Cholesterol lowering agents: update on LDL, how low should they be pushed?

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2016 AHA/ACC Guideline on the Management of Patients With Lower Extremity Peripheral Artery Disease
A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

Lowering LDL is good, but is there a limit?

Reduced or modified dietary fat for preventing cardiovascular disease
Lee Hooper 1, Carolyn G Summerbell 1, Rachel Thompson 1, Darien Sills 1, Felicia G Roberts 1, Helen Moore 1, and Douglas C.D. Glass 1

• Reducing saturated fat/fat modification associated with RRR = 14%; 26 studies, N = 65,508; correlates to LDL lowering
• Total mortality not affected with RR = .85 – 1.04

Authors’ conclusions—The findings are suggestive of a small but potentially important reduction in cardiovascular risk on modification of dietary fat, but not reduction of total fat, in longer trials. Lifestyle advice to all those at risk of cardiovascular disease and to lower risk population groups should continue to include permanent reduction of dietary saturated fat and partial replacement by unsaturated. The ideal type of unsaturated fat is monounsaturated.
Non statin strategies

- RCT of simv 40 + ezetimibe vs simv 40
- N = 18,144
- Recent ACS
- LDL 50-100 mg/dL
- Post LDL = 54 v. 70 (P < .001)
- Composite outcome reduced at 7 yrs

Evolocumab and Clinical Outcomes in Patients with Cardiovascular Disease

- RCT of pts with atherosclerosis and LDL > 70 mg/dL on a statin
- N = 27,564
- F/U = 2.2 yrs
- Composite endpoint

Evolocumab Added to Statin Therapy after Acute Coronary Syndromes

- RCT of pts with atherosclerosis and LDL > 70 mg/dL on a statin
- N = 27,564
- F/U = 2.2 yrs
- Composite endpoint
- No difference in adverse outcomes or side effects
In depth study of 1204 pts

F/U = 19 mo

Cognitive function by Neuropsychological testing

- RCT of pts with atherosclerosis on atorvastatin
- N = 30,449
- Baseline LDL = 61 mg/dL
- Baseline HDL ~ 40 mg/dL
- Increased HDL 104%
- F/U = 4.1 yrs

- RCT of Niacin 1.5-2 gm + simva and ezetimibe
- N = 3414
- HDL: 35 to 42
- LDL: 74 to 62
- Composite outcome
So what about our vascular patients?

- Essentially all symptomatic patients are high risk
- First line is potent statin (rosuvastatin 20 - 40 or atorvastatin 80 qd)
- If cannot get to LDL <70 mg/dL, would add ezetimibe 10 qd
- Consider PCSK9 inhibitors in refractory patients, but not routine, and probably via dedicated clinic

There seems to be no lower limit of LDL in terms of safety (so far)