Differences in Types of Myocardial Infarction Among Patients Aging with HIV

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Background

- The Universal Definition classifies myocardial infarctions (MI) by type according to mechanism of myocardial ischemia
  - Type 1 MI (T1MI) result spontaneously from atherosclerotic plaque instability
  - Type 2 MI (T2MI) are secondary to other causes such as sepsis and cocaine-induced vasospasm resulting in oxygen demand-supply mismatch
- In the general population, most MIs are T1MI; T2MI are a minority of MIs
- In contrast to the general population, almost half of MIs among people living with HIV (PLWH) are T2MI
- Different MI types indicate different prognoses and optimal medical management
- Demographic and clinical characteristics may differ among those with different MI types
- However, most previous studies have not differentiated MI types limiting the ability to understand MIs in PLWH

OBJECTIVE

- We conducted this study to compare MI rates by type and age among PLWH
- We hypothesized that increases in rates with older age would differ by MI type, and that in contrast to the general population, T2MI would be more common in younger individuals
- We also hypothesized that there would be a measurable rate of T1MI even among young (<30 year old) PLWH

Methods

STUDY SETTING

- Longitudinal observational study conducted in the Centers for AIDS Research Network of Integrated Clinical Systems (CNICS), a multisite clinical cohort of PLWH receiving HIV care at sites across the U.S.
- Study participants: PLWH ≥18 years of age receiving HIV care at 6 sites after MI adjudication began (dates varied by site, ~2000-2017)
- We excluded PLWH with MIs before the start of follow-up to ensure incident events
- Data sources: The CNICS Data Repository integrates comprehensive clinical data from outpatient and inpatient encounters including demographic characteristics, clinical and laboratory data, and medications

MIs

- Ascertainment/case identification included multiple criteria to optimize sensitivity:
  - MI diagnoses
  - Cardiac biomarkers
  - Coronary procedures such as coronary artery bypass graft (CABG)
- For each potential MI, sites assembled a de-identified packet that included available provider notes, ECGs, laboratory results, and imaging and procedure results including from cardiac catheterizations
- 2 experts independently reviewed each packet, followed by a 3rd if discrepancies
- Reviewers entered standardized data (based on ECGs, cardiac biomarker abnormalities, and chest pain as well as procedure/imaging results when available) into a web application, thus enabling the application of multiple operational definitions of whether an MI occurred
- Reviewers categorized each probable or definite MI by type, identified causes for T2MIs, and identified PLWH without an MI but with cardiac interventions (CI) such as CABG
- We grouped CI with T1MI, based on prior work evaluating the similarity of PLWH with adjudicated T1MI and CI
- MI types beyond T1MI and T2MI are not discussed further due to low numbers

ANALYSES

- By decade of age, we calculated T1MI and T2MI rates and confidence intervals (CI) per 1000 person-years of follow-up
- Rate ratios were calculated for rates of T2MI vs. T1MI per decade of age

Table 1. *Clinical and demographic characteristics of PLWH by MI type*

Characteristic	T1MI* N=443 N (%)	T2MI N=401 N (%)	P-value
Age, years median (IQR)	52 (45,58)	50 (43,56)	0.006
Age, years by decade			<0.001
<30	2 (<1)	20 (5)	
30-39	30 (7)	46 (11)	
40-49	147 (33)	131 (33)	
50-59	182 (41)	145 (36)	
≥60	82 (19)	59 (15)	
Sex			<0.001
Male sex	378 (85)	294 (73)	
Race/Ethnicity			<0.001
White	216 (49)	99 (25)	
African-American	169 (38)	259 (65)	
Hispanic	42 (9)	34 (8)	
Other/unknown	16 (4)	9 (2)	
HIV Transmission Risk Factor			<0.001
Heterosexual	101 (23)	120 (30)	
Men who have sex with men	229 (52)	122 (30)	
Injection drug use	94 (21)	143 (36)	
Other/unknown	19 (4)	16 (4)	
Antiretroviral therapy at time of MI			<0.001
Yes	378 (85)	284 (71)	
CD4 count closest to event (cells/μl)			<0.001
0-200	92 (21)	174 (43)	
201-350	79 (18)	71 (18)	
>350	270 (61)	156 (39)	
CD4 cell count nadir (cells/μl) median (IQR)	146 (41,295)	98 (17,238)	0.06
HIV-1 RNA closest to event			<0.001
>100,000	25 (6)	70 (17)	

