Associations of Obesity With Lipoprotein Subfractions in Japanese American, African American, and Korean Men

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ABSTRACT

Background: Both indices of obesity and lipoprotein subfractions contribute to coronary heart disease risk. However, associations between indices of obesity and lipoprotein subfractions remain undetermined across different ethnic groups.

Objective: This study aims to examine the associations of indices of obesity in Japanese Americans, African Americans, and Koreans with lipoprotein subfractions.

Methods: A population-based sample of 230 Japanese American, 91 African American, and 291 Korean men ages 40 to 49 was examined for indices of obesity—that is, visceral and subcutaneous adipose tissue (VAT and SAT, respectively); waist circumference; and body mass index—and for lipoprotein subfractions by nuclear magnetic resonance spectroscopy. Multiple regression analyses were performed in each of the 3 ethnic groups to examine the associations of each index of obesity with lipoprotein.

Conclusions: VAT had significant positive associations with total and small low-density lipoprotein (LDL) and a significant negative association with large high-density lipoprotein (HDL) in all 3 ethnicities ($p < 0.01$). SAT, waist circumference, and body mass index had significant positive associations with total and small LDL in only Japanese Americans and Koreans, whereas these indices had significant inverse associations with large HDL in all ethnic groups ($p < 0.01$). Compared with SAT, VAT had larger R^2 values in the associations with total and small LDL and large HDL in all 3 ethnic groups. VAT is significantly associated with total and small LDL and large HDL in all 3 ethnic groups. The associations of SAT, waist circumference, and body mass index with lipoprotein subfractions are weaker than the associations of VAT in all 3 ethnic groups.

Coronary heart disease (CHD) is the leading cause of death in the United States [1] and worldwide [2]. Thus, preventing CHD is of great interest from both a clinical and a public health perspective. Current clinical practice guidelines, such as those by the National Cholesterol Education Program Adult Treatment Panel, recommend measuring standard lipids to assess CHD risk and stratify risk categories [3]. Our ability to estimate the risk of developing CHD is limited, however, and intense efforts have been made to determine whether additional examination would improve the accuracy of CHD risk estimation [4,5]. Such efforts include measuring lipoprotein subfractions.

Lipoprotein subfractions can be quantified by nuclear magnetic resonance spectroscopy [6,7]. Some subfractions are reported to be associated with CHD. Total low-density lipoprotein (LDL) number and small LDL particles, for example, are strong predictors of CHD. Small high-density lipoprotein (HDL) is positively associated with CHD, whereas large HDL is inversely associated [8,9].

Many epidemiological studies have demonstrated strong associations of indices of obesity, such as visceral adipose tissue (VAT), subcutaneous adipose tissue (SAT), waist circumference (WC), and body mass index (BMI), with CHD and its risk factors [10–12]. Evidence suggests body fat distribution, such as VAT, is more strongly associated with CHD than BMI or WC are [11,13].

Recently, several studies have examined the associations between indices of obesity and lipoprotein subfractions. In these studies, VAT is more strongly associated with risk factors and lipoprotein subfractions than SAT is [11,14]. We have reported that VAT and SAT are associated with higher particle concentrations of total, large, and medium very low-density lipoprotein (VLDL), small LDL,

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and large HDL in a population-based sample of U.S. white and Japanese middle-aged men [15]. Our study also indicates the associations of VAT with lipoprotein subfractions are stronger than those for SAT. However, few studies have investigated associations between indices of obesity (i.e., VAT, SAT, WC, and BMI) and lipoprotein subfractions among different ethnicity groups from a community-based population. This study examined the association between indices of obesity and lipoprotein ;subfractions for Japanese Americans (JA), African Americans (AA), and Koreans from a community-based sample.

