INFLAMMATION BUT NOT DERANGED MINERAL METABOLISM MAY EXPLAIN THE PROGRESSION OF CORONARY ARTERY CALCIFICATION IN CKD PATIENTS NOT ON DIALYSIS (CKD-ND)

L Russo (1), Y Battaglia (2), GB Capasso (1), V D'Esposito (3), B di Iorio (4), L di Lullo (5), P Formisano (3), A Perna (1), ML Tramontano (3), D Russo (6).

Objectives:

- Vascular calcifications are present in all stages of the kidney disease even when the mineral metabolism compensation mechanisms are fully active.
- In atherosclerosis, pro-inflammatory signals

such as modified lipoproteins promote macrophage infiltration into the vessel wall.

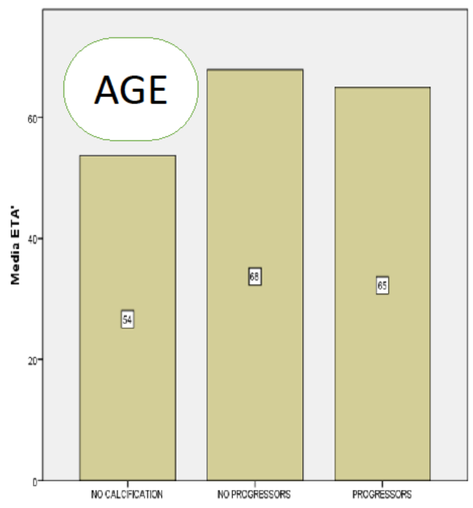
- Macrophages express pro-inflammatory cytokines that induce vascular smooth muscle cells (VSMC) apoptosis and osteogenic differentiation.
- The calcium release associated with apoptotic cells also may induce VSMC vesicle release.
- In the absence of inhibitors and phagocytosis, apoptotic bodies and vesicles can form a nidus for new calcifications and progression of older ones
- Therefore vascular calcification and mainly its progression is likely a process induced by inflammation
- This study aims to evaluate the hypothesis of a major role of inflammation in the pathogenesis of coronary artery calcification (CAC) and their progression in patients with chronic kidney disease not on dialysis (CKD-ND)

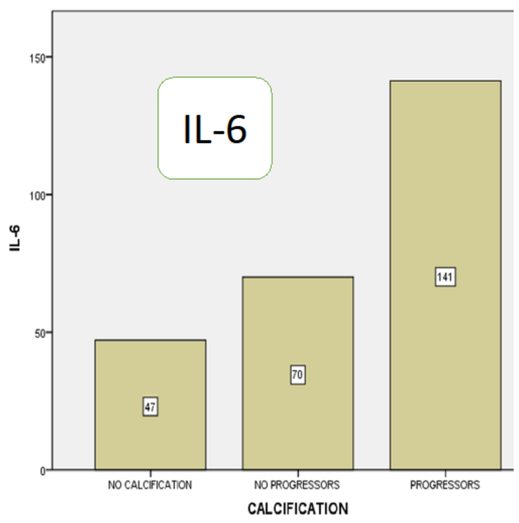
Methods:

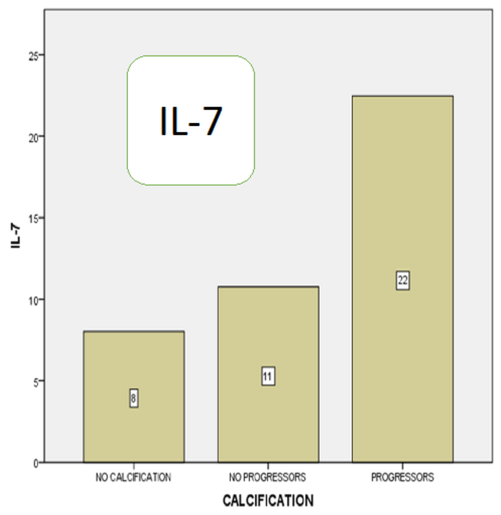
- In this pilot study we evaluated n.76 patients for 18 months who had undergone at least two coronary CT scans for assessment of coronary total calcium score (CTCS)
- Inclusion criteria were: age ≥ 18 years, stage 2-5 CKD-ND, six-month follow-up before enrollment.
- Exclusion criteria were: heart failure and/or coronary artery disease, prior history of myocardial infarction, coronary bypass surgery, angioplasty, stroke, rapidly progressive renal disease, cardiac arrhythmias.
- At enrollment plasma concentrations of calcium, (PTH-i), PCR, homocysteine, triglycerides, total cholesterol, HDL,LDL, PDGF, IL1B, IL1RA, IL4, IL5, IL6, IL7, IL8, IL9, IL10, IL12, IL13, On 17, eotaxin, basic FGF, IFNG, IP10, MCP1, MIP1a, MIP1b, RANTES, TNFa, VEGF were assayed
- Patients were divided on the basis of CT scan in 3 groups:

(1) patients without CAC; (2) patients with stable CAC (no-progressors) (3) patients with CAC and high progression (progressors)

Graphs:







Results:

- Calcified patients were older.
- e-GFR was not different between groups (1=75±41; 2=71,7±25; 3=68,3±43,6)
- In multivariate analyzes potential predictors of CAC presence were: Age (beta =, 507; p = 0.001), IL-6 (Beta = 272; p = 0.05), IL-7 (Beta =, 311; p = 0:05).
- Predictor of CAC progression was found IL-7 both in univariate (r2 =, 397; p = 0.001) and in multivariate analysis (Beta = 1.01; p = 0.001)
- Markers of mineral metabolism, PCR and homocysteine were never significant predictors of CAC presence or progression

Conclusions:

Onset of CAC and progression may have two different times-dependent phases during the course of CKD.
It is likely that in the not advanced stages of CKD inflammation is the predominant pathogenic factor.
Subsequently, in later stages , the disturbances of mineral metabolism prevail and overlap inflammation factors that characterize CKD

1) Department of Cardio-Thoracic and Respiratory Sciences, Second University of Naples. 2) Nephrology Unit, University-Hospital St. Anna, Ferrara. 3) Department of Translational Sciences University FEDERICO II, Naples. 4) Department of Nephrology, Landolfi Hospital, Solofra. 5) Department of Nephrology, Parodi-Delfino Hospital, Rome. 6) Department of Nephrology, University FEDERICO II, Naples

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