CORONARY ARTERY DISEASE IN PEOPLE LIVING WITH HUMAN IMMUNODEFICIENCY VIRUS

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Abstract: *People living with HIV live longer now due to highly active antiretroviral therapy. Due to their increased life expectancy, they have an increased cardiovascular risk cause by the traditional risk factors (smoking, use of ilicit drugs, obesity/lipodystrophy, dyslipidemia, diabetes, hypertension) and particular risk factors (endothelial dysfunction, inflammation, coagulation abnormalities, viral coinfections and antiretroviral therapy. The pathophysiology of accelerated atherosclerosis is complex. Coronary artery disease become an important cause of mortality in these patients. The incidence of coronary artery disease and especially of acute myocardial infarction is generally low among HIV patients, but it may by twice as high as in patients with the similar characteristics. Medical treatment for coronary disease in these patients has no special particularities comparing to general population, but possible drug interactions must be considered. Indication for coronary revascularization, either angioplasty, or aorto-coronary by-pass follows general indications for general population.*
Keywords: *coronary artery disease; HIV; antiretroviral therapy;*

Rezumat: *Persoanele ce trăiesc cu HIV au o supraviețuire mai lungă, datorită terapiei antiretrovirale. Crescând speranța de viață, acești pacienți dezvoltă risc cardiovacular crescut atât prin creșterea factorilor de risc tradiționali (fumat, consum de substanțe inicite, obezitate/lipodistrofie, dislipidemie, diabet zaharat, hipertensiune), cât și prin creșterea factorilor de risc particulari (disfuncție endotelială, inflamație, tulburări de coagulare, co-infecții virale și terapia antiretrovirală. Fiziopatologia aterosclerozei accelerate este complexă. Boala coronariană a devenit o cauză importantă de moratlitate la acești pacienți. Incidența bolii coronariene, în special a infarctului miocardic actut este în general mică în rândul pacienților infectați cu HIV, dar poate fi până la de două ori mai mare față de pacienți din populația generală cu caracteristici asemănătoare. Tratamentul medicamentos al bolii coronariene la acești pacienți nu diferă față de populația generală, însă trebuie avute în vedere potențialele interacțiuni medicamentoase. Indicația de revascularizare coronariană, fie prin angioplastie percutanată, fie prin bypass aortocornarian se pune aidoma populației generale.*
Cuvinte cheie: *boală coronariană, HIV, terapie antiretrovirală.*



Internal Medicine

General Reviews

It is anticipated that by year 2030, 73% of the people living with HIV will be over the age of 50 and 78% of them will by suffer from cardiovascular diseases [1]. This is a consequence of aging of this population and increasing of cardiovascular risk. Among traditional risk factors, most frequently encountered are smoking, use of illicit drugs, obesity/lipodystrophy, dyslipidemia, diabetes, hypertension. Also, particular risk factors such as endothelial dysfunction, inflammation, coagulation abnormalities and viral coinfections (cytomegalovirus, herpes simplex virus, hepatitis C virus), selenium deficiencies and last, but not least, antiretroviral therapy lead to the acceleration of atherosclerosis.

In Europe, cardiovascular death in people living with HIV is reported in a proportion of 6.5% [2], with 8% in France [3] and 15% in North America[6].

The etiology of coronary artery disease is multifactorial and includes the increase of prevalence in traditional and particular risk factor, with chronic inflammation and the activation of the immune system being a key factor.

Antiretroviral therapy, especially protease inhibitors, causes important significant disorders of lipid and carbohydrate metabolism and is associated with early atherosclerosis. This therapy may exacerbate the injury of vascular smooth muscle cells and may induce neointimal hyperplasia. Recent studies show that increased platelet reactivity may also be responsible for the increased cardiovascular risk in these patients so new therapies meant to prevent this effect must be studied[5].

In the era of antiretroviral therapy, coronary artery disease became the most important cardiovascular disease in HIV infected patients in North America[6].

Regarding the association between antiretroviral therapy and myocardial infarction, it was shown that the incidence is increased by recent exposure to reverse transcriptase nucleoside inhibitors and especially by recent or cumulative exposure to protease inhibitors [7]. Laboratory animal research shown that abacavir administration had proinflammatory and prothrombotic effects by increasing of interactions between thrombocytes, leucocytes and endothelium, favouring platelet aggregation and thus increasing the risk of acute myocardial infarction [8]. Exposure to non-nucleoside reverse transcriptase inhibitors was not associated with and increased risk of acute myocardial infarction[9].

The incidence of coronary artery disease and especially of acute myocardial infarction is generally low among HIV patients, but it may by twice as high as in patients with the similar characteristics (sex, age, risk factors). As this population ages, coronary artery disease will

become more common. At this point, the data available in literature are quite variable.

