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# Variations in plasma apolipoprotein C-III levels are strong correlates of the triglyceride response to a high-monounsaturated fatty acid diet and a high-carbohydrate diet☆

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**Abstract**

The objective of this study was to examine how a diet rich in carbohydrates (high-CHO) vs a diet rich in monounsaturated fatty acids (high MUFA) consumed ad libitum modulated plasma apolipoprotein C-III (apo C-III) levels and to examine the extent to which diet-induced changes in plasma apo C-III were associated with concurrent variations in plasma triglyceride (TG) levels. Forty-seven men (mean age, 35.7 ± 11.4 years; body mass index, 29.0 ± 5.1 kg/m$^2$) were randomly assigned to either a high-CHO diet (CHO, 58%; fat, 26%; n = 23) or a high-MUFA diet (CHO, 45%; fat, 40%; MUFA, 22.5%; n = 24), which they consumed for 6 to 7 weeks. Fasting and postprandial lipemia after an oral fat load and fasting plasma apo C-III were measured at the beginning and at the end of the dietary intervention. Ad libitum consumption of the high-CHO diet induced a significant reduction in body weight (−2.6%, $P < .0001$), but had no impact on plasma apo C-III concentrations and on fasting and postprandial plasma TG levels. In contrast, ad libitum consumption of the high-MUFA diet also resulted in a significant reduction in body weight (−2.3%, $P < .01$) as well as in significant reductions in plasma apo C-III (−11%, $P = .05$) and fasting plasma TG (−17%, $P < .01$). Diet-induced variations in plasma apo C-III concentrations were correlated with changes in fasting and postprandial TG levels both in the high-CHO ($r > 0.70$, $P < .001$) and the high-MUFA groups ($r > 0.42$, $P < .05$). These results indicate that variations in plasma apo C-III levels are strong correlates of the fasting and postprandial plasma TG responses to high-MUFA and high-CHO diets.


## 1. Introduction

Hypertriglyceridemia in the general population is quite common with more than 14% of Canadian adults having plasma triglyceride (TG) concentrations above 2.3 mmol/L [1]. It has been demonstrated that apolipoprotein CIII (apo C-III), an essential constituent of very low-density lipoprotein (VLDL) and high-density lipoprotein (HDL), may be an important regulator of intravascular TG metabolism. Apo C-III, a 79–amino acid glycoprotein, is synthesized by the liver and to a lesser extent by the small intestine [2]. Studies in transgenic mice overexpressing apo C-III have demonstrated that apo C-III inhibits the hydrolysis of TG by lipoprotein lipase (LPL) and interferes with the hepatic uptake of lipoproteins causing primary hypertriglyceridemia [3,4]. In humans, prospective studies have shown that level of apo C-III in VLDL is a significant predictor of coronary events [5] and an excellent marker of the metabolic syndrome [6]. Elevated apo C-III levels have also been associated with increased plasma TG concentrations in visceral obese individuals [7], irrespective of an important apo C-III gene polymorphism [8]. Batal et al [9] have demonstrated that the increased plasma apo C-III concentrations observed in hypertriglyceridemic subjects are due

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to the overproduction of apo C-III. Although fibrates effectively decrease the production of apo C-III in the liver through a peroxisome proliferator–activated receptor α down-regulation of hepatic apo C-III messenger RNA levels [6], little is know about the effects of nonpharmacologic therapies such as diet on plasma apo C-III levels.

A growing body of literature has documented the effects of apo C-III gene polymorphisms on TG metabolism in humans [8,10-13]. On the other hand, only a few studies have extended their investigation of apo C-III polymorphisms in relation with diet [14,15] or with the acute effect of a glucose or fat load [8,16]. To the best of our knowledge, the impact of any diet on plasma apo C-III levels per se has yet to be documented. Studies have previously reported a potentially detrimental impact of low-fat diets on plasma TG levels but most of them were conducted under isoenergetic conditions. However, it is now well known that consumption of a low-fat diet under ad libitum conditions, that is, without any imposed energy intake, is closer to a real-life setting and has been shown to be associated with reductions in spontaneous energy intake and subsequent reduction in body weight [17]. The purpose of the present study was therefore to compare the effects of the ad libitum consumption of predetermined and controlled low-fat, high-complex carbohydrates (CHO) diet vs a high-fat, high-monounsaturated fatty acid (MUFA) diet on fasting plasma apo C-III levels. We also investigated the extent to which diet-induced changes in apo C-III levels correlated with the fasting and postprandial TG response to each experimental diet.

