

Heart failure in persons with HIV: A scoping review

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BACKGROUND

The discovery of human immunodeficiency virus (HIV) in the early 1980s marked a significant challenge for healthcare systems worldwide. Initially, an HIV diagnosis was synonymous with high mortality, primarily due to the vulnerability to opportunistic infections such as tuberculosis. However, the advent and continuous development of antiretroviral therapy (ART) revolutionised the management of HIV, enabling individuals to achieve near-normal life expectancy. Longitudinal studies, including one involving HIV-positive veterans in the United States, have demonstrated a significant increase in the median age of individuals with HIV, underscoring the success of ART in extending life expectancy.⁽¹⁾ With adherence to ART, mortality from opportunistic infections has notably decreased. By 2022, an estimated 39 million people were living with HIV globally, and approximately 29.8 million were receiving ART.⁽²⁾

While ART has significantly improved the prognosis for persons living with HIV (PLWH), it has also introduced new healthcare

ABSTRACT

Introduction: Human immunodeficiency virus (HIV) infection remains a global health challenge, marked by substantial morbidity and mortality. The introduction of antiretroviral therapy (ART) has dramatically extended life expectancy for people living with HIV (PLWH), but this increased longevity exposes them to long-term conditions such as cardiovascular diseases, particularly HIV associated cardiomyopathy leading to heart failure (HF). HF in PLWH is a rising cause of morbidity and mortality, yet remains poorly understood. This scoping review aims to systematically examine and synthesise the existing literature on the relationship between HIV and heart failure.

Methods: The review followed the Arksey and O'Malley 6-stage methodological framework for scoping reviews. A systematic search was conducted using Boolean search strings across 4 databases: Scopus, Cochrane, PubMed, and ScienceDirect. The search was restricted to studies published between 2019 - 2023. Core articles yielded from data base search total 83. Twenty additional articles included in references do not form part of those yielded from Boolean string search. Total references 103. The results were analysed and synthesised to explore the prevalence, risk factors, and pathophysiology of heart failure in PLWH. Data analysis included descriptive statistics and thematic organisation.

Results: The scoping review highlights a significant association between HIV and heart failure, with PLWH having a 2-fold increased risk of developing HF compared to HIV-negative individuals ($p < 0.001$). Studies report a shift from heart failure with reduced ejection fraction (HFrEF) to heart failure with preserved ejection fraction (HFpEF) in aging PLWH populations on ART ($p = 0.05$). Additionally, elevated N-terminal pro b-type natriuretic peptide (NT-proBNP) levels were consistently found in PLWH with low CD4 counts, suggesting a persistent inflammatory state affecting the heart ($p = 0.02$). Other significant predictors of heart failure include high viral load ($p = 0.03$), low CD4 counts ($p = 0.01$), and traditional cardiovascular risk factors such as hypertension, diabetes, and dyslipidemia ($p = 0.001$). Protease inhibitors and nucleoside reverse transcriptase inhibitors (NRTIs) were identified as ART classes associated with a higher cardiovascular risk (OR 1.8, 95% CI: 1.5-2.2).

Conclusion: Heart failure is an emerging clinical entity among PLWH, driven by both HIV-related and traditional cardiovascular risk factors. This review underscores the need for integrated cardiovascular management strategies that encompass regular cardiac monitoring, advanced diagnostic tools, and careful selection of ART regimens. Ongoing research is crucial to develop tailored prevention and management approaches for cardiovascular complications in PLWH, ensuring improved clinical outcomes and quality of life for this vulnerable population. SA Heart® 2025;22:88-101

challenges. Non-communicable diseases, particularly cardiovascular diseases, have become increasingly prevalent in this population.^(1,3,4) Among these, heart failure is emerging as a major cause of morbidity and mortality in PLWH.^(5,6) Heart failure is defined as “a clinical syndrome manifesting symptoms and / or signs caused by structural and/or functional cardiac abnormalities, substantiated by elevated natriuretic peptide levels and / or concrete evidence of pulmonary or systemic congestion”.⁽⁷⁾ Globally, an estimated 64 million people were affected by heart failure in 2017.⁽⁸⁾

Despite these global trends, there is a significant gap in data documenting the epidemiology of heart failure in low- and middle-income regions, such as Northern and sub-Saharan Africa. This lack of data is concerning, as these regions bear approximately 80% of the global disease burden.⁽⁹⁾ The extended lifespan of HIV-positive individuals has revealed a direct association between HIV and an increased risk of heart failure. PLWH are more than twice as likely to develop heart failure compared to their HIV-negative counterparts.⁽¹⁰⁾ However, there remains a scarcity of research exploring the link between HIV and heart failure in countries like South Africa, where the healthcare system is already under considerable strain. This underscores the critical need for further research to identify and support HIV-positive individuals at risk of heart failure within these healthcare settings.

AIM

The aim of this scoping review was to examine the published literature that documents the relationship between HIV and cardiac failure.

METHODS

A scoping review was conducted to examine the available literature on the relationship between HIV and cardiac failure, following the 6-stage framework proposed by Arksey, O'Malley, and Levac, et al.^(11,12)

Stage 1 involved formulating a research question, done in collaboration with an expert in the field: “What is currently understood about cardiac failure among people living with HIV?” Following this, a comprehensive search strategy was devised to identify relevant studies from four major databases: Scopus, Cochrane, PubMed, and Science Direct (**Stage 2**). The search employed keywords and Boolean operators (AND / OR / NOT) to form a search string:

(TITLE-ABS-KEY (“heart failure” OR “congestive heart failure” OR “cardiac failure” OR “cardiac insufficiency” OR “HFpEF”

OR “heart failure with preserved ejection fraction” OR “HFrEF” OR “heart failure with reduced ejection fraction”) AND (“HIV+” OR “HIV positive” OR “HIV infected” OR “human immunodeficiency virus positive” OR “seropositive”)) AND (LIMIT-TO (PUBYEAR, 2023) OR LIMIT-TO (PUBYEAR, 2022) OR LIMIT-TO (PUBYEAR, 2021) OR LIMIT-TO (PUBYEAR, 2020) OR LIMIT-TO (PUBYEAR, 2019)).

