MACE Incidence Among HIV and Non-HIV-Infected Patients in a Clinical Care Cohort

Virginia A. Triant,[1,2] Susan Regan,[2] and Steven K. Grinspoon[3]

Division of Infectious Diseases,[1] Division of General Medicine,[2] Program in Nutritional Metabolism,[3] Massachusetts General Hospital, Boston, MA, USA

Contact: Virginia A. Triant, MD, MPH
Infectious Diseases/General Medicine Divisions
Massachusetts General Hospital
Phone: 617-726-5257
Email: vtriant@partners.org
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Introduction

- Non-communicable diseases are an increasingly important component of the clinical management of HIV-infected patients who have achieved virologic suppression on antiretroviral therapy (ART).
- Large cohort studies and clinical studies of subclinical atherosclerosis demonstrate significantly increased rates of acute myocardial infarction (AMI).
- Accumulating data suggest broader cardiovascular and cerebrovascular endpoints are also increased among HIV compared with control groups.
- Risk factors for cardiovascular disease (CVD) among HIV-infected patients likely differ from those of the general population, with contributions from HIV-related immunologic factors as well as traditional CVD risk factors.
- Patient subgroups at high CVD risk may differ in the setting of HIV infection.
- Preliminary data indicate an increased relative risk of AMI and stroke among young and female HIV-infected patients.
- We assessed major adverse cardiac event (MACE) rates individually and as a composite outcome approximating outcomes of large clinical trials in the general population, using a large observational clinical care cohort of HIV and matched control patients.
- We conducted age- and gender-stratified analyses to identify at-risk subgroups among the HIV population.

Hypotheses

- **Incidence rates of a composite CVD endpoint will be increased among HIV-infected patients compared with matched controls.**
- **The CVD incidence rate ratio comparing HIV-infected to control patients will be greater for women and for younger age groups.**

Methods

- Partners HealthCare System HIV longitudinal cohort, comprised of Brigham & Women's Hospital and Massachusetts General Hospital
- 3,109 HIV-infected and 23,237 non-HIV-infected control patients matched on age, gender, and race
- Followed 4.8 years (14,942 person-years [PYs]) for HIV 4.6 years (106,885 PYs) for control patients
- Data derived from the Research Patient Data Registry, a clinical care data registry which includes comprehensive clinical information for over 4.5 million patients
- Observation period 2000 to 2009
- Data censored at first event, last encounter, or December 31, 2009
- All patients ≥age 18 at start of observation
- Composite CVD endpoint ascertained as documentation of ICD-9-CM or CPT codes myocardial infarction (ICD 410), stroke (ICD 433-434), angina (ICD 411.1 inpatient only) or coronary revascularization (CPT 92982, 92984, 92980, 92981, 92995, 92996, G0290, G0291)
- Individual and composite incidence rate ratios calculated overall and after stratification by age and sex

Results

	All		Female		Male	
	HIV	Control	HIV	Control	HIV	Control
N	4467	37044	1467	12782	3000	24262
Age - mean (SD)	42 (10.9)	42 (11.9)	40 (11.8)	39 (12.9)	43 (10.5)	43 (11.2)
Female - N (%)	1467 (33)	12782 (34)	~	~	~	~
Race - N (%)						
White	2303 (52)	19023 (51)	590 (40)	5177 (40)	1713 (57)	13845 (57)
Black	947 (21)	8182 (22)	448 (31)	3956 (31)	499 (17)	4226 (17)
Asian	68 (2)	548 (2)	28 (2)	215 (2)	40 (1)	333 (1)
Hispanic	767 (17)	6622 (18)	275 (19)	2362 (18)	492 (16)	4260 (18)
Other	66 (2)	475 (2)	24 (2)	213 (2)	42 (1)	262 (1)
Unknown	316 (7)	2194 (6)	102 (7)	859 (7)	214 (7)	1335 (6)
HTN - N (%)	567 (13)	1956 (5)	216 (15)	574 (4)	351 (12)	1382 (6)
DM - N (%)	314 (7)	644 (2)	117 (8)	213 (2)	197 (7)	431 (2)
Dyslipidemia - N (%)	501 (11)	1558 (4)	165 (11)	350 (3)	336 (11)	1208 (5)

Table 1: Patient characteristics. Demographic and clinical characteristics are shown overall and in gender-stratified analyses comparing HIV to control groups. Approximate smoking rates are 50% for HIV and 30% for control groups. For HIV-infected patients, mean CD4 cell count 475; 75% virologically suppressed; 50% on ART (approximations from longitudinal cohort).

	All		Female		Male	
	IRR	95% CI	IRR	95% CI	IRR	95% CI
Composite CVD Endpoint	**1.56**	**1.40-1.75**	**2.19**	**1.76-2.70**	**1.35**	**1.17-1.54**
<30	2.04	1.06-3.66	3.67	1.62-7.62	0.92	0.24-2.55
30-39	2.16	1.67-2.78	4.09	2.60-6.33	1.61	1.16-2.21
40-49	1.70	1.41-2.04	2.24	1.55-3.17	1.53	1.22-1.90
50-59	1.18	0.92-1.51	0.98	0.49-1.79	1.22	0.93-1.59
60-69	1.16	0.79-1.65	1.81	0.69-4.01	0.96	0.62-1.44
≥70	0.98	0.55-1.64	0.96	0.34-2.20	0.99	0.46-1.90
AMI	**1.58**	**1.35-1.85**	**2.35**	**1.74-3.12**	**1.33**	**1.10-1.60**
<30	2.74	1.16-5.84	5.14	1.80-13.07	1.00	0.11-4.20
30-39	1.93	1.35-2.72	3.49	1.86-6.30	1.46	0.92-2.25
40-49	1.82	1.43-2.29	2.37	1.48-3.67	1.63	1.22-2.15
50-59	1.09	0.74-1.55	0.88	0.27-2.22	1.12	0.74-1.64
60-69	1.00	0.53-1.76	1.15	0.13-4.65	0.89	0.44-1.64
≥70	0.76	0.24-1.86	1.33	0.25-4.41	0.46	0.05-1.78
Stroke	**1.53**	**1.28-1.83**	**2.10**	**1.49-2.90**	**1.32**	**1.06-1.64**
<30	1.48	0.45-3.79	2.20	0.41-7.63	0.94	0.11-3.93
30-39	2.66	1.76-3.95	6.32	3.02-13.01	1.80	1.05-2.97
40-49	1.51	1.07-2.08	2.01	1.00-3.75	1.34	0.90-1.97
50-59	1.29	0.87-1.86	1.10	0.42-2.45	1.33	0.86-2.01
60-69	1.29	0.74-2.14	2.64	0.79-7.03	0.99	0.51-1.78
≥70	0.97	0.43-1.93	0.77	0.15-2.42	1.12	0.39-2.61

Table 2: Incidence Rate Ratios. Ratios of incidence rates comparing HIV to control groups are shown according to gender, age group, and CVD outcome.

- Rates of composite CVD endpoint were 16.7 events per 1000 PYs (95% confidence interval [CI] 15.1-18.5) for HIV versus 10.7 (95% CI 10.2-11.2) for control group.
- Rates of composite CVD endpoint were 20.8 events per 1000 PYs (95% CI 18.6-23.3) for HIV versus 15.1 (95% CI 14.4-15.9) for control group in patients ≥40 years.
- Of the 332 events observed in patients ≥40 years, 165 (50%) were MI, 124 (37%) were stroke, 35 (11%) were angina and 8 (2%) were revascularization.

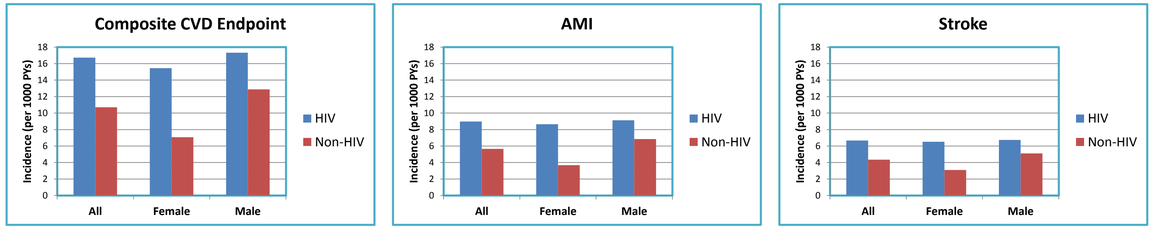


Figure 1: CVD Incidence Rates by Gender. Incidence rates per 1000 PYs are shown for the composite CVD endpoint (including AMI, stroke, angina or coronary revascularization) and for AMI and stroke individually. For each outcome, incidence rates are shown comparing HIV to control groups in all patients and within each gender. All differences in incidence rates comparing HIV to control groups are statistically significant.

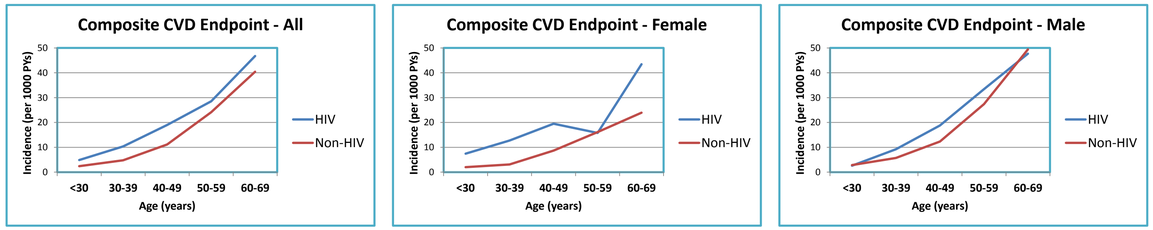


Figure 2: CVD Incidence Rates by Age Group. Incidence rates per 1000 PYs are shown for the composite CVD endpoint (including AMI, stroke, angina or coronary revascularization). For the overall group and each gender, incidence rates are shown comparing HIV to control groups according to age group.

Conclusions

- In a clinical care cohort of HIV-infected and matched control patients, major adverse cardiac events including myocardial infarction, stroke, angina and coronary revascularization were more common among HIV-infected compared with matched control patients.
- The relative increase of approximately 50 percent for HIV was seen for the composite endpoint as well as the individual endpoints of AMI and stroke, corroborating data from earlier time periods from this and other cohorts.
- The pattern of increased rates in HIV was observed for both genders and all age groups.
- The increase in incidence rates comparing HIV to control groups was relatively greater for females versus males for all three outcomes (composite, AMI, and stroke).
- The increase in incidence rates comparing HIV to control groups was relatively greater for younger age groups for all three outcomes (composite, AMI, and stroke).
- The relatively greater risk for female and younger patients may reflect the different distribution of CVD risk factors in HIV, with important contributions from non-traditional risk factors reflecting HIV-related immune dysregulation.
- Targeted interventions are needed to prevent CVD in HIV disease, particularly among patients not traditionally considered to be high-risk.

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