## 2. Methods

### 2.1. Subjects

Forty-seven men of a larger group of 65 men (20-55 years of age) constituted the study sample for the present analyses. Participants were recruited in the Québec metropolitan area to participate in this randomized dietary intervention trial with 2 parallel arms examining the effects of low-fat, high-carbohydrate diet (high-CHO) compared to a high-fat, high-monounsaturated fatty acid diet (high-MUFA) on lipid and lipoprotein metabolism in men [18]. Exclusion criteria included endocrine, cardiovascular, hepatic and renal disorders, use of medication known to affect lipid metabolism, smoking, and significant change in body weight within the year that preceded study onset. Individuals with alcohol intake of more than 1 drink per day or more than 7 drinks per week were also excluded from the study. Each participant signed a consent form approved by the Clinical Research Ethical Committee of Laval University.

### 2.2. Experimental design

As described previously [18], subjects were randomized to either a high-CHO diet or a high-MUFA diet, which they consumed for 6 to 7 weeks. Subjects were instructed to maintain their usual level of physical activity throughout the study and to refrain from intense physical exercise for the 3 days preceding the beginning and the end of the study. Participants and staff performing laboratory measures were blinded to dietary treatments. Compliance to the experimental diets was assessed using riboflavin incorporated in the foods and only 2 subjects were excluded from the analysis because of a low compliance.

On weekdays, subjects came to the metabolic unit daily to consume their noon meal under the supervision of at least one member of the staff, at which time they were also given their evening meal and next day's packaged breakfast to take home. On weekends, all meals were provided by the research unit but were packaged to take home. To achieve ad libitum conditions, participants were blinded to the fact that they were receiving food in quantities that met 150% of their habitual daily energy intake as assessed by 3-day food records (2 weekdays and 1 weekend day), obtained at baseline. The breakfast meal represented 20% of the daily energy intake, whereas the lunch and dinner meals each provided 40% of daily energy intake. Subjects were instructed to consume their entire breakfast, but were asked to eat their lunches and dinners on an ad libitum basis, until satiety was met. All leftovers were returned to the laboratory and weighed to calculate actual energy intakes. For participants used to eating between meals, 836.8-kJ snacks were provided on demand. These high-CHO and high-MUFA snacks were prepared in our kitchen and had the same macronutrient composition as that of the 2 experimental diets.

### 2.3. Experimental diets

The nutritional composition of the experimental diets was calculated with the Canadian Nutrient File database (Health Canada, Ottawa, 1997) and the Nutrition Data System for Research (NDS-R) software (Nutrition Coordinating Center, Minneapolis, Database version 4.03_30, 1999). The experimental diets consisted of usual solid foods that were prepared daily in our metabolic kitchen and

Table 1
Energy intake and nutrient composition of the experimental diets

| | High-CHO (n = 23) | High-MUFA (n = 24) |
|---|---|---|
| Energy (kJ) | 12481 ± 2038 | 13054 ± 2209 |
| Proteins (% kJ) | 15.9 | 15.2 |
| Carbohydrates (% kJ) | 58.3 | 44.7* |
| Total fibers (g/1000 kJ) | 14.2 | 10.1* |
| Fats (% kJ) | 25.8 | 40.1* |
| Saturated (% kJ) | 6.0 | 8.2* |
| Monounsaturated (% kJ) | 13.3 | 22.5* |
| Polyunsaturated (% kJ) | 5.1 | 7.6* |
| Cholesterol (mg/1000 kJ) | 105.8 | 110.1 |
| Polyunsaturated-saturated ratio | 0.87 | 0.93 |

The percentage of macronutrients was predetermined in each of the experimental diets. SD for macronutrients and cholesterol, and ratios in experimental diets were virtually equal to zero and are therefore not shown.

* $P \leq .01$, significantly different from the high-CHO experimental diet.

