High-Fat Meals Do Not Impair Postprandial Endothelial Function in HIV-Infected and Uninfected Men

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Abstract

Prior studies have demonstrated impaired endothelium-dependent flow-mediated dilation (FMD) in healthy subjects following a high-fat meal. Compared to uninfected individuals, HIV-infected persons have been shown to have impaired FMD. We examined the effect of two different high-fat meals on endothelial function in HIV-infected and uninfected men. We performed a randomized, parallel group crossover study comparing 47 white men [18 HIV-uninfected, 9 HIV-infected and antiretroviral therapy (ART)-naïve, and 20 HIV-infected men on ART]. Fasting participants consumed one of two randomly assigned high-fat meals of either saturated or polyunsaturated fat, followed at least 24 h later by the other meal. Brachial artery ultrasound measurements to assess vascular reactivity were performed before and 3 h after each dietary challenge. There was no significant difference in mean baseline or postprandial FMD between HIV-infected and HIV-uninfected participants (mean baseline FMD $\pm$ SD, 9.0% $\pm$ 5 vs. 9.2% $\pm$ 5, $p=0.9$; mean postprandial FMD $\pm$ SD, 9.0% $\pm$ 4.7 vs. 9.1% $\pm$ 4.7, $p=0.96$, respectively). No significant difference in baseline or postprandial change in FMD was found between meals or HIV treatment groups. Fasting lipids and glucose, CD4⁺ count, and viral load did not predict FMD in HIV-infected participants. In contrast to previous reports, this study did not demonstrate impaired endothelium-dependent vasodilation after high-fat meals in either HIV-infected or HIV-uninfected men. Moreover, HIV infection itself may not be the primary explanation for the abnormal endothelial function reported in HIV-infected individuals.

Introduction

A SINGLE HIGH-FAT MEAL has been shown to impair endothelial function, as measured by postprandial flow-mediated dilation (FMD).^{1–6} Highly unsaturated omega-3 fatty acids and dietary antioxidants may reverse this effect.^{6–9} HIV has also been associated with impaired FMD in several studies,^{10–13} though this is not a universal finding.^{14,15} Impaired endothelial function precedes atherosclerosis and is independent of other cardiovascular (CV) risk factors.^{16–19} Premature CV disease is of concern in HIV-infected persons, especially those on antiretroviral therapy (ART). An increase in myocardial infarction and other CV events have been reported with ART^{20,21} as well as metabolic derangements,^{22–24} particularly high triglycerides and low high-density lipoprotein-cholesterol (HDL).²⁵ A recent study found no effect of 24 weeks of

omega-3 fatty acid supplementation on FMD in HIV-infected men on stable ART²⁶; however, to our knowledge, the acute postprandial effects of both polyunsaturated and saturated fat on endothelial function have not been evaluated in HIV-infected individuals. Therefore, the primary aim of this study was to assess the effects of two different high-fat meals, one of saturated and one of polyunsaturated fat, on postprandial FMD in HIV-infected and HIV-uninfected men. We hypothesized that a meal rich in saturated fat, but not one of highly unsaturated fatty acids, would impair FMD in all participants, and that impairment after a saturated fat meal would be greater in HIV-infected individuals.

Conflicting data exist over whether ART or HIV infection itself contributes most to increased cardiovascular risk in HIV infection: ART decreases the risk of death from any cause, including CV disease, compared to no therapy.^{27–29}

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Cross-sectional studies have noted that patients on ART, particularly protease inhibitors, have impaired FMD,^{10–12} while intervention trials report that ART improves FMD in previously ART-naïve individuals.³⁰ Therefore, a secondary purpose of this study was to examine the associations between ART and FMD. We expected that ART-naïve participants would have greater impairment of FMD than ART-treated participants, and that lopinavir/ritonavir (LPV/r)-based regimens would be associated with greater FMD impairment than efavirenz-based regimens.

