Factor analysis on fibroblast growth factor–23 levels in hemodialysis patients with or without cardiovascular diseases.

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OBJECTIVES

- Fibroblast growth factor–23 (FGF23) is a bone–derived hormone regulating renal phosphate reabsorption and vitamin D synthesis in renal proximal tubules[1)].
- Higher circulation levels of FGF23 are associated with increased mortality in both chronic kidney disease (CKD) patients and dialysis patients[2)].
- Also, elevated FGF23 levels relate to increase risks of congestive heart failure but do not raise risks of coronary artery calcifications in CKD patients[3)].
- Although evidences of FGF23 on CKD population have been accumulated, only few reports mentioned on FGF-23 on dialysis patients to date.
- The aim of this study is to evaluate factors associated with FGF23 levels in hemodialysis patients with or without histories of cardiovascular diseases (CVDs).

METHODS

- Randomize-selected maintenance hemodialysis patients (n = 76) at a single hemodialysis center were enrolled in this study.
- Each patient's FGF23 levels were measured and extreme outliers (n = 8) were excluded and finally 68 patients were analyzed.
- In 68 patients, 46 patients had histories of CVDs. Durations of dialysis, time-averaged concentration of urea (TAC–urea), ultrafiltration rates (UFR), blood pressure during hemodialysis session, laboratory data, echocardiographic parameters including interventricular septum thicknesses (IVST), left ventricular mass indexes (LVMI) and ejection fraction in these patients were collected and analyzed.

