THE CHANGING LANDSCAPE OF HIV-ASSOCIATED CARDIOVASCULAR DISEASE IN THE ANTI RETRO VIRAL THERAPY ERA

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Abstract: **Human Immunodeficiency Virus (HIV) once recognized to cause immune deficient state in the infected person. Due to advent of Anti Retro Viral Therapy(ART) Its now being increasingly recognized as a Chronic condition. This Review Article focuses on clinical care that has been altered in a way that is unusual for a disease. Opportunistic infections and illnesses associated with an immunocompromised state dominated in the early phases of the epidemic, and a large corpus of research and therapeutic practice centered on these sequelae. In the present treatment period, HIV patients on suppressive antiretroviral medication face a new set of problems. These chronic, non-infectious disorders, such as cardiovascular disease (CVD), require management approaches that are distinct from those used to treat infectious consequences. An HIV-positive patient's optimal care for cardiovascular disease and other non-infectious consequences may differ from that of a healthy person. New research into the epidemiology, pathophysiology, prevention, and treatment of chronic illness problems, as well as the translation of such research into guidelines and policy creation, is needed as the focus of care for stable treatment for HIV-infected individuals.**

KEYWORDS: **HIV, AIDS, cardiovascular disease, coronary artery disease, antiretroviral therapy, drug interaction**

I. INTRODUCTION

As the HIV epidemic has progressed, the focus of People living with HIV (PLWH) have lived longer with the widespread use of combination antiretroviral medication, with their life expectancy improving by 9 to 10 years in high-income countries between 1996 and 2010. The introduction of ART has also transformed HIV infection into a manageable chronic illness. However, cardiovascular complications have become increasingly prevalent, contributing significantly to non-AIDS-related mortality. The interplay between HIV-related immune activation, chronic inflammation, metabolic derangements, and ART-associated toxicities underlies the heightened cardiovascular risk.

II. EPIDEMIOLOGY

HIV/AIDS has risen to become the world's fourth-leading cause of death due to its rising global epidemic. Since the start of the HIV epidemic, approximately 88.4 million people [71.3–112.8 million] have been infected with the virus. By the end of 2023, an estimated 39.9 million people were living with HIV globally, HIV/AIDS is becoming a significant issue for healthcare professionals and physicians.

In the HAART era, the incidence of opportunistic infections has decreased in these patients. The metabolic effects of HAART, particularly protease inhibitors (PI), have become more prominent in this patient population. Patients with HIV/AIDS are often given prophylaxis for opportunistic infections in addition to HAART therapy, depending on their level of immunity and prior infections.

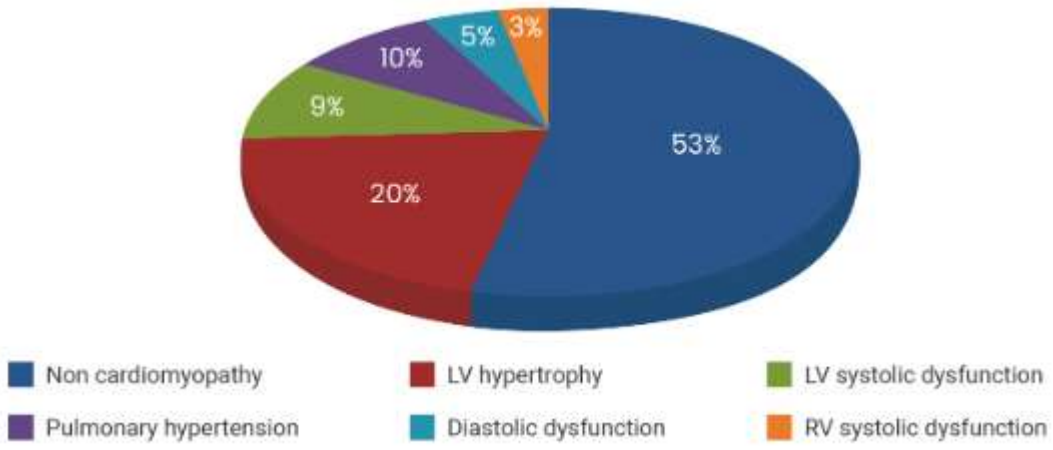

Fig.1: Epidemiology of heart disease in HIV patients

III. ETIOLOGY

Table 1: Etiology of cardiac effects of HIV/AIDs

Etiology of Cardiac Effects of HIV/AIDS
HIV directly affecting the heart
Effects of HAART on the heart
Opportunistic infections or treatment/prophylaxis of opportunistic infections
Mode of acquisition of HIV (intravenous drug use-related complications)
Non-HIV cardiac risk factors (such as diabetes mellitus or hypertension)

