



Simposio  
***Geriatric Crossroads: Osteoporosi e  
Patologia Cardiovascolare***

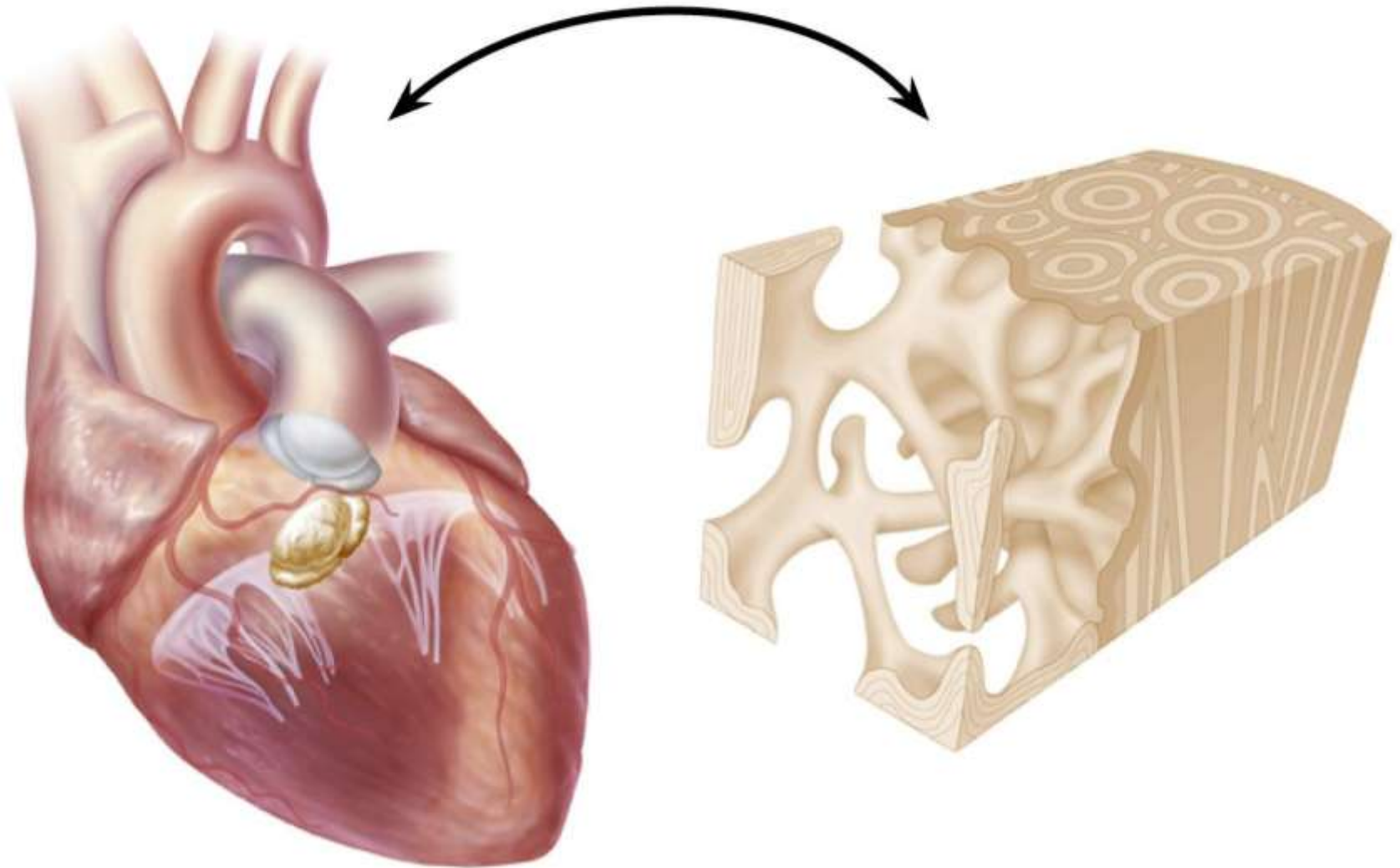
Marcatori osteometabolici  
e patologie cardiovascolari



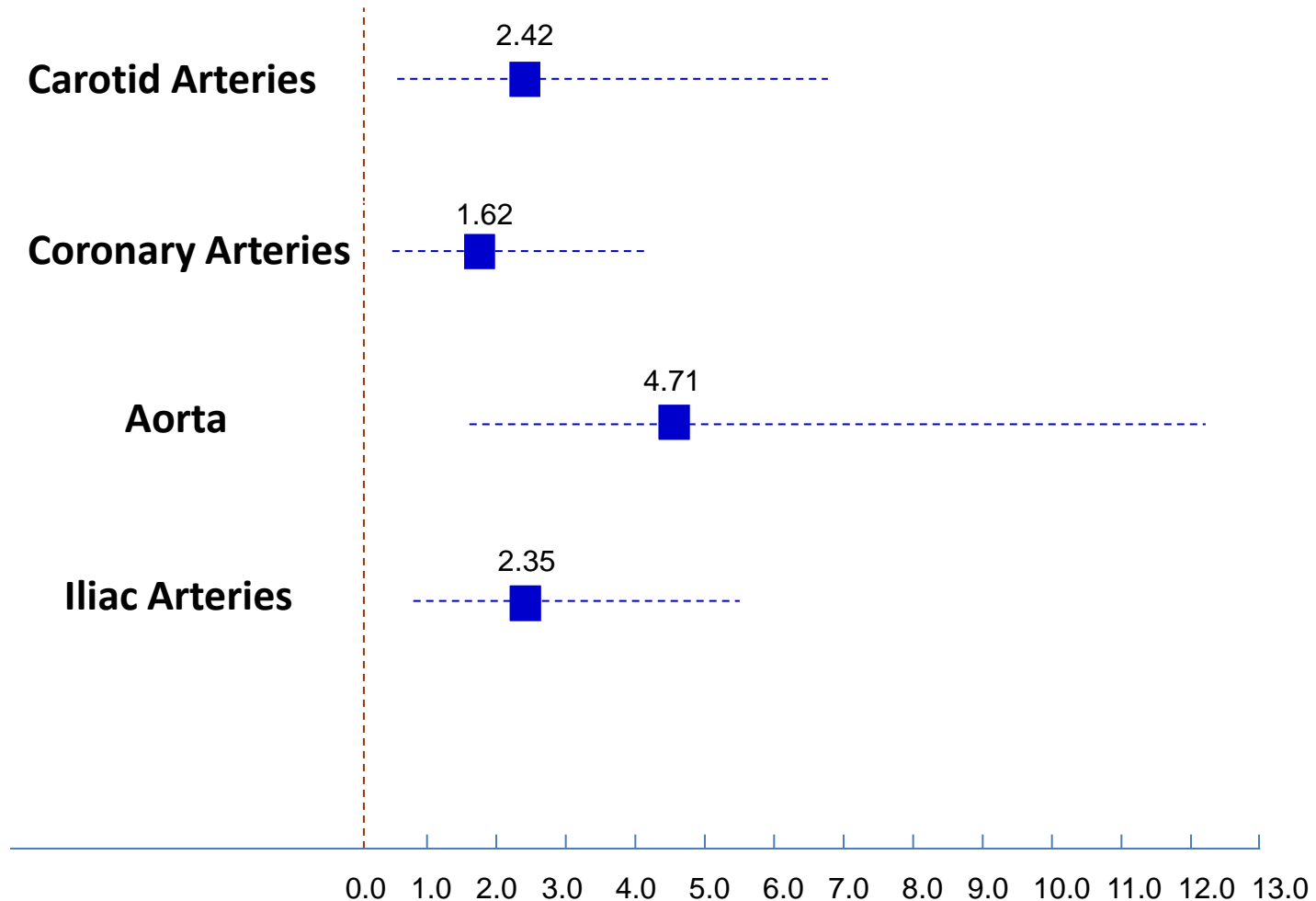
Dario Leosco  
*Cattedra di Geriatria  
Università di Napoli "Federico II"*