The search was applied with necessary filters such as publication year, literature type, and human studies, yielding 1 126 abstracts for initial analysis.

In **Stage 3**, these abstracts were screened based on pre-defined inclusion and exclusion criteria. Articles in Chinese (2), French (3), and Spanish (4) were excluded due to translation limitations, while 8 Russian articles were successfully translated using Google Translate. Additionally, 12 letters to the editor and 13 book chapters were excluded. After excluding 991 irrelevant articles and removing 18 duplicates, a total of 83 abstracts remained for further review.

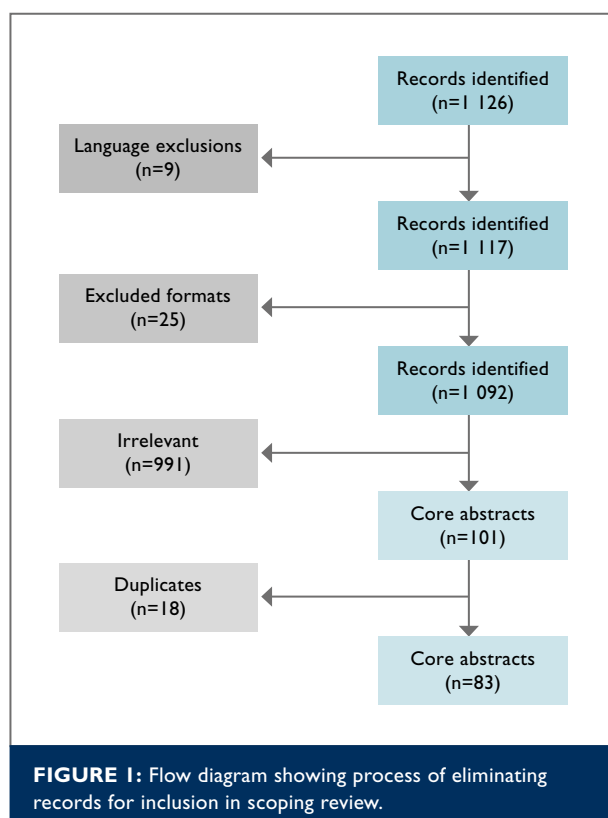
Stage 4 involved critical review and data extraction from the selected publications. The extracted data were thematically organised and summarised (**Stage 5**), leading to the formulation of conclusions in **Stage 6** (Figure 1).

RESULTS

Eighty-three articles were included in this scoping review. A summary of the articles can be found in Appendix 1. Data from the studies has been analysed and thematically categorised below as per the guidelines suggested by Arksey and O'Malley.⁽¹²⁾

Magnitude of the cardiovascular challenges in HIV

The prevalence of cardiovascular disease (CVD) among PLWH has tripled over the past 2 decades, with particularly significant impacts noted in sub-Saharan Africa and the Asia-Pacific regions.⁽¹³⁾ Over the same period, the proportion of CVD-related mortalities in the HIV-positive population has risen from 2.5% to 4.6%.⁽¹⁴⁾ The spectrum of cardiovascular disease in HIV is wide however, HIV cardiomyopathy has emerged as the leading cause of mortality within this cohort.⁽¹⁵⁾ The increasing prevalence of heart failure as a result of HIV cardiomyopathy underpins a growing public health concern. Research indicates that individuals with HIV receiving ART face a 2-fold increased risk of developing cardiac failure compared to their HIV-negative counterparts.⁽¹⁶⁾ Moreover, these individuals experience a significantly higher risk of all-cause mortality



when heart failure is present.⁽¹⁷⁾ Elevated levels of N-terminal pro b-type natriuretic peptide (NT-proBNP) among South African PLWH on ART, especially in those with reduced CD4 counts, further highlight the presence of a persistent inflammatory state contributing to myocardial inflammation.⁽¹⁸⁾ This growing body of evidence calls for a critical shift in the clinical management of HIV, placing greater emphasis on addressing cardiovascular complications.

Classification of heart failure in HIV

The aetiology of heart failure is broad with taxonomic classifications including ischemic heart disease, valvular heart disease, hypertensive heart disease, primary cardiomyopathies, secondary cardiomyopathies, congenital heart disease, pericardial disease, and uncategorised causes.⁽¹⁹⁾ Geographical variances in aetiology exist between developed and developing regions. Industrialised countries experience a lower burden of tuberculosis and access to ART is widespread.⁽²⁰⁾ Thus coronary artery disease presents as the dominant cause of HIV associated heart disease in developed regions. In sub-Saharan Africa, pericardial tuberculosis and cardiomyopathy present as the dominant forms of HIV associated heart disease. HIV cardiomyopathy is characterised by decreased left ventricle ejection fraction (LVEF) or a dilated left ventricle, with or without symptoms of heart failure.⁽⁵⁾ Heart failure may be further classified on

the basis of echocardiographic assessment: Heart Failure with Reduced Ejection Fraction (HFrEF) and Heart Failure with Preserved Ejection Fraction (HFpEF). Historically, HIV-associated cardiomyopathy predominantly presented as HFrEF, which is characterised by marked left ventricular systolic dysfunction and ventricular dilation.⁽²¹⁾ However, with increased ART uptake, an aging HIV-infected population and longer exposure to cardiometabolic risk factors, there has been a shift toward the predominance of HFpEF.^(16,22) This shift reflects the intricate interaction between HIV infection, long-term antiretroviral therapy, and conventional cardiovascular risk factors. As a result, clinical management strategies must adapt to the evolving cardiac presentations in this population, addressing both phenotypes and the complex cardiovascular needs of individuals living with HIV.