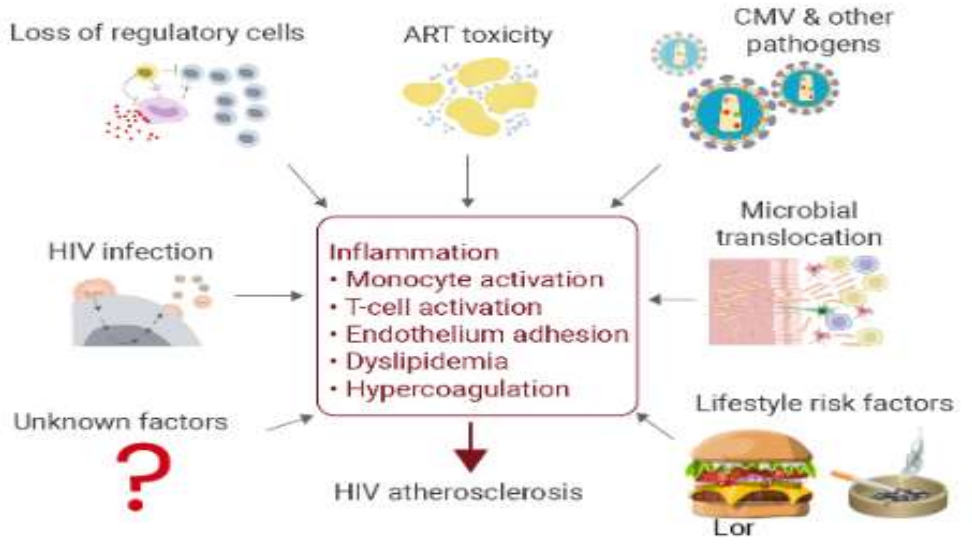

Fig 2: Etiological factors of heart disease in HIV patients

IV. PATHOPHYSIOLOGY

With increasing knowledge about the mechanism of HIV-related CVD, there has been a shift in perspective. Many early studies focused on the impact of classic CVD risk factors and antiretroviral drugs. Recent research is focusing on immunological activation and associated inflammation. The true underlying mechanism is likely to be a complicated interaction of components that is somewhat described by existing cardiovascular disease mechanistic pathways and partially explained by unique effects associated with HIV infection immunologic sequelae.

People living with HIV have lifestyle risk factors, combined antiretroviral therapy, and persistent immune activation. Lifestyle risk factors lead to metabolic dysfunction, and persistent immune activation leads to myocardial fibrosis. All these factors lead to obesity, hypercoaguable state, pro-inflammatory milieu, endothelial dysfunction, and pro-atherogenicity, and these factors lead to metabolic dysfunction and myocardial fibrosis. All these conditions lead to cardiovascular diseases in HIV patients.

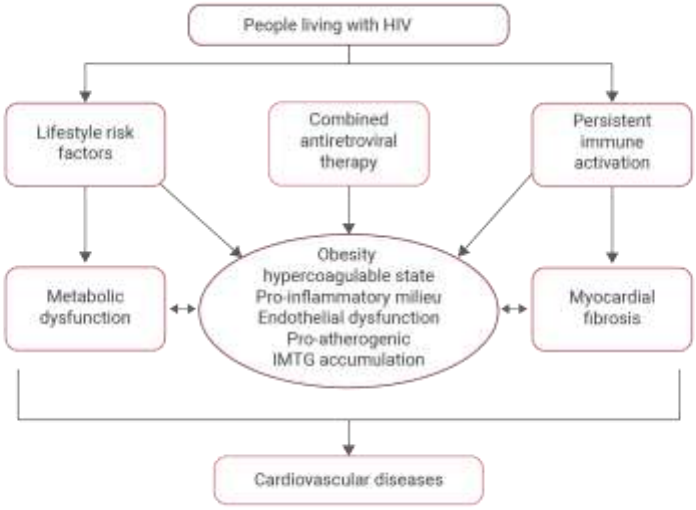

Fig 3: Pathophysiology of heart disease in HIV patients

V. CARDIAC DISEASE IN PATIENTS WITH HIV/AIDS

Pericardial disease

Pericarditis and pericardial effusions are two pericardial diseases reported in HIV/AIDS patients. In this patient population, pericarditis can be caused by bacterial pericarditis, the most prevalent of which is tuberculosis, Kaposi's sarcoma, or lymphomas. Pericardial effusions can occur in these patients; very large effusions producing tamponade are uncommon. Pericardial effusions were seen in up to 20% of patients, with 4% having significant effusions, according to echocardiography. Pericardiocentesis is usually reserved for cases where there is suspicion of tamponade or where diagnostic uncertainty exists. Even if there is no tamponade, the etiology might vary, and treatment is dependent on the unique etiology. In these individuals, the main disadvantage of Pericardiocentesis is the low diagnostic yield for tuberculous pericarditis. The pericardial biopsy may be more sensitive in the diagnosis in this situation, especially if the tuberculin skin test is negative.

