Screening For ACS: Its Main Value Is In Guiding Lipid Treatment: How Low Should LDL-Cholesterol (LDL-C) Be Pushed And What Will It Do To Carotid Plaques

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Arterial Ultrasound Testing to Predict Atherosclerotic Cardiovascular Events: The Cyprus Atherosclerosis Study

n=985

Reclassification of All Individuals[c]

		Predicted 10-Year ASCVE Risk Using Conventional Risk Factors and Total Plaque Thickness (Cox Model 2)					
		Low (<7.5%)		Intermediate (7.5%-20%)		High (>20%)	Total
Predicted 10-y ASCVE risk using conventional risk factors only (Cox model 1)	Low (<7.5%)	422 2%	→	56 13%		0	478 3%
	Intermediate (7.5%-20%)	109 4%	←	177 19%	→	73 19%	359 14%
	High (>20%)	0		41 12%	←	107 41%	148 33%
	Total	531 2%		274 17%		180 31%	985 7%

By adding total plaque thickness and total plaque area from 4 bifurcations (carotid and femoral) to conventional risk factors in a Cox model, net reclassification improvement was 16.6%, and 16.6% (P < 0.0001), respectively.

Nicolaides AN, JACC, 2022

How can the presence of an Ax carotid stenosis (ACS) or common femoral artery stenosis on ultrasonography trigger treatment of dyslipidemia?

- Check if the patient has already an established atherosclerotic disease, e.g. LEAD requiring Tx of dyslipidemia.
- Often guidelines are ignored or interpreted differently across the various specialties.
- Great opportunity to review implementation of BMT.
- Isolated, subclinical atherosclerosis?

What is the current *trial* evidence to treat dyslipidemia in a patient with an isolated ACS? NONE – THERE IS NO RCT!

The Society for Vascular Surgery implementation document for management of extracranial cerebrovascular disease

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European Society for Vascular Surgery (ESVS) 2023 Clinical Practice Guidelines on the Management of Atherosclerotic Carotid and Vertebral Artery Disease☆

Ross Naylor [a,*], Barbara Rantner [a], Stefano Ancetti [a], Gert J. de Borst [a], Marco De Carlo [a], Alison Halliday [a], Stavros K. Kakkos [a], Hugh S. Markus [a], Dominick J.H. McCabe [a], Henrik Sillesen [a], Jos C. van den Berg [a], Melina Vega de Ceniga [a], Maarit A. Venermo [a], Frank E.G. Vermassen [a]

Recommendation 13 — Changed

For patients with asymptomatic carotid stenosis, lipid lowering therapy with statins (with or without ezetimibe) is recommended for the long-term prevention of stroke, myocardial infarction, and other cardiovascular events.

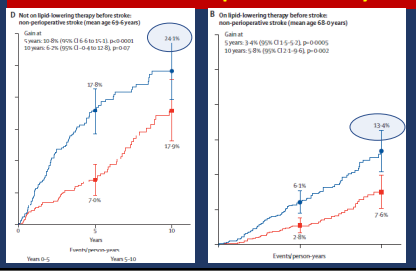
Class	Level	References	ToE
I	B	Zhan *et al.* (2018)[111], Halliday *et al.* (2010)[228], Cholesterol Treatment Trialists Collaboration (2012)[229]	

2023 ESVS carotid guidelines, EJVES

Where does this evidence derive from?

- Observational in nature
- Extrapolation from similar patient populations
- Not all outcomes (e.g. stroke, MI, etc) have been reported

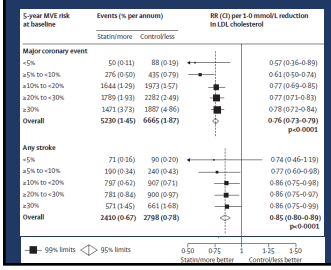
Association of lipid-lowering therapy and long-term stroke in a post hoc analysis of ACST-1



