Vitamin D status, sodium intake and the risk of developing CKD

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Introduction

Vitamin D deficiency is common and has been associated with increased albuminuria and progressive renal function loss in chronic kidney disease (CKD) patients. Treatment with a vitamin D receptor activator (VDRA) provides renoprotection by reducing albuminuria in preclinical and clinical CKD. The albuminuria-lowering effect of vitamin D receptor activators may depend on dietary sodium intake.

Whether the precursor 25-hydroxyvitamin D (25[OH]D) or the active metabolite 1,25-dihydroxyvitamin D (1,25[OH]2D) is associated with the risk of developing CKD is unclear.

Aims

1. To investigate the association of 25(OH)D and 1,25(OH)2D with the risk of developing CKD in a general population-based cohort.
2. To explore a potential interaction of vitamin D with sodium intake on incident albuminuria.

Methods

Circulating 25(OH) and 1,25(OH)2 vitamin D were measured by liquid chromatography tandem mass spectrometry (LS-MS/MS) in the general population-based PREVEND cohort. Participants with CKD at baseline were excluded from the analysis.

The primary outcome was CKD, defined as an eGFR (creatinine/cystatin C-based CKD-EPI formula) <60 ml/min/1.73 m2 and/or urinary albumin excretion (UAE) >30 mg/24h. Secondary outcomes were reduced eGFR and increased albuminuria individually.

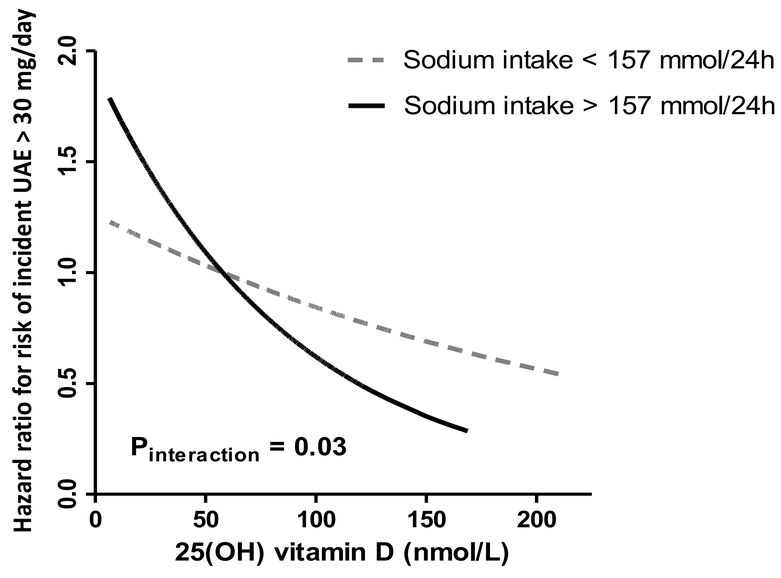
Associations between vitamin D status and the risk of onset CKD was assessed using Cox regression analyses with adjustment for baseline age, sex, DM, history of CV disease, smoking, use of lipid-lowering and/or blood pressure-lowering drugs, BMI, SBP, day of blood sampling, total to HDL cholesterol ratio, triglycerides, eGFR and UAE.

Results

Table 1. *Baseline characteristics*

Male sex, %	2400 (47)
Age, years	48.4 ± 11.7
BMI, kg/m^2	25.7 ± 3.9
Systolic BP, mmHg	125.8 ± 17.9
Diastolic BP, mmHg	72.8 ± 9.1
Antihypertensives, %	589 (12)
25(OH)D, nmol/L	57.8 ± 23.2
1,25(OH)$_2$D, pmol/L	145.5 ± 47.2
eGFR, ml/min/1.73m^2	97.3 ± 14.6
UAE, mg/24h	8.13 [5.94-12.15]

