Cardiac Steatosis Increased in HIV: Related to Gender, Visceral Fat and ARV Exposure

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BACKGROUND

- Cardiac steatosis (i.e. lipid deposition in myocardial tissue) has been identified in diabetes and is associated with impaired myocardial function[5]
- Significant abnormalities of lipid deposition have been seen in HIV-infected patients due in-part to the effects of antiretroviral therapy[1-3]
- HIV-infected patients have an elevated risk for developing cardiovascular disease (CVD) compared to controls, particularly in relationship to abnormal lipid deposition[4]
- Intramyocardial lipid content was determined using magnetic resonance spectroscopy (MRS) in a cohort of HIV-infected adults and healthy volunteers to assess cardiac steatosis

METHODS

- Prospective cross-sectional study of 95 HIV-infected adults and 30 age/sex/race-matched healthy controls
- Participants with known cardiovascular disease were excluded
- Clinical history and past antiretroviral exposure were characterized for all subjects.
- Study measurements included intramyocardial lipid with MRS of the intraventricular septum and visceral abdominal fat volume was measured by MRI
- Laboratory assessments included serum lipids, glucose, insulin, CD4 T-cell count, HIV viral load, and biomarkers of inflammation

PROCEDURE: MRS OF THE INTRAVENTRICULAR SEPTUM

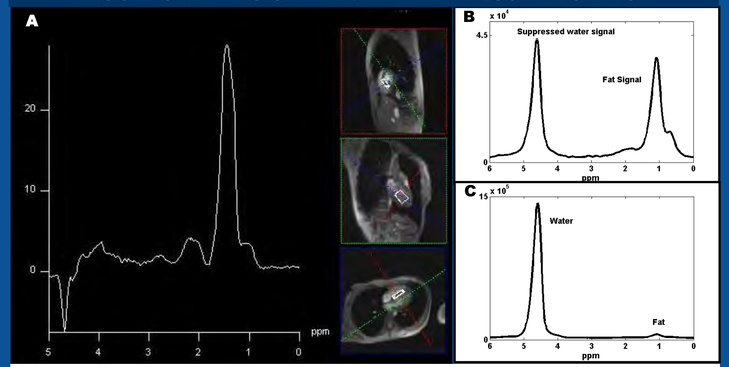


Figure 1. Representative MRS of the intraventricular septum with good spectra results (A) triacylglycerol (TG) peaks, (B) fat peak with water signal suppressed, and (C) water signal unsuppressed

%TG (triglyceride) = (signal amplitude of TG) / (signal amplitude of Water) X 100

PARTICIPANT DEMOGRAPHICS & CLINICAL CHARACTERISTICS

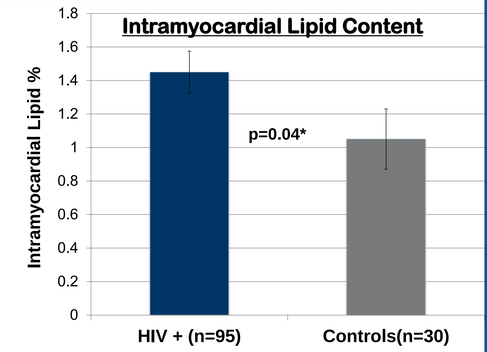
	HIV + (n=95)	Control (n=30)	p-value
Age, years	49±10	46±8	0.16
Sex: Male/ Female, n (%)	71(75)/24 (25)	22(73)/8(27)	0.88
Race: White/Black/Hispanic/Mixed Race/Native American/Asian, n (%)	27(28)/55(58)/9(10)/ 1(1)/0(0)/3(3)	8(27)/18(60)/4(30)/ 0(0)/0(0)/0(0)	0.80
BMI	28±5.4	29.8±4.3	0.07
Ever Smoked, n (%)	62 (65)	10 (33)	0.002
Smoking Pack years	11.3±22.3	1.6±3.7	0.0001
Diabetes, n (%)	9 (9.5)	0 (0)	0.09
Hepatitis C, n (%)	18 (19)	0(0)	0.01
Framingham Risk Score	4.5±4.9	3.4±3.2	0.16
Systolic blood pressure (mmHg)	127±13	123±13	0.13
Diastolic blood pressure (mmHg)	79±9	76±10	0.12
Currently on Lipid Lowering Medications, n (%)	33 (34.7)	5(16.7)	0.06
Current ARV use, n (%)	88 (93)	---	---
Duration of ARV use, years	8.5±6	---	---
CD4	615±276	904±349	0.0002
Nadir CD4	235±182	---	---
Undetectable Viral Load (Viral Load <50), n (%)	80 (84.2)	---	---
Fasting Glucose (mg/dL)	97±18	92±8	0.03
Fasting Insulin (mcU/mL)	9.9±8.3	9.2±5.5	0.63
FFA	0.47±0.21	0.47±0.20	0.99
Cholesterol (mg/dL)	168±30	181±40	0.11
HDL (mg/dL)	47±15	45±13	0.59
LDL (mg/dL)	94±29	112±34	0.01
Triglycerides (mg/dL)	147±102	120±70	0.10
D-Dimer (ug/mL FEU*)	0.32±0.25	0.43±0.31	0.09
CRP (mg/L)	3.6±5.7	3.9±5.3	0.80
Pro BNP (pg/mL)	57.6±133.7	31.6±32.5	0.09

*FEU= fibrinogen equivalent units

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RESULTS



*p-value of the log transformation of intramyocardial lipid content

Overall Univariate Correlations

(HIV+ and Controls)	Intramyocardial Lipid Content (%)	
	r	p-value
Age (n=125)	0.22	0.01
Glucose (n=123)	0.21	0.02
Triglyceride levels (n=123)	0.19	0.04
Visceral abdominal fat (n=114)	0.37	<0.001

- There was no relationship between intramyocardial lipid content and CD4 count, HIV viral burden, CRP, D-dimer, or pro-BNP levels

Univariate Correlation: HIV only

- Years of ARV exposure was positively correlated with intramyocardial lipid (r=0.27, p=0.007), but there were no increases related to NNRTI or PI exposure specifically.
- Visceral fat volume was correlated with ARV years (r=0.31, p=0.004)

Regression Model of HIV subjects:

- Included: age, sex, years of ARVs, visceral fat, glucose, and triglycerides
- Female sex (p=0.02) and visceral fat (p=0.02) were significantly associated with intramyocardial lipid but not years of ARV exposure.

Multivariate Model:

- HIV status (p=0.03),visceral fat volume (p=0.001), and female sex(p=0.02) all remained significant independent predictors of intramyocardial lipid in a model including age, smoking, glucose, triglycerides.
- Of note, among the HIV+, there was significantly higher heart fat in women (1.8%) vs. men (1.3%) (p=0.008)

CONCLUSIONS

- Cardiac steatosis, which is associated with impaired myocardial function, is increased in persons with HIV.
- We showed a 38% increase in myocardial lipid content in HIV-infected adults compared to age/race/sex matched healthy controls.
- Our data suggest that women with HIV may be particularly vulnerable to cardiac steatosis, which may be related to BMI and adiposity.
- Increased intramyocardial lipid was observed in association with metabolic parameters such as glucose and triglycerides.
- Increases in visceral adiposity that occur with ARV exposure may drive some of the observed increases in myocardial lipid and convey an increased risk of myocardial dysfunction