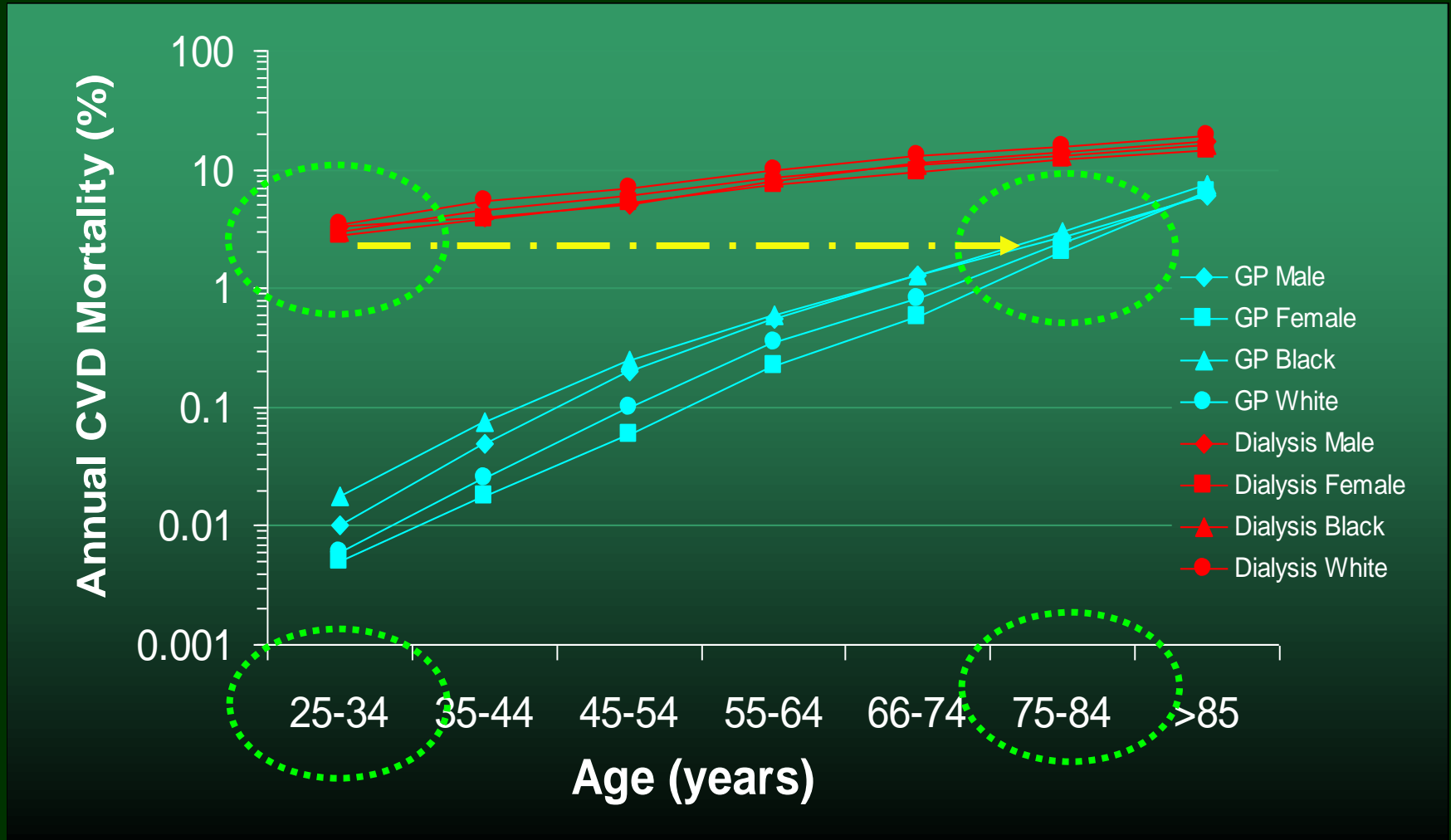


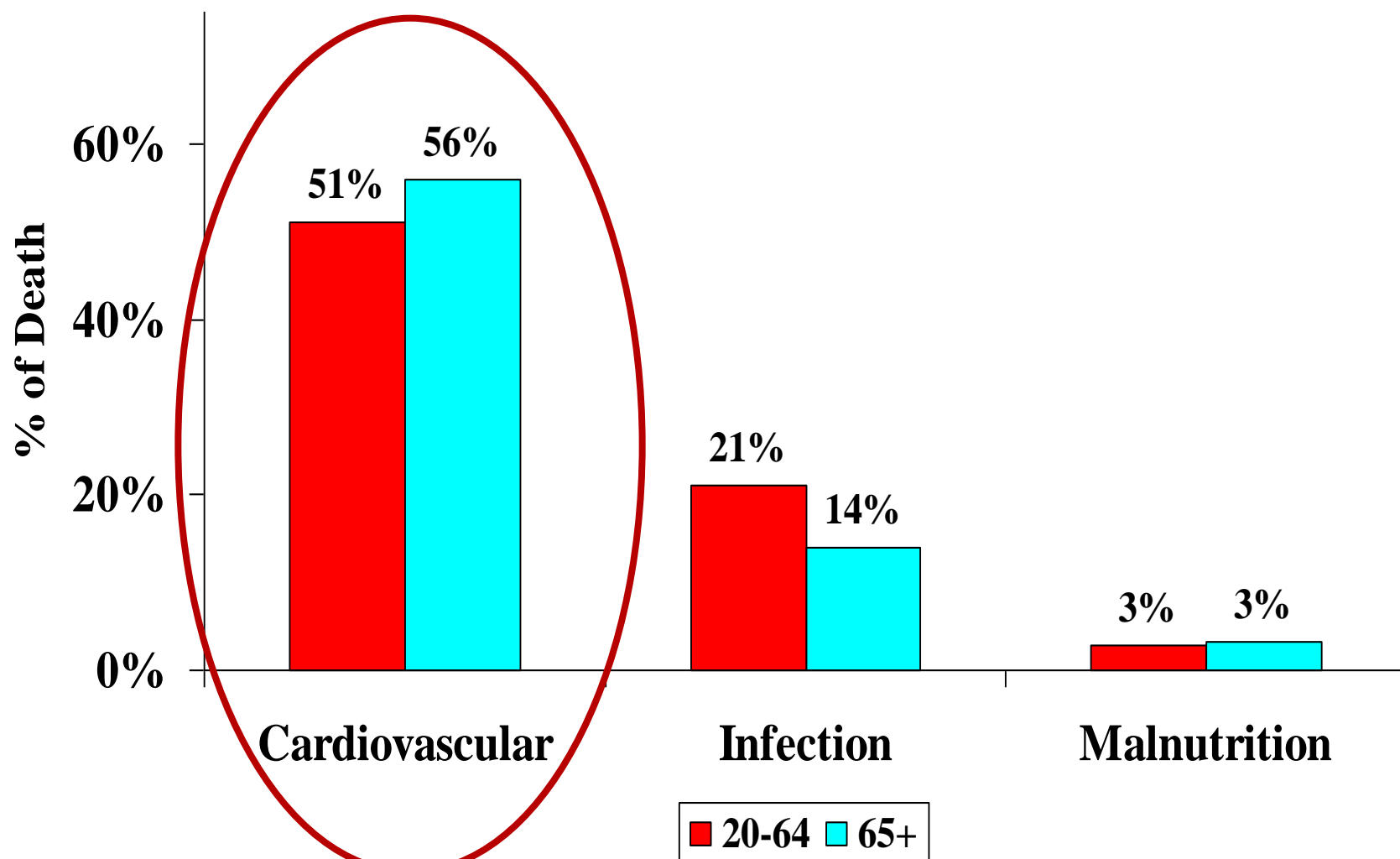
Cardiovascular Mortality:

