



Smoking, Other Substance Use and Coronary Atherosclerosis Among HIV-Infected and Uninfected Men

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Background

- HIV infection is associated with subclinical atherosclerosis.
- Tobacco smoking and other recreational substance use is common among HIV-infected persons. Associations between substance use and subclinical atherosclerosis according to HIV serostatus are not well-characterized.
- We hypothesize that associations between subclinical atherosclerosis and recreational substance use exist and differ by HIV serostatus.

Table 1. Participant Characteristics and Plaque/Stenosis Prevalence

	Non-contrast CT		Non-contrast CT and CT-angiogram	
	HIV+	HIV-	HIV+	HIV-
	N=621	N=384	N=453	N=311
Age in years, Median (IQR)	53(48-58)	55(50-62)	52(47-57)	55(50-62)
Race				
Caucasian (%)	52.7	66.9	50.1	68.5
African American (%)	34	24.7	34.7	23.8
Hispanic/Other (%)	13.4	8.3	15.2	7.7
Systolic BP, mmHg, Median (IQR)	126(115-137)	128(118-137)	126(115-136)	128(118-137)
LDL cholesterol, mg/dL, Median (IQR)	104(81-128)	112(91-137)	104(82-134)	113(91-139)
HDL cholesterol, mg/dL, Median (IQR)	46(38-55)	52(43-61)	45(37-55)	52(43-61)
Taking BP medication (%)	35.9	31.2	32.1	29.8
Taking DM medication (%)	8.7	7.6	7.8	6.5
Taking cholesterol medication (%)	34.9	30.1	33.7	31.6
HIV clinical factors				
Nadir CD4 (cells/ μ L), Median (IQR)	248(144-336)	--	256(159-340)	--
History of AIDS (%)	14.2	--	11	--
HIV RNA >50 copies/mL (%)	17.9	--	19.6	--
Substance use prevalence				
Smoking status				
Never (%)	25.2	25.3	26.2	23.8
Former (%)	43.8	52.9	43.5	54.7
Current (%)	31	21.8	30.4	21.5
Pack years of smoking, Median (IQR)	5.6(0-22.9)	1.8(0-21.5)	5.6(0-21.4)	3.1(0-21.9)
Any ETOH use 1-14 drinks/week (%)	71.7	78.1	72.8	81
Any ETOH use >14 drinks/week (%)	21.4	26.8	23	27.3
Any binge drinking/week (%)	31.2	25.5	33.3	26.4
Any stimulant use (%)	44.8	31	47.7	30.9
Any marijuana use (%)	58.8	54.9	59.8	55.3
Any inhaled nitrite use (%)	50.1	40.6	52.1	40.8
Any erectile dysfunction drug use (%)	48.8	45.6	48.3	44.1
Plaque/Stenosis Prevalence (%)				
Prevalence of coronary artery calcium	53.1	52.1	--	--
Prevalence of any plaque	--	--	77.7	74.6
Prevalence of calcified plaque	--	--	34.9	39.9
Prevalence of non-calcified plaque	--	--	63.1	52.7
Prevalence of mixed plaque	--	--	34.7	31.8
Prevalence of coronary artery stenosis >50%	--	--	16.8	14.5

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Methods

Population

- Multicenter AIDS Cohort Study (MACS): ongoing study of HIV+ and HIV- men who have sex with men (MSM).
- CVD substudy inclusion criteria: age 40-70, no history of cardiac surgery, angioplasty or stent, weight <300 lbs.

Imaging Methods

- Non-contrast CT-scanning was performed on 1005 MSM (621 HIV+, 384 HIV-) to measure coronary artery calcium (CAC).
- 764 of these men (453 HIV+, 311 HIV-) with no contrast allergy and estimated GFR >60 ml/min/m² underwent coronary CT angiography to measure plaque presence, type, and extent.

- Plaque types (based on calcium composition): calcified, non-calcified, mixed (Figure 1)

Substance Use Methods

- Smoking, ETOH and recreational drug use data were self-reported prospectively during semi-annual study visits (used data beginning 10 years prior to CT scanning and ending at CT scanning).

- Recreational drugs: stimulants (smoked or inhaled cocaine, powdered cocaine, methamphetamines, ecstasy), marijuana, inhaled nitrites, and erectile dysfunction drugs (EDD).

- Tobacco use patterns: current and former use at time of CT scanning, and cumulative pack-years.

