Statin-Induced Diabetes: Too Sweet a Deal?

Clinical Question: Do statins increase the risk of diabetes, and does this worsen outcomes?

Bottom Line: Statins modestly increase blood glucose, which leads to an extra one in 250 patients crossing the “diabetic threshold” over 4 years. This should not change statin prescribing, as they reduce cardiovascular events and all-cause mortality in appropriate patients.

Evidence:
Statin versus no statin:
• Meta-analysis of 13 Randomized Controlled Trials (RCTs) with 91,140 patients with, or at high risk for, cardiovascular disease:
  o New diabetes over four years: Statins 4.9%, control 4.5%, Number Needed to Harm (NNH)=250.
• Similar results in meta-analysis of 15 RCTs (91,828 patients): odds ratio 1.11 (95% confidence interval 1.03-1.20).
High versus low/moderate dose statin (e.g. atorvastatin 80 mg versus 10 mg):
• Meta-analysis of five RCTs with 32,752 patients with cardiovascular disease:
  o New diabetes over five years: High-dose 8.8%, low/moderate-dose 8%, NNH=125.
Observational studies confirm increased diabetes diagnosis with statin versus no statin, and higher versus lower statin dose or potency seen in RCTs.

Context:
• Diagnosis of type 2 diabetes is largely based on crossing an arbitrary laboratory threshold, like fasting plasma glucose (FPG) ≥7.0 mmol/L:
  o Baseline FPG 6.0-6.9 mmol/L is a risk factor for developing diabetes with statins.
O In an observational study, FPG increased by 0.1 mmol/L at 2 years in non-diabetics taking statins.\textsuperscript{11}
O Thus, the increase in diabetes diagnoses in statin users is mostly from patients with borderline glucose levels crossing the diagnostic cutoff.

- Genetic studies showed that having mutations that impair HMG-CoA reductase activity is associated with greater FPG and higher incidence of type 2 diabetes.\textsuperscript{2}
  - Confirms that risk of diabetes with statins tied to their LDL-lowering potency.

- Despite the increase in blood glucose, statins reduce important clinical outcomes including mortality in patients with an appropriate indication:\textsuperscript{5,12}
  - In the Heart Protection Study:\textsuperscript{12} for every one person newly diagnosed with diabetes due to statin use over five years, statins prevented five deaths, six non-fatal myocardial infarctions and four strokes.

- Thiazides and beta-blockers also increase the risk of diabetes versus placebo or other antihypertensives.\textsuperscript{14}
  - Both classes\textsuperscript{15,16} provide net benefit in appropriate patients.

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\textbf{References:}

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