SERUM FETUIN-A AND OSTEOPROTEGERIN ARE INDEPENDENTLY ASSOCIATED WITH LEFT ATRIAL SIZE AND FUNCTION IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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Background and Aim

- Osteoprotegerin (OPG) is a cytokine that regulates bone resorption and is implicated in the process of vascular calcification and stiffness. Fetuin-A is secreted by hepatocytes into the circulation, where it forms soluble complexes with calcium and phosphate. Human studies have demonstrated associations between higher serum ostoeprotegerin levels and adverse cardiovascular outcomes in CKD patients. There are only scarce and contradictory data on fetuin A levels in early CKD stages and their effect on cardiovascular health.
- **We aim of this study was to evaluate associations between serum fetuin-A and osteoprotegerin and echocardiografic parameters of LA volume and function in patients with chronic kidney disease (CKD).**

Methods:

- We prospectively enrolled 95 CKD patients (65.1±11.2 years, 67 men) in pre-dialysis. The stage of CKD has been established based on eGFR using CKD-EPI formula.
- ***Laboratory tests***: Fetuin A, OPG, intact parathyroid hormone (iPTH) were measured using xMAP technology (Luminex® 200™).
- ***Echocardiographic evaluation*** was performed using the Vivid 7 ultrasound system, General Electric. End-systolic and end-diastolic volumes were used to calculate left ventricular (LV) ejection fraction (EF) by Simpson biplane method. Impaired LVEF was defined as <45%. Left ventricular filling pressures were assessed using the E/septal E' ratio. Diastolic function was assessed using several parameters including E/A ratio, deceleration time of early filling velocity (DT)and left atrial volume (2). LV mass was calculated with the formula: LV mass (in grams) = 0.8 x {1.04 [(LV internal dimension + septal wall thickness + posterior wall thickness)^3 – LV internal dimension^3]} + 0.6. LV mass was indexed to height$^{2.7}$ (3). We used left ventricular mass index (LVMI) and indexed left atrial volume (LAVI)
  We also performed two-dimensional speckle-tracking echocardiography. We obtain LA reservoir, conduit and contractile (atrial function strain rate – ASr) functions.
- The cardiac clinical functional status was defined according to the New York Heart Association (NYHA) classification.
- We evaluated intima media thickness (IMT) by ultrasonographic study of the common carotid arteries.
- ***Statistical analysis*** was performed using IBM SPSS Statistics Version 21.

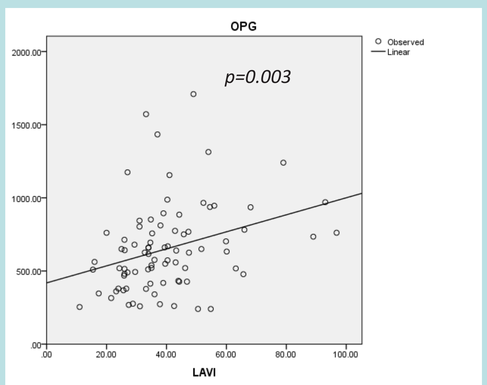
Results:

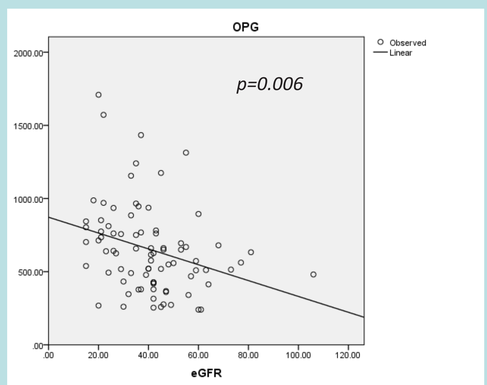
- The etiology of CKD was: diabetic nephropathy (25 pts), nephroangiosclerosis (43 pts), tubulointerstitial nephropathy (24 pts), chronic glomerulonephritis (3).
- - 10 patients CKD stage 2
  - 62 patients CKD stage 3
  - 23 patients CKD stage 4.
  The mean eGFR was 41.5 ± 17.2 ml/min/1.73m^2.
- The baseline characteristics of the patients:

