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Sex differences in postprandial plasma tumor necrosis factor–α, interleukin-6, and C-reactive protein concentrations

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Abstract

Abdominal obesity and insulin resistance are characterized by low-level chronic inflammation most likely implicated in the increased cardiovascular disease risk associated with these conditions. However, not much is known of the acute regulation of circulating inflammatory markers in response to food intake. The aim of this study is to examine changes in inflammatory marker concentrations after the consumption of a high-fat meal in men and women. We measured tumor necrosis factor–α (TNF-α), interleukin-6 (IL-6), and C-reactive protein concentrations in plasma samples collected at 0, 4, and 8 hours after consumption of the meal in 39 men and 41 women. Associations between these variations and physical as well as metabolic variables were then examined. We noted significant increases in plasma IL-6 concentrations at 4 and 8 hours after the meal in men (+34% and +107%, respectively; $P < .005$ vs 0 hour) and women (+78% and +153%, respectively; $P < .0001$ vs 0 hour). Postprandial plasma TNF-α concentrations significantly dropped at 4 hours after the high-fat meal in men (−9.5%, $P < .0005$ vs 0 hour) and women (−5.5%, $P < .05$ vs 0 hour). Plasma CRP concentrations were not affected by food intake in either men or women. We also found that postprandial plasma concentrations of IL-6 were lower in subjects with a normal glucose tolerance (n = 69) compared with individuals with an impaired glucose tolerance (n = 11). Results of the present study show that consumption of a high-fat meal is associated with a transient reduction in circulating concentrations of TNF-α in both men and women as well as an elevation of plasma IL-6 concentrations that was found to be greater in women than in men.

1. Introduction

It is well established that fasting plasma lipid disturbances like high circulating low-density lipoprotein cholesterol and triglycerides (TGs) concentrations as well as low high-density lipoprotein (HDL) cholesterol concentrations are strong independent risk factors for cardiovascular disease (CVD) [1], a leading cause of death in North America and around the globe. Postprandial hyperlipidemia has also been identified as a predictor of CVD [2]. Interestingly, insulin-resistant [3] and abdominally obese [4-6] subjects have been characterized by an exaggerated postprandial lipemia, a condition that has been suggested to contribute to the increased risk of CVD in these individuals. Furthermore, men have been characterized by postprandial hypertriglyceridemia compared with women [7], an observation that likely

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contributes to their higher CVD risk compared with women. We have also previously reported that the sex difference in abdominal visceral fat accumulation may explain, at least in part, the greater plasma TG response after the consumption of a high-fat meal in men than in women [7].

On the other hand, inflammation plays a key role in the initiation and progression of atherosclerosis leading to CVD; and it has been suggested that measuring blood inflammatory markers could be helpful in the evaluation of CVD risk [8]. To that effect, interleukin-6 (IL-6), C-reactive protein (CRP), and tumor necrosis factor–α (TNF-α) have attracted much attention and are frequently used in the assessment of the inflammatory component associated to CVD risk [9]. Obese individuals are characterized by a chronic state of low-grade inflammation, including high circulating IL-6 and TNF-α concentrations that have been suggested to result, to some extent, from the increased production and release of these cytokines by adipocytes [10] and macrophages present in adipose tissue (AT) [11]. Abdominal obesity is also associated with elevated plasma high-sensitivity CRP (hsCRP) concentrations [12]. This peculiar metabolic milieu has been suggested to precede and contribute to the development of complications linked to obesity including insulin resistance, diabetes, and atherosclerosis. We [13] and others [14-17] have previously reported significant variations in circulating inflammatory markers after food intake in male subjects. However, not much is known of the potential differences in postprandial IL-6, TNF-α, and CRP concentrations between men and women. The present study was therefore undertaken to further investigate this issue.

2. Methods

2.1. Subjects

Thirty-nine men and 41 women (36 premenopausal and 5 postmenopausal) were recruited in the Québec City metropolitan area through media advertisement. Participants were selected to cover a wide range of adiposity values (body mass index = 18.7-41.0 kg/m^2) and gave their written consent to participate in the study. All participants were healthy nonsmoking volunteers who were not under treatment of coronary heart disease, diabetes, dyslipidemias, or endocrine disorders. The study was approved by the Medical Ethics Committee of Laval University.

