



Wouldn't Bet On it: What is the risk of muscle symptoms on statins?

CLINICAL QUESTION

What are the effects of statins on muscles?

BOTTOM LINE

Statins increase the risk of muscle symptoms (includes pain, cramps, and weakness) in their first year of use, from 14% (placebo) to 14.8%, but are similar to placebo after 1 year. When patients report muscle symptoms, only 1 in 15 is due to the statin. Statins may increase muscle symptoms with creatine kinase rise 10x normal for 1 in ~3000 patients over placebo.

EVIDENCE

- 7 systematic reviews [11-135 randomized controlled trials (RCTs); 18,192-192,977 patients] from the last 5 years.¹⁻⁷ Focusing on the most recent (23 RCTs; 154,664 patients x4.3 years).¹ Results statistically significant unless indicated.
 - Any muscle symptoms, statin versus placebo,
 - Anytime: 27.1% versus 26.6% (placebo).¹
 - Within 1st year: 14.8% versus 14.0%, number needed to harm=125.
 - After 1st year: 14.8% versus 15.0% (not statistically different).
 - Other systematic reviews²⁻⁷ similar but not statistically different for myalgia,⁵ ≥65 age subgroup,⁴ or intensity subgroups versus placebo.²
 - No difference by statin type,³ lipophilic/hydrophilic statin,⁶ or age groups.^{1,5,6}

- Any muscle symptoms, more versus less-intense statin:
 - Any timepoint: 36.1% versus 34.8% (less intense).¹
 - Other systematic reviews found similar.²
- Creatine kinase >10x upper limit of normal (myopathy): 0.077% versus 0.044% (placebo).¹
 - 4 other systematic reviews:²⁻⁵ No difference.
 - More versus less-intense statin:^{1,2} Results no different for approved statins/doses (excluding simvastatin 80mg).
- Rhabdomyolysis:
 - 3 systematic reviews:^{4,5} No difference.
- Discontinuation for muscle symptoms^{2,4} or any adverse event^{4,5,7} not statistically increased.
- Three n-of-1 trials (8-200 patients, previous statin intolerance due to muscle symptoms) randomized to 3-4 cycles of ~3-8 weeks of statin,⁸⁻¹⁰ placebo,⁸⁻¹⁰ and no-pill⁸ each. Muscle symptom scores:
 - Statin versus placebo:⁸⁻¹⁰ no difference.
 - Statin versus no-pill:⁸ 16 versus 8 (no-pill) (scale=0-100, higher worse).

CONTEXT

- Mean creatine kinase rise¹ with statin therapy ~2%.
- Events like myopathy and rhabdomyolysis are too infrequent to discern statin effects in meta-analysis of >100,000 RCT participants.
 - Statin-induced rhabdomyolysis estimated at 2-3 excess cases/100,000 patient-years.¹¹
- Guidelines recommend:
 - In patients with non-severe muscle-symptoms, offer retreat of same or lower-intensity statin.¹²
 - Monitoring creatinine kinase is generally not encouraged, but check if symptoms or high-risk.^{12,13}

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