Getting to the heart of the matter: the need for tailored cardiovascular prevention strategies in patients with HIV

People diagnosed with HIV today can expect significantly longer lifespans than those diagnosed in previous decades thanks to improved diagnostic tests and effective combination antiretroviral therapy (cART). The Centers for Disease Control and Prevention reported that, in 2018, more than half (51%) of the people living with HIV in the United States and dependent areas were aged 50 years and older [1]. As more individuals diagnosed with HIV join the ranks of older adults, they are likely to face the same health problems as the general aging population, which include living with cardiovascular disease (CVD) and other chronic conditions.

An analysis of nearly 80 000 health insurance claims submitted from 2009 through 2015, collected from a US health care database, showed that individuals living with HIV are at increased risk of developing CVDs, particularly heart failure and stroke, compared with uninfected people [2]. Chronic inflammation caused by HIV has been identified as one of the mechanisms that increase risk for cardiovascular events [3]. In addition, the metabolic complications associated with HIV infection continue to play a role, alongside traditional risk factors, in the pathogenesis of atherosclerosis in HIV-positive individuals, despite aggressive cART [3].

Ischemic heart disease is the most common form of CVD in patients with HIV, according to research [4] presented at the 2019 American Heart Association (AHA) Scientific Sessions. The authors used data collected from 2005 through 2014 in the largest publicly available US national database (National Inpatient Sample) to identify patients with HIV and various forms of CVD. Nearly one-quarter (22.2%) of the HIV-seropositive patients included in the study had CVD. The authors found that patients with HIV and comorbid CVD had higher mortality rates, longer hospital stays, and higher health care costs compared with HIV-seropositive patients without CVD.

Early recognition of patients at high risk for ischemic heart disease has become an important step toward improving the prognosis of HIV-positive individuals. 'Clinicians should be aware that many persons living with HIV will have an underlying higher risk of CVD and, therefore, thresholds for preventive therapy (e.g. statins) may need to be lower and efforts to optimize lifestyles (e.g. smoking cessation) may need to be more intensive [in this patient population],' said Alvaro Alonso, MD, PhD, Associate Professor in the Department of Epidemiology at the Emory University Rollins School of Public Health, who was involved in the analysis of the health care claims [2]. 'Some evidence also suggests that better control of the HIV infection results in lower risk of CVD,' Dr. Alonso added.

To truly optimize primary prevention, clinicians must recognize that patients with HIV have a unique CVD risk profile that may dictate different approaches. In the era of cART, HIV-positive patients often present with subclinical changes in cardiac structure and function rather than symptomatic heart failure [3]. A study [5] published in 2021 showed that individuals with HIV experienced specific changes in cardiac structure and diastolic function that may predispose them to developing heart failure with preserved ejection fraction (HFpEF). Transthoracic echocardiographic examination performed between 2017 and 2019 in nearly 1200 participants in the Multicenter AIDS Cohort Study showed that HIV seropositivity was independently associated with small increases in left ventricular (LV) mass index and mild diastolic abnormalities, but not with LV systolic dysfunction. Reduced LVEF (<50%) was identified in a small percentage of participants with HIV (2.4%). The authors noted that the differences in several cardiac metrics persisted among the patients with HIV who received cART compared with the HIV-seronegative group, suggesting that HIV infection remains a major contributor to subclinical myocardial dysfunction in virally suppressed patients.

'Given that HIV infection is an independent risk factor for subclinical changes in cardiac structure and function, it is critical that not only is the HIV infection treated aggressively but the burden of cardiovascular risk factors should also be reduced,' said Katherine Wu, MD, Associate Professor of Medicine at the Johns Hopkins University School of Medicine, who co-authored the study. 'Lifestyle changes such as smoking cessation, abstinence from illicit drugs, healthy eating and regular, at least moderate-intensity physical activity are important. Equally critical are aggressive monitoring and management of diabetes, hypertension, and hypercholesterolemia. Such measures may offset the added burden of HIV on the heart which is present even among people who are virally suppressed.' HIV-seropositive patients may require prevention tools and therapies that target HFpEF, an

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entity that has become increasingly widespread in clinical practice. 'Vigilance regarding changes in exercise tolerance or development of palpitations is warranted, with further diagnostic testing as needed,' Dr Wu noted.

