

Relationship between Serum Fibroblast Growth Factor 21 Levels and Arteriosclerosis Factors in Chronic Hemodialysis Patients.

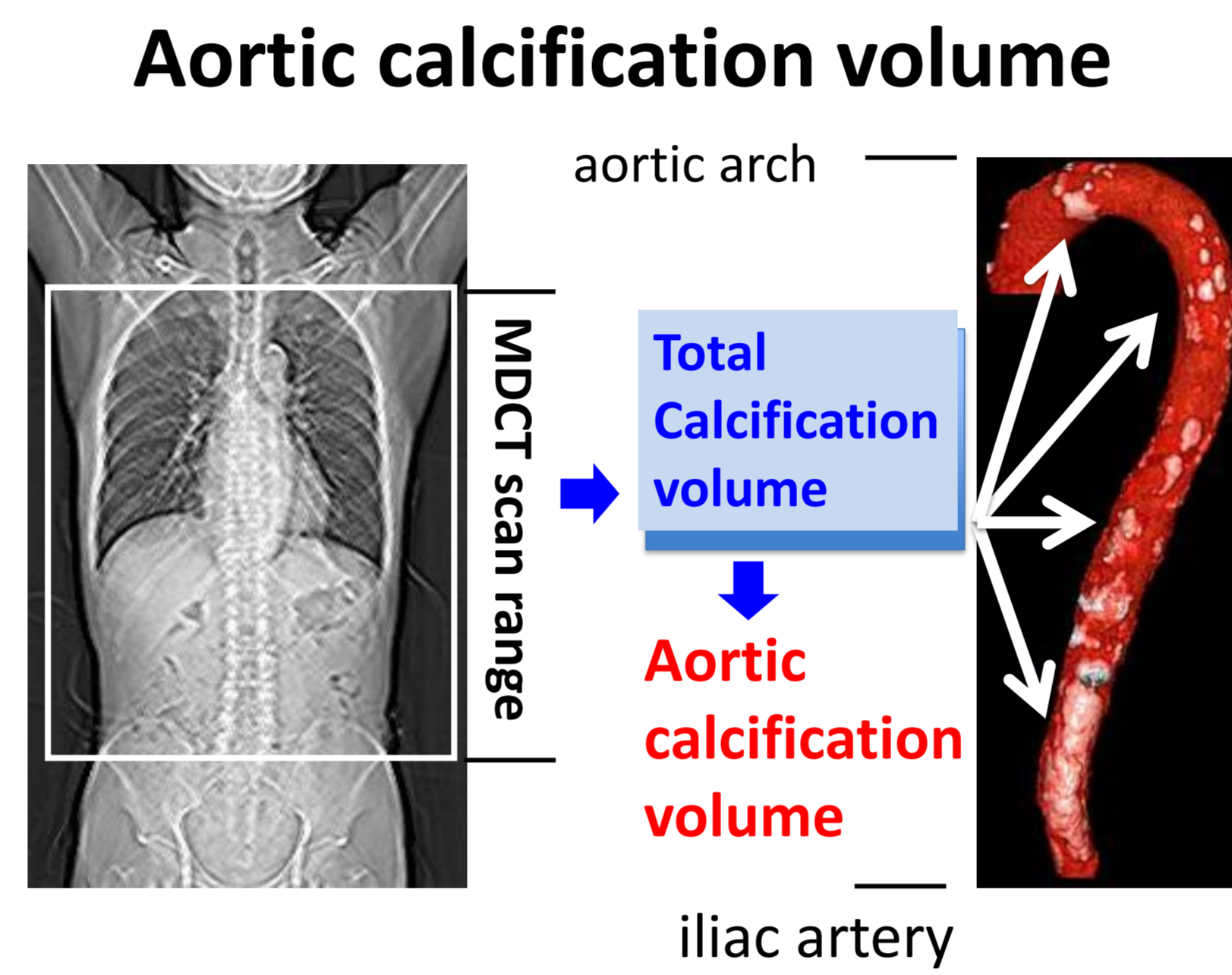
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OBJECTIVES