General Population vs ESRD Dialysis Patients

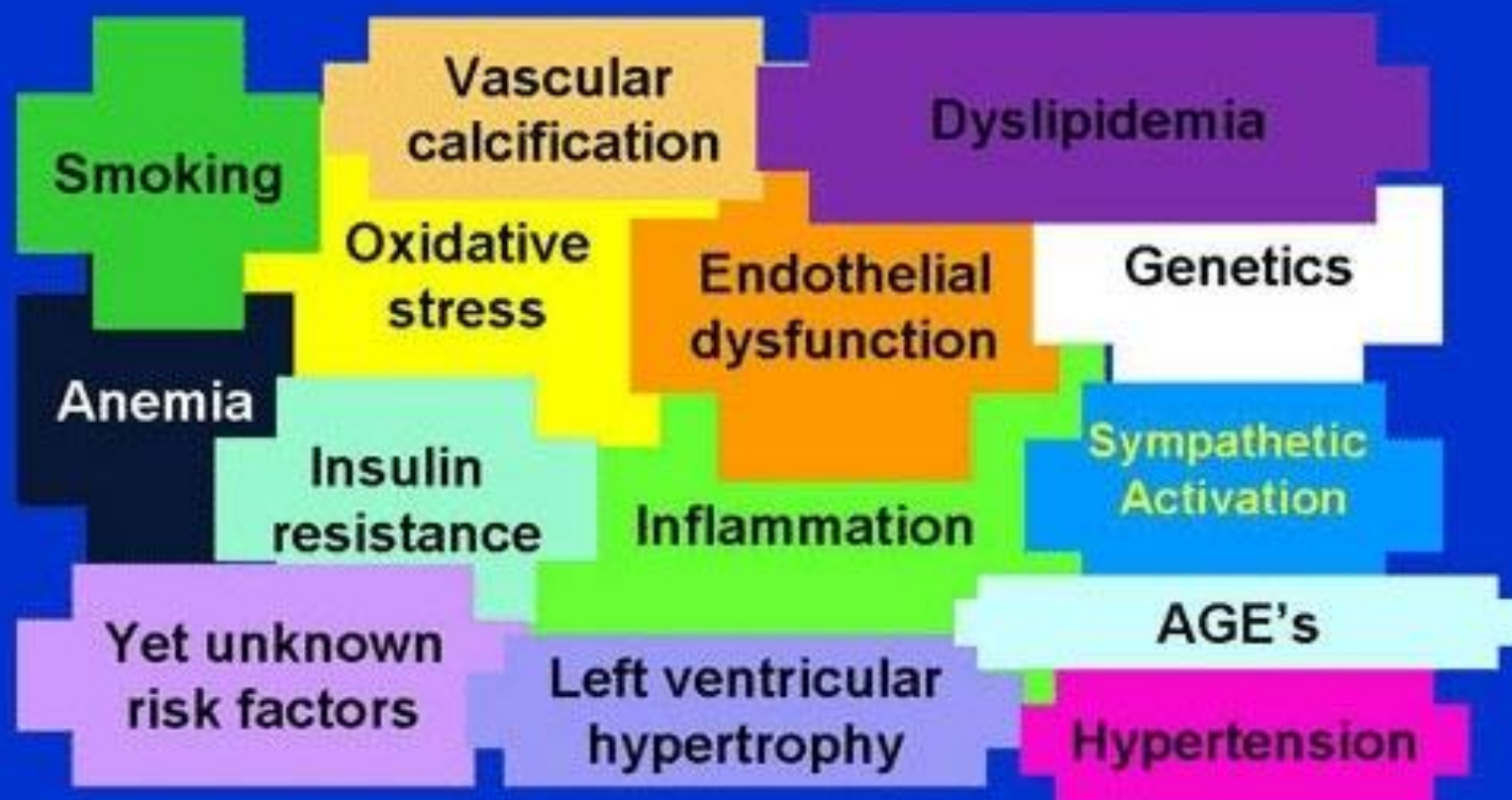


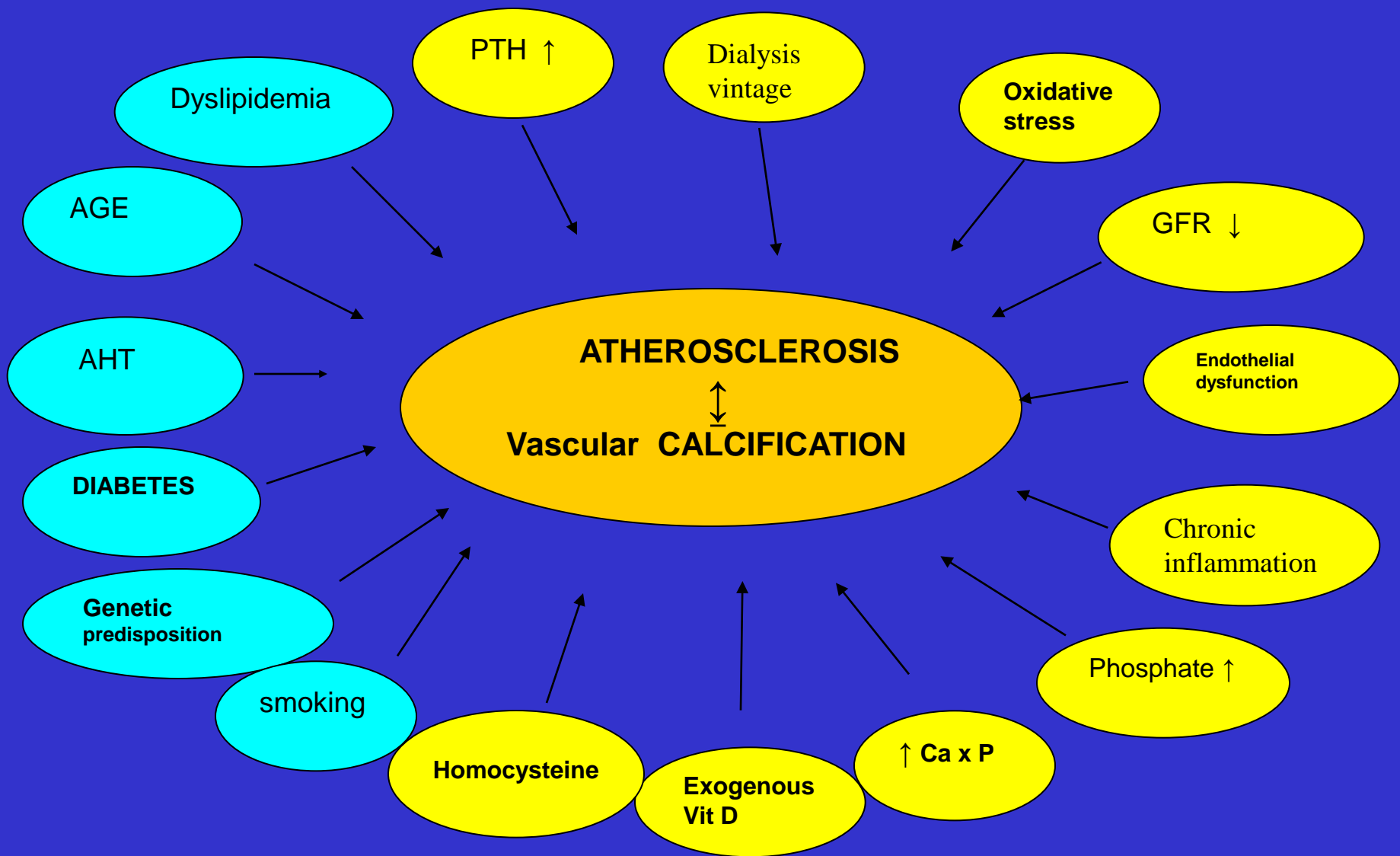
RN Foley, PS Parfrey, and MJ Sarnak; Clinical epidemiology of cardiovascular disease in chronic renal disease AJKD, 1998 32(5):S112-S119

