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Type of lipid lowering therapy impacts atherosclerosis progression in peripheral arterial disease as assessed by CMR

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Introduction

Lipid lowering may improve exercise performance in peripheral arterial disease (PAD), but it is unknown how it affects local vessel wall atherosclerosis as measured by CMR.

Purpose

We hypothesized that lowering LDL cholesterol in PAD would reduce superficial femoral artery (SFA) plaque burden assessed by magnetic resonance imaging.

Methods

Thirty eight patients with mild-to-moderate symptomatic PAD (mean age 64 ± 10 years, ankle brachial index 0.70 ± 0.13) were followed for two years on lipid lowering therapy. Statin-naïve patients were randomized to simvastatin 40 mg or simvastatin 40 mg plus ezetimibe 10 mg (R group, n = 20). Those already on a statin were given openlabel ezetimibe 10 mg (Z group, n = 18). Patients had the first 15-20 cm of the SFA in their most symptomatic leg imaged with black blood multi-slice turbo spin echo CMR annually (Figure 1). Plaque volume (PV) defined as total vessel volume (TVV) minus lumen volume was measured. Changes in parameters within the R and Z groups over the two years were analyzed with one way ANOVA and between group changes were compared with an unpaired t-test.

Results

R group designation remains blinded until 2-year follow-up is finished. LDL at baseline in R was 119 ± 43 mg/dl and fell significantly at one year $(81 \pm 38, p < 0.001)$ and remained decreased at two years (83 ± 45) . The LDL in Z at baseline was 98 ± 27 mg/dl, decreased significantly at one year $(74 \pm 35, p = 0.005)$, and was similar at year 2 (76 ± 27) . Total cholesterol changes were similar in both groups. The baseline LDL and total cholesterol in R were greater than Z (p = 0.04 and p = 0.05 respectively), however the year 1 and 2 values were similar between groups. See Table 1 for absolute changes in plaque volume and TVV over time. When expressed as % change over 2 years

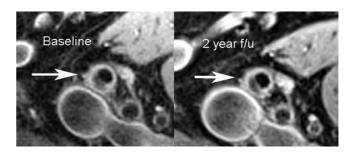


Figure 1
Representative image of SFA (arrow) of R patient with less plaque at year 2.

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Table I: Changes in Vessel Wall Characteristics

	Baseline	One Year	Two Years	ANOVA p
R - Plaque volume (cm3)	11.1 ± 4.7	11.0 ± 5.3	10.5 ± 4.4	0.09
Z - Plaque volume (cm3)	9.6 ± 4.0	10.2 ± 5.1	9.8 ± 4.2	0.21
R - TVV (cm3)	16.4 ± 7.0	16.1 ± 7.3	15.8 ± 6.8	0.22
Z - TVV (cm3)	13.4 ± 6.1	15.9 ± 6.9	16.2 ± 6.3*	0.04

^{*}p < 0.04 vs. baseline

relative to baseline, there was a trend towards plaque regression in R relative to Z at 2 years (-4.5 \pm 13.2% vs. +2.6 \pm 8.8%, p < 0.07). TVV regressed in R compared to Z over the same time period (-3.3 \pm 8.9% vs. +5.9 \pm 9.1%, p < 0.001).

Conclusion

Treating statin-naïve patients with PAD with a statin for two years halted progression of SFA atherosclerosis relative to those already treated with statin begun on ezetimibe, as assessed by CMR. This occurred despite similar final LDL. The mechanism or timing of statin initiation may be more important than the absolute LDL achieved in slowing progression of atherosclerotic plaque in the SFA.

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