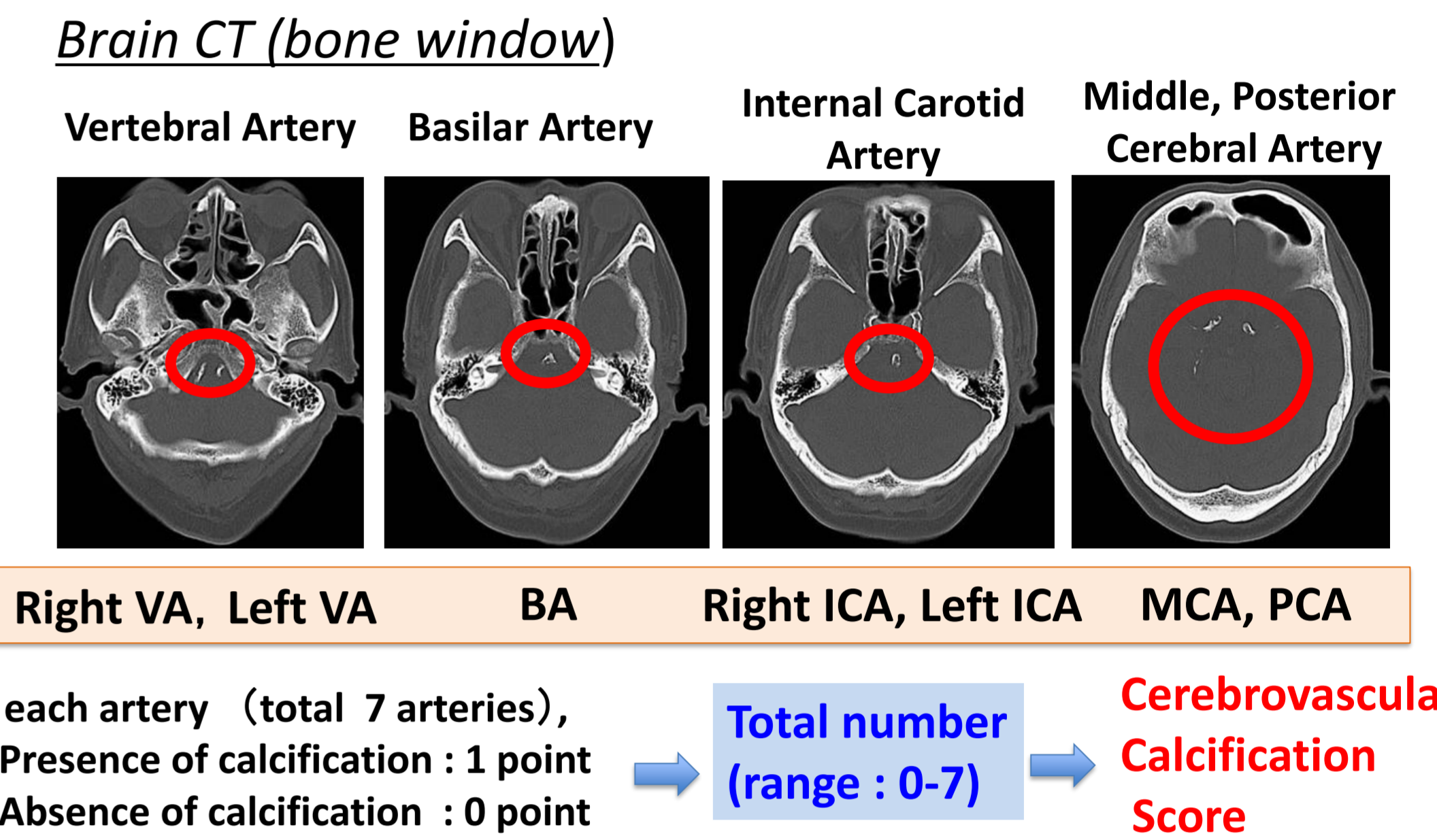
- Fibroblast growth factor 21 (FGF21) is an important metabolic regulator with multiple beneficial effects on glucose and lipid homeostasis. *(Kharitonov A et al. J Clin Invest. 115(6):1627-1635, 2005¹)*
- Circulating FGF21 levels are elevated in obese subjects and patients with impaired glucose tolerance, type 2 diabetes mellitus, dyslipidemia. In addition, circulating FGF21 levels are positively associated with body adiposity index, insulin resistance and hepatic lipid levels. *(Sarruf DA et al. Diabetes. 59(7):1817-24, 2010²). Kharitonov A et al. J Cell Physiol. 215(1):1-7, 2008³)*
- Recently, FGF21 has been demonstrated to be associated with cardiovascular diseases such as carotid atherosclerosis and coronary heart disease. Meanwhile, it has been reported that in patients with CKD, the prevalence of arteriosclerosis (remodelling of large arteries) and cardiomyopathy was higher than in general population. *(Candace C BS et al. J Am Geriatr Soc 60(4), 792-793, 2012⁴). Hindricks, J et al. Clin Endocrinol (Oxf). 80(6):918-24, 2014⁵)*
- The aim of this study is to evaluate arteriosclerosis factors associated with FGF21 levels in hemodialysis patients.

