ApoE and apoC-III-defined HDL subtypes: A descriptive study of their LCAT and CETP content and activity

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Abstract

Background

High-density lipoproteins (HDL) in plasma are strongly and negatively associated with cardiovascular risk, yet interventions to raise HDL have not improved cardiovascular outcomes. HDL functionality and heterogeneity may hold the clue to this paradox. The apolipoprotein composition of HDL may be an important determinant of their functionality. Lecithin-cholesterol acyl transferase (LCAT) and cholesterol-ester transfer protein (CETP) are key enzymes for HDL-mediated reverse cholesterol transport. We assessed the distribution and activity of LCAT and CETP in HDL subspecies defined by their content of apolipoproteins E (apoE) and C-III (apoC-III) in humans.

Methods

We isolated in adult humans of both sexes (mean age 55.6, BMI 26.9 Kg/m², HbA1c 5.4%), four subspecies of HDL containing respectively: No apoE and no apoC-III (E-C-), apoE but not apoC-III (E+C-), apoC-III but no apoE (E-C+) and both apoE and apoC-III (E+C+). In each HDL subspecies, we measured LCAT and CETP concentration and activity using immunoenzymatic and fluorometric methods. Additionally, we determined the size distribution of HDL in each apolipoprotein-defined fraction using non-denaturing electrophoresis and anti-ApoA-I western blot.

Results

Similar to previous studies, HDL in the E-C- fraction was the predominant subtype. The size distribution of HDL was very similar across all four apolipoprotein-defined fractions. LCAT was most abundant in E-C- HDL (3.58 mg/mL, 59.6 % of plasma LCAT mass), while HDL with apoE or apoC-III had much less LCAT (19.8%, 12.2% and 8.37% of plasma LCAT respectively for E+C-, E-C+ and E+C+). Despite a much lower LCAT mass, LCAT activity in E+C- HDL was comparable to that in E-C- HDL. Both CETP mass and CETP activity showed only slight variations across HDL subspecies. There was an inverse correlation between plasma LCAT activity and both E-C+ pre-beta HDL ($r=-0.55$, $p=0.017$) and E-C- alpha 1 HDL ($r=-0.49$, $p=0.041$). Conversely, there was a direct correlation between E-C+ alpha 1 HDL and CETP activity in plasma ($r=0.52$, $p=0.025$).

Conclusions

Our results suggest that LCAT activity in humans is influenced by the presence of small interchangeable apolipoproteins. The presence of apoE in small HDL is correlated with increased LCAT activity and esterification of plasma cholesterol.

Full Text

Due to technical limitations, full-text HTML conversion of this manuscript could not be completed.

However, the manuscript can be downloaded and accessed as a PDF.

Figures

Figure 1

Distribution of plasma apoA-I across HDL subfractions defined by size, apoE and apoC-III content. HDL size ranges are as follows: Prebeta: <7.1 nm, alpha 3: 7.1-8.2 nm, alpha 2: 8.2-9.5 nm, alpha 1: 9.5-12.2 nm (n=18, 10 women and 8 men).

Figure 2

LCAT concentrations and activities in HDL subfractions defined by their apoE and apoC-III content. (A-Top) LCAT concentrations. (B-bottom) LCAT activities (n=18, 10 women and 8 men).

Figure 3

CETP concentrations and activities in HDL subfractions defined by their apoE and apoC-III content. (A-top) CETP concentrations. There was no significant difference across subfractions (overall ANOVA $p=0.48$). (B-bottom) CETP activities. There was no significant

difference across subfractions (overall ANOVA $p=0.50$) ($n=18$, 10 women and 8 men).