Myocardial disease

Cardiomyopathy, myocarditis, cardiac tumors, and medication toxicity are all diseases of the myocardium in HIV/AIDS patients.

Left ventricular dysfunction in patients with HIV/AIDS is frequently clinically undetectable, although it can progress to severe left heart failure. HAART therapy has been shown to significantly reduce the progression of left ventricular dysfunction to heart failure. The etiology of HIV-associated cardiomyopathy is highly complex, involving the direct effects of HIV on the heart. The inflammatory response of the myocardium to HIV, the presence of autoantibodies, and reduced immunity make them susceptible to infection. Myocarditis is common in HIV/AIDS patients, and although pinpointing the cause can be difficult, only 20% of myocarditis in patients with HIV/AIDS can be related to a specific cause. Myocarditis can be caused by various things, including fungus, histoplasmosis, cryptococcosis, aspergillosis, herpes simplex virus, cytomegalovirus, bacterial tuberculosis, or parasitic toxoplasmosis. Because toxoplasma is a potentially curable cause of myocarditis or cardiomyopathy in these patients, toxoplasma serology should be included in the evaluation. Cocaine and methamphetamine usage can cause heart damage. Recently, a link between selenium deficiency and cardiomyopathy has been discovered. Antiretroviral medication has been proven to elicit autoimmune responses in the immune system, leading to cardiac dysfunction.

Endocardial disease

In HIV patients, endocardial or ventricular illness can be caused by bacterial or non-bacterial (marantic) endocarditis. Among the patient population, bacterial endocarditis is usually caused by intravenous drug misuse, with Staphylococcus aureus and Streptococcus viridans being the most prevalent pathogens and the tricuspid valve being the most common valve involved. Unlike the myocardium, HIV has no direct effect on the endocardium. Non-bacterial (marantic) endocarditis damages the tricuspid valve and can cause an embolism into the pulmonary artery, which is normal clinically.

Arrhythmias

Arrhythmias in patients with HIV/AIDS might be caused by drug toxicity or a subsequent symptom of cardiac dysfunction. Pentamidine/pyrimethamine and TMP-SMZ (trimethoprim-sulfamethoxazole), both used to treat toxoplasmosis and PCP (Pneumocystis jirovecii) pneumonia, can produce severe QT prolongation and, as a result, torsades de pointes, which can be deadly. In the absence of pharmacological therapy, most hospitalized patients showed QT prolongation, and torsades de pointes have been reported. The antibiotic ganciclovir, used to treat CMV infections, can produce ventricular tachycardia. Myocardial illness, including

heart failure and myocarditis, can produce arrhythmias in patients with HIV/AIDS, as previously mentioned. Patients who receive interferon-alpha therapy are more likely to have heart blockages and die suddenly.

Coronary artery disease and vascular disease (cerebral and peripheral)

On the one hand, while HAART medication delays the course of HIV-associated cardiomyopathy, it has clinically significant effects on metabolism, including hyperlipidemia, insulin resistance, lipodystrophy, and hyperglycemia, particularly with protease inhibitors. One of the unanticipated side effects of HAART appears to be accelerated atherosclerosis. The link between antiretroviral medication and coronary artery disease is a controversial topic.

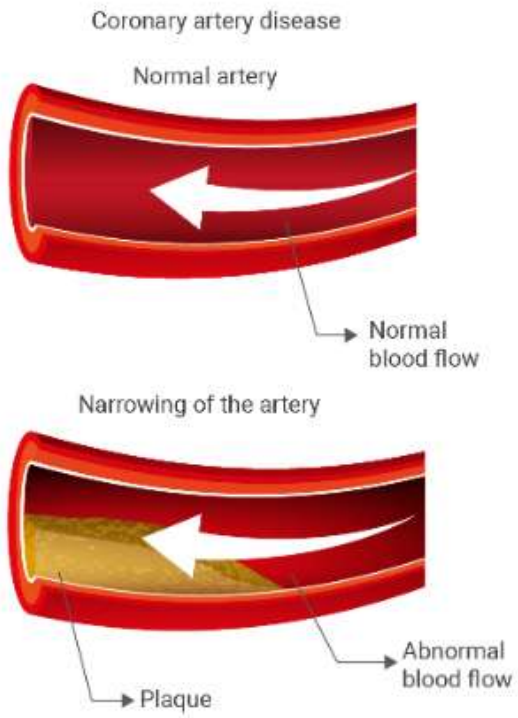

Fig 4: Coronary artery disease in HIV patients

Aneurysmal disease

Patients with HIV have more chances of developing an aneurysmal illness, particularly in the aortic and cerebral blood arteries than the general population. Vasculitis can cause aneurysms, which can be caused by HIV or secondary infections like CMV or tuberculosis. When HIV causes aneurysms, they are frequently unusual and numerous.

