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Assessment of apoB dyslipoproteinemia in Korean population

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ABSTRACT

Objectives: There is sparse data on apoB dyslipoproteinemia in Asian population. The purpose of this study was to assess apoB dyslipoproteinemia and to compare the LDL-C, non-HDL and apoB for risk assessment with percentile equivalent cut off in Korean population.

Methods: With 1193 Korean adult subjects, the prevalence and characteristics of different types of dyslipoproteinemias were analyzed in each age and gender group. The percentile values of direct LDL-C, calculated LDL-C, non HDL-C, HDL-C, apoAI, apoB and apoB/apoAI ratio were estimated.

Results: The prevalences of normoapoB–hyperTG, hyperapoB–normoTG and hyperapoB–hyperTG dyslipoproteinemia were 6.9, 8.9 and 10.9% in men and 3.7, 6.4 and 2.8% in women. The 40th percentile of direct LDL-C, calculated LDL-C, non-HDL-C and apo B were 108, 104.2, 126 and 85 mg/dl, respectively. The individual above optimal cut off was significantly underestimated with LDL-C than with non-HDL and apoB, in groups with adverse risk factors.

Conclusions: This study firstly shows the prevalence of various types of dyslipoproteinemias in Asian population. The percentile values of Korean population were similar to those of NHANES. Integration of lipid markers is needed for making clinical decisions and further research involving various populations and methodologies should be performed.

Introduction

Increased plasma low-density lipoprotein cholesterol (LDL-C) has been a major lipid risk factor for cardiovascular events and LDL-C is a primary target of lipid-lowering therapies on the basis of risk stratification [1–3]. Although lipid-lowering therapy with statins (3-hydroxy-3-methylglutaryl-coenzyme A reductase inhibitors) has successfully resulted in lower LDL-C levels and a significant reduction in the incidence of cardiovascular morbidity and mortality, many clinical and observational studies have demonstrated a significant residual cardiovascular risk [4–6]. The residual risk is most prominent in the conditions such as metabolic syndrome, diabetes and obesity [6–8]. In these conditions, many patients showed elevated apolipoprotein B (apoB)-containing lipoproteins, including very low-density lipoprotein (VLDL), intermediate-density lipoprotein (IDL) or small dense LDL, thus, LDL-C alone could not reflect the overall atherosclerotic burden [3]. Also, many population studies have reported the superior prognostic value of apoB compared to LDL-C in predicting cardiovascular events [9,10]. Recently, Sniderman et al. suggested a simple algorithm based on the plasma levels of apoB, triglyceride (TG) and total cholesterol (TC) for diagnosis of major atherogenic dyslipoproteinemias [11] and reported population-based prevalence of different dyslipoproteinemias in the Dutch population [12]. With rapid economic development and change of lifestyle, the prevalence of dyslipoproteinemia has been estimated to have increasing trend in Asian population in contrast to Western population [13,14]. Moreover, the genetic factors also affect in lipid metabolism and ethnic difference seems to be present in characteristics of dyslipoproteinemias. However, there is sparse data on distribution and percentiles values of various lipid markers in Asian population.

The purpose of this study was to determine the prevalence of dyslipoproteinemias using apoB level and other lipid markers and to evaluate the characteristics of different types of dyslipoproteinemias in Korean population. Moreover, we estimated the percentile value of LDL-C, non-HDL-C and apoB in Korean population and compared these markers for risk assessment with percentile equivalent cut off.

Abbreviations: NCEP, National Cholesterol Education Program; ATP, Adult Treatment Panel; LDL-C, low-density lipoprotein cholesterol; apoB, apolipoprotein B; VLDL, very low-density lipoprotein; IDL, intermediate-density lipoprotein; HDL-C, high-density lipoprotein, TG, triglyceride; TC, total cholesterol; NHANES, National Health and Nutrition Examination Survey; ADA, American Diabetes Association; ACA, American College of Cardiology; BMI, body mass index; MetS, metabolic syndrome; IDF, International Diabetes Federation.

