

Virtual Histology Evaluation of Atherosclerosis Regression During Atorvastatin and Ezetimibe Administration - HEAVEN study (ongoing)

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Aim: to investigate the changes of plaque and lumen volumes by intravascular ultrasound (IVUS) , changes of plaque composition by virtual histology (VH) in segment at least 30 mm and changes of serum inflammatory markers (IL-6, VCAM, ICAM, TNF, CD40 ligand) during aggressive hypolipidemic treatment. Polymorphism of genes for hemoxygenase promoter (HO) and endothelial nitric oxide synthase, exon 7 (ENOS) were studied.

Results: 107 patients with stable angina pectoris was randomly designed for 80mg atorvastatin plus 10mg ezetimibe (group A) or 10mg of atorvastatin (group B). Coronary angiography, IVUS and VH were done during baseline and after 12 months follow-up. Till now 72 patients completed study and 40 were analyzed, 9 patients refused control coronary angiography. Mean length of plaque is 40.8 mm. Changes of volumes, plaque composition, plaque regression and lipids levels are summarized in table. Plaque regression was defined as decrease of plaque volume together with increase of lumen volume. We found interesting relationships among changes of necrotic core (NC), markers and genes. Decreasing amount of NC correlated with lowering of at least four from five inflammatory markers (p=0.05) and was more pronounced in patients with protective polymorphism of ENOS (p=0.03). Decrease of plaque volume was found in patients with protective polymorphism of ENOS compared to risk one (-26.4 mm³ ± 24.3 vs. +2.5mm³ ± 29.1, p=0.05).

Conclusion: Our first results have shown higher occurrence of plaque regression, enlargement of lumen volume and significant decrease of LDL cholesterol in group A compared to group B. Interesting correlations among NC, inflammatory markers and ENOS were seen. Type of ENOS polymorphism influences also plaque regression. No statistical differences in changing of plaque composition were found in both groups.

	group A	group B	p
Δ lumen volume [%]	2.4 ± 6.9	-5.1 ± 9.2	0.015
Δ vessel volume [%]	-0.03 ± 5.3	-4.1 ± 8.4	0.12
Δ plaque volume [%]	-2.6 ± 7.1	-2.7 ± 12.3	0.96
Δ fibrous tissue [%]	-1.7 ± 7.9	-1.05 ± 8.5	0.82
Δ fibro-lipid tissue [%]	-1.9 ± 10.3	-3.1 ± 14.2	0.80
Δ calcification [%]	2.1 ± 4.8	2.0 ± 4.1	0.98
Δ necrotic core [%]	1.9 ± 9.8	2.3 ± 6.8	0.89
plaque regression	57.1 %	21.1 %	0.03
Δ total cholesterol [mmol/l]	-2.6 ± 1.9	-1.6 ± 1.8	0.16
Δ LDL cholesterol [mmol/l]	-1.05 ± 1.5	-0.14 ± 0.9	0.04
Δ HDL cholesterol [mmol/l]	0.12 ± 0.5	-0.06 ± 0.2	0.16
Δ triacyglyceroles [mmol/l]	-0.7 ± 0.8	-0.3 ± 0.8	0.17