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Authors

Shitole, Sanyog G
Kuniholm, Mark H
Hanna, David B
et al.

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Association of human immunodeficiency virus and hepatitis C virus infection with long-term outcomes post-ST segment elevation myocardial infarction in a disadvantaged urban community

Sanyog G. Shitole[a], **Mark H. Kuniholm**[b], **David B. Hanna**[c], **Thomas Boucher**[c], **Angel Y. Peng**[d], **Cecilia Berardi**[e], **Tina Shah**[d], **Anna E. Bortnick**[c,d], **Panagiota Christia**[f], **James Scheuer**[c,d], **Jorge R. Kizer**[a]

[a]University of California San Francisco and San Francisco Veterans Affairs Health Care System, 4150 Clement Street, San Francisco, CA 94121, USA.

[b]University at Albany, 1 University Place, Rensselaer, NY 12144, USA.

[c]Albert Einstein College of Medicine, 1300 Morris Park Avenue, Bronx, NY 10461, USA.

[d]Montefiore Health System, 3311 Bainbridge Avenue, Bronx, NY 10467, USA.

[e]Yale-New Haven Hospital, 20 York Street, New Haven, CT 06510, USA.

[f]Mount Sinai Heart-Mount Sinai Medical Center, 1468 Madison Avenue, New York, NY 10029, USA.

Corresponding Author: Sanyog G. Shitole, 4150 Clement Street, San Francisco, CA 94121, USA. sanyog.shitole@ucsf.edu.

Author Contributions: Sanyog G. Shitole: Conceptualization, Data curation, Formal analysis, Methodology, Writing - original draft, Writing - review and editing. Mark H. Kuniholm: Writing - review and editing. David B. Hanna: Writing - review and editing. Thomas Boucher: Data curation, Writing - review and editing. Angel Y. Peng: Data curation, Writing - review and editing. Cecilia Berardi: Data curation, Writing - review and editing. Tina Shah: Data curation, Writing - review and editing. Anna E. Bortnick: Data curation, Writing - review and editing. Panagiota Christia: Data curation, Writing - review and editing. James Scheuer: Conceptualization, Writing - review and editing. Jorge R. Kizer: Conceptualization, Writing - review and editing.

Credit Author Statement

Sanyog G. Shitole: Conceptualization, Data curation, Formal analysis, Methodology, Writing - original draft, Writing - review and editing.
Mark H. Kuniholm: Writing - review and editing.
David B. Hanna: Writing - review and editing.
Thomas Boucher: Data curation, Writing - review and editing.
Angel Y. Peng: Data curation, Writing - review and editing.
Cecilia Berardi: Data curation, Writing - review and editing.
Tina Shah: Data curation, Writing - review and editing.
Anna E. Bortnick: Data curation, Writing - review and editing.
Panagiota Christia: Data curation, Writing - review and editing.
James Scheuer: Conceptualization, Writing - review and editing.
Jorge R. Kizer: Conceptualization, Writing - review and editing.

Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Abstract

Background: HIV and HCV have been linked to an increased risk of cardiovascular disease (CVD). Their impact on long-term outcomes following ST-segment myocardial infarction (STEMI) has not been previously studied.

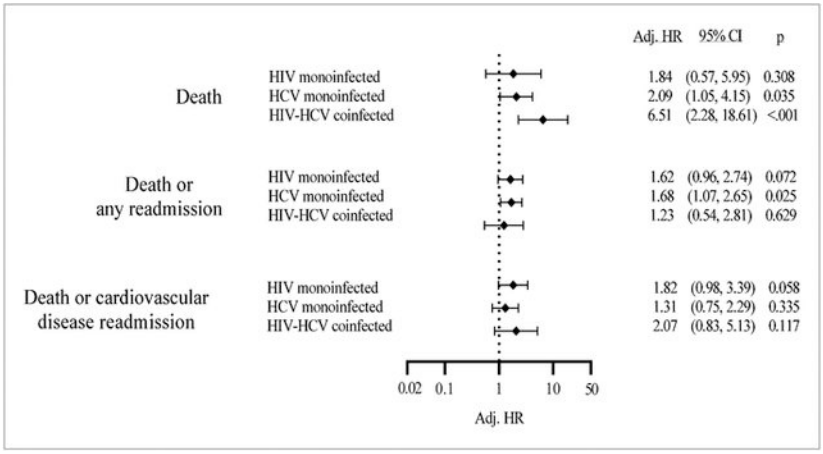
Methods: We leveraged data from a STEMI registry (n=1208) at an inner-city health system to assess the influence of HIV and HCV on post-STEMI outcomes. Cox regression was used to compare HIV-monoinfected (n=22), HCV-monoinfected (n=26) and HIV-HCV-coinfected patients (n=8) with the neither-infected group (n=1152) with regard to death, death or any readmission, and death or CVD readmission.

Results: The cohort was majority black or Hispanic. Median follow-up was 4.3 years. Compared to the neither-infected group, the HIV-monoinfected group showed near-significantly higher risks of death or any readmission (HR=1.62, 95% CI=0.96, 2.74) and death or CVD readmission (HR=1.82, 95% CI=0.98, 3.39) after full adjustment. On similar comparison, the HCV-monoinfected group exhibited significantly higher risks of death (HR=2.09, 95% CI=1.05, 4.15) and death or any readmission (HR=1.68, 95% CI=1.07, 2.65), whereas the HIV-HCV-coinfected group showed higher risk of death (HR=6.51, 95% CI=2.28, 18.61).

Conclusions: In this cohort composed mostly of race-ethnic minorities, HIV monoinfection tended to be associated with 1.6-to-1.8-fold higher death or readmission for any cause or CVD over long-term follow-up compared to neither infection, whereas HCV monoinfection was associated with 1.7-to-2.1-fold higher death and death or any readmission, and HIV-HCV coinfection with 6.5-fold higher death. These associations require further study in larger populations, but highlight the importance of identifying and treating HIV and HCV in patients presenting with STEMI.

