Original Article

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Effects of lipoprotein lipase gene variations, a high-carbohydrate low-fat diet, and gender on serum lipid profiles in healthy Chinese Han youth

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Summary **A high-carbohydrate low-fat (HC/LF) diet and lipoprotein lipase gene (*LPL*) Ser447Stop and *Hind* III polymorphisms have separately been found to be associated with triacylglycerol (TG) and high density lipoprotein cholesterol (HDL-C). This study sought to test the effects of *LPL* polymorphisms and an HC/LF diet on the serum lipid profile of Chinese with a lower incidence of coronary artery disease (CAD) consuming a diet with less fat and more carbohydrates. Fifty-six healthy subjects (22.89 ± 1.80 years) were given a control diet of 30.1% fat and 54.1% carbohydrates for 7 days, followed by an HC/LF diet of 13.8% fat and 70.1% carbohydrate for 6 days; there were no changes in the fatty acid composition or restrictions on total energy. Serum lipid profiles at baseline, before and after the HC/LF diet, and *LPL* polymorphisms were analyzed. After 6 days of the HC/LF diet, TG and the homeostasis model assessment of insulin resistance (HOMA-IR) index were found to increase only in females with S447S. No decrease in HDL-C was noted. In subjects with *Hind* III polymorphism, increased TG was found in all females but not in males. Increased HDL-C, together with apolipoprotein (apo) AI, was found in male H- carriers but not in males with H+/H+ and females. In conclusion, *LPL* Ser447Stop and *Hind* III polymorphisms modified the effects of an HC/LF diet on the serum lipid profiles of a young Chinese population in different ways. Effective strategies for dietary interventions targeted at younger populations should take into account the interplay between genetic polymorphisms, diet, and gender.**

Keywords: High-carbohydrate low-fat diet, lipoprotein lipase, SNP, serum lipids, glucose, insulin resistance

1. Introduction

Numerous studies have indicated that substitution of fat with carbohydrates as dietary energy is an effective way to reduce serum low density lipoprotein cholesterol (LDL-C) (*1*), one of the key factors for coronary artery disease (CAD). However, a high-carbohydrate low-fat (HC/LF) diet can lead to hypertriacylglycerolemia (HPTG) by elevating triglycerides (TG) and decreasing high density lipoprotein cholesterol (HDL-C) in serum, both of which are considered to be key risk factors for CAD (*1*,*2*). However, the mechanism of changes in the lipid profile after an HC/LF diet has yet to be fully elucidated. Genetic factors, and their interaction with diets, are believed to play important roles in the development of carbohydrate-induced HPTG and subsequently lead to CAD (*2*,*3*). Previous studies on carbohydrate-induced HPTG mainly focused on middle-aged or elderly subjects since CAD is often

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diagnosed after 45 years of age (*4*). Few efforts have been made to study younger populations, whose risk of CAD has risen steadily in recent decades (*5*).

Abundant evidence provided by epidemiologic studies has indicated that HPTG is rare and the incidence of CAD is much lower in rice-eating populations of the world and particularly in Chinese (*6,7*). There is ample documentation that the Chinese population has a diet with more carbohydrates and less fat, including less saturated, monounsaturated, and polyunsaturated fat (*8,9*). Additionally, the Chinese population has been found to have a better lipid profile, including less total cholesterol (TC), more HDL-C, and a higher apolipoprotein (apo) AI/B100 ratio (*10*). These findings highlight the importance of environmental, lifestyle, and potential genetic factors in modulating the lipid response to carbohydrate consumption.

Lipoprotein lipase (LPL) catalyzes the hydrolysis of TG in chylomicrons (CM) and very low density lipoprotein (VLDL) to promote cellular uptake of lipoproteins and is thus a key enzyme influencing serum TG. Several polymorphisms of the LPL gene (*LPL*) have been found to be linked to abnormalities of the serum lipid profile and also to the development of CAD (*11*). *LPL* Ser447Stop polymorphism results from a C to G transition at position 1595 in exon 9 that removes two amino acid residues at the C-terminal of LPL. The truncated LPL protein has enhanced LPL activity and has been found to be related to decreased TG and increased HDL-C (*12,13*). *LPL Hind* III polymorphism occurs in intron 8 with a T to G transition at position +495. The H+ allele has been reported to be associated with elevated TG, lower HDL-C, and an increased risk of CAD (*14,15*). However, little is known about the interaction between these two *LPL* polymorphisms and an HC/LF diet and their effects on the serum lipid profiles of young subjects and particularly Chinese.

Previous studies by the present authors have found that polymorphisms in the key enzymes and lipoproteins involved in lipid metabolism, such as *Taq*IB polymorphism of the cholesterol ester transfer protein (*CETP*) gene (*16*) and polymorphism of sterol regulatory element-binding protein (SREBP) genes (Zhang *et al.*, accepted by "Applied Physiology, Nutrition and Metabolism"), may modify the impact of an HC/LF diet on the lipid profile. Therefore, this study sought to test the hypothesis that *LPL* polymorphisms of *Hind* III and Ser447Stop affect changes in serum lipid levels in response to an HC/LF diet. Since *LPL* polymorphisms were found to be associated with insulin resistance (IR) (*17*), effects of the polymorphisms on the response of insulin and IR were also studied.

2. Methods

2.1. *Study population*

Volunteers were recruited *via* an advertisement seeking healthy young students at Sichuan University. Recruitment criteria included no history of metabolic disease, understanding of the procedures involved, and provision of written consent. Volunteers who were on any lipid-lowering drugs or hormones, who consumed alcohol or smoked, or whose physical activity or sleep times varied widely were excluded. Of 209 Chinese Han students recruited, 60 met the above criteria for inclusion in the study. Four subjects dropped out due to personal reasons while the remaining 56 subjects (27 males and 29 females) completed the study. The study protocol was approved by the Human Ethics Committee of Sichuan University.

2.2. *Diets*

This study consisted of 7 days of a control diet as a wash-out period, followed by 6 days with intervention in the form of an HC/LF diet. Each diet was designed to have constant ratios of carbohydrates, proteins, and fat in relation to total energy and the control and HC/LF diets had a similar composition of fatty acids (Table 1). All meals were prepared from foods regularly consumed by locals and were provided by the Department of Nutrition, West China Hospital, Sichuan University. There were no restrictions on total energy

Table 1. Daily intake and fatty acid concentrations during diet consumption

Items	Control diet	HC/LF diet
Protein (% of total energy intake)	15.8 ± 1.8	16.2 ± 1.6
Total fatty acids (% of total energy intake)	30.1 ± 3.6	13.8 ± 1.4
Saturated fatty acids	7.5 ± 0.9	3.6 ± 0.5
Monounsaturated fatty acids	16.1 ± 1.4	7.3 ± 0.8
Polyunsaturated fatty acids	6.4 ± 1.5	2.8 ± 0.3
Carbohydrates (% of total energy intake)	54.1 ± 2.4	70.1 ± 2.8
Fiber (g/d)	11.6 ± 2.3	15.4 ± 3.6
Fatty acid composition (% of total fatty acids by energy intake)		
Palmitic fatty acids (16:0)	15.9 ± 4.4	18.9 ± 5.8
Palmitoleic fatty acids (16:1)	2.1 ± 0.7	2.0 ± 0.4
Stearic fatty acids (18:0)	6.9 ± 1.3	7.4 ± 0.9
Oleic fatty acids (18:1)	30.7 ± 6.5	32.1 ± 3.7
Linoleic fatty acids (18:2)	13.2 ± 3.3	17.0 ± 5.1

in each meal. All subjects ate to satiation as usual. All subjects were informed not to consume anything else in addition to the prepared meal except water. A daily checklist was used to assess each subject's compliance with the study design.

2.3. *Blood collection and laboratory analysis*

Blood samples after 12 hours of fasting were collected on the morning of the first day of the study, the morning of the day the HC/LF diet started, and the morning of the day after the HC/LF diet concluded. Serum TG, TC, glucose, HDL-C, and LDL-C were analyzed using enzymatic methods described previously (*18*). Apo B100 and apo AI were measured by immunoturbidimetry with a Hitachi 7070 Analyzer and insulin concentration was determined by electrochemical luminescence with a Roche E170 Analyzer. The homeostasis model assessment of insulin resistance (HOMA-IR) index was calculated as (insulin × glucose)/22.5. The inter- and intra-assays coefficients of variation were less than 6%. Each variable of a given sample was measured three times, and the average value of the three measurements was used in statistical analysis.

2.4. *Genetic analysis*

Polymerase chain reaction (PCR)-based restriction fragment length polymorphism (RFLP) analysis was used to screen for *LPL* Ser447Stop and *Hind* III polymorphisms using the primers and procedures described previously (*12,14*). The enzyme *Mnl* I was used to detect Ser447Stop polymorphism. Homozygotes of the mutation were designated X447X, homozygotes of the wild type were designated S447S, and heterozygotes were designated S447X. *Hind* III polymorphism was detected by digestion of PCR products with *Hind* III. Homozygotes of the mutation were designated H-/H-, homozygotes of the wild type were designated H+/H+, and heterozygotes were designated H+/H-. Because of the small sample size, S447X and X447X were combined and designated 447X carriers (447XC), and heterozygotes of H+/H- and homozygotes of H-/H- were pooled and designated H- carriers (H-C) for further analyses.

2.5. *Statistical analysis*

Gene-counting was used to calculate the frequencies of genotypes and alleles. SPSS (16.0) was used for statistical analysis. A χ^2 test was used to evaluate the gender difference in the frequency of *LPL* Ser447Stop and *Hind* III. Data were expressed as mean ± S.D. All variables were tested for normality before analyses. The value of TG was log-transformed to reduce skewness. One-way ANOVA was used to evaluate differences in variables among subjects of each gender with different genotypes and the least significant difference (LSD) was used for post-hoc multiple comparisons. A paired *t*-test was used to analyze differences in variables before and after the HC/LF diet. A value of $p < 0.05$ was considered to be statistically significant.

3. Results

3.1. *Frequencies of LPL polymorphisms*

Genotype and allele frequencies of Ser447Stop and *Hind* III polymorphisms of *LPL* in the study population are shown in Table 2. Genotype distributions of the two polymorphisms were found to be in accordance with Hardy-Weinberg equilibrium expectations (p = 0.105 for Ser447Stop and p = 0.075 for *Hind* III). There were no differences in genotype frequencies of the two polymorphisms in males and females (p = 0.639 for Ser447Stop and p = 0.830 for *Hind* III).

3.2. *Effects of an HC/LF diet on lipid and glucose metabolism in subjects with different LPL Ser447Stop genotypes*

Table 3 shows lipid profiles in subjects with different *LPL* Ser447Stop genotypes at baseline, after the wash-

Table 2. Allele and genotype frequencies of *LPL* Ser447Stop and *Hind* III polymorphisms

	Total (n = 56) n (%)	Males (n = 27) n (%)	Females (n = 29) n (%)
Ser447Stop			
S447S	45 (80.4%)	21 (77.8%)	24 (82.8%)
S447X	9 (16.0%)	4 (14.8%)	5 (17.2%)
X447X	2 (3.6%)	2 (7.4%)	0
Hind III			
H+/H+	34 (60.7%)	16 (59.3%)	18 (62.1%)
H+/H-	16 (28.6%)	6 (22.2%)	10 (34.5%)
H-/H-	6 (10.7%)	5 (18.5%)	1 (3.4%)
Allele frequency			
S447	0.88	0.85	0.91
447X	0.12	0.15	0.09
H+	0.75	0.67	0.79
H-	0.25	0.33	0.21

out diet, and after the HC/LF diet. There were no statistically significant differences in variables from the baseline for subjects with the genotype S447S and genotype 447XC who were either male or female (data not shown); the same was true after the wash-out diet and after the HC/LF diet. However, males with the 447X allele had a significantly lower glucose level compared to the level before the HC/LF diet, but males with the S447S genotype did not have a lower glucose level after the HC/LF diet intervention. Females with S447S were found to have increased TG and insulin and a higher HOMA-IR as well as decreased LDL-C in comparison to values after the wash-out diet. Therefore, the increased TG and insulin and higher HOMA-IR level were presumably modified by the *LPL* Ser447Stop polymorphism in healthy females.

3.3. *Effects of an HC/LF diet on lipid and glucose metabolism in subjects with different LPL Hind III genotypes*

Table 4 shows lipid profiles at baseline, after the wash-out diet, and after the HC/LF diet for subjects with different *LPL Hind* III genotypes. There were no significant differences in variables at the baseline and after a 13-day diet intervention for subjects with H+/H+ and H-C who were either male or female (data not shown); the 13-day diet intervention consisted of 7 days of a wash-out diet followed by 6 days of the HC/LF diet. However, females in both two genotype subgroups were found to have increased TG compared to the level before the HC/LF diet, but males had no such increase. Notably, only male H-allele carriers were found to have increased HDL-C and elevated ApoAI after the HC/LF diet. Female H+/H+ homozygotes had increased insulin and a higher HOMA-IR index after the HC/LF diet intervention while female H- allele carriers had significantly decreased glucose. Therefore, HDL-C did not decrease in the young Chinese population on an HC/LF diet. In contrast, male carriers of *LPL Hind* III H- had increased HDL-C while on the HC/LF diet.

4. Discussion

Most previous studies on carbohydrate-induced HPTG focused on middle-aged or elderly subjects because CAD is often diagnosed after 45 years of age (*4*). Much less effort has been made study younger populations,

Table 3. BMI and serum biochemistry of subjects with different *LPL* Ser447Stop genotypes before and after an HC/LF diet

Variables	Males		Females	
	S447S (n = 21)	447XC (n = 6)	S447S (n = 24)	447XC (n = 5)
Frequency (%)	77.78	22.22	82.76	17.24
Age (years)	23.14 ± 2.06	22.33 ± 1.51	22.60 ± 1.83	22.60 ± 0.55
BMI (kg/m^2)				
Before HC/LF diet	22.03 ± 3.87	20.64 ± 5.18	20.13 ± 2.64	20.15 ± 2.29
After HC/LF diet	21.93 ± 3.83	20.45 ± 5.19	20.06 ± 2.63	19.94 ± 2.14
TG (mg/dL)[c]				
Before HC/LF diet	84.43 ± 41.35	71.30 ± 17.84	66.12 ± 15.29	63.32 ± 21.07
After HC/LF diet	92.75 ± 42.39	69.70 ± 15.56	79.48 ± 23.42[b]	78.03 ± 25.05
TC (mg/dL)				
Before HC/LF diet	134.26 ± 23.54	125.68 ± 15.62	138.77 ± 23.42	143.29 ± 19.08
After HC/LF diet	119.13 ± 19.02[b]	119.17 ± 13.17[a]	132.65 ± 18.58[a]	138.08 ± 28.13
LDL-C (mg/dL)				
Before HC/LF diet	68.38 ± 22.36	63.39 ± 13.63	69.61 ± 21.49	74.35 ± 13.91
After HC/LF diet	53.43 ± 16.22[b]	54.63 ± 14.47[a]	57.77 ± 14.49[b]	67.85 ± 22.71
HDL-C (mg/dL)				
Before HC/LF diet	48.03 ± 11.24	51.31 ± 7.05	58.80 ± 10.70	59.71 ± 9.54
After HC/LF diet	52.32 ± 10.81	58.60 ± 10.97	60.14 ± 9.90	58.87 ± 8.57
Glucose (mg/dL)				
Before HC/LF diet	79.43 ± 9.24	87.21 ± 6.54	78.94 ± 9.81	80.84 ± 7.71
After HC/LF diet	78.44 ± 6.30	77.24 ± 7.38[a]	77.72 ± 7.56	76.19 ± 5.88
Insulin (μU/mL)				
Before HC/LF diet	5.70 ± 5.11	4.13 ± 2.26	4.22 ± 2.78	6.22 ± 4.13
After HC/LF diet	5.93 ± 3.43	5.22 ± 2.99	6.02 ± 3.17[b]	6.02 ± 3.40
HOMA-IR				
Before HC/LF diet	1.15 ± 1.06	0.91 ± 0.53	0.84 ± 0.59	1.23 ± 0.74
After HC/LF diet	1.17 ± 0.75	1.02 ± 0.60	1.17 ± 0.65[b]	1.14 ± 0.66
ApoAI (mg/dL)				
Before HC/LF diet	166.95 ± 29.72	169.33 ± 15.58	191.75 ± 22.97	195.20 ± 21.38
After HC/LF diet	168.48 ± 26.66	177.50 ± 21.95[a]	195.88 ± 20.84	198.40 ± 29.11
ApoB100 (mg/dL)				
Before HC/LF diet	59.81 ± 21.70	51.67 ± 11.94	58.04 ± 16.51	64.40 ± 16.83
After HC/LF diet	58.43 ± 23.06	52.50 ± 13.16	57.63 ± 14.96	67.00 ± 23.73

[a] $p < 0.05$ when compared to subjects with the same genotype before the HC/LF diet; [b] $p < 0.01$ when compared to subjects with the same genotype before the HC/LF diet; [c] The value of TG was log-transformed for statistical analysis.

whose risk of CAD has risen steadily in recent decades (*5*). An HC/LF diet may have different effects in younger populations than in middle-aged or older populations; this is especially true for Chinese, who generally have a better lipid profile and consume a diet containing less fat and more carbohydrate (*8*). To the extent known, the present study is the first attempt to investigate the effects of an HC/LF diet on the serum lipid profiles of young, healthy Chinese subjects with different genotypes of *LPL* Ser447Stop and *Hind* III polymorphisms.

The time an HC/LF diet takes to induce HPTG depends on the composition of dietary carbohydrates as part of energy intake, the types of carbohydrates, the physical form of those carbohydrates in the diet, the fiber content in the diet, and even the ethnicity of the subjects (*1*). Previous studies sought to introduce HPTG with an HC/LF diet in 48 hours to several months (*1*). However, Ginsberg *et al.* noted that "during the high carbohydrate period, plasma TG was found to increase in most subjects for 5-7 days before establishing a new plateau (*19*)". In a recent study, Ji (*20*) used a 7-day interval to compare the postprandial lipemic response after a low-fat meal and a high-fat meal consumed by non-obese men with the -1131T>C polymorphism of the apo A5 gene. Holmback *et al.* (*21*) used a 6-day period for HC/LF diet adaptation. Since studies have shown that plasma TG rises and then plateaus after 5-7 days of an HC/LF diet (*22*,*23*), the present study used an intervention of 6 days with a regular diet for 7 days as a wash-out period.

An HC/LF diet (*1*,*2*) and *LPL* Ser447Stop (*12*,*13*) and *Hind* III (*14*,*15*) polymorphisms have been reported to be associated with variations in HDL-C and TG. The present study found no significant differences in HDL-C and TG as well as other serum lipid parameters in carriers and non-carriers of the *LPL* Ser447Stop or *Hind* III mutation after 7 days on a control diet as a wash-out period, followed by 6 days of an HC/LF diet (Tables 3 and 4). A number of factors that are known to be associated with the effects of *LPL* polymorphisms on the lipid profile may account for this finding, including matching for environmental and other genetic factors in carriers and non-carriers of the mutations (*12*,*24*) as well as the small study size. Since most of the genetic and environmental factors for each individual were constant in the 6-day HC/LF diet, a *t*-test was used to compare serum biochemical profiles before and after

Table 4. BMI and serum biochemistry of subjects with different *LPL Hind* III genotype s before and after an HC/LF diet

Variables	Males		Females	
	H+/H+ (*n* = 16)	H-C (*n* = 11)	H+/H+ (*n* = 18)	H-C (*n* = 11)
Frequency (%)	59.26	40.74	62.07	37.93
Age (years)	23.50 ± 2.03	22.18 ± 1.60	23.11 ± 1.97	22.36 ± 0.92
BMI (kg/m^2)				
Before HC/LF diet	21.29 ± 3.00	22.35 ± 5.47	20.33 ± 2.62	19.82 ± 2.51
After HC/LF diet	21.17 ± 2.95	22.23 ± 5.48	20.23 ± 2.67	19.71 ± 2.33
TG (mg/dL)[c]				
Before HC/LF diet	78.14 ± 27.82	86.42 ± 49.54	67.61 ± 16.61	62.41 ± 15.20
After HC/LF diet	87.31 ± 36.29	88.09 ± 44.58	81.52 ± 25.25[b]	75.48 ± 20.12[b]
TC (mg/dL)				
Before HC/LF diet	132.01 ± 16.22	132.84 ± 29.49	139.97 ± 23.35	138.86 ± 22.08
After HC/LF diet	118.83 ± 15.71[b]	119.58 ± 20.97[b]	132.62 ± 18.58[a]	135.18 ± 23.04
LDL-C (mg/dL)				
Before HC/LF diet	65.20 ± 18.50	70.27 ± 23.96	70.94 ± 20.62	69.59 ± 20.60
After HC/LF diet	51.66 ± 14.54[b]	56.67 ± 17.26[b]	58.31 ± 14.42[a]	61.47 ± 19.27[a]
HDL-C (mg/dL)				
Before HC/LF diet	50.97 ± 10.90	45.53 ± 9.22	58.95 ± 10.72	58.97 ± 10.23
After HC/LF diet	54.55 ± 10.65	52.50 ± 11.76[b]	60.43 ± 10.14	59.08 ± 8.93
Glucose (mg/dL)				
Before HC/LF diet	79.64 ± 10.32	83.37 ± 7.17	78.00 ± 10.49	81.35 ± 7.21
After HC/LF diet	78.27 ± 5.30	78.02 ± 8.09	77.46 ± 8.42	77.45 ± 5.07[a]
Insulin (μU/mL)				
Before HC/LF diet	4.99 ± 3.57	5.88 ± 3.40	3.94 ± 2.34	5.59 ± 5.35
After HC/LF diet	5.28 ± 2.47	6.50 ± 4.16	6.03 ± 3.39[b]	6.00 ± 2.87
HOMA-IR				
Before HC/LF diet	1.00 ± 0.71	1.23 ± 1.29	0.78 ± 0.51	1.13 ± 1.13
After HC/LF diet	1.03 ± 0.54	1.29 ± 0.92	1.16 ± 0.68[b]	1.16 ± 0.59
ApoAI (mg/dL)				
Before HC/LF diet	173.00 ± 28.46	159.45 ± 23.57	191.61 ± 24.11	193.55 ± 20.26
After HC/LF diet	173.81 ± 24.06	165.64 ± 28.09[b]	195.33 ± 20.09	197.91 ± 25.50
ApoB100 (mg/dL)				
Before HC/LF diet	56.25 ± 18.11	60.55 ± 23.24	58.00 ± 17.02	61.00 ± 16.08
After HC/LF diet	54.75 ± 19.49	60.55 ± 23.98	57.78 ± 15.92	61.64 ± 18.32

[a] $p < 0.05$ when compared to subjects with the same genotype before the HC/LF diet; [b] $p < 0.01$ when compared to subjects with the same genotype before the HC/LF diet; [c] The value of TG was log-transformed for statistical analysis.

the HC/LF diet. Results revealed that *LPL* Ser447Stop and *Hind* III polymorphisms have different effects on serum glucose, insulin, and the lipid profile after an HC/LF diet (Tables 3 and 4). The 447X allele offers females significant protection from elevated levels of TG and insulin and a higher HOMA-IR index induced by the HC/LF diet but does not offer males that protection; this may be what protects females from HC/LF diet-induced IR.

Recent studies showed that the response of serum lipids to an HC/LF diet may be gender-specific (*25*). An HC/LF diet was reported to be associated with lower HDL-C in males and higher TG in females. The response of TG to the HC/LF diet in this study was basically the same as that reported previously (*1*,*2*). However, there was no significant decrease in HDL-C after the HC/LF diet for this young Chinese population. When *LPL* polymorphism is taken into account, the interaction of the H- allele and HC/LF diet has a significant effect on HDL-C in that HDL-C is elevated after the HC/LF diet. Such an increase in HDL-C after an HC/LF diet has not been reported before. This may result from the interaction between the allele and the diet. Alternatively, the increased HDL-C may reflect environmental and other genetic differences that modify the outcome of interactions between the *LPL Hind* III allele and the diet in this young Chinese population with a high basal HDL-C. The association between 447X and decreased TG was found to be stronger in males than in females in the Danish general population (*13*). In contrast, there was a significant association between the 447X allele and decreased TG in females but not in males in the Singaporean population (*12*). The present study found that the LPL 447X allele provided only females with significant protection from increased TG induced by an HC/LF diet. This finding is consistent with findings for Asian populations.

LPL is reported to be a gene related to IR (*17*). *Hind* III polymorphism has been found to be associated with steady-state plasma glucose concentrations in nondiabetic males with CAD (*26*). Normoglycemic subjects with H+/H+ were found to be more likely to have increased fasting insulin than subjects with H+/H- (*27*). The present study found significantly increased insulin and a higher HOMA-IR index after the HC/LF diet was consumed by female wild-type homozygotes but not by female carriers of *LPL* Ser447Stop and *Hind* III polymorphisms. This result further supports the hypothesis that *LPL* is one of the genes underlying IR. Further studies are needed to confirm the gender specificity of *LPL* Ser447Stop and *Hind* III polymorphisms and to elucidate the mechanisms responsible for the protection from HC/LF diet-induced elevation of insulin and HOMA-IR in these young females.

The effects of particular nutrients, such as the fatty acid composition of the diets, were not tested in this study. However, the purpose of this study was to examine interaction between the ratios of carbohydrate and fatty acids, instead of the fatty acid composition of the diets, and *LPL* polymorphisms and the effect of that interaction on lipid profiles. The ratios of total fatty acids, saturated fatty acids, monounsaturated fatty acids, and polyunsaturated fatty acids to total energy intake were changed accordingly for the control diet and HC/LF diet in this study (Table 1). The percentage of palmitic, palmitoleic, stearic, oleic, and linoleic fatty acids in relation to total fatty acids as energy intake remained constant for the control diet and HC/LF diet in this study (Table 1). In fact, observations pertaining to the different effects of the fatty acid composition may not be valid for diets with extremely low levels of total fat (*28*). More importantly, isolating particular nutrients such as different fatty acids is not possible in everyday life, and especially in developing countries such as China. The present design focusing on diet patterns is much more practical than focusing on particular nutrients in a diet.

In conclusion, *LPL* Ser447Stop and *Hind* III polymorphisms modify the effects of an HC/LF diet on the serum lipid profile, serum levels of insulin, and insulin sensitivity in different ways in a young Chinese population. First, the mutated allele of *LPL Hind* III polymorphism is associated with increased HDL-C and apo AI in males consuming an HC/LF diet. Second, the mutated allele of *LPL* Ser447Stop polymorphism provides only females with significant protection from increased TG induced by an HC/LF diet, although the mutated alleles of both Ser447Stop and *Hind* III polymorphisms provide females with significant protection from increased insulin and a higher HOMA-IR index induced by an HC/LF diet. These findings provide new insight into the interaction of gender, *LPL*, and an HC/LF diet and their effects on risk factors for CAD. These findings are especially relevant to a young Chinese population with a low incidence of CAD consuming a diet with less fat and more carbohydrates. Once confirmed by studies with a large sample size, the current findings may help with the formulation of personalized strategies for diet-based prevention of CAD in a country with a quarter of the world's population.

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