Materials and Methods

Subjects

Forty-seven white men participated in this randomized, observer-blinded, crossover study: 18 HIV-uninfected and 29 HIV-infected men (9 ART-naïve and 10 each on efavirenz or LPV/r-based ART). Exclusion criteria included a preexisting diagnosis of or treatment for hypertension, diabetes, hyperlipidemia, or cardiovascular disease, though one participant regularly took propranolol. Subjects were asked to have no caffeine on the day of the study, to consume no alcohol for 48 h prior to the study, and to discontinue antiinflammatory drugs for 1 week and antioxidants for 2 weeks prior to and throughout the duration of the study. Participants taking omega-3 fatty acid supplements were asked to have a 2-week washout period prior to the study and to resume supplements only after all visits were completed. Smoking was initially a criterion for exclusion, but several participants were found to be smokers at subsequent visits; therefore, other smokers were enrolled to preserve an equal distribution between groups. Subjects were asked to refrain from smoking from the start of fasting to the completion of the study visit. Participants were asked to refrain from exercise on the morning of each visit; blood pressures and serum samples were taken only after subjects had been sitting relaxed for at least 5 min.

Subjects were recruited from current cohorts and prior studies within Tufts University Nutrition/Infection Unit or had identified themselves to the nutrition staff of that department with concerns about diet or cardiovascular disease. Additionally, subjects were recruited from the hospital and from the community through flyers and online advertisements. HIV-infected participants were additionally recruited from community agencies serving HIV-infected persons. All HIV-infected subjects on a treatment regimen had undetectable viral load; naïve subjects were appropriately untreated. All treated participants had been on a stable regimen for 4 weeks prior to the first study visit, except for one subject who began an efavirenz-based regimen 3 weeks prior. The Tufts Health Sciences Campus Institutional Review Board approved this study, and signed informed consent was obtained from all participants. The procedures followed were in accordance with the ethical standards of the institution.

Meal intervention

Fasting participants consumed one of two randomly assigned, high-fat meals containing either saturated or polyunsaturated fats, followed at least 24 h later by the other meal. The median duration between meals was 7 days (IQR 3, 11) as prior studies separated meals by as few as 2–3 days^{9,31} but most by 7 days.^{1,3,4,6} Saturated fat meals (700 kcal, 29 g total

fat, 65 g carbohydrate, 43 g protein, 10 g saturated fat) consisted of 3 ounces of bacon, one slice of processed American cheese, two servings of egg substitute (whites only), five large black olives, one bagel with 1.3 tablespoons of yogurt-based margarine, $\frac{3}{4}$ cup canned pears in water, and 8 fluid ounces of 1% fat milk. Polyunsaturated fat meals were isocaloric (700 kcal, 29 g total fat, 65 g carbohydrate, 44 g protein, 5 g saturated fat, and 4 g omega-3 fatty acids) and consisted of 5 ounces of salmon, one bagel with $2\frac{1}{4}$ tablespoons of yogurt-based margarine, 1 tablespoon of cashew butter, $\frac{1}{2}$ tablespoon of dry grated Parmesan cheese, 1.5 tablespoons of walnuts, $\frac{1}{4}$ cup of canned peaches in water, and 8 fluid ounces of mineral water without ice. The nutritional composition of meals was calculated using the Nutrition Data System for Research software version 2006, developed by the Nutrition Coordinating Center (NCC), University of Minnesota, Minneapolis, MN.³²

Endothelial dysfunction measurements

Serial brachial artery ultrasound measurements of flow-mediated dilation to assess vascular reactivity were performed before and 3 h after each dietary challenge, as postprandial changes in FMD have been seen 2–4 h following a high-fat meal.^{1,2,4,5} Meals were consumed at the study site and FMD measurements were performed according to the following procedure. After measuring the baseline brachial artery diameter using high-resolution ultrasound, a blood pressure cuff placed around the upper arm was rapidly inflated to a suprasystolic pressure for 5 min, causing forearm ischemia. Release of the tourniquet causes dilation of the distal microvasculature, termed reactive hyperemia, and results in the local release of nitric oxide. Sixty seconds after the release of the cuff, the brachial artery diameter was again measured. The endothelium-dependent FMD of the brachial artery is quantified as the maximum percent change in arterial diameter during reactive hyperemia, as determined by high-resolution ultrasound imaging. Our laboratory has reported mean intraobserver and interobserver variability of FMD measurements of 1.9% and 2.8%, respectively, in healthy volunteers.³³