Graphical Abstract.

Adjusted hazard ratios of death, death or any readmission and death or CVD readmission following acute ST-elevation myocardial infarction for HIV monoinfection, HCV monoinfection and HIV-HCV coinfection compared to neither-infection group. Hazard ratios are adjusted for age, sex, race-ethnicity, BMI, summary socioeconomic score, current smoking, heavy alcohol use, cocaine use, diabetes, hypertension, dyslipidemia, prior ASCVD, Prior HF, serum creatinine, Killip class, LVEF, Catheterization within 24 hours, CABG during index hospitalization. ASCVD=Atherosclerotic cardiovascular disease; BMI=Body mass index; CABG=Coronary artery bypass grafting; CI=Confidence interval; HCV=Hepatitis C virus; HF=Heart failure; HIV=Human immunodeficiency virus; HR=Hazard ratio; LVEF=Left ventricular ejection fraction.



Keywords

HIV; HCV; STEMI; Outcomes

Introduction

The advent of combination antiretroviral therapy (ART) has led to an increase in the life expectancy of people living with HIV (PLWH), who now number more than 1.1 million in the United States (1). This survival benefit has come at the cost of an increased burden of chronic disorders, particularly cardiovascular disease (CVD) (2). Like HIV, hepatitis C virus (HCV) affects a considerable fraction of the US population, with an estimated 2.7 to 3.9 million chronic cases (3). The prevalence of chronic HCV is high among people with HIV, with 15-30% affected (4). Apart from being a foremost cause of cirrhosis and hepatocellular carcinoma, chronic HCV leads to various extrahepatic complications, including insulin resistance and diabetes, as well as kidney disease (5). Chronic HCV has also been associated with a heightened risk of atherosclerosis, encompassing both coronary heart disease and stroke (6, 7). Development of direct-acting antiretroviral (DAA) drugs has rendered chronic HCV infection curable (8), and prompted increased screening efforts in at-risk populations (9).

Both HIV and HCV disproportionately affect socioeconomically disadvantaged race-ethnic groups, including blacks and Hispanics (10-12). Available studies assessing the impact of these chronic infections on outcomes after acute coronary syndromes have centered exclusively on HIV, showing increased HIV-related risks of rehospitalization for heart failure (HF) (13) or mortality (14), but have not focused on low-income settings. To date, the separate and combined influence of HIV and HCV on outcomes of acute myocardial infarction has not been examined, particularly in vulnerable populations. We turned to a well-characterized cohort with ST-segment elevation myocardial infarction (STEMI) receiving acute care at an inner-city health system to evaluate the impact of HIV and HCV on long-term outcomes in this predominantly black and Hispanic population. We leveraged data from the Montefiore STEMI Registry (15, 16) over 7 years to examine the baseline

differences at index STEMI hospitalization between groups based on HIV and HCV status and to evaluate differences in outcomes post-STEMI.

Materials and methods

Details of the Montefiore STEMI Registry have been described before (15, 16). Briefly, the registry included all STEMI patients considered for acute revascularization at Montefiore Health System (MHS) from May 2008 to December 2014 and providing informed consent. Sociodemographic characteristics, medical history, physical examination, laboratory results, and other diagnostic test findings were gathered from direct interviews with patients and from chart reviews. In-hospital characteristics and blood values for cardiac markers were obtained from a proprietary database system, Looking Glass Clinical Analytics (LGCA) (Streamline Health, Atlanta, GA) (17). Information collected by abstractors on clinical, laboratory, and imaging data was supplemented using LGCA. Cardiac catheterization data were obtained from an electronic database containing standardized angiographic and procedural information reported to New York State. The STEMI registry protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki and was approved by the Institutional Review Board of Albert Einstein College of Medicine.

HIV-infection status was defined by a positive HIV ELISA or a positive HIV viral load at any time point before and through the index STEMI hospitalization by chart review. Additionally, we linked our cohort of n=1208 patients to the Einstein-Rockefellar-CUNY Center for AIDS Research (ERC-CFAR) HIV Clinical Cohort Database (18). All n=30 HIV cases identified by chart review were confirmed as positive through this linkage and no additional HIV cases were detected. Positive HCV status was defined by the detection of anti-HCV antibodies, detection of HCV RNA in the blood or documented history of HCV infection at any time point before and through the index STEMI hospitalization by chart review. Among the n=34 HCV-positive patients, n=12 had tested positive for HCV RNA, n=12 had tested positive for HCV antibody, and n=10 had a documented history of HCV infection.

Race-ethnicity was self-reported. Summary socioeconomic score was calculated from z-scores of neighborhood-level measures of income, education, and occupation available from U.S. census data using published methods (19). Body mass index (BMI) was derived as weight (kilograms) divided by the square of height (meters). Hypertension, diabetes and dyslipidemia were based on self-reported or documented history, or treatment with corresponding medications. Current smoking was defined as any cigarette use in the past 30 days. Heavy alcohol was defined by a history of alcohol abuse or consumption of more than 14 drinks/week in men or 7 drinks/week in women. Cocaine use was defined as self-reported use in the past 4 weeks or a positive urine cocaine test (15). Family history of coronary heart disease (CHD) was obtained from patient history in the medical record. Prior atherosclerotic cardiovascular disease (ASCVD) included CHD, stroke or peripheral arterial disease. Both, prior ASCVD and prior heart failure (HF) were assessed from patient history or clinical information in the medical record. The TIMI STEMI risk score was calculated in standard fashion (20). Critical coronary disease was defined as ⩾70% luminal narrowing of the left anterior descending, left circumflex or right coronary artery or its branches or ⩾50%

narrowing of the left main coronary artery. Left ventricular ejection fraction (LVEF) was obtained from the left ventriculogram at cardiac catheterization or, in its absence, from the earliest echocardiogram at the index hospitalization. Killip class, laboratory measures, discharge medications, catheterization data and other relevant clinical data were obtained from the medical record. Aspartate aminotransferase to platelet ratio index (APRI) {[(aspartate aminotransferase level/ aspartate aminotransferase upper limit of normal)/ platelet count in 10^9 per L] × 100} and fibrosis-4 (FIB4) score [(age in years × aspartate aminotransferase in units per liter)/(platelet count in 10^9 per liter × square root of alanine aminotransferase in units per liter)] were calculated in standard fashion (21, 22).

