Cholesterol efflux to high density lipoproteins (HDL) in plasma does not reflect cardiovascular risk

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Introduction

High density lipoprotein cholesterol (HDL-C) is inversely correlated with coronary heart disease incidence, but interventional studies failed to show beneficial effects of HDL-C elevation on cardiovascular risk. Cholesterol efflux from macrophages to plasma HDL (HDL-CE) has been proposed as an alternative metrics of HDL function, but its capacity to predict cardiovascular disease remains controversial. We here examined CE among patients with varying cardiovascular risk and compared it to lipoprotein-associated phospholipase A2 (Lp-PLA2) – an independent coronary risk marker.

Methods

168 asymptomatic male subjects attending the lipid outpatient clinic at the University Hospital Münster were enrolled in the study. 10-year cardiovascular risk was calculated using the PROCAM algorithm. Lipid parameters in plasma including HDL-C, low density cholesterol, and triglycerides were measured with routine laboratory procedures. HDL-CE was determined using human THP-1 monocyte-derived macrophages after precipitating apoB-containing lipoproteins. Lp-PLA2 activity was measured using enzymatic test (DiaSys GmbH). Carotid intima-media thickness (cIMT) was measured by Doppler ultrasonography. The exclusion criteria for this study were renal impairment (creatinine > 1.2 mg/dl), latent or manifest hyperthyroidism (TSH <0.20 mU/ml), bronchial asthma, AV- block, psoriasis, treatment with lipid-lowering agents or with antihypertensives and symptomatic coronary heart disease (acute myocardial infarction, angina pectoris, angioplasty or aortocoronary venous bypass).

Study group		range	median	number
age (years)		42-46	65	58
sex	*m*			162
	w			0
smoking	*yes*			40
	no			119
diabetes mellitus	*yes*			26
	no			134
familiar history	*yes*			48
	no			112
10-year-risk		1.22-64.25	12.69	
risk group	*<10%*			53
	10-20%			73
	>20%			33
intima-media thickness (mm)		0.5-1.8	0,8	130
cholesterol (mg/dl)		135-384	240	
triglyceride (mg/dl)		50-621	149	
LDL (mg/dl)		0-269	160	
HDL (mg/dl)		26-89	49	
ApoA1 (mg/dl)		100-197	144	
ApoB (mg/dl)		61-177	122	
Lp-PLA2		256-825	480.55	
efflux (plasma)		0.610-1.4	0.930	
HDL Efflux		0.511-1.232	0.933	

Results

As expected, HDL-C and HDL-CE were closely correlated to each other. However, similar HDL-CE distribution was observed among subjects with low (<10%), moderate (10 – 20%), and high (>20%) cardiovascular risk. In addition, HDL-CE did non correlate with cIMT. By contrast, patients with moderate or high cardiovascular risk presented with increased Lp-PLA2 activities in plasma and the latter parameter was correlated with cIMT. A correlation between calculated cardiovascular risk and cIMT was additionally observed.

Multiple linear-regression analysis	10-year-risk	
	Regression coefficient	**Significance**
Lp-PLA2	0.430**	p<0.01
intima-media thickness	0.207*	p<0.05
HDL	-0.478**	p<0.01
LDL	0.360**	p<0.01
cholesterol	0.306**	p<0.01
triglyceride	0.439**	p<0.01
ApoA1	-0.397**	p<0.01
ApoB	0.350**	p<0.01
HDL-Efflux	-0.087	p>0.05
plasma-Efflux	0.117	p>0.05

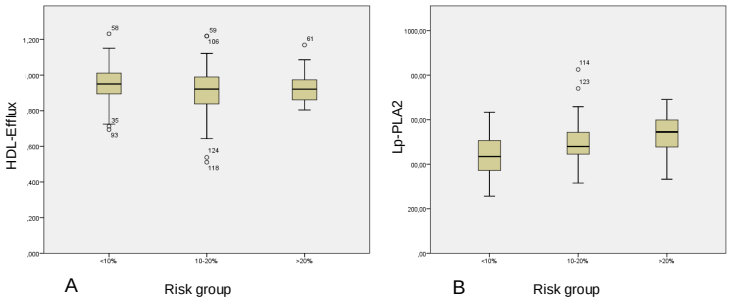

Fig.1: Distribution of HDL-efflux (A) and Lp-PLA2 (B) in the low (<10%), middle (10-20%) and high (>20%) group according to PROCAM risk algorithm. Box-plots contain the 1st and 3rd quartiles, the median, and the whiskers represent the lowest and the greatest values.

Conclusion

Present data do not favour the contention that HDL-CE might be useful as a marker of cardiovascular risk. Determination of Lp-PLA2 might improve cardiovascular risk prediction.

References

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