Clinical practice Assessment

Effect of Calcium Intake on Cardiovascular Events

Clinical Question:
Does calcium supplementation with or without vitamin D increase the risk of cardiovascular events in post menopausal women?

Bottom Line:
Meta-analysis suggests an increased risk of all-cause mortality and myocardial infarction in women on calcium supplements of ≥ 500mg/day (either as Calcium Citrate or Calcium Carbonate) with or without the addition of vitamin D. Those with a high (greater than 1400mg/day) dietary calcium intake also exhibited comparable risk. Other studies suggest vitamin D supplementation has beneficial effects (see Vitamin D Clinical Practice Assessment).

The USPSTF does not recommend supplementation with calcium and vitamin D for primary prevention of osteoporosis.

The IOM recommends a daily total of 1000-1200mg of elemental calcium with 600-800IU of vitamin D for adults.

Synopsis:
In a meta-analysis of 15 placebo controlled trials (1) Bolland found an increase in risk of cardiovascular (CV) events with calcium supplementation of ≥500mg daily. Data was analyzed at the trial level in 11 studies and at the patient level in 5. The 11 studies with trial level data (n = 11921 patients) revealed that the relative risk (RR) of MI was 1.27 (confidence interval (CI) of 1.01-1.59, P=0.038) with 166 MIs in the calcium group and 130 in the control group. No increase in RR of death or strokes was found.

In 5 studies with patient level data (n = 8151) 143 people in the calcium group had MIs compared with 111 on placebo; hazard ratio (HR) of 1.31 (CI of 1.02-1.67, P=0.035). For stroke there was a HR of 1.20 (CI of 0.96-1.5, P=0.11). There was no significant increase in the composite incidence of any MI, stroke or sudden; HR of 1.18 (CI of 1.00-1.39, P = 0.057) or in all causes of death; HR of 1.09 (CI of 0.96-1.23, P=0.18). The number needed to harm (NNH) with five years use of calcium to cause one MI was 69. When analysis included incident and recurrent CV events in the calcium group there were more MIs; RR of 1.32 (CI of 1.02-1.71, P=0.032) and more combined MIs, strokes or sudden deaths; RR of 1.27 (CI of 1.07-1.51, P=0.006).

In a reanalysis of the Women’s Health Imitative excluding the personal use (46% of total women) of calcium (2) women using calcium 1gm and Vitamin D 400IU were compared with placebo. In those on not taking personal calcium at randomization (46%) the RR for CV events with calcium and vitamin D was 1.16, P=0.005 for clinical MI or stroke. The RR was 1.16, P=0.04 for clinical MI or revascularization. However, in women taking personal calcium supplements before randomization, CV risk did not alter with allocation to calcium and vitamin D. Adding this study
to the prior meta-analysis concluded the number needed to harm with five years use of calcium or calcium with Vitamin D to cause one incident event was 240 for MI, 283 for stroke and 178 for the composite end point of either. The number needed to treat (NNT) to prevent 1 fracture is 302 women. Treating 1000 women with five years of calcium or calcium and vitamin D would cause an additional 6 MIs or strokes and prevent 3 fractures.

A large prospective cohort study from Sweden\(^3\) evaluated high dietary calcium intake separate from supplements. The intake of high total calcium intake (dietary and/or supplemental) above 1400mg/day was associated with higher death rates from all causes and cardiovascular disease (CVD) but not stroke. Vitamin D intake did not significantly modify the associations between calcium intake and the rate of death from all causes or CVD.

**Benefit of Calcium and Vitamin D:**

In studies observational and randomized controlled, mostly in the elderly there is evidence of improved calcium balance, bone density and limited support for reduced fragility fracture risk with calcium intakes of 1000mg daily, vitamin D 400IU daily and in those with a 25 OH vitamin D level above 20ng/ml. This has led to recommendations that patients with osteoporosis maintain a total (dietary plus supplementation) of calcium of 1200mg daily and vitamin D of 800IU.

The risks of calcium with or without vitamin D supplements include an increased incidence of renal calculi, myocardial infarction and all-cause mortality.

The USPSTF in 2013 states it does not recommend for the primary prevention of fractures the use of combined calcium and vitamin D supplementation because of inclusive evidence to assess the benefits and harms.\(^4\)

**Strength of Recommendation B**

**Source:**


