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Significant associations between lipoprotein(a) and corrected apolipoprotein B-100 levels in African-Americans

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Abstract

Objectives—Lipoprotein(a), Lp(a), represents an apolipoprotein (apo) B-carrying lipoprotein, yet the relationship between Lp(a) and apoB levels has not been fully explored.

Methods—We addressed the relationship between Lp(a) and apoB-containing lipoprotein levels in 336 Caucasians and 224 African-Americans. Our approach takes unique molecular properties of Lp(a) as well as contribution of Lp(a) to the levels of these lipoproteins into account.

Results—Levels of total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), apoB and apoB/apoA-1 did not differ across ethnicity. African-Americans had higher levels of Lp(a) and high-density lipoprotein cholesterol and lower triglyceride levels compared to Caucasians. Lp(a) levels were correlated with levels of TC ($p<0.005$), LDL-C ($p<0.001$), apoB ($p<0.05$) or apoB/apoA-1 ($p<0.05$) in both ethnic groups. These associations remained significant only in African-Americans after adjustments for the contribution of Lp(a)-cholesterol or Lp(a)-apoB. Furthermore, taking Lp(a)-apoB into account, allele-specific apo(a) levels were significantly associated with apoB levels and the apoB/apoA-1 ratio in African-Americans. The latter associations in African-Americans remained significant for allele-specific apo(a) levels for smaller apo(a) sizes (<26 K4 repeats), after controlling for the effects of age, sex, and BMI.

Conclusions—Although TC, LDL-C, and apoB levels were comparable between African-Americans and Caucasians, the associations of these parameters with Lp(a) and allele specific apo(a) levels differed between these two ethnic groups. In African-Americans, apoB and apoB/apoA-1 remained consistently and positively associated with both Lp(a) and allele-specific apo(a) levels after adjustments for the contribution of Lp(a)-apoB. The findings suggest an interethnic difference with a closer relationship between Lp(a) and apoB among African-Americans.

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DISCLOSURES
None

Keywords

plasma lipids; ethnicity; corrections for the contribution of Lp(a); apo(a) sizes; K4 repeats

INTRODUCTION

Accumulating evidence, including recent Mendelian randomization and genetic studies, support the role of lipoprotein(a), Lp(a), as an independent causal risk factor for atherosclerotic cardiovascular disease [1–3]. Based on this evidence, clinical guidelines have recommended screening for elevated Lp(a) levels [4]. Besides a cholesterol-rich lipid core and one molecule of apolipoprotein (apo) B-100, like an LDL particle, Lp(a) contains a unique glycoprotein, i.e., apo(a) bound to apoB-100 with a single disulfide bond. Apo(a) has repeated loop structures, referred to as Kringles (K), where one motif, K4 type 2, is present in three to more than 40 copies [5]. This extensive size polymorphism in the apo(a) gene is a major predictor of Lp(a) levels, and in general small apo(a) sizes are associated with high Lp(a) levels [6–8]. However, for any given apo(a) size, Lp(a) levels vary across individuals, families, and ethnic groups with most profound differences between individuals of African versus non-African descent [9–11]. We have previously demonstrated a concept of allele-specific apo(a) level which determines the amount of Lp(a) associated with a defined apo(a) allele/isoform size, and reported that these levels were important in assessing the Lp(a)-associated cardiovascular risk across ethnicity [12].

Environmental and lifestyle-related factors and currently available lipid-lowering medications have no or minimal effects on Lp(a) levels [13–18] with exception of niacin [19] and hormone replacement therapy [20]. New evidence on the interactions between Lp(a) and inflammation [21–23] or chronic immune activation [24] has emerged, as studies have suggested an impact of these factors on Lp(a) with a variable effect across ethnicity. Notably, the relationship of Lp(a) with the plasma lipid profile, particularly, apoB-containing atherogenic lipoproteins, has attracted considerable attention, producing inconsistent results. While many studies focused on this topic have reported a positive correlation between Lp(a) and low-density lipoprotein cholesterol (LDL-C) or total cholesterol (TC) [25–31], others report no such association [16, 32, 33].

Furthermore, current assessments of TC, LDL-C and apoB generally do not take the contribution of Lp(a) to the levels of these lipoproteins into account. Considering that cholesterol corresponds to ~30% and apoB contributes to ~16% of Lp(a) mass [34, 35], the contribution of Lp(a) to overall TC, LDL-C and apoB levels can be substantial. This potential is particularly prominent in individuals with elevated Lp(a) levels. In addition, the effects of apo(a) size polymorphism (number of K4 repeats) and ethnicity/race on this association remain elusive.

