

## Calcium Supplements and Heart Disease

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### Abstract:

Calcium supplements are widely used in the United States and other developed nations traditionally to avoid osteopenia and its complications, but now often given along with vitamin D supplementation, for maintenance of optimum health for other physiologic processes. Concern has been expressed that calcium supplementation may increase the risk of atherosclerotic vascular disease. The data is conflicting. The controversy started with a secondary analysis of a randomized placebo controlled trial of calcium supplements versus placebo in post-menopausal women for 5 years, which showed a statistically significant increase in MI. The composite end point of myocardial infarction (MI), stroke or cerebrovascular accident (CVA), or sudden death was higher in calcium group ( $P=0.008$ ), relative risk was 1.66. When the events were attempted to be adjudicated using a national registry, statistical significance was no longer found. The baseline characteristics of the participants in this study were not adjusted for cardiovascular risk, nor was there adequate documentation for concomitant cardiovascular medications. Secondly, a meta-analysis of 11 studies showed that allocation of calcium supplements ( $>500$  mg/day for more than a year) was associated with increased risk of MI, and that calcium supplementation was associated with 30% increase in incidence of MI and smaller no significant increase in risk of CVA and death. None of the trials had CV events as the primary end points, and data on CV events were not gathered in a standardized manner. Incomplete or no data on CV outcomes were available in 7 trials, comprising about 15% of participants. None of the trials were designed to have the baseline characteristics of the subjects equalized, in terms of cardiac risk factors. The trials did not have standardized information about the use of statins, ACE inhibitor therapy or previous history of coronary artery disease (CHD). The Women's Health Initiative trial, another randomized controlled study, did not show any concerning cardiovascular risk from calcium supplements. The trial was a randomized controlled trial (RCT) of calcium (500 mg) plus Vitamin D (200 IU), twice daily versus placebo in 36,282 post-menopausal females, 50 to 79 years at 40 clinical sites, where CVD was a pre-specified secondary efficacy outcome. This study revealed that calcium/vitamin D supplementation neither increased nor decreased the risk for CHD or stroke, in general healthy postmenopausal women throughout the 7-year duration of this randomized trial. A limitation of the trial was that women in the placebo group were allowed to continue their own calcium supplements, and personal use of calcium supplement at randomization could have influenced the effect of randomization to calcium and vitamin D on the risk of cardiovascular events. A prospective cohort study of 34,486 postmenopausal Iowa women, 55-69

years old and without a history of ischaemic heart disease, was analyzed to investigate whether greater intakes of calcium, vitamin D or milk products may protect against ischaemic heart disease mortality. 8 year follow up suggested that among postmenopausal women, the risk of dying of ischaemic heart disease may be reduced by consuming relatively high levels of calcium. There was an estimation of statistically significant 33% reduction in risk for persons in the highest quartile of total calcium intake (i.e. high whether due to diet, supplements or both). Limitation of the study was that the duration of supplemental vitamin and mineral use was not known. Finally, a recent publication was done to evaluate the risk and vascular hospitalization and mortality data from a 5-year randomized, controlled trial of calcium carbonate, and 4.5 years of post-trial follow-up was undertaken. This study used data from a published 5-year randomized, double-blinded, placebo-controlled trial. The participants were 1460 women aged 75 years at baseline recruited from the general population, and randomized to receive 1200 mg of calcium carbonate daily, or an identical placebo. In this intent to treat analysis, the intervention group did not have a higher risk of death or first-time hospitalization from atherosclerotic vascular disease in the 5-year RCT compared to placebo. This trial provides compelling evidence that calcium supplementation of 1200 mg daily does not significantly increase the risk of atherosclerotic vascular disease in elderly women. In summary, when patients are randomized with appropriate risk factors for cardiac health, there is no compelling evidence that the calcium supplementation increase the rate of major cardiovascular events.

There is some evidence that calcium supplements can increase the risk of heart attacks. Calcium supplements are usually taken to treat or prevent bone disease, such as osteoporosis.

A recent analysis of peer-reviewed, double-blind studies concluded that calcium supplements increased the risk of heart disease, particularly in healthy, postmenopausal women. Other studies have said calcium supplements don't increase the risk.

In general, more research is needed before doctors know how calcium supplements affect your overall heart attack risk. What is known is that calcium from food sources, such as dairy products and leafy green vegetables, isn't a concern.