Table 2
Sample 1-day menu for the experimental diets[a]

| | High-CHO diet (g) | High-MUFA diet (g) |
|---|---|---|
| Breakfast | | |
| Orange juice | 183 | 131 |
| Wheat germ muffin | 134 | 108 |
| 1% Fat milk | 361 | 310 |
| Margarine | 5 | 10 |
| Lunch | | |
| Cod fillets | 120 | 150 |
| Barbecue sauce | 47 | 62 |
| Vegetable couscous | 227 | 238 |
| Broccoli | 194 | 97 |
| Whole wheat bread | 68 | - |
| Margarine | 5 | - |
| Strawberry/rhubarb pudding | 232 | 223 |
| Dinner | | |
| Mexican pie (with veal) | 245 | 248 |
| Potatoes | 240 | 112 |
| Cauliflower | 114 | 38 |
| Broccoli | 77 | 39 |
| Peach crumb dessert | 250 | 208 |

[a] Based on a 10460-kJ daily menu.

weighed in individual portions. Both experimental diets were formulated to have a similar food composition and differed mainly with respect to macronutrients (Tables 1 and 2). The diets were composed of nonhydrogenated unsaturated fats, mostly olive oil, with whole grains and vegetables as the main forms of carbohydrates. Simple sugars were used only in the preparation of muffins and some desserts. Alcohol was forbidden during the entire dietary intervention, whereas caffeine-containing beverages were restricted to 2 per day, but subjects had free access to water and to diet, caffeine-free beverages.

### 2.4. Postprandial study

Before and at the end of the dietary intervention, each participant consumed a test meal rich in fat, of similar macronutrient composition to the high-MUFA diet and representing 40% of their daily intake as assessed by the 3-day food record. Participants were asked to eat the meal within 15 minutes. No other food was provided for the subsequent 8 hours until the last postprandial blood sample was collected, but subjects had free access to water throughout the day. Blood samples were collected in the fasting state and at 2, 4, 6, and 8 hours after the consumption of the test meal.

### 2.5. Laboratory methods

At the beginning and at the end of the study, plasma lipid levels were measured as described previously [18] on blood samples collected into tubes containing disodium EDTA (0.03%) after a 12-hour fasting period and at 2, 4, 6, and 8 hours after the consumption of the test meal. Blood samples were immediately centrifuged at 4°C for 10 min at 1500*g* to obtain plasma and were stored at 4°C with benzamidine (0.03%) until analyzed for plasma lipid and apolipoprotein levels. Very low-density lipoproteins were isolated using a fixed angle rotor. Plasma fasting apo C-II and C-III concentrations were measured by nephelometry (BN-100, Dade-Behering, Marburg, Germany) using polyclonal antibodies against human apo C-II and C-III, respectively (Kamiya Biomedical Co, Seattle, Wash). Intra- and interassay coefficients of variation for this measurement were both 6.0% or less as described previously [8]. Postheparin (60 IU/kg body weight) LPL and hepatic lipase (HL) activities were measured using a modification of the method of Nilsson-Ehle and Engert [19], as previously described [20], and expressed as nanomoles of oleic acid released per milliliter of plasma per minute.

### 2.6. Statistical procedures

Data were analyzed using SAS (version 8.2, SAS Institute Inc, Cary, NC). Differences among as well as between dietary groups were tested by the MIXED procedure for repeated measurements after adjustment for body weight changes. Multivariate adjustment for the diet composition at baseline, which was assessed using 3-day food records [18], had no impact on the results. Fasting plasma TG, VLDL-TG, and apo C-II and C-III levels were log-transformed to normalize their distribution before statistical analysis. Areas under the curve of TG were determined by the trapezoid method. Spearman correlation coefficients were calculated to test for associations between diet-induced changes in plasma fasting apo C-III and changes in fasting and postprandial TG levels. Multiple regression analyses were conducted using the general linear model procedure to assess independent correlates of the

Table 3
Anthropometric characteristics of subjects before and after ad libitum consumption of the experimental diets

| | High-CHO diet (n = 23) | | | High-MUFA diet (n = 24) | | | Between-diet |
|---|---|---|---|---|---|---|---|
| | Pre | Post | $P^a$ | Pre | Post | $P^a$ | $P^b$ |
| Weight (kg) | 87.3 ± 12.6 | 84.9 ± 12.2 | <.0001 | 88.6 ± 16.6 | 86.8 ± 16.2 | <.01 | .45 |
| Waist circumference (cm) | 93.4 ± 13.4 | 90.7 ± 11.8 | <.001 | 96.5 ± 16.9 | 94.7 ± 16.5 | .01 | .36 |
| Body mass index (kg/m$^2$) | 28.6 ± 4.4 | 27.8 ± 4.4 | <.0001 | 29.3 ± 5.7 | 28.7 ± 5.6 | <.01 | .51 |

Values are mean ± SD.
[a] *P* value related to the repeated-measure analysis (within-diet effect) of the absolute change compared with the baseline value.
[b] *P* value related to the comparison of the absolute change between the 2 diets (between-diet effect).

