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Optimal high-density lipoprotein cholesterol cutoff for predicting cardiovascular disease: Comparison of the Korean and US National Health and Nutrition Examination Surveys

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BACKGROUND: Serum high-density lipoprotein cholesterol (HDL-C) has been reported to be lower in Asians than in Caucasians.

OBJECTIVE: We compared HDL-C levels between the Korean and US populations using stratified analysis according to age and sex and estimated the optimal cutoff value for HDL-C that best predicts the risk of cerebrovascular accidents (CVAs) and ischemic heart disease (IHD) in Koreans.

METHODS: The Korean National Health and Nutrition Examination Survey (KNHANES) 2010-2012 and the National Health and Nutrition Examination Survey (NHANES) 2011-2012 were used for the Korean and US populations, respectively. HDL-C levels were compared using general linear models. To estimate the optimal HDL-C cutoff value that predicts CVAs and IHD, sensitivity and specificity of different HDL-C levels were calculated.

RESULTS: The mean HDL-C level was significantly lower in KNHANES in both sexes (46.1 [standard error, 0.2] mg/dL in KNHANES and 47.7 [0.5] mg/dL in NHANES, $P = .003$ in men, and 51.2 [0.2] mg/dL in KNHANES and 58.3 [0.8] mg/dL in NHANES, $P < .001$ in women). The optimal HDL-C cutoff to predict CVA-IHD was 43 mg/dL and 48 mg/dL for Korean men and women, respectively, and 41 mg/dL and 56 mg/dL for US men and women, respectively.

CONCLUSION: HDL-C levels are significantly lower in both sexes in the Korean population than the US population. The optimal cutoff HDL-C value to predict the risk of CVA-IHD was 43 mg/dL for men and 48 mg/dL for women in the Korean population.

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Metabolic syndrome is a condition characterized by the presence of multiple metabolic risk factors for cardiovascular disease.[1] Low levels of high-density lipoprotein cholesterol (HDL-C), which is a component of metabolic syndrome, are associated with an elevated risk of atherosclerotic disorders such as cerebrovascular accidents

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(CVAs)[2] and ischemic heart disease (IHD).[3,4] The National Cholesterol Education Program (NCEP) Adult Treatment Panel (ATP) III adopted HDL-C levels of <40 mg/dL in men and <50 mg/dL in women to indicate the cutoff for low HDL-C in metabolic syndrome[5] based on epidemiologic studies conducted in insulin resistant men[6] and women.[7,8] However, the inverse association between HDL-C concentrations and IHD risk is continuous, and a threshold relationship has not yet been identified.[9] Despite this limitation, this HDL-C cutoff is frequently used to estimate the risk of several metabolic and cardiovascular diseases in Korea.[10–12]

Interestingly, nationwide surveys conducted in the Korean and US populations have shown that the prevalence of low HDL-C in the Korean population is significantly higher than that in the US population, especially in women.[13] In the Korean National Health and Nutrition Examination Survey (KNHANES) 2001-2007, 59.3% to 61.2% of Korean women had low HDL-C, which was almost double that of US women (33.8%) in the National Health and Nutrition Examination Survey (NHANES) 1998-2006.[13] However, the incidence of cardiovascular disease in the Korean population is not higher than that in the US population.[14]

Serum HDL-C concentrations differ by ethnicity, with reportedly lower HDL-C levels in Asians than in Caucasians.[15] Furthermore, in the Korean population, the sex difference in HDL-C levels may not be as significant. On average, HDL-C levels are 10 mg/dL lower in adult Caucasian men than in Caucasian women[9,16]; however, the difference in mean (standard error [SE]) HDL-C levels between sexes was lower in KNHANES 2005 (43.8 [0.2] and 46.3 [0.2] mg/dL in men and women, respectively).[17]

Considering the ethnic differences in HDL-C, the estimation of an adequate cutoff for low HDL-C level to predict cardiovascular disease in the Korean population is important for the prevention and management of cardiovascular disease. However, there have been few studies to investigate HDL-C levels for this purpose in the Korean population. In the present study, we compared HDL-C levels based on the presence of CVA and IHD between the Korean and US populations using nationwide surveys conducted in the early 2010s. In addition, we estimated the cutoff value for HDL-C that best predicts the risk of CVA and IHD in the Korean population.

Methods

Subjects

The Korean Ministry of Health and Welfare designed the KNHANES, which has been conducted since 1998, to be representative of the Korean population using a stratified, multistage, probability sampling method; the survey has been described in detail elsewhere.[13,18] We analyzed data from the KNHANES V, which was conducted from January 2010 to December 2012 with 25,533 individuals (participation rate, 80.8%), representing 11,400 households and 576 sampling frames.

For the analysis of the US population, the NHANES was used. It is a cross-sectional, nationwide study conducted by the Centers for Disease Control and Prevention (CDC) and is designed to evaluate the health and nutritional status of the noninstitutionalized US population. Further details are described elsewhere.[19] Data from NHANES 2011-2012 were used for analysis, including 9756 individuals.

Subjects aged ≥30 years with HDL-C measurement were included in the analysis. In KNHANES (n = 25,533), 17,292 (67.7%) subjects were aged ≥30 years, and serum HDL-C was measured in 15,074 (87.2% of age ≥30 years) subjects. In NHANES (n = 9756), 4566 (46.8%) subjects were aged ≥30 years, and 4033 (88.3% of age ≥30 years) measured HDL-C.

Measurement of metabolic parameters and disease definitions

Anthropometric and laboratory measurements in the KNHANES were as described in the following. Height was measured to the nearest 0.1 cm using a stadiometer (seca 210, seca, Hamburg, Germany), and weight was measured to the nearest 0.1 kg (GL-6000-20, G-tech, Uijeongbu City, Korea). Body mass index (BMI) was calculated as body weight (kg) divided by height squared (m^2). Waist circumference was measured to the nearest 0.1 cm (seca 200, seca). A mercury sphygmomanometer (Baumanometer, Baum, Copiague, NY, USA) was used to measure blood pressure to the nearest 2 mm Hg.

Blood samples were drawn from the antecubital vein in the morning after fasting for at least 8 hours. Samples were properly processed, immediately refrigerated at 2°C to 8°C, and sent to a central laboratory. Total cholesterol, HDL-C, low-density lipoprotein cholesterol (LDL-C), triglycerides (TGs), and fasting glucose were measured enzymatically (Hitachi Automatic Analyzer 7600, Hitachi, Tokyo, Japan). Glycated hemoglobin was measured by high-performance liquid chromatography (HLC-723G7, Tosoh, Tokyo, Japan).

The revised HDL-C value was determined, following reference values from the Clinical and Laboratory Standards Institute for metrological traceability. To verify the accuracy of HDL-C, traceability analysis was conducted by KNHANES in 2013 to confirm the accuracy of HDL-C measurement. Difference of HDL-C values from Korean central laboratory and US CDC were 5.3% to 9.2% for 2008 to 2011, and 2.3% to 3.5% for 2012. For this reason, new regression formula of HDL-C was necessary to verify HDL-C value, especially for 2008 to 2011. Commutable frozen serum samples were taken according to Clinical and Laboratory Standards Institute guideline, and samples were sent to CDC. Samples were analyzed with gold-standard