantly elevated VCAM-1 levels in HIV-positive patients with ACS compared to control patients who were either HIV negative or HIV positive without ACS. Similarly, in our cohort of HIV+/ACS patients, we found significantly higher levels of VCAM-1 compared to HIV-negative patients, findings that are in concert with previous reported results.

VCAM-1 is a member of the immunoglobulin super-family and is involved in cellular adhesion and transmigration of leucocytes through endothelial cells, and is thought to play a role in the development of atherosclerosis. With the stimulation of endothelial cells by inflammatory cytokines there is increased expression of VCAM-1 and this is associated with an increased predictive value for future cardiovascular events. Therefore VCAM-1 may be an informative biomarker for predicting the risk of HIV disease progression, morbidity and mortality.

The pro-inflammatory cytokine, IL-6, induces expression of adhesion molecules such as VCAM-1 and ICAM-1 and may be seen as an early modulator of leukocyte trafficking in the vascular wall. However, we did not find significantly elevated levels of IL-6 in HIV-positive and HIV-negative patients with ACS. Lack of a significant difference in IL-6 and other markers of endothelial dysfunction in HIV-infected and non-infected controls have also been previously reported.

Non-invasive surrogate tools such as CIMT and coronary computer tomography angiography indicate an increased prevalence of sub-clinical atherosclerosis in HIV-positive compared to HIV-negative patients. A meta-analysis of 13 observational studies suggests a trend towards increased CIMT in HIV-infected patients. As early as childhood, HIV-infected children receiving cART were found to have increased CIMT, suggesting that IHD risk may already be heightened in HIV-infected patients at a young age.

CIMT has been shown to decrease with cART and less CIMT progression was associated with suppressed viral load at baseline. In our cohort, CIMT measurements were unexpectedly lower in the HIV+/ACS compared to the HIV- ACS patients. The HIV+/no ACS patients also had low CIMT measurements. One possible explanation for the finding of lower CIMT in HIV+/ACS patients is the relative lack of traditional risk factors for atherosclerosis, such as hypertension, diabetes and low LDL levels in the HIV+/ACS group. It has been shown that the presence of high cardiovascular risk-factor profiles in HIV-positive patients is associated with increased CIMT.

This study has the following limitations. First, the study is a single-centre study with a small sample size. Given the nature of the study, it took almost three years to recruit 20 HIV-positive patients presenting with ACS to our centre. With the small sample size we were not able to perform multivariate analyses. Second, given the type of the clinical presentation of patients in the study we were unable to completely match case–control patients for age, gender and cardiovascular risk factors. Although the HIV+/no ACS group were gender matched, they could not be matched for age as the majority of HIV+/no ACS patients, who were cART-naive, presenting at the HIV clinic were young. Lastly, HIV+/no ACS patients in the study were newly diagnosed and therefore the duration of infection was not known.

Conclusion

Endothelial dysfunction as assessed by brachial FMD was similar in HIV-positive patients with ACS compared to HIV-negative patients with ACS. Endothelial biomarkers such as VCAM-1 and ICAM-1 were significantly raised in HIV-positive patients compared to HIV-negative patients. However, VCAM-1 was the only endothelial marker that was significantly raised in HIV-positive patients with ACS compared to HIV-negative patients with ACS. Our cohort of HIV-positive patients with ACS had impaired FMD but near-normal CIMT and PWV measurements. Given that FMD, CIMT and PWV were similar in HIV-positive and HIV-negative patients with ACS, the use of endothelial biomarkers may provide a more promising modality to investigate endothelial activation and subsequent dysfunction.
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References