Fibroblast Growth Factor 21 plasma levels and future cardiovascular outcome among non-dialysis chronic kidney disease patients

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Background

Patients with CKD have substantial metabolic alterations, which comprise insulin resistance, hypertriglyceridemia and low HDL-cholesterolemia.

Recently discovered FGF 21 is a central regulator of glucose and lipid metabolism and plays a important role in cardiac remodeling.

The effects of CKD on circulating plasma FGF 21 concentration, and the association of plasma FGF 21 with incident cardiovascular disease and CKD progression have not yet been assessed in large-scale cohorts.

Methods

467 patients with CKD G2 – 4 within the CARE FOR HOMe cohort were analysed. All patients were followed for

cardiovascular events (acute myocardial infarction, stroke, amputation, any surgical or interventional coronary/cerebrovascular or peripheral-arterial revascularization, heart failure, or death of any cause)

and **renal events** (halving of eGFR, ESRD or death of any cause).

Table 1 Baseline characteristica of CARE FOR HOMe participants

	All patients (n = 467)	FGF 21 1st Quartile (n = 117)	FGF 21 2nd Quartile (n = 117)	FGF 21 3rd Quartile (n = 117)	FGF 21 4th Quartile (n = 116)	p
Age (years)	65 ± 12	63 ± 15	65 ± 11	66 ± 12	66 ± 11	0.048
Gender (female)	187 (40 %)	48 (41 %)	49 (42 %)	45 (39 %)	45 (39 %)	0.938
Smoking (yes)	48 (10 %)	9 (8 %)	18 (15 %)	8 (7 %)	13 (11 %)	0.124
DM (yes)	178 (38 %)	31 (27 %)	41 (35 %)	47 (40 %)	59 (51 %)	0.002
Prevalent CVD (yes)	148 (32 %)	30 (26 %)	34 (29 %)	40 (34 %)	44 (38 %)	0.189
BMI (kg/m²)	30 ± 5	28 ± 5	31 ± 6	30 ± 5	32 ± 6	< 0.001
Waist circumference (cm)	103 ± 15	99 ± 15	104 ± 13	104 ± 14	107 ± 17	< 0.001
Hip circumference (cm)	107 ± 12	104 ± 11	108 ± 11	107 ± 11	109 ± 14	0.002
Total FGF 21 (ng/ml)	0.8 ± 1.5	0.2 ± 0.1	0.4 ± 0.2	0.6 ± 0.2	2.0 ± 2.6	< 0.001
Active FGF 21 (ng/ml)	0.4 ± 0.7	0.1 ± 0.03	0.2 ± 0.03	0.3 ± 0.1	1.0 ± 1.2	< 0.001