Taking calcium — with vitamin D — does provide a benefit for those who have too little calcium or bone loss. As with any health issue, it's important to talk to your doctor to determine what's most appropriate in your case. Check with your doctor before taking any type of supplement to determine if there's a need.

After analyzing 10 years of medical tests on more than 2,700 people in a federally funded heart disease study, researchers at Johns Hopkins Medicine and elsewhere conclude that taking

calcium in the form of supplements may raise the risk of plaque buildup in arteries and heart damage, although a diet high in calcium-rich foods appears to be protective. When it comes to using vitamin and mineral supplements, particularly calcium supplements being taken for bone health, many Americans think that more is always better,” says Erin Michos, M.D., M.H.S., associate director of preventive cardiology and associate professor of medicine at the Ciccarone Center for the Prevention of Heart Disease at the Johns Hopkins University School of Medicine. “But our study adds to the body of evidence that excess calcium in the form of supplements may harm the heart and vascular system.”

The researchers were motivated to look at the effects of calcium on the heart and vascular system because studies already showed that “ingested calcium supplements — particularly in older people — don’t make it to the skeleton or get completely excreted in the urine, so they must be accumulating in the body’s soft tissues,” says nutritionist John Anderson, Ph.D., professor emeritus of nutrition at the University of North Carolina at Chapel Hill’s Gillings School of Global Public Health and a co-author of the report. Scientists also knew that as a person ages, calcium-based plaque builds up in the body’s main blood vessel, the aorta and other arteries, impeding blood flow and increasing the risk of heart attack.

The investigators looked at detailed information from the Multi-Ethnic Study of Atherosclerosis, a long-running research project funded by the National Heart, Lung, and Blood Institute, which included more than 6,000 people seen at six research universities, including Johns Hopkins. Their study focused on 2,742 of these participants who completed dietary questionnaires and two CT scans spanning 10 years apart.

The participants chosen for this study ranged in age from 45 to 84, and 51 percent were female. Forty-one percent were white, 26 percent were African-American, 22 percent were Hispanic and 12 percent were Chinese. At the study’s onset in 2000, all participants answered a 120-part questionnaire about their dietary habits to determine how much calcium they took in by eating dairy products; leafy greens; calcium-enriched foods, like cereals; and other calcium-rich foods. Separately, the researchers inventoried what drugs and supplements each participant took on a daily basis. The investigators used cardiac CT scans to measure participants’ coronary artery calcium scores, a measure of calcification in the heart’s arteries and a marker of heart disease risk when the score is above zero. Initially, 1,175 participants showed plaque in their heart arteries. The coronary artery calcium tests were repeated 10

years later to assess newly developing or worsening coronary heart disease. For the analysis, the researchers first split the participants into five groups based on their total calcium intake, including both calcium supplements and dietary calcium. After adjusting the data for age, sex, race, exercise, smoking, income, education, weight, smoking, drinking, blood pressure, blood sugar and family medical history, the researchers separated out 20 percent of participants with the highest total calcium intake, which was greater than 1,400 milligrams of calcium a day. That group was found to be on average 27 percent less likely than the 20 percent of participants with the lowest calcium intake — less than 400 milligrams of daily calcium — to develop heart disease, as indicated by their coronary artery calcium test.

Next, the investigators focused on the differences among those taking in only dietary calcium and those using calcium supplements. Forty-six percent of their study population used calcium supplements.

The researchers again accounted for the same demographic and lifestyle factors that could influence heart disease risk, as in the previous analysis, and found that supplement users showed a 22 percent increased likelihood of having their coronary artery calcium scores rise higher than zero over the decade, indicating development of heart disease.

“There is clearly something different in how the body uses and responds to supplements versus intake through diet that makes it riskier,” says Anderson. “It could be that supplements contain calcium salts, or it could be from taking a large dose all at once that the body is unable to process.”

Among participants with highest dietary intake of calcium — over 1,022 milligrams per day — there was no increase in relative risk of developing heart disease over the 10-year study period.

“Based on this evidence, we can tell our patients that there doesn’t seem to be any harm in eating a heart-healthy diet that includes calcium-rich foods, and it may even be beneficial for the heart,” says Michos. “But patients should really discuss any plan to take calcium supplements with their doctor to sort out a proper dosage or whether they even need them.”

According to the U.S. Centers for Disease Control and Prevention, coronary heart disease kills over 370,000 people each year in the U.S. More than half of women over 60 take calcium supplements — many without the oversight of a physician — because they believe it will reduce their risk of osteoporosis.