Causes of death in ESRD Patients

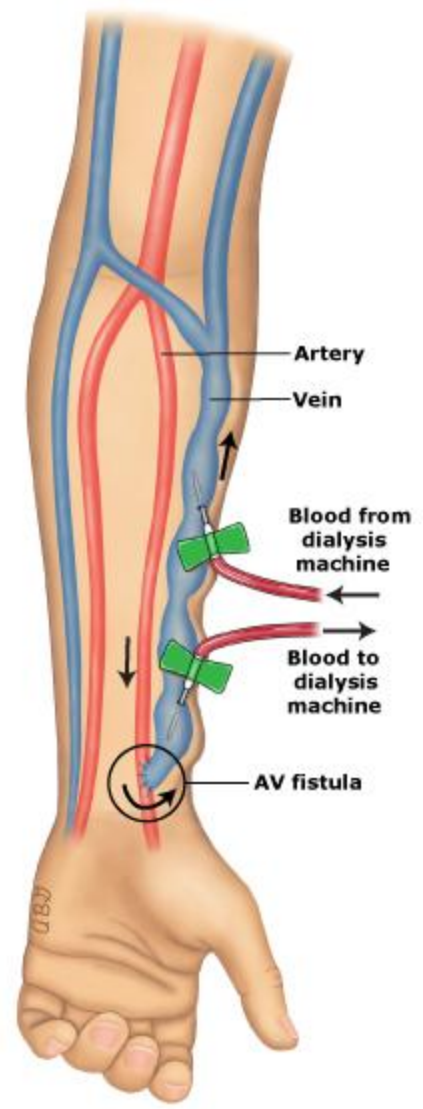


Causes of cardiovascular disease in CKD/ESRD – A puzzle with many pieces

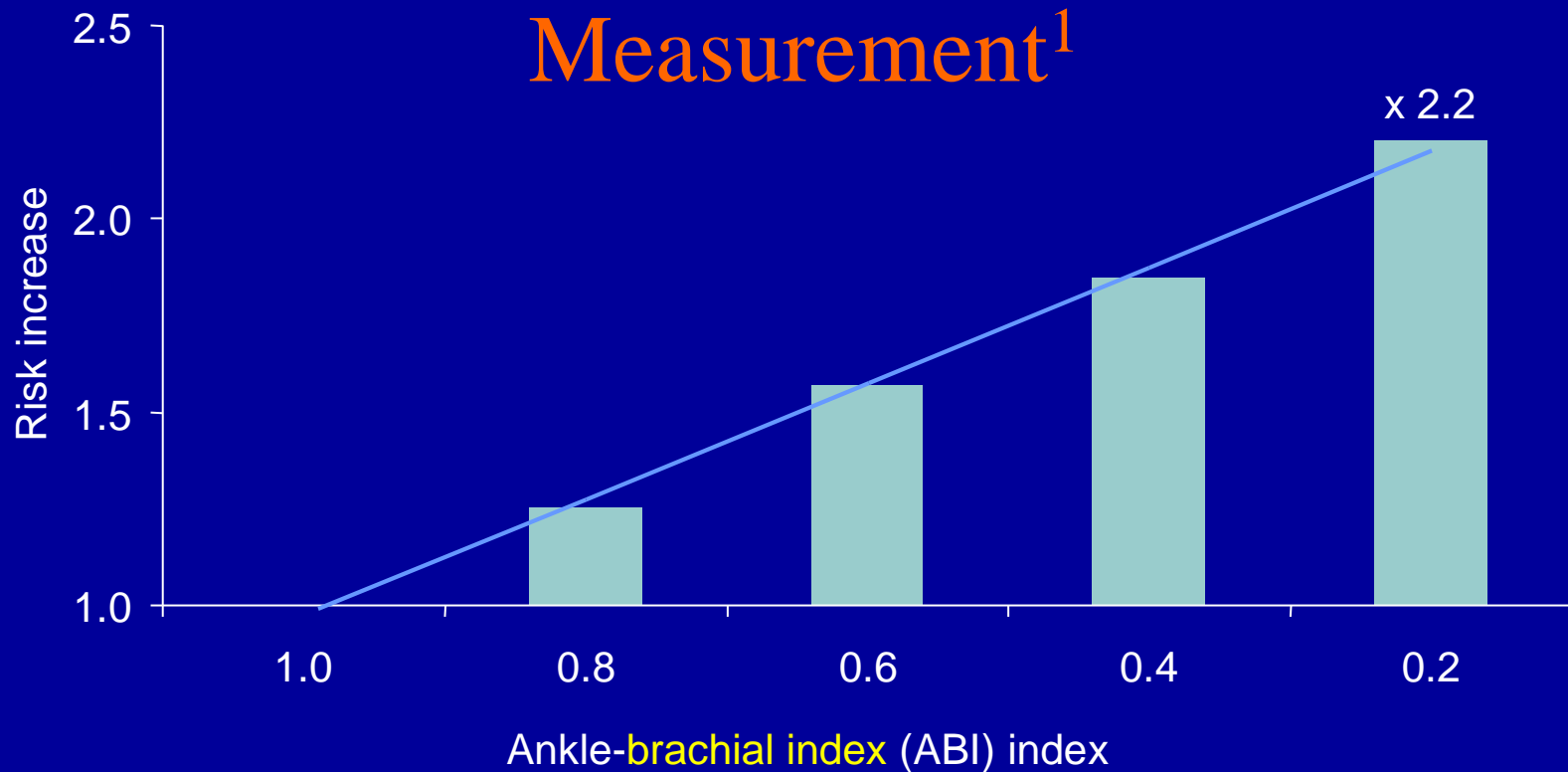




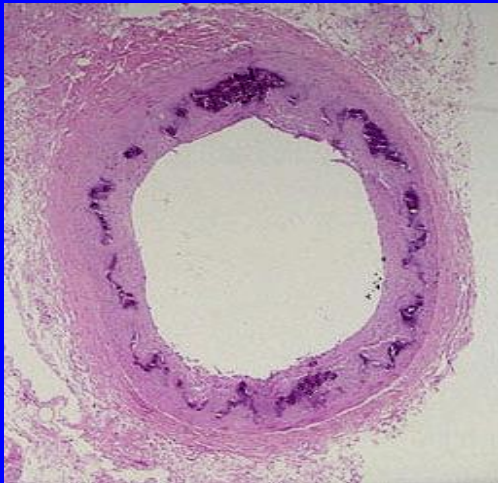
Pathogenesis of cardiovascular disease in CKD



Atherothrombosis is a Systemic Disease: Increase for Myocardial Infarction and Stroke as a Function of ABI