Clinical characteristics and laboratory data

Data were collected via personal interview with a study coordinator on smoking, exercise frequency, drug/alcohol use, past medical history, and current medications. Participant height was measured via a stadiometer at the initial visit, and weight and blood pressure were measured at each visit by a trained study coordinator or nurse using a digital scale and automated blood pressure cuff, respectively. Blood samples were collected for measurement of CD4⁺ count and HIV RNA for HIV-infected subjects and for C-reactive protein (CRP), fasting triglycerides, fasting total cholesterol, fasting HDL-cholesterol, fasting glucose, and fasting insulin for all participants. Glucose, insulin, and lipid measurements were repeated 3 h after each experimental meal. The quantitative insulin sensitivity check index (QUICKI), a measure of insulin sensitivity, was calculated from baseline fasting insulin and glucose according to the following formula: QUICKI = $1/[\log(\text{fasting insulin concentration, } \mu\text{U/ml}) + \log(\text{fasting glucose concentration, mg/dl})]$.³⁴

Statistical analysis

We employed repeated measures analysis of variance to evaluate differences in mean FMD_{%Δbase} between HIV-infected and HIV-uninfected participants, between treated and untreated participants, and between all four groups (HIV-uninfected, HIV-infected/ART-naïve, HIV-infected/LPV/r therapy, and HIV-infected/efavirenz therapy group). We compared mean FMD_{%Δbase} between saturated fat and polyunsaturated fat meals within and between HIV treatment groups. Preprandial and postprandial metabolic parameters were compared via paired *t*-test or signed rank test/sign test where data were not normally distributed. Normally distributed variables were reported as mean ± SD, while variables with nonnormal distributions were reported as median (interquartile range). We employed mixed models to evaluate the random effect of subject and the fixed effects of meal type, meal order, and HIV status on preprandial FMD, postprandial FMD, and the difference between preprandial and postprandial FMD. Demographic, clinical, and HIV-associated variables were also entered into univariate models as possible predictors of FMD.

Demographic variables included current smoking, drug use (ever), recent drug use (in the last 6 months), alcohol use, and current exercise. Clinical and laboratory variables included the following: body mass index; CRP; systolic blood pressure, diastolic blood pressure, and pulse (each averaged

over three measurements); initial preprandial values for cholesterol, LDL, HDL, triglycerides, glucose, insulin, and QUICKI; and baseline arterial diameter. For HIV-infected participants, ART use (Y/N), ART type (LPV/r vs. efavirenz), HIV viral load, absolute CD4 cell count, and percent CD4 cell count were also evaluated. Mixed models were then repeated for each variable, adjusting for age and meal type. As the extent of significant impairment of endothelial reactivity after a high-fat meal is not known in the HIV-infected population, a formal power calculation could not be performed. However, sample size was determined by prior intervention studies demonstrating a statistically significant difference in mean FMD_{%Δbase} between groups of 8–10 participants.^{1,3,4} Statistical significance was defined by a *p*-value of <0.05. Analyses were performed using SAS software, Version 9.2 (SAS Institute, Cary, NC).

Results

Baseline demographic and clinical characteristics, brachial artery diameter, and fasting lipids, glucose, and insulin are shown in Table 1. All participants were white males. Groups were similar in terms of body mass index, baseline lipids, and lifestyle factors. LPV/r users were older than HIV-infected, ART-naïve participants (50.1 ± 5.1 years vs. 36.8 ± 11 years, respectively, *p* = 0.008), but no other significant differences in age were found between groups. Baseline cholesterol and