The primary outcomes were death, death or any readmission, and death or CVD readmission. Mortality data were obtained by linkage to the National Death Index (NDI). LGCA was also used to capture readmissions at MHS and direct chart review was used to identify readmissions at the adjacent Jacobi Medical Center and North Central Bronx Hospital (together forming the North Bronx Health Network [NBHN]). Follow-up for all outcomes was through 2015. CVD readmission comprised myocardial infarction, percutaneous or surgical revascularization, stroke, HF, ventricular tachycardia/ventricular fibrillation, and atrial fibrillation/flutter, based on appropriate Current Procedural Terminology, Fourth Edition (CPT4), codes or discharge International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), codes in the primary position, as previously reported (15).

Patients were divided into four groups based on their HIV and HCV status as HIV monoinfection, HCV monoinfection, HIV-HCV coinfection and neither-infection. Continuous variables are described by their medians and interquartile ranges, while categorical variables are presented as counts and percents. Comparisons of continuous variables applied the Wilcoxon rank-sum test, while those of categorical variables used the chi-square or Fisher's exact test, as appropriate. Crude incidence rates for the outcomes were calculated per 100 person years and differences as compared to the neither-infection group were computed with Poisson-based 95% confidence intervals. The relationship between HIV/HCV status groups and time to events was described using Kaplan-Meier plots, and unadjusted comparisons between status groups were performed with the logrank test. Figures 1, 2 and 3 showing the Kaplan-Meier plots with numbers at risk were generated using STATA, version 16.1, and the *p* value is for the logrank test for difference in the survival plots across groups. Adjusted comparisons were performed by fitting Cox proportional hazards models. Covariates were selected based on observed differences in levels between HIV and/or HCV positive groups in comparison with the neither-infected group, in conjunction with known biology or previously reported associations with exposures and outcomes. Although some factors could act not just as confounders but also as causal intermediates, all such covariates were included in the adjustment in order to define the associations of HIV and HCV status groups themselves with adverse post-STEMI outcomes. An initial model adjusted for age, sex and race-ethnicity. A subsequent model adjusted additionally for BMI, summary socioeconomic score, current smoking, heavy alcohol use and cocaine use. A third model additionally adjusted for diabetes, hypertension, prior ASCVD, prior HF and initial creatinine. Finally, a fourth model (main model) additionally adjusted for Killip class, left ventricular ejection fraction (LVEF),

catheterization within 24 hours of presentation and whether patient underwent coronary artery bypass grafting (CABG) during the index hospitalization. The proportional hazards assumption was tested by Schoenfeld residuals, which revealed no violations. Analyses were performed with SAS, version 9.4 (SAS Institute, Cary, NC). A two-tailed $p<0.05$ defined statistical significance.

Results

Table 1 presents the sociodemographic and clinical characteristics of the study cohort stratified by HIV and HCV infection status and their comparisons to the neither-infection (referent) group. Among the n=30 patients with HIV infection, n=21 (70%) were on ART, the median CD4+ T-cell count was 372 (IQR 135, 570) cells/μL and n=11 (37%) had a detectable viral load within an year of the index STEMI. Figures 1, 2 and 3 show Kaplan-Meier curves for the four HIV and HCV status groups in relation to the primary outcomes of death, death or any readmission, and death or CVD readmission. Median follow-up for the entire cohort was 4.3 (IQR 2.4, 6.0) years.

Cumulative numbers and incidence rates for the main outcomes in the four groups are presented in Table 2, along with comparisons to the referent (neither-infection) group. There were no significant differences in crude incidence rates between the HIV mononfection group and the neither-infection group, but the HCV monoinfection group did show significantly higher rates of death and death or any readmission as compared to the referent group. The HIV-HCV coinfection group showed a significantly higher crude incidence rate of death in comparison to the neither-infection group.

Table 3 details the adjusted relationships with the primary outcomes for HIV monoinfected, HCV monoinfected, and HIV-HCV coinfected patients in comparison to patients with neither infection. There was no significant association between the HIV monoinfected group and death at any level of adjustment. In models adjusting for demographic factors, however, HIV monoinfection was significantly associated with a 1.7 and 2.0-fold higher risk of death or any readmission, and death or CVD readmission, respectively. These risks were minimally attenuated with serial adjustment for socioeconomic and lifestyle factors and clinical covariates (1.6 and 1.8-fold higher risk of death or any readmission, and death or CVD readmission, respectively, in the final [main] model), but became marginally non-significant. For the HCV monoinfection group, there were significantly increased risks of death and death or any readmission in the minimally adjusted model, which were moderately attenuated with serial adjustment for covariates. These higher risks of death and death or any readmission remained significant at 2.1 and 1.7-fold, respectively, in the final model. There was no significant association between HCV monoinfection and death or CVD readmission at any level of adjustment. The HIV-HCV coinfected group was significantly associated with a 7.0-fold higher risk of death in the minimal model which was not meaningfully changed at 6.5-fold in the final model. This group did not show any significant association for either death or any readmission, or death or CVD readmission.

Discussion

This investigation of patients presenting with acute STEMI in a socioeconomically disadvantaged urban area focusing on HIV and HCV status and associated long-term outcomes yielded several notable findings. When compared to the neither-infected group, the HIV-monoinfected group had higher risks of death or any readmission and death or CVD readmission, but not death only, although these fell slightly short of statistical significance after full adjustment for sociodemographic and clinical covariates. The HCV-monoinfected group had higher risks of death and death or any readmission, but not death or CVD readmission, as the neither-infected group, which remained statistically significant in fully adjusted models. In turn, the HIV-HCV coinfected group showed a markedly increased risk of death as compared with the neither-infected group that maintained significance after full adjustment, but no significant associations were detected with either of the composite outcomes including readmission.