2.2. Anthropometric and body composition measurements

Body weight, height, and waist circumference were measured following standardized procedures [18]. Body density was measured by the hydrostatic weighing technique [19]. The mean of 6 measurements was used in the calculation of percentage body fat from body density using the equation of Siri [20]. Fat mass was obtained by multiplying body weight by percentage body fat. Abdominal AT accumulation was assessed by computed tomography, which was performed on a Siemens Somatom DRH scanner (Erlangen, Germany) using previously described procedures [21].

2.3. Oral lipid tolerance test

In the morning after an overnight fast, each participant was given a test meal containing 60 g fat per square meter of body surface area as previously described [4]. Briefly, the meal consisted of eggs, cheese, toasts, butter, peanut butter, peaches, whipped cream, and milk. Energy content of the meal was 64% fat, 18% carbohydrates, and 18% protein and ranged from 1600 from 2200 kcal depending on body surface area of the participants. The test meal was well tolerated by all subjects. After the meal, subjects were not allowed to eat for the next 8 hours but were given free access to water. An intravenous catheter was inserted into the subject's forearm vein for blood sampling before meal ingestion, and blood samples were drawn before the meal and every 2 hours for the 8-hour postprandial period. Data presented in the present article consist of measures made in the 0-, 4-and 8-hour plasma samples.

2.4. Fasting plasma lipoprotein and lipid concentrations

Blood samples were collected under EDTA, and plasma was immediately separated after blood collection by centrifugation at 3000 rpm for 10 minutes at 4°C. Triglycerides and cholesterol concentrations in total plasma were determined enzymatically on a Technicon RA-500 (Bayer, Tarrytown, NY) as previously described [22]. Each plasma sample (4 mL) was then subjected to a 12-hour ultracentrifugation (50 000 rpm) in a Beckman 50.3 Ti rotor (Beckman, Palo Alto, CA) at 4°C in a 6-mL Beckman Quickseal tube, which yielded 2 fractions: the top fraction containing TG-rich lipoprotein (density [d] <1.006 g/mL) and the bottom fraction (d > 1.006 g/mL) containing TG-poor lipoproteins. The HDL particles were isolated from the bottom fraction (d > 1.006 g/mL) after precipitation of apolipoprotein (apo) B–containing lipoproteins with heparin and $MnCl_2$ [23]. Fasting total apo B concentration was measured in plasma by the rocket immunoelectrophoretic method of Laurell [24]. The lyophilized serum standard for apo B measurement was prepared in our laboratory and calibrated with reference standards obtained from the Centers for Disease Control and Prevention (Atlanta, GA).

2.5. Insulin and glucose concentrations

Each participant was given a 75-g oral glucose tolerance test, and blood samples were taken at −15, 0, and 120 minutes, allowing assessment of the glucose tolerance of subjects. Glucose concentrations were measured enzymatically [25], whereas plasma insulin was measured by radioimmunoassay with polyethylene glycol separation [26]. The homeostasis model assessment of insulin resistance (HOMA-IR) was calculated in each subject according to the equation of Matthews et al [27]. The same techniques were used for the measurements of glucose and insulin in

Table 1
Physical characteristics and metabolic profile in the fasting state of men and women