>10% reduced rates at 10 years i.e. ~ 1% per year

Halliday, Lancet 2010

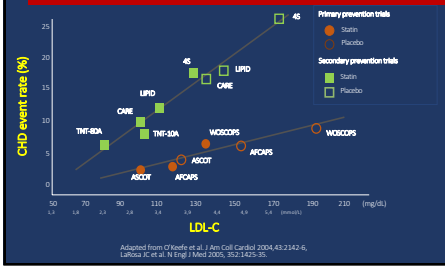
Effects on major coronary events and strokes, per 1.0 mmol/L reduction in LDL cholesterol at different levels of risk



Meta-analysis of 27 RCTs (n=174,149): Statins were associated with statistically significant reductions in stroke (RR 0.85) and major coronary events (RR 0.76)

Cholesterol Treatment Trialists' (CTT) Collaborators Lancet 2012

LDL reduction with statins reduces cardiovascular events in the setting of secondary and primary prevention



What about isolated ACS and asymptomatic atherosclerosis in general?

LDL target for Ax patients

At present, evidence is lacking to support specific LDL-C targets in ACS patients (2023 ESVS GLs)

BUT

2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases. Eur Heart J, 2018

In patients with PADs, it is recommended to reduce LDL-C to < 1.8 mmol/L (70 mg/dL) or decrease it by ≥ 50% if baseline values are 1.8–3.5 mmol/L (70–135 mg/dL).[25]	I	C

PADs = peripheral arterial diseases.

Statins reduce carotid plaque volume progression

Three-dimensional ultrasound imaging: An effective method to detect the effect of moderate intensity statin treatment in slowing carotid plaque progression

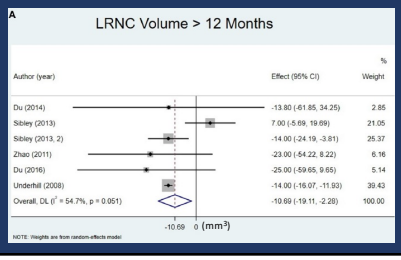
Yuhui Chen MD[1,2] | Haiying Xing MD[1,2] | Jiexi Wen MD[1,2] | Qing Peng MD[1,2] |

TABLE 3 Baseline, 2-year follow-up, and change from baseline characteristics for carotid plaques

	Total (n = 73)	Statin-group (n = 48)	Control group (n = 25)	*P* value[a]
Number of plaques				
Baseline	2 [1–3]	2 [1–3]	2 [1–3]	1.00
2 years	2 [2–3]	2 [1-2.75]	2 [2–3]	.07
Change	0 [0–0]	0 [0–0]	0 [0-1]	.04
P value[b]	0.15	0.99	0.03	
Total plaque volume (mm^3)				
Baseline	270 [160-500]	295 [145-510]	210 [170-420]	.62
2 years	290 [190-515]	290 [170-497.5]	280 [225-715]	.37
Change	50 [–40-100]	15 [–57.5-90]	70 [25–150]	.02
P value[b]	0.02	0.59	0.001	

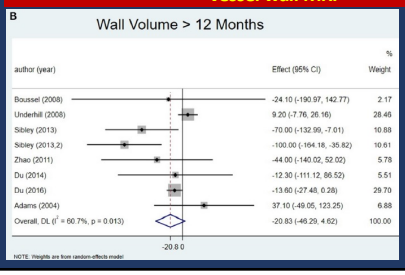
J Clin Ultrasound. 2021

Statins reduce lipid-rich necrotic core (LRNC) volume of carotid plaques on vessel wall MRI



Zhou P, et al. Front. Cardiovasc. Med 2021

Statins do not reduce plaque volume of carotid plaques on vessel wall MRI



Zhou P, et al. Front. Cardiovasc. Med 2021

Conclusions

- Statins positively affect atherosclerotic plaque composition.
- Statins reduce cerebrovascular events in patients with ACS, based on OBSERVATIONAL data.
- Lipid lowering Tx (e.g. statins, PCSK9 inhibitors, inclisiran, etc) and LDL targets should be tested further by future RCTs in this setting.