Diet, Gut Integrity Markers, and Cardiovascular Disease Risk in HIV+ Adults

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Introduction

- HIV+ adults have an increased risk of cardiovascular disease (CVD), compared to those not infected with HIV
- This increased CVD risk is, at least, partially driven by monocyte activation and inflammation
- Lifestyle factors, including dietary intake, have been linked to microbial translocation and CVD
- Yet the impact of diet on microbial translocation, inflammation and subsequent CVD in HIV adults, has not yet been explored
- **Our purpose** was to describe relationships among diet, markers of gut integrity, inflammation and subclinical CVD in HIV+ adults
- Our **hypothesis** was that higher dietary intake of fat would be related to worse gut integrity (intestinal fatty acid binding protein (IFAB) and lipopolysaccharide binding protein (LBP)), increased inflammation (hsCRP, IL-6, and sTNFRII) and worse markers of subclinical CVD (carotid intima-media thickness (CIMT) and coronary calcification)

Methods

Design: Secondary analysis of a longitudinal randomized clinical trial (SATURN-HIV) at a single site in the United States

Sample: 147 HIV+ adults who were undergoing successful ART and had normal low-density lipoprotein cholesterol levels (<130 mg/dl), but who had elevated levels of inflammation and immune activation were enrolled between March 2011 and August 2012

Measures:

Diet: was assessed using a standardized 24-hour dietary recall interview. Diet was assessed at each of the four time points. Responses are converted into daily food group, nutrient units and % of daily diet.

Gut Integrity: was assessed using two serum measures at baseline, 24 weeks and 48 weeks.

- *Intestinal fatty acid binding protein (IFAB)* was measured using the R &D Systems Human FABP2 Duoset ELISA system: Minneapolis, MN and analyzed according to recommend protocols.
- *Lipopolysaccharide binding protein* (LBP)), was measured using the Hycult Biotech LBP Human ELISA kit: Plymouth Meeting: PA

Inflammation was assessed using three measures of systemic inflammation (hsCRP, IL-6 , and sTNFR11) baseline, 24 weeks, 48 weeks and 96 weeks. All were analyzed according to the recommended protocols.

Subclinical Cardiovascular Disease: was assessed by two common measures.

- *Mean-max common carotid intima-media thickness*: the maximum IMT of the distal 1cm of the CCA far wall was measured at 3 angles bilaterally (anterior, lateral, and posterior; 6 total measurements). The mean of the 6 maximum measurements was used for analyses.
- *Coronary calcification* was quantified from a from gated, non-contrast coronary calcium scan of the chest, performed on a 64-slice multi-detector CT scanner

Analysis:

- Descriptive statistics were used to examine the sample characteristics
- Quintile regression and general estimating equations were used to study the associations among integrity, inflammation and subclinical CVD

Results

Table 1: Sample Characteristics at Baseline(*n*=147)	
Demographic	
	Mean (± SD)
Age at baseline (years)	45.4 (9.9)
Gender	
Male (%)	115 (78)
Race	
African American (%)	100 (68)
Caucasian/Hispanic/Other (%)	47 (32)
Currently Smoking (%)	93 (63%)
Body Mass Index (kg/m^2)	28.07 (6.5)
HIV Disease	
Number of Years Since HIV Diagnosis	12.2 (6.9)
CD4+ T cell count (cells/ul)	639.9 (300)
CD4+ T cell nadir (cells/ul)	200.4 (146.2)
Number of Subjects with Viral Suppression (<75) (%)	127(86)
Gut Integrity	
Intestinal fatty acid binding protein (pg/ml)	4530 (3206)
Lipopolysaccharide binding protein (µg/ml)	20.8 (10.8)
Inflammation	
HsCRP (mg/dL)	5.6 (12.4)
IL-6 (pg/ml)	4.48 (9.4)
STNFR11 (pg/ml)	233.53 (837)
Indicators of Subclinical Cardiovascular Disease	
Carotid intima-media thickness (mm)	0.71 (0.14)
Coronary calcification (Agatston units)	31.5 (89.5)

Table 2. Longitudinal dietary characteristics

	Recommend Range [1]	Baseline (*n*=147)	24 weeks (*n*=135)	48 weeks (*n*=127)	96 weeks (*n*=118)
kcals	1800-2400	2395 (1547)	2111 (1323)	2061 (1374)	1996 (1190)
Total fat (g)	65-70	108.4 (70.3)	94.3 (61.1)	91.5 (61.8)	88.1 (56.7)
Saturated fat (g)	22-24	36.0 (23.0)	31.60 (20.3)	31.09 (21.2)	29.8 (20.0)
Polyunsaturated fat (g)	<22 g	21.9 (15.0)	19.1 (13.1)	18.0 (12.8)	17.6 (11.6)
Fiber (g)	22.4-33.6	19.2 (15.6)	16.2 (12.5)	16.1 (13.5)	15.8 (10.9)
Carbohydrate (g)	130	265.5 (185.9)	234.2 (162.5)	227.2 (167.2)	224.3 (141.2)
Protein (g)	46-56	15.6 (5.9)	15.1 (3.2)	15.2 (3.3)	15.9 (8.07)
Average number of beers/week	n/a	1.5 (4.6)	1.6 (3.0)	2.1 (4.4)	2.8 (4.5)
Average glasses of wine /week	n/a	0.6 (1.5)	0.5 (1.2)	0.7 (1.3)	1.1 (1.4)
Average servings of liquor/week	n/a	1.2 (3.7)	1.0 (2.7)	1.5 (3.0)	3.0 (6.2)