In the present study, we investigated the relationship between Lp(a), allele-specific apo(a) and apoB-containing atherogenic lipoprotein levels, while taking into account the contribution of Lp(a) to the latter. The inclusion of two ethnic groups with very different Lp(a) and allele-specific apo(a) levels, but with similar apoB-containing lipoprotein levels

(Caucasians and African-Americans) allowed us to directly assess the relationship between apoB and Lp(a) under a range of conditions.

MATERIALS AND METHODS

Subjects

Subjects were recruited from a patient population scheduled for diagnostic coronary angiography either at Harlem Hospital Center in New York City or at the Mary Imogene Bassett Hospital in Cooperstown, NY. The clinical characteristics of the study population and the study design including inclusion and exclusion criteria have been described previously, and notably, exclusion criteria included use of lipid lowering drugs, as well as hormone replacement therapies [12, 36]. Briefly, a total of 648 patients, self-identified as Caucasian (n=344), African American (n=232), or other (n=72) were enrolled. The present report is based on the findings in 560 subjects (336 Caucasians, 224 African Americans); 16 subjects were excluded due to incomplete data. The apo(a) allele sizes, circulating apo(a) isoforms, and allele-specific apo(a) levels were available on 426 subjects (167 African Americans, 259 Caucasians). This cohort has been extensively studied with regard to Lp(a) and apo(a) size distributions and detailed information can be found in our previous studies [12, 21–23, 37]. The study was approved by the Institutional Review Boards at Harlem Hospital, the Mary Imogene Bassett Hospital, Columbia University College of Physicians and Surgeons, and University of California, Davis, and informed consent was obtained from all subjects.

Measurement of plasma lipids and lipoproteins

Participants were asked to fast for 12 hours, and blood samples were drawn approximately 2 to 4 hours before the catheterization procedure. Serum and plasma samples were separated and stored at −80°C prior to analysis. Concentrations of triglycerides (Sigma Diagnostics, St. Louis, MO), TC and high density lipoprotein cholesterol (HDL-C) (Roche, Sommerville, NJ) were determined using standard enzymatic procedures [38, 39]. HDL-C levels were measured after precipitation of apoB-containing lipoproteins with dextran sulfate [40], and LDL-C levels were calculated in subjects with triglyceride levels of <400 mg/dL with the formula of Friedewald [41]. ApoB-100 levels were determined by rate immunonephelometry (Array 360, Beckman, Brea, CA) using manufacturer' supplied calibrator and bi-level quality controls which were within the recommended precision for each test [42]. The interassay coefficient of variation was consistently less than 6%. These biochemical assays were performed at a core laboratory certified in lipid and lipoprotein measurements by the Center for Disease Control (Mary Imogene Basset Research Institute, Cooperstown, NY). Plasma Lp(a) levels were measured by an apo(a) size insensitive sandwich enzyme-linked immunosorbent assay (ELISA) (Sigma Diagnostics, St Louis, MO) and expressed as nmol/L [12]. The interassay coefficient of variation was 8.4% at an apo(a) level of 19.9 nM and 9.0% at an apo(a) level of 67.1nM [12, 36].

As Lp(a) levels were measured in nmol/L and other plasma lipids and lipoproteins were expressed in mg/dL, we converted Lp(a) values into mg/dL by use of a conversion factor of 2.4 nmol/L=1 mg/dL [12]. TC, LDL-C, and apoB levels were adjusted for the Lp(a)

contribution [25], according to compositional data in which cholesterol accounts for ~30% and apoB-100 for ~16% of total Lp(a) mass [34, 35]. Thus, the level of Lp(a) mass (mg/dL) multiplied by 0.3 was subtracted from TC and LDL-C values in all subjects. Similarly, total Lp(a) mass multiplied by 0.16 was subtracted from apoB-100 values. For corrected apoB-100/ApoA-1 ratio, the latter values were divided by apoA-1 levels.

To verify our findings on the relationship between Lp(a) and apoB-100 levels, we performed additional analyses. First, we converted apoB-100 values in mg/dL into nmol/L, using a molecular weight of approximately 512 kDa for ApoB-100 [43]. Thus, we recalculated particle concentration of apoB-100 by use of a conversion factor of 0.0512 mg/dL = 1 nmol. Second, Lp(a) values expressed as nmol/L were subtracted from the apoB-100 values expressed as nmol/L to obtain non-Lp(a)-apoB values. These values were used to describe the relationship between Lp(a) and apoB-100 at a molecular level.

