Clinical Practice Assessment

Do statins increase the risk for developing type 2 Diabetes Mellitus?

Clinical Question:
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Bottom Line: Yes.
Meta-analyses of statin trials demonstrate that statin use is associated with a statistically significant increase in the risk of developing type 2 Diabetes Mellitus, especially in those on more potent statins and those with risk factors for diabetes. Strength of recommendation: B. However the reduction in major cardiovascular events with statin use outweighs the risk of developing diabetes in most patients. Strength of recommendation: A.

Synopsis:
One earlier study, the West of Scotland Coronary Prevention Study (WESCOPS) published in 2001 showed a 30% reduction in the risk of developing diabetes in patients assigned to pravastatin compared with placebo (1). This study included 5974 men aged 45-64. Diabetes was defined as 2 glucose measurements above 6.9 mmol/L (124 mg/dL) with at least one glucose measurement greater than 1.9 mmol/L (34 mg/dL) above baseline.

More recent studies however show an increased incidence of diabetes with statin use. A meta-analysis of 13 randomized statin trials including 91,140 participants demonstrated a 9% increased risk of incident diabetes in patients on statins (2). This translated to one additional case of diabetes for every 255 patients treated. However not all 13 studies showed an increased rate of diabetes, and for 7 of the 13 trials incident diabetes data was not published in the original reports.

Another meta-analysis evaluated 32,752 participants in 5 studies comparing diabetes incidence with high dose vs. moderate dose statins (3). High dose statins increased the risk for diabetes by 12%, but reduced the risk of cardiovascular events by 16%. Compared with moderate dose statin, the number needed to harm per year with high dose statin was 498 for new-onset diabetes; the number needed to treat per year to prevent cardiovascular events was 155 for high dose statin compared with moderate dose statin.

A population-based cohort study of 471,250 people over age 66 in Ontario who were started on statin therapy from August 1, 1997 to March 31, 2010 also showed an increase incidence of diabetes in those receiving higher potency statins (rosuvastatin, atorvastatin, simvastatin) compared with lower potency statins (pravastatin, lovastatin, fluvastatin) (4).
Analyses of the Treating to New Targets, Incremental Decrease in End Points Through Aggressive Lipid Lowering, and Jupiter trials all showed an increase incidence of diabetes with statin use in patients with multiple risk factors for diabetes, but not in patients without risk factors (5, 6). The risk factors included: a) fasting glucose > 100 mg/dL; b) fasting triglycerides > 150 mg/dL; c) body mass index > 30 kg/m2; d) history of hypertension.

The Diabetes Subpanel of the National Lipid Association Expert Panel on Statin Safety has published the following statement:

*Given the well-established benefits of statin therapy in the primary and secondary prevention of cardiovascular events among those with indications for treatment, no changes to clinical practice are recommended other than the measurement of HbA1c or fasting glucose in those deemed to also be at elevated diabetes risk after initiating statin therapy, and potentially before initiation in selected patients considered to be at elevated risk of developing diabetes.* (7)

This statement is consistent with the 2013 American College of Cardiology/American Heart Association guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults (8).

**References:**


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