It is well recognized that PLWH are at increased risk of CVD, a risk that extends beyond atherosclerotic disease to heart failure and cardiac dysrhythmias (23). Such cardiovascular complications of ART-treated HIV, much like non-cardiovascular disorders in this population, are deemed to result from chronic immune activation or inflammation from viral persistence, microbial translocation, and co-infections (24). All such processes are accentuated in the setting of more advanced HIV disease, lack of effective ART, or unsuppressed viremia. In addition, it is documented that people with chronic HCV infection are prone not only to hepatic complications, but also to extrahepatic disorders such as diabetes, chronic kidney disease and, with them, atherosclerotic CVD (5). These disorders result from HCV-induced hepatic inflammation and systemic immune dysregulation, with consequences within and without the liver (5). Fewer data are available regarding the clinical profile and, especially, long-term outcomes following acute MI in these susceptible individuals.

In a nationwide administrative database of acute myocardial infarction (AMI) cases in France, most of which were STEMIs, patients with HIV had an increased risk of rehospitalization for HF, but not mortality, at 1-year, as compared with their HIV-negative counterparts (13). Detailed information on clinical factors, however, including HIV-specific factors, was not available. Another study comparing outcomes between HIV-infected and -uninfected patients after acute coronary syndromes (ACS) in a large integrated health system in Northern California found higher HIV-related mortality, but no association with ACS recurrence, during follow-up restricted to 3 years (14). The increased risk of death was observed in HIV-positive patients with CD4+ T-cell count<500 cell/uL, but not higher. Similar to the foregoing finding, it is likely that the low median CD4+ T-cell count among HIV-positive patients in our sample, the fact that nearly a third were not on ART and that over a third had a detectable viral load contributed to the near-significant or significant associations with adverse outcomes post-MI documented here.

As distinct from HIV, no study to our knowledge has previously evaluated the impact of HCV on outcomes post-MI. Nor have existing studies of HIV in ACS concurrently accounted for, or evaluated, HCV infection. As such, our study provides new information on

the presenting features of these often concurrent infections, both alone and in combination, in the context of acute STEMI, and particularly on long-term outcomes thereafter. As in previous studies, STEMI patients with HIV monoinfection were younger than those without HIV, and they also had a higher burden of smoking and cocaine use. There was no increased risk of all-cause mortality, for which the number of events was small, but there were near-significant increases in death or any readmission and death or CVD readmission after full adjustment, which accords with prior findings (13, 14).

By contrast, STEMI patients with HCV monoinfection were not distinctly younger than those with neither infection, but they too exhibited more unhealthful habits, particularly, heavy alcohol use. HCV monoinfected patients also had worse Killip class, higher peak troponin T and TIMI risk score, and showed evidence of worse liver, kidney, and cardiac systolic function. They less frequently underwent catheterization within 24 hours of presentation, had a longer length of stay, and were less often discharged on beta-blockers and statins. In keeping with their greater event severity and comorbidity status, HCV-monoinfected patients had nearly a 3-fold higher risk of death and over 2-fold higher risk of death or any readmission than their counterparts with neither infection. These elevated risks were attenuated to approximately 2-fold and 1.7-fold, respectively, after full adjustment. Unlike HIV monoinfection, no similar association was seen in relation to death or CVD readmission, which may reflect the preponderance of liver and non-cardiovascular extrahepatic disorders known to supervene in this population (5), as seen in their clinical profile documented herein.

A similarly adverse profile was observed in the HIV-HCV coinfected group, which, though of small size, showed high adverse habits, low BMI, and elevated serum creatinine as compared with the neither-infection group. This group showed the numerically largest risk of death, with a 6.5-fold higher hazard than the neither-infection group, although no significant differences were noted for either death or readmission outcome. This group was of particularly small size, however, limiting both power and precision of the estimates, and precluding direct assessment of effect-modification by HIV-HCV coinfection as compared to HIV or HCV monoinfection. But the finding for this group does suggest that the impact of coinfection, attendant high-risk behaviors, and comorbidities on survival in the context of acute STEMI may be pronounced, a premise that will require testing in larger studies.

The results of this study have important implications. DAA agents now offer a high likelihood of cure for chronic HCV infection, with treatment considered cost effective (25). Indeed, sustained virologic response to treatment has been associated with improved survival in patients with advanced liver disease (26), as well as with lower incidence of CVD events more generally in HCV infection (27). Hence, the poor outcomes documented with HCV infection herein call for heightened awareness of HCV in the AMI setting and for appropriate HCV testing in the in-hospital setting. Recent guidelines have in fact extended recommendations for HCV screening to all adults ages 18 to 79 (28). At a miminum, such testing would apply to groups with history of injection drug use, HIV, or high-risk sex behaviors (25), as well as patients with suspicious abnormalities in liver function tests. Detection of HCV viremia should trigger prompt referral for treatment. In addition,

appropriate counseling is essential in high-risk groups as relates to adverse habits, as are referrals for treatment or harm-reduction programs for substance abuse (8).

Our study has a number of strengths. It focuses on a disadvantaged population primarily composed of race-ethnic minority groups that remains understudied as relates to HIV and HCV status in the setting of acute STEMI. It leverages inclusive data from MHS, the principal care provider for Bronx County, New York, and employs its clinical and administrative information systems to capture multi-layer data pertaining to STEMI care and outcomes. Also, our study includes detailed data on social habits, such as current smoking, heavy alcohol use and cocaine use, as well as detailed clinical and laboratory data, that are important in this context but often not available in larger registries.

