VASCULAR CALCIFICATION [VC]

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Introduction

- Vascular calcification (VC) is a common pathological condition in patients with chronic kidney disease (CKD), characterized by the accumulation of calcium and phosphate deposits in the walls of blood vessels.

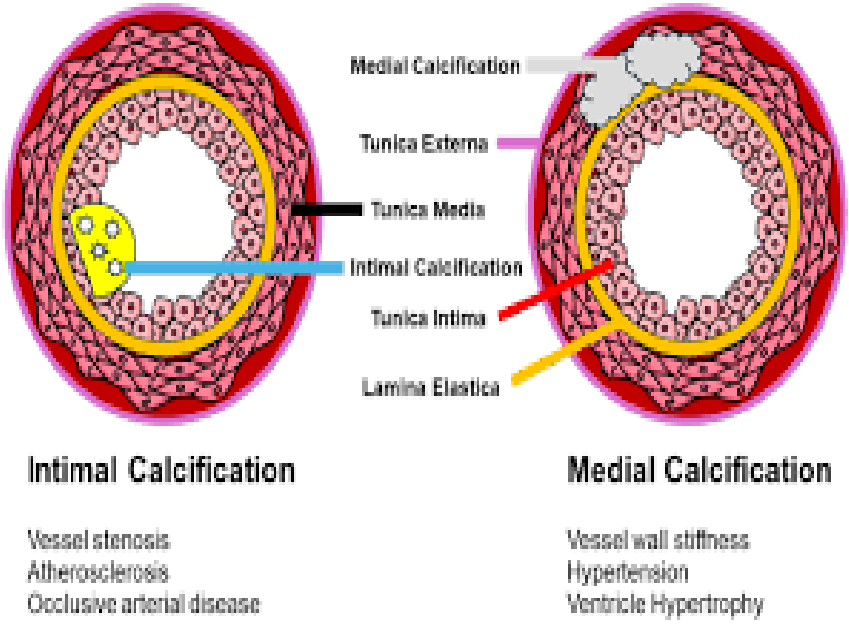
- CKD patients exhibit a significantly higher risk of cardiovascular mortality compared to the general population, primarily due to their increased predisposition to vascular calcification.

- **Risk** Factors: Age ,sex, smoking, hypertension, diabetes, dyslipedemia , dialysis vintage , disordered mineral metabolism, calcium, phosphate , oxidative stress and inflammation.

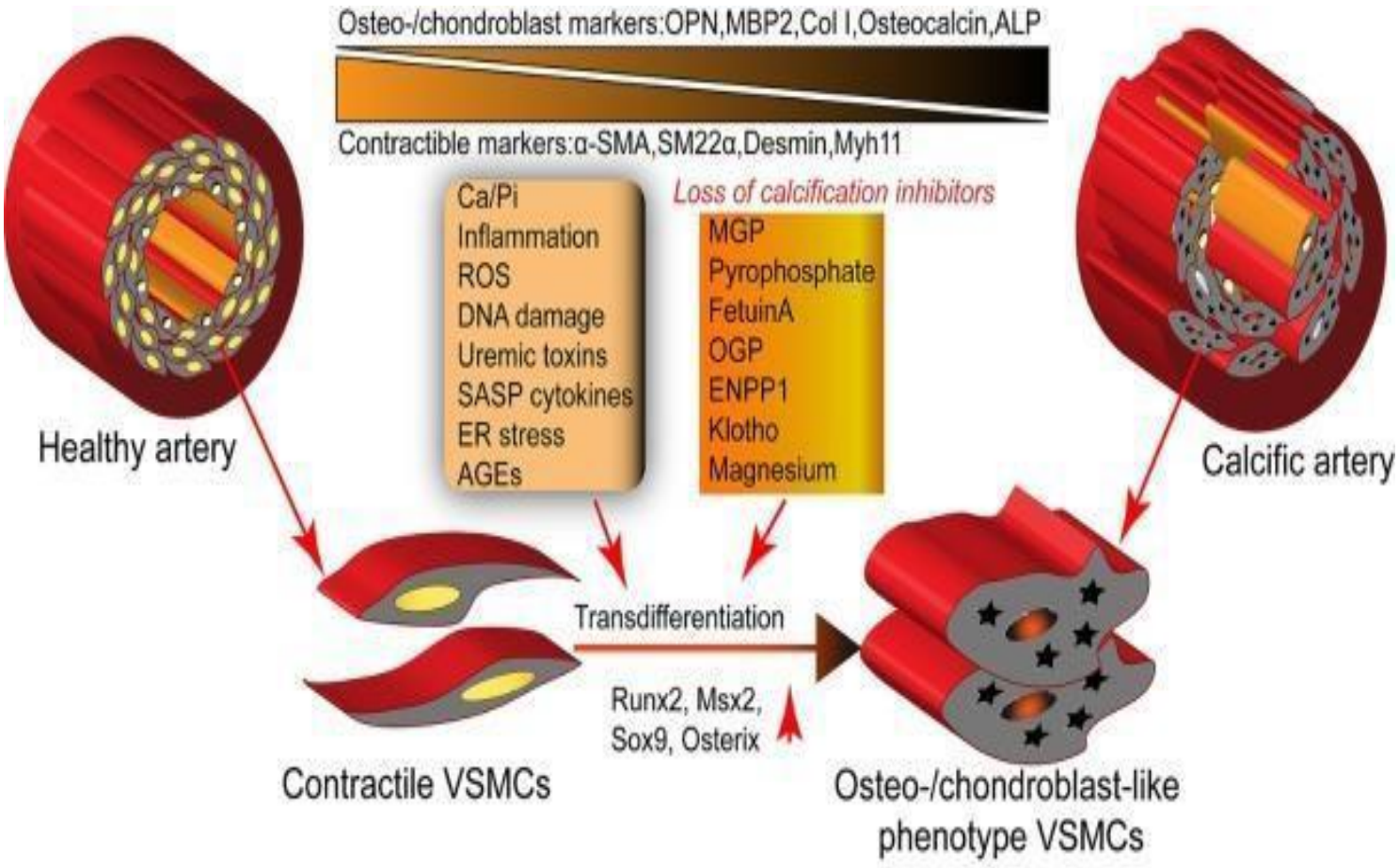
- **Other** risk factoes : FGF-23 soluble Klotho, osteopontin, Calprotectin , Sclerostin, osteoprotegerin, bone morphogenic proteins, matrix Gla protein gene, fetuin-A, calciprotein particles (CPP), magnesium, zinc, microbiome, uremic toxin, and advanced glycation end-products.

