Ethnicity differences in plasma apoC-III levels between African American and Caucasian youths

Ji-Young Lee, Hye-Ryun Hong, Hyun-Sik Kang

Suwon, Republic of Korea

Original article

Background: **Little is known about the association between apoC-III and lipoprotein-lipids in African American (AA) and Caucasian (CA) youths. The aim of this study was to investigate if plasma apoC-III level is associated with ethnicity differences in atherogenic lipoprotein-lipids between AA and CA youths.**

Methods: **A total of 202 youths (mean age 16.1±1.3 y, range 13.8-18.9 y) consisting of 122 AA (boys/girls, 52/70) and 80 CA (boys/girls, 40/40) youths were recruited via flyers sent to local high schools. For AA youths, body mass index (BMI) values were 22.5±5.0 kg/m^2 and 25.0±6.8 kg/m^2 for boys and girls, respectively. For CA youths, BMI values were 22.0±4.8 kg/m^2 and 22.1±5.0 kg/m^2 for boys and girls, respectively. Anthropometric variables were measured using standard procedures. Body fat was measured by dual-energy X-ray absorptiometry. Fasting glucose and insulin, lipoprotein-lipids, and apolipoproteins were measured in fasting plasma samples.**

Results: **AA youths had significantly lower values in apoC-III (P<0.001), triglyceride (P<0.001), and total cholesterol/high-density lipoprotein cholesterol (P=0.011) and higher values in HDLC (P=0.004), apoE (P=0.016), insulin (P=0.027), and homoeostasis model of assessment-insulin resistance (HOMA-IR) (P=0.025) than CA youths. Body composition and insulin resistance parameters were significantly associated with apoC-III levels in CA youths, but not in AA youths. Regression analyses showed that waist circumference and HOMA-IR were significant predictors for apoC-III in CA, not AA, youths.**

Conclusions: **The findings of the current study suggest that ethnicity differences in atherogenic lipids between AA and CA youths may be associated with differences in apoC-III and apoE levels.**

World J Pediatr 2011;7(2):136-142

Key words: **adiposity; ethnicity; lipoprotein-lipids; pediatrics; risk factors**

Introduction

High triglyceride (TG) levels coupled with low high-density lipoprotein cholesterol (HDLC) levels in circulating plasma are the hallmarks of hypertriglyceridemia[1] as well as a major risk factor for diabetes and cardiovascular diseases.[2-3] It is well known that African American (AA) adults and children have higher rates of obesity, diabetes and hypertension than Caucasian (CA) adults and children.[4] Paradoxically, AA adults and children have a lower prevalence of metabolic syndrome due to lower TG and higher HDLC levels,[4] as well as larger low-density lipoprotein cholesterol (LDLC)-particle sizes.[5-6] However, the mechanism(s) responsible for the ethnicity differences in atherogenic lipoprotein-lipid profiles are not clear, especially in youths.

One explanation for the ethnic differences in atherogenic lipoprotein-lipid profiles may be that AA children have lower visceral adiposity than CA children.[7] In a Bogalusa study, Freedman et al[8] found that the relationship of waist circumference with TG and very low-density lipoprotein (VLDL) subclasses was much greater in white youths than in black youths, suggesting that the magnitude of the deleterious effect of abdominal adiposity differs between the two ethnic groups. Similarly, Burns et al[5] found that lower visceral adiposity partially explained the ethnic differences in lipoprotein profiles in that black children had lower TG and VLDL concentrations and larger LDL particle sizes than white children.

Apolipoprotein C-III (apoC-III) plays a critical role

Author Affiliations: Division of Humanities and Social Sciences, Pohang University of Science and Technology, Pohang, Republic of Korea (Lee JY); School of Sports Science, Sungkyunkwan University, Suwon, Republic of Korea (Hong HR, Kang HS)

Corresponding Author: Hyun-Sik Kang, PhD, School of Sports Science, Sungkyunkwan University, 300 Chenchen-dong, Jangan-gu, Suwon, Republic of Korea (Tel: +82-31-299-6911; Fax: +82-31-299-6929; Email: hkang@skku.edu)

doi: 10.1007/s12519-011-0266-8

in TG metabolism and therefore the TG concentrations in circulating plasma. ApoC-III consisting of 79-amino acids (8.8 kD) is synthesized predominantly in the liver and to a lesser extent in the intestine.[9] ApoC-III is a major component of VLDL and chylomicrons and a minor component of HDL.[9]