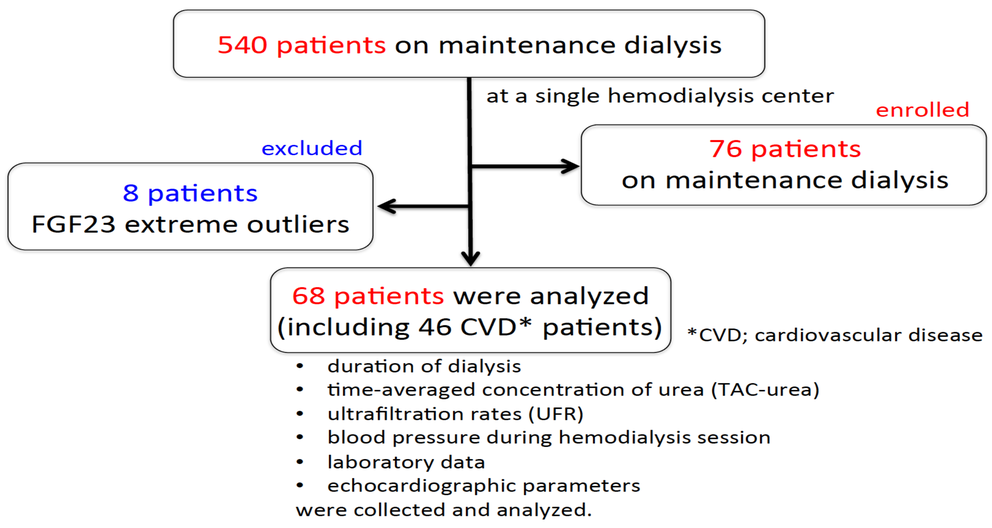


Table 1. BASIC PATIENTS' CHARACTERISTICS

		Overall	with CVDs	without CVDs	P value
Age		64.4 ± 12.1	65.8 ± 10.2	61.4 ± 15.1	NS
Male: Female		48 : 20	34 : 12	14 : 8	NS
duration of hemodialysis	years	12.7 ± 7.1	13.1 ± 7.4	11.9 ± 6.6	NS
FGF23	pg/ml	17039 ± 19178	14633 ± 16563	22068 ± 23376	NS
TAC-urea	mg/dl	45.2 ± 9.7	43.9 ± 8.5	49.9 ± 9.7	0.01
UFR	L/hour	0.70 ± 0.27	0.66 ± 0.23	0.80 ± 0.34	NS
blood pressure	mmHg	147 ± 21	144 ± 22	151 ± 16	NS
CRP (C-reactive protein)	mg/dl	0.34 ± 0.70	0.43 ± 0.86	0.24 ± 0.30	NS
ALP (alkaline phosphatase)	mg/dl	265 ± 106	267 ± 116	252 ± 74	NS
cCa (corrected serum calcium)	mg/dl	8.90 ± 1.17	9.05 ± 0.80	8.98 ± 0.65	NS
iP (serum phosphate)	mg/dl	5.64 ± 1.30	5.52 ± 1.25	6.22 ± 1.07	0.03
intact PTH	pg/dl	207 ± 173	212 ± 191	225 ± 141	NS
IVST (interventricular septum thickness)	mm	10.6 ± 2.0	10.7 ± 2.1	10.7 ± 2.1	NS
LVMI (left ventricular mass index)	g/m^2	109 ± 34	114 ± 32	107 ± 36	NS
EF (ejection fraction)	%	63.1 ± 11.1	61.5 ± 12.9	65.9 ± 7.7	NS

RESULTS

Table2. The relationship between FGF23 and basic patients' characteristics.

	Univariate analysis		Multiple-regression analysis	
	r	P value	F	P value
age	− 0.12	< 0.01		
gender	− 0.03	0.41		
duration of hemodialysis	− 0.11	< 0.01		
TAC-urea	0.29	0.01	0.08	0.78
UFR	0.26	0.04	3.94	0.05
blood pressure	0.17	0.17		
CRP	− 0.04	0.72		
ALP	− 0.27	0.03	5.34	0.03
cCa	0.32	< 0.01	25.6	< 0.001
iP	0.57	< 0.01	22.5	< 0.001
intact PTH	0.38	< 0.01	19.2	< 0.001
IVST	0.30	0.01	0.04	0.83
LVMI	0.26	0.04	1.13	0.29
EF	0.05	0.86		

Figure1. The relationship between FGF23 and ultrafiltration rate.

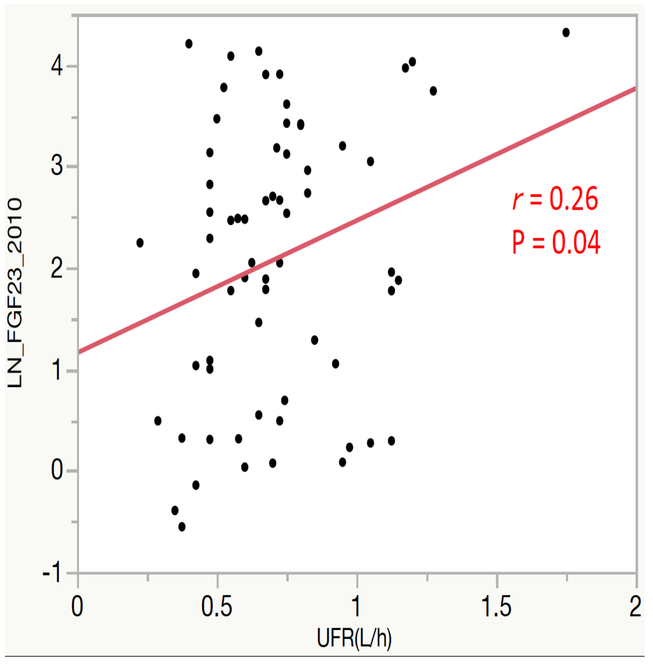
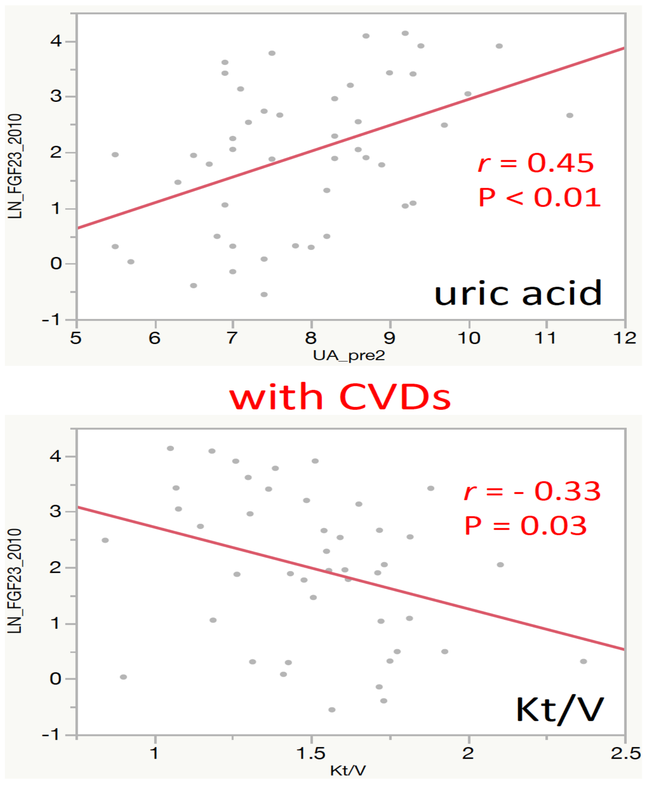


