FIBROBLAST-GROWTH-FACTOR-23 AND PARATHYROID HORMONE PREDICT AORTIC VALVE CALCIFICATIONS EXTENT IN MILD TO MODERATE CHRONIC KIDNEY DISEASE

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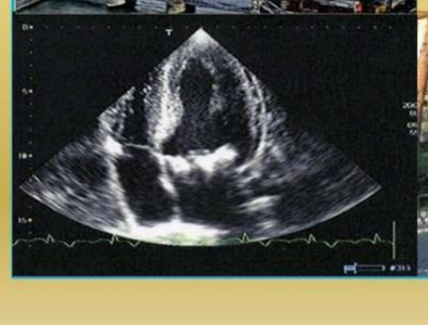


Background

- ✓ Rate of cardiovascular mortality is high in incident and prevalent patients on dialysis (ESRD) as well as in patients with chronic kidney disease not requiring dialysis (CKD-ND)
- ✓ Presence of cardiac valve calcification is frequently observed in CKD patients and it is associated to increased risk for cardiovascular events
- ✓ Derangement of mineral metabolism is regarded as the leading factor responsible for cardiac valve calcification. The association between mineral metabolism and cardiac valve calcification has been extensively evaluated in patients on dialysis but seldom in patients with CKD-ND
- ✓ The present study aimed at assessing among several markers of mineral metabolism the best predictor(s) of cardiac valve calcification extent in naïve CKD-ND patients. To our knowledge, this issue has never been addressed before by simultaneously measuring serum concentration of intact parathyroid hormone (i-PTH), phosphorus, calcium, 25-OH vitamin D, Fibroblast-Growth-Factor-23 (FGF-23), Klotho, high sensitivity C-Reactive protein (hs-CRP).

Patients and Methods

- ✓ This is a multicenter study carried out in 125 consecutive naïve out-patients admitted to five Nephrology Units for clinical assessment. Inclusion criteria were: age>18 years, CKD stage 3-4, presence of either aortic or mitral valve calcification ascertained by echocardiography as routine clinical evaluation.
- ✓ Patients underwent clinical examination and routine biochemistry measurements. Blood specimens were collected in the morning in overnight fasting state. Levels of 25–OH Vitamin D, Klotho, FGF-23, calcium, phosphorus, i-PTH, hs- CRP and 24-h urinary phosphate excretion were measured. Glomerular filtration rate was assessed by EPI formula (e-GFR).
- ✓ Extent of mitral and aortic valve calcification was evaluated and scored by two-dimensional echocardiography using a 3.3-mHz multiphase array probe. Extent of mitral valve calcification was measured with Wilkins calcification score and graded from 0 to 4. Semi–quantitative method was used for assessing the extent of aortic valve calcification (1= partial calcification on single cusp; score 2= partial calcification on two cusps; score 3 = extended calcification on two cusps; score 4 = extended calcification on all three cusps)

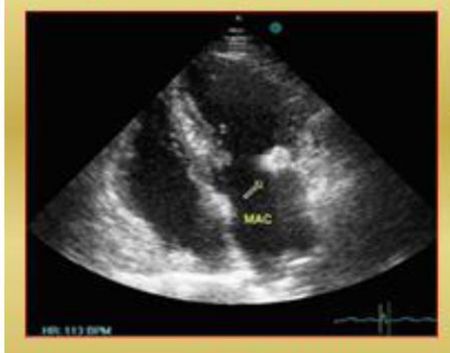
Results 1

- ✓ One hundred patients had aortic and ninety-six mitral valve calcification. Population was represented by middle-aged patients with not far advanced stages of CKD and moderate derangement of mineral metabolism.
- ✓ Extent of aortic valve calcification was moderate in 68 patients; remaining patients had mild calcification extent. Score of mitral valve calcification was 1, 2, 3 in 61, 34, and 1 patients, respectively.
- ✓ Inverse association was found between FGF-23 and PTH (r2 = -0.252; p=0.01), 25- 0H vitamin D (r2 = -0.605; p=0.01); positive association was found between FGF-23 and serum phosphorus (r2= 0.248; p=0.01), 24h-urinary phosphorus excretion (r2=0.513; p=0.01) and hs-CRP (r2 =0.398; p=0.01).
- ✓ In univariate analysis, mitral valve calcification score was associated with serum calcium (r2 = 0.565; p=0.01); no association was found between mitral valve calcification score and e-GFR (r2 = -0.146), serum phosphorus (r2 = -0.08), PTH (r2=0.17), FGF-23 (r2 =0.052), Klotho (r2 =0.098), 25-OH vitamin D (r2 = 0.020), 24-h urinary phosphorus excretion (r2 = 0.099) and hs-CRP (r2 = 0.030).