TABLE 1. BASELINE CHARACTERISTICS

	HIV-uninfected (n = 18)	ART naïve (n = 9)	LPV/r-based ART (n = 10)	Efavirenz-based ART (n = 10)	p-value
Age (years)	40 ± 11	37 ± 11	50 ± 5 ^a	47 ± 8	0.008
Current smoker, no (%)	4 (22)	3 (33)	1 (10)	2 (20)	0.68
Total cholesterol (mg/dl)	167 ± 38	178 ± 32	182 ± 23	184 ± 43	0.55
LDL (mg/dl)	104 ± 31	122 ± 23	102 ± 33	113 ± 37	0.46
HDL (mg/dl)	42 ± 12	35 ± 9	43 ± 17	40 ± 7	0.50
Triglycerides [mg/dl (IQR)] ^b	89 (53,141)	74 (50,113)	198 (91,249)	121 (88,225)	0.12
Fasting glucose (mg/dl)	85 ± 9	80 ± 11	86 ± 13	94 ± 5	0.03
Fasting insulin [μIU/ml (IQR)] ^b	6 (3,12)	6 (5,13)	13 (5,14)	10 (6,21)	0.35
QUICKI (IQR) ^b	0.2 (0.1,0.2)	0.2 (0.1,0.2)	0.1 (0.2,0.2)	0.1 (0.1,0.2)	0.21
C-reactive protein [mg/liter (IQR)] ^b	0.6 (0.4,4)	1.0 (0.4,2)	1.1 (0.7,5)	1.8 (1,2)	0.23
BMI (kg/m ²)	26 ± 4	27 ± 6	24 ± 2	24 ± 4	0.47
Blood pressure, systolic (mm Hg) ^c	122 ± 10	117 ± 11	122 ± 13	118 ± 11	0.62
Blood pressure, diastolic (mm Hg) ^c	73 ± 5	74 ± 9	76 ± 9	77 ± 7	0.48
Antiretrovirals, no. (%)					
Tenofovir			6 (60)	9 (90)	
Abacavir			3 (30)	1 (10)	
Lamivudine			5 (50)	0	
Emtricitabine			3 (30)	9 (90)	
Zidovudine			5 (50)	0	
Stavudine			0	1 (10)	
Amprenavir/ritonavir			0	1 (10)	
Raltegravir			0	1 (10)	
Exercise, min/week (IQR) ^b	160 (120,225)	270 (135,273)	120 (80,480)	240 (60,315)	0.71
Recent drug use, no. (%)	2 (11)	2 (22)	1 (10)	1 (10)	0.82
Baseline arterial diameter (mm)	0.4 ± 0.04	0.4 ± 0.04	0.4 ± 0.04	0.4 ± 0.07	0.08

^aSignificant difference compared to naïve group using ANOVA with Bonferroni adjustment.

^bMedian value expressed; Kruskal–Wallis test used for comparisons.

^cAverage of three separate measurements.

Data are mean ± SD and ANOVA is statistical test used unless otherwise noted.

ART, antiretroviral therapy; HDL, high-density lipoprotein; LDL, low-density lipoprotein; LPV/r, lopinavir/ritonavir; BMI, body mass index.

TABLE 2. FLOW-MEDIATED DILATION BY TREATMENT GROUP AND MEAL TYPE

	Preprandial FMD% _{Abase} (mean ± SD)	Postprandial FMD% _{Abase} (mean ± SD)	FMD difference
Saturated fat (n=46)	9.8 ± 5	10.1 ± 6	0.3 ± 4
Polyunsaturated fat (n=47)	9.1 ± 5	9.0 ± 4	-0.2 ± 6
HIV uninfected (n=18), saturated fat	9.0 ± 5	9.2 ± 5	0.1 ± 5
HIV uninfected (n=18), polyunsaturated fat	9.4 ± 5	9.2 ± 5	-0.2 ± 7
ART naïve (n=8), saturated fat	9.4 ± 4	10.7 ± 5	1.4 ± 3
ART naïve (n=9), polyunsaturated fat	8.2 ± 3	10.1 ± 4	1.8 ± 5
LPV/r-based ART (n=10), saturated fat	8.6 ± 5	8.2 ± 4	-0.4 ± 4
LPV/r-based ART (n=10), polyunsaturated fat	8.9 ± 5	8.1 ± 3	-0.8 ± 5
Efavirenz-based ART (n=10), saturated fat	12.9 ± 7	13.1 ± 7	0.3 ± 4
Efavirenz-based ART (n=10), polyunsaturated fat	9.5 ± 4	8.1 ± 4	-1.4 ± 6