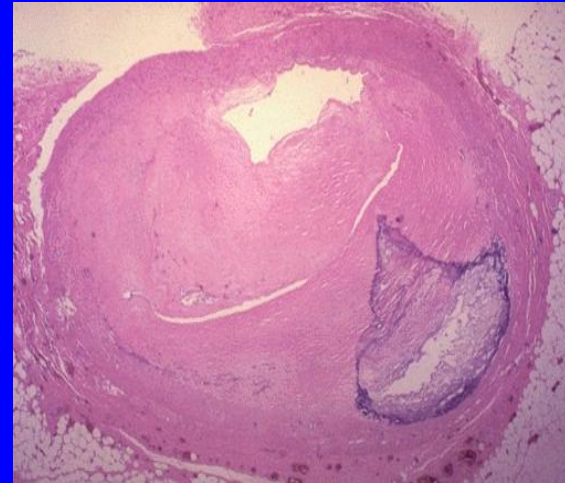


Medial calcifications



Medialcosis = Monckeberg

Intimal calcifications



Intimal = atherosclerosis

Intimal Calcification

Medial Calcification

Femoral
Artery



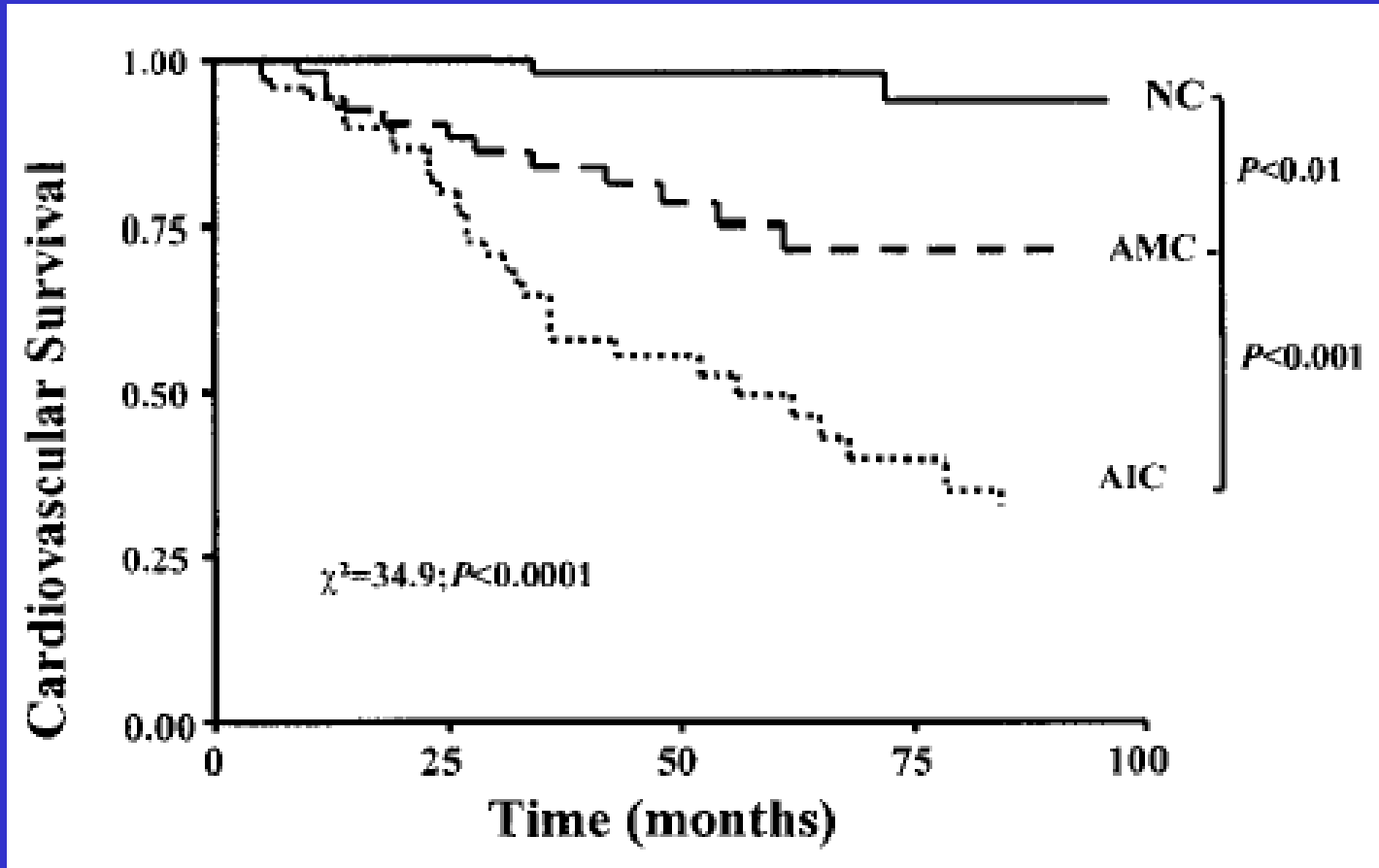
Pelvic
Arteries



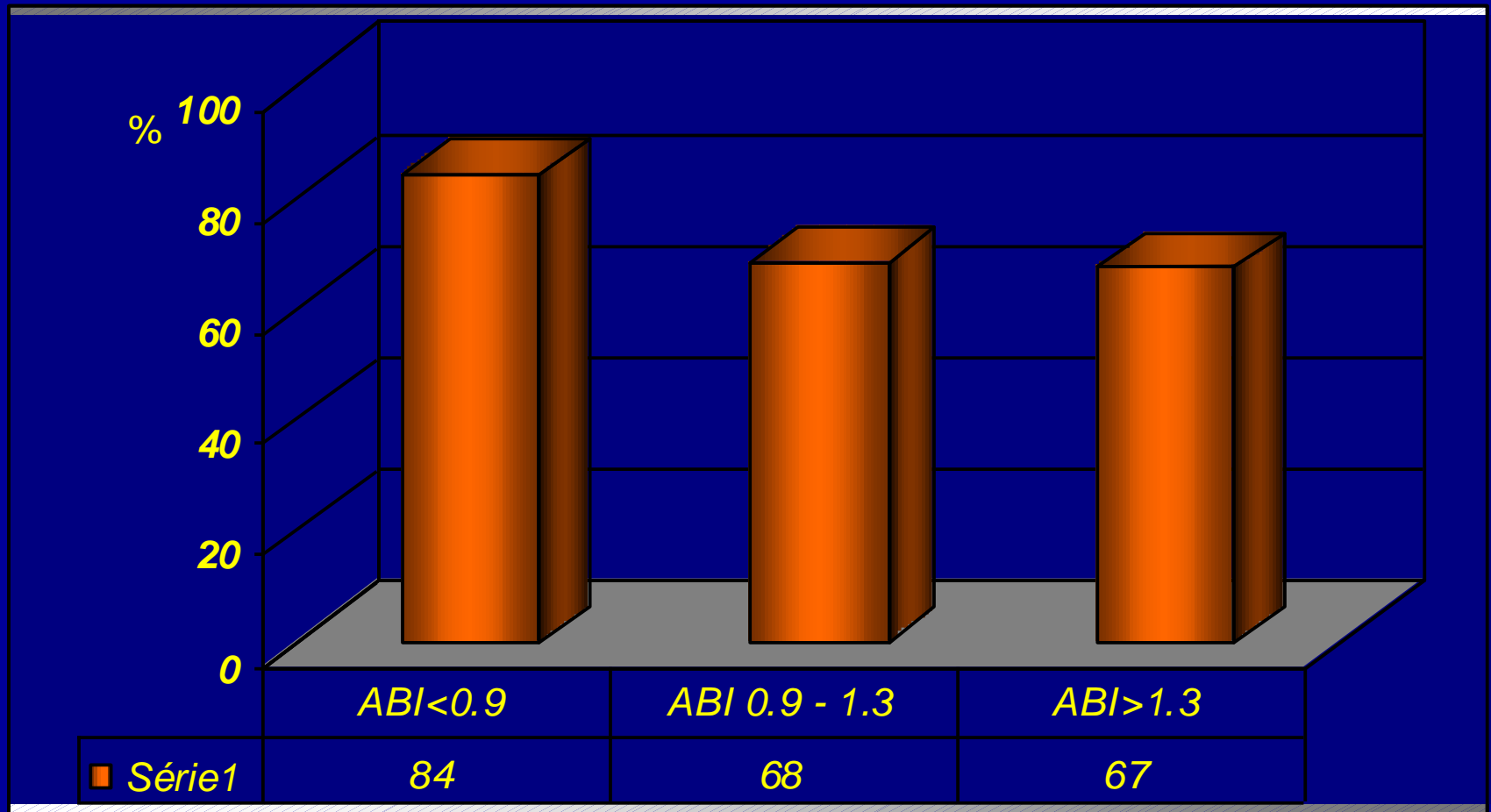
Medial Calcification

Mixed Calcification

Calcification Status & Cardiovascular Survival in ESRD



Frequency of calcified aortic arch*



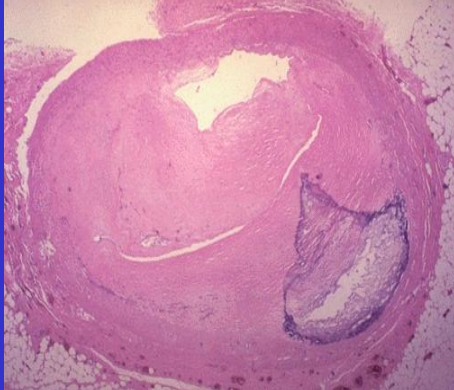
* x-ray radiography

Atherosclerosis: causes

ACCELERATED ATHEROSCLEROSIS IN PROLONGED MAINTENANCE HEMODIALYSIS

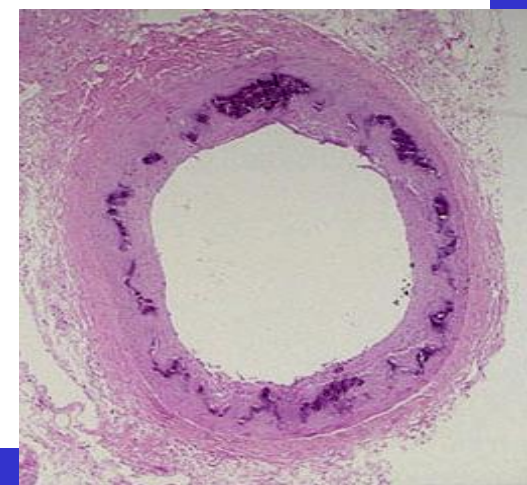
ARMANDO LINDNER, M.D., BERNARD CHARRA, M.D., DONALD J. SHERRARD, M.D., AND
BELDING H. SCRIBNER, M.D.

- Older age
- Hypertension
- Male gender
- Elevated LDL and Decreased HDL cholesterol
- Diabetes mellitus
- Tobacco use
- Psychosocial stress
- Family history of CVD
- ECF overload
- Anemia
- Abnormal mineral metabolism
- Malnutrition
- Inflammation/Infection
- Thrombogenic factors
- Oxidative stress
- Proteinuria
- Uremic toxins



Two types of risk factors

Risk Factor	Intimal/Atherosclerotic Calcification	Medial/Mönkeberg's Calcification
Dyslipidemia	Yes	No
Advanced age	Yes	Yes
Elevated blood pressure	Yes	Reciprocal (medial lesions worsen blood pressure)
Male	Yes	No
Smoking	Yes	No
Inflammation	Yes (local)	Yes (systemic mediators)
Diabetes/glucose intolerance	Yes	Yes
Kidney disease		
Reduced GFR	No	Yes
Calcium		
Hypercalcemia	No	Yes
Positive balance	No	Yes
Hyperphosphatemia	Yes	Yes
PTH abnormalities	No	No
Vitamin D administration	No	Yes
Duration of treatment with dialysis	No	Yes



Biomarkers of vascular calcification

Promoters

- High blood glucose levels
- High LDL Cholesterol
- Low HDL Cholesterol
- Uremic serum
- Hyperphosphatemia
- Increased CaxP product
- High intake of Vitamin D
- High iPTH levels
- Hypercalcemia
- Elevated leptin levels
- TNF α
- TGF β
- AGEs
- Oxidised lipids