METHODS

- Randomize-selected 47 hemodialysis patients (age: 67.6 ± 10.5 years, Male:68 %, BMI: 21.7 ± 3.3 kg/m²), who had undergone multi detector computed tomography (MDCT), were enrolled in this study.
- We evaluated relationship between FGF21 and atherosclerosis or related factors, such as BMI, dry weight and blood pressure during hemodialysis session, the presence of diabetes mellitus, hemoglobin (Hb) levels, albumin levels, β 2-microglobulin levels, total cholesterol (LDL-C) levels, high-density lipoprotein-cholesterol (HDL-C) levels, triglyceride (TG) levels, pulse wave velocity (PWV), ankle-brachial index (ABI), aortic calcification and cerebrovascular calcification.
- Aortic calcification volume** was evaluated by calcification volume from aortic arch to iliac artery bifurcation using MDCT.
- Cerebrovascular calcification score** was evaluated by total number as one point which was defined in case of calcification existence in each artery of the brain, which was right or left internal carotid artery, middle cerebral artery, posterior cerebral artery, right or left vertebral artery or basilar artery, using MDCT.

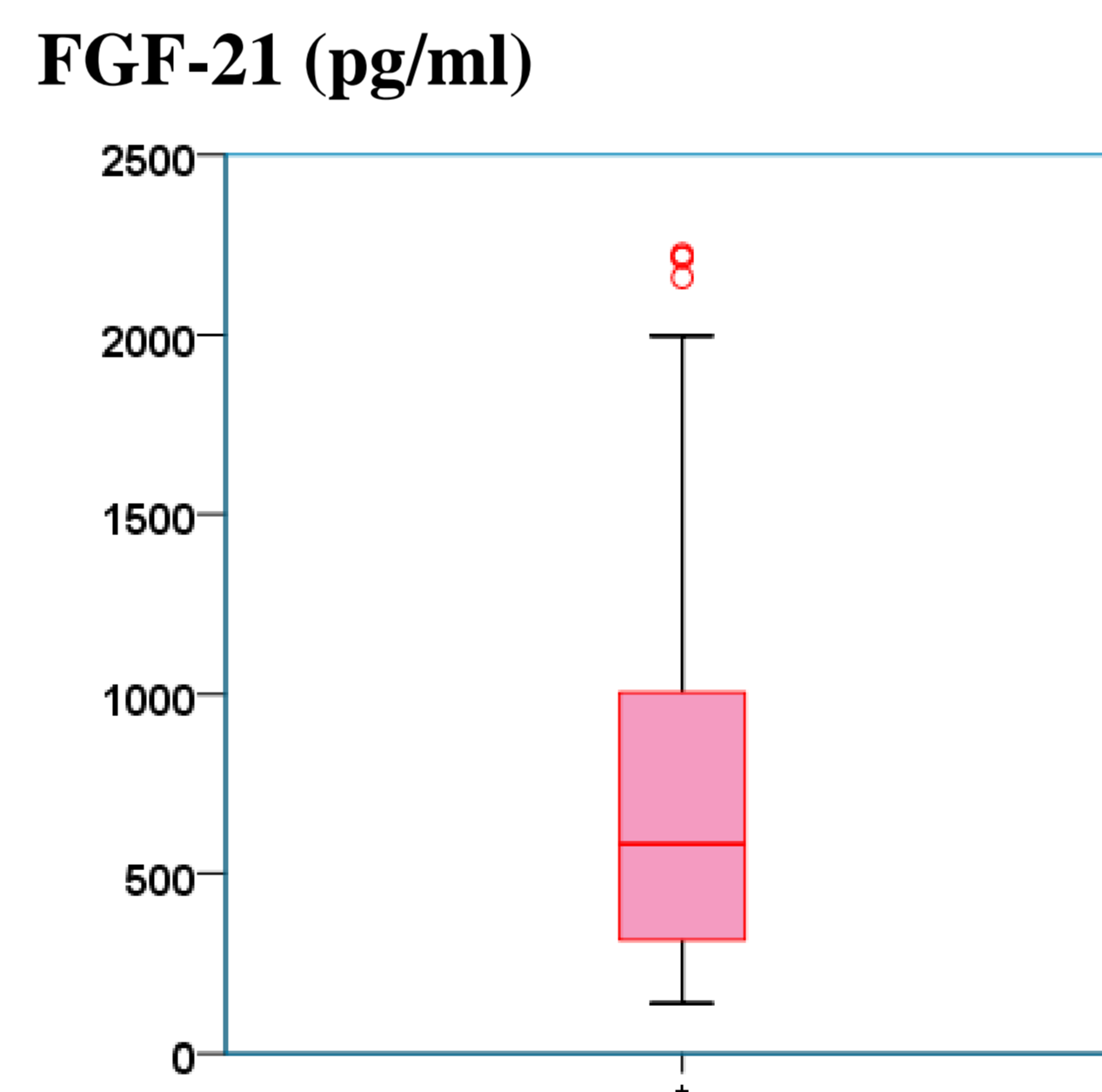


Cerebrovascular calcification score



RESULTS

Serum FGF-21 levels in HD patients

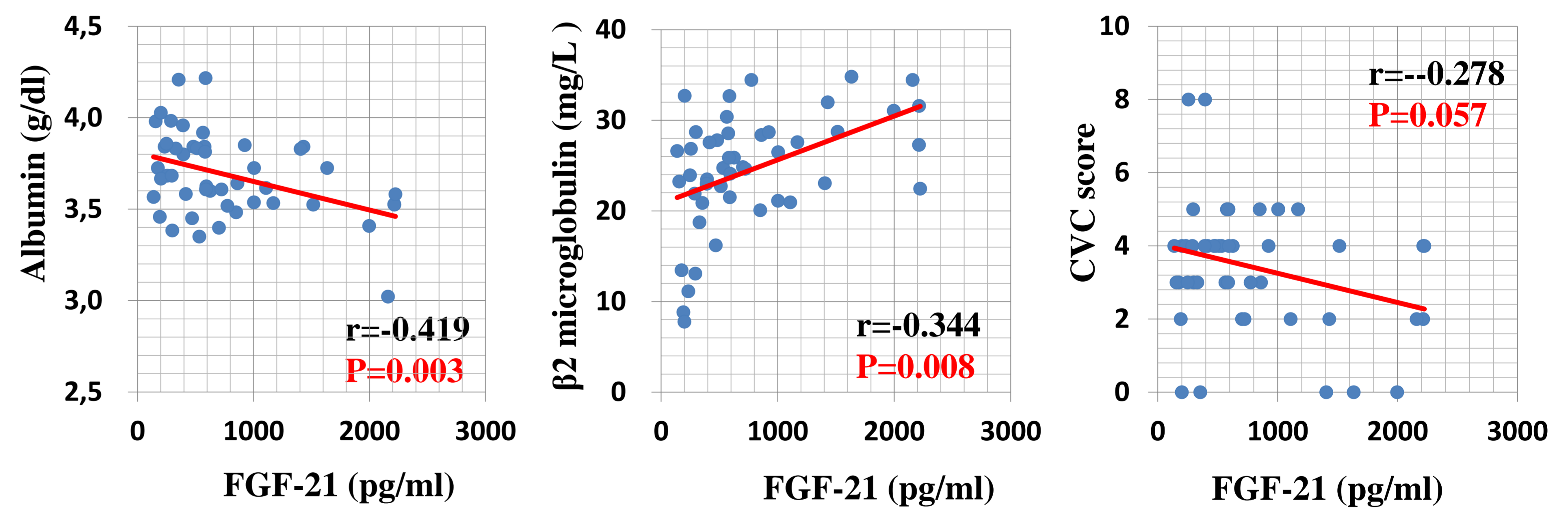


The correlation between FGF-21 and related parameters

