Journal Scan

Effect of Calcium Supplements on Risk of Myocardial Infarction and Cardiovascular Events: Meta-analysis

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BMJ 2010, Jul 29;341:C3691, DOI:10.1136/bmj.C3691

ABSTRACT

Objective

To investigate whether calcium supplements increase the risk of cardiovascular events.

Design

Patient level and trial level meta-analyses.

Data Sources

Medline, Embase, and Cochrane Central Register of Controlled Trials (1966-March 2010), reference lists of meta-analyses of calcium supplements, and two clinical trial registries. Initial searches were carried out in November 2007, with electronic database searches repeated in March 2010.

Study Selection

Eligible studies were randomized, placebo controlled trials of calcium supplements (≥ 500 mg/day), with 100 or more participants of mean age more than 40 years and study duration more than 1 year. The lead authors of eligible trials supplied data. Cardiovascular outcomes were obtained from self-reports, hospital admissions and death certificates.

Results

Fifteen trials were eligible for inclusion, five with patient level data (8,151 participants, median follow-up 3.6 years, interquartile range 2.7-4.3 years) and 11 with trial level data (11,921 participants, mean duration 4.0 years). In the five studies contributing patient level data, 143 people allocated to calcium had a myocardial infarction compared with 111 allocated to placebo (hazard ratio 1.31, 95% confidence interval 1.02-1.67, p = 0.035). Nonsignificant increases occurred in the incidence of stroke (1.20, 0.96-1.50, p = 0.11), the composite end point of myocardial infarction, stroke, or sudden death (1.18, 1.00 to 1.39, p = 0.057), and death (1.09, 0.96-1.23, p = 0.18). The meta-analysis of trial level data showed similar results: 296 people had a myocardial infarction (166 allocated to calcium, 130 to placebo), with an increased incidence of myocardial infarction in those allocated to calcium (pooled relative risk 1.27, 95% confidence interval 1.01-1.59, p = 0.038).

Conclusion

Calcium supplements (without coadministered vitamin D) are associated with an increased risk of myocardial infarction. As calcium supplements are widely used these modest increases in risk of cardiovascular disease might translate into a large burden of disease in the population. A reassessment of the role of calcium supplements in the management of osteoporosis is warranted.

Long-term Calcium intake and Rates of all Cause and Cardiovascular Mortality: Community based Prospective Longitudinal Cohort Study

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BMJ 2013;346:f228. Published online, Feb 12,2013, DOI: 10.1136/bmj.f228

ABSTRACT

Objective

To investigate the association between long-term intake of dietary and supplemental calcium and death from all causes and cardiovascular disease.

Design

Prospective longitudinal cohort study.

Setting

Swedish mammography cohort, a population-based cohort established in 1987-90.

Participants

A total of 61,433 women (born between 1914 and 1948) followed-up for a median of 19 years.

Main Outcome Measures

Primary outcome measures, identified from registry data, were time to death from all causes (n = 11,944) and cause specific cardiovascular disease (n = 3,862), ischemic heart disease (n = 1,932), and stroke (n = 1,100). Diet was assessed by food frequency questionnaires at baseline and in 1997 for 38,984 women, and intakes of calcium were estimated. Total calcium intake was the sum of dietary and supplemental calcium.

Results

The risk patterns with dietary calcium intake were non-linear, with higher rates concentrated around the highest intakes (≥1400 mg/day). Compared with intakes between 600 and 1,000 mg/day, intakes above 1400 mg/day were associated with higher death rates from all causes (hazard ratio 1.40, 95% confidence interval 1.17-1.67), cardiovascular disease (149, 1.09-2.02), and ischemic heart disease (2.14, 1.48-3.09) but not from stroke (0.73, 0.33-1.65). After sensitivity analysis including marginal structural models, the higher death rate with low dietary calcium intake (<600 mg/day) or with low and high total calcium intake was no longer apparent. Use of calcium tablets (6% users; 500 mg calcium per tablet) was not on average associated with all cause or cause specific mortality but among calcium tablet users with a dietary calcium intake above 1,400 mg/day the hazard ratio for all cause mortality was 2.57 (95% confidence interval 1.19 to 5.55).

Conclusion

High intakes of calcium in women are associated with higher death rates from all causes and cardiovascular disease but not from stroke.

Journal of South Asian Federation of Obstetrics and Gynaecology

The Effect of Calcium Plus Vitamin D on Risk for Invasive Cancer: Results of the Women's Health Initiative Calcium Plus Vitamin D Randomized Clinical Trial

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Nutr cancer 2011;63(6):827-841, Published online, Jul 20, 2011, DOI: 10.1080/01635581.2011.594208

ABSTRACT

In the Women's Health Initiative (WHI) trial of calcium plus vitamin D (CaD), we examined the treatment effect on incidence and mortality for all invasive cancers. Postmenopausal women (N = 36,282) were randomized to 1,000 mg of elemental calcium with 400 IU vitamin D_3 or placebo. Cox models estimated risk of cancer incidence and mortality. After 7 years, 1,306 invasive cancers were diagnosed in the supplement and 1,333 in the placebo group [hazard ratio (HR) = 0.98; CI = 0.90, 1.05, unweighted p = 0.54]. Mortality did not differ between supplement (315, annualized (%) = 0.26) and placebo [(347, 0.28%; p = 0.17; HR = 0.90 (0.77, 1.05)]. Significant treatment interactions on incident cancer were found for family history of cancer, personal total intake of vitamin D, smoking, and WHI dietary trial randomized group. Calcium/vitamin D supplementation did not reduce invasive cancer incidence or mortality. Supplementation lowered cancer risk in the WHI healthy diet trial arm and in women without a first-degree relative with cancer. The interactions are only suggestive given multiple testing considerations. The low vitamin D dose provided, limited adherence, and lack of serum 25(OH)D values should be considered when interpreting these findings.

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