Among the study's limitations, the present sample contained HIV and HCV monoinfected groups, and particularly an HIV-HCV coinfected group, of modest size. This led to reduced study power and precision of the risk estimates, and constrained the study's ability to discern differences in the co-infected *versus* monoinfected groups. In the case of HIV, this precluded analysis by HIV-specific factors, including CD4 T-cell count, viral load or medications. Nonetheless, our source population, the Bronx, New York, has high prevalences of HIV and HCV, and therefore even our modest number of HIV and HCV patients with STEMI would be difficult to accrue in other populations (29). Classification of HIV and HCV status was based on either medical history or a positive result if testing was conducted at any time point before and through the index hospitalization, but in the absence of a test, the patient was considered negative. This might lead to some patients being misclassified and would tend to bias the comparisons of interest toward the null hypothesis. Data on intravenous drug use, important in the context of HIV and HCV infections (30, 31), was unavailable in this cohort. We did not have systematic data on HCV RNA status, such that some participants classified as HCV-infected could have had self-cleared or previously treated infection. Since such individuals would tend to have a better prognosis than patients with chronic HCV infection, this would likewise tend to bias our findings toward the null. Although the NDI afforded comprehensive assessment of mortality, the study was only able to capture readmissions to MHS and NBHN. This may have led to underascertainment of readmissions and potentially misclassification bias of uncertain direction. However, results for readmission were broadly similar to patterns seen for mortality, suggesting that such bias, if any, did not meaningfully influence our findings. Last, the present findings pertain specifically to STEMI, and are not necessarily generalizable to non-STEMI or other populations. Still, HIV and/or HCV may well worsen outcomes following non-STEMI as well, as documented elsewhere for HIV. Pending further study, the current findings should be borne in mind in the care of patients with acute coronary syndromes generally.

In this urban population presenting for acute care of STEMI, HIV monoinfection tended to show 1.6-to-1.8-fold higher risks of death or readmission for any cause or CVD compared to neither infection over long-term follow-up after full adjustment for covariates. Meanwhile, HCV monoinfection showed corresponding 1.6-to-2.1-fold higher risks of death or any readmission or mortality alone, while for HIV-HCV coinfection, the risk of death was 6.5-fold higher than for neither infection. Although these associations require further evaluation in larger samples, our findings underscore the impact of HCV and related conditions, both

alone and in combination with HIV, on morbidity and mortality post-STEMI. Given that available regimens of direct acting antiretrovirals for the treatment of HCV infection can achieve sustained virologic response rates of 90-95%, even in HIV-HCV coinfection (32-36), these results highlight the need for attention to appropriate screening, counseling, and initiation of treatment in this setting.

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Highlights

- In patients presenting with STEMI, compared to the neither-infected group, HIV monoinfected group has an increased risk of death or any readmission and death or cardiovascular disease readmission on long-term follow-up.
- On similar comparison, the HCV monoinfected group also has increased risk of death and death or any readmission.
- Similarly, the HIV-HCV coinfected group has a highly increased risk of death on long-term follow-up.
- These findings are significant considering highly effective direct acting antivirals against HCV making it almost completely curable and highly effective anti-retroviral therapy against HIV making it a long-term manageable disease.
- It is extremely important to identify and treat HIV and HCV in patients presenting with STEMI to reduce risk of future adverse outcomes.

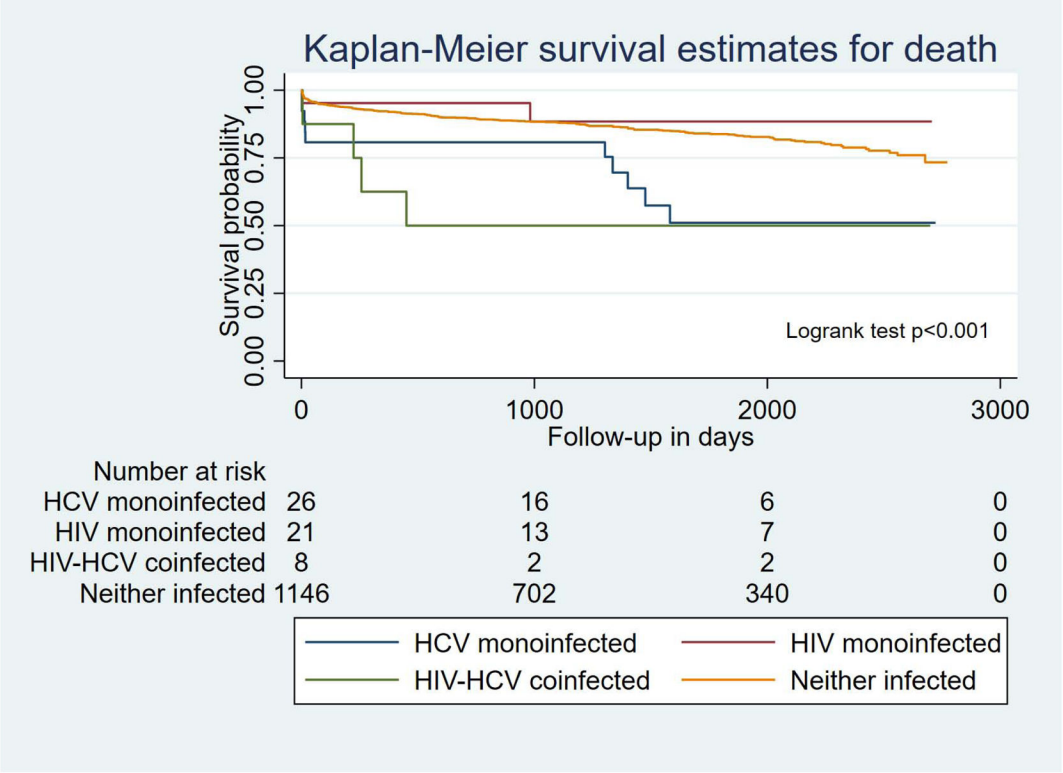

Figure 1.

Kaplan-Meier survival estimates by HIV and HCV status for death. HCV=Hepatitis C virus; HIV=Human immunodeficiency virus.