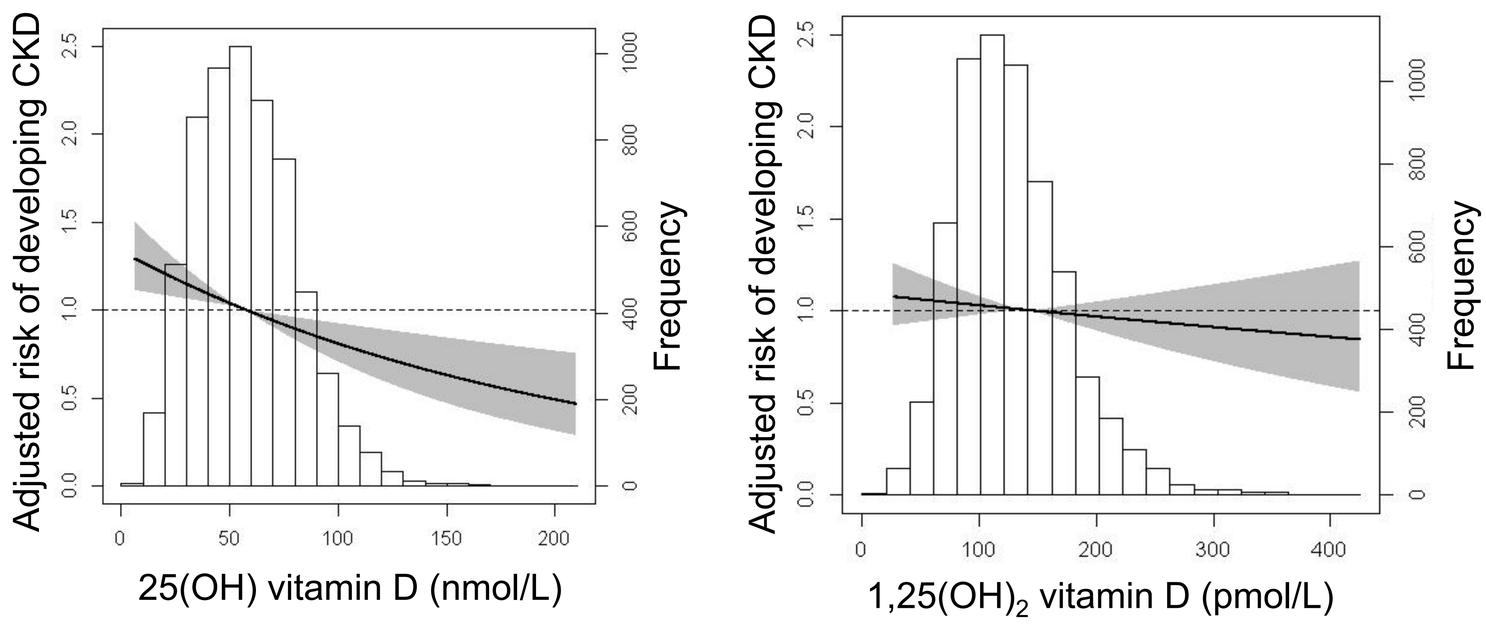
Figure 2. *Interaction of sodium intake and 25(OH)D on incident albuminuria*



During a median follow-up period of 10.4 [IQR, 6.2-11.4] years, 828 out of 5082 (16%) participants developed CKD. Each standard deviation (SD) increase in 25(OH)D was associated with a 14% lower risk of developing CKD after adjustment (HR 0.86 [95% CI 0.79-0.93], *P*<0.001, Figure 1A). Plasma 25(OH)D was inversely associated with the risk of incident increased albuminuria (adjusted HR 0.86 [0.79-0.95], *P*=0.003, n=634), but not with incident reduced eGFR (events 261).

Plasma 1,25(OH)$_2$D was not significantly associated with incident CKD (adjusted HR per SD increase 0.99 [0.92-1.07], *P*=0.8, Figure 1B), nor with microalbuminuria or reduced eGFR separately.

Figure 1. *The relative risk of developing CKD*



The association between 25(OH)D levels and the development of albuminuria was modified by baseline sodium intake (*P-interaction*=0.03).The association between 25(OH)D and onset microalbuminuria was more pronounced in subjects within the highest tertile of sodium intake (> 157 mmol/day, representing >3.6 grams sodium) than in those with low or intermediate sodium intake tertiles (Figure 2).

Conclusion

Low plasma 25(OH)D is associated with an increased risk of developing CKD, mainly driven by an association with incident micro- or macroalbuminuria. Especially subjects with low plasma 25(OH)D and high sodium intake have a high risk of developing albuminuria.

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