Rev Port Cardiol. 2019;38(7):471–472

Portuguese Society of CARDIOLOGY

Revista Portuguesa de
Cardiologia
Portuguese Journal of Cardiology
www.revportcardiol.org

EDITORIAL COMMENT

Cardiovascular risk in HIV-infected patients

Risco cardiovascular em doentes infetados com HIV

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Available online 13 September 2019

With the advent of antiretroviral therapy (ART), survival of human immunodeficiency virus (HIV)-infected patients has increased, and HIV has become, in those who adhere to ART, a chronic disease with long life expectancy.

In these circumstances, degenerative diseases, particularly cardiovascular disease (CVD), sometimes premature, have become important problems in the follow-up of these patients.

Cardiovascular disorders initially associated with HIV included left ventricular dysfunction, pericardial effusion, infective endocarditis, arrhythmias associated with long QT interval and pulmonary hypertension, as well as atherosclerosis.[1]

However, in recent years, accelerated atherosclerosis and coronary artery disease have emerged as major causes of cardiovascular mortality and morbidity in HIV-infected patients. Although total mortality in HIV patients has fallen in the last 10 years, cardiovascular mortality has increased significantly over the same period.[2]

The reasons for this accelerated atherosclerosis and the increased incidence of myocardial infarction in HIV patients are not fully known. The causes are probably multiple, with associations of factors, including endothelial dysfunction with increased expression of adhesion molecules and platelet aggregation,[3] side effects of ART including protease inhibitor-associated dyslipidemia and insulin resistance, and a heavy burden of traditional risk factors such as smoking. Paradoxically, in general, the cardiovascular risk factors of HIV-infected individuals are treated less than those of uninfected persons.[4,5]

HIV infection itself appears to be an independent risk factor for coronary artery disease. HIV patients without major cardiovascular risk factors present about twice the risk of myocardial infarction compared to non-infected individuals.[6]

After a coronary event, HIV-infected individuals appear to present a worse prognosis, with unexpectedly high restenosis rates after percutaneous coronary intervention.[7,8]

Against this background, the current issue of the *Journal* presents a paper by Policarpo et al. on cardiovascular risk estimation in HIV-infected patients, assessing and comparing the usefulness of three cardiovascular risk algorithms.[9]

Considering the importance of CVD in HIV-infected individuals, all papers in this field are to be welcomed, since they focus on what is clearly an unsolved problem.

In their study, the authors estimate cardiovascular risk using the European Systematic Coronary Risk Evaluation (SCORE), the Framingham risk score (FRS) and the Data Collection on Adverse Events of Anti-HIV Drugs (DAD) score. The latter is designed to assess the cardiovascular risk of HIV-infected individuals and includes exposure to HIV treatment as well as traditional risk factors.[10]

Analyzing 571 patients from a total of 3000 HIV-infected patients followed at their Department of Infectious Diseases, Policarpo et al. conclude that there are significant correlations between the three risk scores, with 4.4% of the patients being classified as high-risk with SCORE, 10.3% with DAD, and 20.5% with the FRS. This result was predictable, as

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https://doi.org/10.1016/j.repc.2019.08.007

all risk algorithms share the same parameters (conventional risk factors) to estimate overall cardiovascular risk.

At the same time, the authors found a high level of conventional risk factors in HIV patients, with 53% being smokers, waist circumference above the cut-off in 42%, obesity or overweight in 40% and metabolic syndrome in nearly 33%. In general, the group on ART presented a worse risk profile than the treatment-naive group, reflecting the older age of the former group as well as the atherogenic potential of the therapy.

The article has several positive points, including the importance of the subject, the large sample under analysis, the identification of conventional cardiovascular risk factors in an HIV population, and the use of three algorithms to estimate cardiovascular risk in HIV-infected individuals.

On the other hand, there are also some limitations. From my standpoint, the main limitation of the paper is the lack of a gold standard for assessing cardiovascular risk.

The authors compare three risk algorithms, with significant correlations but quite different results (the proportion of subjects classified as at high risk ranging from 4.4% to 20.5%).

Bearing in mind the high cardiovascular risk of HIV patients, it could be assumed that the most inclusive score (FRS) is the most applicable, but in fact we do not know which is the most appropriate to assess the actual cardiovascular risk in HIV patients. Moreover, different scores analyze different endpoints, leading to different results. SCORE assesses cardiovascular mortality over 10 years, while the FRS assesses the incidence of CVD, including fatal and non-fatal events, over the same period. In these circumstances, the FRS is bound to be more inclusive than SCORE.

Only a prospective study to assess what happens to patients at different risk levels could validate a particular risk score. Such a study would present ethical limitations: HIV patients with conventional risk factors must be treated, not observed.

An alternative to validate the utility of a risk score in these patients could be to assess intermediate end-points, such as carotid intima-media thickness or coronary artery calcium score. Demonstration of a close relationship between a risk score and an intermediate end-point would support the usefulness of that score to access coronary risk in HIV patients.

Finally, what advice can be given to physicians and HIV patients to prevent CVD?

HIV patients under ART should be aware that CVD is a real threat to their life, in terms of survival as well as quality, and should adopt healthy habits, not smoking and actively controlling their cardiovascular risk factors.

Physicians should be aware of HIV patients' cardiovascular risk, assess that risk and, whatever the algorithm, bearing in mind the high baseline cardiovascular risk of these patients, be prepared to intervene to achieve control of their cardiovascular risk factors.

Infectologists should aim to use ART drugs that are less likely to cause cardiovascular harm and should remain aware of their HIV patients' cardiovascular status.

Cardiologists should perform routine systematic cardiac monitoring, assessing traditional risk factors, paying special attention to major cardiovascular risk factors(smoking, hypertension, diabetes and dyslipidemia), and monitor risk factors and the cardiovascular status of HIV patients, bearing in mind that a first cardiac accident can be fatal. Cardiac assessment, including echocardiography and other cardiac exams, is often needed to determine whether generic symptoms, such as fatigue, result from the infectious disease or from a cardiac complication.

Considering the high risk level of these patients, after behavioral intervention, cardiovascular medication should begin early in the follow-up of cardiovascular risk factors. When prescribing cardiovascular drugs such as statins, it is important to take into account the particular characteristics of these patients and to choose drugs that do not interfere with ART.

The initial approach to HIV patients was based on control of the infection. When this is achieved, to maintain the increase in life expectancy of HIV-infected individuals, it is necessary to prevent and treat late complications of the disease, including CVD.

Conflicts of interest

The author has no conflicts of interest to declare.

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