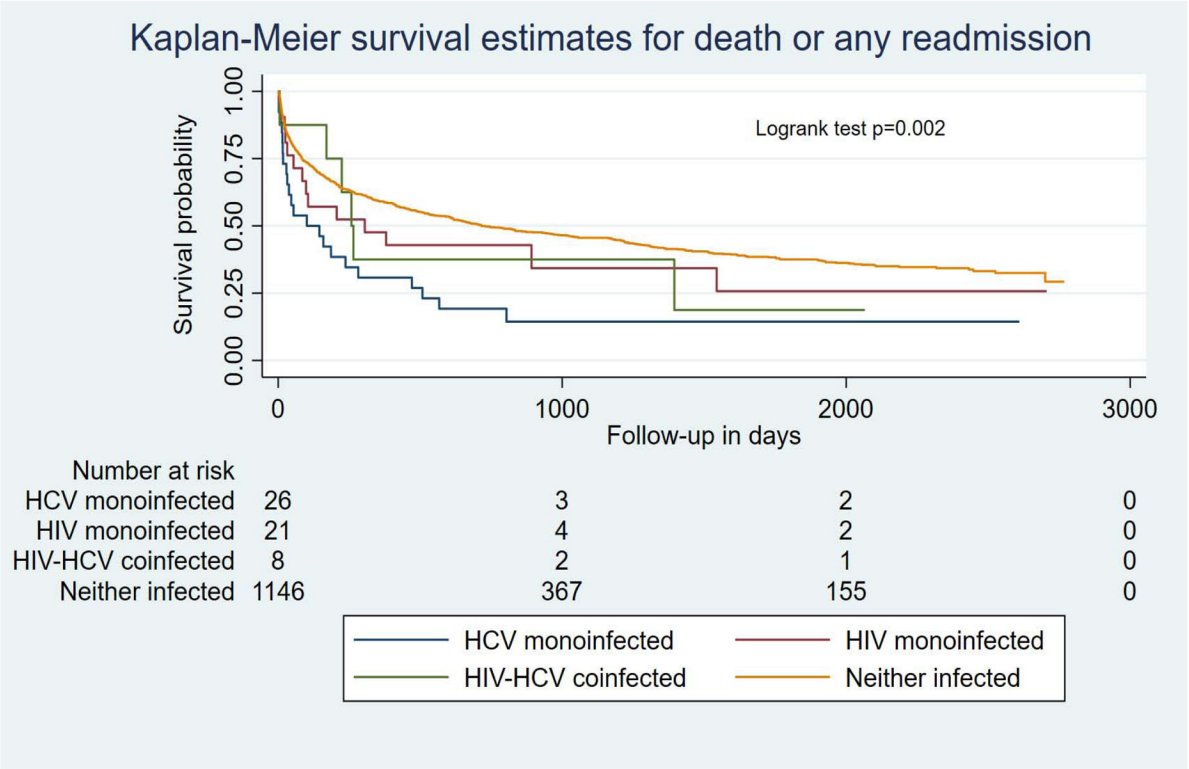

Figure 2.

Kaplan-Meier survival estimates by HIV and HCV status for death or any readmission. HCV=Hepatitis C virus; HIV=Human immunodeficiency virus.

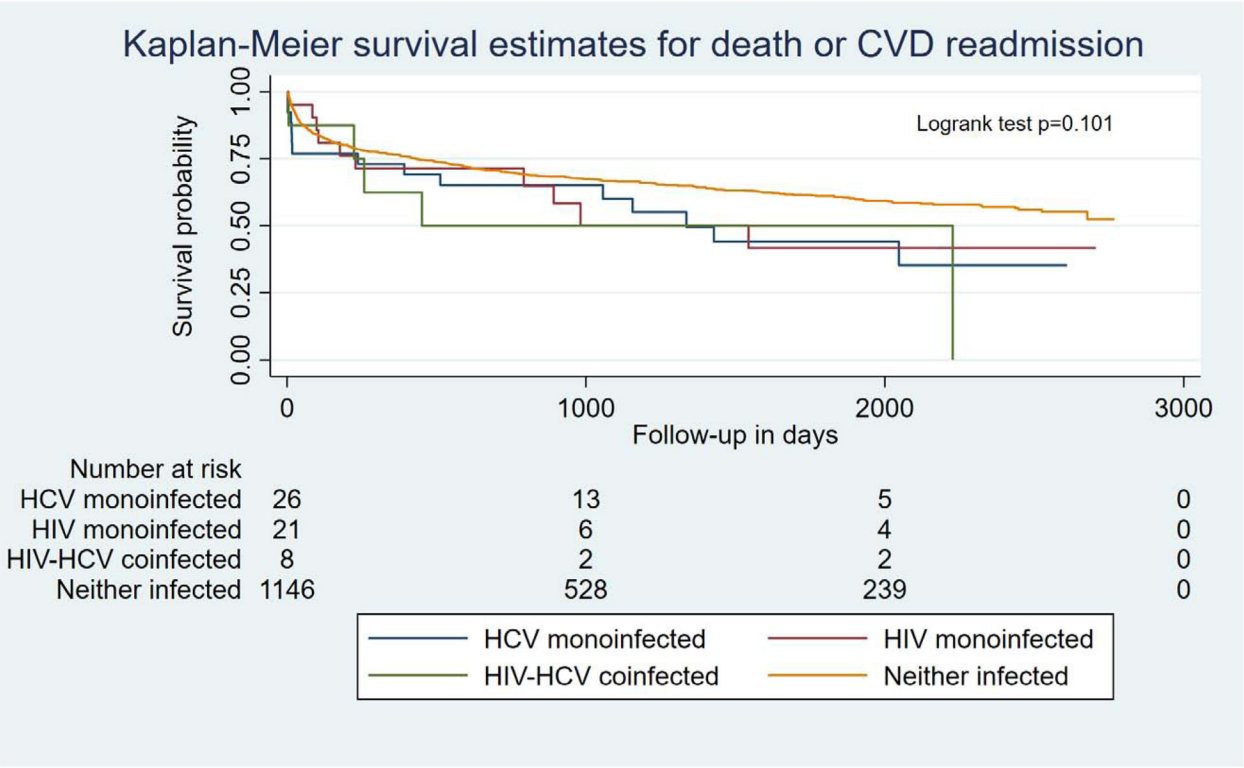

Figure 3.