Determinations of apo(a) isoform size and allele-specific apo(a) levels

Apo(a) isoform sizes were determined by Western blotting technique with SDS-agarose gel electrophoresis of plasma samples, followed by immonoblotting as previously described [7, 37]. The protein isoform dominance pattern was assessed by optical analyses of the apo(a) protein bands on the Western blots, and the visual estimations were validated by computerized scanning. To determine allele-specific apo(a) levels, for each of the apo(a) protein bands, Lp(a) levels were apportioned according to the degree of intensity of the bands on the Western blot as previously described [37].

Statistics

Statistical analysis was performed with SPSS software (SPSS Inc, Chicago, IL). Results were expressed as mean ± standard deviation (SD) for normally distributed variables, or median with interquartile range for non-normally distributed variables. Triglyceride levels were logarithmically transformed, and Lp(a) and allele-specific apo(a) levels were square root transformed to achieve normal distributions. Both the larger and smaller apo(a) isoforms of subjects with two distinguishable bands and one isoform of subjects with a single band were considered for statistical analyses. Unadjusted and adjusted (partial) Pearson's correlation coefficients for age, sex, and body mass index (BMI) were calculated to describe the magnitude and direction of the association of Lp(a) or allele-specific apo(a) levels with other variables for each ethnic group, respectively. Group means were compared using Student's *t*-test. All analyses were two-tailed, and *p*-values less than 0.05 were considered statistically significant.

RESULTS

Clinical characteristics of study population

Caucasians were slightly older and obese as compared with African-Americans (Table 1). There was no difference in the gender distribution between the two ethnic groups. Levels of TC, LDL-C or apoB did not differ significantly between Caucasians and African-Americans. However, African-Americans had significantly higher levels of HDL-C (*p*<0.001) and apoA-1 (*p*=0.003) and significantly lower levels of triglycerides (*p*<0.001) and apoB/apoA-1

ratio (*p*=0.008) compared to Caucasians. Furthermore, as expected, Lp(a) levels were significantly higher in African-Americans compared to Caucasians (*p*<0.001).

Relationship of Lp(a) with plasma lipid and lipoprotein levels before and after correction

First, we assessed the relationship of Lp(a) with plasma lipid and lipoprotein levels before corrections for each ethnic group separately. In both ethnic groups, Lp(a) levels were significantly and positively correlated with levels of TC, LDL-C, apoB and apoB/apoA-1 ratio regardless of adjustment for the covariates of age, sex, and BMI (Table 2). In addition, triglyceride levels were weakly but significantly associated with Lp(a) levels in African-Americans (*p*=0.028) before adjustment for the covariates. However, analyses controlling for the effects of the covariates resulted in disappearance of the latter significant association (*p*=0.052). HDL-C or apoA-1 levels were not significantly associated with Lp(a) levels in either ethnic group.

Second, we tested the effects of correction for the contribution of Lp(a) to apoB-containing lipoprotein levels on the relationship. Corrected values of TC, LDL-C, apoB and apoB/apoA-1 were calculated according to the formulas as described in Methods. As seen in Figure 1, the largest differences between corrected and uncorrected levels were seen for African-Americans. Thus, percentage changes in TC, LDL-C, and apoB levels from before correction levels were significantly greater in African-Americans than Caucasians (*p*<0.001 for all). We observed an interethnic difference as Lp(a) remained significantly associated with levels of TC, LDL-C, apoB and apoB/apoA-1 ratio in African-Americans, but not in Caucasians (Table 2). Furthermore, analyses controlling for the effects of covariates of age, sex, and BMI revealed a loss of significant associations between Lp(a) levels with TC or LDL-C levels in African-Americans.

To verify our finding on the relationship between Lp(a) and apoB levels at a molecular basis, we first converted apoB levels in mg/dL into nmol/L, and then recalculated non-Lp(a)-apoB (nmol/L) values as described in Methods. As shown in Figure 2, particle concentrations of Lp(a) were correlated with particle concentrations of apoB in African-Americans, but not in Caucasians, after correction for the contribution of Lp(a)-apoB content (Figure 2C and D), confirming the findings when using mg/dL.