HIV and heart failure: A significant correlation

A growing body of evidence strongly links HIV infection with an increased risk of cardiovascular disease and heart failure.^(1,23-25) People living with HIV who develop heart failure are at a higher risk of hospital readmissions and mortality compared to HIV-negative individuals.^(26,27) The progression towards heart failure in HIV-infected individuals is often insidious, with clinical symptoms typically emerging in advanced stages. Studies have revealed a higher incidence of subclinical left ventricular systolic dysfunction (LVSD) in HIV-infected paediatric populations receiving ART compared to non-infected controls,⁽²⁸⁾ a pattern similarly observed in a Zimbabwean cohort.⁽²⁹⁾

An inverse relationship has been established between the age at HIV diagnosis and the prevalence of LVSD.⁽²⁸⁾ A study in Malawi found an increased rate of left ventricular hypertrophy (LVH) amongst PLWH.⁽²⁴⁾ HIV-positive veterans with heart failure, for instance, tend to present at a younger age than their HIV-negative peers.⁽³⁰⁾ Among individuals who have not initiated ART, significant cardiac structural changes have been noted, including increased left ventricular end-diastolic internal diameter (LVEDD), left ventricular mass index (LVMI), and left atrial volume (LAVI), though without significant differences in systolic function.^(31,32) HIV seropositivity is associated with increased LVMI, enlargement of left atrial and right ventricular dimensions, and impaired right ventricular function,^(22,33) suggesting that HIV directly contributes to cardiac remodelling and the development of left ventricular diastolic dysfunction.⁽³⁴⁾

Furthermore, Global Longitudinal Strain (GLS), a key indicator of cardiac systolic function, is reduced in individuals with HIV, reflecting a heightened risk of heart failure in this population.^(35,36)

Risk factors for cardiac failure in HIV

Cardiovascular disease risk factors in PLWH encompass both HIV-specific and traditional determinants. HIV infection itself is an independent risk factor for CVD and heart failure,⁽³⁷⁻³⁹⁾ with a meta-analysis indicating that HIV increases the risk of heart failure by 48%.⁽⁴⁰⁾ The pathogenesis of HIV-associated cardiac failure is multifactorial with multiple risk factors working synergistically to produce a state of persistent myocardial inflammation.⁽⁴¹⁾ Chronic inflammation may occur as a result of direct viral effects, opportunistic infections, ART side effects, and the mode of HIV transmission.⁽³⁹⁾ By inference, it is appropriate to assume that a reduction in inflammation may result in a reduced risk of HIV associated cardiac failure. Conventional risk factors include type 2 diabetes mellitus, dyslipidaemia, smoking, hypertension, and impaired glucose metabolism. Epidemiological studies have reported varying incidences of these conditions among PLWH, with certain studies highlighting elevated risks of CVD.^(42,43)

Notably, hypertension, a well-recognised risk factor for CVD, affects approximately 35% of PLWH on ART⁽⁴⁴⁾ and is associated with left ventricular hypertrophy.⁽²⁴⁾ Additionally, HIV infection accelerates the development of atherosclerosis,⁽⁴⁵⁾ with coronary artery disease playing a significant role in the cardiovascular complications linked to HIV.^(46,47) Changes in body fat distribution, including increased cardiac adiposity, have been implicated in the development of atherosclerosis and Heart Failure with Preserved Ejection Fraction (HFpEF) in PLWH.^(48,49) Furthermore, weight gain, particularly associated with certain ART regimens, is a risk factor for diabetes, dyslipidaemia, hypertension, and CVD.^(50,51)

An inverse relationship exists between CD4 cell counts and viral load with CVD risk, with lower CD4 counts, particularly below 200 cells/ml, being associated with more severe heart failure.⁽⁵²⁻⁵⁴⁾ Gender differences also play a crucial role in risk stratification, as women living with HIV experience higher cardiovascular risks compared to men.⁽⁵⁵⁻⁵⁷⁾ Smoking and poly-substance use further exacerbate cardiovascular risks, with their impact varying across PLWH.⁽⁵⁸⁻⁶⁰⁾ This multifactorial landscape of HIV-specific and conventional risk factors necessitates a comprehensive approach to cardiovascular risk management in this population.

Pathophysiology of HIV-associated cardiomyopathy

The pathophysiological mechanisms driving HIV-associated cardiomyopathy are complex and multifactorial, involving direct viral effects on the myocardium, immune system dysregulation,

systemic inflammation, ischaemic cardiac conditions, pulmonary arterial hypertension, adverse effects of ART, and psychiatric comorbidities.^(16,21,61,62) A prevailing hypothesis suggests that the interplay of lifestyle factors, prolonged ART, and chronic immune activation leads to a pro-inflammatory state that promotes atherogenesis, endothelial dysfunction, and myocardial fibrosis.⁽⁵²⁾ Persistent immune activation is considered a key contributor to the onset and progression of cardiovascular diseases in PLWH.^(14,63,64) Systemic inflammation in this population is known to trigger thrombotic events, endothelial damage, and myocardial fibrosis, which are integral to the development of heart failure.⁽¹⁴⁾

Importantly, myocardial fibrosis, a critical factor in heart failure pathogenesis, is frequently observed in HIV-infected individuals even in the absence of overt cardiovascular disease.^(57,65,66) Additionally, myocardial steatosis, which results from metabolic dysregulation, has been implicated in the onset of diastolic dysfunction,⁽⁶⁷⁾ with certain metabolites being identified as potential therapeutic targets for intervention.^(68,69) HIV-encoded proteins such as NEF and TAT further exacerbate cardiovascular pathology by impairing endothelial function and facilitating atherosclerosis.⁽⁵⁸⁾ These mechanisms underscore the complexity of HIV-associated cardiac dysfunction, highlighting the need for targeted therapeutic strategies to mitigate cardiovascular risk in this population.

