

Calcium supplements increase heart attack risk?! Making Sense of the Confusing Data...

By Jannet Huang, MD, FRCPC, FACE, ABIHM, CCD, NCMP.

August 2010

Calcium supplementation appears to increase the risk of myocardial infarction, a meta-analysis showed. Among studies of patients with or at risk for osteoporosis, those who took calcium supplements were about 30% more likely to have an MI than those who did not, Ian Reid, MD, of the University of Auckland in New Zealand, and colleagues reported online in *BMJ*.

Reid and his colleagues analyzed data from 15 randomized controlled trials that evaluated the use of calcium supplementation (at least 500 mg/day). They excluded studies that also administered vitamin D, which has been shown to have a cardiac benefit, in order to get a clearer picture of calcium's effect on the heart.

None of the individual studies was designed to assess the risk of cardiovascular events. None of the individual trials found a significantly increased risk, although six had non-significant trends in that direction.

In the analysis of patient-level data, calcium supplementation was associated with an increased risk of MI in participants who had a dietary calcium intake above the median of 805 mg/day, but not in those with lower dietary intake.

Previous studies evaluating dietary calcium intake showed a reduced cardiovascular risk with greater consumption. The difference between those results and the findings of the current study suggests "cardiovascular risks from high calcium intake might be restricted to use of calcium supplements," according to the researchers.

The study authors noted that the analysis was limited in that it excluded trials in which calcium supplements were co-administered with vitamin D. In addition, they noted, only two of the trials had data adjudicated by blinded trial investigators and seven -- which accounted for 15% of the participants -- had incomplete or missing data.

Statement from the Council for Responsible Nutrition

"Adequate calcium intake is vital to building and maintaining healthy bones, and to preventing osteoporosis. Most people do not get enough calcium from diet alone, and this is where a calcium supplement can be important to consumers of all ages," said Andrew Shao, PhD, senior vice president, scientific & regulatory affairs, Council for Responsible Nutrition. "The results from this meta-analysis do not undermine the value calcium supplements offer to those concerned with maintaining or increasing bone density, as years of research shows these products do."

The authors of the meta-analysis examined the effects of calcium supplements on the risk of cardiovascular events, concluding there is an increased risk, and calling for a reassessment of the role of calcium supplements for osteoporosis. According to CRN, these conclusions are dramatically overstated, considering the limitations of meta-analysis, in general, and this meta-analysis, specifically.

For example, the analysis could have potentially included over 300 scientific studies on calcium supplementation's effect on bone, but only 15 randomized clinical trials were deemed "eligible for analysis." Further, seven of the 15 trials evaluated had no, or incomplete, data on cardiovascular outcomes, and only five of the 15 studies accounted for almost all of the cardiovascular outcomes. Further, because the researchers chose to exclude any trials administering calcium plus vitamin D, many large, important trials— including the Women's Health Initiative, which found calcium plus vitamin D had no effect on the risk of coronary heart disease or stroke—were not included.

"The authors characterize these findings as though all of the selected studies suggest increased risk. In fact, the opposite is true: most of the studies do not suggest increased risk," says Dr. Shao. "Bone health is one of the most common reasons why healthcare professionals recommend calcium supplements; there are other health benefits that may be associated with calcium supplementation, such as reduction of colon cancer risk. This is not even considered by the authors. It's unfortunate that these researchers are making sweeping judgments about the value of calcium supplements by only assessing a handful of handpicked studies."

Dr. Shao also pointed out that none of the original studies included in the meta-analysis were designed to evaluate cardiovascular outcomes. Additionally, the data on cardiovascular events was never previously published, so the meta-analysts had to track the information down separately, in some cases, 10 even 20 years after the original study was published.

"Meta-analysis can be a useful tool for scientific evaluation, but we have to recognize its limitations, and keep in mind that its findings are based on a collection of past studies that may have different designs, doses and study populations," says Dr. Shao. "This analysis should not dissuade consumers, particularly young women, from taking calcium supplements. They should talk with their doctors about their current and long-term needs and determine how much calcium they are getting from their diets, and supplement accordingly—likely in combination with vitamin D."

Making the Case for Appropriate Use of Calcium Supplements – Advice from Dr. Jannet Huang

When we look at the recently published meta-analysis with the finding of seemingly increased cardiac risk with calcium supplementation, we must carefully consider these following points.

- First, none of the studies were designed to evaluate cardiovascular outcome. Out of the 190 studies identified as potentially relevant, the authors chose 15 "eligible" studies which were mostly studies of calcium effect on osteoporosis (two

studies were regarding colorectal adenoma). Study participants were mostly women with an average age of 72.