Variables	Men	Women	*P*
n	39	41	
Age (y)	44.0 ± 9.1	43.7 ± 9.4	.88
Weight (kg)	87.0 ± 12.4	68.7 ± 16.3	<.0001
Body mass index (kg/m^2)	28.9 ± 4.3	26.5 ± 5.7	.04
Body fat (%)	27.6 ± 6.8	34.1 ± 10.4	.002
Fat mass (kg)	24.6 ± 8.5	24.4 ± 12.5	.93
Waist circumference (cm)	98.2 ± 9.8	82.6 ± 13.5	<.0001
Hip circumference (cm)	103.7 ± 7.8	103.5 ± 12.8	.93
Waist-to-hip ratio	0.95 ± 0.05	0.80 ± 0.06	<.0001
Abdominal visceral AT (cm^2)	147.3 ± 62.6	102.0 ± 52.8	<.001
Abdominal subcutaneous AT (cm^2)	286.3 ± 106.7	332.0 ± 190.4	.19
Total cholesterol (mmol/L)	5.23 ± 0.80	4.83 ± 0.93	.05
LDL cholesterol (mmol/L)	3.53 ± 0.70	3.22 ± 0.81	.08
HDL cholesterol (mmol/L)	0.98 ± 0.19	1.21 ± 0.29	<.0001
Cholesterol/HDL cholesterol	5.55 ± 1.41	4.20 ± 1.25	<.0001
TGs (mmol/L)	1.99 ± 0.99	1.24 ± 0.68	<.001
Apo B (g/L)	1.10 ± 0.21	0.96 ± 0.22	.005
Insulin (pmol/L)	95.2 ± 55.5	78.8 ± 35.5	.12
Glucose (mmol/L)	5.00 ± 0.56	4.69 ± 0.54	.01
HOMA-IR	2.98 ± 2.05	2.04 ± 1.37	.02
TNF-α (pg/mL)[a]	1.69 (1.37-2.13)	1.55 (1.23-1.93)	.93
IL-6 (pg/mL)[a]	1.95 (1.43-2.97)	2.29 (1.60-2.81)	.33
CRP (mg/L)[a]	1.14 (0.48-2.73)	1.19 (0.45-3.43)	.76

Values are means ± standard deviation. LDL indicates low-density lipoprotein.
[a] Values are presented as median (25th-75th percentile). Statistical analyses were performed on log-transformed values.

plasma from blood samples taken after ingestion of the high-fat meal.

2.6. Determination of CRP, IL-6, and TNF-α concentrations

The hsCRP, IL-6, and TNF-α measurements were performed in blood samples collected at 0, 4, and 8 hours after the high-fat meal. Concentrations of CRP concentrations were measured using the Behring Latex-Enhanced highly-sensitive CRP assay performed with a Dade Behring BN-ProSpec nephelometer (Dade Behring, Mississauga, Ontario, Canada) [28]. The run-to-run coefficient of variation at hsCRP concentrations ranging from 1.0 to 10 μg/mL was less than 5%. Plasma IL-6 and TNF-α were quantified by commercially available high-sensitivity enzyme-linked immunosorbent assay kits (R&D Systems, Minneapolis, MN) according to the manufacturer's instructions. The minimum detectable concentrations by these methods were estimated to be 0.039 pg/mL for IL-6 and 0.12 pg/mL for TNF-α by the manufacturer.

2.7. Statistical analyses

Data are presented as means ± standard deviation unless indicated otherwise. Because there was no difference between pre- and postmenopausal women (data not shown), we combined both subgroups of women for the analyses. Differences between men and women were tested

Table 2
Postprandial plasma proinflammatory cytokine concentrations in 39 men and 41 women

	0 h	4 h	8 h	*P* across time
Men				
IL-6 (pg/mL)	2.40 ± 1.36	2.85 ± 1.72 [b]	4.38 ± 2.35[b,c]	<.0001
TNF-α (pg/mL)	1.74 ± 0.48	1.57 ± 0.50 [b]	1.65 ± 0.57	.0031
CRP (mg/L)	2.02 ± 2.30	1.98 ± 2.03	1.86 ± 2.02	.87
Women				
IL-6 (pg/mL)	2.77 ± 1.81	4.36 ± 3.15 [a,b]	5.83 ± 3.49 [a,b,c]	<.0001
TNF-α (pg/mL)	1.91 ± 1.35	1.80 ± 1.29 1	1.84 ± 1.36	.0383
CRP (mg/L)	1.96 ± 2.03	2.05 ± 2.10	2.06 ± 2.14	.93

Values are means ± standard deviation. Statistical analyses were performed on log-transformed values.
[a] Significantly different from men.
[b] Significantly different from 0 hour.
[c] Significantly different from 4 hours.