- Alcohol use: cumulative years of low/moderate use (1-14 drinks/week), heavy use (>14 drinks/week) and binge drinking (\geq 5 drinks at least once over past 30 days).

- Use patterns of all other substances were weighted by frequency of use (standardized to monthly use).

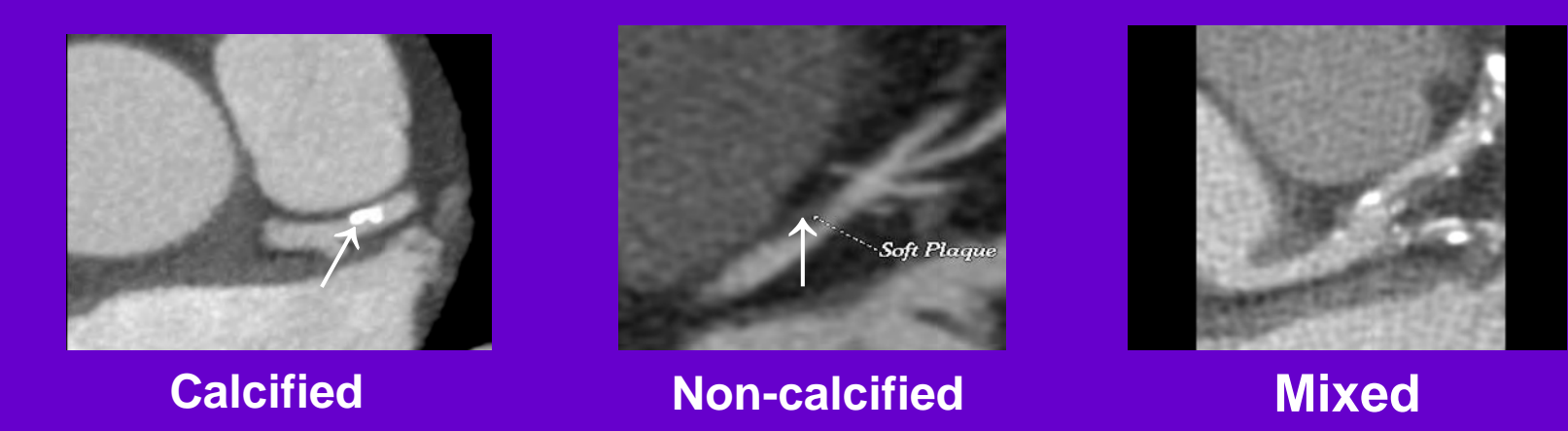
Statistics

- Logistic regression: to assess associations between plaque presence and substance use

- Linear regression: to assess associations between plaque extent and substance use

- Models were adjusted for age, race, study center, socioeconomic status, traditional cardiac risk factors (hypertension, diabetes mellitus, hyperlipidemia, obesity and smoking) and stratified by HIV serostatus. All of these factors were included simultaneously and were adjusted for each other.