Relationship of allele-specific apo(a) with plasma lipid and lipoprotein levels before and after correction

To assess an impact of apo(a) size on the relationship between Lp(a) and apoB, we analyzed the associations between Lp(a) levels associated with a defined apo(a) allele/isoform size, i.e., allele-specific apo(a) levels and other plasma lipid and lipoproteins levels. Before corrections, reflecting the Lp(a) findings, allele-specific apo(a) levels were significantly and positively correlated with levels of TC (*p*<0.001), LDL-C (*p*<0.001), apoB (*p*<0.05) and apoB/apoA-1 (*p*<0.05) ratio in both Caucasians and African-Americans (Supplementary Table 1). Adjustments for the effects of covariates (age, sex, and BMI) did not alter the findings, except for triglyceride in African-Americans. When corrected levels were taken into account, significant associations between allele-specific apo(a) levels and the above parameters were no longer seen in Caucasians. In African-Americans, however, allele-

specific apo(a) levels remained significantly and positively associated with apoB ($p<0.001$) and apoB/apoA-1 ($p=0.001$) levels, but not with TC and LDL-C levels (Supplementary Table 1). Again, these finding were not impacted by adjustments for the covariates. The correlations of allele-specific apo(a) levels (nmol/L) with apoB levels (nmol/L) before and after correction for the contribution of Lp(a)-apoB content across ethnicity are shown in Supplementary Figure 1. As for the findings in mg/dL, particle concentrations of allele-specific apo(a) were associated with particle concentrations of apoB even after taking the contribution of Lp(a)-apoB into account.

Relationship of allele-specific apo(a) levels for smaller versus larger apo(a) sizes with plasma lipid and lipoprotein levels before and after correction

To assess the impact of apo(a) size on the relationship between allele-specific apo(a) levels and apoB in more depth, we divided study subjects into two groups based on the median apo(a) size, i.e., 26 K4 repeats (for both ethnic groups). For smaller apo(a) sizes (<26 K4 repeats), allele-specific apo(a) levels were significantly and positively correlated with levels of TC, LDL-C and apoB, but not with apoB/apoA-1 in Caucasians (Table 3). In African-Americans, all four parameters (TC, LDL-C, apoB and apoB/apoA-1) were consistently associated with allele-specific apo(a) levels for smaller apo(a) sizes. For larger apo(a) sizes (26 K4 repeats), we observed an interethnic difference. Thus, allele-specific apo(a) levels for larger apo(a) sizes did not correlate with any of the parameters in Caucasians, but significantly correlated with all four parameters (TC, LDL-C, apoB and apoB/apoA-1) in African-Americans. Notably, as seen in Table 3, these results remained essentially the same when adjusted for the covariates of age, sex, and BMI.

We then assessed the effects of correction on the relationship. Not surprisingly, the corrections eliminated previously observed significant associations of TC, LDL-C and apoB with allele-specific apo(a) levels for smaller (<26 K4 repeats) apo(a) sizes in Caucasians (Table 3). In African-Americans, a similar effect was observed for larger (26 K4 repeats) apo(a) sizes as the previously observed significant associations of all four parameters vanished after corrections. For smaller apo(a) sizes, however, both apoB and apoB/apoA-1 remained consistently associated with allele-specific apo(a) levels in African-Americans even after corrections, and these associations were independent of the effects of covariates.

DISCUSSION

In the present study, we demonstrate a differential association of plasma Lp(a) and allele-specific apo(a) levels with other apoB-containing atherogenic lipoproteins across African-American-Caucasian ethnicity, despite similar levels of these apoB-containing lipoproteins in the two groups. Lp(a) and allele-specific apo(a) levels were significantly and positively correlated with TC, LDL-C, apoB and apoB/apoA-1 levels in both ethnic groups. However, after adjustment for the contribution of Lp(a)-cholesterol or -apoB content, only apoB levels and apoB/apoA-1 ratio remained consistently and positively associated with both Lp(a) and allele-specific apo(a) levels in African-Americans. These findings were independent of the effects of age, sex, and BMI. Notably, we were able to verify our findings on the relationship between Lp(a) and apoB levels at a molecular basis. In addition, in African-

Americans, there was a significant association between apoB and allele-specific Lp(a) levels for smaller, but not for larger apo(a) sizes.

