A New Face of Cardiac Emergencies

Human Immunodeficiency Virus–Related Cardiac Disease

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KEYWORDS

• Human immunodeficiency virus • HIV-associated acute cardiovascular diseases
• Antiretroviral drug interactions • Emergency department

KEY POINTS

- Patients positive for the human immunodeficiency virus (HIV) present a unique challenge to emergency physicians as they may present to the emergency department with a variety of cardiovascular diseases related to the HIV infection.
- Common cardiovascular emergencies include acute coronary syndromes, HIV-associated cardiomyopathy, pericardial effusion, infective endocarditis, pulmonary embolism, and cardiac arrhythmias.
- Important drug interactions between antiretroviral therapy and common cardiovascular therapies exist and should be taken into consideration when treating such patients.

INTRODUCTION

The human immunodeficiency virus (HIV) epidemic is a major health challenge of the twenty-first century with an estimated 36.7 million people living with HIV globally and more than 1.2 million HIV-positive patients living in the United States.[1,2] The improved access to combination antiretroviral therapy (cART) has not only increased life expectancy, but has also changed the spectrum of disease. Thus HIV-positive patients present a unique challenge to emergency physicians, as they may present with a variety of cardiovascular diseases related to the HIV infection (**Fig. 1**). In this review we discuss the presentation, management, and prognosis of common acute cardiovascular diseases affecting HIV-positive patients presenting to the emergency department (ED).

CORONARY ARTERY DISEASE

HIV infection carries an overall 1.5 to 2.0-fold increased risk for developing coronary artery disease (CAD).[3] Current data suggest that immunodeficiency (CD4 <200 cells/mm^3) is significantly associated with a higher risk of myocardial infarction (MI).[4,5] HIV-related inflammation and immune activation together with endothelial dysfunction and coagulation abnormalities contribute to CAD in these patients.

Studies indicate a high prevalence of traditional CAD risk factors in HIV-positive populations.[4,6] However, prevalence estimates vary due to differences in study populations, risk cutoffs, genetic background, geographic location, and access to cART. Smoking is the most common risk factor and has been reported to be two-fold higher in

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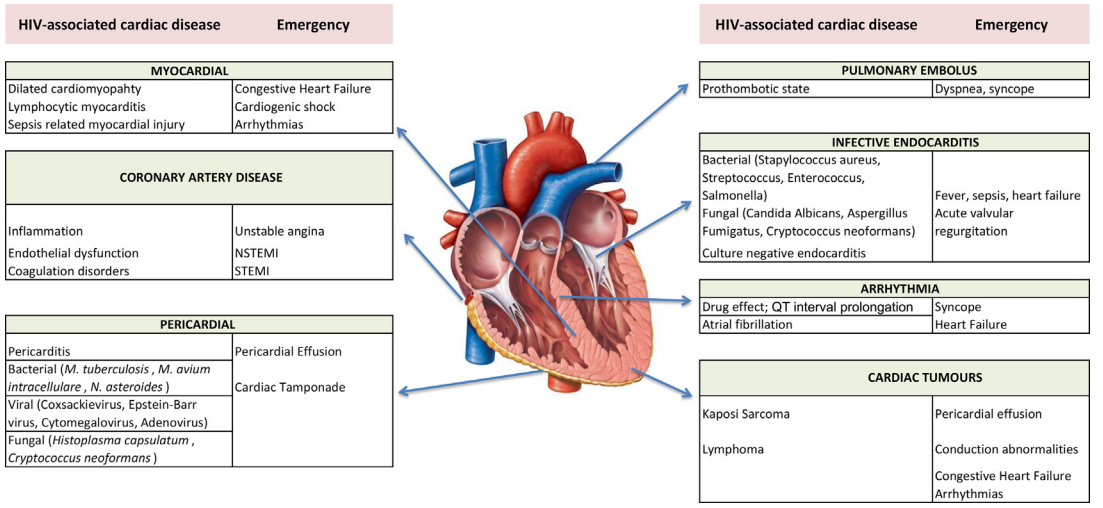

Fig. 1. Cardiac emergencies in HIV. NSTEMI, non-STEMI.

HIV-positive patients.[7,8] Thus, smoking cessation should be strongly advocated, as the life expectancy of HIV-infected smokers has been found to be on average 8 years less than that of HIV-infected nonsmokers.[9]

Clinical Presentation and Management

As compared with the general population, HIV-positive patients presenting with acute coronary syndrome (ACS) are younger (mean 50 years), predominantly male, and usually have single-vessel CAD on coronary angiography.[10–12] Most commonly, HIV-positive patients present with ST elevation MI (STEMI).[11] It is important to consider the type of MI among HIV-positive individuals to guide prevention and treatment strategies. A recent study from 6 US centers found that half (50.4%) of all HIV-positive patients presenting with ACS had Type 2 MI, which occurs in the setting of supply and demand mismatch.[13] The etiology of these MIs was attributed to sepsis, bacteremia, and recent use of cocaine or other illicit drug use.[13]

Patients presenting with ACS should be managed similar to HIV-negative patients according to standard guidelines.[14,15] There are no data to guide which is the most appropriate thrombolytic agent to administer in HIV-positive patients presenting with MI; however, tenecteplase would be the agent of choice, as it can be administered quickly as a bolus dose.

Antiplatelet agents should be standard of care in all patients with ACS. Aspirin 300 to 325 mg together with P2Y12 inhibitors (clopidogrel, ticagrelor, prasugrel) should be administered at the time of presentation. Thienopyridines are metabolized by several cytochrome P450 liver enzymes and may interact with antiviral agents such as efavirenz as well as certain drugs used to treat opportunistic infections, such as antifungals, rifampicin, and isoniazid (**Table 1**).[16,17] Prasugrel should not be combined with ritonavir because this may decrease prasugrel's efficacy. Ticagrelor, which is predominantly metabolized by the CYP3A4/5 isoenzyme, also should be used with caution in patients on protease inhibitor (PI) therapy, as there may be an increased risk of bleeding.[16,17]

Statins should be prescribed for all patients with ACS. Statins not only reduce low-density lipoprotein levels but there is evidence that they may also indirectly reduce immune activation.[18] There are several interactions between cART and statins and one should be mindful when prescribing these drugs.[19] PIs can significantly increase statin levels, thus increasing the risk of toxicity. With regard to fibrate therapy, fenofibrate is preferred over gemfibrozil due to fewer drug interactions.[20]

Combination antiretroviral therapy, particularly PIs, have been implicated in inducing dyslipidemia (elevated total cholesterol and triglyceride levels), as well as endothelial dysfunction.[21,22] On the other hand, non-nucleoside reverse transcriptase inhibitors, integrase inhibitors, and CCR5 antagonists have thus far shown to have neutral lipid effects with no increased risk of CAD.[23] The START study found that initiation of cART in all HIV-infected patients with CD4 counts greater than 500 cells/mm^3 significantly reduced serious AIDS-related events and death at a mean follow-up of 3 years.[24] As a result, the World Health Organization now recommends cART to all HIV-infected patients regardless of CD4 count.[25]