Impact of antiretroviral therapy on cardiac failure

The advent of ART has significantly improved survivability of HIV. The pathogenesis of cardiac failure amongst PLWH is multifactorial notwithstanding persistent viral replication and immune activation being key role players. Ntusi, et al. found that ART naïve PLWH had lower left ventricular ejection fraction values when compared to those on ART.⁽⁷⁰⁾ ART is crucial for achieving virological suppression and improving CD4 cell count, thereby reducing the direct impact of HIV infection on the immune system. ART generally involves a combination of protease inhibitors (PIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), and nucleoside reverse transcriptase inhibitors (NRTIs). In South Africa, first line ART is provided in the form of a fixed dose combination tablet (TLD) which includes tenofovir disoproxil fumarate (TDF), lamivudine (3TC), and dolutegravir (DTG).⁽⁷¹⁾ Modern ART has improved cardiovascular risk safety profiles. A meta-analysis found that DTG had no significant effect on the risk of adverse cardiac events.⁽⁷²⁾ Integrase strand transfer inhibitors (INSTIs) and the CCR5 antagonist maraviroc have shown atheroprotective properties, indicating their potential role in mitigating the development of

atherosclerosis.^(10,73,74) This is corroborated by a Kenyan study which found that ART does not significantly increase the risk of cardiovascular disease in PLWH.⁽⁷⁵⁾ In contrast, certain classes such as NRTIs and PIs have been linked to a higher risk of cardiovascular complications.⁽⁷⁶⁻⁷⁹⁾ The cardiovascular risks associated with ART are thought to arise from a complex interaction of factors, including persistent systemic inflammation, the development of metabolic syndrome, and oxidative DNA damage.⁽⁷⁴⁾ These effects underscore the need for a nuanced approach to managing ART, balancing its benefits in controlling HIV with its potential to elevate cardiovascular risk. This highlights the importance of individualised treatment strategies to optimise both virological outcomes and cardiovascular health in people living with HIV.

Management strategies for cardiac failure in PLWH

The management of cardiac failure in PLWH requires a comprehensive strategy that addresses both HIV viral suppression and the reduction of cardiovascular risk factors.⁽⁸⁰⁻⁸²⁾ Ensuring adherence to ART is critical not only for maintaining virological control but also for mitigating the economic burden of cardiovascular complications in this population.⁽⁸³⁾ The presence of subclinical changes in cardiac morphology and the unique cardiovascular risks associated with PLWH necessitate a personalised approach to risk assessment and management by healthcare providers.^(65,84) Despite the increasing burden of cardiac failure amongst PLWH, general risk assessment models may underestimate the cardiac risk this unique group is exposed to.⁽⁸⁵⁾ Features suggestive of cardiac failure in PLWH may be detected by imaging before clinical symptoms develop. Thus, basic and advanced imaging modalities are increasingly being used to understand the pathophysiology of subclinical cardiovascular disease. So far they have proven useful in identifying and risk stratifying patients at risk for myocardial dysfunction. While conventional echocardiography provides invaluable insight into cardiac structure and function, 3D speckle-tracking echocardiography (3DSTE) has proven to be more sensitive in detecting early myocardial dysfunction.⁽⁸⁶⁾ 3DSTE is able to detect subclinical biventricular dysfunction in PLWH. 3DSTE identified lower left ventricular global longitudinal strain (GLS) and global area strain (GAS) in PLWH when compared to uninfected controls.⁽⁸⁷⁾ Increased left ventricular mass index and diastolic dysfunction are also seen in HIV-associated cardiac dysfunction.⁽⁸⁸⁾ In addition, weak negative correlation exists between left ventricular GLS and nadir CD4 count.⁽⁸⁷⁾ Cardiac magnetic resonance imaging and spectroscopy (CMR) is useful to establish cardiac structure and function. It is also able to detect the presence of HIV-associated cardiac fibrosis, steatosis,

diastolic dysfunction, and subclinical systolic dysfunction.^(89,90) Subclinical atherosclerosis is a separate disease entity resulting in HIV-associated cardiovascular disease. PLWH are at an increased risk for developing accelerated atherosclerosis which predisposes to cardiovascular disease.^(91,92) There have been great strides in using imaging modalities to detect subclinical atherosclerosis. However, this is beyond the scope of this review.

Systemic immune dysregulation plays a key role in the development of cardiac disease. Certain biomarkers have been associated with cardiac dysfunction in PLWH. HIV infection causes CD4 T cell activation which in turn are recruited to the heart. This is associated with expression of enzymes involved in cardiac calcium regulation. Overexpression of RyR2 and calcium regulatory enzymes induces expression of cardiac foetal genes, MYH6 and MYH7.⁽⁹³⁾ This results in deterioration of cardiac muscle function. Excessive calcium release in cardiac myocytes is also associated with increased expression of cytokines and chemokines, which portend opportunistic infections.⁽⁹⁴⁾ These findings are further supported by the INHALE study which found increased levels of CRP, VCAM-1, TNF alpha, ST2 and GDF-15 in HIV infected children when compared to controls.⁽⁹⁵⁾ Furthermore, a 1 unit increase in CRP and GDF-15 was associated with increased odds of cardiac abnormality. N-terminal pro b-type natriuretic peptide (NT-proBNP) levels, offer significant benefits for nuanced risk stratification and targeted therapeutic management of cardiovascular conditions in PLWH.^(89,96-97)

Statin therapy is used to lower the risk of cardiovascular disease by reducing LDL cholesterol and hence development of atherosclerosis. In addition, statin therapy also reduces inflammation in PLWH, providing an additional benefit beyond lowering LDL cholesterol.^(98,99) A phase 3 randomised control trial demonstrated that taking pitavastatin conferred a lower risk of major adverse cardiovascular events amongst PLWH when compared to placebo.⁽¹⁰⁰⁾ While pharmacological interventions like statins and antithrombotic agents play a crucial role in CVD management, their use must be carefully evaluated to avoid potential drug-drug interactions with ART regimens.^(44,101)

Heart transplantation, the ultimate treatment for end-stage heart failure, remains a subject of ongoing investigation in HIV-positive individuals, with its feasibility and outcomes still under review by the medical community.^(102,103) This underscores the critical need for further research and the development of tailored clinical protocols to optimise cardiovascular care for PLWH.