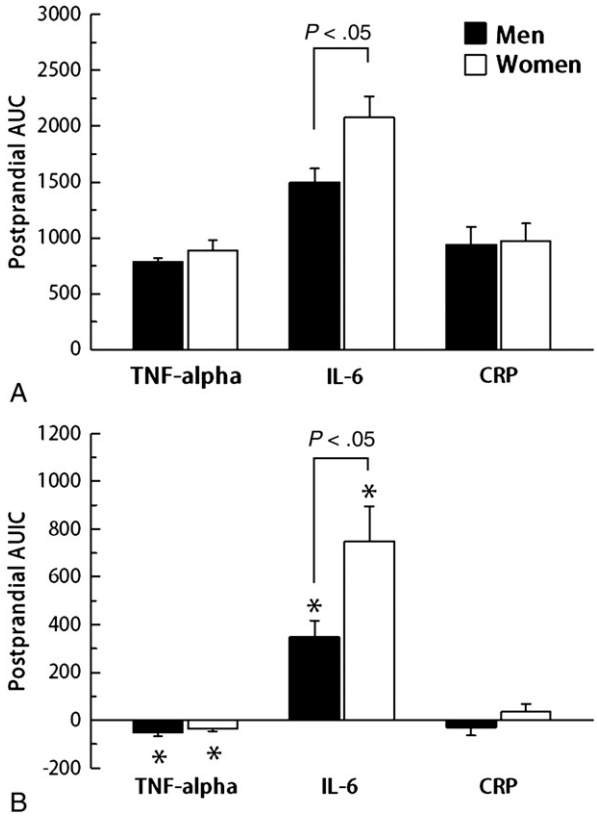

Fig. 1. Postprandial (A) AUC and (B) AUIC of plasma TNF-. Postprandial (A) AUC and (B) AUIC of plasma TNF-α (in picograms per milliliter per 8 hours), IL-6 (in picograms per milliliter per 8 hours), and CRP (in milligrams per liter per 8 hours) concentrations in men (black bars, n = 39) and women (white bars, n = 41). *Significant change in the postprandial response (AUIC).

by analysis of variance (ANOVA). Postprandial changes in TNF-α, IL-6, and CRP were tested by ANOVA for repeated measures, whereas significance of change for each time point vs baseline values was tested by paired *t* tests. Furthermore, we compared inflammatory marker concentrations in subjects separated on the basis of their glucose tolerance, that is, normal (NGT; 2-hour glucose <7.8 mmol/L, n = 69) and impaired (IGT; 2-hour glucose between 7.8 and 11.1 mmol/L, n = 11) according to accepted guidelines [29]. Multiple comparisons were made with 2-way ANOVA followed by post hoc analysis (Tukey test) to locate significant between-group differences identified by ANOVA. A *P* value of less than .05 was considered statistically significant, and all statistical procedures were performed with the SAS statistical package (version 8.2; SAS Institute, Cary, NC).

3. Results

Physical characteristics and fasting metabolic profiles of men and women are shown in Table 1. Overall, men were more obese than women according to body mass index values ($P < .05$) and were characterized by abdominal obesity as indicated by higher waist circumference ($P < .0001$) and abdominal visceral AT area ($P < .001$). Although women showed approximately 15% more subcutaneous AT in the abdominal region than men, this difference did not reach statistical significance. Sex difference was noted in the metabolic profile, with men displaying higher fasting plasma cholesterol, TG, apo B, and glucose concentrations compared with women ($P < .05$). Men also showed lower plasma HDL cholesterol concentrations than women ($P < .0001$) and were also more insulin resistant than women as indicated by a significantly higher HOMA-IR value ($P < .05$). However, there was no significant difference in circulating IL-6, TNF-α, and CRP concentrations in the fasting state between both sexes (Table 1).