Table 4
Effects of both diets on fasting lipid profile and on postprandial triglyceridemia

| | High-CHO diet (n= 23) | | | High-MUFA diet (n = 24) | | | High-CHO vs High-MUFA |
|---|---|---|---|---|---|---|---|
| | Pre | Post | $P^a$ | Pre | Post | $P^a$ | $P^b$ |
| Plasma cholesterol (mmol/L) | 4.30 ± 0.91 | 3.67 ± 0.85 | <.001 | 4.40 ± 0.89 | 3.74 ± 0.64 | <.001 | .92 |
| VLDL-C (mmol/L) | 0.40 ± 0.27 | 0.38 ± 0.25 | .73 | 0.44 ± 0.17 | 0.34 ± 0.16 | <.05 | .06 |
| LDL-C (mmol/L) | 2.84 ± 0.75 | 2.32 ± 0.69 | <.001 | 3.00 ± 0.84 | 2.47 ± 0.59 | <.001 | .77 |
| HDL-C (mmol/L) | 1.06 ± 0.15 | 0.97 ± 0.19 | <.05 | 0.96 ± 0.14 | 0.93 ± 0.18 | .67 | .17 |
| Plasma TG (mmol/L) | 1.24 ± 0.62 | 1.23 ± 0.64 | .78 | 1.33 ± 0.43 | 1.08 ± 0.42 | <.01 | <.05 |
| VLDL-TG (mmol/L) | 0.88 ± 0.54 | 0.88 ± 0.57 | .85 | 0.95 ± 0.41 | 0.76 ± 0.40 | <.05 | <.05 |
| Postprandial TG (mmol × min/L) | 945.1 ± 456.4 | 883.6 ± 426.3 | .48 | 953.1 ± 316.3 | 813.1 ± 320.7 | .35 | .19 |
| Apo C-II (mg/L) | 36.9 ± 14.4 | 34.5 ± 12.0 | .42 | 36.1 ± 12.1 | 33.5 ± 10.3 | .07 | .44 |
| Apo C-III (mg/L) | 93.7 ± 35.0 | 87.1 ± 34.2 | .91 | 94.7 ± 22.5 | 84.5 ± 24.9 | .05 | .14 |
| Apo C-II/C-III ratio | 0.40 ± 0.10 | 0.41 ± 0.12 | .30 | 0.39 ± 0.10 | 0.40 ± 0.09 | .93 | .35 |
| HL (nmol/mL per minute)[c] | 177.5 ± 72.8 | 166.8 ± 56.7 | <.05 | 186.5 ± 68.2 | 168.5 ± 68.1 | <.01 | .64 |
| LPL (nmol/mL per minute)[c] | 79.4 ± 37.8 | 72.6 ± 28.4 | .93 | 74.1 ± 42.7 | 69.0 ± 38.3 | .96 | .97 |
| LPL/HL ratio | 0.55 ± 0.39 | 0.50 ± 0.28 | .94 | 0.50 ± 0.42 | 0.58 ± 0.67 | .26 | .35 |

Values are mean ± SD.

[a] $P$ value related to the repeated-measure analysis (within-diet effect) based on the absolute change compared with the baseline value after adjustment for concurrent changes in body weight.

[b] $P$ value related to the comparison of the absolute change between the 2 diets (between-diet effect) after adjustment for changes in body weight.

[c] n = 23 for HL and lipoprotein lipase in the high-MUFA diet.

diet-induced response in plasma apo C-III, fasting TG, and postprandial TG concentrations. Differences were considered statistically significant at $P < .05$.