METHODS

Study participants

During 2002 to 2006, 712 men ages 40 to 49 were randomly selected: 303 JA men from a representative sample of offspring to fathers who participated in the Honolulu Heart Program, Honolulu, Hawaii, USA [16]; 107 AA men from Allegheny County, Pennsylvania, USA [17]; and 302 Korean men from Ansan, Gyeonggi-do, South Korea. JA men were the third or fourth generation of JA without ethnic admixture. All the participants were without clinical cardiovascular disease or other severe diseases [17]. Men in Honolulu were randomly selected from the offspring of the members of the Honolulu Heart Program [18]. Men in Allegheny County, Pennsylvania, USA, were randomly selected from the voter registration list. The voter registration list is very complete. Men in South Korea were randomly selected from the Korean Health and Genome Study, an ongoing population-based prospective cohort study [19]. The rate of participation was about 50% at each site. This rate of participation is much higher than for the MESA (Multi-Ethnic Study of Atherosclerosis) [20] and is comparable with the CARDIA (Coronary Artery Risk Development in Young Adults) [21] and the CHS (Cardiovascular Health Study) [22].

Of the original sample, we excluded men taking lipid-lowering medications (n = 83) and individuals with missing values (n = 17). The final sample was 612 subjects (230 JA, 91 AA, and 291 Koreans). Written informed consent was obtained from each participant. The study was approved by the institutional review boards of the following institutions: the Kuakini Medical Center, Honolulu, Hawaii, USA; the University of Pittsburgh, Pittsburgh, Pennsylvania, USA; and Korea University, Seoul, South Korea.

All participants underwent a physical examination and laboratory assessment and completed a lifestyle questionnaire (e.g., smoking and alcohol consumption), as described previously [17]. Venipuncture was performed after a 12-h fast, early in the morning of the clinic visit. Samples were stored at −80°C and shipped on dry ice to the University of Pittsburgh to determine lipids, glucose, and other factors. Serum lipids were determined using standardized methods by the Centers for Disease Control and Prevention. Intra-assay coefficients of variation for total cholesterol, triglycerides, and HDL-C were 1.8%, 1.8%, and 3.5%, respectively. Serum glucose was determined by an enzymatic assay. An intra-assay coefficient of variation for glucose was 1.8%. Data collection was standardized across the research centers.

Body mass index and abdominal adiposity indices

BMI was calculated using body weight and height (kg/m^2). WC was measured twice at the umbilical level using a measuring tape while the participant was standing upright in underwear. An average of the 2 measurements was used. VAT and SAT were determined as previously described [23]. Briefly, VAT and SAT areas were measured at the level between the fourth and fifth lumbar vertebrae using computed tomography images obtained with the same apparatus at each site (GE-Imatron C150; GE Medical System, South San Francisco, California, USA). All computed tomography images were read at the Cardiovascular Institute, University of Pittsburgh, using image analysis software by 1 trained reader (AccuImage; AccuImage Diagnostic Corporation, San Francisco, California, USA).

Lipoprotein measurement

Nuclear magnetic resonance spectroscopy (LipoScience, Inc., Raleigh, North Carolina, USA) was performed to quantify serum lipoproteins of different sizes [24]. Particle concentrations of the following lipoproteins were determined: VLDL (large: >60 nm; medium: 35−60 nm; small: 27−35 nm); LDL (intermediate-density lipoprotein: 23−27 nm; large: 21.3−23 nm; small: 18.3−21.2 nm); and HDL (large: 8.8−13.0 nm; medium: 8.2−8.8 nm; small: 7.3−8.2 nm) [8]. Weighted average particle sizes were calculated from the subclass levels.

Statistical analyses

Values of lipoprotein subfractions were positively skewed and log-transformed to approximate the normality. To examine the correlations among obesity indices, we used the Spearman rank correlation. To examine the association of each obesity index— BMI, WC, SAT, and VAT (a primary predictor variable)—with each lipoprotein (an outcome variable), multiple linear regression analyses were performed. In the regression model, values of lipoprotein were log-transformed to approximate the normality, and age, pack-year smoking, and amount of alcohol consumption per day were adjusted. Statistical significance level was considered to be 0.01. All statistical analyses were performed with IBM SPSS Statistics (version 20, IBM, Armonk, New York, USA).

RESULTS

The baseline characteristics of study subjects are presented in Table 1. Mean BMI (kg/m^2) differed significantly among the 3 groups: 27.3 for JA; 29.6 for AA; and 24.7 for Koreans. JA had significantly higher VAT and serum