	Univariate analysis		Multivariate analysis	
	r	P value	β	P value
albumin	-0.419	0.003	-0.270	0.049
β2 microglobulin	0.458	0.001	0.344	0.008
T-cho	-0.248	0.092	-0.098	0.922
PWV	0.293	0.048	0.217	0.086
systolic pressure	-0.251	0.089	-0.117	0.499
diastolic pressure	-0.303	0.038	-0.117	0.500
CVC score	-0.278	0.057	-0.287	0.016
presence of DM	-0.254	0.084	-0.232	0.064

CVC : Cerebrovascular calcification

The correlation between FGF-21 levels and albumin, β2 microglobulin levels or cerebrovascular calcification(CVC) score



BASIC PATIENTS' CHARACTERISTICS in HD patients

(n=47)

Age	(years)	67.6 ± 10.5
Gender	(M : F)	32 : 15
BMI	(kg/m ²)	21.7 ± 3.3
SBP	(mmHg)	151.9 ± 19.4
DBP	(mmHg)	74.3 ± 9.1
Ht	(%)	33.5 ± 1.4
TP	(g/dl)	6.6 ± 0.3
ALB	(g/dl)	3.7 ± 0.2
K	(mEq/L)	4.9 ± 0.5
Ca	(mg/dl)	8.6 ± 0.5
P	(mg/dl)	5.1 ± 0.8
Mg	(mg/dl)	2.6 ± 0.3
i-PTH	(pg/ml)	174.5 ± 86.2
TG	(mg/dl)	102.0 ± 47.3
T-cho	(mg/dl)	156.4 ± 30.6
HDL	(mg/dl)	43.8 ± 13.1
β2 microglobulin	(mg/L)	24.6 ± 6.4
PWV	(cm/s)	1993.3 ± 418.8
ABI		1.14 ± 0.20
VFA	(cm ²)	107.3 ± 73.8
MF	(cm ²)	13.3 ± 6.7
AoC volume	(cm ³)	17.3 ± 20.1
CVC score		3.43 ± 1.75
Serum FGF-21	(pg/ml)	778.7 ± 611.6

VFA: visceral fat area, MFA: mediastinal fat area, AoC: Aortic calcification, CVC : Cerebrovascular calcification

SUMMURIES and DISCUSSIONS

