

HIV, cardiology, and ageing-navigating complex health dynamics

Description

The outlook of HIV treatment has dramatically transformed since the advent of combined Antiretroviral Therapy (cART), notably improving life expectancy for People Living with HIV (PLWH). Research shows that the life expectancy of HIV-1 virally suppressed, non-smoker, PLWH may be comparable to that of the general population from the age of 35. However, mortality rates among PLWH remain higher compared to the uninfected population and in terms of non-communicable diseases, Cardiovascular Diseases (CVD) have emerged as a major cause of death, alongside other non-AIDS related malignancies (particularly non-Hodgkin lymphoma) and liver diseases often exacerbated by co-infections such as hepatitis C [1]. Chronic HIV infection significantly increases CVD risks, presenting a complex challenge by introducing an additional layer of HIV-specific factors which stem from chronic inflammation and subsequent endothelial dysfunction with accelerated atherosclerosis. Some imaging studies have revealed myocardial inflammation, oedema, and fibrosis even in asymptomatic PLWH, which are linked to decreased cardiac function. Such findings underscore the critical need for regular comprehensive cardiovascular risk assessment and management in HIV care, advocating for tailored interventions such as lifestyle modifications and adjustments in antiretroviral treatment to mitigate these risks [2].

The interplay of traditional and HIV-specific factors and cardiovascular health

PLWH are estimated to be 1.5-2 times greater risk of developing CVD than that observed in age-matched HIV-uninfected individuals. This increased risk is influenced by a combination of traditional CVD risk factors and HIV-specific factors. Among the traditional risk factors, smoking is particularly prevalent in the HIV-infected population. Research indicates that PLWH are more likely to smoke and are less likely to quit smoking compared to the general U.S. population [3]. Some factors that were independently associated with higher smoking prevalence were homelessness, substance abuse, excessive alcohol intake, mental health issues and not achieving HIV viral load suppression.

Furthermore, certain cART regimens have been associated with cardiovascular toxicities that can exacerbate this risk over time. Specifically, Protease Inhibitors (PIs) are linked to metabolic disturbances, including hypertriglyceridemia, hypercholesterolemia, and insulin resistance which are major risk factors for CVD. Additionally, some studies suggest that the antiretroviral drug abacavir has an increased risk of myocardial infarction and has led to a decreased use globally [4-6]. Although it is important to consider that while these drugs carry potential CVD risks, the benefits of controlling HIV infection and preventing AIDS-related complications greatly outweigh these risks. Therefore, the selection of cART should be individualised, considering the CVD risk profile of each patient.

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Role of inflammation and immune activation

Chronic inflammation and ongoing immune activation play pivotal roles in increasing the CVD risk among PLWH. These physiological changes are closely associated with HIV infection itself and are partly sustained even with effective antiretroviral therapy. Chronic inflammation contributes to the development of atherosclerosis by damaging tunica intima and media, leading to plaque formation and arterial stiffness. This process can begin without noticeable symptoms and progresses to compromise CVD function [7].

Furthermore, immune activation in PLWH continues to engage immune cells and inflammatory markers, which exacerbate vascular inflammation and contribute to clot formation and arterial blockages. Studies indicated that high levels of IL-6 are a significant marker of CVD disease risk and all-cause mortality in HIV disease. Monocytes from HIV-infected adults produce high levels of IL-6, which promotes the development of atherosclerosis by influencing vascular cell function and increasing inflammation. This risk persists even in well-controlled HIV individuals as PLWH with well-controlled viral loads have 50%-100% higher IL-6 levels compared to the general population [8]. This state of heightened immune response not only accelerates the natural progression of atherosclerosis but may also induce changes in the cardiac myocyte and its function.

Subclinical cardiac changes

The introduction of advanced imaging techniques such as Cardiovascular Magnetic Resonance (CMR) has revolutionized the detection of subclinical cardiac changes in asymptomatic PLWH. CMR has revealed significant myocardial inflammation, oedema, and fibrosis with changes in myocardial structure and function in treated PLWH, compared to that of the general population [9]. Chronic systemic inflammation involving the myocardium and pericardium disrupts the electrical transmission and impairs overall systolic function while oedema of myocytes further reduces the preload of the heart, predisposing to heart failure. Similarly, in PLWH, pericardial effusions and myocardial fibrosis were 3 and 4 folds more common, respectively, compared to the general population. These subclinical abnormalities are often precursors to any overt CVD symptoms, making CMR a useful tool for early detection and intervention which can significantly impact the long-term CVD health of PLWH.

Premature ageing and HIV

The premature ageing process in PLWH is often accelerated due to a phenomenon known as immune senescence. Immune senescence refers to the gradual deterioration of the immune system brought on by the natural age advancement compounded by chronic HIV infection. This condition can precipitate the early onset of various

geriatric syndromes such as frailty, a decline in physical strength, and cognitive functions that are not typically observed until later in life in the general population. Frailty in PLWH can manifest as decreased muscle mass and strength, reduced endurance, slower walking speed, and unintended weight loss. Cognitive decline may range from subtle deficits in memory and executive function to more pronounced forms of HIV-Associated Neurocognitive Disorders (HAND) [10].

As PLWH ages, these age-related conditions add layers of complexity to healthcare management for PLWH and demand an integrated care approach that goes beyond standard HIV treatment protocols. Comprehensive geriatric assessment, which is a multidimensional process designed to evaluate an older person's functional ability, physical health, cognition, and mental health, has become increasingly important. The goal is to develop a coordinated and integrated plan for treatment and long-term follow-up.

Conclusion

The interaction of chronic HIV infection, cardiovascular disease, and premature ageing presents intricate challenges that require a tailored and multidisciplinary approach to care in an outpatient setting. By integrating specialized cardiovascular care with HIV treatment and geriatric support, Healthcare Providers (HCP) and multidisciplinary teams can offer more effective preventive and active management strategies that enhance the quality of life and health outcomes for ageing PLWH. Therefore, HCPs are challenged with developing a holistic approach that balances the suppression of HIV with the mitigation of CVD risks and the promotion of overall good health and well-being.

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