In the Monitored Atherosclerosis Regression Study, the amount of apoC-III in VLDL was found to be an independent predictor of the progression or severity of coronary artery disease.[10] In the Etude cas-témoin sur l' infarctus du myocarde study, elevated apoC-III levels were associated with myocardial infarction in non-diabetic subjects.[11] In young adults, increased apoC-III was an independent predictor of a family history of coronary artery disease that remained significant even after adjustment of apoB and TG levels.[12] However, it is not known if ethnic differences in apoC-III levels explain the ethnic differences in both lipoprotein-lipid profiles and their relationship with body fat, including abdominal differences between AA and CA youths.

The goals of the current study were: (i) to determine if plasma apoC-III levels differ between AA and CA youths; and (ii) to investigate how body fatness and markers of insulin resistance are associated with plasma apoC-III levels and atherogenic lipoprotein-lipids in AA and CA youths.

Methods

Subjects

In a cross-sectional design, a total of 202 children (mean age: 16.1±1.3 y, range: 13.8-18.9 y) consisting of 122 AA (boys/girls, 52/70) and 80 CA (boys/girls, 40/40) youths were recruited via flyers sent to local high schools. For AA youths, body mass index (BMI) values were 22.5±5.0 kg/m^2 (range: 16.8-40.7) and 25.0±6.8 kg/m^2 (range: 16.6-43.8) for boys and girls, respectively. For CA youths, BMI values were 22.0±4.8 kg/m^2 (range: 17.1 -38.1) and 22.1±5.0 kg/m^2 (range: 16.7- 45.5) for boys and girls, respectively. Interested youths and parents signed consent forms in accordance with the procedures of the Institutional Human Subject Committee.

Weight was assessed with a balance scale, and height was assessed using a stadiometer. These values were then used to calculate BMI (kg/m^2). Waist and hip circumferences were measured at the level of the umbilicus and at the maximum posterior extension of the buttocks, respectively, with a commercially-available tape measure (MyoTape, AccuFitness, CO, USA), and waist-to-hip ratio (WHR) was calculated. A trained expert measured all body composition variables in triplicate, and the mean values were used. Total body composition was measured by dual energy X-ray absorptiometry (DXA) using the Hologic QDR-4500W (Waltham, MA, USA).

Plasma lipid, lipoprotein, and apolipoprotein measurements

A 20 mL fasting blood sample was obtained from an antecubital vein into Vacutainers® containing EDTA. Samples were separated by low speed centrifugation (1400 rpm) and stored at -80ºC. Plasma concentrations of total cholesterol (TC), LDLC, HDLC, TG, and glucose were determined by methods previously described.[13] Fasting insulin concentrations were also measured in duplicate using a commercially available ELISA immunoassay kit (ALPCO Diagnostics, Salem, NH, USA). The index of insulin resistance was assessed using the homoeostasis model of assessment-insulin resistance (HOMA-IR), as HOMA-IR = [fasting insulin (μIU/mL) × fasting glucose (mmol)]/22.5.[14] The coefficients of variations (CVs) for intra- and inter-assays of insulin were 4.3% and 6.8%, respectively.

Apolipoprotein A1, B and E were measured in duplicate using commercially available nephelometric immunoassays (Dade Behring, Marburg, Germany). The inter-assay CV for apoA-I, apoB and apoE was 4.7%, 6.6%, and 6.6%, respectively, and the intra-assay CV for apoA-I, apoB and apoE was 2.8%, 3%, and 4.4%, respectively. Serum apoC-III levels were measured in duplicate using a turbid metric immunoassay kit (Wako APO C3-HA, Wako Pure Chemical Inc., Osaka, Japan). The inter- and intra-assay variability for the assay was less than 10%.

LDL diameters were determined in duplicate using segmental gradient polyacrylamide gel (S-GGE 2.8/8.30) as previously described.[15] Briefly, plasma samples were pre-stained for 2 hours at room temperature with 0.6% Sudan black in ethylene glycol (3:1) prior to loading onto the gel. A single load of 10 μL of prestained plasma solution was applied to individual troughs (GA-50 sample applicator, Isolabs). Electrophoresis was performed at room temperature for 18-20 hours (50 mA and 80 V). The position of the LDL bands was determined using a LKB laser densitometer (LKB Pharmacia, Piscataway, NJ, USA). The inter- and intra-assay CVs for the LDL particle diameter were 1.16% and 0.47%, respectively.

