How low do statins have to drive LDL-C to produce carotid plaque regression and improved echogenicity; value of Ezetimibe in getting there and of 3D ultrasound in detecting regression

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Disclosure
None

Glagov trial: evolocumab in statin-treated patients
PCSK9 antibody, coronary IVUS
Placebo Evolocumab
LDL (mg/dL) 93 46
% with regression 47.3% 64.3%
Nicholls SJ et al. JAMA 2016 online Nov 15

Paradigm change:
Treating arteries, not risk factors
Instead of treating risk factors to target, since 2003 we treat patients more intensively if their plaque is progressing, regardless of their level of LDL or other risk factors
i.e. – since 2003
our target is now plaque regression

What happened in high-risk patients with asymptomatic carotid stenosis?
>80% ↓ of MI and stroke

Annual rate of plaque progression in ACS patients before and since 2003

“Resistant atherosclerosis”

• Patients whose plaque progresses despite achieving target LDL
• They have something else causing much of their atherosclerosis
• All we can do now is treat the thing we know how to treat (LDL) to lower levels
• We need to figure out what’s causing it
• ? Intestinal microbiome

Neither achieved LDL-C nor change in LDL-C predicted plaque regression (n = 4531)

Percent of patients with regression with LDL <68 mg/dL
<38 mg/dL

Solo K, Spence JD 2016 Submitted for publication

How low does LDL have to go to achieve regression?
• It’s individual
• Target LDL levels for all patients do not work
• I have 231 patients with LDL < 38 mg/dL
  and 6 with LDL < 19 mg/dL because that’s what it took to stop progression

How quickly do plaques change in size and composition? Months

Spence JD  Time course of atherosclerosis regression. Atherosclerosis 235 (2014) 347e348
Role of ezetimibe

Bogiatzi C, Spence JD. Stroke 2012, 43:1153-1155

231 patients with plaque measurements for 2 years before and 2 years after initiation of ezetimibe

95 mg/dL
84 mg/dL
71 mg/dL

Placebo
Atorvastatin
Treatment group

Change in plaque volume (mm3) ± SE

3-month progression of carotid plaque volume with placebo vs. atorvastatin 80mg

P<0.0001


3D carotid ultrasound is the best way to measure effects of treatment: 200 times better than IMT; Much better than IVUS:

In Glagov trial n = 484 per group followed 76 weeks²

Treating arteries without measuring plaque is like treating hypertension without measuring blood pressure

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