** T1MI also includes patients with coronary interventions*

Results

- We followed 27,671 PLWH during the study
- We included 443 T1MI (52%) and 401 T2MI (48%)
- A higher proportion of PLWH who had a T1MI were ≥40 years of age, male, White, and on ART compared with those with a T2MI (Table 1)
- The median CD4 cell count was higher among those with a T1M1 vs. those with a T2MI (420 vs. 253, p<0.001)
- T1MI occurred in all adult age groups including young adults
- The rates of T1MI increased for each decade of older age (Table 2) with much higher rates among those ≥70 (10.5 T1MI per 1000 person-years)
- T2MI also occurred in every decade of adult PLWH and rates increased with age among PLWH ≥40 (Table 2)
- When comparing rates between T1MI and T2MI, T2MI rates were higher than T1MI rates for younger PLWH (Table 2) with the comparison of T2MI to T1MI rates highest in those <30 (rate ratio 10.0; 2.4-88.2)
- Rates of T1MI and T2MI were not significantly different among those 30-49
- However, among PLWH 50-59, and 60-69 years of age, rates of T1MI were significantly higher (rate ratio of T2MI to T1MI 0.8; 0.6-1.0 and 0.7; 0.4-1.0, respectively)
- Sepsis (37%), respiratory failure (11%) and cocaine or other drug-induced vasospasm (10%) were the most frequently identified T2MI causes (Figure 1)
- In every decade, more T2MI were associated with sepsis than any other T2MI cause
- However, while sepsis was always the most common cause, the proportion of T2MIs due to sepsis varied over time with more T2MIs due to sepsis among the younger adult PLWH (e.g. 50% of T2MI among those <30) and older adults (47% of T2MI among those ≥60) and a lower percentage of T2MI among those who were middle aged (e.g. 27% of T2MI among those 40-49)

Table 2. *Rates of T1MI and T2MI per 1000 person-years of follow-up*

Age category	T1MI Rate (CI)	T2MI Rate (CI)	T2MI vs T1MI Rate ratio (CI)	T2MI vs T1MI P-value
<30	0.1 (0.04-0.6)	1.4 (0.9-2.2)	10.0 (2.4-88.2)	<0.001
30-39	0.8 (0.5-1.1)	1.2 (0.9-1.5)	1.5 (1.0-2.5)	0.07
40-49	2.4 (2.0-2.8)	2.1 (1.8-2.5)	0.9 (0.7-1.1)	0.3
50-59	4.2 (3.6-4.8)	3.3 (2.8-3.9)	0.8 (0.6-1.0)	0.04
60-69	5.7 (4.4-7.2)	3.7 (2.7-5.0)	0.7 (0.4-1.0)	0.03
≥70	10.5 (6.7-16.5)	10.0 (6.3-15.9)	1.0 (0.5-1.9)	0.9

CI: confidence interval; MI: myocardial infarction

LIMITATIONS

- We had >800 MIs allowing us to evaluate T1MI and T2MI separately. However, T2MI are due to heterogenous causes. A larger number of outcomes are needed to further separate T2MIs by cause
- We focused on initial MI. While this has many advantages, it limits comparisons to some general population studies where those with T2MI are more likely to have had a prior MI

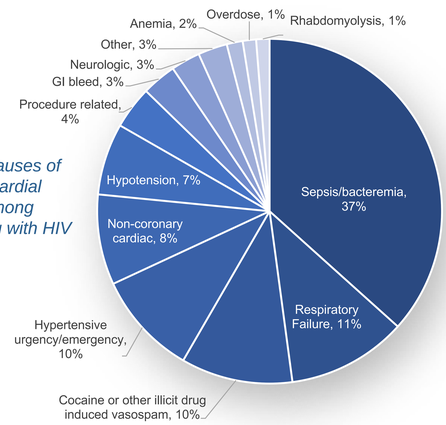

Figure 1. *Causes of type 2 myocardial infarction among people living with HIV*

STRENGTHS

- We used centrally adjudicated MIs and differentiated T1MI and T2MI
- We used multiple ascertainment criteria; this is crucial given how poorly prior studies have found diagnoses codes alone work to accurately identify MIs

Conclusions

- PLWH with T2MI were younger than those with a T1MI on average. This is in contrast to general population studies
- We found that among PLWH rates of T2MI were higher than T1MI in younger adults, rates of T1MI were higher among those 40-60, and rates of both were very high among older PLWH
- Causes of T2MI differed by age
- These results highlight the importance of evaluating MI by type among PLWH and understanding causes of T2MI
- A better understanding of these important comorbidities, who is impacted, when, and why, is needed to further comprehend the underlying mechanisms and successfully intervene to improve longterm outcomes for older PLWH as the population continues to age

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