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Materials and methods

Subjects

From August 2012 to November 2012, we included 1200 adult individuals who visited at health care center for a general examination in a university- affiliated hospital located in Seoul city, Korea (Konkuk University Medical Center). After persons without available data were excluded, the study population comprised 1193 subjects, aged 18–84 years, which evenly distributed through all age groups. The major characteristics of the study population are described in Table 1. For diagnosis of dyslipoproteinemia, we classified participants based on apoB, TG, TC and LDL as suggested by Sniderman et al. [11]. The prevalence of different types of dyslipoproteinemia in each age and gender group were estimated based on this classification except TG cut off (we used cut off of 150 mg/dl). The cut off levels of optimal non-HDL and apoB were based to the equivalent population percentile in the National Health and Nutrition Examination Survey (NHANES) 2007 to 2008 [15] and target value in the American Diabetes Association (ADA) and American College of Cardiology (ACA) recommendation [16]. The persons with BMI of 25 or more were classified as obesity [17]. The presence of the metabolic syndrome (MetS) was determined using the guidelines of the International Diabetes Federation (IDF) [18]. Since there were significant differences of demographic, lifestyle factors and lipid profiles between men and women, most of the analyses were performed separately in each gender and age group. The Framingham Risk Score (FRS) was calculated based on age, gender, TC, HDL-C, systolic blood pressure, treatment of hypertension and cigarette smoking [2]. According to FRS, individuals were categorized as "low" (<10% 10-year risk), "intermediate" (10–20% risk) or "high" risk (≧20% risk). The study protocol was approved by the Institutional Review Boards of Konkuk University Medical Center.

Blood sample collection and analysis

Blood samples were drawn after at least 12 h overnight fasting. After venous blood collection using gel separator tubes, the samples were centrifuged at 2500–3000 rpm for 10 min within 1 h of collection [19] and the serum fraction was used for measurement. The serum samples were stored at −70 °C until measurement. The lipid markers including TC, LDL-C, HDL-C and TG were measured using commercially available enzymatic reagents (Kyowa reagent, Japan) on chemical analyser (TBA-200FR NEO, Toshiba Medical Systems Co., Tokyo, Japan). The calculated LDL-C was also determined by using the Friedewald Formula [20]. Non-HDL-C was calculated as TC minus HDL-C. The measurement of apoB and apoAI levels was performed using immunoturbidimetric assay (Abbott Diagnostics, Chicago, IL, USA).

Statistics

The relationships between the continuous variables of the different groups were analyzed using Student's *t*-test, the Mann–Whitney test and ANOVA. The significance of categorical variables was assessed by the chi-square test, McNemar test and Cochran–Armitage test for trend. Statistical analysis was performed using PAWS Statistics software, version 17.0 (SPSS Inc., Chicago, IL, USA) and MedCalc Statistical software 12.3.0.0 (Mariakerke, Belgium). *P*-values of less than 0.01 were considered to be statistically significant.

Results

Prevalence of different types of dyslipoproteinemia in Korean men and women according to age group

Among 1193 subjects, 436 men (73.3%) and 521 (87.1%) women had normal apoB (<120 mg/dl) and normal TG levels (<150 mg/dl) (normoapoB–normoTG). The group of normal apoB and increased TG (normoapoB–hyperTG) were 6.9% in men and 3.7% in women. In this type of dyslipoproteinemia, most men (38/41, 92.7%) were because of increased VLDL (TC: apoB <2.4), but lower proportion was seen in women (15/22, 68.2%). Normal TG and increased apoB (hyperapoB–normoTG) were seen in 8.9% of men and 6.4% of women. Increased TG and increased apoB (hyperapoB–hyperTG) were seen in 10.9% of men and 2.8% of women (Table 2). The prevalence of hyperapoB–normoTG dyslipoproteinemia in men and women and hyperapoB–hyperTG dyslipoproteinemia in men significantly increased according to increased age group (*P* for trend, all <0.0001). Of note, the prevalence of

Table 1
Baseline characteristics of enrolled population.