CONCLUSION

The management of HIV has undergone transformative advancements, particularly with the development of potent ART, which has significantly extended the life expectancy of PLWH. However, this increased lifespan has introduced complex healthcare challenges, most notably a rising prevalence of cardiovascular diseases (CVD). The intricate interplay between HIV infection, ART, and traditional CVD risk factors necessitates a comprehensive and nuanced approach to managing heart failure and other cardiovascular conditions in this population. The evolving understanding of the pathophysiology of HIV-associated cardiomyopathy characterised by chronic immune activation, myocardial fibrosis, and metabolic disturbances highlights the critical need for continued research and individualised treatment strategies. Advanced imaging modalities show promise in early detection of cardiac failure amongst PLWH. Furthermore the identification of novel biomarkers may assist in developing risk stratification models for myocardial dysfunction.

LIMITATIONS

This scoping review is subject to several limitations. First, the exclusion of non-English language studies may have resulted in the omission of relevant data, particularly from regions where HIV is prevalent, such as sub-Saharan Africa and Latin America. Additionally, the use of Google Translate for some non-English abstracts may introduce translation inaccuracies. Second, the review was restricted to studies published between 2019 - 2023, which may limit insights from earlier research on the topic. The studies included also vary in terms of study design, population size, and geographical distribution, introducing heterogeneity that may affect the generalisability of the findings. Furthermore, the reliance on observational studies for much of the evidence raises concerns about potential bias, including confounding factors that were not accounted for, such as the presence of comorbidities or differences in ART adherence. Finally, there was a paucity of randomised controlled trials (RCTs) specifically examining heart failure in PLWH, limiting the ability to draw strong causal conclusions from the data. These limitations highlight the need for further high-quality, longitudinal research to better understand the relationship between HIV and heart failure across diverse populations and healthcare settings.

Conflict of interest: none declared.

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APPENDIX I: Articles that were included in the scoping review.

Title	Author	Year	Participants	Country of study	Study design	Male (%)	Duration	Age group
Two decade trends in cardiovascular disease outcomes and cardio-vascular risk factors among US veterans living with HIV. ⁽¹⁾	Haji M, et al	2022	50 284	USA	Observational retrospective cohort	96	20 years	Adults
UNAIDS. The path that ends AIDS: UNAIDS Global AIDS Update 2023. ⁽²⁾	UNAIDS	2023	N/A	N/A	N/A	N/A	N/A	N/A
National trend of heart failure and other cardiovascular diseases in people living with human immunodeficiency virus. ⁽³⁾	Park DY, et al.	2022	2 483 868	USA	Observational retrospective cohort	65	10 years	Adults
The epidemiology, mechanisms, diagnosis and treatment of cardiovascular disease in adult patients with HIV. ⁽⁴⁾	Henning RJ, et al.	2023	N/A	USA	Review article	N/A	N/A	N/A
Heart failure in patients with human immunodeficiency virus infection: Epidemiology, pathophysiology, treatment, and future research. ⁽⁵⁾	Remick J, et al.	2014	N/A	USA	Review article	N/A	N/A	Variable
A systematic review exploring the effect of human immunodeficiency virus on cardiac diseases. ⁽⁶⁾	Alzubaidee MJ, et al.	2022	12 318 120	USA	Systematic review	N/A	N/A	Adults
Global burden of heart failure: A comprehensive and updated review of epidemiology. ⁽⁷⁾	Savarese G, et al.	2023	N/S	Sweden	Systematic review	N/A	N/A	N/A
Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990 - 2017: A systematic analysis for the Global Burden of Disease Study 2017. ⁽⁸⁾	James SL, et al.	2018	N/S	195 countries	Systematic review	N/A	27 years	Variable
Cardiovascular risk and events in 17 low-, middle-, and high-income countries. ⁽⁹⁾	Yusuf S, et al.	2014	156 424	Bangladesh, India, Pakistan, Zimbabwe, Argentina, Brazil, Chile, China, Colombia, Iran, Malaysia, Poland, South Africa, Turkey, Canada, Sweden, and the United Arab Emirates	Observational prospective cross sectional	42	4.1	Adults
Adjudicated heart failure in HIV-infected and uninfected men and women. ⁽¹⁰⁾	Feinstein MJ, et al.	2018	8 890	USA	Observational retrospective cohort	82	16 years	Adults
Scoping studies: Advancing the methodology: Implementation science. ⁽¹¹⁾	Levac D, et al.	2010	N/A	USA	Article	N/A	N/A	N/A
Scoping studies: Towards a methodological framework. ⁽¹²⁾	Arksey H, et al.	2005	N/A	N/A	Article	N/A	N/A	N/A
Global burden of atherosclerotic cardiovascular disease in people living with HIV: Systematic review and meta-analysis. ⁽¹³⁾	Shah ASV, et al.	2018	793 635	154 countries	Meta-analysis	N/A	25 years	variable
HIV-related myocardial fibrosis: Inflammatory hypothesis and crucial role of immune cells dysregulation. ⁽¹⁴⁾	Teer E, et al.	2022	N/A	N/A	Review article	N/A	N/A	N/A

APPENDIX I: Articles that were included in the scoping review, continued.

