Vitamin D status and long-term outcomes after kidney transplantation

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Introduction

- Vitamin D is a hormone with a central role in mineral homeostasis. Concordant evidence sustains a wide range of vitamin D effects beyond mineral metabolism including immunological, cardiovascular, and renal effects.
- A recent study linked low levels of 25(OH) (inactive) but not 1,25$(OH)_2$ (active) vitamin D to an increased risk of interstitial fibrosis, tubular atrophy, and lower measured GFR one year after kidney transplantation. Whether this discrepancy also holds for long-term hard outcomes is not well described in this population.

Aims

1. To investigate the value of circulating 25(OH)D and 1,25$(OH)_2$D levels as risk factors for graft failure and mortality in stable renal transplant recipients (RTR).
2. To investigate the relation between vitamin D and annual change in eGFR.

Methods

Plasma 25(OH)D and 1,25$(OH)_2$D levels were measured by LC MS/MS in a cohort of stable RTR (N=437) transplanted in our center (UMCG), with a functioning graft for ≥1 year.

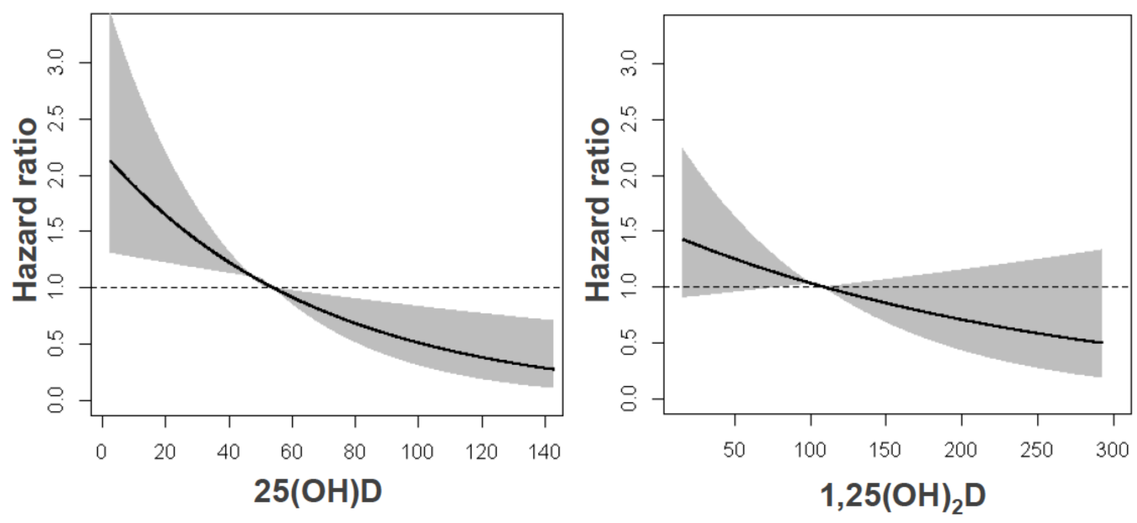
After a median follow-up of 7.1 [6.2-7.5] years, associations of vitamin D status with death-censored graft failure or all-cause mortality were investigated by Cox regression analyses adjusted for known risk factors. The association of vitamin D with annual change in eGFR was assessed using linear regression analyses.

Results

Table 1. Baseline characteristics of the cohort (N=437)

Male gender, n (%)	223 (51)
Age, years	51.9 ± 11.9
Time after transplantation, years	6.4 [3.1-11.8]
Pre-transplant dialysis, n (%)	399 (91)
BMI, kg/m^2	25.9 ± 4.3
SBP, mmHg	152 ± 24
Current smoking, n (%)	93 (21)
Current diabetes, n (%)	77 (18)
LDL cholesterol, mmol/L	3.53 [2.98-4.08]
PTH, pmol/L	9.1 [6.0-13.4]
eGFR, ml/min	46.5 ± 16.4
Proteinuria, g/24h	0.20 [0.00-0.50]
25(OH) vitamin D, nmol/L	53.8 ± 23.0
1.25 $(OH)_2$ vitamin D, pmol/L	108.4 ± 45.7

Figure 1. Vitamin D status and the risk for all-cause mortality.

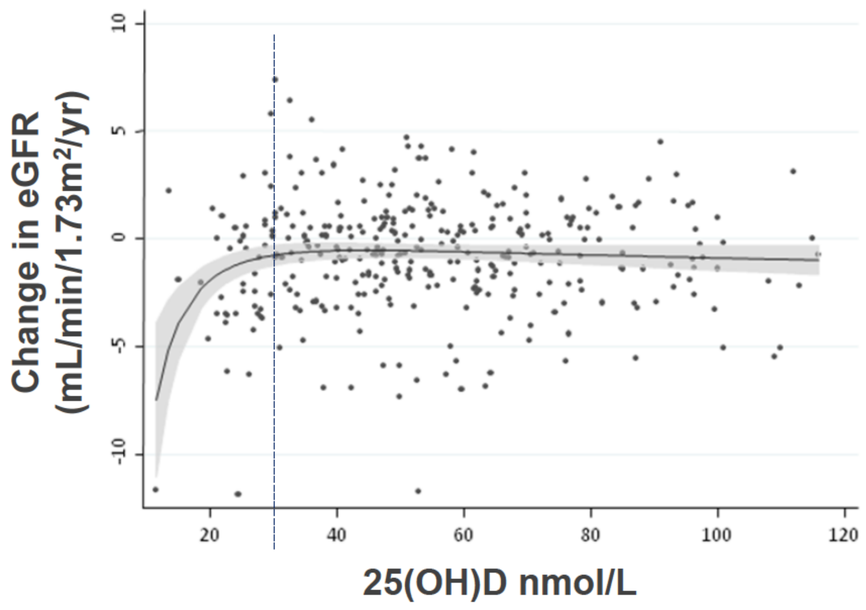


Bold line represents the risk for all-cause mortality, whereas the grey area represents the 95% confidence interval of the hazard ratio. Cox regression model adjusted for age, gender, current smoking, systolic blood pressure, waist circumference, LDL cholesterol, diabetes mellitus, PTH, dialysis vintage and eGFR.

In multivariable Cox regression, plasma 25(OH)D was associated with all-cause mortality (HR 0.69 [95%CI 0.53 to 0.91] per SD increase; *P*=0.007; 99 events). Plasma 1,25$(OH)_2$D was associated with all-cause mortality in univariable analysis (HR 0.69 (0.55 to 0.87) per SD increase; *P*=0.002) but not in analyses adjusted for renal function (HR 0.86 (0.66 to 1.11); *P*=0.2).

Neither 25(OH)D nor 1,25$(OH)_2$D was associated with death-censored graft failure in multivariable analyses adjusting for renal function (44 events).

Figure 2. Scatter plot of the annual change in eGFR



In multivariable linear regression analyses, 25(OH)D levels <30 nmol/L were significantly associated with a higher annual change in eGFR (β -0.11, *P*=0.03).

Conclusion

Low plasma 25(OH)D is an independent risk factor for all-cause mortality after kidney transplantation. In addition, very low levels of 25(OH)D are associated with higher annual decline in eGFR. Future studies should address whether vitamin D supplementation improves long-term outcomes after kidney transplantation.

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