## 3. Results

The group of 47 men who participated in the postprandial studies was comparable to the entire study group of 65 men in terms of obesity indices and plasma lipid profile at baseline (data not shown). Participants randomized to the high-CHO and high-MUFA dietary groups were of similar age (mean age, 35.7 ± 11.4 years), had comparable physical characteristics (Table 3), and a similar baseline lipid profile (Table 4). As reported previously [18], ad libitum consumption of the experimental diets led to moderate but significant reductions in body weight and in waist circumference that were comparable between the high-CHO and high-MUFA diets (Table 3).

The high-CHO diet induced a significant reduction in HL activity (6%) but had no significant effect on fasting plasma apo C-III levels, on postheparin LPL, and on plasma and VLDL-TG levels. As reported previously [18], the high-CHO dietary group was associated with significant reductions in plasma cholesterol (−14%), LDL-C (−18%), and HDL cholesterol (HDL-C) (−8%) concentrations. Ad libitum consumption of the high-MUFA diet led to significant reductions in fasting plasma apo C-III (−11%), TG (−17%), and VLDL-TG levels (−18%) and in HL activity (−10%). The high-MUFA diet significantly reduced plasma cholesterol (−14%), VLDL-C (−24%), and low-density lipoprotein cholesterol (LDL-C) levels (−15%), but had no impact on plasma HDL-C levels and LPL activity. Fig. 1 depicts the individual diet-induced variations in plasma apo C-III in each dietary group.

The comparison of the impact of the 2 experimental diets on plasma lipid and apolipoprotein levels as well as on postheparin lipase activities is also shown in Table 4. The

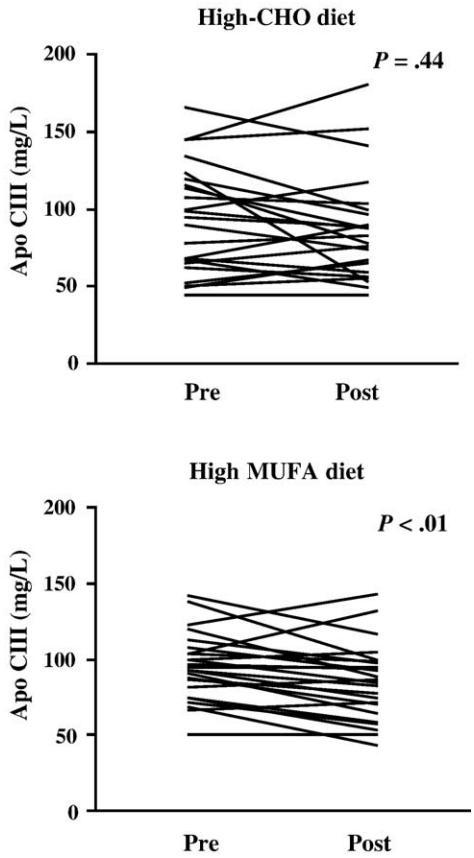


Fig. 1. Individual diet-induced changes in plasma apo C-III levels in each dietary group.

