

Intravascular Ultrasound Evaluation of Coronary Plaque Regression by Low Density Lipoprotein-Apheresis in Familial Hypercholesterolemia

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Object : This paper shows the efficacy of aggressive lipid-lowering therapy using the combination of LDL-apheresis LDL-A and lipid-lowering drugs on regression of coronary plaque in familial hypercholesterolemia (FH) as the result of one-year multicenter controlled study. Of 18 heterozygous FH with coronary heart disease, 11 were treated with LDL-A combined with lipid-lowering drugs (LDL-A group) and 7 were with medication only (medication group). Change in coronary plaque area (PA) and minimal lumen diameter (MLD) during one-year treatment were compared between two groups using coronary angiography and intravascular ultrasound (IVUS).

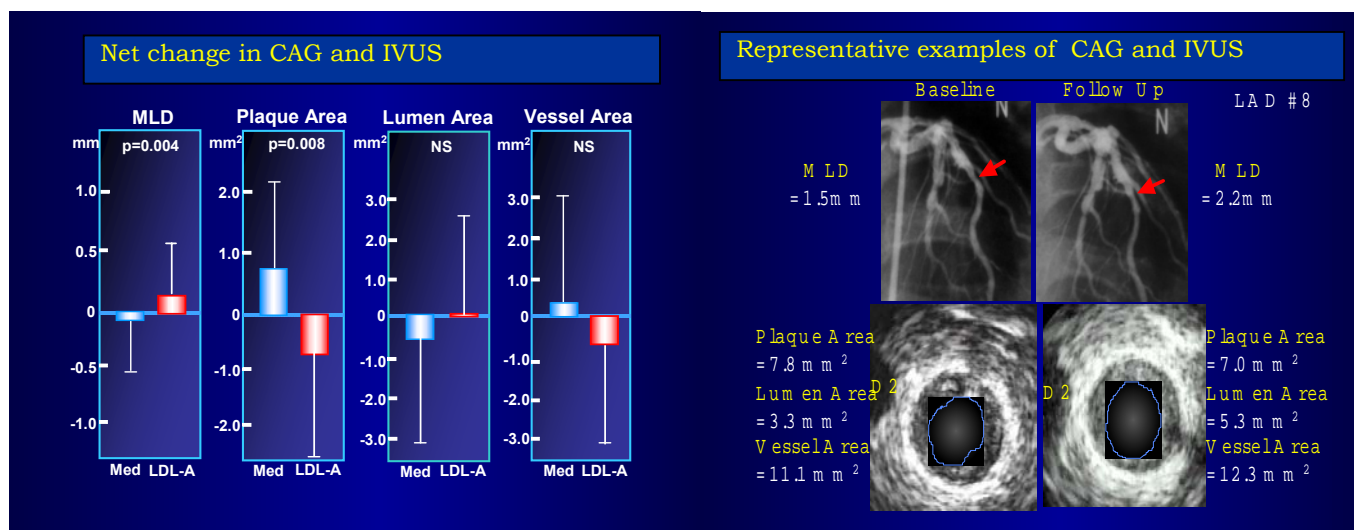
Basic Characteristics of Patients : LDL-A group have more severe symptoms than medication group.

	LDL-A (n=11)	Medication (n=7)		LDL-A (n=11)	Medication (n=7)
Age (old)	50±13	54±15	No. of vessels with significant stenosis		
Gender			1	1 (9)	2 (29)
male	8 (73)	5 (71)	2	3 (27)	2 (29)
female	3 (27)	2 (29)	3	7 (64)	3 (43)
Risk factor			Medication		
Hypertension	4 (36)	4 (57)	Statin	11 (100)	7 (100)
Diabetes Mellitus	2 (18)	0 (0)	Probucol	5 (45)	3 (43)
Smoking	7 (64)	4 (57)	Cholestyramine	3 (27)	1 (14)
Case history			Fibrate	1 (9)	0 (0)
Angina Pectoris	8 (73)	4 (57)	Achilles' tendon thickness (mm)		
Myocardial Infarction	6 (55)	2 (29)	Right	14.3±3.5	9.3±5.5
PTCA	5 (45)	5 (71)	Left	14.5±4.3	10.0±6.0
CABG	2 (18)	1 (14)			

Change in cholesterol : The LDL cholesterol level in medication increased a little from 174±39 mg/dL to 181±53 mg/dL. On the other hand the LDL cholesterol level in LDL-A decreased from 213±25 mg/dL to 140±27 mg/dL (34%). The difference between two groups was statistically significant (p=0.0001).

	LDL-A (n=11)			Medication (n=7)			p Value
	Baseline	Follow-Up	Reduction (%)	Baseline	Follow-Up	Reduction(%)	
TC (mg/dL)	275±27	197±19	28.4	251±57	254±38	-1.1	0.0001
TG (mg/dL)	143±74	139±93	2.8	163±70	147±41	9.8	0.65
HDL-C (mg/dL)	33±20	36±16	-9.1	44±20	45±22	-2.3	0.79
LDL-C (mg/dL)	213±25	140±27	34.3	174±39	181±53	-4.0	0.0001

Evaluation by CAG and IVUS : Minimal lumen diameter (MLD) was measured by coronary angiography (CAG) and the plaque area was by IVUS. MLD significantly increased in LDL-A group (p=0.008) and decreased in medication group. The plaque area significantly decreased in LDL-A group (p=0.01) and increased in medication group.



	LDL-A			Medication			
	Baseline	Follow-Up	Net Change	Baseline	Follow-Up	Net Change	p
MLD(mm)	1.99±0.73	2.11±0.81	0.12	2.24±0.89	2.16±0.84	-0.08	0.008
Plaque area(mm ²)	8.45±4.22	7.76±4.34	-0.69	7.19±2.88	8.08±3.14	0.88	0.01
Lumen area(mm ²)	9.84±5.43	9.87±5.55	0.03	9.13±4.33	8.63±3.18	-0.51	0.52
Vessel area(mm ²)	18.29±8.84	17.63±9.05	-0.66	16.4±5.63	16.7±4.36	0.3	0.26

Conclusion : It was clearly shown by IVUS evaluation that LDL apheresis may induce regression of coronary atherosclerotic plaque with one year treatment for medication refractory heterozygous FH with coronary heart disease.

Editorial Comment; Coronary Plaque Regression: Role of LDL-A

There is now a consensus that lowering the level of low density lipoprotein cholesterol (LDL-C) prevents and reduces cardiovascular morbidity and that the guideline of LDL-C with coronary heart disease should be below 100mg/dl. However, it is not clear whether more aggressive lowering of LDL-C is necessary or not. From this viewpoint there is an Atorvastatin Simvastatin Atherosclerosis Progression (ASAP) study which compares the effects of moderate versus aggressive lowering of LDL-C to heterozygous FH by measuring the change in carotid intima media thickness (IMT). In the LACMART study, one year LDL apheresis (LDL-A) treatment, which lowers the LDL-C of FH patients aggressively, reduces the plaque area and increases the MLD with statistically significant rate. This study is quite unique and new from the viewpoint of the combination of CAG and IVUS.

Although Mabuchi et al. have already reported the efficacy of LDL-A on the reduction in the rate of total coronary arterial events, this LACMART study showed efficacy of LDL-A as treatment more clearly. It will also need to demonstrate that the benefits of LDL-A are substantial when used in the setting of a much more aggressive super-statin such as atorvastatin.

Barter PJ. *J Am Coll Cardiol* 2002;40:228-230.