Figure 1. Examples of coronary artery plaques



Results

Table 2: Associations Between Substance Use and Plaque in HIV+ Men

Substance	Logistic Regression: Associations Between Substance Use and Plaque Type and Presence						Linear Regression: Associations Between Substance Use and Plaque Type and Extent				
	Total Agatston Score >0	Total Plaque Score >0	Total Calcified Plaque Score >0	Total Non-calcified Plaque Score >0	Total Mixed Plaque Score >0	Stenosis >50%	Total Agatston Score	Total Plaque Score	Total Calcified Plaque Score	Total Non-calcified Plaque Score	Total Mixed Plaque Score
	N=621 OR (95% CI)	N=453 OR (95% CI)	N=453 OR (95% CI)	N=453 OR (95% CI)	N=453 OR (95% CI)	N=453 OR (95% CI)	N=330 β (SE)	N=352 β (SE)	N=158 β (SE)	N=286 β (SE)	N=157 β (SE)
Current smoking	2.26** (1.31-3.88)	2.27* (1.11-4.67)	2.03* (1.07-3.85)	1.6 (0.88-2.93)	1.75 (0.93-3.29)	2.55* (1.09-6.0)	0.96** (0.27) \uparrow	0.24 (0.13)	0.28 (0.2)	-0.07 (0.12)	0.13 (0.18)
Past smoking	1.59 (0.99-2.53)	1.63 (0.88-3.02)	2.17** (1.24-3.78)	1.22 (0.72-2.06)	1.46 (0.85-2.51)	2.22* (1.05-4.7)	0.72** (0.23) \uparrow	0.24* (0.11) \uparrow	0.043 (0.17)	0.06 (0.11)	0.22 (0.16)
Cumulative pack-years [†]	1.02** (1.01-1.03)	1.03** (1.01-1.05)	1.02** (1.01-1.03)	1.0 (0.99-1.02)	1.01* (1.0-1.02)	1.01 (1-1.03)	0.01 (0.004)	0.01* (0.002) \uparrow	0.01** (0.003) \uparrow	-0.001 (0.002)	0.01 (0.003)
Cumulative drinking 1-14 drinks/week [†]	1.13 (0.73-1.76)	0.87 (0.47-1.62)	1.18 (0.71-1.97)	0.74 (0.45-1.22)	1.14 (0.69-1.89)	1.04 (0.54-2.0)	0.07 (0.21)	-0.02 (0.1)	-0.04 (0.15)	-0.01 (0.1)	0.06 (0.14)
Cumulative drinking >14 drinks/week [†]	2.01 (0.75-5.4)	1.93 (0.36-10.23)	1.04 (0.37-2.92)	2.12 (0.64-7.05)	2.4 (0.87-6.59)	4.71** (1.5-14.76)	0.44 (0.38)	0.35 (0.2)	0.34 (0.29)	0.34 (0.19)	-0.28 (0.26)
Cumulative binge drinking [†]	1.24 (0.52-2.95)	1.23 (0.35-4.27)	2.62 (0.95-7.23)	0.52 (0.18-1.47)	1.74 (0.65-4.69)	1.13 (0.31-4.08)	0.57 (0.4)	0.27 (0.22)	0.15 (0.28)	-0.03 (0.25)	0.26 (0.29)
Cumulative stimulant use [†]	1.0 (0.99-1.01)	1.0 (0.99-1.01)	0.99 (0.98-1.01)	0.52 (0.18-1.47)	1.0 (1.0-1.01)	1.0 (0.96-1.01)	0.001 (0.01)	-0.002 (0.002)	0.001 (0.01)	-0.002 (0.002)	0.001 (0.003)
Cumulative marijuana use [†]	1.0 (1.0-1.01)	1.0 (1.0-1.01)	1.0 (1.0-1.004)	1.0 (0.99-1.01)	1.0 (1.0-1.004)	1.0 (1.0-1.004)	-0.001 (0.001)	0 (0.001)	0 (0.001)	0 (0.001)	0 (0.001)
Cumulative inhaled nitrite use [†]	1.0 (0.99-1.01)	1.0 (0.99-1.01)	1.0 (1.0-1.01)	1.0 (1.0-1.002)	1.0 (0.99-1.01)	1.0 (1.0-1.01)	-0.004 (0.003)	-0.001 (0.002)	-0.001 (0.002)	-0.001 (0.002)	0.001 (0.002)
Cumulative EDD use [†]	1.01 (0.94-1.09)	0.95 (0.85-1.06)	1.01 (0.93-1.09)	1.0 (0.99-1.01)	1.06 (0.98-1.15)	1.05 (0.95-1.15)	0.03 (0.03)	0.02 (0.02)	0.06* (0.02) \uparrow	0.001 (0.02)	-0.01 (0.02)

Table 3: Associations Between Substance Use and Plaque in HIV- Men

Substance	Logistic Regression: Associations Between Substance Use and Plaque Type and Presence						Linear Regression: Associations Between Substance Use and Plaque Type and Extent				
	Total Agatston Score >0	Total Plaque Score >0	Total Calcified Plaque Score >0	Total Non-calcified Plaque Score >0	Total Mixed Plaque Score >0	Stenosis >50%	Total Agatston Score	Total Plaque Score	Total Calcified Plaque Score	Total Non-calcified Plaque Score	Total Mixed Plaque Score
	N=384 OR (95% CI)	N=311 OR (95% CI)	N=311 OR (95% CI)	N=311 OR (95% CI)	N=311 OR (95% CI)	N=311 OR (95% CI)	N=200 β (SE)	N=232 β (SE)	N=124 β (SE)	N=164 β (SE)	N=99 β (SE)
Current smoking	1.85 (0.82-4.18)	1.76 (0.63-4.9)	2.04 (0.83-5.02)	0.84 (0.38-1.86)	1.79 (0.7-4.48)	2.55 (0.76-8.63)	0.61 (0.42)	0.28 (0.17)	0.49* (0.23) \uparrow	-0.08 (0.16)	-0.07 (0.31)
Past smoking	0.93 (0.51-1.71)	0.92 (0.43-1.95)	0.71 (0.36-1.38)	0.77 (0.43-1.39)	0.95 (0.47-1.92)	1.21 (0.48-3.08)	-0.36 (0.31)	-0.02 (0.131)	-0.14 (0.18)	0.11 (0.12)	-0.26 (0.23)
Cumulative pack-years [†]	1.02* (1.0-1.03)	1.01 (0.98-1.03)	1.01 (1.0-1.03)	0.99 (0.98-1)	1.01 (0.99-1.03)	1.02* (1.0-1.04)	0.01 (0.01)	0.01* (0) \uparrow	0.01 (0.004)	0.004 (0.003)	0 (0.004)
Cumulative drinking 1-14 drinks/week [†]	1.18 (0.67-2.08)	1.24 (0.61-2.51)	0.96 (0.51-1.78)	0.88 (0.51-1.53)	0.79 (0.42-1.48)	0.59 (0.25-1.4)	-0.69* (0.28) \downarrow	-0.16 (0.12)	-0.22 (0.15)	0.03 (0.11)	-0.34 (0.2)
Cumulative drinking >14 drinks/week [†]	0.83 (0.33-2.11)	2.55 (0.69-9.45)	1.09 (0.38-3.11)	1.58 (0.61-4.13)	0.46 (0.14-1.46)	0.68 (0.16-2.89)	-1.14* (0.51) \downarrow	-0.32 (0.2)	-0.89** (0.27) \downarrow	-0.004 (0.18)	-0.47 (0.38)
Cumulative binge drinking [†]	0.44 (0.13-1.46)	0.48 (0.13-1.76)	0.33 (0.09-1.2)	0.61 (0.21-1.71)	0.33 (0.08-1.46)	2.23 (0.49-10.1)	0.70 (0.66)	0.28 (0.24)	0.85* (0.37) \uparrow	0.36 (0.23)	0.29 (0.53)
Cumulative stimulant use [†]	1.02 (1.0-1.04)	1.04* (1.001-1.08)	1.02 (1.0-1.04)	1.0 (1.0-1.02)	1.01 (0.99-1.03)	0.99 (0.97-1.02)	0 (0.01)	0 (0.003)	-0.01 (0.004)	-0.003 (0.004)	0.01 (0.01)
Cumulative marijuana use [†]	1.0 (1.0-1.0)	1.0 (0.99-1.01)	1.0 (0.99-1.004)	1.0 (1.0-1.01)	1.0 (1.0-1.01)	1.0 (1.0-1.01)	0.01* (0.002) \uparrow	0 (0.001)	0 (0.001)	0.001 (0.001)	0 (0.002)
Cumulative inhaled nitrite use [†]	1.01 (1.0-1.03)	1.0 (0.98-1.02)	1.0 (0.98-1.02)	1.01 (0.99-1.02)	1.0 (1.0-1.02)	1.0 (0.98-1.02)	-0.01 (0.01)	0 (0.003)	0 (0.01)	0 (0.003)	-0.002 (0.01)
Cumulative EDD use [†]	1.03 (0.93-1.14)	0.93 (0.81-1.06)	0.99 (0.89-1.11)	0.96 (0.87-1.07)	1.03 (0.92-1.16)	0.87 (0.73-1.04)	0.08 (0.05)	-0.01 (0.02)	0.03 (0.03)	-0.04 (0.02)	-0.01 (0.04)

*p \leq 0.05, **p \leq 0.01, [†]per pack-year, [‡]per year

Summary

- Current smoking was more prevalent in HIV+ men than HIV- men.
- Among HIV+ men, smoking (current, past and cumulative) was associated positively with more plaque parameters than was smoking among HIV- men.
- Erectile dysfunction drug use (HIV+ men), stimulant and marijuana use (HIV- men) demonstrated a weak positive association with coronary artery plaque presence or extent.
- The putative protective effect of ETOH on cardiovascular disease (CVD) appears present among HIV- men but was not observed in HIV+ men.

Conclusions

- Our findings underscore the importance of effective smoking cessation strategies targeting HIV+ men to decrease CVD burden.
- Use of recreational drugs appears to have minimal impact on coronary atherosclerosis in both HIV+ and HIV- men.
- HIV infection may diminish the potential benefits of ETOH consumption in the protection against coronary atherosclerosis, however this area needs further study.