[1]Ranges based on an adult who consumes a daily diet of 1800-2400 kcals. Variations exist by age, sex and activity level. Source: *2015-2020 Dietary Guidelines for Americans 2015-2020. Eighth Edition.*

Table 3: Median Regression of IFAB at Baseline					
Variable	Beta Coefficient	SE	*p*-value	95% Confidence Interval	
Saturated Fat	-0.2568	0.12	0.04	-0.50	-0.01
Duration of Protease Inhibitor Use (months)	0.00014	0.00	0.36	0	0
Age (years)	0.0037	0.01	0.62	-0.20	0.01
Male Sex	-0.5587	0.21	0.01	-0.98	-0.14
Race (African American)	0.2715	0.16	0.09	-0.05	0.59
Body Mass Index (kg/m^2)	0.0057	0.01	0.66	-0.02	0.03
Constant	9.2035	0.76	0.00	7.70	10.71
IFAB					
Variable	Beta Coefficient	SE	*p*-value	95% Confidence Interval	
Polyunsaturated Fat	-0.2208	0.13	0.08	-0.50	-0.01
Duration of Protease Inhibitor Use (months)	0.0014	0.00	0.33	0	0
Age (years)	0.0002	0.01	0.62	-0.01	0.02
Male Sex	-0.4755	0.21	0.02	-0.88	-0.06
Race (African American)	0.3457	0.16	0.03	0.03	0.66
Body Mass Index (kg/m^2)	0.0099	0.01	0.44	-0.02	0.04
Constant	8.4293	0.65	0.00	7.15	9.71

Table 4: Generalized Estimating Equations Examining the Associations Among IFAB, sTNFR11 and Markers of Subclinical Cardiovascular Disease					
sTNFR11 a					
Variable	Beta Coefficient	SE	*p*-value	95% Confidence Interval	
IFAB (pg/ml)	-0.00	-6.39^{e-06}	0.02	-0.00	-2.42^{e-06}
Age (years)	0.01	0.00	0.02	0.00	0.01
Male Sex	0.09	0.07	0.20	-0.22	0.05
Race (African American)	-0.05	0.05	0.40	-0.15	0.06
Body Mass Index (kg/m^2)	0.00	0.00	0.55	-0.01	0.01
Constant	7.73	0.18	0.00	7.37	8.10
Coronary Calcification					
Variable	Beta Coefficient	SE	*p*-value	95% Confidence Interval	
IFAB (pg/ml)	-0.00	0.00	<0.01	-0.00	-0.00
Age (years)	0.08	0.03	<0.01	0.03	0.13
Male Sex	-0.58	0.63	0.35	-1.81	0.64
Race (African American)	-0.61	0.48	0.20	-1.55	0.33
Body Mass Index (kg/m^2)	0.06	0.04	0.15	-0.01	0.13
Constant	-0.30	1.92	0.88	-4.06	3.46
Common carotid intima-media thickness					
Variable	Beta Coefficient	SE	*p*-value	95% Confidence Interval	
IFAB (pg/ml)	-3.73^{e-06}	-1.97^{e-06}	0.06	-7.6^{e-06}	1.38^{e-06}
Age (years)	0.01	0.00	<0.01	0.08	0.01
Male Sex	-0.03	0.04	0.371	-0.10	0.04
Race (African American)	0.04	0.03	0.10	-0.01	0.09
Body Mass Index (kg/m^2)	0.00	0.00	0.65	-0.00	0.00
Constant	-0.89	0.09	<0.01	-1.07	-0.72

Variables were log-transformed to normalize distributions

Conclusions

- Dietary composition was outside of the recommended range, with high intake of saturated fat and carbohydrates, and low fiber and protein intake throughout the 96 weeks study duration.
- We unexpectedly found that high IFAB was associated with more favorable subclinical markers of CVD
- Dietary fat, both saturated and unsaturated, was associated with IFAB in HIV+ adults.
- Negative association between IFAB and markers of subclincal CVD further illustrates the complex relationships among gut integrity, inflammation and CVD and suggests that further research is warranted
- Further analyses are planned to better explore the effect of dietary composition on markers of gut integrity and CVD in this population (e.g., alcohol use, type of carbohydrates)