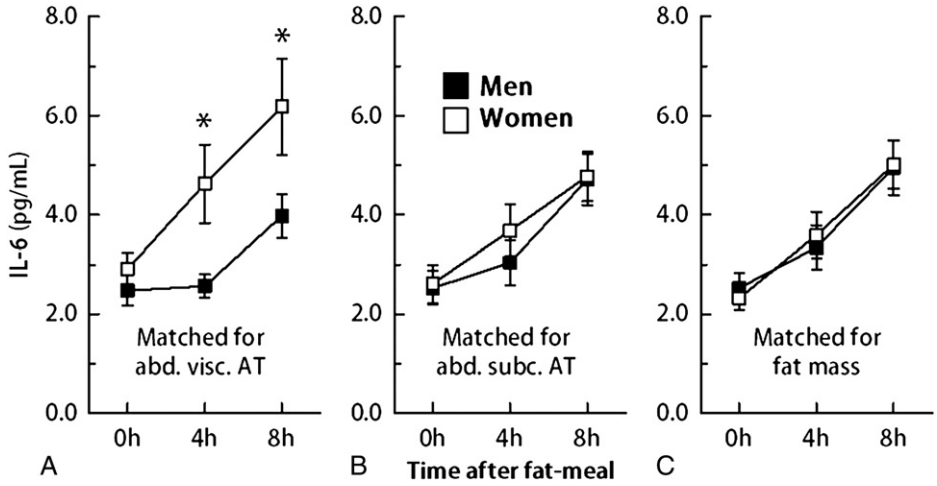

Fig. 2. Postprandial variations of plasma IL-6 concentrations in men (black squares) and women (white squares) individually matched for (A) abdominal visceral AT accumulation (n= 21 pairs), (B) abdominal subcutaneous AT accumulation (n = 20 pairs), and (C) total body fat mass (n = 21 pairs). *Significantly different from men.

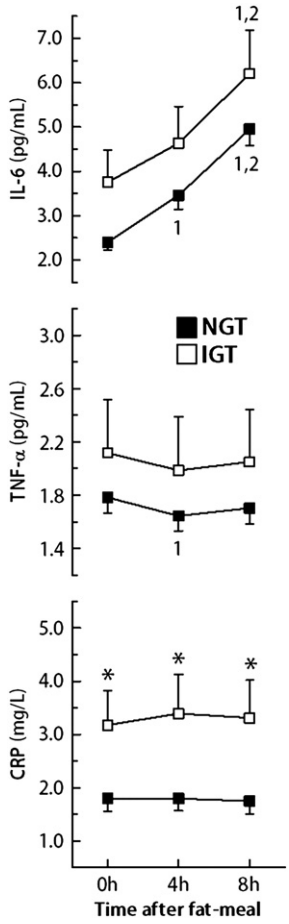

Fig. 3. Postprandial variations in plasma IL-6, TNF-α, and CRP in NGT (black squares, n = 69) and IGT (white squares, n = 11) participants. *Significantly different from NGT subjects. [1]Significantly different from 0 hour. [2]Significantly different from 4 hours.

As shown in Table 2, plasma IL-6 concentrations increased significantly after the high-fat meal in men at 4 hours (+34%, $P < .005$ vs 0 hour) and 8 hours (+107%, $P < .0001$ vs 0 hour). Circulating IL-6 concentrations also increased in women at 4 hours (+78%, $P < .0001$ vs 0 hour) and 8 hours (+153%, $P < .0001$ vs 0 hour) after the meal. Furthermore, women showed significantly higher concentrations of plasma IL-6 both at 4 and 8 hours after food intake compared with men. On the other hand, both men (−9.5%, $P < .0005$ vs 0 hour) and women (−5.5%, $P < .01$ vs 0 hour) showed significant decreases in plasma TNF-α concentrations 4 hours after the meal. There was no significant acute effect of food intake on plasma CRP concentrations. Fig. 1 illustrates the postprandial total (AUC) and incremental (AUIC) areas under the curve for plasma TNF-α, IL-6, and CRP concentrations in men and women. We found no difference in both the postprandial AUC and AUIC of TNF-α and CRP between men and women. However, women displayed significantly greater AUC ($P = .0129$) and AUIC ($P = .0164$) of IL-6 in response to the meal compared with men.