The relationship of Lp(a) with other traditional cardiovascular risk factors, including atherogenic plasma lipids and lipoproteins levels, has attracted considerable attention and has been a focus of investigation in many studies. Studies focused on the relationship between Lp(a) and the plasma lipid profile, however, have produced conflicting results, and notably, most studies have not taken the contribution of Lp(a) cholesterol content to TC or LDL-C levels into account. Furthermore, limited information is available regarding any roles of apo(a) size polymorphism or ethnicity on the relationship of Lp(a) with apoB-containing lipoproteins. A positive correlation of Lp(a) with TC, LDL-C and/or triglyceride levels has been reported in non-diabetics [25–28] as well as diabetics [29]. Lp(a) levels were significantly associated with TC, LDL-C and apoB levels in patients with chronic renal failure [44], or with LDL size in patients with coronary artery disease [30]. In both Caucasians and African-Americans, Lp(a) levels were correlated with apoB but not with other lipoprotein levels [16]. Another study conducted among Caucasians and African-Americans from the Seychelles Island reported a positive correlation of Lp(a) with TC, LDL-C, and apoB levels regardless of ethnic background [27]. In line with these findings, prior to any correction for the contribution of Lp(a), we observed significant and positive correlations of Lp(a) with TC, LDL-C and apoB levels in both Caucasians and African-Americans.

Compositional data indicates that cholesterol accounts for ~30% and apoB for ~16% of Lp(a) mass [34, 35]. Therefore, in particular, among individuals with elevated Lp(a) levels, such as subjects of African descent, the contribution of Lp(a) to TC, LDL-C or apoB levels can be substantial. Among Caucasians enrolled in the Framingham Offspring Study, the observed positive correlations of Lp(a) with TC and LDL-C levels were abolished after appropriate adjustments [25]. Our findings in Caucasians were in line with this observation as the significant associations of Lp(a) with TC and LDL-C disappeared after correction for Lp(a)-cholesterol content. These findings suggest that the observed significant associations were mainly due to the contribution of Lp(a) cholesterol to TC or LDL-C levels. However, relatively little attention has been paid to the impact of any contribution of Lp(a) on the relationship between Lp(a) and apoB-containing lipoproteins across ethnicity. In contrast to findings in Caucasians, Lp(a) remained significantly associated with TC, LDL-C, apoB and apoB/apoA-1 in our African-American subjects even after adjustment for Lp(a)-cholesterol or -apoB. These findings are notable as African-Americans, in general, have higher Lp(a) levels than Caucasians. One might therefore expect that a subtraction of an amount equal to 30% of Lp(a) mass from TC or LDL-C (or 16% of Lp(a)-apoB mass from apoB) would result in a much greater degree of level change (Figure 1), and thus consequently might lead to a lack of correlation of Lp(a) levels with these parameters. Our results were, however, contrary to this assumption.

Similar to our results for Lp(a) levels, allele-specific apo(a) levels were significantly correlated with apoB-containing lipoproteins in both ethnic groups. In Caucasians, corrections for the contribution of Lp(a) led to a loss of significant associations. However, in African-Americans, the findings were somewhat different as allele-specific apo(a) levels

remained significantly associated with apoB and apoB/apoA-1 levels. Further analyses stratified by the median apo(a) size provided an in-depth insight into this relationship as circulating apoB levels showed the strongest correlation with allele-specific apo(a) levels carried by smaller apo(a) sizes in African-Americans.

The underlying mechanisms through which these associations are mediated are unclear, although many factors, including differences in hepatic apo(a) synthesis rate, Lp(a) assembly mechanisms, and recruitment of various apoB sources in the formation of Lp(a) may contribute. In this context, the question of assembly site for Lp(a) has been a subject of much debate, and it is unclear to what extent intracellular, extracellular, and/or plasma membrane-associated assembly contributes and whether differences might occur between individuals [45–47]. An *in vivo* kinetic study conducted in human subjects reported two sources for Lp(a)-apoB with about equal portions derived from preformed lipoproteins, such as IDL or LDL, and from newly synthesized hepatic apoB [46]. Another study using multi-compartmental modelling in healthy controls and patients undergoing hemodialysis suggested that the majority (>90%) of Lp(a)-apoB is synthesized from the liver [48]. It is tempting to suggest that the differences noted for the relationship between Lp(a) and apoB levels across ethnicity and/or apo(a) size groups might be related to differences in synthetic pathway. Further studies aimed at elucidating Lp(a) synthesis in different population groups are needed. It is in this context of interest that the production rate for apoB from LDL differed substantially from the production rate for apoB from Lp(a), suggesting different apoB kinetic pools for the formation of LDL and Lp(a) [47]. In contrast, Demant et al., reported results supporting an extracellular assembly [46]. Our findings of a differential association of apoB with allele-specific apo(a) levels with smaller versus larger apo(a) sizes in African-Americans may provide additional insights, and lend support for the concept that the source of apoB for Lp(a) production may vary between different groups and/or conditions.