Pulmonary hypertension

Pulmonary hypertension can occur in patients with HIV/AIDS, which is caused by a combination of inflammation and genetic factors. This patient population has been linked to plexogenic arteriopathy.

Primary pulmonary hypertension affects less than 0.5% of patients with HIV, and the prognosis is usually dismal. Echocardiography can diagnose and rule out secondary types of pulmonary hypertension. The gold standard for diagnosis is still right cardiac catheterization. Plexogenic arteriopathy is the most common histological result, identical to what is seen in immunocompetent patients. Veno-occlusive disease and thrombotic arterial lesions are significantly more uncommon. Intravenous drug users are more likely to develop pulmonary hypertension linked to foreign material injected intravenously. Poor compliance frequently exacerbates pulmonary hypertension. Calcium channel blockers, diuretics, anticoagulants, and prostacyclin analogs are all used to treat pulmonary hypertension. In patients with HIV, the latter, specifically epoprostenol, effectively lowers pulmonary artery pressure both abruptly and over time. Pulmonary hypertension linked with HIV/AIDS varies from idiopathic/primary pulmonary hypertension in that it progresses more quickly, is unrelated to CD4 level, and is associated with a worse prognosis than non-AIDS patients.

Venous thrombosis

Patients with HIV/AIDS are at an increased risk of developing deep venous thrombosis (DVT). The prothrombotic state in these patients is likely due to a combination of factors, including elevated levels of plasminogen activator inhibitor (PAI), heparin cofactor II, D-dimer, and reduced protein S levels.

Valvular heart disease

IV drug users are at high risk for infective endocarditis due to HIV, but not nonusers. In the pre-ART era, the frequency of infective endocarditis ranged from 6% to 34%, with the right heart being the most commonly affected. Cases of nonbacterial thrombotic endocarditis have been documented in patients with severe immunosuppression and wasting syndrome. On echocardiography, Kaposi's sarcoma and non-Hodgkin type B lymphoma can be mistaken for infective endocarditis, and atypical endocarditis with negative hemocultures and immunosuppression must be invoked.

Tumors

Cardiac tumors affecting the heart are more typically secondary than primary in patients with HIV/AIDS. Kaposi's sarcoma frequently occurs in the context of diffuse mucocutaneous involvement. The heart is the only site of involvement. Asymptomatic lesions are common. Lymphomas can damage the heart; lymphomas in patients with HIV/AIDS are mostly non-lymphomas (Hodgkin's), which can be secondary or primary, with the former being far more prevalent. Primary non-lymphoma Hodgkin's that starts in the heart is extremely uncommon. Primary cardiac lymphomas, which are predominantly B-cell lymphomas, usually affect the right atrium and can cause conduction abnormalities, arrhythmias, superior vena cava blockage, or heart failure due to infiltration of the conduction system. In some patients, chemotherapy and radiation therapy have had mixed effects.

VI. Clinical Approach to Heart Disease in HIV/AIDS Patients

In patients with HIV/AIDS, the history and physical examination must be used to detect symptoms and indicators of cardiovascular disease. Details of previous opportunistic infections, classic atherosclerotic risk factors, and current and prior antiretroviral therapy must all be included in the history. One of the most crucial issues clinicians should consider is whether an HIV-positive person is immunocompetent or immunodeficient based on a recent CD4 count, which would be required for further diagnostic evaluation, treatment, and prognosis decisions. If the patient does not currently have antiretroviral therapy and has cardiac symptoms, he or she may need to be referred to an infectious disease specialist for antiretroviral therapy decision-making. Coordination of care between infectious disease and cardiology can help to improve care quality and design a tailored treatment plan based on all of the above considerations. Electrocardiography or echocardiography should not be used routinely in these individuals, especially because there is no evidence that they can detect subclinical illness. Dyspnea is a common complaint in HIV/AIDS patients, and the etiologies of cardiomyopathy and pulmonary hypertension must be considered.

For a thorough examination, a transthoracic echocardiogram is required. Except for consideration of drug-drug interactions, especially with antiretroviral therapy, drug therapy for heart failure is the same as for HIV-negative people. In HIV/AIDS patients with ventricular failure on echocardiography, an endomyocardial biopsy may be required to detect possibly treatable causes of myocarditis or cardiomyopathy. Finally, patients with pre-existing or newly developed serious cardiovascular illnesses may need to discontinue using cardiotoxic drugs.

