HIV-infected patients on combined antiretroviral treatment had a similar level of arterial stiffness to the patients with ST-segment elevation myocardial infarction

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DOI: 10.33963/KP.a2021.0183

Received:
September 12, 2021

Accepted:
December 16, 2021

Early publication date:
December 16, 2021

INTRODUCTION

Human immunodeficiency virus (HIV) is an independent risk factor for cardiovascular disease, and HIV-infected patients have a higher risk of myocardial infarction than HIV-negative patients. Consequently, age-related comorbidities, such as cardiovascular disease, have become more common in this population [1, 2]. We can use invasive and non-invasive methods to assess endothelial function and arterial stiffness. One of the non-invasive techniques is reactive hyperemia peripheral arterial tonometry (RH-PAT) that allows for the evaluation of peripheral microcirculation vessels [3]. The study by Kikuya et al. [4] presented another non-invasive method for evaluation of arterial stiffness. The authors confirmed the significance of periodic changes in blood pressure and their influence on arterial stiffness. Nadel et al. [5] compared HIV-infected patients to the non-HIV-infected over a median period of 38 months and showed an increased risk of acute coronary syndrome without ST-segment elevation (NSTEMI) in HIV-infected patients. Moreover, they showed that HIV-infected patients had more severe coronary atherosclerosis on computed tomography (CT) angiography and higher rates of NSTEMI compared to uninfected patients [5]. The attention was focused on the influence of combined antiretroviral therapy (cART) on lipid metabolism and increased cardiovascular risk, especially in patients treated with protease inhibitors (PIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), and nucleoside reverse transcriptase inhibitors (NRTIs) [6].

Evaluating cardiovascular risk among HIV-infected people is not an easy assignment. The Framingham score used in HIV-infected patients is underestimated. Moreover, the importance of cART treatment, drugs interaction, and side effects are underlined [7, 8].

In terms of the goal of the study, because the cardiovascular risk in HIV-infected patients is higher than in the HIV-negative and the pathomechanism of these changes is still unknown, we decided to compare the arterial stiffness and the endothelial dysfunction in adult HIV-infected patients with non-HIV-infected persons at week 4 after ST-elevation myocardial infarction (STEMI).

METHODS

From January to December 2016, we recruited 63 patients, including 34 HIV-infected (18 on cART) and 29 HIV-negative patients at week 4 after STEMI. On the visit day, each HIV-infected patient underwent a basic medical examination. The body mass index (BMI) and laboratory results were collected. Despite the fact that the Centers for Disease Control and Prevention (CDC) defines tobacco smokers as people who smoked at least 100 cigarettes in their lifetime and who currently smoke cigarettes [9], we defined current tobacco smokers as individuals who smoked at least 20 cigarettes/day for more than 5 years (5 pack-years). The arterial stiffness was calcu-

Table 1. Baseline patient characteristics

	HIV group (n = 34)	STEMI group (n = 29)	*P*-value
Age, years, mean (SD)	38.9 (11.7)	55.3 (8.6)	<0.01
Male gender, n (%)	30 (88.2)	26 (89.7)	1.00
BMI, kg/m^2, mean (SD)	23.8 (4.1)	28.4 (3.4)	<0.01
Active smoking, n (%)	19 (55.9)	21 (72.4)	0.20
Hypertension, n (%)	2 (5.9)	17 (58.6)	<0.01
Diabetes mellitus, n (%)	0 (0.0)	4 (13.8)	0.04
ACEI, n (%)	1 (2.9)	28 (96.6)	<0.01
Statins, n (%)	2 (5.9)	29 (100.0)	<0.01
Systolic blood pressure, mm Hg, mean (SD)	125 (18)	129 (19)	0.41
Diastolic blood pressure, mm Hg, mean (SD)	78 (12)	82 (12)	0.19
Heart rate, bpm, mean (SD)	77 (12)	70 (9)	0.01
Hemoglobin, g/dl, mean (SD)	13.8 (2.1)	14.4 (1.7)	0.15
White blood cells, 1000/mcL, mean (SD)	6.2 (2.3)	9.2 (2.8)	<0.01
AI, %, mean (SD)	1.5 (18.2)	11.4 (18.7)	0.04
AI@75, %, mean (SD)	3.3 (14.0)	8.2 (16.8)	0.21
lnRHI, mean (SD)	0.7 (0.3)	0.5 (0.2)	<0.05

Abbreviations: ACEI, angiotensin-converting-enzyme inhibitors; BMI, Body Mass Index; AI, augmentation index; AI@75, AI corrected for a heart rate of 75 beats per minute; lnRHI, natural logarithm of reactive hyperemia index

lated by the EndoPAT 2000 (ITAMAR®, Caesarea, Israel) and the endothelial function with Peripheral Arterial Tonometry (PAT®; ITAMAR). The endothelial dysfunction was defined for the natural logarithm of the reactive hyperemia index (lnRHI) ≤0.51. Arterial stiffness was assessed as the augmentation index (AI) and AI adjusted for a heart rate of 75 beats per minute (AI@75). Among HIV-negative patients after STEMI, similar procedures were carried out at week 4 since admission to the hospital, except for laboratory tests performed at the time of acute coronary syndrome (ACS). The exclusion criterion in the HIV-infected group was having experienced myocardial infarction. It was a retrospective analysis in parallel groups.