The findings of the current study have several important implications. First, they demonstrate an interethnic difference in the relationship between Lp(a) and apoB-containing lipoproteins. Second, they emphasize the importance of taking into account the contribution of Lp(a)-cholesterol and -apoB content to apoB-containing lipoprotein levels. This could potentially be clinically relevant for individuals with high Lp(a) levels due to a higher contribution of Lp(a) to LDL-C levels. As currently available lipid-lowering drugs, except niacin, do not appreciably impact Lp(a) levels, a failure to reduce LDL-C levels in some individuals despite an aggressive lipid-lowering treatment, including statins, might partially be explained by the contribution of Lp(a)-cholesterol and -apoB to LDL. It was therefore interesting to note the closer relationship between Lp(a) and corrected apoB levels in one ethnic group, but not in the other. Furthermore, the present study was the first to investigate the relationship of apoB-containing atherogenic lipoprotein levels with allele-specific apo(a) levels, i.e., Lp(a) levels associated with a defined apo(a) allele size.

We acknowledge some limitations of this study as subjects in our study were recruited from patients scheduled for coronary angiography, and are likely more typical of a high-risk patient group than the healthy population at large. The mean ApoB level in our study was higher than that of reported for the general population [49], but was closer to that of reported

for diabetic adults enrolled in the National Health and Nutrition Examination Survey (115 mg/dL) [50]. However, other clinical and laboratory parameters were in agreement with differences generally observed between healthy African-American and Caucasian populations from other studies. Moreover, the generalizibilty of these findings to other ethnic groups is unknown.

In conclusion, although TC, LDL-C, and apoB levels were comparable between African-Americans and Caucasians, the associations of these parameters with Lp(a) and allele specific apo(a) levels differed between these two ethnic groups. In African-Americans, apoB and apoB/apoA-1 remained consistently and positively associated with both Lp(a) and allele-specific apo(a) levels after adjustments for the contribution of Lp(a)-apoB. The findings suggest a close relationship between Lp(a) and apoB among African-Americans.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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HIGHLIGHTS

- Lp(a) levels associate with TC, LDL-C and ApoB levels across ethnicity.

- After appropriate corrections, Lp(a) levels correlate with ApoB in African-Americans.

- Apo(a) sizes may potentially influence the associations of Lp(a) with apoB levels.

- Contribution of Lp(a) to apoB-containing lipoprotein levels can be substantial.

- Consideration of Lp(a) is important for risk assessment and treatment modification.
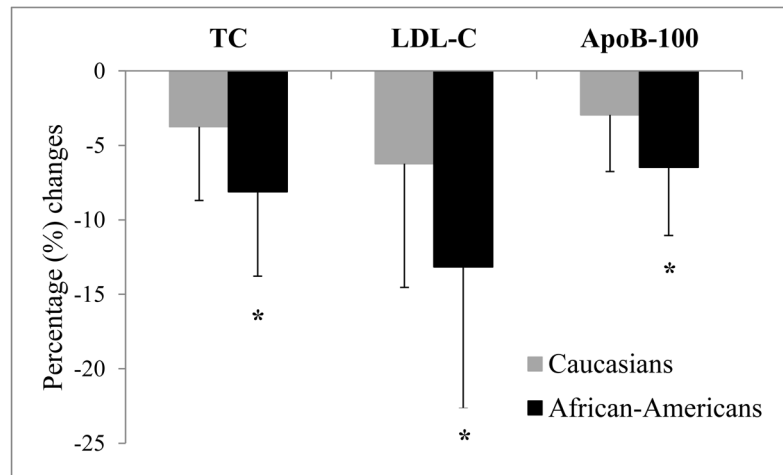
Figure 1. The effects of correction for the contribution of Lp(a)-cholesterol or -apoB content on apoB-containing atherogenic lipoprotein levels in Caucasians versus African-Americans
Differences in TC, LDL-C and ApoB levels before and after correction for the contribution of Lp(a)-cholesterol or -apoB content were calculated per each individual, and expressed as a percentage (%) change from the before correction level. Based on the individual percentage change, the mean percentage changes in TC, LDL-C, and apoB levels per each ethnic group were computed, and are shown in the graph. For details on calculations of corrected levels, see the footnote of Table 2 or the Methods section.

