

Does calcium supplementation increase risk of myocardial infarction?

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Clinical question

Do calcium supplements increase risk of myocardial infarction (MI) and other cardiovascular disease (CVD)?

Evidence

Three systematic reviews had differing conclusions.

- The first reviewed 15 RCTs comparing calcium supplementation (≥ 500 mg/d) with placebo.¹
 - Only 1 CVD outcome reached statistical significance.
 - Calcium increased MI risk: relative risk (RR) 1.27 (95% confidence interval [CI] 1.01 to 1.59).
 - Absolute risk was less than 1% and the number needed to harm (NNH) for 1 MI was 135 to 211 over 4 years.
 - Concern: overinterpretation of data, including calculating NNH for non-significant outcomes.
- Another systematic review examined 17 studies comparing vitamin D, calcium, or both with placebo.²
 - No comparisons reached statistical significance.
 - Concerns: excluded relevant studies, small sample size, and no analysis of different outcomes.
 - More than 99% of data for calcium and vitamin D versus placebo were from the Women's Health Initiative (WHI),³ and 54% of participants were taking extra calcium.⁴
- A subgroup (similar to per-protocol) analysis of WHI data⁵ excluding those taking extra calcium found borderline-significant increases in hazard ratios for MI (1.22 [95% CI 1.00 to 1.50]) and MI or stroke (1.16 [95% CI 1.00 to 1.35]).
 - Updating the previous meta-analysis¹ with these data, calcium (with or without vitamin D) significantly increased⁵
 - MI (NNH 240 over 5 years, $P = .004$) and
 - MI or stroke (NNH 178 over 5 years, $P = .009$).
 - Concerns: large number of comparisons, subgroup analyses, and possible conflict of interest.

Context

- No RCT of calcium supplementation was designed to assess CVD outcomes.^{1,2} These meta-analyses¹⁻³ represent post-hoc analyses of secondary or unplanned outcomes, possibly inadequately reported.⁶
- Trials of vitamin D alone do not suggest CVD harm.⁷
- Calcium (88% with vitamin D) reduces fracture (any type); number need to treat is 63 over 3.5 years.⁸
 - Calcium alone just failed to reach statistical significance.
 - Other studies suggest calcium alone does not reduce nonvertebral fracture and might increase hip fracture.^{9,10}

Bottom line

Evidence suggests that calcium supplementation might

slightly increase the risk of MI and perhaps other CVD. Although there are limitations to the evidence and the increased CVD risk is likely less than 1%, the benefit-to-harm ratio might not favour calcium supplementation.

Implementation

It is difficult to help patients weigh probability of risk against benefit. Both patients and physicians tend to react more strongly to RR differences than to absolute differences.¹¹ Framing outcomes positively ("survival") will lead to different patient decisions than framing them negatively ("mortality").¹² In this case, it might suffice to tell patients that if 100 patients take calcium supplements, we expect that less than 1 will have a fracture prevented and less than 1 will develop a heart attack or stroke. For the other 98 patients, calcium will have no effect at all (on these outcomes). 🌿

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