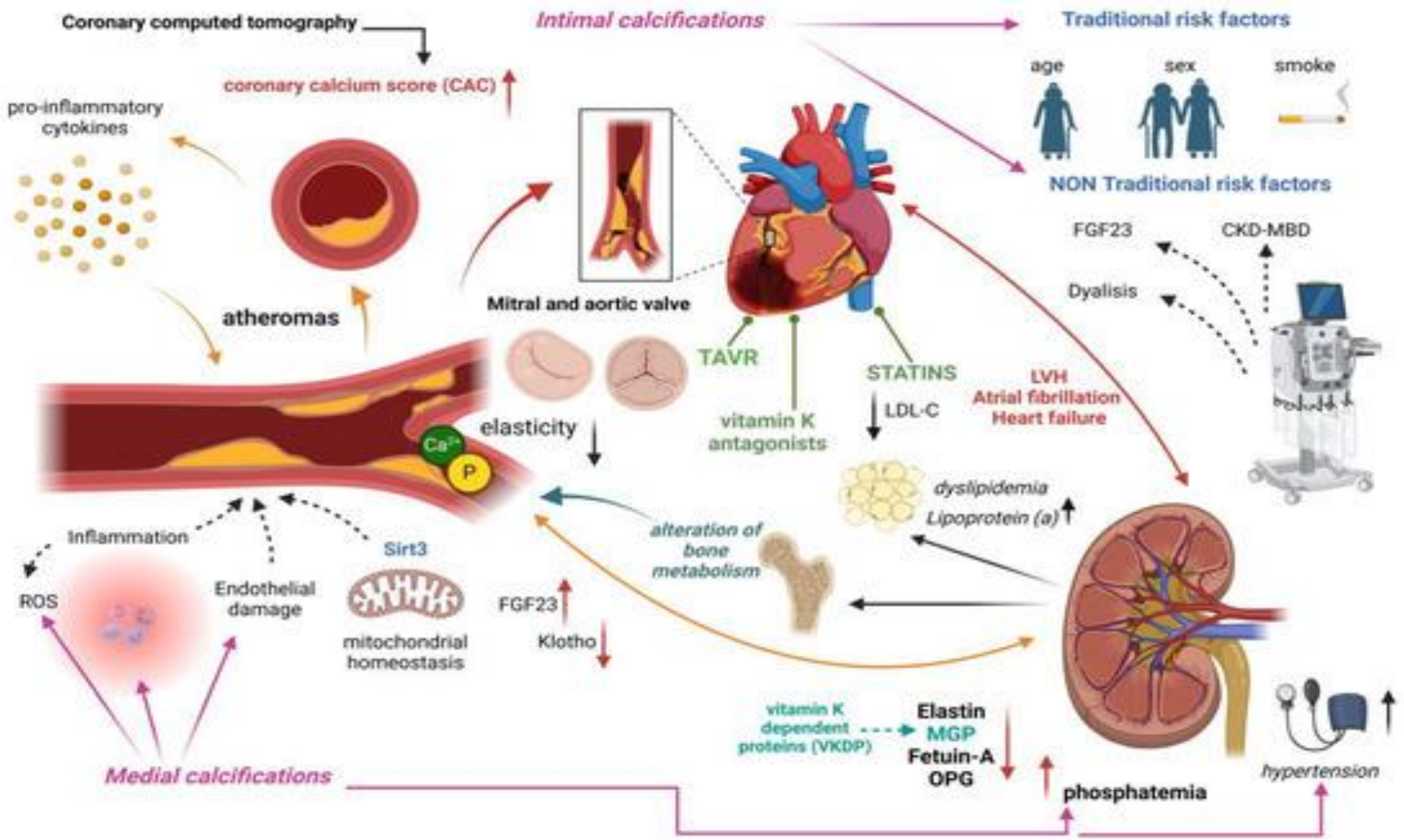
	Intimal calcification	Medial calcification
Distribution	Focal	Diffuse
Mechanism	Associated with lipid deposition and inflammatory infiltration	Can occur without lipid deposition and immune cell infiltration
Deposits	Cholesterol	Hydroxyapatite
Type of ossification	Endochondral	Intramembranous
Pathogenic mechanism	Atherosclerosis Plaque rupture	Arteriosclerosis Increased Cardiac after load
Risk factors	Hypertension DM Hypercholesteremia Smoking.	More prevalent in patients with CKD

