Abstract 630

Hepatitis C Virus and Incident Type 1 And Type 2 Myocardial Infarction in HIV

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STUDY QUESTIONS

Is active infection with Hepatitis C virus (HCV) at start of follow-up associated with higher risk of myocardial infarction (MI) in people living with HIV? And does any such risk differ by MI type?

BACKGROUND

- HCV increases the risk of atherosclerosis[1] and cardiovascular disease (CVD)[2,3] but effect on MI is less conclusive[4,5].
- HIV is associated with a higher risk of CVD[6], including MI[7], and prevalence of HCV coinfection is 10-30%[8].
- Thus, it is **important to establish if HCV infection is independently associated with a greater risk of MI** in people living with HIV.
- We hypothesized that impact of HCV on MI would differ between Type 1 MI[9] due to atherothrombotic plaque rupture and Type 2 MI[9] due to supply-demand mismatch because of different underlying pathophysiology.

METHODS

- **CFAR Network of Integrated Clinical Systems (CNICS),** a multi-center HIV cohort with comprehensive clinical data
- **Incident Type 1 MI** and **Type 2 MI** were adjudicated based on review of medical records, laboratory results, and echocardiograms. For Type 2 MIs, reviewers identified a probable cause of the supply-demand mismatch.
- Estimated association of **positive HCV RNA test** and time to MI using **Cox regression** adjusting for age, sex, race, ethnicity, site, smoking, substance use, cholesterol measures, diabetes, treated hypertension, statin use, nadir CD4 count, HIV viral load, and antiretroviral therapy use.
- We used **multiple imputation** by chained equations. Proportion missing was: body mass index (12%), cholesterol measures (24-33%), self-reported substance use (50-70%).

Figure 1. Sunburst plot showing number of myocardial infarction (MI) events in this study by type and attributed cause.

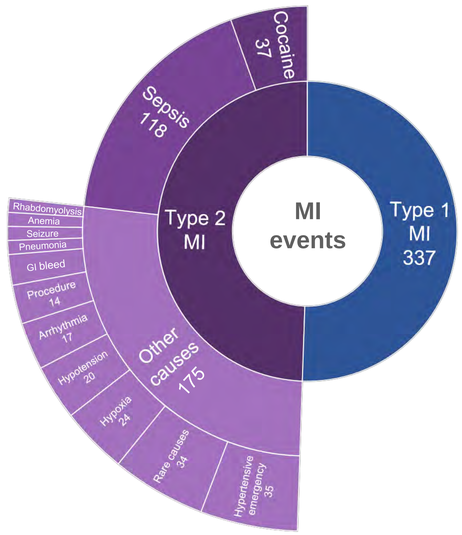


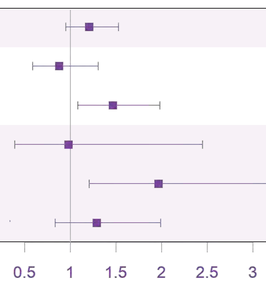
Table 1. Characteristics of participants at 6 CNICS sites across the U.S. at start of MI follow-up during 1995 through 2016

	HCV-	HCV+	Total
n	21,164	2,280	23,444
Demographics & behaviors			
Age, mean (sd)	40 (10)	45 (9)	41 (10)
Male	81%	78%	81%
Non-Hispanic, black	40%	43%	40%
History of IDU	15%	62%	20%
Comorbidities			
Diabetes	5%	7%	5%
Hypertension	11%	15%	12%
Statin use	8%	4%	7%
FIB-4 score* > 3.25	3%	17%	5%
HIV-related factors			
Nadir CD4+ <200†	39%	43%	40%
HIV viral load ≤200‡	56%	54%	56%
Receiving ART	85%	84%	85%

IDU, injecting drug use; ART, antiretroviral therapy
*calculated as $(age \times AST)/(platelet\ count \times \sqrt{ALT})$
†cells/ml ‡RNA copies/mL

Figure 2. Association of active Hepatitis C virus infection with time to myocardial infarction (MI) events

Outcome	Events	Hazard Ratio (95% CI)
All MI	667	1.2 (0.9 - 1.4)
Type 1 MI	337	0.9 (0.6 - 1.3)
Type 2 MI	330	**1.5 (1.1 - 2.0)**
Type 2 MI, cocaine	37	1.0 (0.4 - 2.5)
Type 2 MI, sepsis	118	**2.0 (1.2 - 3.2)**
Type 2 MI, other causes	175	1.3 (0.8 – 2.0)



Hazard ratios are adjusted for site, demographic factors, measures of cholesterol, diabetes, treated hypertension, statin use, nadir CD4 count, HIV viral load, ART use, smoking, and substance use.

MAIN FINDINGS

- 5.0 MI events (4.6 among HCV-negative, 8.2 among HCV-positive participants) per 1000 person-years
- No association between HCV and Type 1 MI
- HCV infection associated with approximately 47% higher risk of Type 2 MI in people living with HIV
- **HCV infection associated with approximately 2-fold higher risk of Type 2 MI attributed to sepsis in people living with HIV**

CONCLUSIONS

- HCV does not appear to impact risk of classical, plaque-rupture-event Type 1 MI in this cohort
- Association between active HCV in people living with HIV and Type 2 MI driven by Type 2 MI attributed to sepsis
- **HCV-infected people living with HIV may have a higher risk of Type 2 MI, likely as a complication of sepsis**
- Reasons for association with Type 2 MI may be related to consequences of HCV infection, such as liver dysfunction and chronic inflammation, or differences in sepsis risk factors between HCV-infected and uninfected individuals
- MI type analysis allowed a more detailed understanding of the cardiovascular risks associated with HCV in this cohort

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CNICS CFAR Network Of Integrated Clinical Systems

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