Statistical analyses

SPSS-PC version 10.1 was used for all statistical analyses. The distributions of the dependent variables were checked for normality prior to the analyses by plotting standardized residuals for each variable

from regression models using ethnicity and gender as independent variables. Because BMI and waist circumference (WC) were not normally distributed, a $\log_{10}$ transformation was conducted, which adequately normalized the distributions of these variables.

Analyses of variance were used to compare gender and ethnic groups. Pearson correlations were calculated among body composition parameters, fasting insulin and HOMA-IR, apolipoproteins, and lipoprotein-lipids. Linear regression analyses were used to determine the degree to which gender, ethnicity, adiposity, and HOMA-IR explained the variance in apoC-III and other primary lipid variables. We chose WC as the primary index of central adiposity in the regression analyses for several reasons. Specifically, there were substantial inter-correlations among the adiposity indices; thus, we chose one index to avoid problems of colinearity. WC was more closely related to several measured lipoprotein-lipids including apoC-III than other adiposity indices (Table 2). Moreover, WC has consistently shown to be strongly associated with obesity-related metabolic disorders in adults[1] as well as in children,[8] perhaps because it focuses on abdominal adipose tissue. Finally, the use of WC avoided any problems associated with the use of ratios such as body fat percentage and BMI.[16]

Results

Table 1 shows the characteristics of the subjects. Ages were similar between AA and CA youths and between boys and girls. Girls had higher body fat than boys, while boys had higher WHR than girls, suggesting that girls have higher overall body fatness than boys, while boys are more centrally obese than girls. AA youths had significantly higher values in body weight and BMI values than CA youths. A further analysis showed that these differences in body composition were limited to the girl sample since AA girls had significantly higher body weight and BMI values than CA girls, with no such differences between AA and CA boys. The ethnicity differences in body weight and BMI may imply that AA girls have higher lean body mass including muscle mass and/or bone mineral density than CA girls. No significant differences in percent body fat, WHR, and WC were found between the two ethnicity groups.

With respect to lipoprotein-lipids and apolipoproteins, girls had generally more favorable lipoprotein-lipids profiles than boys, especially in HDLC and apoA-I. AA youths had more favorable lipoprotein-lipids featuring of low TG, low TC/HDLC, and high HDLC than CA youths. In particular, AA youths had lower apoC-III levels along with higher apoE levels than CA youths,

Table 1. Description of study participants (mean±SD)

Variables	Boys		Girls		*P* value for gender	*P* value for ethnicity
	CA (*n*=40)	AA (*n*=52)	CA (*n*=40)	AA (*n*=70)		
Age, y	16.0±1.2	16.2±1.3	16.3±1.1	16.1±1.3	0.714	0.851
Weight, kg	66.6±16.6	69.0±14.4	59.4±14.5	67.6±22.0	0.242	0.038
BMI, kg/m^2	22.0±4.8	22.5±5.0	22.1±5.0	25.0±6.8	0.056	0.018
WHR	0.82±0.05	0.80±0.06	0.74±0.04	0.75±0.06	<0.001	0.257
WC, cm	78.7±13.1	75.8±12.3	72.9±12.8	75.5±13.6	0.193	0.970
BF, %	20.0±8.9	16.4±9.4	30.0±7.2	30.2±8.7	<0.001	0.979
TG, mmol/L	0.96±0.63	0.57±0.23	0.85±0.40	0.55±0.18	0.143	<0.001
TC, mmol/L	3.63±0.67	3.79±0.65	3.99±0.63	3.87±0.70	0.061	0.956
HDLC, mmol/L	1.06±0.25	1.19±0.19	1.20±0.23	1.28±0.27	0.002	0.005
TC/HDLC	3.53±0.76	3.25±0.64	3.45±0.78	3.15±0.82	0.308	0.011
LDLC, mmol/L	2.29±0.57	2.38±0.60	2.73±1.41	2.40±0.69	0.174	0.282
LDL-PPD, nm	25.4±0.6	25.6±0.8	25.4±1.0	25.7±0.8	0.718	0.087
ApoA, mg/dL	113.8±24.5	117.1±24.8	125.1±22.3	126.9±27.4	0.014	0.409
ApoB, mg/dL	73.0±21.1	69.3±21.2	77.5±21.2	71.4±22.0	0.508	0.191
ApoC-III, mg/dL	11.5±3.3	9.3±2.6	11.2±3.5	9.5±2.6	0.669	<0.001
ApoE, mg/dL	4.1±1.1	4.5±1.4	4.3±1.1	4.8±1.5	0.144	0.016
FBG, mmol/L	5.2±0.3	5.2±0.4	4.9±0.3	5.0±0.4	<0.001	0.529
†Insulin, μIU/mL	18.3±10.0	16.3±8.9	14.0±5.4	20.6±10.5	0.456	0.027
†HOMA-IR	4.3±2.4	3.8±2.2	3.1±1.3	4.7±2.7	0.787	0.025