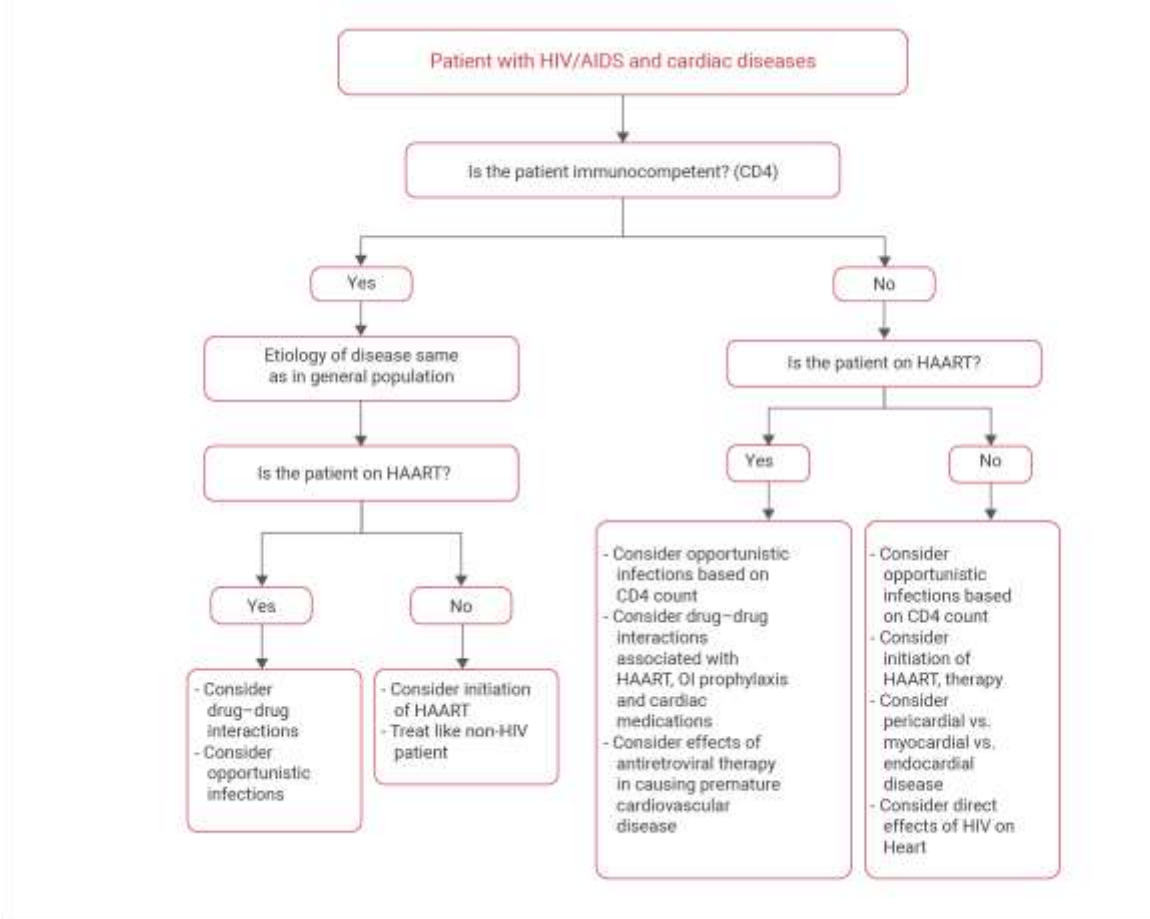

Fig 5: Clinical approach to heart disease in HIV patients

VII. DIAGNOSTIC APPROACH

Authority: IDSA/HIVMA

Recommendations/guidelines:

i. Fasting lipid levels should be checked before and after commencing HAART for 4–6 wk.
ii. Fasting glucose levels should be measured before and during HAART; currently, routine monitoring of insulin levels and/or oral glucose tolerance testing is not recommended.
iii. For clinical practice, routine body weight measurements and patient self-reports of body shape changes are sufficient.

Authority: The New York State Department of Health AIDS Institute

Recommendations/guidelines:

i. Before commencing antiretrovirals, obtain a fasting lipid profile and fasting blood glucose, as well as within 3–6 mo before starting a new regimen and annually thereafter.
ii. Obtain a fasting lipid profile and fasting blood glucose at baseline and yearly for individuals who are not on HAART.
iii. Clinicians should screen all HIV-positive patients for the use of illicit drugs or tobacco at least once a year.

Authority: The Australasian Society for HIV Medicine

Recommendations/guidelines:

i. Fasting lipids (total cholesterol, HDL-C, LDL-C, triglycerides) and glucose levels should be measured at baseline and periodically during HAART, at least once a year if normal and more frequently if abnormal.
ii. Directly question patients about perceived changes in body shape regularly.
iii. Assess smoking status, blood pressure, and weight at each visit.

IDSA: Infectious Diseases Society of America, HIVMA: HIV Medicine Association

VIII. ASSESSMENT OF CVD IN PATIENTS WITH HIV

Despite the debate over clear end objectives like myocardial infarction, multiple studies reveal that HIV patients on sustained combination antiretroviral therapy (cART) display early, subclinical indications of atherosclerosis. As a result, early symptoms of atherosclerosis may be necessary for identifying and monitoring HIV-infected patients at risk. The methods for such monitoring currently accessible in the general population will be discussed here, focusing on research conducted on HIV-infected patients.