Furthermore, we compared men and women matched for different adiposity indices to sort out the contribution of the sex difference in adiposity and fat distribution to our results. Fig. 2 shows postprandial variations in plasma IL-6 concentrations in men and women individually matched for abdominal subcutaneous AT, visceral AT, or total body fat mass. We found that matching men and women for either abdominal subcutaneous AT accumulation or total body fat mass eliminated the sex difference in circulating IL-6 concentrations after the ingestion of the high-fat meal. On the other hand, matching men and women for abdominal visceral AT accumulation had no impact on the sex difference in postprandial plasma IL-6 concentrations (Fig. 2).

We also examined the impact of glucose tolerance on the postprandial inflammatory response; and therefore, we separated the subjects into those with a normal (NGT, n = 69) or impaired (IGT, n = 11) glucose tolerance. We found (Fig. 3) that NGT individuals showed a larger increase in plasma IL-6 concentrations at 4 hours (+58%, $P < .0001$ vs

Table 3
Postprandial plasma glucose and proinflammatory cytokine concentrations according to the glucose tolerance of men and women separately

	NGT				IGT			
	0 h	4 h	8 h	P^c	0 h	4 h	8 h	P
Men								
Glucose (mmol/L)	4.93 ± 0.48	5.43 ± 0.54 [a]	5.12 ± 0.39 [a,b]	<.0001	5.41 ± 0.82	6.33 ± 0.22 [a]	5.11 ± 0.65 [b]	<.05
IL-6 (pg/mL)	2.31 ± 0.22	2.51 ± 0.17	4.17 ± 0.36 [a,b]	<.0001	2.85 ± 0.81	4.75 ± 1.36	5.56 ± 1.42 [a]	<.05
TNF-α (pg/mL)	1.74 ± 0.09	1.57 ± 0.09 [a]	1.64 ± 0.11	<.05	1.78 ± 0.07	1.59 ± 0.11	1.73 ± 0.16	NS
CRP (mg/L)	1.98 ± 0.41	1.92 ± 0.35	1.83 ± 0.37	NS	2.26 ± 0.86	2.30 ± 0.88	2.03 ± 0.68	NS
Women								
Glucose (mmol/L)	4.60 ± 0.46	5.30 ± 0.41 [a]	4.99 ± 0.42 [a,b]	<.0001	5.30 ± 0.77	5.62 ± 0.30	5.07 ± 0.21 [b]	NS
IL-6 (pg/mL)	2.48 ± 0.25	4.34 ± 0.55 [a]	5.67 ± 0.59 [a,b]	<.0001	4.84 ± 1.15	4.51 ± 0.99	6.99 ± 1.40 [a]	.056
TNF-α (pg/mL)	1.83 ± 0.21	1.71 ± 0.20 [a]	1.76 ± 0.21	<.05	2.52 ± 0.90	2.46 ± 0.88	2.44 ± 0.86	NS
CRP (mg/L)	1.64 ± 0.31	1.68 ± 0.30	1.68 ± 0.31	NS	4.28 ± 0.79	4.71 ± 1.02	4.85 ± 0.99 *	NS

Values are means ± standard deviation. When necessary, statistical analyses were performed on log-transformed values. NGT men: n = 33; IGT men: n = 6; NGT women: n = 36; IGT women: n = 5. NS indicates not significant.

[a] Significantly different from 0 hour.

[b] Significantly different from 4 hours.

[c] P value across time points.

* $P = .0521$ vs 0 hour.

Table 4
Effects of sex and glucose tolerance on postprandial AUC and AUIC of proinflammatory cytokine concentrations

	Sex	Glucose tolerance	Interaction
IL-6 AUC	F(1,75): 7.05 $P = .0097$	F(1,75): 3.0 $P = .0873$	F(1,75): 0.11 $P = .7396$
IL-6 AUIC	F(1,75): 7.05 $P = .0097$	F(1,75): 0.34 $P = .5623$	F(1,75): 4.47 $P = .0379$

P values of 2-way ANOVA with Tukey post hoc analysis.

