

Calcium supplementation in people with diabetes – is caution needed?

Habitual calcium supplementation is associated with an increased risk of cardiovascular disease (CVD) amongst people with diabetes but not in those without diabetes, according to this study of UK Biobank data published in *Diabetes Care*. Over a median follow-up of 8.1 years, 26 374 cardiovascular events were recorded amongst the 435 000 participants studied, and over a median follow-up of 11.2 years there were 20 526 deaths, of which around 4000 were designated as cardiovascular deaths. Amongst those with diabetes, habitual calcium supplementation was significantly associated with higher risks of cardiovascular events (HR 1.34), cardiovascular mortality (HR 1.67) and all-cause mortality (HR 1.44) compared to no calcium supplementation. In contrast, calcium supplementation in those without diabetes was not associated with significantly increased risk of these outcomes. Since habitual calcium supplementation is common in older people keen to reduce the risk of osteoporotic fractures, and since cardiovascular risk is already higher in those with diabetes, any potential increases in risk of CVD or other adverse events associated with calcium supplementation are important.

People with diabetes are known to have a 2–4-fold increased risk of cardiovascular disease (CVD) (Harding et al, 2019) and a slightly [increased risk of fractures](#) (Moayeri et al, 2017). Calcium supplementation is common, particularly amongst older people and women aiming to reduce their risk of osteoporosis and fractures, but previous studies of the associations between calcium supplementation and cardiovascular disease amongst the general population have been inconclusive, with positive, negative and null results (Jenkins et al, 2018).

Calcium supplements result in a sudden increase in blood calcium levels, and it has been suggested that this may increase the risk of CVD, particularly in those already at high risk or with chronic kidney disease (West et al, 2010). In contrast, dietary calcium intake has not been associated with increased cardiovascular risk, possibly related to the smaller amounts of calcium absorbed over a longer part of the day compared with supplement intake.

In the present study, published in *Diabetes Care*, Qiu and colleagues used UK Biobank data from 434 374 people, including 21 676 with diabetes, to further explore associations between calcium supplementation and cardiovascular

events, cardiovascular mortality and all-cause mortality in cohorts with and without diabetes. UK Biobank is a large cohort study which recruited nearly half a million people aged 40–69 years between 2006 and 2010. For this analysis, people who were known to be pregnant or to have CVD or cancer were excluded, and those who died in the first 2 years of follow-up or who had missing data were excluded. Habitual calcium supplementation was identified by self-report at baseline.

Results

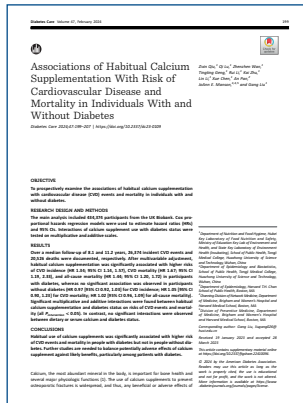
A total of 29 360 participants (6.8%) took calcium supplements, and these were evenly distributed between those with and without diabetes. Over a median of 8.2 years of follow-up, there were 26 374 cardiovascular events amongst the whole cohort. Adjustments were made for dietary and lifestyle factors, other supplement use and higher serum vitamin D.

Amongst those with diabetes, habitual calcium supplementation was significantly associated with an increased risk of cardiovascular events compared to those with diabetes not taking calcium supplements (hazard ratio [HR] 1.34; 95% CI 1.14–1.57). Amongst those



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without diabetes, however, habitual calcium supplementation was not associated with significant increase in cardiovascular events compared to no supplementation (HR 0.97; 95% CI 0.92–1.03).

Over 11.2 years of median follow-up, there were 20 526 deaths, including 4007 designated as cardiovascular deaths. Again, habitual calcium supplementation in those with diabetes was associated with increased risk of both cardiovascular death (HR 1.67; 95% CI 1.19–2.33) and all-cause mortality (HR 1.44; 95% CI 1.20–1.72). Amongst those without diabetes, calcium supplementation was not associated with significant increases in either cardiovascular (HR 1.05; 95% CI 0.90–1.23) or all-cause death (HR 1.02; 95% CI 0.96–1.03).

When people with diabetes taking calcium supplements were compared to those without diabetes and not on supplements, those with diabetes had hazard ratios of 1.67 for incident cardiovascular events, 2.84 for cardiovascular mortality and 2.20 for all-cause mortality. Similar results were identified in a variety of stratified and sensitivity analyses, including when only those with type 2 diabetes (instead of all diabetes types) were analysed and when adjustments were made for total energy and dietary calcium intake.

When dietary calcium intakes and cardiovascular risk were reviewed in those who had completed dietary assessments, there was a U-shaped curve, with decreased risk in those with moderate calcium intakes (900–1000 mg/day), with or without diabetes. In this study, the highest risk of CVD and mortality was seen in those with diabetes taking calcium supplements with low intakes of dietary calcium.

Discussion

What are the underlying mechanisms here? Adequate calcium intake could influence insulin secretion, lipid metabolism and body weight. Rapid increases in serum calcium levels, as occur even after supplementation with 500 mg of calcium, may increase vascular calcification and coagulability.

The authors outline the strengths of this study: a large population of almost half a million, assessment of dietary calcium, calcium supplements and blood calcium levels, assessment of confounding factors including vitamin D levels, diet and lifestyle factors, and consistent findings in sensitivity analyses. However, limitations include the fact that this was a cohort study, so we should remember these are associations only. Furthermore, calcium supplementation coding was based on a single self-reported assessment at baseline, and no details of whether supplementation practices changed during follow-up are available, and the individual doses and types of calcium supplements are unknown. The study included a predominantly white, UK-based cohort.

The authors call for further studies to clarify the benefits and risks of calcium supplementation amongst people with diabetes. In the meantime, they conclude that people with diabetes “might need to be cautious about the long-term use of calcium supplements.”

Implications for practice

This study will certainly prompt me to audit and re-evaluate our use of calcium supplementation in people with diabetes, particularly those most at risk of CVD, and to consider a discussion with our renal colleagues. I will continue providing advice about how to increase dietary calcium intake, which I already do given the potential impact on weight and bones. ■

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