BMI: body mass index; WHR: waist-to-hip ratio; WC: waist circumference; BF: body fat; TG: triglycerides; TC: total cholesterol; HDLC: high-density lipoprotein cholesterol; LDLC: low-density lipoprotein cholesterol; Apo: apolipoprotein; PPD: peak particle diameter; FBG: fasting blood glucose; HOMA-IR: homoeostasis model of assessment-insulin resistance. For statistical analyses, values were $\log_{10}$ transformed for normalization, but actual values were presented. Further analyses showed that AA girls had higher values in insulin (P<0.001) and HOMA-IR (P=0.001) than CA girls, with no differences between AA and CA boys; CA: Caucasian; AA: African American.

while the former had higher fasting insulin and higher HOMA-IR than the latter. Boys had higher fasting glucose levels than girls (Table 1).

Significant Pearson correlations were found among body fatness, lipids, apolipoproteins, and markers of insulin resistance. In boys, TG levels were significantly correlated with WC (r=0.526), percent body fat (r=0.501), insulin (r=0.505), and HOMA-IR (r=0.495). TC/HDLC was significantly correlated with BMI (r=0.248), WHR (r=0.264), WC (r=0.305), percent body fat (r=0.351), insulin (r=0.406), and HOMA-IR (r=0.403). In girls, HDLC and TC/HDLC were significantly correlated with BMI (r=-0.301 & r=0.361, respectively), WHR (r=-0.376 & r=0.365, respectively), WC (r=-0.308 & r=0.395, respectively), and percent body fat (r=-0.321 & r=0.334, respectively). In addition, TG and apoB levels were significantly correlated with WHR (r=0.264 & r=0.254, respectively), WC (r=0.292 & r=0.245, respectively), and percent body fat (r=0.226 & r=0.231, respectively). Serum apoC-III levels were significantly correlated with WC (r=0.311 & r=0.228, respectively) in both boys and girls and with fasting insulin (r=0.299) and HOMA-IR (r=0.276) in boys only. Regardless of gender, no further significant correlations were found between the measured variables (data not shown).

Tables 2 and 3 represent Pearson correlations among the measured variables by ethnicity. In CA youths, most of body composition parameters were positively associated with apoC-III, TG, and TC/HDLC and negatively associated with HDLC. In AA youths, WC, BMI, and WHR were positively associated with TG and/or TC/HDLC and negatively associated with HDLC. Regardless of ethnicity, fasting insulin and HOMA-IR were positively associated with TG and TC/HDLC. In CA, not AA, youths, insulin and HOMA-IR were also positively associated with circulating apoC-III and apoE.

Table 4 shows the final regression models for apoC-III and other major lipid variables for both CA and AA youths, respectively. WC and HOMA-IR were significant predictors for apoC-III in CA youths, but not in AA youths. HOMA-IR was a significant predictor for TG in both CA and AA youths. WC was a predictor for both HDLC and TC/HDLC in CA and AA youths.