Mean FGF-21 level was 778.7 ± 611.6 pg/ml. In univariate analysis, FGF21 level was significantly correlated with albumin (r=-0.149, P=0.003), β 2 microglobulin (r=0.458, P=0.001), PWV (r=0.293, P=0.048), diastolic pressure (r=-0.303, P=0.038). In the multivariate regression model, all variables with a P value less than 0.1 in the univariate analysis were included. Multivariate analysis showed that albumin levels (β value=-0.270, P=0.049), β 2 microglobulin levels (β value=0.344, P=0.008) and cerebrovascular calcification (β value=-0.287, P=0.016) were significant independent determinants of FGF21 levels.

CONCLUSIONS

In the current literature^{6, 7}, clinical studies suggest that β 2 microglobulin level is an independent, significant predictor of mortality and seems to be a factor strongly linked to the presence and severity of cardiovascular diseases. In this study, as β 2 microglobulin levels were significant independent determinants of FGF21 levels, FGF21 levels in hemodialysis patients may associate not only with atherosclerosis related factors but also with cerebrovascular calcification.

CONFLICT of INTERESTS

: None

- REFERENCES
- 1) Kharitonov A et al. J Clin Invest. 115(6):1627-1635, 2005
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- 6) Cheung CL et al. Int J Cardiol. 168(5):4811-, 2013
- 7) Okuno S et al. Nephrol Dial Transplant 24(2):571-7, 2009