# The Bone Paradox

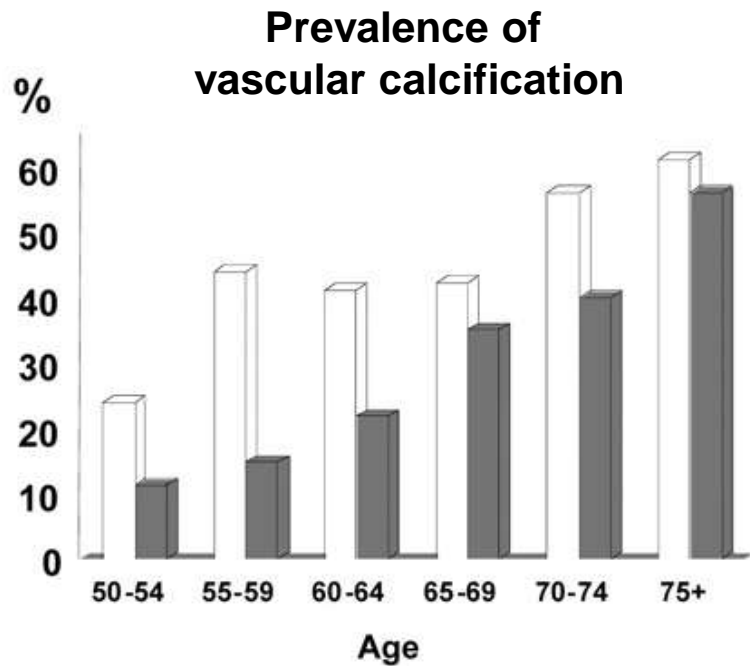
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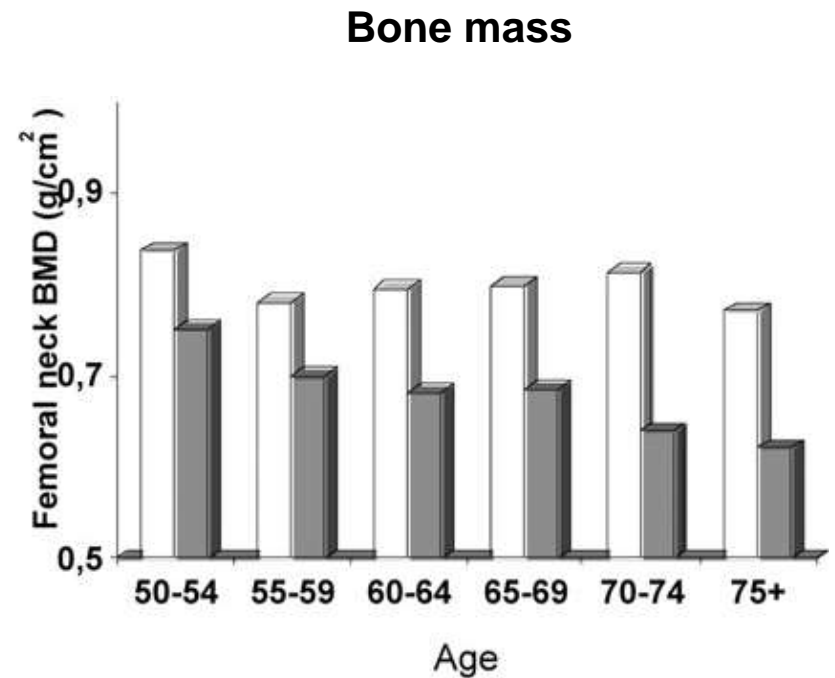
# ORs of Ca<sup>++</sup> in a given arterial bed associated with BMD lower than median in the general population



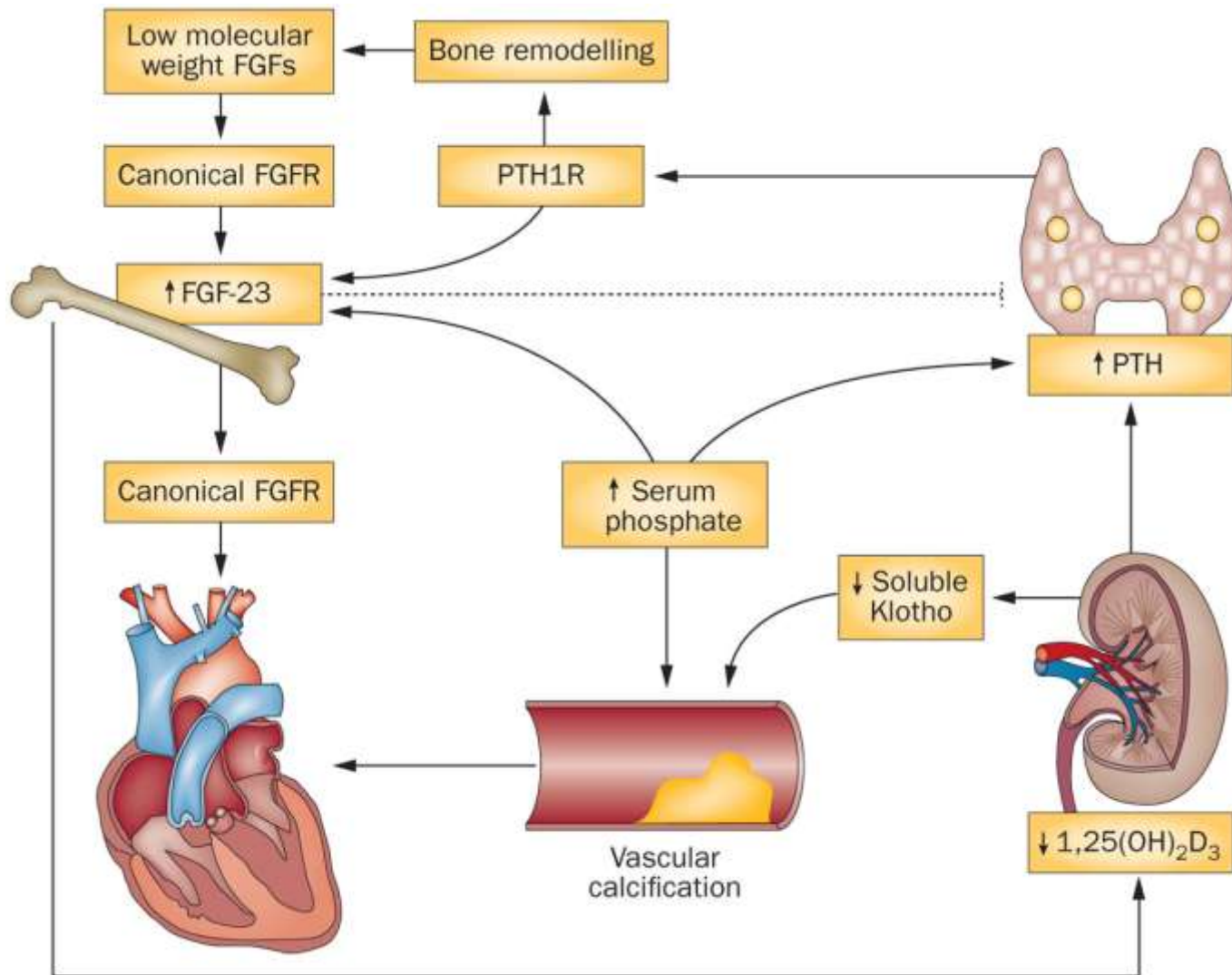
# Prevalence of aortic calcifications in men and women from the European Vertebral Osteoporosis Study (EVOS)



□ Men      ■ Women

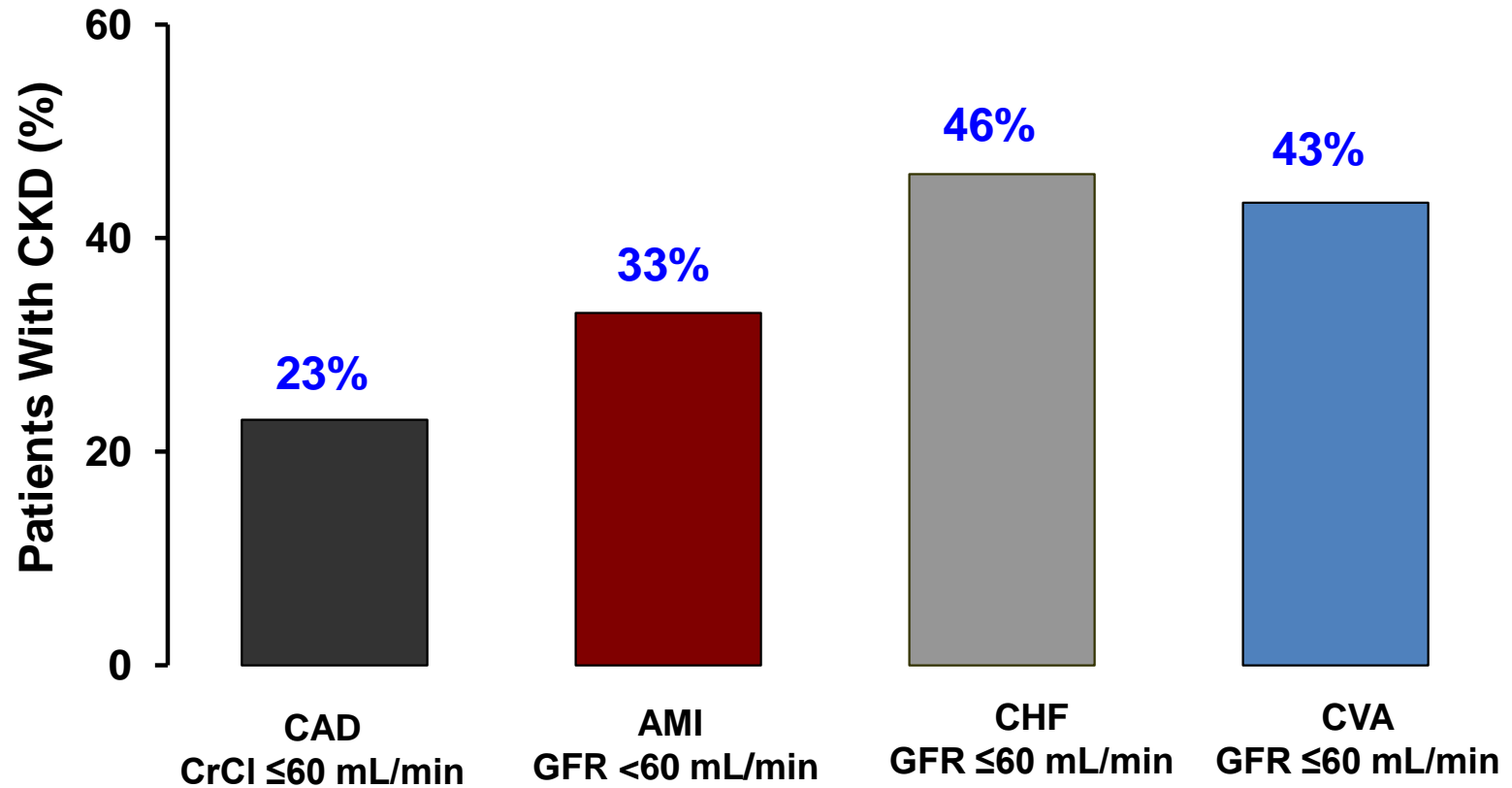


# The bone paradox in CKD



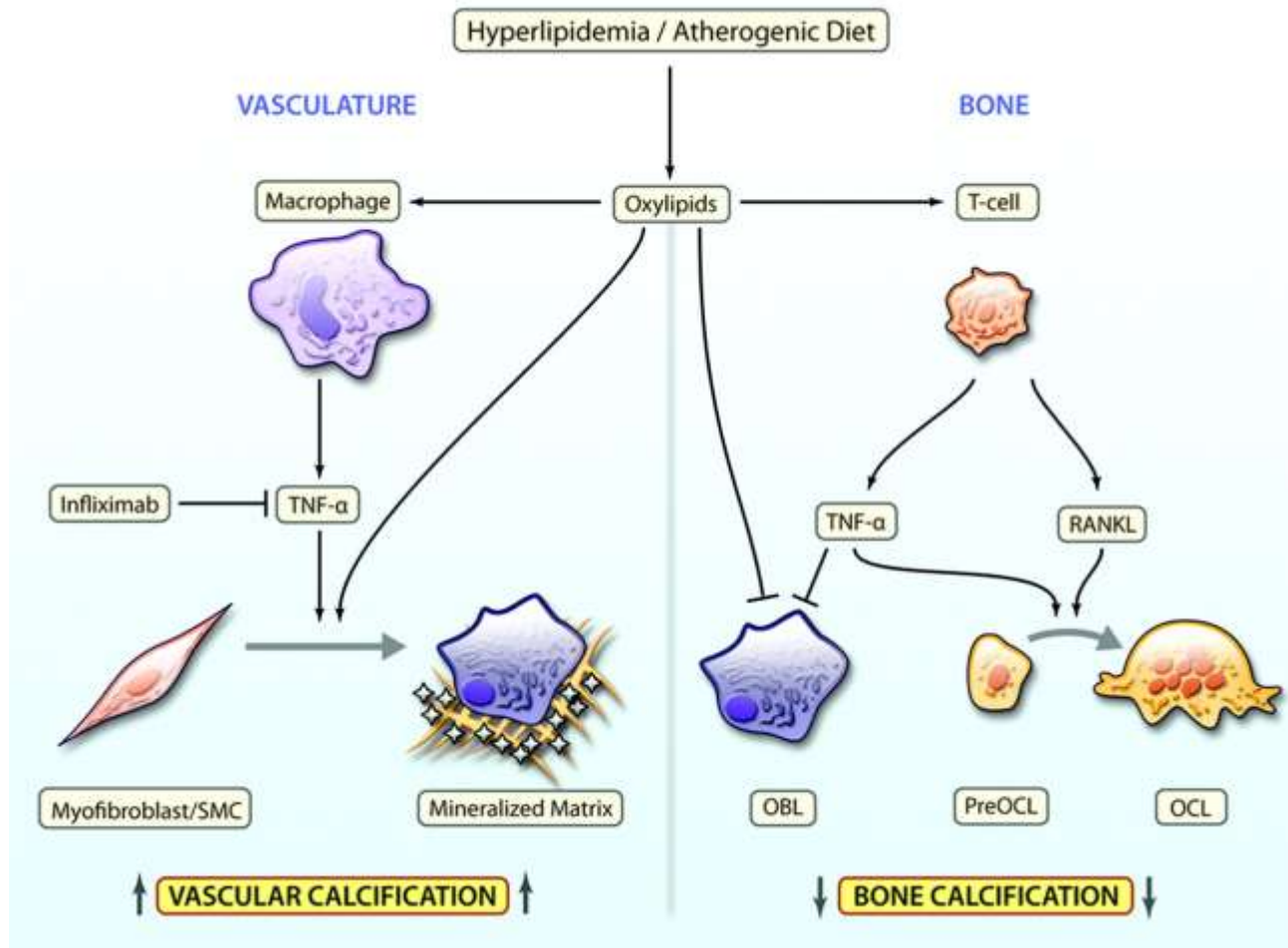
# CKD is prevalent in CVD

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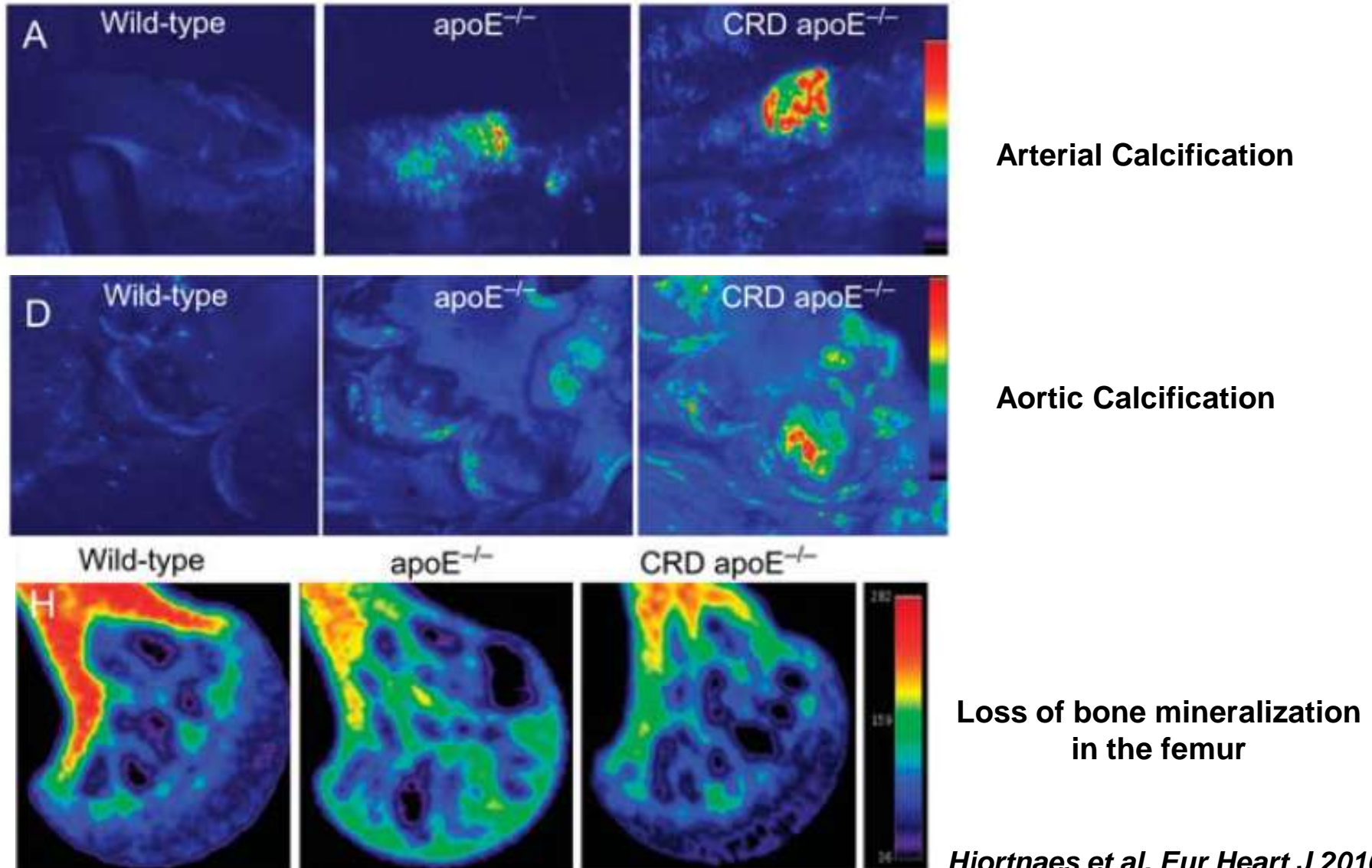


*Ix, et al., 2003; Anavekar, et al., 2004; Shlipak, et al., 2004, McClellan et al, 2006.*

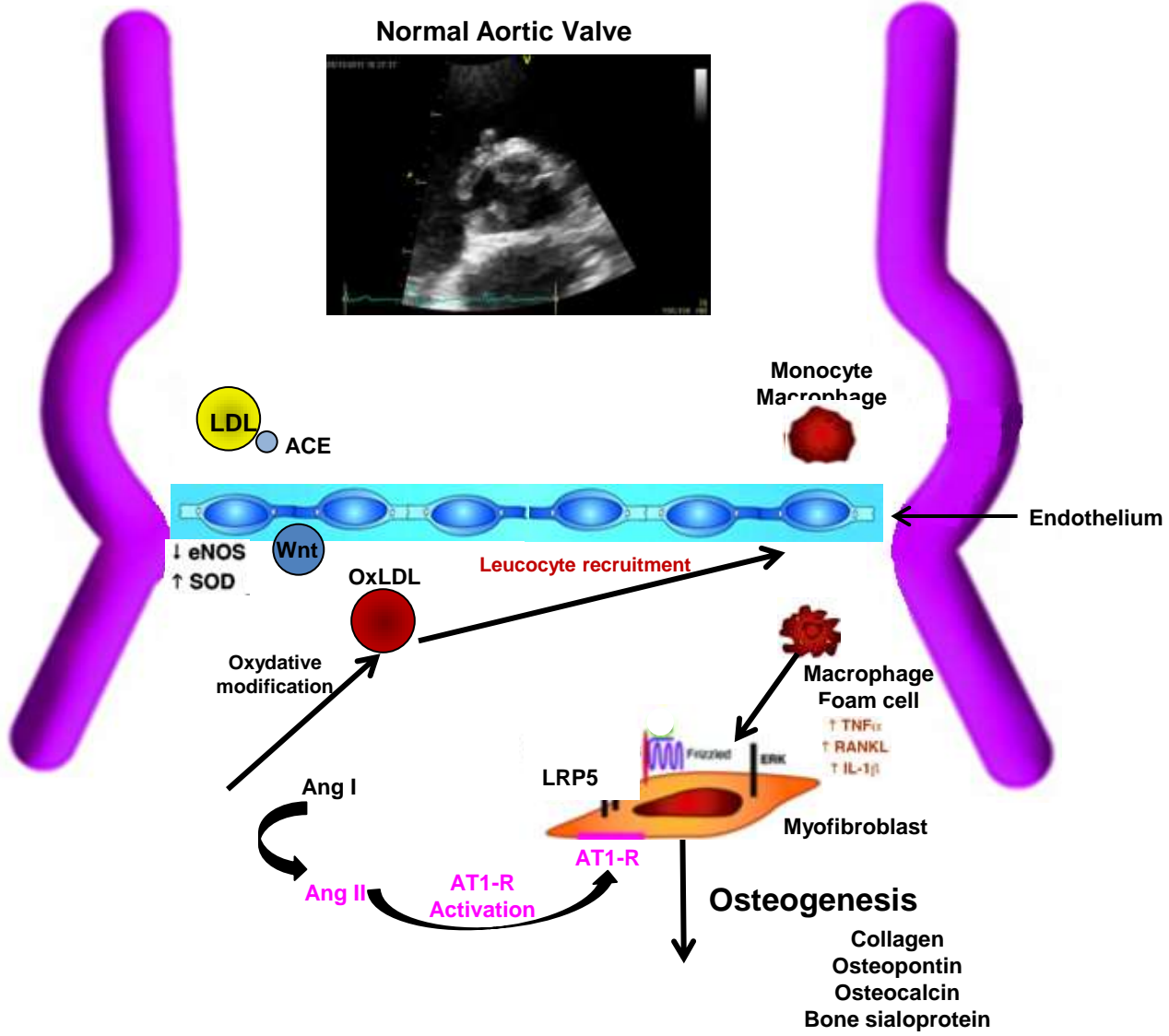
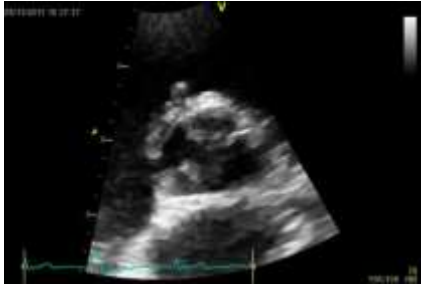
# The bone paradox and the lipid theory

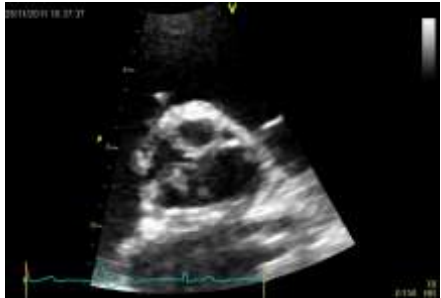
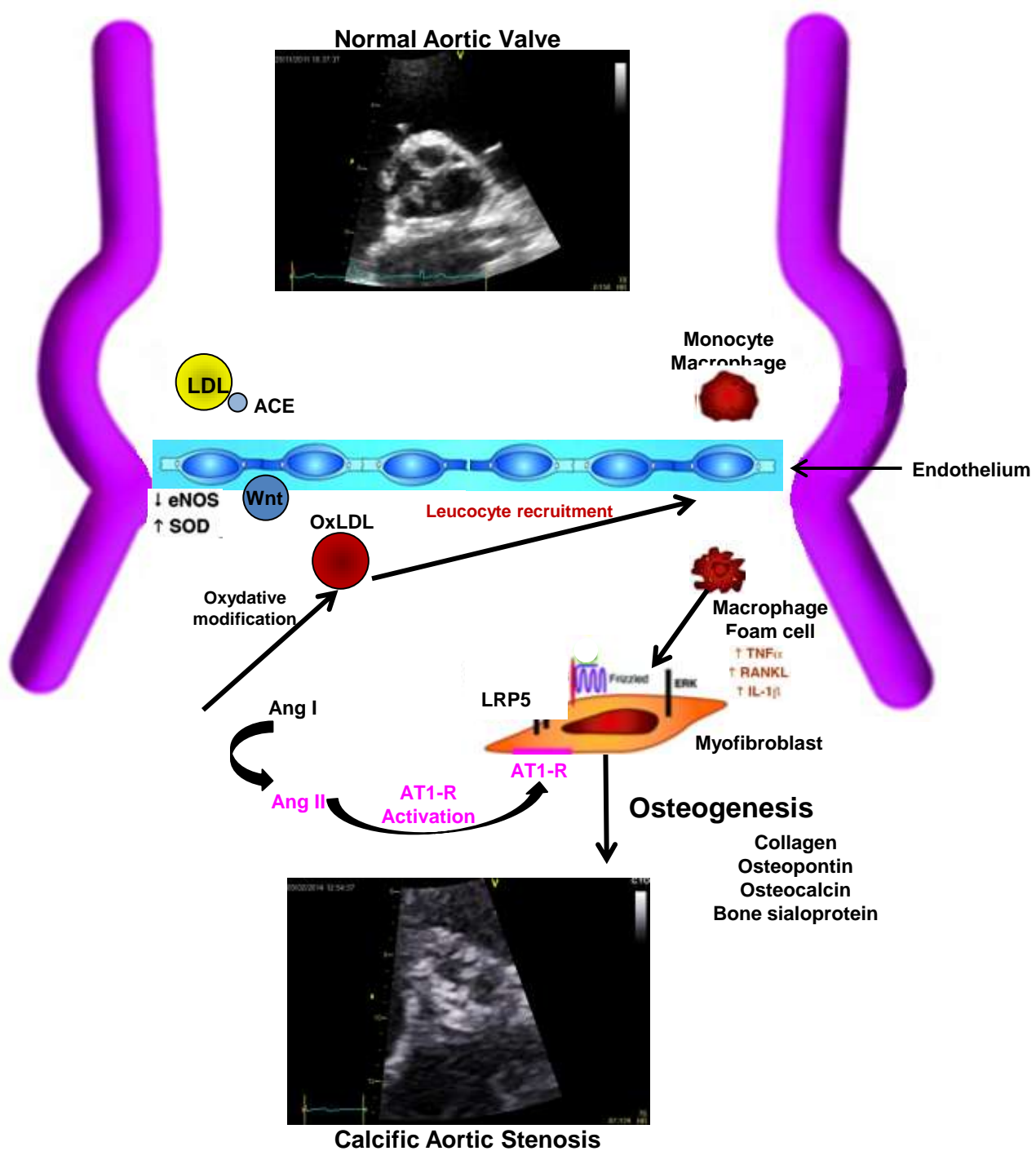


# Arterial and aortic valve calcification inversely correlates with osteoporotic bone remodelling

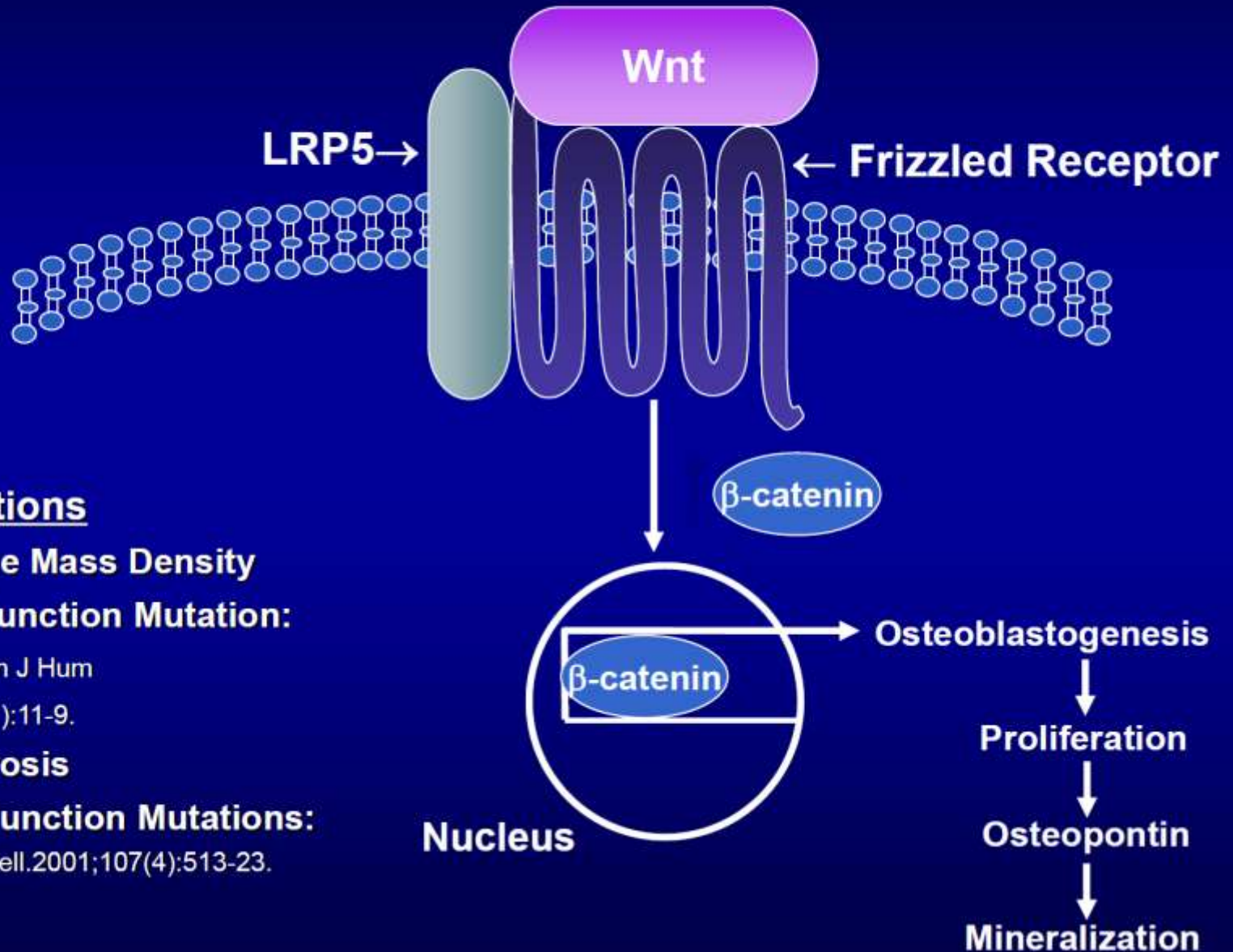


# Normal Aortic Valve





# Lrp5/WNT Regulation of Osteoblastogenesis



## Lrp5 Mutations

### 1) High Bone Mass Density

#### Gain of Function Mutation:

Little et al, Am J Hum

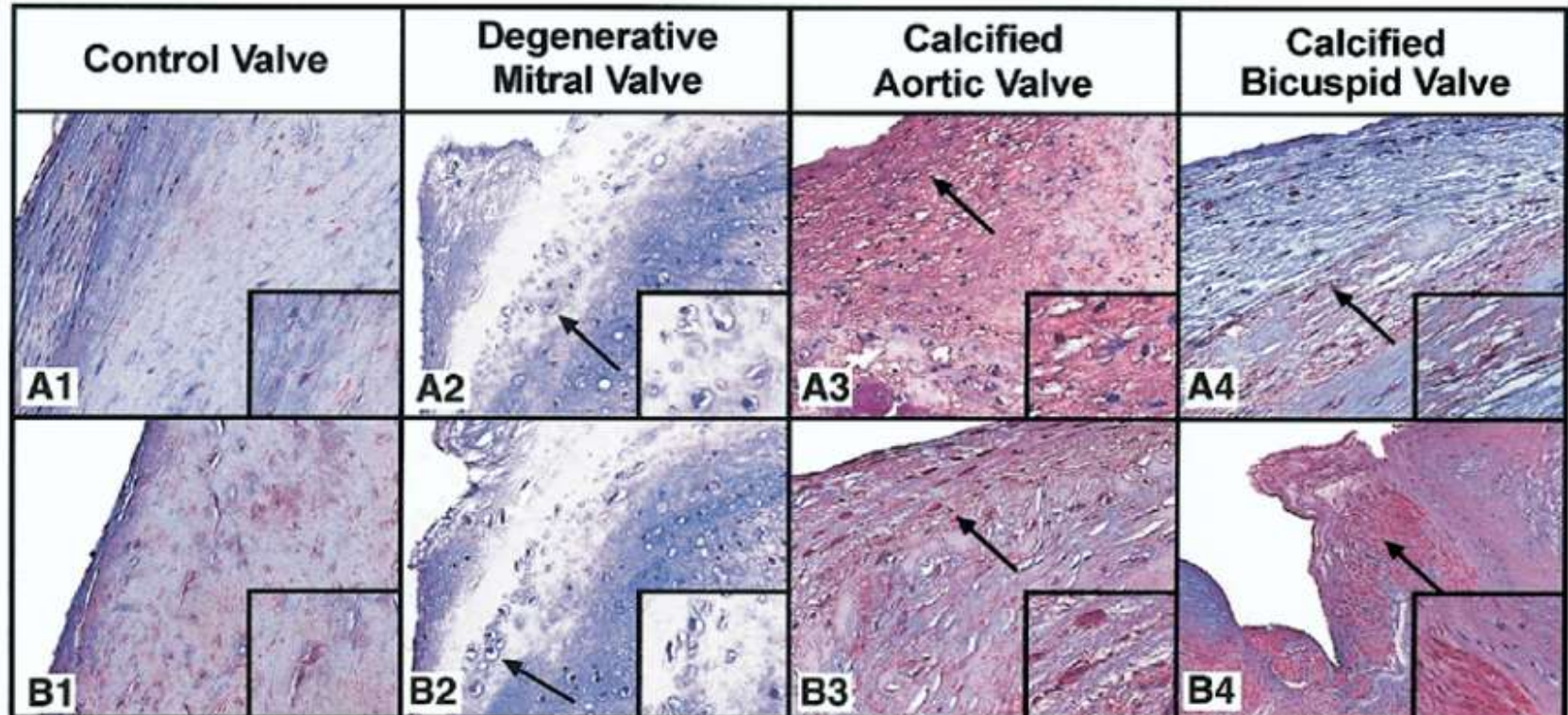
Genet,2002;70(1):11-9.

### 2) Osteoporosis

#### Loss of Function Mutations:

Gong et al, Cell.2001;107(4):513-23.

# Lrp5 Signaling in Human Valvular Heart Disease

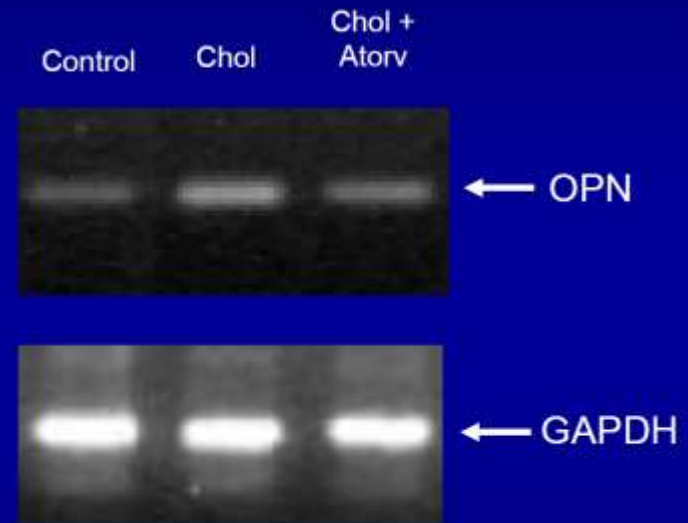


# New Insights Into the Progression of AS Implications for Secondary Prevention

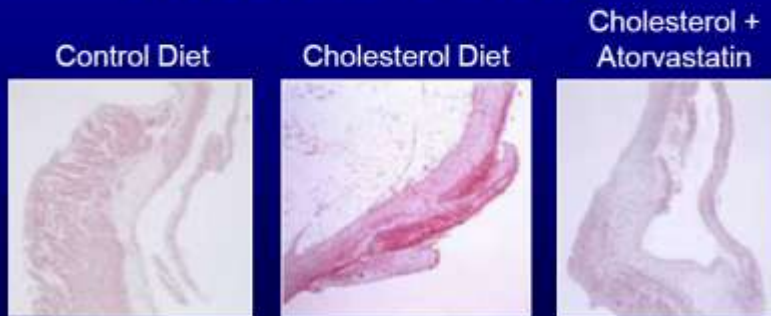
## Macrophage Marker



## Osteopontin Bone Matrix Expression



## Osteopontin Bone Marker

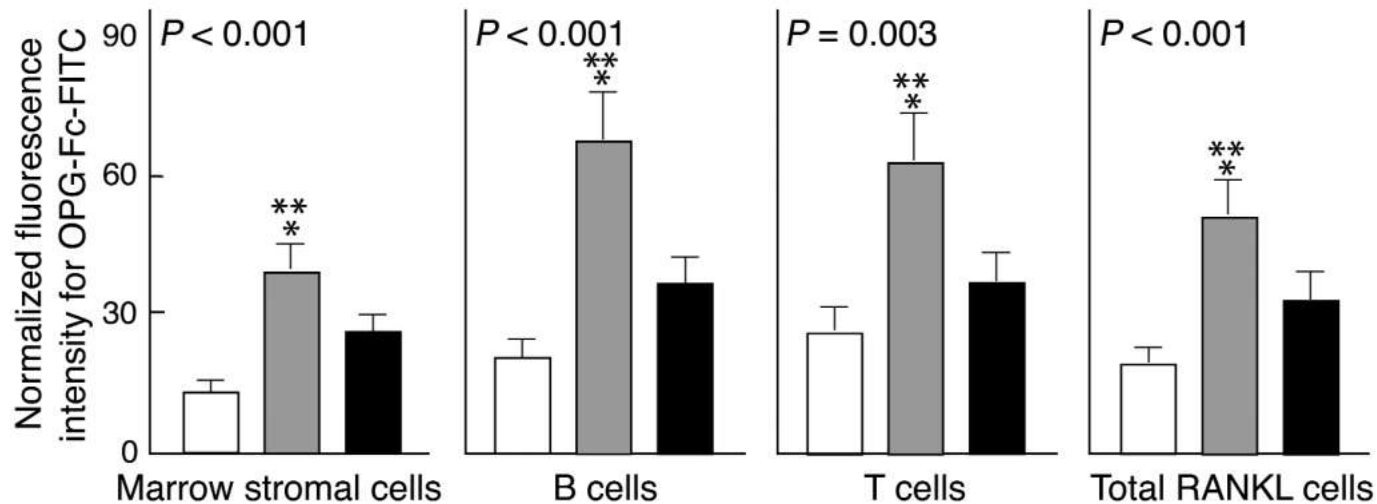


Rajamannan et al, *Circulation*  
2002;105(22): 2660-2665



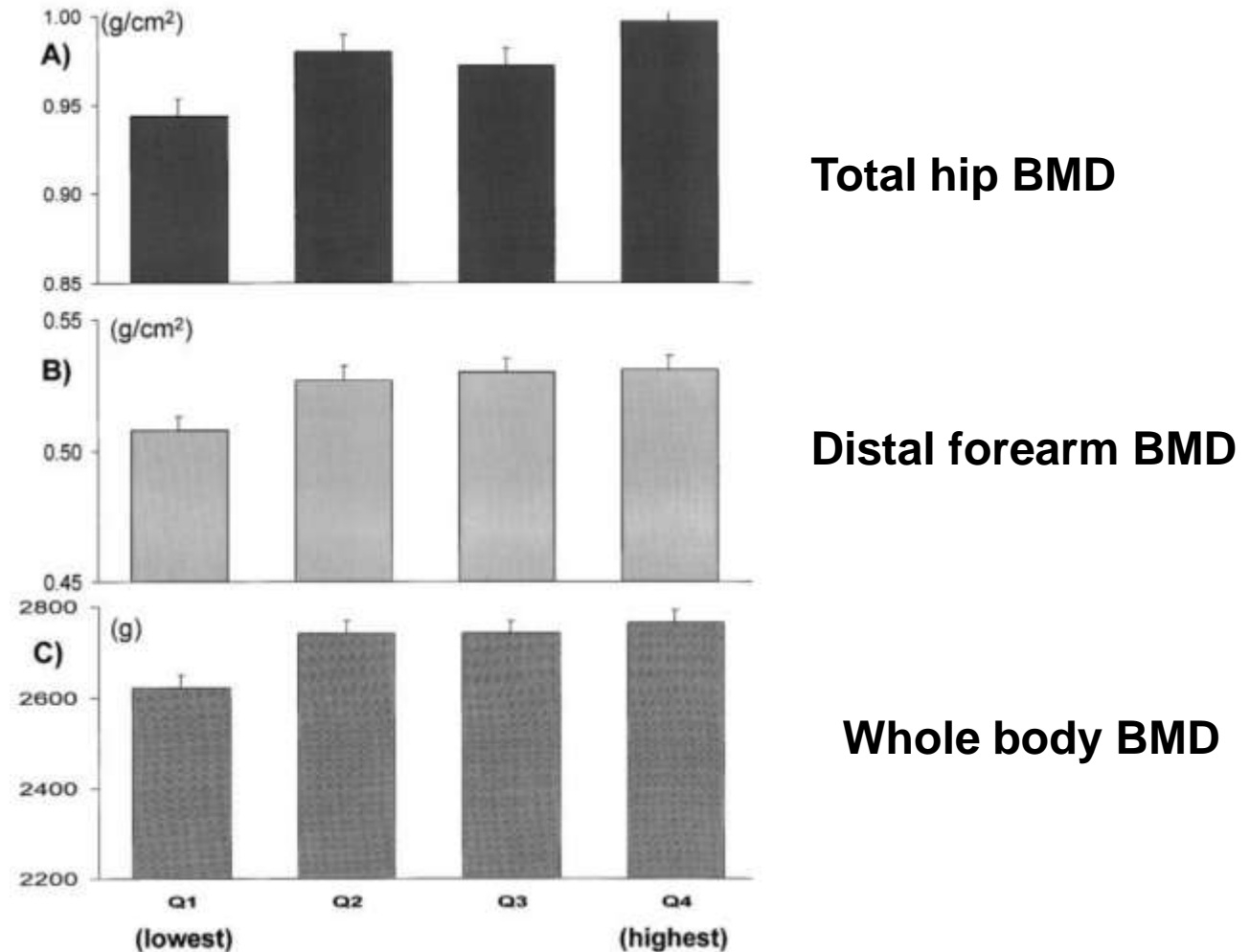
# Role of RANK ligand in mediating increased bone resorption in postmenopausal women

## RANKL expression on cell surface

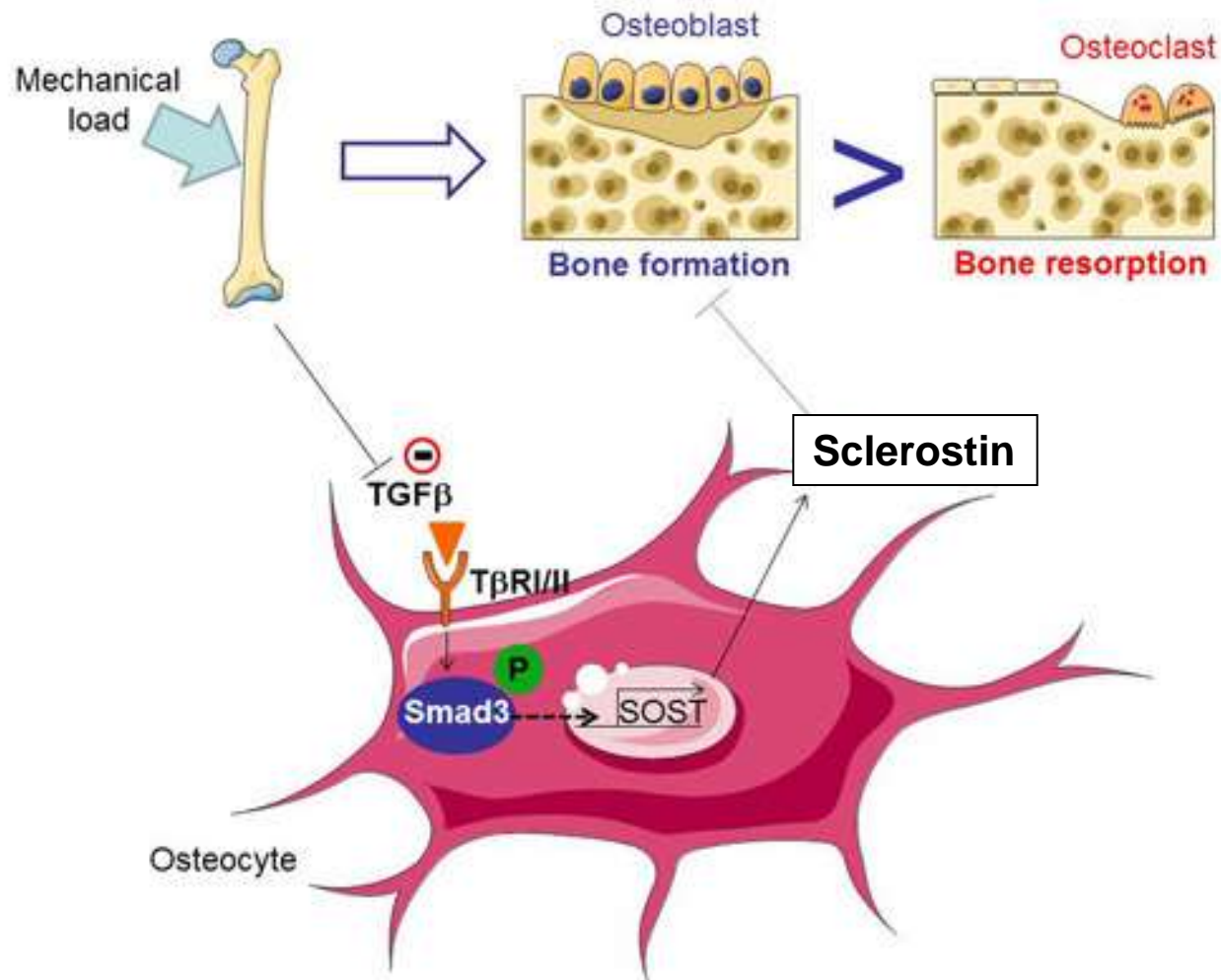


- Pre-menopausal women
- Untreated Post-menopausal women
- Estrogen Treated Post-menopausal women

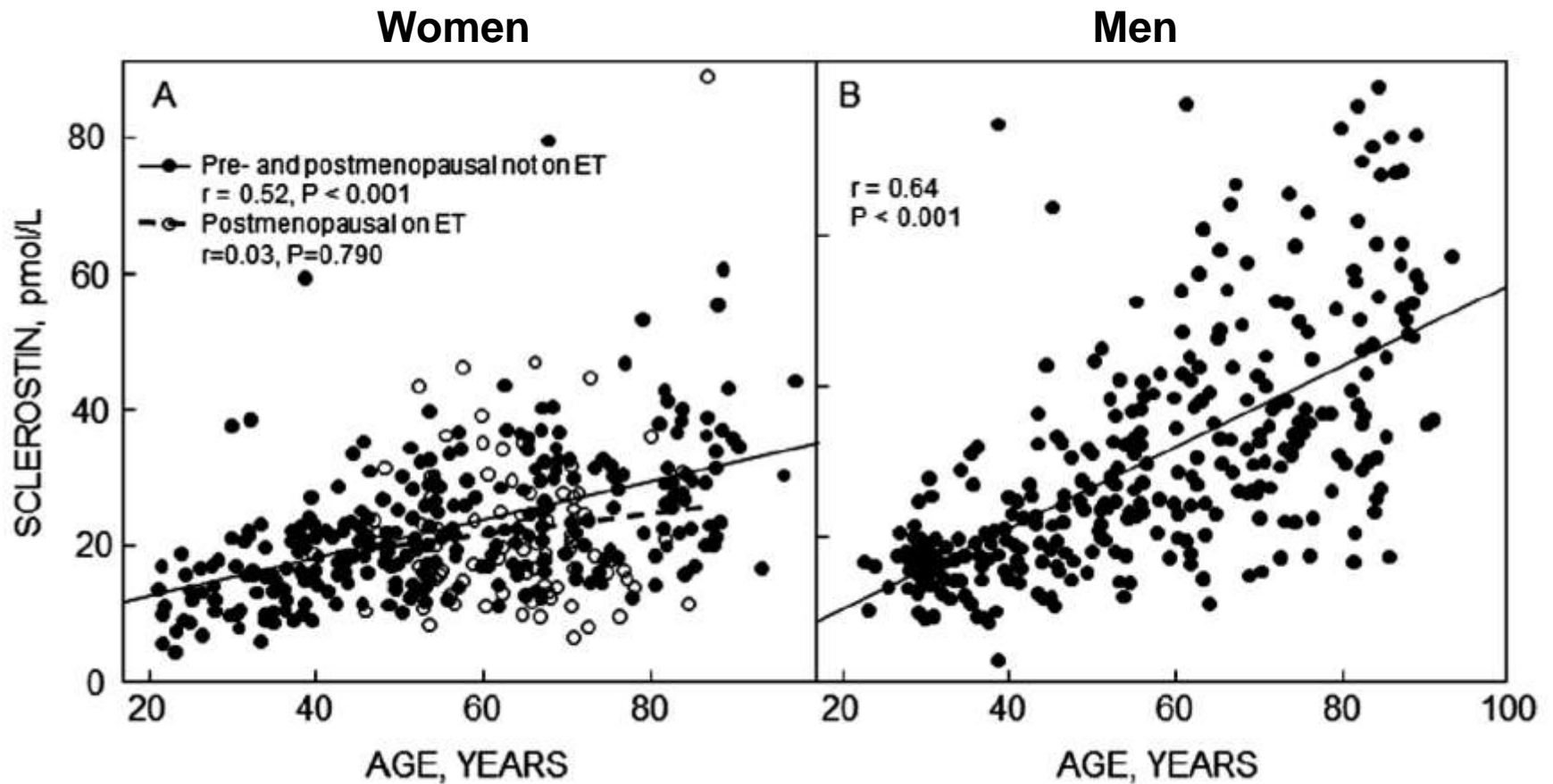
# BMD in elderly men according to quartiles of bioavailable estradiol: The MINOS study