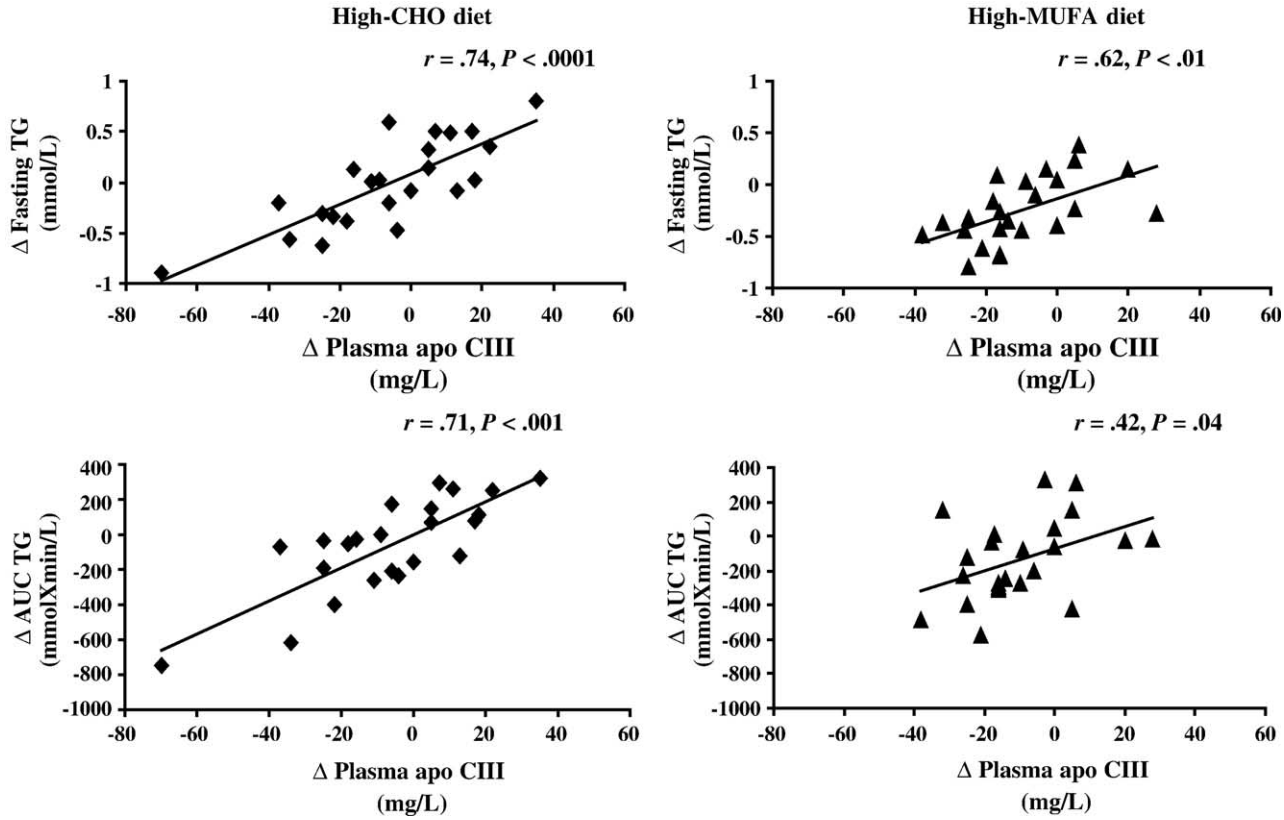


Fig. 2. Correlations between diet-induced changes in plasma apo C-III levels and changes in plasma fasting and postprandial TG levels in each dietary group.

high-MUFA diet was associated with a significantly greater reduction in plasma TG and VLDL-TG levels compared with the high-CHO diet. Changes in other characteristics of the lipoprotein-lipid profile including apo C-II and C-III levels and in the lipase activities were comparable between the 2 dietary groups. Changes in the apo C-II/C-III ratio were also not statistically different between the 2 dietary groups.

In both dietary groups, as shown in Fig. 2, diet-induced variations in plasma apo C-III levels were associated with changes in fasting plasma TG concentrations (high-CHO, $r = 0.74$, $P < .0001$; high-MUFA, $r = 0.62$, $P < .01$) and variations in postprandial TG levels (high-CHO, $r = 0.71$, $P < .001$; high-MUFA, $r = 0.42$, $P = .04$). Although there was no mean change in plasma apo C-II levels after the 2 diets, there were important interindividual variations in the response of apo C-II to both diets. We found that diet-induced variations in plasma apo C-III concentrations also correlated with concurrent variations in plasma apo

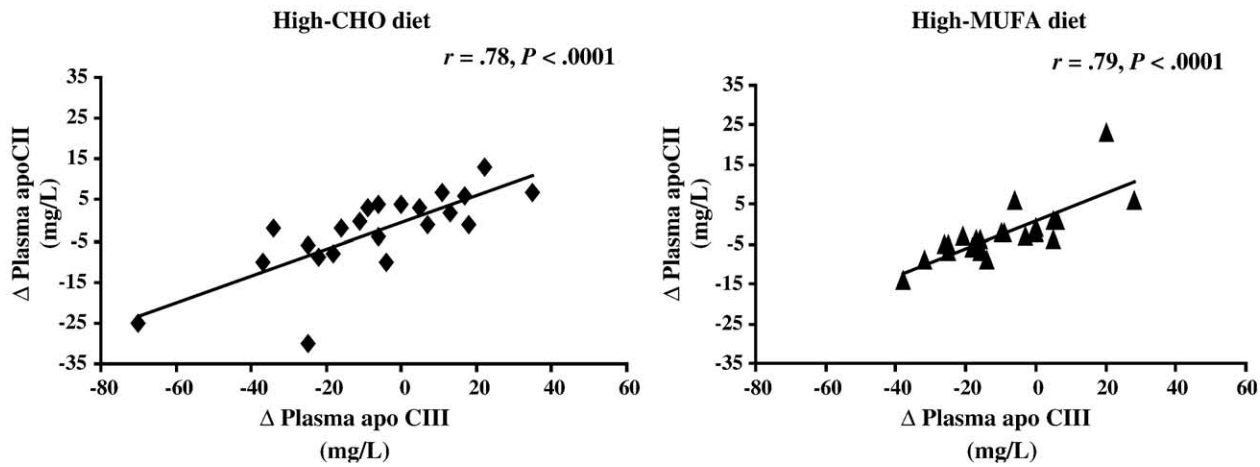


Fig. 3. Correlations between diet-induced changes in plasma apo C-III levels and apo C-II levels in each dietary group.

C-II levels (Fig. 3). No relationship was observed between changes in apo C-III levels and changes in postheparin LPL and HL activities in either dietary group (not shown).

Multiple regression analyses of all study participants showed that diet-induced variations in apo C-II levels (54.9%, $P < .0001$) and in body weight (7.3%, $P < .001$), age (3.4%, $P = .02$), and the experimental dietary group (high-CHO vs high-MUFA, 2.3%, $P = .05$) accounted for more than 60% of the diet-induced variation in plasma apo C-III concentrations. In this model, the difference in energy intake before vs after the experiment also tended to contribute to the apo C-III response to the diets (2.1%, $P = .06$). Finally, diet-induced changes in plasma apo C-III concentrations correlated with variations in both fasting plasma TG concentrations (3.9%, $P = .06$) and postprandial TG concentrations (9.1%, $P < .05$) in a model adjusted for age, experimental dietary group, and diet-induced changes in waist circumference, apo C-II, LPL, and HL activities.

## 4. Discussion

Hypertriglyceridemia has been associated with higher risk of cardiovascular disease [21]. Apo C-III, a major surface constituent of VLDL and HDL, is believed to play an important role in the development of hypertriglyceridemia [22]. To the best of our knowledge, our study is the first to document the impact of any diet consumed ad libitum on apo C-III levels and the extent to which diet-induced variations in apo C-III concentrations account for concurrent changes in fasting and postprandial triglyceridemia. We found that ad libitum consumption of a high-CHO diet had no effect on mean plasma apo C-III levels, whereas the high-MUFA diet was associated with significantly reduced apo C-III concentrations. In both dietary groups, however, variations in fasting TG levels were highly correlated to variations in plasma apo C-III, suggesting that diet-induced variations in apo C-III concentrations may have been responsible at least partly for the differential impact of the high-MUFA and high-CHO diets on fasting TG levels.

Numerous studies have investigated the acute or prolonged effect of individual meals or diet on plasma lipid levels according to various polymorphisms in the apo C-III gene [8,14-16]. The *Sst*I polymorphism within the apo AI-CIII-AIV gene cluster is the variant site that has been most strongly correlated with variations in plasma TG levels and in coronary artery disease risk [12], the rare S2 allele being associated with raised plasma apo C-III levels and hypertriglyceridemia [8,10,12,13]. However, Waterworth et al [16] found that the postprandial TG response to an oral saturated fat load was not modulated by the *Sst*I polymorphisms among participants of the European Atherosclerosis Research Study II. In healthy young men, the *Sst*I polymorphism accounted for only 5% of the LDL-C response to the isoenergetic consumption of a high-MUFA diet [14]. These data suggest that the *Sst*I polymorphism in the apo C-III gene may not be considered as an important modulator of the diet-induced variations in plasma TG levels. We could not study the impact of the *Sst*I polymorphism on diet-induced plasma TG levels in the present study because of the lack of adequate statistical power attributable to a low prevalence of this polymorphism among white populations, which has been shown to vary from 8% to 21% [15].

High-CHO diets have long been promoted as the primary dietary strategy for the prevention of cardiovascular disease. However, their potentially undesirable impact on plasma TG levels and other features of the metabolic syndrome such as lowered plasma HDL-C levels and small dense LDL particles has fueled the debate as to whether low-fat diets should still be advocated as the best dietary recommendation [23,24]. On the other hand, diets rich in MUFA have generally not been associated with undesirable changes in plasma TG and HDL-C levels, although this is not a unanimous finding [25,26]. A strong positive association between triglyceridemia and plasma apo C-III levels has been observed in healthy individuals and patients with type 2 diabetes [27]. In our study, baseline plasma apo C-III concentrations correlated strongly with fasting and postprandial TG levels as well as with age, body mass index, and waist circumference.

In an attempt to better understand the differential impact of various diets on TG metabolism, we undertook the study of the apo C-III as a modulator of the diet-induced changes in fasting and postprandial TG levels. We have previously reported in the same cohort of men that ad libitum consumption of a high-CHO diet, when associated with moderate but significant weight loss, was not associated with fasting and postprandial hypertriglyceridemia, whereas the high-MUFA diet significantly reduced fasting TG levels [28]. Accordingly, plasma apo C-III concentrations were not altered in the high-CHO group but were significantly reduced in the high-MUFA group. In addition, diet (high-CHO vs high-MUFA) was a significant determinant of changes in apo C-III levels after adjustment for diet-induced weight loss and age of study participants. These results suggest that changes in apo C-III levels may represent one of the key factors responsible for the discrepancy in the TG response to a high-MUFA and a high-CHO diet. However, it must be stressed that our results do not exclude the possibility that aside from apo C-III, other factors that have yet to be investigated may also be responsible in the differential impact of both experimental diets on TG levels.

Stable isotope kinetic studies in humans have demonstrated that the hypertriglyceridemia associated with elevated apo C-III levels might originate from the overproduction of apo C-III [9]. The mechanisms involved are not fully understood but investigators have hypothesized that the overproduction of apo C-III, which is directly reflected by increased plasma and VLDL–apo C-III levels, may hamper the lipolytic processing and catabolism of TG-rich lipoproteins (TRL), particularly in hypertriglyceridemic subjects [9]. Indeed, transgenic mice overexpressing human and mouse apo C-III have been shown to have markedly

inhibited LPL activity, thus leading to the accumulation of fasting and postprandial TRL that are less rapidly catabolized [4]. Furthermore, apo C-III gene knockout mice remained hypotriglyceridemic even when fed a high-fat diet [2,29]. In addition, patients with apo C-III deficiency display an accelerated conversion of VLDL to IDL and LDL resulting in lowered TRL levels [30]. These in vitro and in vivo studies confirmed that LPL-mediated lipolysis of TRL is largely modulated by apo C-III levels [30]. Whereas apo C-III is an inhibitor of LPL, apo C-II acts as its cofactor [31]. Thus, the apo C-II/C-III ratio has been suggested to reflect the ability of LPL to exert its lipolytic functions on chylomicrons and VLDL [32]. Neither of the 2 experimental diets had any effect on the ratio of apo C-II to C-III, which is consistent with the absence of effect of the 2 diets on LPL activity. However, the high-MUFA diet was associated with a lowered post-heparin HL activity. These observations are inconsistent with the reported increase in LPL and HL activities after the isoenergetic consumption of a high-fat diet by healthy normolipidemic men [33]. It is believed that high LPL activity coupled with a low HL activity results in a cardioprotective lipid profile [34]. In our study, reduction in apo C-III levels associated with lowered HL activity and plasma TG levels after the ad libitum consumption of the high-MUFA diet suggests that compared with a high-CHO diet, the high-MUFA diet may be more effective in beneficially modulating TG metabolism, thus contributing to an overall lowering of cardiovascular disease risk.

One of the limitations of the present study is its parallel experimental design. However, because weight loss was expected with the high-CHO diet and not necessarily with the high-MUFA diet, a crossover design could have imposed a rather peculiar analytical problem because body weight at the start of each diet would most likely have been different.

In conclusion, diet-induced change in apo C-III appears as one of the key factors modulating the differential effect of high-CHO and high-MUFA diets on fasting and postprandial TG levels. Kinetic studies of apo C-III are needed to better assess the underlying mechanisms through which a high-MUFA diet may induce hypotriglyceridemia compared with a high-CHO diet.

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