FMD, flow-mediated dilation; ART, antiretroviral therapy; LPV/r, lopinavir/ritonavir.

t-test was used for all comparisons between groups. There were no comparisons for which the *p*-value was <0.05.

triglycerides were not significantly different between groups. For treatment-naïve subjects, the median HIV-1 RNA was 4,529 log₁₀ copies/ml (IQR 228, 12,116), compared to ≤75 log₁₀ copies/ml for treated participants (75, 75) (*p*<0.001). Median CD4⁺ counts did not differ between naïve and treated HIV-infected subjects: 512 cells/μl (419, 740) and 531 cells/μl (343, 880), respectively; *p*=0.87.

Flow-mediated dilation

There were no differences in FMD at baseline between HIV-infected and HIV-uninfected subjects (9.6% ± 4.9 vs. 9.2% ± 5, respectively, *p*=0.7). For both polyunsaturated and saturated fat meals, no significant differences were seen in preprandial or postprandial FMD between HIV-infected and HIV-uninfected subjects, between ART-naïve and ART-treated participants, or among all four groups (Table 2). Three hours postprandially, there were no significant differences in FMD from baseline, regardless of meal type, meal order, or HIV treatment group. After adjusting for age, only QUICKI was significantly associated with preprandial FMD: for each 0.1 unit increase in QUICKI, preprandial FMD increased by 4.8% (95% CI, 0.14, 9.6; *p*=0.044). After ad-

justing for age and meal type, only diastolic blood pressure was associated with postprandial FMD in multivariate analysis (postprandial FMD, -0.2%; 95% CI, -0.4, -0.003%; *p*=0.05). Recent drug use, defined as any use of street drugs (cocaine, crack, heroin, street methadone, sedatives, tranquilizers, speed, crystal meth, poppers, ecstasy, special K or GHB) in the past 6 months, was associated with a postprandial decrease in FMD (FMD difference, -4.0%; 95% CI, -6.7, -1.3%; *p*=0.005). CD4⁺ percentage (natural log) was associated with an increase between preprandial and postprandial FMD (FMD difference, 2.1%; 95% CI, 0.1, 4%; *p*=0.04). The intraclass correlation coefficient for FMD within subjects was 0.38 (95% CI, 0.18, 0.64). There were no significant differences between the two preprandial FMD, baseline arterial diameter, or hyperemic arterial diameter measurements (by paired *t*-test) in either the HIV-infected or HIV-uninfected group (data not shown).

Metabolic parameters

Preprandial and postprandial glucose, lipids, and insulin are shown in Table 3 for the three HIV-infected groups and one uninfected group, separated by meal type. LDL-cholesterol