Title	Author	Year	Participants	Country of study	Study design	Male (%)	Duration	Age group
Heart health in the age of highly active antiretroviral therapy: A review of HIV cardiomyopathy. ⁽¹⁵⁾	Belkin MN, et al.	2018	N/A	N/A	Review article	N/A	N/A	N/A
Human immunodeficiency virus infection and incident heart failure: A meta-analysis of prospective studies. ⁽¹⁶⁾	Chen Y, et al.	2021	8 848 569	USA, Taiwan, UK, France	Meta-analysis	N/A	1-10	Adults
Human immunodeficiency virus infection and risks of morbidity and death in adults with incident heart failure. ⁽¹⁷⁾	Avula HR, et al.	2021	425 454	USA	Observational cohort	87	16 years	Adults
Elevated N-terminal prohormone of brain natriuretic peptide among persons living with HIV in a South African peri-urban township. ⁽¹⁸⁾	Peterson TE, et al.	2020	224	South Africa	Observational cross sectional		N/A	Adults
Cardiovascular disease among persons living with HIV: New insights into pathogenesis and clinical manifestations in a global context. ⁽¹⁹⁾	M Ntsekhe, et al.	2023	N/A	N/A	Review article		N/A	N/A
High rate of left ventricular hypertrophy on screening echocardiography among adults living with HIV in Malawi. ⁽²⁰⁾	Hoffman RM, et al.	2022	202	Malawi	Observational cross sectional		N/A	Adults
Cardiac dysfunction among people living with HIV: A systematic review and meta-analysis. ⁽²¹⁾	Erqou S, et al.	2019	125 382	India, USA, UK, Iran, Italy, Netherlands, Portugal, Tanzania, Morocco, Germany, Canada, Zimbabwe, Cameroon, Spain, Nigeria, Denmark, Congo, China, Ghana, Rwanda.	Meta-analysis	82	N/A	Adults 47
Risk of death and readmission among individuals with heart failure and HIV: A systematic review and meta-analysis. ⁽²²⁾	Zhou Y, et al.	2024	59 085	China, USA	Systematic review	N/A	N/A	Adults
Heart failure outcomes and associated factors among veterans with human immunodeficiency virus infection. ⁽²³⁾	Erqou S, et al.	2020	39 244	USA	Retrospective cohort	98	19	Adults
Correlate of left ventricular systolic function in children with human immunodeficiency virus infection on combined highly active antiretroviral medications in Aminu Kano Teaching Hospital, Kano State. ⁽²⁴⁾	Garba NA, et al.	2023	200	Nigeria	Observational cross sectional	49	N/A	Children
Incidence and progression of echocardiographic abnormalities in older children with human immunodeficiency virus and adolescents taking antiretroviral therapy: A prospective cohort study. ⁽²⁵⁾	Majonga ED, et al.	2019	175	Zimbabwe	Prospective cohort	52	3 years	Children
Age at diagnosis of heart failure in United States veterans with and without HIV infection. Journal of the American Heart Association. ⁽²⁶⁾	Erqou S, et al.	2021	1 425 897	USA	Retrospective cohort	97	18	Adults

APPENDIX I: Articles that were included in the scoping review, continued.

Title	Author	Year	Participants	Country of study	Study design	Male (%)	Duration	Age group
Echocardiographic assessment of left cardiac structure and function in antiretroviral therapy (ART)-naïve people living with HIV / AIDS. ⁽²⁷⁾	Hu X, et al.	2023	195	China	Observational cross sectional	84	N/A	Adults
HIV infection is associated with greater left ventricular mass in the multicentre AIDS cohort study. AIDS Research and Human Retroviruses. ⁽²⁸⁾	Hutchins E, et al.	2019	721	USA	Observational cross sectional	100	N/A	Adults
HIV status, and measures of cardiac stress and fibrosis in Uganda. ⁽²⁹⁾	Kipke J, et al.	2021	200	Uganda	Observational cross sectional	38	N/A	Adults
Associations between HIV serostatus and cardiac structure and function evaluated by 2-Dimensional echocardiography in the multicentre AIDS cohort study. ⁽³⁰⁾	Doria d Vasconcellos H, et al.	2021	1 195	USA	Observational cross sectional	100	N/A	Adults
Diastolic dysfunction in patients with human immunodeficiency virus receiving antiretroviral therapy: Results from the CHART Study. ⁽³¹⁾	Butler J, et al.	2020	195	USA	Observational cross sectional	70	N/A	Adults
Global longitudinal strain to predict mortality in patients with acute heart failure. ⁽³²⁾	Park JJ, et al.	2018	4172	South Korea	Prospective cohort	53	31,7 months	>18
Cardiac strain is lower among women with HIV in relation to monocyte activation. ⁽³³⁾	Toribio M, et al.	2022	34	USA	Observational cross sectional	0	N/A	Adults
Human immunodeficiency virus infection-associated cardiomyopathy and heart failure. ⁽³⁴⁾	Papamanoli A, et al.	2022	N/A	USA	Systematic review	N/A	N/A	N/A
Variation in heart failure risk by HIV severity and sex in people with HIV infection. ⁽³⁵⁾	Lam Jo, et al.	2022	425 437	USA	Observational cross sectional	88	N/A	Adults
Human immunodeficiency virus infection and variation in heart failure risk by age, sex and ethnicity: The HIV HEART Study. ⁽³⁶⁾	Alan S, et al.	2022	425 454	USA	Observational retrospective cohort	87	16	Adults
Human immunodeficiency virus increases the risk of incident heart failure. ⁽³⁷⁾	Yen Y-F, et al.	2019	120 765	Taiwan	Observational prospective cohort	N/A	5,85	Adults
HIV infection and risk of heart failure: A meta-analysis and systematic review. ⁽³⁸⁾	Li X, et al.	2022	303 734	USA, Taiwan	Meta-analysis	N/A	6-17	Adults
Trends of age-related non-communicable diseases in people living with HIV and comparison with uninfected controls: A nationwide population-based study in South Korea. ⁽³⁹⁾	Kim JH, et al.	2021	296 182	South Korea	Observational cross sectional	91	12	Adults
Incidence of cardiometabolic diseases in people with and without human immunodeficiency virus in the United Kingdom: A population-based matched cohort study. ⁽⁴⁰⁾	Gooden TE, et al.	2021	44 954	UK	Observational cross sectional	66	20	Adults
Characteristics, prevention, and management of cardiovascular disease in people living with HIV: A scientific statement from the American Heart Association. ⁽⁴¹⁾	Feinstein MJ, et al.	2019	N/A	USA	Review article	N/A	N/A	N/A
Coronary artery disease in patients with human immunodeficiency virus infection. ⁽⁴²⁾	Mondal P, et al.	2021	N/A	USA	Review article	N/A	N/A	N/A