0 hour) and 8 hours (+136%, $P < .0001$ vs 0 hour and +65%, $P < .0001$ vs 4 hours) after the meal, whereas IGT subjects showed a significant increase only at 8 hours (+93%, $P = .01$ vs 0 hour) after the meal. Although IGT individuals displayed higher plasma IL-6 concentrations at each time point after the meal compared with NGT subjects, between-groups differences failed to reach statistical significance. On the other hand, we noted a statistically significant decrease in plasma TNF-α in NGT subjects (−7.5%, $P < .0001$ vs 0 hour) but not in IGT individuals (−6.8%, $P = .16$ vs 0 hour). There was no variation in plasma CRP in the postprandial state when subjects were separated on the basis of glucose tolerance. Finally, we noted similar patterns of variations when we compared men and women with varying glucose tolerance. As shown in Table 3, irrespective of the glucose tolerance status, there was a significant increase in postprandial IL-6 concentrations in men, whereas in women, this increase in circulating IL-6 concentrations after the high-fat meal only reached statistical significance in NGT women. Furthermore, a 2-way ANOVA (sex × glucose tolerance, Table 4) showed a significant effect of sex ($P < .01$) on postprandial total AUC and AUIC of circulating IL-6 concentrations as well as a sex × glucose tolerance interaction effect ($P < .05$) on postprandial plasma IL-6 concentrations AUIC.

4. Discussion

Postprandial hyperlipidemia is a known metabolic disturbance associated with increased risk of heart disease [30]. We have reported that postprandial hyperlipidemia was associated with abdominal obesity [4] and that higher abdominal visceral fat accumulation in men was a major contributor to the sex difference in postprandial lipemia noted between men and women [7]. More recently, we reported that consumption of a high-fat meal was associated with an increase in plasma IL-6 concentrations and transient decrease in circulating TNF-α concentrations in overweight men [13]. In the present study, we show that plasma IL-6 increases postprandially in both men and women but that this increase is significantly more important in women. We also report that men and women show a similar transient decrease in plasma TNF-α observed 4 hours after food intake. Our results are in line with previous observations that showed that a high-fat meal induced an increase in plasma concentration of IL-6 in lean healthy men [31] as well as in diabetic [14,16] and coronary heart disease [32] patients and detrained individuals [15]. To the best of our knowledge, this is the first study to investigate the sex difference in the postprandial variations of circulating inflammatory markers.

Interleukin-6 is a proinflammatory cytokine that is secreted by many cell types, including immune, endothelial, and muscle cells [33]. Among the potential mechanisms explaining the postprandial IL-6 response, an increase in the production and secretion of IL-6 by leukocytes could be suspected. Indeed, a postprandial increase of leukocyte counts and increased activation of monocytes and neutrophils have been shown postprandially [34]. These changes may correspond to an increased adhesive capacity of these cells contributing to the inflammatory component of atherosclerosis. Unfortunately, these measures were not available in the present study.

Furthermore, to our knowledge, a sex difference in postprandial neutrophil activation and recruitment has not yet been reported. On the other hand, approximately one third of total circulating IL-6 concentrations appears to be secreted by AT [35], with a large contribution from cells of the visceral depot [36]. In the present study, women were characterized by a lower abdominal visceral AT accumulation than men, which does not support a major contribution of visceral AT in the observations we report herein. However, our results also suggest that the higher total fat accumulation may be a more important contributor to higher postprandial circulating IL-6 concentrations in women compared with men. This is suggested by the lack of difference in postprandial plasma IL-6 concentrations between men and women after they had been individually matched for abdominal subcutaneous AT accumulation or total body fat mass, but not after matching individuals on the basis of abdominal visceral AT accumulation. It has been previously shown that there are differences in the gene expression of adipocytes from the subcutaneous and omental depots [36,37] and that hypertrophic fat cells display a higher gene expression than smaller adipocytes [38]. Unfortunately, the potential role of fat cell size and number in the sex difference of postprandial plasma IL-6 concentrations we report herein could not be investigated in the present study.

