

Calcium, With or Without Vitamin D, Raises Risk for Adverse Cardiovascular Events

Vascular calcification is one proposed mechanism.

A recent meta-analysis showed that calcium supplementation without vitamin D elevates cardiovascular (CV) risk ([JW Gen Med Aug 31 2010](#)). However, whether calcium and vitamin D taken together elevate CV risk is unclear. Although the Women's Health Initiative (WHI) previously reported that calcium and vitamin D supplements taken together did not elevate CV risk, about half the 36,000 participants were taking nonprotocol calcium and vitamin D at randomization — potentially obscuring the association. To determine whether calcium and vitamin D taken together elevate CV risk, investigators reanalyzed WHI data according to personal use of calcium and incorporated these data in a meta-analysis of eight additional studies.

In the reanalysis of WHI data, women who did not report baseline calcium use who were randomized to daily calcium (1 g) and vitamin D (400 IU) had significantly elevated risks for myocardial infarction, MI or revascularization, and MI or stroke (hazard ratio, 1.2 for each outcome), compared with placebo recipients. In contrast, users of calcium at baseline who were randomized to calcium and vitamin D did not have excess CV risk compared with placebo recipients.

In a meta-analysis of three randomized trials with 20,000 participants, calcium and vitamin D supplementation raised risks for MI, stroke, and a composite of MI or stroke, compared with placebo (relative risk, 1.2 for each outcome). A meta-analysis of nine trials that involved 28,000 participants showed that calcium or calcium and vitamin D supplementation significantly raised risks for MI and a composite of MI or stroke compared with placebo (RR, 1.2 for each outcome). The average duration of the trials was about 6 years.

Comment: These results suggest that calcium supplements, with or without vitamin D, raise risk for adverse CV events. The authors note "calcium supplements acutely increase serum calcium concentration . . . an effect that is sustained during long term treatment, as evidenced by lower levels of parathyroid hormone" and might promote vascular calcification. That baseline users of calcium in the WHI study who were randomized to calcium and vitamin D did not have excess CV risk suggests a dose-response relation does not exist. The authors speculate "the abrupt change in plasma calcium after supplement ingestion" rather than total calcium load causes the adverse effect. What should clinicians do until these results are confirmed or refuted by additional research? One approach would be to advise patients to increase calcium intake through food sources (e.g., milk products), as the aforementioned studies say nothing about this type of calcium intake. Another approach would be to avoid calcium supplementation in patients at high CV risk.

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