Inhibitors

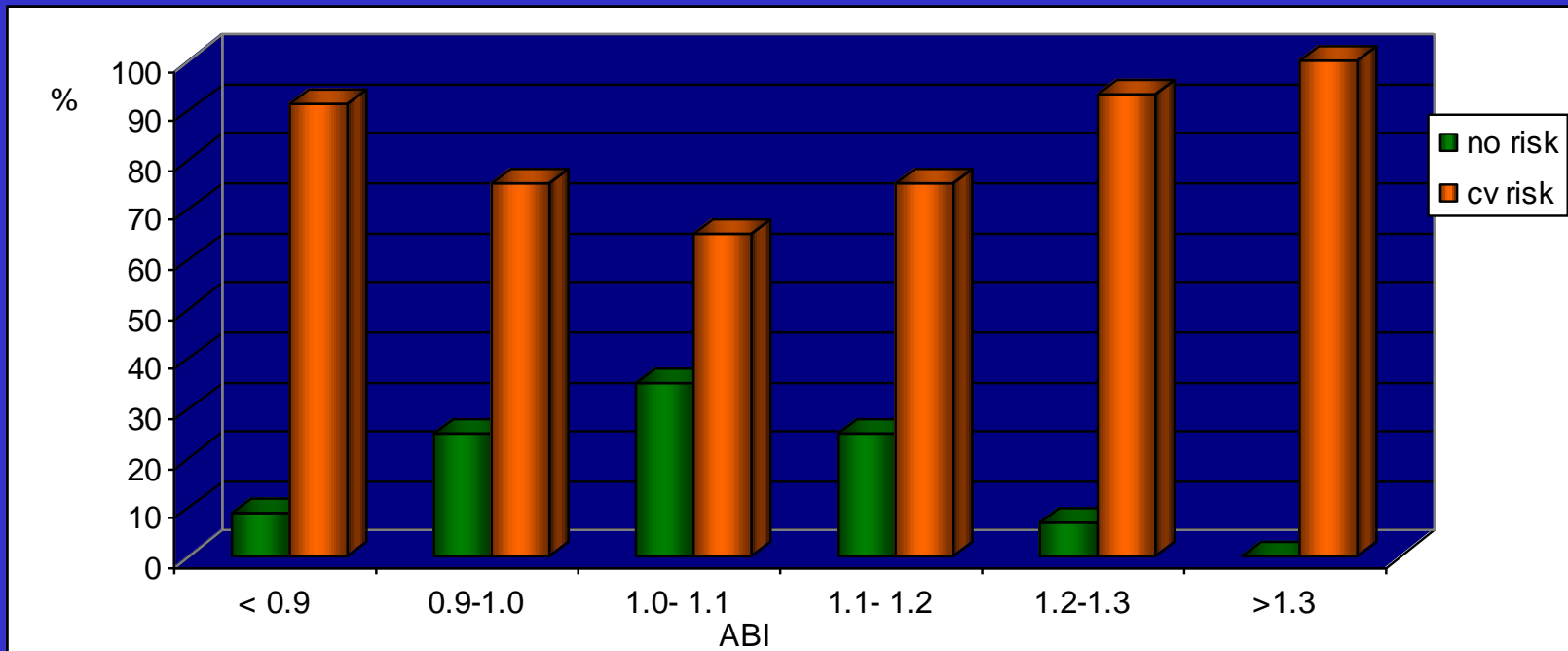
Circulating inhibitors

- fetuin A
- bone morphogenic protein -7
- PTHrP
- HDL
- Magnesium

Locally acting inhibitors

- Matrix Gla protein
- Osteopontin
- Pyrophosphate
- Osteoprotegerin (OPG)

Distribution of 83 HD patients according to CV risk and ABI



At least one cv complication:
LVH; MI; stroke; Heart failure

Mechanisms of vascular calcifications

Established general favouring conditions

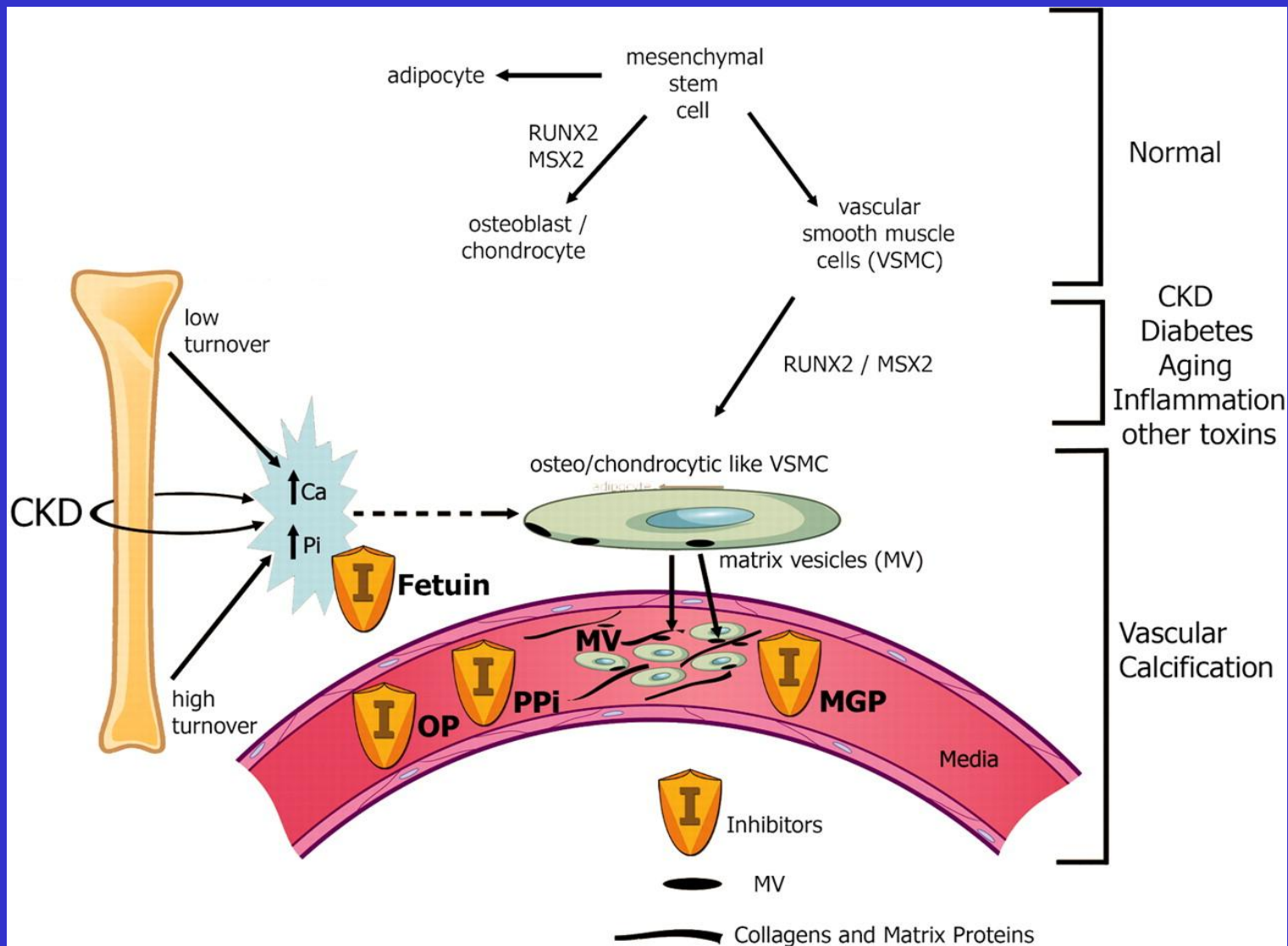
- age +++
- male gender
- hypertension
- diabetes mellitus
- vitamin D intoxication