Characteristics	Male	Female	Total	*P*-value
N (%)	595 (49.9)	598 (50.1)	1193 (100.0)	
Age	47.9 ± 12.2 (20–86)	47.6 ± 13.2 (18–84)	47.7 ± 12.7 (18–86)	0.656
Diabetes mellitus, n (%)	56 (9.4)	37 (6.2)	93 (7.8)	0.0489
Fatty liver*, n (%)	132 (22.2)	46 (7.7)	178 (14.9)	<0.0001
Metabolic syndrome*, n (%)	122 (25.8)	73 (13.9)	195 (16.3)	0.0001
Current smoking*, n (%)	163 (27.4)	11 (1.8)	174 (14.6)	<0.0001
Pack years of smoking*	10.7 ± 13.4 (0–112.5)	0.3 ± 2.2 (0–40.0)	5.6 ± 11.0 (0–112.5)	<0.0001
Alcohol intake (g/day)*	17.8 ± 22.0 (0–200.0)	2.6 ± 6.5 (0–62.9)	10.7 ± 18.3 (0–200.0)	<0.0001
Exercise, MET min/week	2,239 ± 2,922 (0–29,700)	2,089 ± 3,071 (0–29,934)	2166 ± 2,995 (0–29,934)	0.1783
Body mass index*, kg/m^2	24.7 ± 2.8 (16.2–39.1)	22.8 ± 3.3 (16.4–48.7)	23.8 ± 3.2 (16.2 – 48.7)	<0.0001
Waist circumference*, cm	88.2 ± 7.4 (63.4–122.3)	77.4 ± 8.7 (58.2 128.0)	82.8 ± 9.7 (58.2–128.0)	<0.0001
Systolic blood pressure*, mm Hg	119.9 ± 14.5 (84–179)	111.8 ± 15.0 (78–170)	115.9 ± 15.3 (78–179)	<0.0001
Diastolic blood pressure*, mm Hg	75.7 ± 11.7 (40–128)	67.6 ± 10.3 (44–108)	71.7 ± 11.8 (40–128)	<0.0001
Anti-hypertensive therapy, n (%)	98 (16.5)	75 (12.5)	173 (14.5)	0.0651
Lipid-lowering therapy, n (%)	41 (6.9)	51 (8.5)	92 (7.7)	0.3413
Fasting glucose*, mg/dl	91.9 ± 16.9 (64–254)	87.8 ± 13.2 (52–200)	89.8 ± 15.3 (52–254)	<0.0001
Hemoglobin A_{1c}, %	5.59 ± 0.71 (3.8–12.2)	5.53 ± 0.56 (4.5–10.6)	5.56 ± 0.64 (3.8–12.2)	0.109
Triglyceride*, mg/dl	142.4 ± 95.0 (33–991)	98.3 ± 58.8 (28–598)	120.3 ± 81.9 (28–991)	<0.0001
Total cholesterol, mg/dl	194.5 ± 32.4 (108–319)	191.3 ± 34.3 (98–351)	192.9 ± 33.4 (98–351)	0.104
LDL cholesterol*, mg/dl	120.3 ± 28.1 (36–212)	114.4 ± 31.6 (29–284)	117.3 ± 30.1 (29–284)	0.0007
HDL cholesterol*, mg/dl	51.9 ± 12.1 (25–132)	59.3 ± 12.7 (31–138)	55.2 ± 13.1 (25–138)	<0.0001
Non-HDL cholesterol*, mg/dl	143.4 ± 31.7 (44–251)	132.0 ± 34.9 (44–306)	137.7 ± 33.8 (44–306)	<0.0001
ApoAI, mg/dl	158.1 ± 32.8 (93–301)	158.5 ± 23.4 (100–287)	158.3 ± 28.4 (93–301)	0.805
ApoB*, mg/dl	100.3 ± 23.9 (35–197)	88.0 ± 22.7 (31–179)	94.1 ± 24.1 (31–197)	<0.0001
ApoB/AI ratio*	0.65 ± 0.17 (0.22–1.27)	0.57 ± 0.17 (0.11–1.54)	0.61 ± 0.17 (0.11–1.54)	<0.0001

Values are presented as mean ± SD (range) unless indicated otherwise.
*$P < .01$ between men and women.
Abbreviations: MET, metabolic equivalent of task; LDL, low-density lipoprotein; HDL, high-density lipoprotein; ApoAI, apolipoprotein AI, ApoB, apolipoprotein B.