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Review

A systematic review of the time course of atherosclerotic plaque regression

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ABSTRACT

Objective: We sought to determine the time required for lipid treatment to produce regression of atherosclerotic plaques.
Background: The cholesterol content of atherosclerotic plaques contributes to their instability, and most acute cardiac events including myocardial infarction and sudden death are produced by coronary plaque disruption. We systematically reviewed the literature on atherosclerosis regression to identify the time required for cholesterol egress, plaque regression, and possible plaque stabilization. Such information may help decide when patients with statin side effects or other reasons for statin discontinuation could consider a reduction in the intensity of treatment.
Methods: We performed a PubMed search to identify English language articles reporting atherosclerotic regression. Articles pertinent to the topic were reviewed in detail.
Results: We identified 189 articles, 50 of which provided sufficient information to establish a rate of regression and 31 of which demonstrated plaque regression with statin therapy in the carotid ($n = 11$), coronary ($n = 16$), and aortic ($n = 4$) vascular beds. Plaque regression occurred after an average of 19.7 months of treatment.
Conclusion: Regression of atherosclerotic plaque using statin therapy in those studies documenting regression occurred after an average time of 19.7 months. This suggests that patients should undergo approximately two years of aggressive lipid reduction before considering a reduction of statin therapy.

Contents

Statin discontinuation or a reduction in the intensity of treatment may be necessary in patients with statin side effects. We systematically reviewed the literature on atherosclerosis regression to identify the time required for cholesterol egress, plaque regression, and possible plaque stabilization. Fifty articles were selected, 31 of which demonstrated plaque regression with statin therapy in

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Table 1
Studies examining change in atherosclerotic disease in the coronary arteries.

Author	RCT	Participants	% Women	Mean age (years)	Measure technique	Treatment drug, dose (mg/d), and number on statin	Time (months)	Baseline coronary measurements of treatment group	Imaging analysis	Baseline LDL (mg/dL) of treatment groups	% Change of LDL in treatment groups	Baseline HDL (mg/dL) of treatment groups	% Change of HDL in treatment groups	Baseline triglyceride (mg/dL) of treatment groups	% Change of triglycerides in treatment groups
Blankenhorn et al. (MARS) 1993	Y	270	9	58	QCA	L 80 vs. placebo ($n = 123$)	26.4	Diamter stenosis of all lesions 38%	Mean change in MOD (mm): T: −0.03 C: −0.06 ($p = 0.20$)	151	−38	43	9	159	−22
Jukema et al. (REGRESS) 1995	Y	778	0	56.2	QCA	P 40 vs. placebo ($n = 450$)	24	MOD: 1.85	Mean change in MOD (mm): T: −0.03 C: −0.09 ($p = 0.001$)	166.2	−29	35.9	10	157	−7
Callister et al., 1998	N	149	39	56.3	EBCT	NA ($n = 105$)	13.5	Mean CVS Initial LDL >120: 1017 Initial LDL <120: 980	Annual CVS progression T: 5% C: 52% ($p < 0.001$)	NA	NA	NA	NA	NA	NA
Teo et al. (SCAT) 2000	Y	460	11	61	QCA	S 40 vs. placebo ($n = 230$)	47.8	MOD (mm) 2.03	Mean change in MOD (mm): T: −0.09 C: −0.16 ($p = 0.0001$)	131	−31	38.2	NA	164	NA
Budoff et al., 2000	N	299	24	58	EBCT	"Statin" vs. placebo ($n = 60$)	26.4	NA	Annual CAC score progression (%) T: 15 C: 39 ($p < 0.001$)	NA	NA	NA	NA	NA	NA
Schartl et al. (GAIN) 2001 [48]	Y	131	15	60.2	IVUS	A 20–80 vs. usaual care ($n = 65$)	12	Mean plaque volume (mm^3) T: 121.3 C: 104.7	Change in atheroma volume (%): T: 2.5 C: 11.8 ($p = 0.14$)	155	−42	45	9	145	−9
Achenbach et al., 2002	N	66	NA	NA	EBCT	C 0.3 vs. untreatment period ($n = 66$)	14	CVS 155 mm^3	Annual CAC score progression (%): T: 8.8 C: 25 ($p < 0.0001$)	164	−35	51	2	184	−17
Hecht et al., 2003	N	149	17	58.7	EBCT	A 14.2 ± 8.1 vs. S 23.7 ± 11.8 ($n = 149$)	14.4	Mean CAC score A: 469.1 S: 388.3	Annual CAC score progression (%) A: 10.8 S: 7.5 ($p = NS$)	A: 137.2 S: 121.2	A: −39.8 S: −34.7	A: 50.6 S: 48.7	A: 15.6 S: 14.9	A: 143.9 S: 163.0	A: −22.1 S: −18.8
Hecht et al., 2003	N	182	23	58.5	EBCT	Intensive statin Rx–LDL <80 mg/dl vs. liberal statin Rx: A ($n = 115$) S ($n = 51$) P ($n = 13$) F ($n = 2$) C ($n = 1$) (Total: $n = 182$)	14.4	Mean CAC Score Rx to >80 LDL: 385 Rx to < 80 LDL: 513	Annual CAC score progression (%): >80: 9.1 <80: 9.3 ($p = NS$)	>80: 138 <80: 123	>80: −27 <80: −47	>80: 51 <80: 50	>80: 3.7 <80: 13.7	>80: 166 <80: 149	>80: −25 <80: −35.5