In a retrospective study of patients hospitalised for acute myocardial infarction, of which 0.22% (n=608) was infected with HIV, the prevalence of ischemic cardiomyopathy was reported almost double among patients infected compared with those without infection (7.6% vs 4.2%, p=0.003) [10].

Regarding the evolution of these patients, if the in-hospital and one-year mortality was similar between the two groups, HIV infected patients were more often readmitted for heart failure decompensation (3.3% vs 1.4% p=0.020) [10].

A study review which included almost 800 000 HIV patients has shown an incidence of cardiovascular diseases at 62 events at 10 000 patients and a risk ratio of 2.19 (1.79 for myocardial infarction and 2.56 for stroke), higher compared with patients without HIV infection[11].

Recent data have shown that in-hospital risk of cardiac and cerebrovascular events at patients with acute coronary syndrome and HIV is similar with the risk of HIV negative ones, but the risk of recurrence of ischemic events and the readmission for decompensation of heart failure after a first episode of coronary syndrome is higher among HIV patients [5]. Also, according with older studies, the hospitalization rate for coronary disease is significantly higher among HIV infected patients [12].

In HIV patients, clinical presentation in the case of an acute coronary syndrome can often be atypical, as in the case of patients with other chronic diseases such as diabetes or chronic kidney disease [13]. Due to the polymorphism of symptoms, the diagnosis of acute coronary syndrome in this type of patients is more difficult to establish. A necropsy study in Romania have showed a prevalence of myocardial infarction in of 7.05% (6 patients), of which only one case was diagnosed antemortem[14].

Regarding the degree of coronary impairment, some older studies showed that it can be compared with the degree of coronary impairment in the general population. The prevalence of damage to the common trunk of the left coronary artery in HIV patients is about 6%, as in the general population [15][17]. Coronary artery bypass grafting is considered to be the gold standard in patients with common trunk lesions. Boccara and colleagues compared 27 HIV patients with a control group formed from 57 patients without infections who underwent coronary artery bypass grafting and the results showed that at 30 days the rate of major cardiovascular events was the same. But, at longer follow-up (after 41 months), it has been shown that the rate of recurrence of ischemic events was higher in HIV patients, requiring reintervention, usually percutaneous coronary revascularization of native arteries[16].

Nowadays, the epidemiological data regarding coronary artery in HIV infected patients have changed, due to new information on the pathophysiology of HIV infection, to the new developments of preventive cardiology and due to the progress of imaging techniques able to reveal subclinical cardiac dysfunction, such as cardiac echography by speckle tracking, scintigraphy, cardiac magnetic resonance imaging or coronary artery computed tomographic angiography.

Recent studies on coronary artery disease in patients who associate HIV infections are very extensive regarding the investigations, aiming to improve the confirmation strategies and to diminish the confounding factors. Therefore, patients with HIV have an



increase risk of developing coronary artery disease and of ischemic recurrences after an acute coronary syndrome. [6,11,18]

The most recent multicentric trial [19] compared patients with acute coronary syndrome with and without HIV infection (60 patients versus 107 patients, respectively), males 95,8%, mean age 48 years old. Both study groups had very similar conventional cardiovascular risk factors, but the use of ilicit substances was most frequently seen in HIV patients compared to control group (20,7% versus 4,6%; p = 0.006) (19). In the same time, HIV patients had higher values of reactive protein C (CRP): 31,1 ± 52,3 mg/dl vs 14,0 ± 23,1 mg/dl [19]. The study analysed the angiographic particularities of the coronary arteries in both groups studied and the findings showed that HIV patients had especially diffuse coronary lesions, higher rate of coronary aneurysms, nonobstructive lesions and also higher values of residual SYNTAX score, even though the initial score was similar. In counterpart, HIV patients had better rates of coronary reperfusion.

Another observation was that despite the fact that HIV patients with acute coronary syndromes have greater number of coronary lesions at angiography, these lesions are less complex, with mild calcification, but therefore, probably more vulnerable to complications compared to patients without HIV infection[19].

Medical treatment for coronary disease in these patients has no special particularities comparing to general population, but possible drug interactions must be considered and adaptation of therapeutical recommendations is necessary, consulting the infectionist is mandatory.

Indication for coronary revascularization, either angioplasty, or aorto-coronary by-pass follows general indications for general population.

Conclusions

HIV patients may have accelerated and diffuse atherosclerosis, with extensive and, in many cases, severe coronary artery disease. Therefore, in this particular situation, coronary artery disease becomes an important cause of mortality in these patients.

Clinical presentation of acute coronary syndromes in HIV patients may be atypical and requires special attention, especially when cardiovascular risk factors coexist.

