

HIV linked with increased risk of sudden cardiac death

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People living with human immunodeficiency virus (HIV) have a higher risk of sudden cardiac death than people who do not have HIV, especially if the virus is not well-controlled or if they have other heart

disease risk factors, according to new research published today in the *Journal of the American Heart Association*.

"People living with HIV are already known to have a higher risk of heart attack, stroke, heart failure, blood clots in the lungs and peripheral artery disease," said Matthew S. Freiberg, M.D., M.Sc., lead author of the study, the Dorothy and Laurence Grossman Chair in Cardiology and a professor of medicine at Vanderbilt University School of Medicine in Nashville, Tennessee.

"We know that among people with HIV, those who have a compromised immune system, for example a low total CD4⁺ T cell count, they seem to have a higher risk of cardiovascular disease than those who have high CD4⁺ T cell counts," Freiberg said. "It is unclear if a compromised immune system is a risk factor for sudden cardiac death."

Sudden cardiac death occurs when the heart unexpectedly stops beating (usually due to a sudden electrical malfunction causing a lethal heart rhythm), preventing blood flow to the brain and vital organs, resulting in death within minutes if not treated. Investigators used standard World Health Organization criteria plus detailed review of medical records to define sudden cardiac death in the study.

A previous, single-center study of 2,800 people at an HIV clinic in San Francisco in 2012, discovered the rate of sudden cardiac death was 4-times higher in people with HIV. The current study examines the rate of sudden cardiac death on a national scale, along with the influence of HIV viral loads and other heart disease risk factors on the risk of sudden cardiac death.

Researchers evaluated participants from a national study of people with HIV infection that has a matched participant group without HIV—the Veterans Aging Cohort Study (VACS). VACS is an ongoing, long-term,

national study that follows veterans with and without HIV (two uninfected to each HIV-positive participant), and matched by age, sex, race/ethnicity and the VA site where they receive care. The study explores the role of HIV and HIV disease status, along with other health conditions.

Among the more than 144,000 veterans in the VACS study, 30% were diagnosed with HIV and evaluated at VA hospitals across the country. Overall, participants were 97% male, 47% were African American, and the average age was 50 years at enrollment. Each participant entered the study at an initial medical appointment on or after April 2003, and were followed through December 31, 2014, for the occurrence of sudden cardiac death. During the median follow-up of 9 years, sudden cardiac death was cited as the cause of death for 3,035 of the veterans, 26% (777) of whom had HIV.

After adjusting for numerous factors, including age, sex, race/ethnicity, the presence of heart or kidney disease, cocaine or alcohol dependence or abuse, and various heart disease risk factors, the analysis found the risk of sudden cardiac death was:

- not higher in people with HIV who had healthy levels of infection-fighting CD4⁺ T cells or among those who had a low level of the HIV virus in their blood;
- progressively higher with each risk factor for sudden cardiac death that was present, including existing cardiovascular disease, high blood pressure, smoking, hepatitis C infection, anemia, alcohol dependence or abuse, and chronic obstructive pulmonary disease, regardless of whether or not they had HIV;
- 14% higher in people with HIV;
- 57% higher in people with HIV whose blood tests showed low levels of CD4⁺ T cells over time, an indicator that HIV was progressing, and the immune system was compromised; and

- 70% higher in people with HIV whose blood tests showed that antiretroviral therapy had not suppressed the HIV viral load in their blood over time.

"Addressing risk factors related to both cardiovascular disease and HIV is essential to prevent the higher rates of sudden cardiac death in people with HIV," said Zian H. Tseng, M.D., M.A.S, senior author of the study and a professor of medicine in residence, Murray Davis Endowed Professor at the University of California, San Francisco. "Clinicians should consider screening for specific warning signs of sudden cardiac death such as fainting or heart palpitations. And, if indicated, clinicians should request additional testing such as echocardiograms or continuous rhythm monitoring."

Results from this overwhelmingly male sample of study participants may not be generalizable to women. The study is also limited by the fact that autopsies were rarely available, and autopsies are the definitive way to diagnose sudden cardiac death. Tseng and colleagues recently reported that when people with HIV and presumed sudden cardiac death (based on paramedic records) had detailed, research-level autopsies, half were confirmed to have had a cardiac cause, however, many were found to have died of non-cardiac conditions, such as drug overdose, a blood clot in the lungs or a stroke. People with HIV also had higher levels of scar tissue in the heart muscle (myocardial fibrosis) than people without HIV, which may account for the higher rate of death due to lethal arrhythmias among people with HIV.

"In addition to HIV and cardiovascular risk factors, it is important for health care professionals to screen for and treat substance use disorders especially in people with HIV because they have a three times higher rate of overdose deaths presenting as cardiac arrest in our previous research," Tseng said.

More information: Matthew S. Freiberg et al, HIV Infection and the Risk of World Health Organization–Defined Sudden Cardiac Death, *Journal of the American Heart Association* (2021). DOI: 10.1161/JAHA.121.021268

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