Correlates of osteoprotegerin and association with cardiovascular status in patients with chronic kidney disease

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OBJECTIVES

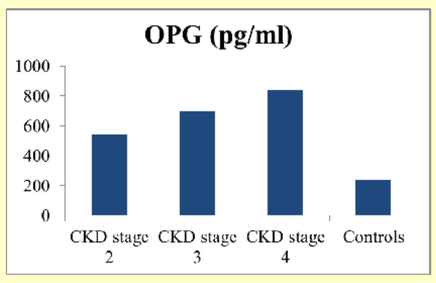
- Osteoprotegerin (OPG) is a cytokine that regulates bone resorption and is implicated in the process of vascular calcification and stiffness. Human studies have demonstrated associations between higher serum osteoprotegerin levels and adverse cardiovascular outcomes in CKD patients .
- The aim of the present study is to evaluate the association between serum osteoprotegerin and cardiovascular status evaluated by heart failure symptoms, echocardiography, vascular stiffness and common carotid intima-media thickness (IMT) in chronic kidney disease (CKD) patients.

METHODS

- We enrolled 95 CKD patients (65.1 11.2 years, 67 men) in pre-dialysis:
  - 10 patients with CKD stage 2
  - 62 patients with CKD stage 3
  - 23 patients with CKD stage 4
  - 20 healthy controls.
- OPG was measured using xMAP technology (Luminex® 200™).
- Echocardiographic evaluation was performed in order to evaluate cardiac structure, left atrial volume index (LAVI), left ventricular mass index (LVMI), left ventricular function, including transmitral peak early diastolic velocity (E), peak late filling diastolic velocity (A), E/A ratio. The cardiac clinical functional status was defined according to the New York Heart Association (NYHA) classification.
- Arterial stiffness measurements were performed with the SphygmoCor device.
- We evaluated IMT and the presence of atheroma plaques by ultrasonographic study of the common carotid arteries.
- Statistical analysis was performed using IBM SPSS Statistics Version 21.

RESULTS

- The mean OPG serum level was 717.0±307.6, and was significantly higher ($p<0.05$) in CKD patients than in healthy controls.



- Diastolic dysfunction was present in 80% patients, arterial hypertension in 95.8%, metabolic syndrome in 54.7% patients.
- Echocardiographic results showed LAVI=40.5±16.3 ml/m2, LVMI=116.8±28.8 g/m2, E/A=0.91±0.37.
- Mean IMT and mean pulse wave velocity values were significantly elevated in CKD patients versus control group.

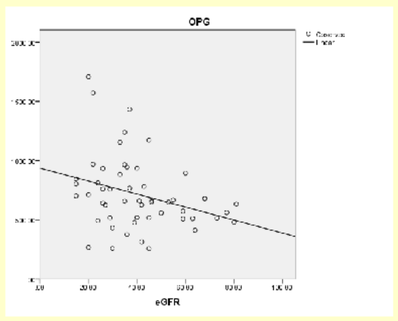
Variable (mean value)	CKD stage 2	CKD stage 3	CKD stage 4
LVMI (g/m²)	106.8	118.1	117.3
LAVI (g/m²)	35.2	39.2	46.3
NYHA class	1	2	2
E/A	0.87	0.94	0.86
E/E'	9.0	12.8	11.6
IMT (mm)	0.69	0.75	0.77
PWV (m/s)	9.46	9.86	9.62

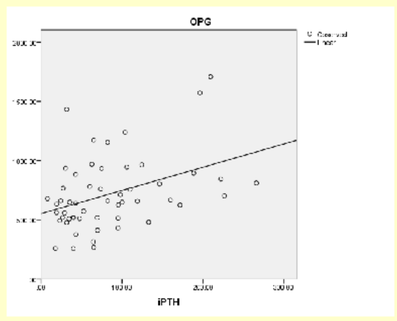
- A stepwise multiple regression analysis of model 3 revealed that E/A ratio was independently correlated with OPG level, diastolic blood pressure and subendocardial viability ratio (SEVR), suggested an association between OPG and diastolic dysfunction.

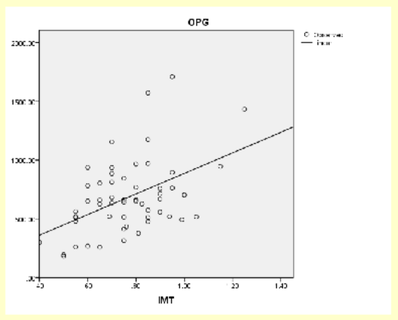
- Univariate analysis showed a significant association between higher plasma OPG levels and higher iPTH and CRP, and with lower eGFR, hemoglobin, albumin and calcium. Also, OPG correlated positively with age, LAVI, NYHA class and IMT. OPG level was significantly higher in CKD patients with metabolic syndrome and mitral valve regurgitation.

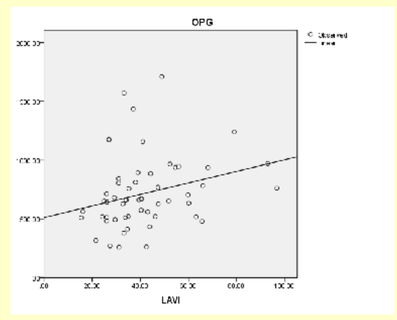
Variable	OPG	
	Correlation coefficient	P-value
eGFR	- 0.334	0.014
iPTH	0.381	0.005
hemoglobin	- 0.456	0.001
albumin	- 0.544	0.0001
calcium	- 0.326	0.02
CRP	0.717	0.03

Variable	OPG	
	Correlation coefficient	P-value
age	0.336	0.014
LAVI	0.372	0.006
NYHA class	0.336	0.014
Mitral valve regurgitation	0.316	0.02
IMT	0.280	0.04
PWV	0.108	0.47
Metabolic syndrome	0.316	0.02









CONCLUSIONS

- Our study shows that OPG is correlated with heart failure clinical symptoms, diastolic dysfunction and atherosclerosis in CKD patients.
- Our data underscore that cardiovascular disease occurs even from early stages of CKD and OPG could be used as surrogate biomarker for cardiovascular complications among patients with CKD.

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