Table 2. Pearson correlations among body composition, lipids, apolipoproteins, fasting insulin, and HOMA-IR in Caucasian youths (n=80)

Variables	BMI	WHR	WC	Body fat percentage	INS	HOMA-IR
ApoC-III	0.443†	0.472†	0.706†	0.446†	0.301*	0.317†
TG	0.374†	0.483†	0.615†	0.431†	0.576†	0.586†
TC	0.080	0.080	0.124	0.303*	0.073	0.049
HDLC	-0.286*	-0.389†	-0.291*	-0.044	-0.226	-0.244*
TC/HDLC	0.421†	0.457†	0.438†	0.348†	0.323†	0.321†
LDLC	0.154	0.171	0.225	0.247*	0.156	0.138
ApoA-I	0.045	-0.157	0.046	0.191	-0.058	-0.078
ApoB	0.213	0.120	0.090	0.230	0.020	-0.002
ApoE	0.129	0.058	0.203	0.254*	0.256*	0.267*
LDL-PPD	-0.035	-0.105	-0.045	0.014	0.034	0.035

BMI: body mass index; WHR: waist-to-hip ratio; WC: waist circumference; INS: insulin; HOMA-IR: homoeostasis model of assessment-insulin resistance; Apo: apolipoprotein; TG: triglycerides; TC: total cholesterol; HDLC: high-density lipoprotein cholesterol; LDLC: low-density lipoprotein cholesterol; PPD: peak particle diameter. *: P<0.05; †: P<0.001. TG was $\log_{10}$ transformed for normalization.

Table 3. Pearson correlations among body composition, lipids, apolipoproteins, fasting insulin, and HOMA-IR in African American youths (n=122)

Variables	BMI	WHR	WC	Body fat percentage	INS	HOMA-IR
ApoC-III	-0.116	-0.132	-0.154	-0.130	0.014	-0.005
TG	0.178	0.106	0.206*	0.075	0.209*	0.213*
TC	0.078	-0.068	0.069	0.069	0.066	0.069
HDLC	-0.222*	-0.243*	-0.245*	-0.067	-0.110	-0.118
TC/HDLC	0.313†	0.182	0.316†	0.174	0.225*	0.231*
LDLC	0.181	0.062	0.174	0.128	0.104	0.104
ApoA-I	-0.134	-0.096	-0.138	-0.068	0.088	0.084
ApoB	0.156	-0.075	0.142	0.099	-0.015	0.001
ApoE	0.033	-0.021	0.032	0.130	0.064	0.038
LDL-PPD	-0.078	0.015	-0.096	-0.083	-0.144	-0.142

BMI: body mass index; WHR: waist-to-hip ratio; WC: waist circumference; INS: insulin; HOMA-IR: homoeostasis model of assessment-insulin resistance; Apo: apolipoprotein; TG: triglycerides; TC: total cholesterol; HDLC: high-density lipoprotein cholesterol; LDLC: low-density lipoprotein cholesterol; PPD: peak particle diameter. *: P<0.05; †: P<0.001. TG was $\log_{10}$ transformed for normalization.

Table 4. The regression models for estimating apoC-III and atherogenic lipids for Caucasian and African American youths

DV	IV	CA youths		AA youths	
		β	R^2 (%)	β	R^2 (%)
ApoC-III	WC	0.412	32.5	NS	NS
	Insulin	NS	NS	NS	NS
	HOMA-IR	0.317	26.5	NS	NS
	R^2 for the model		40.4		
TG	WC	0.433	36.2	NS	NS
	Insulin	NS	NS	NS	NS
	HOMA-IR	0.360	31.7	0.251	6.3
	R^2 for the model (%)		46.3		6.3
HDLC	WC	-0.291	8.5	-0.245	6.0
	Insulin	NS	NS	NS	NS
	HOMA-IR	NS	NS	NS	NS
	R^2 for the model (%)		8.5		6.0
TC/HDLC	WC	0.430	19.2	0.316	10.0
	Insulin	NS	NS	NS	NS
	HOMA-IR	NS	NS	NS	NS
	R^2 for the model (%)		19.2		10.0

DV: dependent variable; IV: independent variable; CA: Caucasian; AA: African American; Apo: apolipoprotein; TG: triglycerides; HDLC: high-density lipoprotein cholesterol; TC: total cholesterol; WC: waist circumference; HOMA-IR: homoeostasis model of assessment-insulin resistance.