APPENDIX I: Articles that were included in the scoping review, continued.

Title	Author	Year	Participants	Country of study	Study design	Male (%)	Duration	Age group
Clinical profile, anatomical features and long-term outcome of acute coronary syndromes in human immunodeficiency virus-infected patients. ⁽⁴³⁾	Postigo A, et al.	2020	92	Spain	Observational retrospective cohort	92	18	Adults
Conceptualising the risks of coronary heart disease and heart failure among people aging with HIV: Sex-specific considerations. ⁽⁴⁴⁾	Abelman RA, et al.	2019	N/A	USA	Review article	N/A	N/A	N/A
Cardiac adiposity as a modulator of cardiovascular disease in HIV. ⁽⁴⁵⁾	Bonou M, et al.	2021	N/A	Greece	Review article	N/A	N/A	N/A
Myocardial steatosis among antiretroviral therapy-treated people With human immunodeficiency virus participating in the REPRIEVE trial. ⁽⁴⁶⁾	Neilan TG, et al.	2020	82	South Africa, USA	Randomised control trial	88	1,5	Adults
Association of concurrent changes in metabolic health and weight on cardiovascular disease risk: A nationally representative cohort study. ⁽⁴⁷⁾	Bae YS, et al.	2019	205 394	South Korea	Prospective cohort	59	9	Adults
Association between weight gain and the incidence of cardiometabolic conditions among people living with HIV-1 at high risk of weight gain initiated on antiretroviral therapy. ⁽⁴⁸⁾	McComsey GA, et al.	2022	1 252	USA	Retrospective cohort	41	2	Adults
Associations between HIV viremia during antiretroviral therapy and cardiovascular disease. ⁽⁴⁹⁾	Elvstam O, et al.	2022	6 562	Sweden	Prospective cohort	N/A	21	>15
Risk factors for the development of severe chronic heart failure in patients infected with human immunodeficiency virus. ⁽⁵⁰⁾	Goryacheva OG, et al.	2021	8 848 569	USA, Taiwan, UK, France	Meta-analysis	N/A	1-10	Adults
Heart failure and adverse heart failure outcomes among persons living with HIV in a US tertiary medical centre. ⁽⁵¹⁾	Alvi RM, et al.	2019	2 308	USA	Prospective cohort	54	2 years	Adults
Heart failure with preserved ejection fraction in women living with HIV: Another inflammatory comorbidity? ⁽⁵²⁾	Moayed Y, et al.	2019	N/A	Canada	Editorial	N/A	N/A	N/A
Sex- and poverty-specific patterns in cardiovascular disease mortality associated with human immunodeficiency virus, New York City, 2007 – 2017. ⁽⁵³⁾	Hanna DB, et al.	2020	147 915	USA	Retrospective cohort	73	11	>13
Myocardial fibrosis among antiretroviral therapy-treated persons with human immunodeficiency virus in South Africa. ⁽⁵⁴⁾	Shuldiner SR, et al.	2020	229	South Africa	Case-control	35	N/A	>18
HIV infection and pathology of the cardiovascular system. Cardiovascular therapy and prevention. ⁽⁵⁵⁾	Shekhovtsova TA, et al.	2023	N/A	Russia	Review article	N/A	N/A	N/A
Association of syndemic, unhealthy alcohol use, smoking, and depressive symptoms on incident cardiovascular disease among veterans with and without HIV-infection. ⁽⁵⁶⁾	Chichetto NE, et al.	2021	5 621	USA	Prospective cohort	94	12	>18
HIV and drug use: A tale of synergy in pulmonary vascular disease development. Comprehensive physiology. ⁽⁵⁷⁾	Cook CM, et al.	2023	N/A	USA	Review article	N/A	N/A	N/A

APPENDIX I: Articles that were included in the scoping review, continued.