TABLE 3. DIFFERENCES BETWEEN PREPRANDIAL AND POSTPRANDIAL METABOLIC PARAMETERS BY TREATMENT GROUP

	HIV-uninfected (n=18)	ART naïve (n=9) ^a	LPV/r-based ART (n=10)	Efavirenz-based ART (n=10)
Total cholesterol (mg/dl), saturated fat	-3.1 ± 13	-7.8 ± 7 ^b	-7.6 ± 8 ^b	-5.8 ± 11
Total cholesterol (mg/dl), polyunsaturated fat	-1.9 ± 8	-2.2 ± 7	-6.4 ± 5 ^b	-6.5 ± 11
LDL (mg/dl), saturated fat	-13.0 ± 13 ^b	-11.5 ± 9 ^b	-9.5 ± 13 ^b	-20.2 ± 17 ^b
LDL (mg/dl), polyunsaturated fat	-11.5 ± 8 ^b	-11.7 ± 11 ^b	-9.1 ± 9 ^b	-14.8 ± 16 ^b
HDL (mg/dl), saturated fat	-0.6 ± 3	-2.1 ± 2 ^b	-1.3 ± 3	-0.8 ± 2
HDL (mg/dl), polyunsaturated fat	-0.2 ± 2	0.4 ± 2	-2.7 ± 3 ^b	-1.3 ± 3
Triglycerides [mg/dl (IQR)] ^c , saturated fat	57 (21, 74) ^{b,d}	31 (17, 71)	25 (-47, 63)	88 (39, 114) ^{b,d}
Triglycerides [mg/dl (IQR)] ^c , polyunsaturated fat	44 (16, 74) ^{b,d}	51 (22, 79) ^{b,d}	33 (5, 51)	58 (41, 90) ^{b,d}
Glucose (mg/dl), saturated fat	-2.4 ± 14	3.5 ± 12	-6.4 ± 21	-4.9 ± 16
Glucose (mg/dl), polyunsaturated fat	-4.5 ± 12	0.2 ± 12	-3.6 ± 19	-3.3 ± 15
Insulin [μIU/ml (IQR)] ^c , saturated fat	2.1 (-1, 8)	3.3 (1, 8)	1.3 (0.4, 8)	3.5 (-1, 13)
Insulin [μIU/ml (IQR)] ^c , polyunsaturated fat	5.6 (-0.1, 11) ^{b,d}	-0.04 (-2, 0.3)	11.9 (1, 20) ^{b,d}	1.6 (-0.7, 13)

^aFor saturated fat meal, *n*=8.

^b*p*-value <0.05 for difference between preprandial and postprandial values.

^cMedian value expressed.

^dNonparametric signed rank/sign test; otherwise two-tailed paired *t* test.

Data are mean ± SD unless otherwise noted.

ART, antiretroviral therapy; HDL, high-density lipoprotein; LDL, low-density lipoprotein; LPV/r, lopinavir/ritonavir.

decreased postprandially for both HIV-infected and HIV-uninfected subjects, but total and HDL-cholesterol decreased in HIV-infected subjects only. Triglycerides rose significantly in all postprandially, except in LPV/r users and the naïve group (saturated fat meal only). Although not statistically significant, there was a trend toward higher triglycerides in the LPV/r group at baseline. All participants had fasting glucose values within normal limits. QUICKI at baseline was compared between groups; no significant differences were seen. CRP measurements did not differ between the HIV-infected and HIV-uninfected groups.

After the completion of the study, one participant was discovered to have been taking both efavirenz and a boosted protease inhibitor during the study protocol; his data were removed and the FMD and metabolic analyses were repeated, without any significant alterations to the results (data not shown).

Discussion

High-fat meals, of predominately saturated or polyunsaturated fat, did not alter endothelium-dependent vasodilation in this study, regardless of HIV infection status. This could be due to several factors. First, even light smoking is associated with endothelial dysfunction,³⁵ and very few smokers were enrolled. Second, most participants engaged in regular exercise at least once per week, which has been associated with improved endothelial function.³⁶ A single episode of aerobic exercise has been shown to reverse the unfavorable effects of a high-fat meal on FMD,^{3,31} and this effect can be seen even if the exercise is performed 16–18 h prior to ingestion of the meal.³ We did not ask participants to abstain from exercise except on the morning of each study visit; this could explain the lack of effect of the high-fat meals on the mean FMD of either group. Lastly, although the mean FMD response to either meal did not differ significantly between groups, individual responses to each meal varied markedly, as previously reported.¹⁶ Therefore, for some participants, FMD was impaired following a high-fat meal.

In this study, HIV-infected individuals did not display impaired endothelial function at baseline when compared to uninfected individuals. In contrast to several previous trials,^{11,13} HIV-infected and HIV-uninfected participants in this study were homogeneous with respect to gender, race, and diagnosis of/treatment for hyperlipidemia. Despite differences between HIV treatment groups, age and lipid values were similar between the HIV-infected and HIV-uninfected groups. In addition, other studies have also shown no FMD impairment in HIV-infected individuals compared to matched uninfected participants, despite differences in baseline lipid profiles.^{14,15} Subjects on ART were older than antiretroviral-naïve subjects, as would be expected; this difference would presumably enhance any deleterious effects of ART on FMD, which were, however, not observed. Baseline brachial artery diameter measurements differed minimally, but not significantly, between ART groups; in addition, FMD is calculated as the percentage change from baseline, accounting for any differences in baseline brachial artery diameter between groups. Furthermore, multivariate analysis did not reveal any associations between baseline brachial artery diameter and either preprandial or postprandial FMD or FMD difference following either meal.

In the present study, we found an association between increasing diastolic blood pressure and impaired FMD in multivariate analysis; also, recent drug use was associated with a postprandial decline in FMD. Previously both traditional and novel risk factors have been implicated in endothelial dysfunction and cardiovascular disease risk in HIV-infected individuals. For example, increasing insulin resistance predicted endothelial dysfunction in an HIV-infected cohort whose mean FMD was similar to that of matched HIV-uninfected controls,¹⁵ and current injection drug use and hazardous drinking have also been shown to be associated with impaired FMD.¹³ Current evidence suggests that endothelial dysfunction caused by circulating inflammatory mediators precedes and contributes to hypertension^{37,38}; therefore, rather than causing impaired FMD, elevated diastolic blood pressure may, in fact, reflect a downstream effect of antecedent peripheral vascular dysfunction. Although some groups have shown that antihypertensives improve endothelial function,³⁹ others have demonstrated that treatment does not reverse endothelial dysfunction in hypertensives and that endothelial function may be impaired even in normotensive subjects.³⁸

We did not identify any HIV-specific risk factors associated with FMD or any associations with ART, although HIV viral load was associated with endothelial dysfunction in several previous studies.^{13,40} In a retrospective cohort study, soluble endothelial and platelet activation markers were higher in HIV-infected persons than in uninfected controls; initiation of ART decreased all markers except for P-selectin, while participants remaining ART naïve maintained higher concentrations of all markers.⁴¹ ART-treated participants had lower FMD than both uninfected and ART-naïve participants in another trial, although the difference between ART-treated and ART-naïve subjects was not statistically significant.¹¹

Metabolic parameters changed as expected following meal consumption: LDL-cholesterol declined and triglycerides rose postprandially. However, total and HDL-cholesterol declined significantly only in the HIV-infected individuals, suggesting that differential metabolic responses to meals may exist even in the absence of previously diagnosed dyslipidemia.

There may be several possible limitations to the present study. The sample size is small ($n=47$); however, prior studies have shown impairment of FMD by 45–76% after a single high-fat meal in as few as 10 subjects.^{1,4,5} We could not evaluate differences in postprandial FMD based on treatment duration, as information on length of time on antiretrovirals was not collected. Several smokers were included in the study, but numbers of smokers were similar between HIV-infected and HIV-uninfected groups. Some HIV-infected subjects were recruited after expressing concerns about diet or cardiovascular disease, which may have biased the sample toward a more health-conscious group. Yet, this bias may have mitigated some of the cardiovascular risk in HIV-infected individuals that has previously been attributed to lifestyle factors. Lastly, we provided breakfast in order to achieve a fasting state, which limited both the quantity and the fat content of food that could be comfortably consumed by participants; therefore, the 37% overall fat in the experimental meals was somewhat less than that used in previously published reports.^{1,9} However, the 13% saturated fat and 4 g omega-3 fatty acids in these meals were consistent with those used in these prior studies.^{1,6,9}

In conclusion, we did not demonstrate reduced endothelial function in HIV-infected subjects compared to uninfected subjects, nor did we observe differences in FMD following a single high-fat meal. This finding was consistent regardless of use of ART therapy or ART type. Furthermore, we investigated, for the first time to our knowledge, the acute impact of a high saturated fat meal on HIV-infected persons, which did not appear to affect postprandial FMD. Differential metabolic responses to meals may contribute to excess cardiovascular risk in HIV-infected persons; however, this risk is unlikely to be mediated by greater impairment of postprandial vascular reactivity compared to HIV-uninfected persons. Future research into the specific mechanisms of increased cardiovascular risk in HIV infection is needed to reduce morbidity in a population subject to many cardiovascular risk factors.

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Author Disclosure Statement

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