Kaplan-Meier survival estimates by HIV and HCV status for death or CVD readmission. CVD=Cardiovascular disease; HCV=Hepatitis C virus; HIV=Human immunodeficiency virus.

Table 1.

Baseline characteristics of the Montefiore STEMI registry population, 2008-2014.

	Neither infection (n=1152)	HIV monoinfection (n=22)	HCV monoinfection (n=26)	HIV-HCV coinfection (n=8)
Age, years	60 (51, 70)	50 (43, 57)[a]	60 (55, 70)	55 (50, 59)
Men	768 (66.7)	16 (72.7)	21 (80.8)	5 (62.5)
Race-ethnicity				
Non Hispanic White	266 (23.1)	2 (9.1)	2 (7.7)	0 (0)
Hispanic	418 (36.3)	12 (54.6)	12 (46.2)	6 (75.0)
Non Hispanic Black	234 (20.3)	5 (22.7)	7 (26.9)	2 (25.0)
Other/unknown	234 (20.3)	3 (13.6)	5 (19.2)	0 (0)
Summary socioeconomic score	−2.1 (−5.2, −0.7)	−3.5 (−7.1, −1.3)	−3.3 (−5.8, −1.6)	−4.7 (−5.8, −2.9)
BMI, kg/m^2	28.2 (25.2, 31.7)	25.7 (23.1, 28.4)[a]	27.4 (25.9, 29.5)	23.6 (20.4, 28.0)[a]
Heart rate, beats per minute	79 (69, 90)	82 (73, 92)	83 (71, 102)	90 (85, 105)[a]
Hypertension	773 (67.1)	13 (59.1)	16 (61.5)	5 (62.5)
Diabetes	385 (33.4)	5 (22.7)	11 (42.3)	4 (50.0)
Dyslipidemia	623 (54.1)	11 (50.0)	14 (53.9)	4 (50.0)
Current smoking	424 (36.8)	15 (68.2)[a]	16 (61.5)[a]	7 (87.5)[a]
Cocaine use	54 (4.7)	4 (18.2)[a]	3 (11.5)	2 (25.0)
Heavy alcohol use	106 (9.2)	2 (9.1)	8 (30.8)[a]	4 (50.0)[a]
Family history of premature CHD	350 (30.6)	6 (27.3)	5 (19.2)	2 (25.0)
Prior ASCVD	288 (25.0)	9 (40.9)	4 (15.4)	1 (12.5)
Prior HF	58 (5.0)	2 (9.1)	2 (7.7)	0 (0.0)
Killip class				
1	975 (84.6)	19 (86.4)	17 (65.4)[a]	6 (75.0)
2	57 (5.0)	2 (9.1)	3 (11.5)[a]	2 (25.0)
3	31 (2.7)	1 (4.6)	1 (3.9)[a]	0 (0.0)

	Neither infection (n=1152)	HIV monoinfection (n=22)	HCV monoinfection (n=26)	HIV-HCV coinfection (n=8)
4	89 (7.7)	0 (0.0)	5 (19.2)[a]	0 (0.0)
TIMI STEMI risk score	3 (2, 5)	3 (1, 5)	5 (2, 7)[a]	3 (3, 5)
Peak CPK, units per liter	1507 (679, 2979)	2583 (964, 3933)	1849 (769, 3270)	912 (167, 1609)
Peak troponin T, ng/mL	4.4 (1.9, 8.3)	6.6 (3.9, 10.9)	7.1 (2.3, 16.8)[a]	2.9 (1.3, 6.6)
Initial creatinine, mg/dL	1.0 (0.8, 1.2)	0.9 (0.8, 1.1)	1.1 (0.8, 1.9)[a]	1.3 (1.0, 2.2)[a]
Platelets, ×1000 per mL	234 (193, 278)	215 (194, 264)	198 (164, 224)[a]	187 (132, 276)
Initial WBC count, ×1000 per μL	10.8 (8.6, 13.6)	9.3 (7.7, 11.2)[a]	10.2 (8.3, 14.1)	7.1 (5.8, 10.8)[a]
AST, U/L	36 (23, 92)	55 (42, 215)[a]	79 (48, 189)[a]	62 (40, 98)
ALT, U/L	27 (18, 43)	41 (28, 52)[a]	42 (30, 71)[a]	40 (23, 45)
Albumin, g/dL	4.1 (3.7, 4.3)	4.0 (3.4, 4.4)	3.9 (3.3, 4.2)[a]	4.0 (2.9, 4.3)
APRI	0.4 (0.2, 1.1)	0.6 (0.5, 2.4)[a]	1.3 (0.9, 2.0)[a]	0.8 (0.4, 1.6)
FIB4	2.0 (1.2, 4.2)	2.7 (2.0, 6.4)	4.5 (3.2, 5.1)[a]	3.4 (1.2, 4.6)
Catheterized within 24 hours	1097 (95.2)	20 (90.9)	22 (84.6)[a]	8 (100.0)
Number of critically diseased vessels[b]				
0	95 (8.7)	2 (10.0)	4 (18.2)	1 (12.5)
1	514 (46.9)	8 (40.0)	8 (36.4)	3 (37.5)
2	309 (28.2)	6 (30.0)	6 (27.3)	4 (50.0)
3	179 (16.3)	4 (20.0)	4 (18.2)	0 (0.0)
CABG during index hospitalization	51 (4.4)	1 (4.6)	2 (7.7)	1 (12.5)
LVEF, %	50 (40, 59)	45 (30, 55)	39 (28, 50)[a]	38 (34, 52)
Length of stay, days	4 (3, 7)	3 (3, 4)	8 (4, 12)[a]	5 (4, 13)
Discharge medications[c]				
Aspirin	1097 (98.8)	20 (100.0)	20 (95.2)	7 (100.0)

	Neither infection (n=1152)	HIV monoinfection (n=22)	HCV monoinfection (n=26)	HIV-HCV coinfection (n=8)
Beta-blocker	1039 (93.6)	18 (90.0)	17 (81.0)[a]	7 (100.0)
RAAS antagonist	824 (74.2)	16 (80.0)	17 (81.0)	4 (57.1)
Statin	1073 (96.7)	18 (90.0)	16 (76.2)[a]	6 (85.7)
Thienopyridine	1043 (94.0)	18 (90.0)	19 (90.5)	6 (85.7)

Median (interquartile range) for continuous variables; n (%) for categorical variables.

