Correlation of Cholesterol Efflux Capacity with Femoral and Carotid Plaque Volume as measured by three-dimensional ultrasound

Noflatscher M.[1], Hunjadi M.[2], Schreinlechner M.[1], Sommer P.[1], Deutinger P.[1], Lener D.[1], Mair F.[1], Theurl M.[1], Kirchmair R.[1], Bauer A.[1], Ritsch A.[2], Marschang P.[1, 3]

[1] Medical University of Innsbruck, Department of Internal Medicine III, [2]Medical University of Innsbruck, Department of Internal Medicine I, [3] Department of Internal Medicine, Central Hospital of Bolzano

Background

Atherosclerosis is a systemic multifocal disease that can cause the narrowing and occlusion of arteries resulting in cardiovascular disease (CVD). Hypercholesterolemia plays a pivotal role in the pathogenesis of atherosclerotic plaques by the accumulation of cholesterol in the arterial wall. Cholesterol efflux mediated by HDL is capable of transporting cholesterol from the periphery back to the liver in a process called reverse cholesterol transport. Cholesterol efflux capacity (CEC) is inversely correlated with cardiovascular risk and has been proposed as a surrogate marker for reverse cholesterol transport. In this study, we set out to study a possible association between CEC and peripheral atheroslcerotic plaque volume.

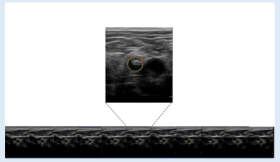

Fig. 1. 3D plaque volumetry measurement using an automated software on a Philips iU22 system equipped with a VL 13-5 probe (1)

Methods

Since lipid lowering therapy interferes with CEC, we studied a subset of 177 patients (median age 64; 48.6% women) without lipid-lowering medication that had been included in a study of 443 patients with at least one cardiovascular risk factor or established CVD. CETP-mediated cholesterol ester transfer was measured by quantifying the transfer of cholesterol ester from radiolabelled exogenous HDL to apoB-containing lipoproteins. CEC was determined using cAMP treated 3H-cholesterol-labeled J774 cells. Plaque volume in the carotid and the femoral artery was measured using a 3D ultrasound system equipped with a semi-automatic software. High total plaque volume was defined above the 75th percentile.

Results

We found a inverse correlation between CEC and high total plaque volume ($p = 0.027$) in patients without lipid-lowering therapy. On the other hand, there was no correlation between LDL cholesterol, lipoprotein(a), or CETP-mediated cholesterol ester transfer with atherosclerotic plaque volume.

	Total population (n=442)	Low Total Plaque Volume (n=333, 0-500 mm³)	High Total Plaque Volume (n= 109, 501-2048 mm³)	p Value
Age, years	64 (57-72)	62 (55-70)	68 (61.5-75)	<0.001
Sex (female)	184 (41.6)	153 (45.9)	31 (28.4)	0.001
Body mass index, kg/m2	25.6 (23.65-28.4)	25.4 (23.45-28.4)	25.9 (24.15-27.85)	n.s.
Hypertension, n(%)	294 (66.5)	203 (61)	91 (83.5)	<0.001
Family history for CV-diseases, n(%)	108 (24.4)	88 (26.4)	20 (18.3)	n.s.
Smoking (pack years)	12.89 (± 19.45)	10.91 (± 17.43)	18.62 (±23.55)	0.003
Hyperlipidaemia, n(%)	392 (88.7)	295 (88.6)	97 (89)	n.s.
Diabetes mellitus, n(%)	55 (12.4)	37 (11.1)	18 (16.5)	n.s.
hs-CRP, mg/dl	0.18 (0.09-0.41)	0.17 (0.08-0.39)	0.205 (0.10-0.42)	n.s.
Total cholesterol, mg/dl	189 (160.8-223.3)	195 (164-227.25)	175.5 (154.25-198)	<0.001
LDL-cholesterol, mg/dl	113 (90-144)	119 (94-148.5)	104 (83.25-127.5)	<0.001
HDL-cholesterol, mg/dl	57 (46-71)	58 (48-73)	52.5 (43-64)	0.004
Triglyceride, mg/dl	132 (95-179)	128 (92.75-172)	140 (99-202.5)	0.039
Lipoprotein (a), mmol/l	20 (20-98.7)	20 (20-91.48)	20.8 (20-119.1)	n.s.
Lipid lowering therapy, n(%)	266 (60.2)	185 (55.6)	81 (74.3)	0.001
Antihypertensive therapy, n(%)	241 (54.5)	159 (47.7)	82 (75.2)	<0.001
Antidiabetic therapy, n(%)	44 (10)	28 (8.4)	16 (14.7)	n.s.
CKD, n(%)	59 (13.3)	34 (10.2)	25 (22.9)	0.001
CAD, n(%)	160 (36.2)	103 (30.9)	57 (52.3)	<0.001
CBVD, n(%)	42 (9.5)	26 (7.8)	16 (14.7)	0.034
PAD, n(%)	33 (7.5)	11 (3.3)	22 (20.2)	<0.001

Table 1. Characteristics of the study population.
Parameters are median (interquartile range) or mean (± standard deviation) as indicated for continuous variables or number (percentage) for categorical variables.
CV-disease = cardiovascular disease, hs-CRP = high-sensitive C-reactive protein, LDL = low density lipoprotein, HDL = high density lipoprotein , CKD= chronic kidney disease, CAD= coronary artery disease, CBVD= cerebrovascular disease, PAD= peripheral arterial occlusive disease

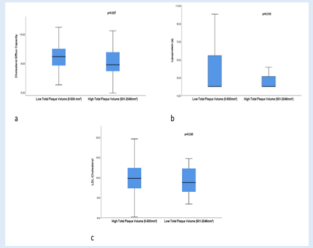

Figure 1: Association of total plaque volume with cholesterol efflux capacity, lipoprotein (a) and LDL-cholesterol in patients without lipid-lowering therapy

Conclusion

We conclude that CEC correlates inversely with peripheral atherosclerosis in patients not taking lipid-lowering therapy, further strengthening its role as a cardiovascular biomarker.