TYPES OF VASCULAR CALCIFICATION

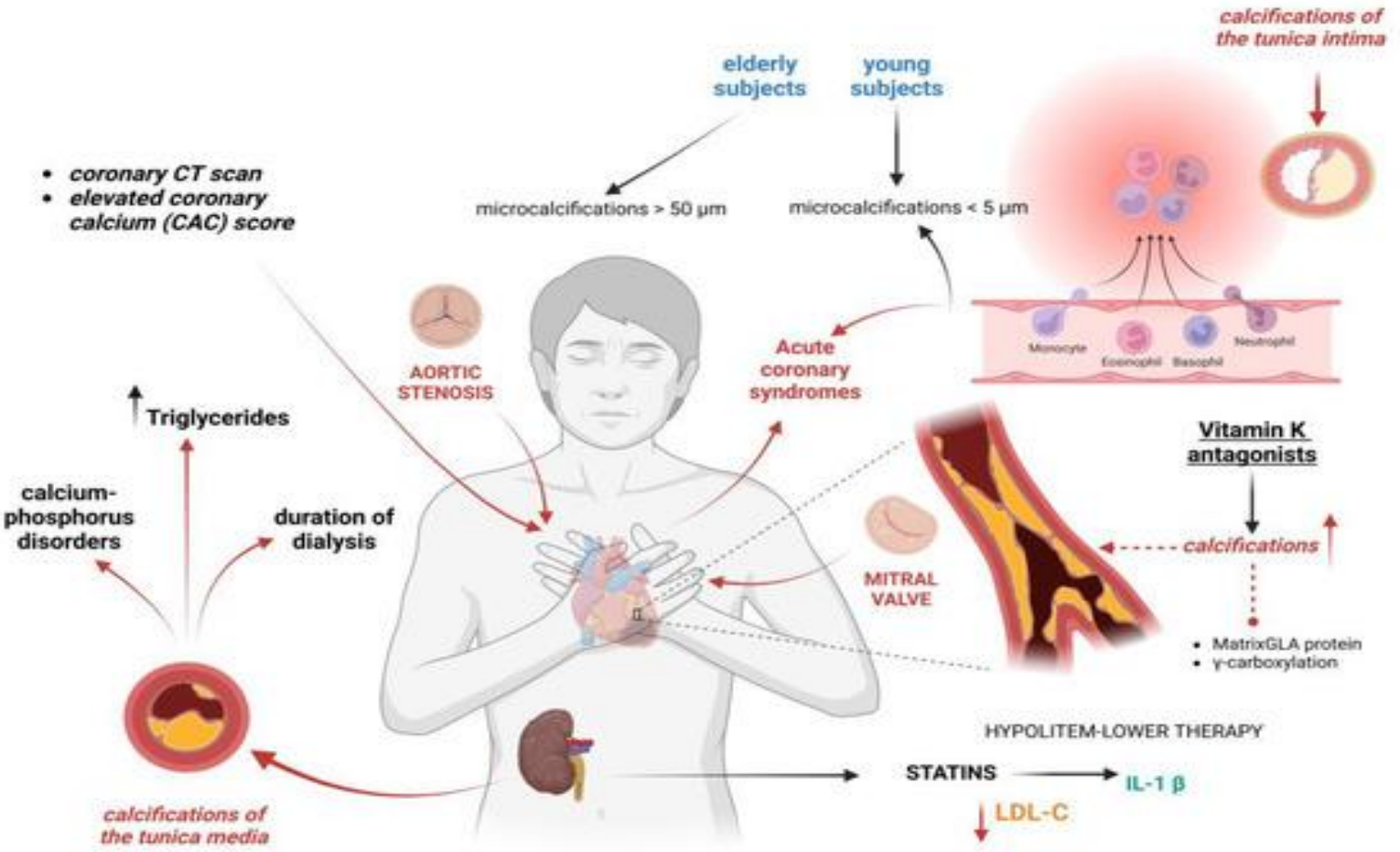


Mechanism of Vascular Calcification





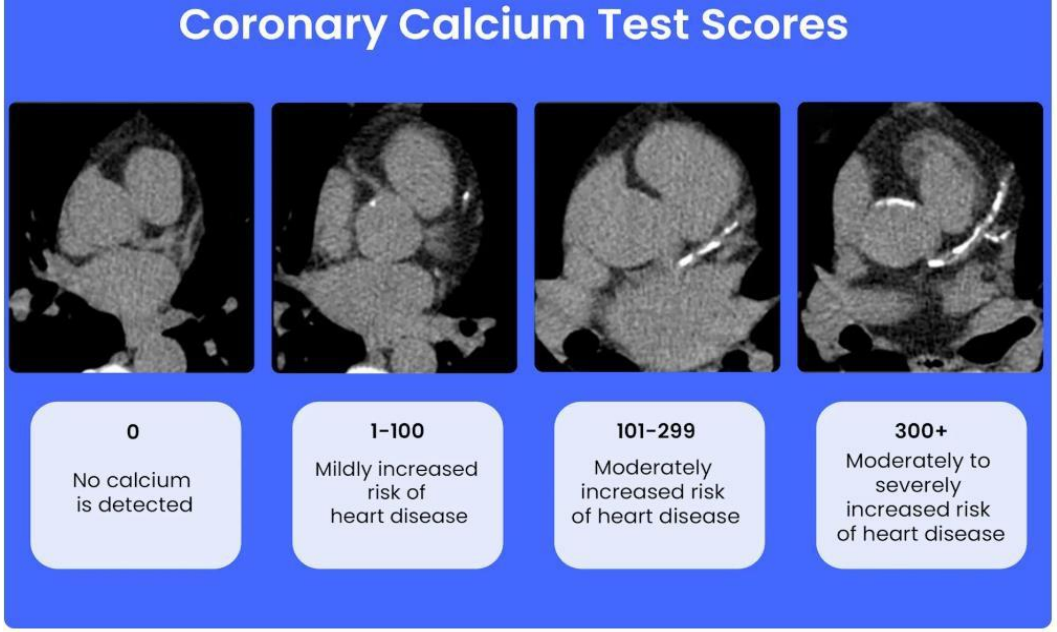
Pathogenic mechanisms of vascular calcification (VC) in chronic kidney disease (CKD). Hyperphosphatemia and hypercalcemia with loss of calcification inhibitors such as fetuin A, osteoprotegerin, and matrix GLA protein (MGP) promote osteochondrogenic differentiation of vascular cells. VC is, furthermore, influenced by traditional risk factors (e.g., aging, smoking) and non-traditional factors related to calcium-phosphorus metabolism dysfunction and increased FGF23. The accumulation of minerals in the arterial walls and the degradation of elastin lead to progressive vascular stiffness.