Discussion

The findings of the present study are in line with those of previous studies, i.e., AA youths have more favorable lipoprotein-lipids than CA youths.[4-5,7] To our knowledge, this is the first article to report that AA youths have significantly lower apoC-III and higher apoE levels in circulating plasma even with higher fasting insulin and HOMA-IR than CA youths. Low apoC-III levels along with high apoE appear to be associated with the more favorable lipoprotein-lipids featuring of lower values in TG and TC/HDLC and higher values in HDLC and LDL particle size in AA youths compared with CA youths. Several potential explanations can be given for those ethnicity differences in atherogenic lipids between AA and CA youths.

First, lipoprotein lipase hydrolyzes TG components of circulating TG-rich lipoproteins (TRL) including VLDL and chylomicrons, thereby removing TG from the circulation. ApoC-III is a constituent of VLDL and chylomicrons that is a noncompetitive inhibitor of lipoprotein lipase.[17,18] Previous mice studies have demonstrated that apoC-III level has a direct and dramatic influence on plasma TG levels.[18,19] Similarly, clinical studies reported that apoC-III levels were positively associated with elevated plasma TG levels via delayed clearance of TRLs.[20-22] In a HERITAGE study, Despres et al[23] found that post-heparin-releasable lipoprotein lipase activity was higher while HL activity was lower in AAs versus CAs. In the present study, therefore, elevated apoC-III levels in CA youths compared with AA youths may indicate that TRL clearance from the circulation is less efficient in the former than in the latter, leading to elevated TG levels along with a higher prevalence of relatively smaller LDL particles.

Second, ethnicity differences in those lipoprotein-lipids might be associated with apoE-mediated hepatic uptake of TRL remnants. Plasma apoE increases the clearance rate of TRL remnants through recognition and uptake by hepatic receptors,[24,25] while apoC-III reduces the apoE-mediated hepatic uptake of TRL remnants.[26] In the present study, we found that AA youths had a significantly higher apoE level and a lower apoC-III level than CA youths, suggesting that hepatic uptake of TRL remnants from the circulation might be more efficient in the former than in the latter.

With respect to the ethnicity difference in apoC-III between AA and CA youths, no clear explanation can be given due to the cross-sectional nature of the present study. The apoC-III gene has an insulin-response element on its promoter that negatively affects gene expression.[27] And it has also been suggested that the normal suppression of hepatic apoC-III expression by insulin is diminished in the insulin resistant state, which leads to increased apoC-III expression and TG-rich VLDL particles in the circulation. For example, epidemiologic studies showed that plasma apoC-III was positively associated with hyperinsulinemia,[28] metabolic syndrome,[20] and type 2 diabetes.[21] In the present study, we found that even with higher insulin and HOMA-IR levels, AA youths had a significantly lower apoC-III level than CA youths. In CA, not AA, youths, HOMA-IR along with waist circumference was an independent predictor for plasma apoC-III. Thus it is certainly possible that unlike CA youths, insulin resistance may not lead to increased apoC-III gene expression and its protein levels in AA youths, implying that the functional influence of insulin on the apoC-III gene expression and thereby its protein expression may differ between CAs and AAs. Considering the cross-sectional nature of this study, however, we cannot provide further information on this question.

Finally, several studies have demonstrated the presence of a complex interaction of genetic variants within apoC-III and the apoA-I/C-III/A-IV/A-V cluster with plasma TG concentrations.[29,30] Waterworth et al[29] reported that the -482T allele frequency in the insulin response element of the apoC-III gene promoter was significantly higher in AAs than in CAs. The -482T allele was also associated with higher concentrations of fasting insulin and TG in CAs, while it was related to lower fasting insulin

and glucose concentrations in AAs. However, how the apoC-III genotype influences the associations among insulin resistance and plasma apoC-III and thereby lipoprotein-lipids in both AA and CA youths needs to be investigated in a future study.

In summary, the findings of the present study suggest that compared with CA youths, AA youths have a favorable lipoprotein-lipids profile featuring of low TG and high HDLC along with relatively larger LDL particles, and they appear to be associated with relatively low apoC-III and high apoE levels. Considering the fact that AAs have a higher risk for cardiovascular diseases than CAs; however, one important implication of the present findings is that clinical practitioners and health care professionals need to be aware of that lipoprotein-lipids profile alone in AA youths may not appropriately reflect the future risk for cardiovascular diseases including type 2 diabetes mellitus and hypertension.