- Second, studies in which Vitamin D was co-administered with calcium were excluded from the analysis. Moreover, there was a wide range of dosing and type of calcium supplementation (eg. carbonate, gluconate, citrate, etc).
- Third, patient level data was available for only 5 of the 15 studies, whereas trial level data was available for 6 studies and no cardiovascular outcome data was available for the remaining 4 studies! Cardiovascular outcome data included unadjudicated self-reports, hospital discharge information and some independently adjudicated events.
- Fourth, there was considerable heterogeneity of participant baseline characteristics. Daily dietary calcium intake reported in the trials ranged from 405mg to 1240mg (ie. from clearly deficient to adequate). 25-hydroxy-Vitamin D levels were measured in 7 studies and ranged from deficient (18ng/mL) to sufficient (37ng/mL). Giving calcium supplementation alone without vitamin D would certainly not be optimal in the setting of vitamin D insufficiency. When we look at the presence of traditional heart disease risk factors in the studies included, the incidence of hypertension ranged from 8-37%, diabetes from 0-10%, current smoking from 0.4-19% and lipid disorder from 1-32%, and many of the studies did not include this information!
- Last but not least, a meta-analysis does not provide any new data but rather it is a review of previously published studies. There are many inherent limitations of meta-analyses and one must be careful not to come to sweeping conclusions from the findings of a meta-analysis.

This recently published meta-analysis came to a conclusion very different from the totality of the literature evidence. Previously published studies have suggested high calcium intake may have a protective effect from vascular disease. The Iowa women's health study found a one third reduction in deaths from cardiovascular events in women whose calcium intakes (diet or supplements) were in the highest fourth compared with those in the lowest fourth. The Boston nurses' health study found that women in the highest fifth for calcium intake had an adjusted relative risk of ischemic stroke of 0.69 compared with those in the lowest fifth. A study in the United Kingdom reported a strong inverse relation between calcium intake and standardized mortality ratios for ischemic heart disease.

Calcium is the most abundant mineral in the human body, making up about 2% of body weight, and participating in the functions of virtually all cells and tissues. Ninety-nine percent of the body's calcium is present in the bones and teeth, to which it gives strength and structure. The remaining 1% of the body's calcium is widely distributed in our tissues and bodily fluids. The vital role of this small amount of calcium is reflected in the precise control of calcium in the blood which always remains within a very narrow range, regulated by hormones including PTH (parathyroid hormone).

This circulating calcium is essential for normal muscle contraction and relaxation, regulation of the heart beat, nerve functioning, blood clotting, secretion of hormones, and the activation of a number of enzymes, including lipase, which is needed to break down dietary fats.

The calcium stored in bones acts as a “reserve” of calcium to the circulation so that blood levels of the mineral can be kept constant at all times. Calcium must be supplied to the body through diet. However, only 20-30% of calcium in the average diet is absorbed from the intestinal tract and taken into the bloodstream. When intake of calcium is inadequate, parathyroid hormone is activated, increasing bone resorption (bone “breakdown”) to “take calcium out from the bone reserve” to keep the blood calcium within the tight range required for physiologic function.

The richest food sources of calcium are dairy products such as cheese, yogurt, ice cream, and milk, greens including collards and kale, almonds, flour, fish, tofu, and egg yolks. In the U.S., 75% of the calcium consumed is in the form of dairy products. Of the nutrients that must be provided by the foods we eat, calcium is one of the most likely to be lacking. Considering the vital functions calcium serves in our physiology, I would argue that calcium supplementation should be used in an appropriate and judicious way. The total daily calcium supplement dose should be individualized, taking into account the individual’s dietary calcium intake and medical history. Vitamin D3 supplementation should be used to optimize an individual’s blood level of 25-hydroxy-vitamin D (I recommend a target 50-100ng/mL) not only for strong bones, but also for multiple health benefits including potentially reducing risk of diabetes/insulin resistance, cardiovascular disease, autoimmune diseases (eg. Multiple sclerosis), breast/colon cancer, dementia and Parkinson’s disease.

I personally take Chelated Cal-Mag capsules by GNLD every evening (and I give this to my now 9 year old daughter as well). The calcium in Chelated Cal-Mag is a food-sourced calcium from eggshells and the double amino acid chelation technology utilizing glycine enhances absorption and bioavailability. I believe that is preferable to select a supplement which supports our body according to the laws of nature, that is why I chose a food-sourced calcium for myself and my family.