It is well documented that TNF-α impairs insulin signaling through the inhibition of the tyrosine kinase activity of the insulin receptor [39]. In the present study, we noted a small but significant decrease in plasma TNF-α 4 hours after the high-fat meal in both men and women. These observations are concordant with previous results showing a decrease in postprandial plasma TNF-α concentrations in lean men [31] as well as patients with diet-controlled type 2 diabetes mellitus [16]. In the latter, the authors suggested that the significant decrease in plasma TNF-α concentration could lessen its impact on insulin sensitivity at a time when it is mostly needed, that is, after food intake. On the other hand,

the potential role of IL-6 as an anti-inflammatory cytokine [40] was not investigated in the present analysis and would need to be addressed in future study. However, not all studies have found such a decrease in plasma TNF-α concentrations after food intake [14,15,17,41]; and as indicated in our previous publication [13], the timing of blood sampling during the postprandial period may have prevented us from noting an early increase in plasma TNF-α concentrations that has been previously reported [14].

Equivocal results have been reported on the postprandial variations in plasma CRP concentrations; some studies showed a significant rise in circulating CRP concentrations after food intake in diabetic patients [42], whereas others found that plasma CRP concentrations were slightly decreased at 2 and 4 hours after consumption of a high-fat meal [43]. In the present study, there was no impact of food intake on plasma CRP concentrations in men and women, an observation that is concordant with previous observations in lean individuals [31].

Adiposity and fat distribution cannot be considered the only contributors to low-grade chronic inflammation of abdominally obese individuals. Indeed, there is mounting evidence indicating that glucose could be a potent modulator of circulating inflammatory cytokine concentrations [16,44], an observation that is further supported by the fact that suppression of postprandial glucose elevation after consumption of a high-carbohydrate meal with an α-glucosidase inhibitor is associated with a lower postprandial increase in plasma IL-6 concentrations [45]. In this regard, we compared the postprandial response of TNF-α and IL-6 of subjects separated on the basis of glucose tolerance. We found that, although IGT subjects showed higher plasma IL-6 and TNF-α concentrations compared with NGT individuals, these differences failed to reach statistical significance. A possible explanation for this observation may reside in the fact that glucose concentrations that were found to acutely affect plasma cytokine concentrations were approximately 10 mmol/L. Although characterized by an impairment of glucose tolerance as defined by accepted guidelines [29], plasma glucose concentrations in IGT individuals were approximately 5.7 mmol/L throughout the entire postprandial period, which remains far from concentrations previously studied. This could be explained, at least in part, by the fact that high-fat meals are not known to dramatically affect glycemia. Nevertheless, our results suggest that further research needs to be conducted on the impact of mild to moderate hyperglycemia on the postprandial inflammatory response.

It also appears important to acknowledge that the speculative nature of association studies does not allow the identification of the physiologic role of inflammatory cytokine variations after food intake with certainty. In this regard, it must be emphasized that the hypotheses we put forward in the present article will have to be validated in future studies. Furthermore, the clinical significance of our results with regard to CVD risk remains to be established. Considering that inflammation is associated with CVD risk, it could be argued that increased postprandial IL-6 levels in women compared with men could put them at greater risk to develop CVD. However, we must keep in mind that the association between inflammation and CVD risk is mostly linked to low-grade chronic inflammation in the fasting state; and in this regard, we found no difference in fasting plasma IL-6 concentrations between men and women. Secondly, because of its role in the immune defense system of an individual, the circulating IL-6 concentration is likely to frequently vary; and the impact of such variations on CVD risk is still unknown. The same rationale applies to the acute increase in plasma IL-6 concentration after food intake. On the other hand, in the present study, we suggest that differences in overall adiposity (women > men) is of importance in the greater postprandial response of plasma IL-6 concentrations in women compared with men. In this sense, postprandial changes in plasma inflammatory cytokines could be implicated more closely with the short-term regulation of AT physiology (fatty acid and glucose metabolism), although this assumption will need to be further studied.

In summary, results from our study suggest that consumption of a fat-rich meal induces an increase in plasma IL-6 concentrations in both women and men but that this increase is larger in women. A small and comparable decrease in plasma TNF-α is noted 4 hours after food intake in both sexes. Our results also suggest that glucose tolerance may determine postprandial IL-6 response differently in men and women. Further studies are needed to better understand the relationship between food intake and proinflammatory cytokines and the relevance in CVD prevention or risk in men and women.

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