Best medical treatment for asymptomatic carotid disease – optimal LDL levels are achievable!

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Best medical treatment for asymptomatic carotid disease: treating arteries instead of treating risk factors!

- LDL-C does not predict plaque progression or regression
- Plaque progression vs regression predicts events
Disclosure

Speaker name: J. David Spence

I have the following potential conflicts of interest to report:

✓ Consulting: Amgen
✓ Stockholder of a healthcare company: Vascularis Inc.
✓ Lecture fees: BMS, Pfizer
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
Treating arteries instead of risk factors: implemented in 2003

In high-risk patients with asymptomatic carotid stenosis, “treating arteries”

• reduced microemboli on transcranial Doppler from 12.6% of patients to 3.7%
• Reduced the 2-year risk of stroke and myocardial infarction by > 80%

TPA and plaque change before and after 2003

Total Plaque Area*  

Plaque progression

* Probably due to a change in referral patterns

- 47.5% of patients with LDL-C <1.8 mm had plaque progression
In the course of “treating arteries” we realized that to achieve plaque regression, many patients required LDL-C much lower than consensus targets.
Resistant Atherosclerosis

• Some patients require extraordinarily low levels of LDL-C to stop progression or achieve regression of atherosclerosis. This may be termed “resistant atherosclerosis”.
• This means that something other than LDL-C is causing their disease
• However, since we don’t know what’s causing it, all we can do is treat the things we know how to treat – such as LDL-C – more intensively

Resistant atherosclerosis

Neither achieved LDL-C nor change in LDL-C was correlated with progression/regression

N = 4512
Resistant Atherosclerosis

Even with LDL-C <1 mmol/L (38 mg/dL), half had plaque progression, and only 35% had regression (Because the ones who were more resistant were the ones being treated more intensively)

Spence JD, Solo K. Stroke. 2017;48:1624-1629
Distribution of LDL-C by progression/regression status

Regression
Mean = 2.22
Std. Dev. = .976
N = 1,301

Stable
Mean = 2.52
Std. Dev. = .995
N = 1,264

Progression
Mean = 2.24
Std. Dev. = .975
N = 1,947
Resistance increases with age and serum creatinine*
Achieved LDL-C < 1 mmol/L

*Probably because impaired renal function raises homocysteine, thiocyanate, ADMA, TMAO and other GDUT

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Whoa! aren’t you worried about very low LDL?

Não: it’s a myth

Stroke, Death or MI by LDL-C
No safety concerns down to LDL-C of 0.2 mmol/L (7.6 mg/dL)

The optimal LDL-C is the level that achieves plaque regression.

Treating arteries without measuring plaque is like treating hypertension without measuring risk factors.
• If you can’t measure plaque, LDL-C should be as low as possible
• Ezetimibe should be routinely added to statins
• Some patients may need PCSK9 antibody injections as well

What’s next?

• RCT of repopulation of intestinal microbiome of patients with unexplained resistant atherosclerosis with the bacteria of patients protected from atherosclerosis