[a] $p<0.05$ when compared to the neither infection group

[b] only for those undergoing catheterization within 24 hours

[c] only for those discharged alive.

To convert creatinine from mg/dL to mmol/L, multiply by 0.0884; to convert albumin from g/dL to g/L, multiply by 10.

ALT=Alanine transaminase; APRI=AST to Platelet Ratio Index; ASCVD=Athresclerotic cardiovascular disease; AST=Aspartate transaminase; BMI=Body mass index; CABG=Coronary artery bypass grafting; CHD=Coronary heart disease; CPK=Creatine phosphokinase; CVD=Cardiovascular disease; FIB4=Fibrosis 4; HCV=Hepatitis C virus; HF=Heart failure; HIV=Human immunodeficiency virus; LVEF=Left ventricular ejection fraction; RAAS=Renin-angiotensin-aldosterone system; STEMI=ST-segment elevation myocardial infarction; TIMI=Thrombolysis in Myocardial Infarction; WBC=White blood cell.

Table 2.

Number of events and incidence rates for outcomes based on HIV and HCV status

Group	Outcome measures	Death	Death or any readmission	Death or CVD readmission
Neither infection (n=1152)	N	185	677	425
	IR (95% CI)	4.2 (3.7, 4.9)	26.8 (24.9, 28.9)	12.4 (11.3, 13.6)
HIV monoinfection (n=22)	N	3	15	11
	IR (95% CI)	3.7 (0.9, 9.9)	40.6 (23.6, 65.5)	19.1 (10.0, 33.1)
HCV monoinfection (n=26)	N	10	22	14
	IR (95% CI)	11.3 (5.8, 20.2)[a]	74.1 (47.7, 110.4)[a]	19.4 (11.0, 31.7)
HIV-HCV coinfection (n=8)	N	4	6	5
	IR (95% CI)	20.3 (6.4, 48.9)[a]	41.5 (16.8, 86.2)	27.1 (9.9, 60.2)

[a] $p<0.05$ when compared to the neither-infection group.

CI=Confidence interval; CVD=Cardiovascular disease; HCV=Hepatitis C virus; HIV=Human immunodeficiency virus; IR=Crude incidence rate per 100 person years; N=Number of events over follow-up.

Table 3.

Hazard Ratios for outcomes for HIV and HCV monoinfection groups compared to neither infection group (n=1152).

Outcome		HIV monoinfected (n=22)		HCV monoinfected (n=26)		HIV-HCV coinfected (n=8)	
		HR (95% CI)	*p value*	HR (95% CI)	*p value*	HR (95% CI)	*p value*
Death	Model 1	1.85 (0.58, 5.86)	0.296	2.79 (1.47, 5.30)	0.002	6.99 (2.56, 19.13)	<0.001
	Model 2	1.84 (0.57, 5.90)	0.306	2.47 (1.27, 4.80)	0.008	6.59 (2.36, 18.43)	<0.001
	Model 3	1.65 (0.51, 5.36)	0.401	2.74 (1.40, 5.36)	0.003	5.49 (1.94, 15.58)	0.001
	Model 4	1.84 (0.57, 5.95)	0.308	2.09 (1.05, 4.15)	0.035	6.51 (2.28, 18.61)	<0.001
Death or any readmission	Model 1	1.73 (1.03, 2.91)	0.037	2.20 (1.44, 3.37)	<0.001	1.49 (0.66, 3.33)	0.335
	Model 2	1.67 (0.99, 2.81)	0.056	1.99 (1.28, 3.12)	0.003	1.37 (0.61, 3.11)	0.448
	Model 3	1.66 (0.98, 2.80)	0.059	1.99 (1.27, 3.13)	0.003	1.31 (0.58, 2.99)	0.516
	Model 4	1.62 (0.96, 2.74)	0.072	1.68 (1.07, 2.65)	0.025	1.23 (0.54, 2.81)	0.629
Death or CVD readmission	Model 1	2.00 (1.09, 3.68)	0.025	1.52 (0.89, 2.60)	0.123	2.26 (0.93, 5.47)	0.072
	Model 2	2.02 (1.09, 3.74)	0.025	1.51 (0.87, 2.61)	0.139	2.29 (0.93, 5.63)	0.070
	Model 3	1.81 (0.97, 3.37)	0.063	1.59 (0.92, 2.75)	0.099	2.09 (0.85, 5.17)	0.111
	Model 4	1.82 (0.98, 3.39)	0.058	1.31 (0.75, 2.29)	0.335	2.07 (0.83, 5.13)	0.117

Neither-infected is the referent group. Model 1 adjusts for age, sex, race-ethnicity; Model 2 adjusts for Model 1, BMI, summary socioeconomic score, current smoking, heavy alcohol use, cocaine use; Model 3 adjusts for Model 2, diabetes, hypertension, dyslipidemia, prior ASCVD, Prior HF, serum creatinine; Model 4 adjusts for Model 3, Killip class, LVEF, catheterization within 24 hours, CABG during index hospitalization.

ASCVD=Athresclerotic cardiovascular disease; BMI=Body mass index; CABG=Coronary artery bypass grafting; CI=Confidence interval; HCV=Hepatitis C virus; HF=Heart failure; HIV=Human immunodeficiency virus; HR=Hazard ratio; LVEF=Left ventricular ejection fraction.