*: *p*<0.001 versus Caucasians

Abbreviations: TC, total cholesterol, LDL-C, low-density lipoprotein cholesterol, apoB, apolipoprotein B;
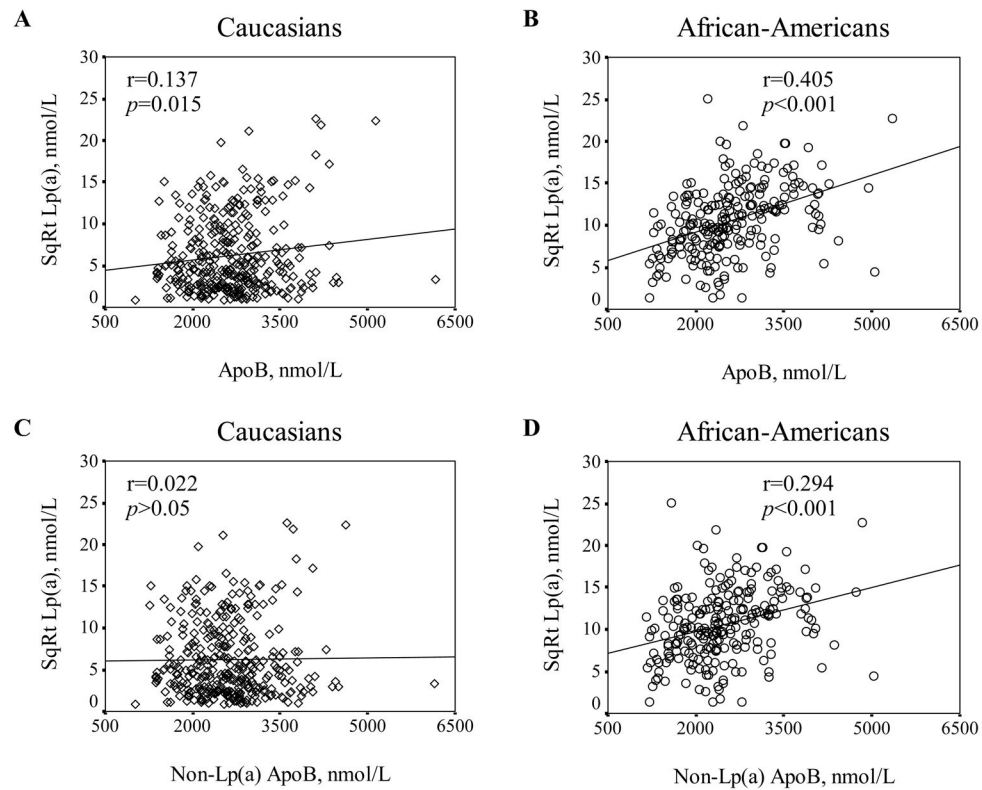
Figure 2. Association of Lp(a) (nmol/L) level with apoB (nmol/L) level before and after correction for the contribution of Lp(a)-apoB content in Caucasians versus African-Americans
The relationship between apoB and square root transformed Lp(a) levels before (A and B) and after (C and D) correction for the contribution of Lp(a)-apoB content is described by partial correlation coefficients controlling for the effects of age, sex, and BMI. At molecular level, Lp(a) remained significantly and positively associated with apoB levels after corrections in African-Americans (D), but not in Caucasians (C). For conversion of apoB levels in mg/dL into nmol/L and calculations of non-Lp(a) apoB levels, see the Methods section.
Abbreviations: SqRt, square root; apoB, apolipoprotein B;

Table 1

Characteristics of study population

Characteristics	Caucasians[†] (n=336)	African-Americans (n=224)	*p*-value
Men/women (n)	217/119	126/98	NS
Age (years)	56.8±10.3	54.8±9.2	0.025
Body mass index (kg/m^2)	29.7±6.0	28.5±6.1	0.043
Total cholesterol (mg/dL)	197±41	198±45	NS
LDL cholesterol (mg/dL)	122±35	126±42	NS
HDL cholesterol (mg/dL)	41±12	49±17	<0.001
Lipoprotein(a) (nmol/L)	24 (7–79)	108 (59–180)	<0.001
Triglycerides (mg/dL)	153 (114–222)	106 (80–144)	<0.001
ApoB-100 (mg/dL)	136±36	134±40	NS
ApoA-1 (mg/dL)	122±23	130±28	0.003
ApoB/ApoA-1	1.15±0.33	1.07±0.37	0.008

Data are expressed as mean ± standard deviation or median (interquartile range) for non-normally distributed variables. Logarithmically transformed triglyceride and square root transformed Lp(a) values were used for statistical analyses.

[†]The results for Lp(a), apoB, apoA-1, and apoB/apoA-1 ratio were based on the data of 304 subjects.

Abbreviations: Apo, apolipoprotein; HDL, high-density lipoprotein; LDL, low-density lipoprotein, NS, not significant.