Summarizing the assessment

i. Biomarker of early atherosclerosis
ii. Carotid Intima-Media thickening
iii. Arterial Stiffness
iv. Flow mediated dilation
v. Coronary endothelial function and Flow reserve studies with PET scan
vi. Coronary artery calcium scoring
vii. Framingham Risk Score

Biomarkers of early atherosclerosis

Because HIV-infected patients usually have blood samples drawn every 3–6 months to assess the effects of cART, a blood-borne marker is an obvious candidate for screening.

Biomarkers for CVD screening are receiving much attention in the general population. Initially, hs-CRP has been extensively studied as a marker of current CVD as well as a predictor of future events, leading to the American Heart Association (AHA)/CDC recommending hs-CRP measurement in patients with an intermediate risk of coronary heart disease (Framingham risk score [FRS] of 10%–20%) to improve risk stratification. Using hs-CRP in the HIV-infected population is controversial, as levels are elevated before cART and during therapy regardless of regimen and appear to either stay elevated despite normalized CD4 cell counts and suppressed viral loads or decrease even though the risk is thought to be associated with cART exposure. Changes in medication regimen have been linked to rises in hs-CRP in certain studies; therefore, it may still be relevant in patients on stable cART with normalized CD4 cell counts and suppressed viral load.

Other endothelial dysfunction biomarkers linked to an elevated risk of CVD in the general population include E-selectin, sICAM-1, sVCAM-1, tPAI-1, MMP9, and MPO, all of which appear to decrease after starting cART

Carotid intima-media thickness

In the most recent version of the American College of Cardiology Foundation/American Heart Association guidelines, carotid intima-media thickness (cIMT) has been granted a level II recommendation for cardiovascular risk evaluation. Commercial software with automated measuring algorithms has made the procedure simple to use and highly reproducible. The approach for measuring cIMT is still being debated, which we will not get into here, but we advocate using an automated edge-detection tool built for measuring the far wall of the common carotid artery. Enlargement of the cIMT in HIV patients has been thoroughly studied over the last decade, and strong evidence shows both an enlargement of the cIMT and faster development of the cIMT than normal. More long-term studies are needed; however, cIMT assessment in HIV-infected patients could prove to be a useful tool in the risk classification of HIV patients.

Arterial stiffness

The idea of enormous vessel stiffness is linked to cIMT and vascular thickening, and it may play a role in the etiology of cardiovascular disease in HIV. Noninvasive assessments of the compliance and distensibility of major arteries may provide indications of early subclinical illness because atherosclerosis is not exclusively a disease of small vessels.

These measures can be done using pulse wave velocity or ultrasound to look for signs of changes in distensibility, which could indicate early atherosclerotic disease. The vascular compliance of the carotid arteries was found to be poorer in HIV-infected patients compared to matched controls using ultrasonography.

Flow-mediated dilation

Endothelial function is critical for a healthy vasculature, and failure occurs when the endothelium loses its capacity to respond appropriately to blood flow (shear stress) and vasoactive blood-borne chemicals, causing the appropriate constriction or dilatation. Following cuff-induced blood stasis, ultrasonography of the brachial artery can be used to evaluate arterial dilatation.

There is a strong association between impaired FMD and cardiovascular events in both HIV-infected and uninfected individuals, with endothelial dysfunction serving as a significant predictor of cardiovascular risk in HIV patients.

Coronary endothelial function and flow reserve studied with PET

Using PET, the approach evaluates myocardial perfusion in absolute values (mL/g/min). Typically, either 13NH3 or 15O-H2O is employed as a PET tracer, and dynamic PET imaging allows for perfusion kinetic modeling. These approaches have been thoroughly verified in non-HIV populations. They are exceedingly reproducible and powerful for evaluating even slight changes in myocardial flow. Thus, there are changes in integrated coronary vasomotor function. In HIV patients on cART, myocardial perfusion reserve is

often reduced compared to the general population, likely due to chronic immune activation and vascular dysfunction, even in the presence of controlled viral loads. However, myocardial perfusion reserve may worsen after the initiation of cART in previously untreated patients.

Coronary artery calcium scoring

Coronary artery calcium scoring (CACS) has been immediately examined in the general population, and the AHA recommends it as a possible supplement to FRS for modifying risk prediction and changing medication in people with intermediate risk.

Framingham risk score

The use of FRS and its ability to accurately estimate the risk of CVD in HIV-infected patients is currently controversial. Efforts have been made to create a version that is more suitable for HIV-infected patients. While the data collection on adverse events of anti-HIV drugs (D: A:D) study group has launched a model that includes exposure to various types of cART. The general agreement appears to be that FRS is helpful, with the caveat that it may underestimate the actual risk among HIV-infected patients in their earlier years, particularly smokers.

IX. TREATMENT OF HIV-ASSOCIATED ASCVD AND HF

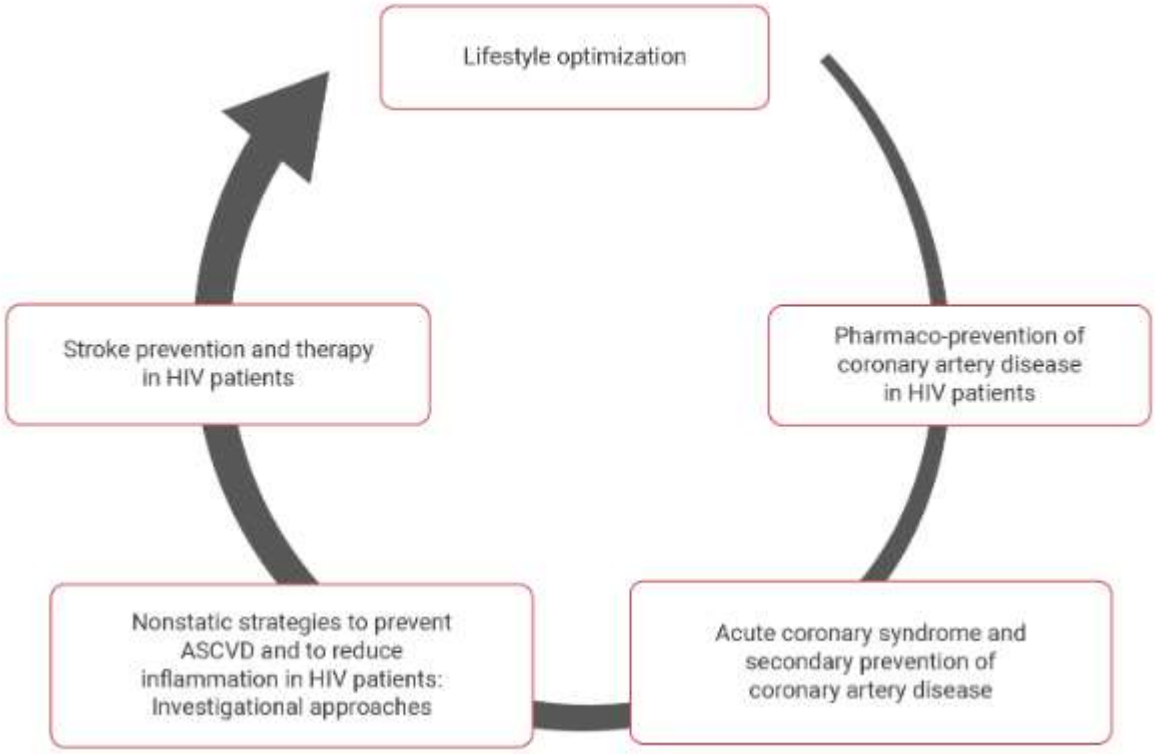

Fig: Cyclical approach to cardiovascular health in HIV patients

Lifestyle optimization

Following a healthy lifestyle, as in the general population, is an important initial step in the primary and secondary prevention of CVD in PLWH. Given the high incidence of smoking among PLWH and the proven involvement of smoking in atherosclerosis and MI, smoking cessation is critical. Limiting alcohol use is also crucial, given the potential for alcohol to play a disproportionate role in HIV-related CVD.

Pharmaco-prevention of coronary artery disease in HIV

A major goal for PLWH is to lower the risk of ASCVD through primary prevention. Statins prevent CVD events in patients without HIV who have high inflammation and low LDL-C levels. Despite effective ART, PLWH often has normal LDL but elevated systemic and arterial inflammation, as well as prolonged immunological activation. The traditional CVD risk factor is smoking, which is more prevalent and should be addressed in HIV. Potential drug interactions complicate statin use in HIV, while new statin and antiretroviral regimens have more benign drug-drug interaction patterns.

Acute coronary syndromes and secondary prevention of coronary artery disease

PLWH with acute coronary syndrome detected ST-segment elevation or non-ST-segment elevation MI. It results in lower overall coronary plaque burden, more single-vessel disease, lower TIMI (thrombolysis in myocardial infarction) risk, and a higher likelihood of proximal lesions than uninfected people.

Stroke prevention and therapy in HIV

Even though HIV increases the risk of ischemic stroke, there is a scarcity of data on HIV-related medication for stroke prevention. While systemic atherosclerosis is a likely cause of increased stroke risk in HIV, atrial fibrillation, which is more frequent overall in HIV but not after controlling for typical CVD risk factors, is responsible for 30% of ischemic stroke in PLWH. Using risk stratification techniques, such as the CHA2DS2-VASc and HAS-BLED scores, to assess cardio embolic stroke and hemorrhagic consequences of antithrombotic medication in general, and maybe in HIV, is an essential step toward rationalizing primary and secondary intervention.