	CKD patients
OPG (pg/ml)	581.0 ± 316.4
Fetuin A (pg/ml)	530.8 ± 133.5
iPTH (pg/ml)	79.2 ± 66.4
LAVI g/m^2	40.5 ± 16.3
LVMI g/m^2	116.8 ± 28.8
IMT (mm)	0.74 ± 0.15

Osteoprotegerin

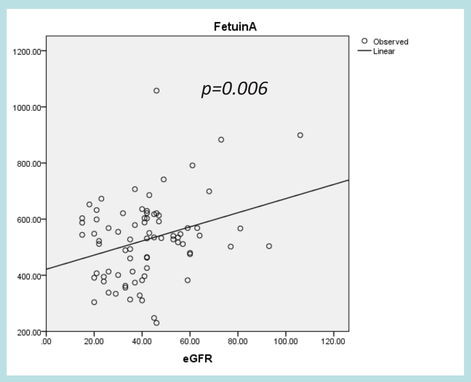
- A significant correlation was found between higher plasma OPG level and higher age (p=0.018), LAVI (p=0.003), sistolic arterial pressure (p=0.0016), IMT (p=0.005), iPTH (p=0.0001), and with lower eGFR (p=0.006), hemoglobin (p=0.0001), and albumin (p=0.002).

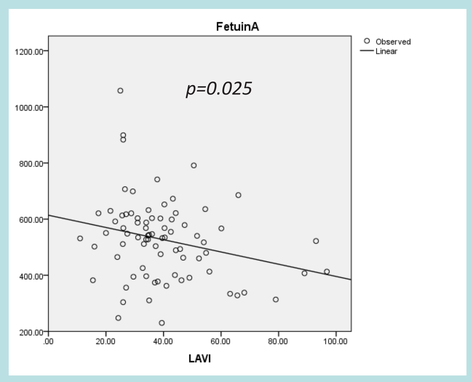


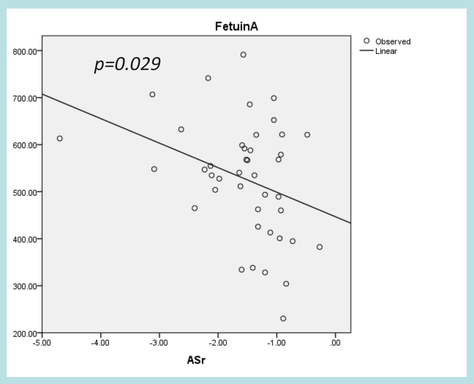


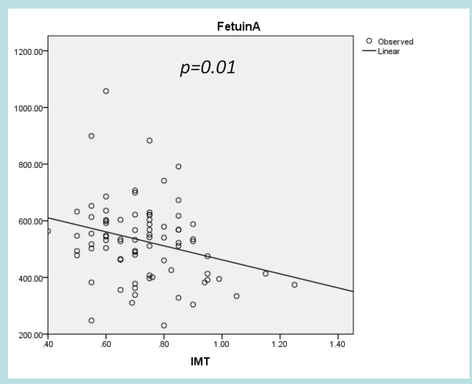
Fetuin A

Higher fetuin A level was also significantly associated with increased eGFR (p=0.006) and hemoglobin (p=0.029), and negatively associated with LAVI (p=0.025), ASr (p=0.029), LVMI (p=0.014), IMT (p=0.01), arterial pressure (p=0.046).









Left atrial size and function

- LAVI and was significanly increased in patients with heart failure symptoms.
- **A stepwise multiple regression analisys revealed that left atrial contractile function parameter (ASr) was independentely correlated with fetuin-A level (β= -0.381, p=0.018) and age (β=0.559, p=0.001).**
  Furthermore on stepwise multiple regression, only ASr was independenly associated with the presence of cardiac failure symptoms.

Conclusions:

- **Our study shows that fetuin-A correlated with LA function, and both OPG and fetuin-A correlated with LAVI. LA contractile dysfunction was the main factor associated with the presence of symptoms, suggesting that it could better reflect cardiac involvement with clinical consequences in CKD patients.**
- **Our data underscore that cardiovascular disease appear even from early stages of CKD and mineral-bone disease serology parameters could be used as surrogate biomarkers for cardiac complications among patients with CKD.**

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