Funding: This study was supported by a grant from the Korean Research Foundation (KRF-2009-32A-G00046).
Ethical approval: This study was approved by the committee of Sungkyunkwan University for Human Subject Research.
Competing interest: No conflicts of interest are declared by the authors.
Contributors: Kang HS conceived and designed the study, analyzed the data, and wrote the first draft. Lee JY and Hong HR contributed to data analysis and interpretation and writing and critical revisions of the manuscript. All the authors reviewed and approved the final version of the manuscript.

References

1 Lemieux I, Pascot A, Couillard C, Lamarche B, Tchernof A, Alméras N, et al. Hypertriglyceridemic waist: a marker of the atherogenic metabolic triad (hyperinsulinemia; hyperapolipoprotein B; small, dense LDL) in men? Circulation 2000;102:179-184.
2 Game FL, Jones AF. Coronary heart disease risk assessment in diabetes mellitus—a comparison of PROCAM and Framingham risk assessment functions. Diabetic Med 2001;18:355-359.
3 Pereira MA, Schreiner PJ, Pankow JS, Williams RR, Higgins M, Province MA, et al. The Family Risk Score for coronary heart disease: associations with lipids, lipoproteins, and body habitus in a middle-aged bi-racial cohort: The ARIC study. Ann Epidemiol 2000;10:239-245.
4 Sumner AE. Ethnic differences in triglyceride levels and high-density lipoprotein lead to underdiagnosis of the metabolic syndrome in black children and adults. J Pediatr 2009;155(Suppl 7):e7-e11.
5 Burns SF, Lee S, Arslanian SA. *In vivo* insulin sensitivity and lipoprotein particle size and concentration in black and white children. Diabetes Care 2009;32:2087-2093.
6 Haffner SM, D'Agostino R Jr, Goff D, Howard B, Festa A, Saad MF, et al. LDL size in African Americans, Hispanics, and non-Hispanic whites: the insulin resistance atherosclerosis study. Arterioscler Thromb Vasc Biol 1999;19:2234-2240.
7 Bacha F, Saad R, Gungor N, Janosky J, Arslanian SA. Obesity, regional fat distribution, and syndrome X in obese black versus white adolescents: race differential in diabetogenic and atherogenic risk factors. J Clin Endocrinol Metab 2003;88:2534-2540.
8 Freedman DS, Bowman BA, Otvos JD, Srinivasan SR, Berenson GS. Levels and correlates of LDL and VLDL particle sizes among children: the Bogalusa Heart Study. Atherosclerosis 2000;152:441-449.
9 Breslow JL. Familial disorders of high density lipoprotein metabolism. In: Scriver CR, Beaudet Al, Sly WS, Valle D, eds. The metabolic basis of inherited disease. New York: McGraw-Hill, 1995: 1251-1266.
10 Hodis HN, Mack WJ, Azen SP, Alaupovic P, Pogoda JM, LaBree, et al. Triglyceride- and cholesterol-rich lipoproteins have a differential effect on mild/moderate and severe lesion progression as assessed by quantitative coronary angiography in a controlled trial of lovastatin. Circulation 1994;90:42-49.
11 Gervaise N, Garrigue MA, Lasfargues G, Lecomte P. Triglycerides, apo C3 and Lp B:C3 and cardiovascular risk in type II diabetes. Diabetologia 2000;43:703-708.
12 Tiret L, Gerdes C, Murphy MJ, Dallongeville J, Nicaud V, O'Reilly DS, et al. Postprandial response to a fat tolerance test in young adults with a paternal history of premature coronary heart disease-the EARS II study. Eur J Clin Invest 2000;30:578-585.
13 DCCT Research Group. DCCT manual of operations (Publ. No. 93-183382). Springfield, VA: National Technical Information Service, 1993.
14 Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner R. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia 1985;28:412-419.
15 Le NA, Innis-Whitehouse W, Li X, Bakker-Arkema R, Black D, Brown WV. Lipid and apolipoprotein levels and distribution in patients with hypertriglyceridemia: effect of triglyceride reduction with atorvastatin. Metabolism 2000;49:167-177.
16 Allison DB, Paultre F, Goran MI, Poehlman ET, Heymsfield SB. Statistical considerations regarding the use of ratios to adjust data. Int J Obes Relat Metab Disord 1995;19:644-652.
17 Wang CS, McConathy WJ, Kloer HU, Alaupovic P. Modulation of lipoprotein lipase activity by apolipoproteins. Effect of apolipoprotein C-III. J Clin Invest 1985;75:384-390.
18 Aalto-Setälä K, Fisher EA, Chen X, Chajek-Shaul T, Hayek T, Zechner R, et al. Mechanism of hypertriglyceridemia in human apolipoprotein (apo) C-III transgenic mice. Diminished very low density lipoprotein fractional catabolic rate associated with increased apo C-III and reduced apo E on the particles. J Clin Invest 1992;90:1889-1900.
19 Zheng C, Khoo C, Ikewaki K, Sacks FM. Rapid turnover of apolipoprotein C-III-containing triglyceride-rich lipoproteins contributing to the formation of LDL subfractions. J Lipids Res 2007;48:1190-1203.
20 Olivieri O, Bassi A, Stranieri C, Trabetti E, Martinelli N, Pizzolo F, et al. Apolipoprotein C-III, metabolic syndrome, and risk of coronary artery disease. J Lipid Res 2003;44:2374-2381.
21 Cohn JS, Patterson BW, Uffelman KD, Davignon J, Steiner G. Rate of production of plasma and very-low density lipoprotein