Table3. The relationship between FGF23 and basic patients' characteristics classified by CVDs.

	with CVDs		without CVDs	
	r	P value	*r*	P value
age	0.01	0.94	− 0.24	0.27
duration of hemodialysis	− 0.16	0.29	0.02	0.91
TAC-urea	0.45	< 0.01	0.02	0.77
Kt/V	− 0.33	0.02	− 0.06	0.80
UFR	0.22	0.14	0.28	0.24
blood pressure	0.11	0.47	0.28	0.21
CRP	− 0.06	0.71	0.26	0.70
ALP	− 0.25	0.10	− 0.33	0.13
cCa	0.34	0.02	0.29	0.20
iP	0.41	< 0.01	0.43	0.06
intact PTH	0.39	0.01	0.38	0.10
uric acid	0.45	< 0.01	− 0.32	0.15
IVST	0.24	0.12	0.53	0.04
LVMI	0.21	0.16	0.39	0.08

Figure2. The relationship between FGF23 and uric acid, Kt/V in patients with CVDs.



SUMMARIES & DISCUSSIONS

- Overall mean FGF23 level, FGF23 in CVD patients, and FGF23 in non–CVD patients were 17039 ± 19178, 14633 ± 16563, and 22068 ± 23376 pg/ml, respectively.
- We analyzed relationship between FGF-23 and collected data mentioned above. In univariate analysis, TAC–urea, UFR, corrected serum calcium (cCa), serum phosphate (iP), ALP, intact PTH (iPTH), IVST, and LVMI were suggested to be associated with FGF23. In multiple-regression analysis of FGF23 and these factors represented that cCa, iP, iPTH, ALP, and UFR were suggested to be associated factors with FGF23.
- In addition, we classified patients with or without CVDs and also did univariate analysis for FGF23 and these factors in each group. In patients with CVD, cCa, iP, iPTH, uric acid, TAC–urea, Kt/V were suggested to be associated with FGF23, though in patients without CVD, only IVST was suggested to be associated with FGF23.

Both high FGF23 and a large UFR are associated with mortality and recent data suggest a role of FGF23 in volume regulation. *Humalda JK, et al*[4)] reported that FGF23 correlates with UFR in hemodialysis patients and our study support this data. Also, in Turkish pediatric peritoneal dialysis population[5)], FGF23 correlated with Kt/V and some repots[6)] suggested that short daily dialysis patients had lower FGF23. These data suggest higher efficacies of dialysis may lower FGF23. In our study, cCa, iP, iPTH, uric acid, TAC–urea, Kt/V were suggested to be associated with FGF23 in CVD patients but not in non–CVD patients. As studies on dialysis patients and are few today, meanings of this difference is unknown and further studies are needed.

CONCLUSIONS

FGF23 levels in hemodialysis patients are associated not only with mineral–bone–disease factors but also with ultrafiltration rate.
Also, to maintain lower serum calcium, uric acid and higher efficacies of dialysis may decrease FGF23 levels in CVD hemodialysis patients.

***CONFLICT of INTERESTS**: None*

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