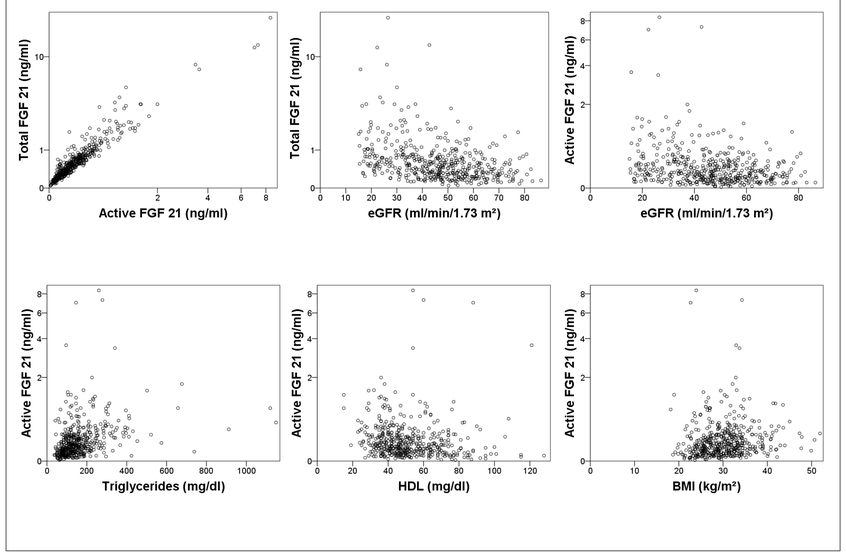
Methods

	All patients (n = 467)	FGF 21 1st Quartile (n = 117)	FGF 21 2nd Quartile (n = 117)	FGF 21 3rd Quartile (n = 117)	FGF 21 4th Quartile (n = 116)	p
Syt. BP (mmHg)	153 ± 24	152 ± 25	152 ± 24	154 ± 24	153 ± 24	0.512
Diast. BP (mmHg)	86 ± 13	87 ± 13	86 ± 12	88 ± 14	85 ± 13	0.618
eGFR (ml/min/1.73 m²)	46 ± 16	49 ± 15	48 ± 16	45 ± 16	40 ± 15	< 0.001
Albuminuria (mg/g)	37 (8 – 202)	22 (6 – 155)	27 (6 – 112)	27 (13 – 176)	111 (24 – 357)	0.011
Total Cholesterol (mg/dl)	193 ± 43	190 ± 37	194 ± 44	192 ± 42	197 ± 49	0.306
Triglycerides (mg/dl)	166 ± 120	115 ± 57	142 ± 80	170 ± 89	238 ± 178	< 0.001
HDL-C (mg/dl)	51 ± 17	58 ± 20	51 ± 15	49 ± 15	48 ± 18	< 0.001
LDL-C (mg/dl)	116 ± 36	114 ± 32	120 ± 37	117 ± 36	112 ± 40	0.558
CRP (mg/l)	2.7 (1.1-5.3)	2.1 (0.8 – 4.0)	2.7 (1.1 – 4.3)	2.8 (1.4 – 4.9)	4.1 (1.5 – 9.7)	0.001

Indicated are means ± standard deviation, or patient numbers (percentages), as appropriate. CVD = cardiovascular disease; BMI = body mass index; BP sys/diast = systolic/diastolic blood pressure; eGFR = estimated glomerular filtration rate; HDL-C = high density lipoprotein-cholesterol; LDL-C = low density lipoprotein-cholesterol; CRP = C-reactive protein.

Results

Figure 1 Correlation between active FGF 21, total FGF 21, eGFR and metabolic markers



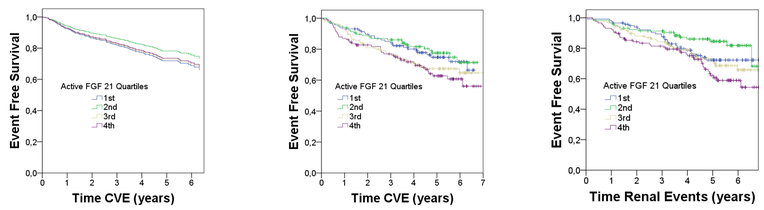
Results

Table 2 Cox regression analysis; CVE and renal events statified by FGF 21 Quartiles

	Univariate Analysis		Adjustment for eGFR and Albuminuria		Adjustment for eGFR, Albuminuria and BMI		Adjustment for eGFR, Albuminuria, BMI, Mean BP, Diabetes mellitus and Current Smoking	
	HR (95 % CI)	p	HR (95 % CI)	p	HR (95 % CI)	p	HR (95 % CI)	p
Renal Events								
1st Quartile	Reference	-	-	-	-	-	-	-
2nd Quartile	0.60 (0.26 -1.38)	0.23	0.68 (0.29 – 1.60)	0.38	0.69 (0.29 – 1.62)	0.39	0.60 (0.24 – 1.47)	0.26
3rd Quartile	1.03 (0.50 – 2.14)	0.94	0.71 (0.34 – 1.48)	0.36	0.71 (0.34 – 1.49)	0.37	0.62 (0.29 – 1.32)	0.22
4th Quartile	1.76 (0.91 – 3.41)	0.09	0.83 (0.42 – 1.61)	0.57	0.83 (0.42 – 1.61)	0.58	0.60 (0.35 – 1.41)	0.31
CV Events								
1st Quartile	Reference	-	-	-	-	-	-	-
2nd Quartile	0.86 (0.50 – 1.47)	0.58	0.82 (0.47 – 1.40)	0.46	0.81 (0.47 – 1.40)	0.45	0.75 (0.43 – 1.30)	0.75
3rd Quartile	1.24 (0.75 – 2.05)	0.39	1.04 (0.63 – 1.72)	0.88	1.03 (0.62 – 1.72)	0.90	0.96 (0.57 – 1.60)	0.87
4th Quartile	1.58 (0.96 – 2.56)	0.06	1.07 (0.65 – 1.75)	0.80	1.06 (0.64 – 1.76)	0.83	0.93 (0.55 – 1.56)	0.79

BMI = body mass index; Mean BP = mean blood pressure; CV events = cardiovascular events; hazard ratio; 95% CI = 95% confidence interval.

Figure 2 Multivariate Cox regression (left) and univariate Kaplan-Meier Curves (middle, left) for CVE and renal events



Conclusions

Our study results demonstrate an increase of plasma FGF 21 levels in CKD patients.

Despite its role in glucose and lipid metabolism, plasma FGF 21 does not independently predict adverse cardiovascular and renal outcome among CKD patients.