The future of HIV management will be defined by the identification of CVD phenotypes that manifest in seropositive patients, with the aim of targeting therapies toward those entities. Physicians who treat HIV-positive individuals with atrial fibrillation face a unique set of challenges, including the optimization of anti-coagulation strategies to prevent thromboembolic events. Recent research has raised questions about the use of conventional strategies for the prevention of thromboembolic events in this patient population. An analysis [6] of data from the Veterans Affairs HIV Clinical Case Registry showed that the CHA_2DS_2-VASc score was not a strong predictor of thromboembolic events in HIV-infected veterans with atrial fibrillation. The study included 914 patients who received a diagnosis of atrial fibrillation between 1997 and 2011 and had no prior thromboembolic events. Warfarin did not appear to be effective at preventing thromboembolic events, suggesting that the pathophysiologic mechanisms of HIV-associated atrial fibrillation may be more complex than those of arrhythmias in non-infected individuals.

Given the specific structural changes detected in their cardiovascular systems, patients with HIV may have risk factors for developing atrial fibrillation that are not found in the general population. These differences may include a younger age of atrial fibrillation onset, according to researchers who analyzed the prevalence and risk of atrial fibrillation in nearly 500 HIV-positive patients treated at the Jackson Memorial and University of Miami Hospitals between 2007 and 2018. Their review [7] of demographic, clinical, and laboratory data showed that patients with HIV, who had a mean age of 57.2 years, had a higher prevalence of atrial fibrillation when compared with HIV-negative adults younger than 60 years living in the United States. Additionally, patients with HIV and atrial fibrillation had lower $CD4^+$ cell counts and lower rates of viral load suppression compared with those without atrial fibrillation, as well as a trend toward higher rates of cerebrovascular events.

Future research may clarify whether patients with HIV are susceptible to diseases such as atrial fibrillation at a young age. In the meantime, routine screening for certain comorbidities could reduce the incidence of CVD in HIV-positive patients if implemented in clinical practice. A significant proportion of patients with HIV have hepatitis C virus (HCV) infection [8], which has been associated with cardiac dysfunction and heart failure even in the absence of coronary artery disease. A study [9] published in August 2021 explored the relationships of HIV and HCV infections with incident LV dysfunction (systolic or diastolic) in participants in The Women's Interagency HIV Study. The analysis included 311 women, of which 70% were HIV-positive and 20% were HCV-positive. Repeat echocardiography over a period of 12 years showed that nearly 14% of participants developed LV dysfunction. Women with HIV–HCV co-infection had a significantly increased risk for incident LV dysfunction compared with non-infected patients. HCV monoinfection was also associated with an elevated risk of developing LV dysfunction. While the causal relationship between HCV infection and LV dysfunction has not been fully elucidated, screening patients with HIV for HCV co-infection could optimize their treatment and prevent cardiovascular complications.

In 2019, the AHA provided clinicians with a roadmap for risk assessment and prevention of atherosclerotic CVD in patients with treated HIV infection [3]. 'HIV is [now] recognized as a risk enhancer for the development of CVD,' Dr. Wu added. 'However, there remain large gaps in specific strategies to address screening, diagnosis, and management of cardiovascular disorders in the aging HIV population, particularly in the areas of heart failure, atrial fibrillation, stroke, and peripheral arterial disease. This is due to the lack of large prospective studies and randomized controlled trials focusing on people living with HIV.' Although new research continues to shape the future of clinical care, understanding the interplay between traditional CVD risk factors and HIV-specific factors marks a first step in the direction of HIV-specific cardiovascular prevention strategies.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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