Apolipoprotein E-containing high-density lipoprotein (HDL) cholesterol is a better indicator for anti-atherosclerotic function of HDL than total HDL cholesterol: a community-based cohort study

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Aim: APOE-containing HDL (APOE-HDL) particle may be necessary to stimulate the reverse cholesterol transport process, and was associated with CHD reported by either underpowered or hospital-based studies. We assessed that whether APOE-HDL cholesterol is causally associated with atherosclerotic CVD risk and this association is independent of total HDL cholesterol.

Methods: APOE-HDL cholesterol and HDL cholesterol were measured in 5417 cardiovascular disease-free participants (women, 51.8%) aged 45-79 years at baseline in the Chinese Multi-provincial Cohort Study. APOE-HDLC/HDLC ratio was calculated to assess the relative proportion of APOE-HDL cholesterol in total HDL cholesterol. Multivariate Cox regression was employed to assess the association between HDL related biomarkers and 10-year CHD incident risk.

Results: Mean levels of baseline APOE-HDL cholesterol and APOE-HDLC/HDLC ratio were 5.15 ± 1.60 mg/dL and 9.05 ± 0.94 %, respectively. HDL cholesterol was strongly correlated with APOE-HDL cholesterol (partial r: 0.978), and moderately with APOE-HDLC/HDLC ratio (partial r: 0.604). Total of 100 incident CHD events occurred during 10-year follow-up. High levels of baseline HDL related biomarkers were significantly negatively associated with incident CHD risk. However, there were no overlaps in 95% confidence interval of absolute risk for the comparison of APOE-HDLC/HDLC ratio (0.48, 95% CI=0.44-0.52) with HDL cholesterol (0.83, 95% CI=0.78-0.88) among participants with the highest level of these parameters. Furthermore, among participants with different levels of HDL cholesterol, baseline APOE-HDLC/HDLC ratio was negatively associated with incident CHD risk, but participants in the highest category of HDL cholesterol had the lowest HR associated with APOE-HDLC/HDLC ratio.

Figure. Cox regression analysis of APOE-HDLC/HDLC ratio associated with the risk of CHD incidence among HDLC subgroup

Conclusions: In conclusion, our findings revealed that APOE-HDLC/HDLC ratio was significantly associated with 10-year increased risk of incident CHD, even beyond HDL cholesterol, suggesting that APOE containing HDL can serve as a better indicator for the anti-atherosclerotic function of HDL than total HDL cholesterol.

Table. Cox regression analysis of HDL related biomarkers on the long-term risk of CHD incidence

Clinical Features	Subgroup of HDL related biomarkers			
	Group 1	Group 2	Group 3	Group 4
APOE-HDLC/HDLC ratio (%)	<8.6	8.6-9.2	9.3-9.9	≥10.0
No. of participants	1367	1628	1643	779
No. of CHD events	29	33	30	8
Incidence rate (per 100,000 person-years)	342	290	273	129
Multivariate adjusted HR(95% CI)	Reference	0.98 (0.55-1.75)	0.84 (0.48-1.46)	0.26 (0.10-0.71)
Absolute risk (%)	4.18 (3.96-4.36)	2.69 (2.58-2.82)	2.45 (2.35-2.59)	0.48 (0.44-0.52)
HDLC (mg/dl)	<40(M) <50(F)	40-49(M) 50-59(F)	50-59(M) 60-69(F)	≥60(M) ≥70(F)
No. of participants	1056	1820	1370	1171
No. of CHD events	31	34	23	12
Incidence rate (per 100,000 person-years)	415	273	244	156
Multivariate adjusted HR(95% CI)	Reference	0.65 (0.39-1.11)	0.54 (0.29-1.02)	0.39 (0.18-0.88)
Absolute risk (%)	4.08 (3.87-4.38)	2.36 (2.20-2.46)	1.69 (1.62-1.78)	0.83 (0.78-0.88)
APOE-HDLC (mg/dl)	<4.0(M) <5.0(F)	4.0-4.9(M) 5.0-5.9(F)	5.0-5.9(M) 6.0-6.9(F)	≥6.0(M) ≥7.0(F)
No. of participants	1925	1483	990	1019
No. of CHD events	46	31	13	10
Incidence rate (per 100,000 person-years)	355	302	193	142
Multivariate adjusted HR(95% CI)	Reference	0.81 (0.49-1.33)	0.58 (0.28-1.21)	0.42 (0.20-0.86)
Absolute risk (%)	4.09 (3.91-4.29)	2.74 (2.61-2.90)	1.89 (1.76-2.02)	1.51 (1.41-1.61)

Abbreviations: APOE-HDLC/HDLC ratio, the ratio of apolipoprotein E-containing HDL cholesterol to total HDL cholesterol; CI, confidence interval; F, female; HR, hazard ratio; M, male.

†All substantial models are additionally adjusted for sex, age (5 year), BMI, smoking status, SBP (10 mmHg), LDLC (30 mg/dl), DM, high TG (≥150 mg/dl), anti-dyslipidemic medication, and log-transformed hs-CRP.