(VLDL) apolipoprotein C-III is strongly related to the concentration and level of production of VLDL triglyceride in male subjects with different body weights and levels of insulin sensitivity. J Clin Endocrinol Metab 2004;89:3949-3955.
22 Florez H, Mendez A, Casanova-Romero P, Larreal-Urdaneta C, Castillo-Florez S, Lee D, et al. Increased apolipoprotein C-III levels associated with insulin resistance contribute to dyslipidemia in normoglycemic and diabetic subjects from a triethnic population. Atherosclerosis 2006;188:134-141.
23 Després JP, Couillard C, Gagnon J, Bergeron J, Leon AS, Rao DC, et al. Visceral adipose tissue, plasma lipids, and lipoprotein lipase activity in men and women: the Health, Risk Factors, Exercise Training, and Genetics (HERITAGE) Family Study. Arterioscler Thromb Vasc Biol 2000;20:1932-1938.
24 Mahley RW, Rall SC Jr. Apolipoprotein E: far more than a lipid transport protein. Annu Rev Genomics Hum Genet 2000;1:507-537.
25 Kashyap VS, Santamarina-Fojo S, Brown DR, Parrott CL, Applebaum-Bowden D, Meyn S, et al. Apolipoprotein E deficiency in mice: gene replacement and prevention of atherosclerosis using adenovirus vectors. J Clin Invest 1995;96:1612-1620.
26 Sehayek E, Eisenberg S. Mechanisms of inhibition of apolipoprotein C on apolipoprotein E-dependent cellular metabolism of human triglyceride-rich lipoproteins through the low density lipoprotein receptor pathway. J Biol Chem 1991;266:18259-18267.
27 Chen M, Breslow JL, Li W, Leff T. Transcriptional regulation of the apoC-III gene by insulin in diabetic mice: correlation with changes in plasma triglyceride levels. J Lipid Res 1994;35:1918-1924.
28 Castro Cabezas M, de Bruin TW, de Valk HW, Shoulders CC, Jansen H, Willem Erkelens D. Impaired fatty acid metabolism in familial combined hyperlipidemia. A mechanism associating hepatic apolipoprotein B overproduction and insulin resistance. J Clin Invest 1993;92:160-168.
29 Waterworth DM, Talmud PJ, Humphries SE, Wicks PD, Sagnella GA, Strazzullo P, et al. Variable effects of the apoC3-482C>T variant on insulin, glucose and triglyceride concentrations in different ethnic groups. Diabetologia 2001;44:245-248.
30 Peacock RE, Temple A, Gudnason V, Rosseneu M, Humphries SE. Variation at the lipoprotein lipase and apolipoprotein AI-CIII gene loci are associated with fasting lipids and lipoprotein traits in a population sample from Iceland: Interaction between genotype, gender, and smoking status. Genet Epidemiol 1997;14:265-282.

Received September 14, 2010
Accepted after revision December 20, 2010