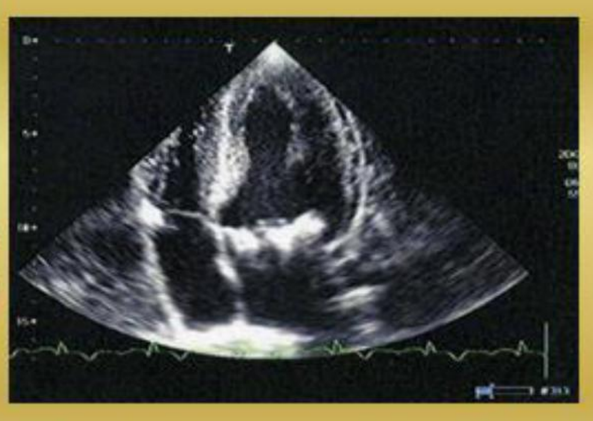
Results 2

- ✓ Aortic valve calcification score was positively associated with PTH (r2 = 0.212; p=0.03), FGF-23 (r2 = 0.272; p=0.01), and negatively with Klotho (r2 = - 0.208; p=0.03)
- ✓ No association was found between aortic valve calcification score and e-GFR (r2 = -0.029), serum phosphorus (r2 =0.094), serum calcium (r2= -0.057), 25-OH vitamin D (r2 = -0.122), 24-h urinary phosphorus excretion (r2 = 0.108) and hs-CRP (r2 = 0.054).
- ✓ FGF-23 and PTH were significantly associated with aortic valve calcification score.

Fig. 1 - Distribution of mitral valve calcifications

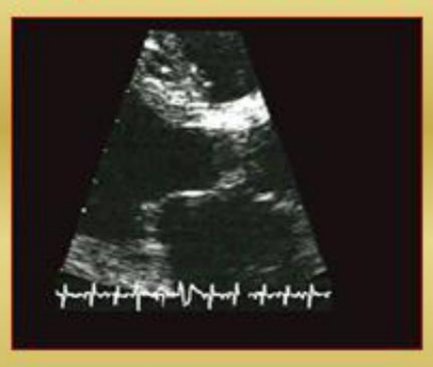


Mitral valve's anulus calcification

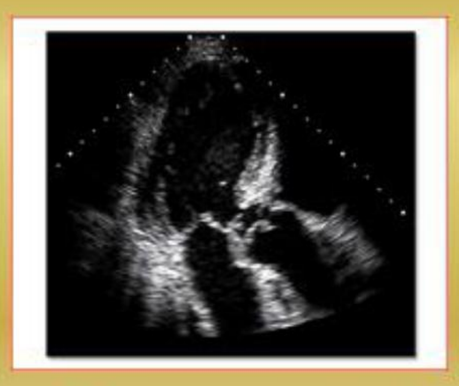


Mitral valve's anulus and leafs calcifications

Fig. 2 - Distribution of aortic valve calcifications



Moderate aortic stenosis



Sub – valvular aortic stenosis

Conclusions

- ✓ FGF-23 and PTH were significantly associated to the extent of aortic valve calcification. No association was found with e-GFG, serum phosphorus, calcium, Klotho, 24h phosphaturia, vitamin D and hs-CRP. An association between FGF-23 and aortic valve calcification has never been reported before in CKD-ND patients, to our knowledge.
- ✓ In the present study different association was found between patients with aortic and mitral valve calcification. Variables significantly associated to aortic valve calcification were different from those predicting mitral valve calcification and vice-versa.
- ✓ Other interesting finding of the present study is that no association was found between cardiac valve calcification extent and serum phosphorus, that is the foremost studied marker of mineral metabolism and main pathogenetic factor of vascular calcification in CKD

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