To assess distributions of continuous variables the Shapiro-Wilk test was used. For all analyzed continuous variables, normal distributions were found. Continuous variables were presented as mean values and standard deviations (SD). Differences between subgroups were calculated with Fisher's exact test and Student's t-test, respectively, for categorical and continuous variables. In the case of 3 subgroups, analysis of variances (ANOVA) and paired Student's t-tests were performed. Tests were considered significant for *P*-values $P < 0.05$ and $P < 0.017$ for multiple comparisons, according to Bonferroni correction.

To reduce the age as a confounding variable, propensity score matching was used, with the 1:1 ratio for numbers of patients in each subgroup. Statistical analysis was performed using SAS® software, version 9.4 (SAS Institute, Cary, NC, US).

The study was approved by the Bioethics Committee of the Medical University of Warsaw. All participants signed written informed consent.

RESULTS AND DISCUSSION

The mean (SD) of cART duration was 172.3 (90.6) weeks and contained: NRTIs–13, NNRTIs–4, PIs–14, and integrase strand transfer inhibitors (INSTIs) — 4 patients. Among 18 patients on cART 5 (27.7%) had endothelial dysfunction, and 10 (55.5%) smoked cigarettes. In the group of 16 patients without cART, 7 (43.7%) had endothelial dysfunction, and 9 (62.5%) smoked cigarettes (Table 1).

In the STEMI group, a high percentage of patients with diabetes and hypertension (13.8% and 58.6%, respectively) was observed in comparison to the HIV group (0% and 5.9%, respectively). Comparisons of AI, AI@75, and lnRHI values in analyzed groups: HIV on cART, HIV without cART, and STEMI are presented in Supplementary material, *Table S1*.

There are several studies concerning the effect of HIV and cART on arterial stiffness augmentation. In the study by Alvi et al. [10], ritonavir-boosted protease inhibitors (PIs/r) had a significant impact on serum lipids and enhanced atherosclerotic lesions [11]. Our results may confirm the negative influence of cART (especially PIs) on arterial stiffness.

We got lnRHI results significantly lower in the STEMI group than HIV-infected patients, which may suggest more intense endothelial dysfunction in the STEMI group. This trend was also observed after analysis of groups matched by age and number. The significant difference in the degree of endothelial dysfunction was for the STEMI group and the cART-treated HIV-infected group, which may suggest the protective effect of cART on endothelial function. However, we did not find any differences for lnRHI in HIV-infected patients on and without cART.

Subsequently, we compared the HIV and STEMI groups, each consisting of 20 patients matched in terms of age and parity (1:1). Data are presented as mean (SD) for the HIV and STEMI groups respectively. Subsequently, we compared age, AI, AI@75 bpm and lnRHI of the HIV and STEMI groups, each consisting of 20 patients matched in terms of age and parity (1:1). Age results as mean (SD) for the HIV and

STEMI groups were respectively — 45.8 (10.3) years and 50.8 (5.8) years with $P = 0.07$. Results of AI as mean (SD) for the HIV and STEMI groups were respectively — 6.9 (19.3) % and 12.0 (21.1) % with $P = 0.43$. Results of AI@75 bpm as mean (SD) for the HIV and STEMI groups were respectively — 8.3 (13.6) and 9.1 (18.8) % with $P = 0.88$. Results of lnRHI as mean (SD) for the HIV and STEMI groups were respectively — 0.71 (0.34) % and 0.52 (0.24) % with $P = 0.06$.

After the 1:1 matching, we confirmed that the arterial stiffness in the HIV-infected group is similar to the STEMI patients, which may be an indirect proof of the severity of cardiovascular changes in this group of patients.

Cigarette smoking is one of the main factors that increase endothelial abnormalities and is also an independent cardiovascular risk factor [12]. We observed a high percentage of patients who smoked cigarettes in both groups. We did not show a statistically significant difference in the rate of smoking between studied groups, but the risk of coronary vascular injury caused by smoking was similar in all patients.

CONCLUSIONS

We report that HIV-infected patients on cART may have similarly high values of arterial stiffness as non-HIV-infected persons at week 4 after STEMI. Assessing cardiovascular risk is very important especially in infected patients on cART therapy. Modification of risk factors should be the basic element of care for HIV-infected patients. More studies are required to validate our observation concerning arterial stiffness and elevated risk of cardiovascular disease in this group of patients, independently of age, smoking status, and concomitant chronic diseases.

Supplementary material

Supplementary material is available at https://journals.viamedica.pl/kardiologia_polska.

Article information

Conflict of interest: None declared.

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