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CLINICAL UPDATE

Statins in older patients – who benefits?

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KEY MESSAGES

- Secondary prevention with a statin at all ages unless limited life expectancy
- Primary prevention for over 75s only if high cardiovascular risk
- Use atorvastatin or rosuvastatin to reduce drug-drug interactions
- Initiate with a lower dose (e.g. atorvastatin 20 mg; rosuvastatin 10 mg) before increasing to achieve target.
- Avoid combining statin with macrolide antibiotics, antifungal azoles, and cyclosporine. Reduce the doses of non-dihydropyridine calcium channel blockers
- Measure CK if muscle pain develops (>10x ULN is significant).
- Reduce, replace or rechallenge for SAMS without myopathy.

Statins are amongst the most commonly prescribed drugs on the PBS. Statin enthusiasm is well justified because a large number of randomised controlled trials have shown long lasting secondary prevention in patients of all ages.

There is less direct evidence from trials for a benefit in patients older than 75 in primary prevention. It is generally believed that statin therapy is warranted in those at high risk of cardiovascular events. Risk estimators are available online or via apps (ASCVD Plus and Heart Risk) but generally, data is not provided for over 80-year-olds.

Cardiovascular events

WOSCOPS randomised 45 to 64-year-old men with a high LDL to pravastatin 40 mg or placebo for around 5 years; electronic health records enabled an analysis 20 years later showing those allocated to pravastatin were 21% less likely to die of a cardiovascular cause, reduced coronary events (including myocardial infarction), and a 35% reduction in heart failure[2].

Uncertainty about statin efficacy and safety among older people led to a recent meta-analysis of participant data from 28 randomised controlled trials[3] and of 186,854 participants, 14,483 (8%) were older than 75. Those older patients had a history of vascular disease (55%), myocardial infarction (29%), other symptomatic coronary disease (31%), diabetes (17%), and treated hypertension (60%) and had a baseline LDL level of 3.2 and HDL of 1.3. Statin therapy resulted in a statistically significant 21% proportional reduction in major vascular events, a 25% reduction in risk of coronary revascularization procedures, and a 16% reduction in stroke per 1.0 mmol per litre reduction in LDL cholesterol – across all age groups.

Muscle symptoms

About 10% of patients stop their statins because of perceived side effects, most often muscle symptoms (statin-associated muscle symptoms (SAMS)). Studies show little difference in muscle symptoms between statins and placebo (at most 1%). However, SAMS can be severe, despite the absence of a pharmacological or serological basis in the overwhelming majority of cases. Significant myopathy should be excluded by measuring CK (CK <10x ULN). Rechallenge with lower dose, reduced frequency of dosing such as every other day, or with a different statin can restore therapy for patients at greatest risk of an atherosclerotic cardiovascular event.

Myopathy in older patients is about twice that of younger people but the absolute risk remains low. Contributors are drug interactions (less so with atorvastatin and rosuvastatin than other statins) and major comorbidities, in particular hypothyroidism, pre-existing muscle disease, and renal impairment. Higher statin levels and therefore the risk of myopathy is large with macrolide antibiotics, antifungal azoles, and cyclosporine, especially in the elderly, and combining these drugs and a statin should be avoided. Be aware of the need to reduce the doses of non-dihydropyridine calcium channel blockers (verapamil, diltiazem).

Because of the increased risk of side effects and drug interactions in the elderly, starting with a lower dose of statin before increasing to achieve a target LDL level (generally <1.6 mMol/L for secondary prevention) seems prudent.

Impaired cognition?

Are statins associated with impaired cognition? Reassuringly, a meta-analysis of studies investigating use of statins were associated with a reduced risk of all-cause dementia and mild cognitive impairment but, perhaps surprisingly, not of vascular dementia[4].

A cognitive substudy of over 70 year-olds in the HOPE-3 study of primary prevention with candesartan 16 mg plus hydrochlorothiazide 12.5 mg, versus placebo and rosuvastatin 10 mg, versus placebo concluded that only those with baseline systolic BP >145 mm Hg and LDL >3.7 showed slower cognitive decline over 5.7 yrs[5].

References: (1) Newman CB Arterioscler Thromb Vasc Biol 2018; 39: e38–e81. (2) Ford I Circulation. 2016;133(11):1073-80 (3) Cholesterol Treatment Trialists' Collaboration Lancet 2019; 393: 407–15 (4) Che-Sheng Chu Scientific Reports 8, Article number: 5804 (2018) (5) Bosch J Neurology 2019 DOI: https://doi.org/10.1212/WNL.0000000000007174

ED. **Giving statins beyond 75-years does not seem backed by evidence, except perhaps those at high risk of cardiovascular events.**

Harms vs Benefits of Statin R_x in 10,000 people (over 5y) achieving 2 mMol/L in LDL-C[1]

BENEFITS	HARMS
1o prevention: first major vascular event - 500 pts	New diagnosis diabetes mellitus - 100 pts
2o prevention: recurrent major vascular event - 1,000 pts	Small absolute ↑ in HbA1c
	Statin-associated muscle symptoms (no sig. CK elevation) - <100 pts
	Myopathy (CK elevation >10x ULN) - 5 pts
	Rhabdomyolysis - 1 pt
	Haemorrhagic stroke - 10 pts
	Severe liver disease < 1pt