The Optimal Dietary Calcium Intake for Preventing Incident and Recurrent Symptomatic Kidney Stone Disease

Until the early 1990s, it was presumed that dietary calcium intake should be limited for preventing the onset and recurrence of calcium kidney stone formation, assuming that frequent consumption of milk and dairy products could unfavorably influence urinary calcium excretion. However, a prospective investigation conducted on 45,619 men without baseline history of kidney stones, published in 1993, showed an inverse relationship between baseline dietary calcium intake, assessed by a semiquantitative food frequency questionnaire, and the risk of incident symptomatic kidney stone disease after a 4-year follow-up period.1 In 2002, a randomized controlled trial comparing a low-calcium (10 mmol/d) diet vs a normal-calcium (30 mmol/d), low-salt (50 mmol of sodium chloride per day), low-animal protein (52 g/d) diet in recurrent calcium oxalate stone formers with hypercalciuria found that a low-calcium diet was associated with a significantly higher rate of further recurrence during a 5-year follow-up period.2

These studies contributed to shift the paradigm of nonpharmacologic prevention of recurrent kidney stone disease, moving the focus from calcium to salt and animal protein intake. Limiting dietary salt intake is nowadays considered a paramount measure for counteracting calcium kidney stone formation because a renal load of sodium is associated with calcium excretion and increased risk of calcium oxalate crystallization.3

However, not all forms of calcium kidney stone disease are salt responsive or associated with hypercalciuria. Some recurrent calcium stone formers may exhibit elevated urinary calcium excretion even in the presence of reduced dietary salt intake. In these situations, in which absorptive hypercalciuria of intestinal origin may be present, a mild dietary calcium restriction could still be regarded as a reasonable option for mitigating the risk of stone recurrence.3

In this issue of Mayo Clinic Proceedings, Chewcharat and colleagues5 contribute to shed light on the relationship between dietary calcium intake and risk of idiopathic kidney stone disease. In their longitudinal study, they enrolled 411 symptomatic stone formers after the first episode of renal colic and followed them up for a median of 4.1 (interquartile range, 1.3 to 5.6) years. The baseline intake of several nutrients, including calcium, assessed by a validated electronic food frequency questionnaire, was significantly different in comparison with a group of 384 non–stone-forming controls. In stone formers, baseline calcium intake was the only dietary factor inversely associated with the risk of symptomatic stone recurrence after adjustment for covariates. Interestingly, a daily calcium intake of 1200 mg/d, equal to that recommended by the US Department of Agriculture for the general population, was the amount associated with the lowest risk of kidney stone formation. Sodium intake, instead, was not significantly associated with either first-episode or recurrent kidney stone disease.

Overall, these results reinforce the recommendation of maintaining an adequate dietary calcium intake for both primary and secondary prevention of nephrolithiasis, whatever the pathophysiologic mechanisms involved in kidney stone formation. The relationship between calcium intake and stone risk was U shaped, with increased risk for dietary extremes.3 Notably, participants to the study were not selected by stone composition or urine chemistry but
represented a reliable sample of the general population experiencing renal colic. Furthermore, the design of the study allowed, for the first time in the scientific literature on stone disease, dietary factors associated with both incident and recurrent episodes of nephrolithiasis to be explored.

The pathophysiologic mechanisms underlying the complex epidemiologic relationship between calcium intake and risk of symptomatic kidney stone disease are not fully understood. Dietary calcium is able to modulate the intestinal absorption of oxalate, influencing delivery of this compound to the kidney and the risk of hyperoxaluria, one of the main urinary abnormalities associated with calcium oxalate stone formation. Diets with a good balance between calcium and oxalate content are generally associated with reduced absorption of oxalate, whereas low-calcium diets promote oxalate absorption because of reduced formation of unabsorbable calcium oxalate complexes in the gut lumen. Furthermore, low-calcium diets can also promote 1,25-dihydroxyvitamin D synthesis, with unfavorable effects in terms of urinary calcium excretion.

In the past decade, several studies have also investigated the role of the intestinal microbiome in the pathophysiologic process of kidney stone disease. According to these

FIGURE. Pathophysiologic model showing how the balance between dietary oxalate and calcium intake can influence the pathogenesis of calcium oxalate kidney stone formation. PTH, parathyroid hormone. (Parts of the image are distributed under Creative Commons Licence and are freely available at the following links: https://smart.servier.com and https://pixabay.com.)
studies, recurrent calcium oxalate kidney stone formers have reduced representation of intestinal bacterial populations involved in oxalate degradation. Because diet represents a powerful modulator of the gut microbiota composition, it can be hypothesized that diet influences lithogenesis through mediation of the gut microbiota (Figure). Interestingly, in one of the largest studies comparing microbiota composition between recurrent calcium oxalate stone formers and healthy controls, low calcium intake was the only dietary difference detected in stone formers.\(^9\) The role of the intestinal microbiota as mediator of the lithogenic effect of low-calcium diets should thus be further investigated in the future.

Kidney stone disease is increasingly regarded as a systemic disease whose pathophysiological processes do not merely involve the urinary tract but depend on intestinal, endocrinologic, and metabolic conditions, strongly interacting with genetic background and the environment.\(^10\) Unfortunately, effective and sustainable long-term strategies for preventing kidney stone recurrence are lacking in clinical practice, and there is still some uncertainty on the best nutritional advice that should be given to stone formers. Stressing the need of maintaining a balanced intake of milk and dairy products, compliant with the US Department of Agriculture recommendations for calcium intake, could represent a cornerstone advice for stone formers, and future research should focus on a better understanding of the mechanisms of this association.

**POTENTIAL COMPETING INTERESTS**
The authors report no competing interests.