Short-term prognosis of HIV patients and acute coronary syndromes is similar with that of negative HIV patients, but long-term evolution is characterised by major cardiovascular adverse events.

Recent studies of coronary disease in HIV infection recommend extensive investigations to better confirm the diagnosis

and reduce potential confounding factors.

Early non-invasive diagnostic methods for atherosclerosis by echocardiography or coronary angio CT, as well as cardiac magnetic resonance, myocardial perfusion scintigraphy for myocardial ischemic lesions should be extensively used in HIV patients with high risk of atherosclerosis.

BIBLIOGRAPHY

1. Smit M, Brinkman K, Geerlings S, Smit C, Thyagarajan K, van Sighem A V., et al. Future challenges for clinical care of an ageing population infected with HIV: A modelling study. Lancet Infect Dis. 2015;

2. Freiberg MS, Chang CCH, Kuller LH, Skanderson M, Lowy E, Kraemer KL, et al. HIV infection and the risk of acute myocardial infarction. JAMA Intern Med. 2013;

3. May M, Gill J, Lewden C, Saag M, Mugavero M, Reiss P, et al. Causes of death in HIV-1-Infected patients treated with antiretroviral therapy, 1996-2006: Collaborative analysis of 13 HIV cohort studies. Clin Infect Dis. 2010;

4. Palella FJ, Baker RK, Moorman AC, Chmiel JS, Wood KC, Brooks JT, et al. Mortality in the Highly Active Antiretroviral Therapy Era. JAIDS J Acquir Immune Defic Syndr. 2006;

5. Boccara F, Mary-Krause M, Potard V, Teiger E, Lang S, Hammoudi N, et al. Hiv infection and long-term residual cardiovascular risk after acute coronary syndrome. J Am Heart Assoc. 2020;

6. Boccara F, Lang S, Meuleman C, Ederhy S, Mary-Krause M, Costagliola D, et al. HIV and coronary heart disease: Time for a better understanding. Journal of the American College of Cardiology. 2013.

7. Bavinger C, Bendavid E, Niehaus K, Olshen RA, Olkin I, Sundaram V, et al. Risk of Cardiovascular Disease from Antiretroviral Therapy for HIV: A Systematic Review. PLoS One. 2013;

8. Collado-Diaz V, Andujar I, Sanchez-Lopez A, Orden S, Blanch-Ruiz MA, Martinez-Cuesta MA, et al. Abacavir induces arterial thrombosis in a murine model. In: Journal of Infectious Diseases. 2018.

9. Class of Antiretroviral Drugs and the Risk of Myocardial Infarction. N Engl J Med. 2007;

10. Lorgis L, Cottenet J, Molins G, Benzenine E, Zeller M, Aube H, et al. Outcomes after acute myocardial infarction in HIV-infected patients: Analysis of Data from a french nationwide hospital medical information database. Circulation. 2013;

11. Shah ASV, Stelzle D, Lee KK, Beck EJ, Alam S, Clifford S, et al. Global Burden of Atherosclerotic Cardiovascular Disease in People Living With HIV. Circulation. 2018;

12. Triant VA, Lee H, Hadigan C, Grinspoon SK. Increased acute myocardial infarction rates and cardiovascular risk factors among patients with human immunodeficiency virus disease. J Clin Endocrinol Metab. 2007;

13. Seecheran VK, Giddings SL, Seecheran NA. Acute coronary syndromes in patients with HIV. Coronary Artery Disease. 2017.

14. Ia IŢ, Sida HI V. Leziuni ischemice aterosclerotice în infec ţ ia hiv/sida. 2012;(20):7882.

15. Escaut L, Monsuez JJ, Chironi G, Merad M, Teicher E, Smadja D, et al. Coronary artery disease in HIV infected patients. Intensive Care Med. 2003;

16. Boccara F, Cohen A, Angelantonio E, Meuleman C, Ederhy S, Dufaitre G, et al. Coronary Artery Bypass Graft in HIV-Infected Patients: A Multicenter Case Control Study. Curr HIV Res. 2008;

17. Mehta NJ, Khan IA. HIV-associated coronary artery disease. Angiology. 2003;

18. Hsue PY, Waters DD. HIV infection and coronary heart disease: mechanisms and management. Nature Reviews Cardiology. 2019.

19. Raphael Robert, Yves Cottin, Valerie Potard, Murielle Mary-Krause, Silvie Lang, Emmanuel Tieger FB. Coronary Angiographic Features and Major Adverse Cardiac or Cerebrovascular Events in People Living With Human Immunodeficiency Virus Presenting With Acute Coronary Syndrome. 2022;(June):13.