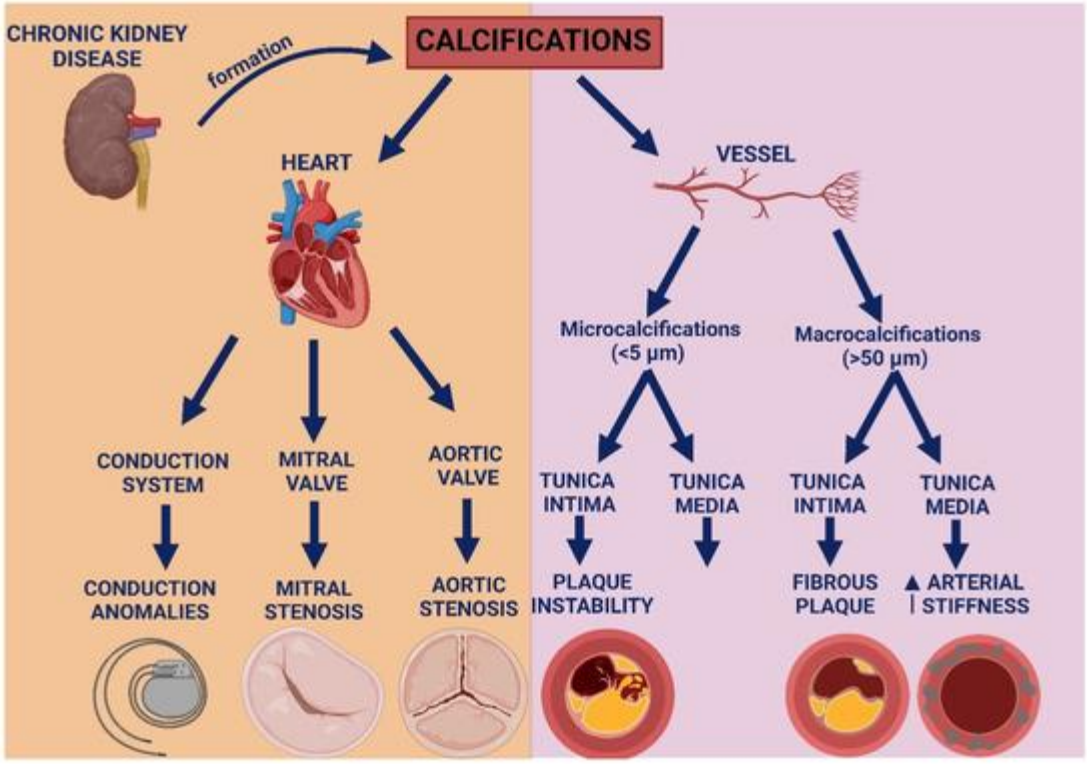
Clinical management of vascular calcifications in CKD patients and intervention strategies to delay the progression.

Investigations

- **Plain Xray-** lateral abdominal Xray.
- **Coronary Artery Calcification** scoring using CT (Agatson, Adragao, Kaupilla)
- **Echo**



American Heart Association/© 2021 The Authors (CT scans)



Role of micro- and macro-calcifications in the large vessels, heart valves, and cardiac conduction system.

Treatment

- No specific therapy to reverse vascular calcification in chronic kidney disease.
- Controlling hyperphosphatemia and optimising CKD-MBD therapies.
- Tenapanor - Reduces intestinal phosphate absorption by inhibiting sodium/hydrogen exchanger 3 (NHE3). Lowers serum phosphate - potentially slows VC.
- Micro RNA therapies and gene therapies [experimental]
- Denosumab - Inhibits osteoclast activity and may reduce vascular osteogenic signaling. [investigational for VC].

- Intensification of dialysis.
- For Calciphylaxis:-
  - Wound care- antibiotics for infected wound, debridement of necrotic wounds.
  - Replace warfarin with LMWH or DOACs .
  - Stop vit D analogues
  - Sodium thiosulphate.
  - Hyperbaric oxygen therapy.

Newer therapies

- **Vitamin K-** Cofactor for Matrix Gla Protein (MGP) activation, an endogenous inhibitor of vascular calcification. Vitamin K2 (menaquinone) is most effective.Trials ongoing (VitaVasK, VIKTORY).

- **SNF472 (Myo-inositol hexaphosphate / Phytate):** Direct inhibitor of hydroxyapatite crystal growth (a key step in calcification) without interfering with calcium and phosphorus metabolism. CaLIPSO trial (in hemodialysis patients) showed reduced coronary artery calcification progression. Phase 3 trials ongoing with promising results.

- **Magnesium** : Competes with calcium; inhibits phosphate-induced calcification of VSMCs. [ongoing trial –DIALMAG- Canada].

- **Etelcalcetide**: Suppress PTH → reduce calcium/phosphate release from bone. May slow progression of VC in dialysis patients (EVOLVE trial – secondary outcomes).