Table 2

Pearson's correlation coefficients on the relationship between plasma Lp(a) levels (mg/dL) and other lipid and lipoproteins with and without adjustment for the covariates of age, sex, and body mass index

	Caucasians				African-Americans			
	Unadjusted		Adjusted		Unadjusted		Adjusted	
	r	p	r	p	r	p	r	p
Before correction								
Total cholesterol (mg/dL)	0.159	0.004	0.179	0.002	0.391	<0.001	0.377	<0.001
LDL cholesterol (mg/dL)	0.217	<0.001	0.220	<0.001	0.411	<0.001	0.401	<0.001
ApoB-100 (mg/dL)	0.127	0.021	0.142	0.013	0.415	<0.001	0.405	<0.001
ApoB/ApoA-1(mg/dL)	0.138	0.012	0.153	0.007	0.334	<0.001	0.330	<0.001
HDL cholesterol (mg/dL)	−0.061	NS	−0.067	NS	−0.022	NS	−0.025	NS
Triglycerides (mg/dL)	−0.005	NS	0.029	NS	0.145	0.028	0.130	0.052
ApoA-1	−0.039	NS	−0.039	NS	0.016	NS	−0.022	NS
After correction								
Total cholesterol (mg/dL)	−0.083	NS	−0.079	NS	0.139	0.034	0.117	NS
LDL cholesterol (mg/dL)	−0.073	NS	−0.078	NS	0.138	0.036	0.118	NS
ApoB-100 (mg/dL)	−0.022	NS	−0.010	NS	0.272	<0.001	0.258	<0.001
ApoB/ApoA-1	0.005	NS	0.014	NS	0.213	0.001	0.206	0.002

Lp(a) levels were measured in nmol/L and converted to mg/dL by use of a conversion factor of 2.4 nmol/L = 1 mg/dL. Corrected levels were calculated as described in Methods [34, 35]. The formulas used were for TC, TC (mg/dL) − [Lp(a) (mg/dL) × 0.3]; for LDL, LDL (mg/dL) − [Lp(a) (mg/dL) × 0.3]; and for apoB-100, apoB-100 (mg/dL) − [Lp(a) (mg/dL) × 0.16], respectively. For corrected apoB/apoA-1 ratio, the latter apoB-100 values were divided by apoA-1 values. Logarithmically transformed triglyceride and square root transformed Lp(a) values were used for statistical analyses. For abbreviations see the footnote of Table 1.

Table 3

Pearson's correlation coefficients on the relationship of allele-specific apo(a) levels (mg/dL) for smaller (<26 K4) versus larger (≥26 K4) apo(a) sizes with apoB-containing lipoproteins with and without adjustment for the covariates of age, sex, and body mass index

Correction	Caucasians								African-Americans							
	≥26 K4				<26 K4				≥26 K4				<26 K4			
	Unadjusted		Adjusted		Unadjusted		Adjusted		Unadjusted		Adjusted		Unadjusted		Adjusted	
	r	p	r	p	r	p	r	p	r	p	r	p	r	p	r	p
Before																
TC	0.002	NS	0.014	NS	0.178	0.020	0.227	0.004	0.232	0.003	0.278	<0.001	0.280	0.002	0.276	0.002
LDL-C	0.065	NS	0.051	NS	0.250	0.001	0.265	0.001	0.244	0.002	0.288	<0.001	0.311	<0.001	0.307	0.001
ApoB-100	−0.021	NS	−0.005	NS	0.183	0.017	0.234	0.003	0.243	0.002	0.289	<0.001	0.310	0.001	0.302	0.001
ApoB/ApoA-1	0.024	NS	0.043	NS	0.135	NS	0.199	0.013	0.165	0.038	0.196	0.014	0.326	<0.001	0.323	<0.001
After																
TC	−0.067	NS	−0.058	NS	−0.051	NS	−0.034	NS	0.069	NS	0.119	NS	0.111	NS	0.096	NS
LDL-C	−0.017	NS	−0.033	NS	−0.022	NS	−0.023	NS	0.064	NS	0.113	NS	0.140	NS	0.127	NS
ApoB-100	−0.060	NS	−0.043	NS	0.034	NS	0.080	NS	0.151	NS	0.200	0.013	0.220	0.015	0.208	0.023
ApoB/ApoA-1	−0.015	NS	0.003	NS	0.011	NS	0.071	NS	0.093	NS	0.125	NS	0.245	0.007	0.239	0.009

Square root transformed allele-specific apo(a) values were used for statistical analyses. For calculations of corrected levels, please see the footnote of Table 2 or the Methods section.

Abbreviations: Apo, apolipoprotein; K, kringle; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol;