Are Calcium Supplements Harmful to Cardiovascular Disease?

Calcium is the most abundant mineral in the body and is crucial for the maintenance of strong bones and teeth. Furthermore, calcium is required for the body’s basic functions, such as nerve transmission, blood clotting, blood pressure, muscle contraction, enzyme activation, and hormone regulation. Although most people think of calcium they think of dairy sources, nondairy foods, such as spinach, kale, soybeans, and white beans, also contain calcium. Calcium is available as dietary supplements and is often taken in combination with vitamin D to improve calcium absorption. Many women are encouraged to take calcium supplements. Approximately 43% of the US population uses dietary supplements that contain calcium. Given the extensive use of calcium supplements, any beneficial or harmful effect of supplemental calcium on health is of great clinical and public health importance.

Calcium supplements, with or without vitamin D, have been widely used for the prevention and treatment of osteoporosis. In a meta-analysis of 29 randomized controlled trials (RCTs), calcium supplementation was associated with a 12% reduction in fracture risk and a reduced rate of bone loss in adults 50 years and older. In addition, a large body of evidence from experimental, clinical, and epidemiological research indicates that getting enough calcium may lower the risk of colorectal cancer. It has also been postulated that calcium may have a role in reducing the risk of cardiovascular disease (CVD) because calcium supplementation has been demonstrated to improve serum lipid levels and modestly reduce blood pressure.

Calcium supplements have traditionally been considered a safe alternative to meet calcium requirements. However, recent research has raised concerns about a possible adverse effect of calcium supplementation on CVD and related mortality. Excessively high intakes of calcium in the form of supplements can lead to hypercalcemia, which in turn can cause renal insufficiency, vascular and soft-tissue calcification, hypercalcuria, and kidney stones. No RCTs have specifically examined the effect of calcium supplementation on CVD morbidity or mortality, but several RCTs have conducted secondary analyses to evaluate the effect of calcium supplement use on CVD events. For example, a recent reanalysis of the Women’s Health Initiative Calcium/Vitamin D Supplementation Study (WHI CaD Study) received much attention because it questioned the safety of calcium supplements. Results from the WHI CaD Study revealed that among women not taking personal calcium supplements at randomization, the risk of myocardial infarction, coronary revascularization, or stroke was 13% to 22% higher in the group allocated to calcium and vitamin D supplementation (1 g of calcium and 400 IU of vitamin D daily). In addition, in a meta-analysis of 8 RCTs, including the WHI CaD Study, calcium supplements with or without vitamin D increased the risk of myocardial infarction by 24% (95% CI, 7%-45%) and stroke by 15% (95% CI, 3%-27%).

In this issue of the journal, Xiao and coworkers report results of the National Institutes of Health (NIH)–AARP Diet and Health Study, which provides further support for the theory that too much supplemental calcium might have an adverse effect on cardiovascular health. This large prospective cohort study of 219,059 men and 169,170 women (including 7904 and 3874 CVD deaths in men and women, respectively) followed up for 12 years revealed that high intakes of supplemental calcium (>1000 mg/d) from multivitamins or individual calcium supplements were associated with a significant 20% (95% CI, 9%-36%) increase in CVD mortality in men. Moreover, in men, a high supplemental calcium intake from individual calcium supplements was associated with a nonsignificant 24% (95% CI, −3% to 57%) increase in CVD mortality and a significant 37% (95% CI, 6% to 77%) increase in heart disease death. The authors observed no association between supplemental calcium intake and CVD mortality in women or between calcium intake from foods and CVD mortality in either men or women. However, there was a J-shaped relationship between total calcium intake from both food and supplements and CVD mortality in men. Total CVD mortality decreased with increasing total calcium intake up to an intake of approximately 1200 mg/d, but above that intake, the trend was positive. Because the NIH-AARP Diet and Health Study is an observational study, confounding from other unmeasured behaviors cannot be excluded. Nevertheless, the study is prospective, well conducted, and large, with a large number of CVD deaths. The lack of association of calcium supplement use with CVD mortality in women is perplexing, especially given the results from the WHI CaD Study reporting an increased risk of CVD in women allocated to calcium supplementation.

The findings from the NIH-AARP Diet and Health Study add to the mounting evidence indicating that calcium supplements may be harmful to CVD. The results are consistent with some but not all previous pro-
spective studies on calcium supplement use in relation to CVD morbidity or mortality. Use of calcium supplements with or without vitamin D was associated with a significant 24% increase in risk of coronary heart disease in a cohort of 10 555 Finnish women. Likewise, in a prospective cohort of German men and women, calcium supplement users had a significant 86% increased risk of myocardial infarction and users of only calcium supplements had a 2.4-fold higher risk compared with nonusers of any supplement. In contrast, 2 prospective US studies suggested an inverse relation between calcium supplement use and CVD mortality or fatal ischemic heart disease.

Available data are suggestive of adverse cardiovascular effects with an excessive intake of supplemental calcium. More large studies are needed to further assess the potential health risks or benefits of calcium supplement use on CVD morbidity and mortality. Meanwhile, a safe alternative to calcium supplements is to consume calcium-rich foods, such as low-fat dairy foods, beans, and green leafy vegetables, which contain not only calcium but also a cocktail of essential minerals and vitamins. These non-dairy food sources of calcium have the added health benefits and have recently been reported to improve glycemic control in persons with diabetes. The paradigm "the more the better" is invalid for calcium supplementation.

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