Mechanisms of vascular calcifications

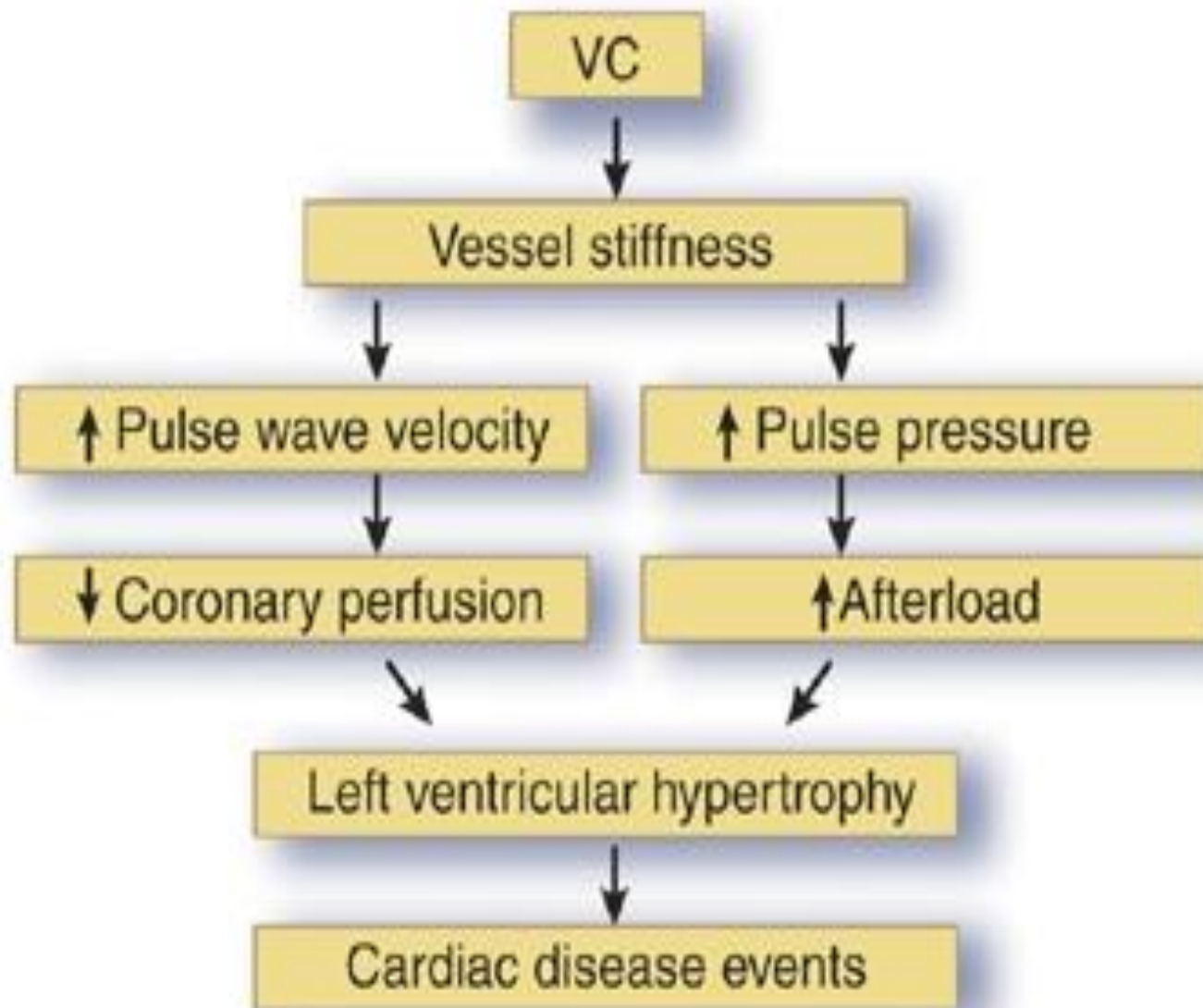
Established favoring conditions linked to CKD

- severe 2ary hyperparathyroidism
- low bone turnover (hypoPTH, Al)
- high-dose active vitamin D metabolites
- high serum P or Ca; high Ca x P product
- excessive oral calcium intake
- duration of dialysis

Vascular calcification



Vascular calcification causes cardiac disease



Vascular calcifications

Ectopic calcification in the vessel wall is very common in ESRD

Localization

arterial calcifications

- atheromatous (*intima, sub-intima*)
- medial (*media*)

arteriolar calcifications

- calcific uremic arteriolopathy (“*calciophylaxis*”)