Vitamin D Deficiency and Elevated PTH but not FGF23 Predict All-Cause Mortality in People with Chronic Kidney Disease Stage 3 in Primary Care

Renal Risk in Derby

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Introduction

Vitamin D deficiency, elevated fibroblast growth factor 23 (FGF23) and elevated parathyroid hormone (PTH) have each been associated with increased mortality in people with chronic kidney disease (CKD). We have previously reported that, in CKD stage 3, FGF23 becomes elevated early in people who are vitamin D replete, but PTH becomes elevated earlier in those with vitamin D deficiency or insufficiency.[1] In this analysis, we aimed to evaluate the relative importance of vitamin D deficiency, elevated PTH and elevated FGF23 as risk factors for all-cause mortality in people with CKD stage 3 recruited from primary care.

Methods

1,741 people were prospectively recruited from 32 local primary care practices.[2] All participants had CKD stage 3 prior to study entry (2 eGFR measurements in the range 30-59 ml/min/1.73m^2 at least 90 days apart.). Demographic and medical details, anthropometric measurements, urine and serum biochemistry were collected at baseline, year 1 and year 5 follow-up visits. Date and cause of death was obtained from the office of national statistics. 25(OH)Vitamin D, PTH and FGF23 were measured in serum (stored at -80°C) from the baseline visit.

Results

1,664 participants were included (mean age 73±9 years; mean eGFR at baseline 54±12 ml/min/1.73m2). Of this group 289 died prior to year 5 follow-up. Participants who died had higher median FGF23 (45, IQR 34-59 pg/ml) and PTH (56, IQR 39-85 pg/ml), as well as lower median 25(OH)vitamin D (48, IQR 31-67 nmol/l) compared to those who survived (FGF23: 42, IQR 33-52 pg/ml; PTH: 45, IQR 33-62 pg/ml; 25(OH)Vitamin D: 54, IQR 39-72 nmol/l; $p < 0.01$ for all variables). 67 participants (3.8 %) were on vitamin D supplementation at the baseline visit and 104 (6.3 %) were vitamin D deficient (<25 nmol/l).

Elevated FGF23 and PTH as well as vitamin D deficiency were associated with increased risk of all-cause mortality in univariate analyses but the association with FGF23 was no longer significant after correction for age, gender, eGFR and uACR, whereas vitamin D deficiency and elevated PTH remained significant. (Figure 1.)

In a fully adjusted model, using variables previously shown to predict mortality, vitamin D deficiency (HR 1.64, 1.03-2.61) and elevated PTH (HR 1.41, 1.08-1.83) were independent predictors of all-cause mortality but elevated FGF23 was not (HR 0.95, 0.73-1.23). (Table 1.)

Results

Figure 1. Adjusted and Unadjusted Hazard ratios of All-Cause Mortality by Baseline levels of Vitamin D, FGF23 and PTH

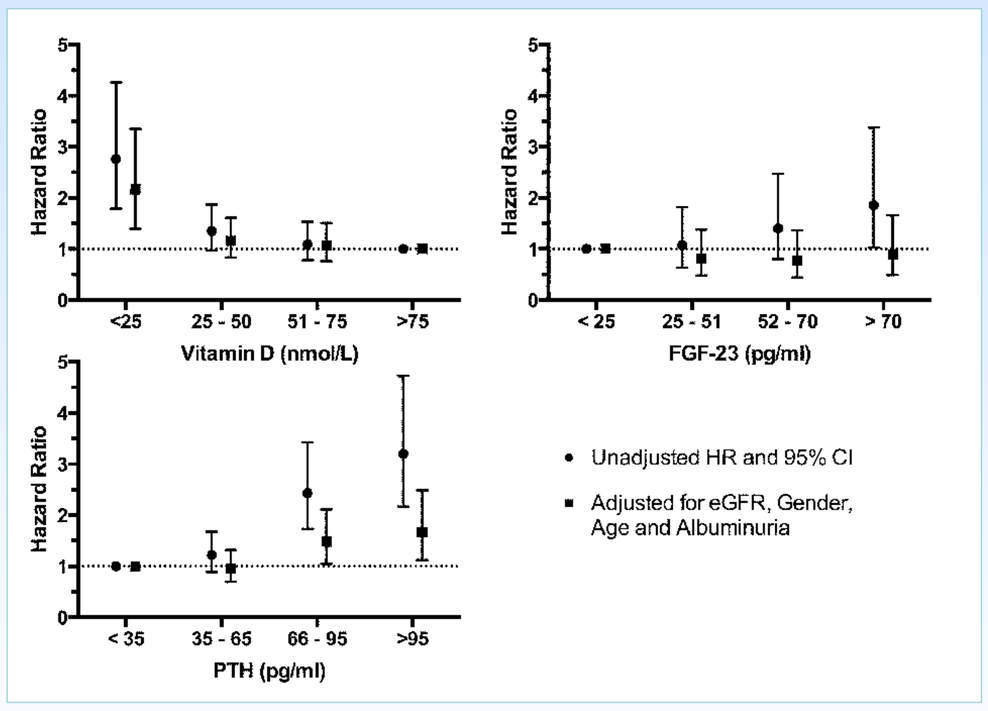

Table 1. Cox Proportional Hazards Models – Univariate and Multivariable Associations of All-Cause Mortality

Variable	Univariate Hazard Ratio (95 % CI)	Multivariable Model	
		Hazard Ratio (95 % CI)	P value
CKD-EPI eGFR	0.95 (0.94-0.95)	0.97 (0.96-0.99)	<0.001
Age	1.10 (1.08-1.12)	1.07 (1.05-1.09)	<0.001
Male Gender	2.01 (1.60-2.54)	1.74 (1.35-2.25)	<0.001
Log uACR	1.30 (1.20-1.41)	1.13 (1.03-1.22)	0.007
Previous CVD	2.45 (1.94-3.11)	1.73 (1.35-2.21)	<0.001
Haemoglobin	0.81 (0.75-0.88)	0.92 (0.84-1.00)	0.07
Albumin	0.91 (0.89-0.94)	0.94 (0.91-0.98)	0.001
Bicarbonate	0.98 (0.94-1.03)	1.04 (1.00-1.09)	0.07
Vitamin D			
< 25	2.76 (1.79-4.26)	1.64 (1.03-2.61)	0.036
25 – 50	1.35 (0.97-1.87)	0.95 (0.67-1.34)	0.76
50 – 75	1.09 (0.78-1.54)	1.01 (0.71–1.43)	0.98
> 75	1 (reference)	1 (reference)	
FGF-23 >51	1.45 (1.14-1.85)	0.95 (0.73-1.23)	0.70
PTH > 65	2.35 (1.86-2.97)	1.41 (1.08-1.83)	0.01

Conclusion

In this cohort of predominantly older people with relatively early CKD, vitamin D deficiency and elevated PTH were independent risk factors for all-cause mortality but elevated FGF23 was not. This suggests that correction of vitamin D deficiency may be more important than targeting FGF23 in this population but randomised trials will be required to test this hypothesis.

References

1. Taal M.W. et al Kidney Int 2014; 86:407-413
2. McIntyre N.J. et al. Nephron Clin Prac 2011; 199(4):269-76

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