Title	Author	Year	Participants	Country of study	Study design	Male (%)	Duration	Age group
Etiology and pathophysiology of heart failure in people with HIV. ⁽⁵⁸⁾	Choi H, et al.	2021	N/A	USA	Review article	N/A	N/A	N/A
Mechanisms of cardiovascular disease in the setting of HIV infection. ⁽⁵⁹⁾	Hsue PY.	2019	N/A	USA	Review article	N/A	N/A	N/A
HIV and cardiovascular diseases risk: Exploring the interplay between T-cell activation, coagulation, monocyte subsets, and lipid subclass alterations. ⁽⁶⁰⁾	Teer E, et al.	2019	80	South Africa	Observational cross sectional	35	N/A	>18
The importance of inflammation in the formation of chronic heart failure in patients infected with human immunodeficiency virus. ⁽⁶¹⁾	Koziova NA, et al.	2022	100	Russia	Observational cross sectional	60	N/A	>18
Myocardial fibrosis and inflammation by CMR predict cardiovascular outcome in people living with HIV. ⁽⁶²⁾	De Leuw P, et al.	2021	156	Germany	Prospective cohort	62	19 months	>18
Immune dysregulation in myocardial fibrosis, steatosis, and heart failure: Current insights from HIV and the general population. ⁽⁶³⁾	Sinha A, et al.	2021	N/A	USA	Review article	N/A	N/A	N/A
Heart failure among people with HIV: Evolving risks, mechanisms, and preventive considerations. ⁽⁶⁴⁾	Toribio M, et al.	2019	N/A	USA	Review article	N/A	N/A	N/A
Metabolomic profiling of cardiac fibrosis and steatosis in women with or at risk for HIV. ⁽⁶⁵⁾	Shitole SG, et al.	2023	153	USA	Observational cross sectional	0	N/A	N/A
Transmethylamine-N-Oxide is associated with diffuse cardiac fibrosis in people living with HIV. ⁽⁶⁶⁾	Colaco NA, et al.	2021	195	USA	Retrospective cohort	71	N/A	>18
Cardiomyopathy and heart failure in patients with HIV infection. ⁽⁶⁷⁾	Savvoulidis P, et al.	2019	N/A	USA	Review article	N/A	N/A	N/A
Cardiovascular toxicity of contemporary antiretroviral therapy. ⁽⁶⁸⁾	Vos AG, et al.	2021	N/A	South Africa, Netherlands	Review article	N/A	N/A	N/A
HOPX plays a critical role in antiretroviral drugs induced epigenetic modification and cardiac hypertrophy. ⁽⁶⁹⁾	Kashyap S, et al.	2021	N/A	USA	Experimental interventional	N/A	N/A	N/A
Incidence of cardiometabolic outcomes among people living with HIV-1 initiated on integrase strand transfer inhibitor versus non-integrase strand transfer inhibitor antiretroviral therapies: A retrospective analysis of insurance claims in the United States. ⁽⁷⁰⁾	Rebeiro PF, et al.	2023	14 076	USA	Retrospective cohort	76	2	>18
HIV infection and coronary heart disease: Mechanisms and management. ⁽⁷¹⁾	Hsue PY, et al.	2019	N/A	USA	Review article	N/A	N/A	N/A
Epidemiology, pathophysiology, and prevention of heart failure in people with HIV. ⁽⁷²⁾	Sinha A, et al.	2020	N/A	USA	Review article	N/A	N/A	N/A
Management of cardiovascular diseases in HIV / AIDS patients. ⁽⁷³⁾	Ashwitha SK, et al.	2021	N/A	UK	Review article	N/A	N/A	N/A
Prevention of heart failure, tachyarrhythmias and sudden cardiac death in HIV. Current opinion in HIV and AIDS. ⁽⁷⁴⁾	Wu KC, et al.	2022	N/A	USA	Review article	N/A	N/A	N/A

APPENDIX I: Articles that were included in the scoping review, continued.

Title	Author	Year	Participants	Country of study	Study design	Male (%)	Duration	Age group
Factors associated with incidence of stroke and heart failure among people living with HIV in Ghana: Evaluating Vascular Event Risk while on Long-Term Antiretroviral Suppressive Therapy (EVERLAST) Study. ⁽⁷⁵⁾	Sarfo FS, et al.	2021	255	Ghana	Prospective cohort	17	1	>18
Association of adherence to antiretroviral therapy with economic burden of cardiovascular disease in HIV-infected population. ⁽⁷⁶⁾	Liao C-T, et al.	2020	18 071	Taiwan	Retrospective cohort	N/A	11	>18
Getting to the heart of the matter: The need for tailored cardiovascular prevention strategies in patients with HIV. ⁽⁷⁷⁾	Fillip I.	2022	N/A	USA	Review article	N/A	N/A	N/A
Myocardial fibrosis and inflammation by CMR predict cardiovascular outcome in people living with HIV. ⁽⁷⁸⁾	De Leuw P, et al.	2021	156	Germany	Prospective cohort	62	19 months	>18
Assessment of biventricular function by 3-Dimensional speckle-tracking echocardiography in adolescents and young adults with human immunodeficiency virus infection: A pilot study. ⁽⁷⁹⁾	Capototso L, et al.	2019	63	Italy	Retrospective cohort	N/A	N/A	N/A
Imaging modalities for cardiovascular phenotyping in asymptomatic people living with HIV. ⁽⁸⁰⁾	Bonou M, et al.	2021	N/A	Greece	Review article	N/A	N/A	N/A
The role of cardiac imaging in the management of non-ischaemic cardiovascular diseases in human immunodeficiency virus infection. ⁽⁸¹⁾	Aljizeeri A, et al.	2020	N/A	Saudi Arabia, Canada, Australia, USA	Review article	N/A	N/A	N/A
Amino-terminal Pro-B-Type natriuretic peptide among patients living with both human immunodeficiency virus and heart failure. ⁽⁸²⁾	Alvi RM, et al.	2019	2 578	USA	Retrospective cohort	50	1	>18
Cardiovascular disease and risk assessment in people living with HIV: Current practices and novel perspectives. ⁽⁸³⁾	Fragkou PC, et al.	2023	N/A	Greece	Review article	N/A	N/A	N/A
Guidance for timely and appropriate referral of patients with advanced heart failure: A scientific statement from the American Heart Association. ⁽⁸⁴⁾	Morris AA, et al.	2021	N/A	USA	Review article	N/A	N/A	N/A
Heart transplantation survival outcomes of HIV positive and negative recipients. ⁽⁸⁵⁾	Doberne JW, et al.	2021	29 923	USA	Retrospective cohort	71	14	>18
Heart transplantation in a well-controlled human immunodeficiency virus infected patient: The first case of Taiwan. ⁽⁸⁶⁾	Chen CH, et al.	2022	1	Taiwan	Case report	100	N/A	>18
Advanced heart failure therapies in patients with stable HIV infection. ⁽⁸⁷⁾	Brozzi NA, et al.	2020	1	USA	Case report	100	N/A	>18