X. MANAGEMENT OF CARDIOVASCULAR DISEASES IN HIV INFECTION

Pericardial Disease:

Anti-tuberculous therapy and corticosteroids are used to treat confirmed tuberculous pericarditis, which requires careful attention. In AIDS patients with suspected tuberculous pericarditis and undetected pericardial effusions, empiric anti-tuberculous treatment should be considered only if there is clinical suspicion. In these patients, adding steroids has been shown to provide considerable mortality benefits. Tuberculous effusions may occasionally necessitate pericardial fenestration.

Myocardial Disease:

The introduction of highly active antiretroviral therapy (HAART) regimens has significantly altered the course of HIV disease, extending patients' lives and enhancing their quality of life. There is also strong evidence that HAART lowers the risk of HIV-related cardiovascular complications. HAART regimens have lowered the prevalence of HIV-associated cardiomyopathy by nearly 7-fold compared to the pre-HAART era by limiting opportunistic infections and reducing the incidence of myocarditis.

Endocardial Disease:

HIV-positive patients receive the same treatment as HIV-negative patients for infective endocarditis.

Arrhythmias:

In the context of AIDS, antiarrhythmic medication aims to address the underlying cause as well as the correction of numerous triggering variables.

Coronary artery disease and vascular disease (cerebral and peripheral):

In the first direct comparison of drug-eluting stents (DES) against bare-metal stents (BMS) for HIV+ people, a single-center retrospective study indicated that HIV+ people who received DES were less likely to have target vessel and lesion revascularization than those who received BMS.

Aneurysmal disease:

The medical care of patients with HIV-related vasculopathy includes a mix of HAART, hyperlipidemia medication, and control of traditional cardiovascular risk factors.

Pulmonary hypertension:

In these patient subgroups, bosentan/PDE inhibitors and heart–lung transplants are frequently the sole therapy choices.

Venous thrombosis:

Long-term prophylaxis with low molecular weight heparin and warfarin for individuals with recurrent thrombosis should be used in HIV-infected patients as it is in non-HIV-infected patients with established VTE.

Cardiovascular Medications	Interaction with Anti-Retroviral
Dihydropyridine calcium-channel blockers	Interaction with protease inhibitors (PIs) leading to increased blood levels of calcium-channel blockers (e.g., nifedipine)
Sildenafil, Beta-blockers, digoxin, and non-dihydropyridine calcium-channel blockers	Increased levels with protease inhibitors (PIs) can lead to potential hypotension Interaction with PIs, risk of increased blood levels leading to bradycardia or other side effects
Statins metabolized by CYP3A4	Atorvastatin, lovastatin, simvastatin - Increased risk of statin toxicity when combined with PIs due to CYP3A4 inhibition
Statins not metabolized by CYP3A4	Fluvastatin, pravastatin - Preferred options with fewer interactions with PIs
Anticoagulants and antiarrhythmics	Warfarin, amiodarone, antiplatelets (ASA, clopidogrel) - Can interact with both PIs and NNRTIs, requiring dose adjustments
Protease inhibitors (PIs)	CYP3A4 inhibitors and substrates (e.g., ritonavir, cobicistat) - Can increase levels of cardiovascular drugs, requiring dose adjustments
Nucleoside reverse transcriptase inhibitors (NRTIS)	Some NRTIs act as substrates; fewer significant interactions with CYP enzyme system
Non-nucleoside Reverse Transcriptase Inhibitors (NNRTIS)	CYP enzyme inducers (e.g., efavirenz) and CYP enzyme inhibitors (e.g., delavirdine) - Interaction varies based on the NNRTI
Antibiotics	Cotrimoxazole - Interacts with PIs and NNRTIs, may affect cardiovascular drug metabolism
Antiviral class of acyclovir	May interact with cardiovascular drugs, though to a lesser extent than other antivirals
Anti-fungal azoles	Fluconazole, itraconazole - Strong CYP inhibitors, significant interaction with cardiovascular drugs and PIs
Anti-tuberculous therapy	Rifampin, isoniazid - Rifampin is a strong CYP inducer and can reduce levels of PIs and cardiovascular drugs

CONCLUSION

In clinical practice, a patient with HIV/AIDS and symptoms suggestive of heart illness, an increasing concern, poses a diagnostic and therapeutic difficulty. In the differential diagnosis, a thorough understanding of opportunistic infections that affect the heart, the effects of HAART medication, and treatment for opportunistic infections on the heart are required. The effects of HAART therapy, particularly protease inhibitors, on lipid and glucose metabolism and their impact on the course of pre-vascular disease must be taken into account. Finally, because of drug interactions, changes in response, and other considerations, the management of these individuals may differ from that of non-infected patients, and further research is needed in this area.

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