

Abstract

Human immunodeficiency virus (HIV) is a major virus that can deteriorate immune system function while simultaneously resulting in numerous adverse side effects that affect the cardiovascular system. Clinical trials for HIV have been historically prominent, however, those trials tend to exclude patients with comorbid cardiology concerns such as hypertension and arrhythmia. In fact, an analysis of data from clinicaltrials.gov found that HIV clinical trials excluded patients with comorbid cardiovascular conditions approximately 94.75% of the time, which was deemed statistically significant. Given the complexity and severity of HIV, it's paramount that future HIV clinical trials include patients with comorbid cardiovascular conditions to improve concurrent treatment efficacy and patient quality of life.

Background

Known as one of the most serious viruses, human immunodeficiency virus (HIV) can cause catastrophic damage to the body's immune system function. Similarly, HIV is believed to be responsible for an increased risk of cardiovascular disease. While the effect of HIV on cardiovascular disease appears to be geographically dependent, HIV patients are roughly twice as likely to be diagnosed with cardiovascular disease than those living without the virus (Shah et al., 2018, 1100-1112; So-Armah et al., 2020, e279-293). Similarly, HIV doubles the likelihood of myocardial infarction (MI), commonly referred to as a heart attack. The increased risk of MI is attributed to traditional cardiovascular disease risk factors such as hypertension, dyslipidemia, and smoking which are more common in HIV patients (Rao et al., 2019, 224).

While there is no known cure for HIV, some treatments can increase survival duration and the quality of life in those living with HIV. Even so, some HIV medications have been tied to major adverse effects including sudden cardiac death. Research has attributed such cases to antiretroviral (ART) medications although major adverse effects appeared to occur in those with previous heart conditions such as arrhythmias. The exact cause of such adverse effects is unknown but anticipated to be a result of non-ART polypharmacy, electrolyte imbalances, and substance use. (Brouillette et al., 2019, 310-319). Regardless of the cause, it's clear that HIV treatments warrant further investigation to minimize adverse cardiovascular events and to concurrently treat patients with comorbid HIV and cardiovascular conditions.

Methods

This study used Python3.9.10 to collect data from clinicaltrials.gov, analyzing the inclusion and exclusion frequency of cardiology terms in HIV clinical trials from 1990 to date. All terms were organized and tallied to compare inclusion and exclusion frequencies and their cumulative statistical significance.

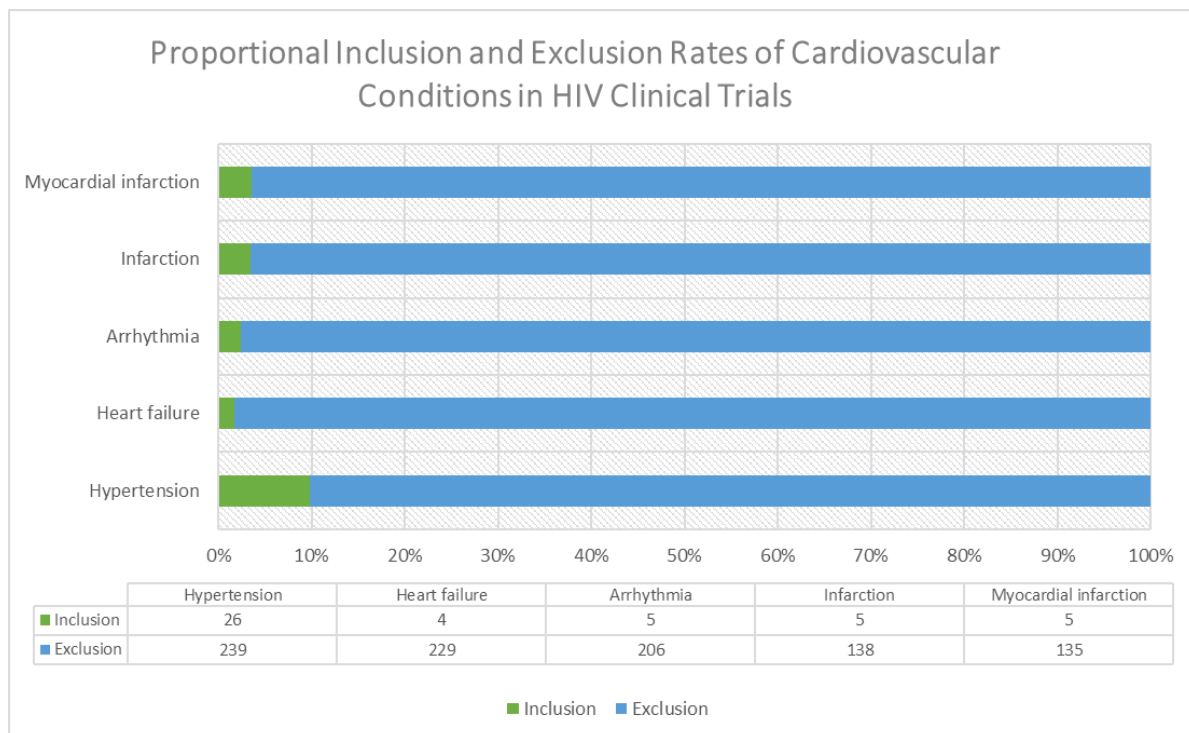
Microsoft Excel was used to sort all collected terms by total frequency. Additionally, Excel was used to determine the statistical significance between the inclusion and exclusion data using a one-tail t-test and Pearson correlation. All data were included in the statistical analysis and any

additional trends were noted to be included within the results section. Figure 1 displays the statistical results while Figure 2 illustrates the proportions of inclusion and exclusion frequencies in cardiology terms that appeared the most frequently in HIV inclusion and exclusion criteria.

Figure 1. T-test paired for two sample means using the inclusion and exclusion criteria of cardiology terms in HIV clinical trials.

Statistical Measure	Inclusion	Exclusion
Mean	1.95	35.175
Variance	20.1	4109.019872
Observations	40	40
Pearson Correlation	0.714158014*	
P(T<=t) one-tail	0.000688289*	

Figure 2. Comparison of inclusion and exclusion frequencies of renal-related terms in hypertension clinical trials.



Results and Discussion

Researchers collected 1485 cardiology terms within HIV clinical trials. Of those terms, 1407 (94.75%) were within the exclusion criteria compared to 78 (5.25%) within the inclusion criteria. The most common cardiology terms were hypertension, heart failure, arrhythmia, infarction, and myocardial infarction which accounted for 947 of the 1407 excluded terms (67.31%).

Collectively, cardiology terms or conditions were 18.05 times more likely to be excluded from HIV clinical trials. The statistical analysis found a significant difference between the inclusion and exclusion criteria ($p < .01$) and a large effect was noted via the Pearson correlation (0.714).

Human immunodeficiency virus is a major virus that can cause severe side effects which are sometimes fatal. Research has established a clear relationship between HIV and cardiovascular risk factors and conditions, although the geographical location may play a role in the magnitude of that relationship. Overall, HIV clinical trials exclude patients with comorbid cardiovascular conditions at an alarming rate considering the increased prevalence of such conditions in HIV patients. A more proportional inclusion of HIV patients with comorbid cardiovascular conditions should be pursued in clinical trials to improve treatment outcomes in a largely affected population.

References

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