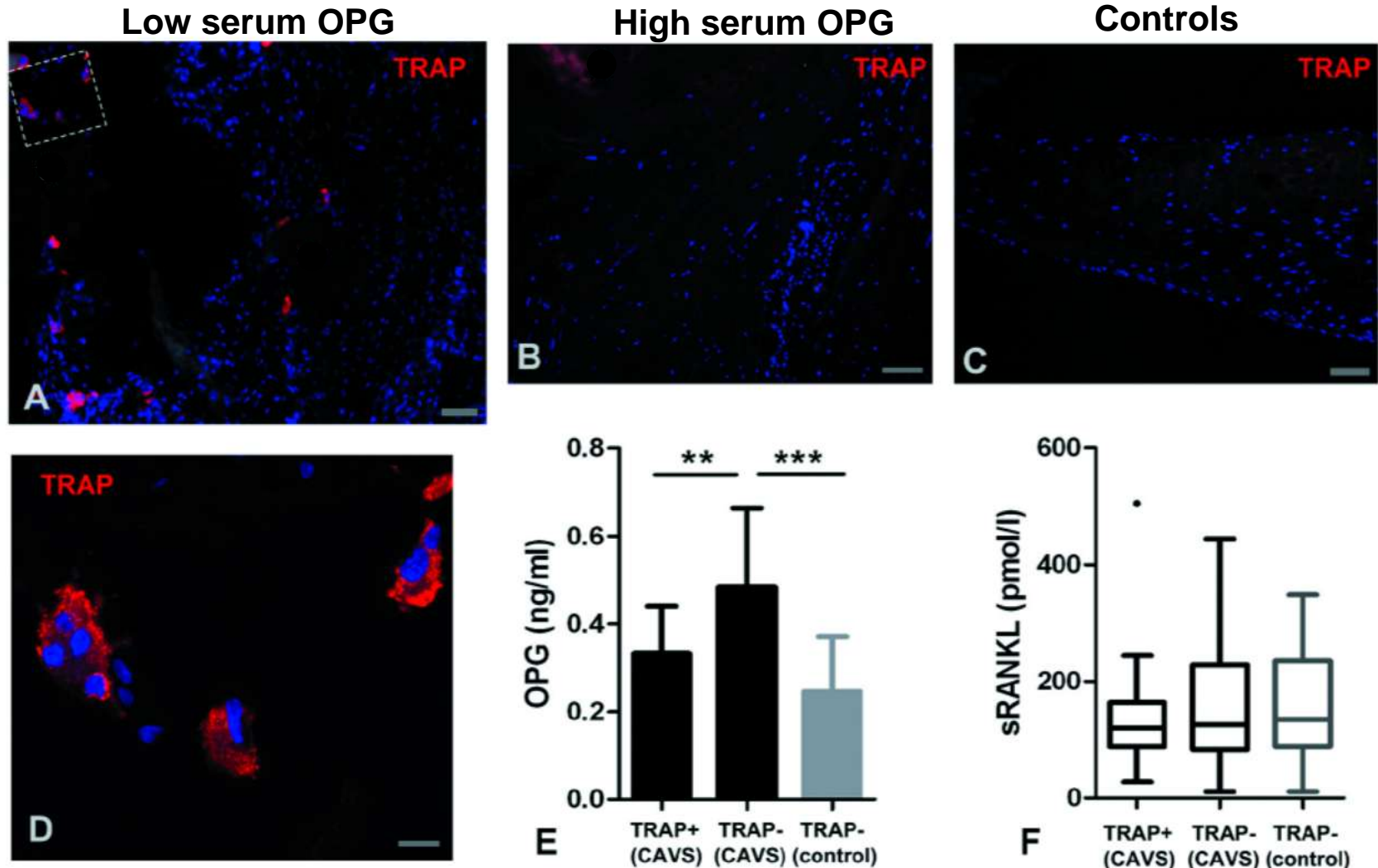
# Load Regulates Bone Formation and Sclerostin Expression through a TGF $\beta$ -Dependent Mechanism



# Serum sclerostin levels increase markedly with age in women and in men



# Serum osteoprotegerin and presence of osteoclasts in human stenotic aortic valves



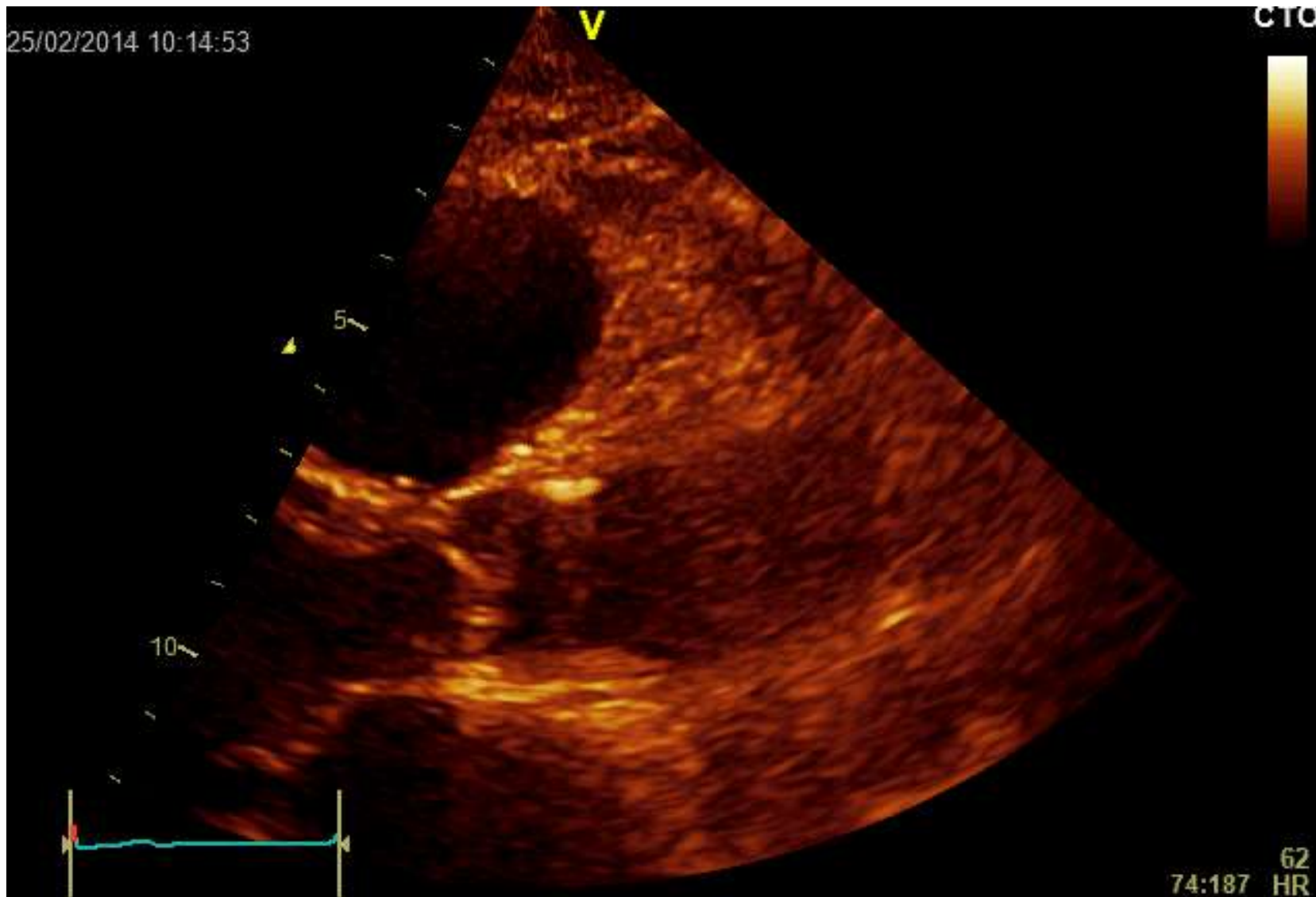
# Reciprocal Relations of Subcutaneous and Visceral Fat to Bone Structure and Strength

	Standardized coefficient	SE	<i>P</i> value	95% CI
<b>Femoral CSA (cm<sup>2</sup>)</b>				
Subcutaneous fat (cm <sup>2</sup> )	0.437	0.13	<0.001	0.19 to 0.69
Visceral fat (cm <sup>2</sup> )	-0.323	0.11	0.005	-0.54 to -0.10
<b>Femoral CBA (cm<sup>2</sup>)</b>				
Subcutaneous fat (cm <sup>2</sup> )	0.419	0.12	0.001	0.17 to 0.67
Visceral fat (cm <sup>2</sup> )	-0.371	0.11	0.001	-0.59 to -0.15
<b>Principal moment, maximum (cm<sup>4</sup>)</b>				
Subcutaneous fat (cm <sup>2</sup> )	0.400	0.13	0.002	0.15 to 0.65
Visceral fat (cm <sup>2</sup> )	-0.336	0.11	0.004	-0.56 to -0.11
<b>Principal moment, minimum (cm<sup>4</sup>)</b>				
Subcutaneous fat (cm <sup>2</sup> )	0.393	0.13	0.003	0.13 to 0.65
Visceral fat (cm <sup>2</sup> )	-0.287	0.12	0.014	-0.52 to -0.06

**Epicardial adipose tissue: emerging  
physiological, pathophysiological  
and clinical features**

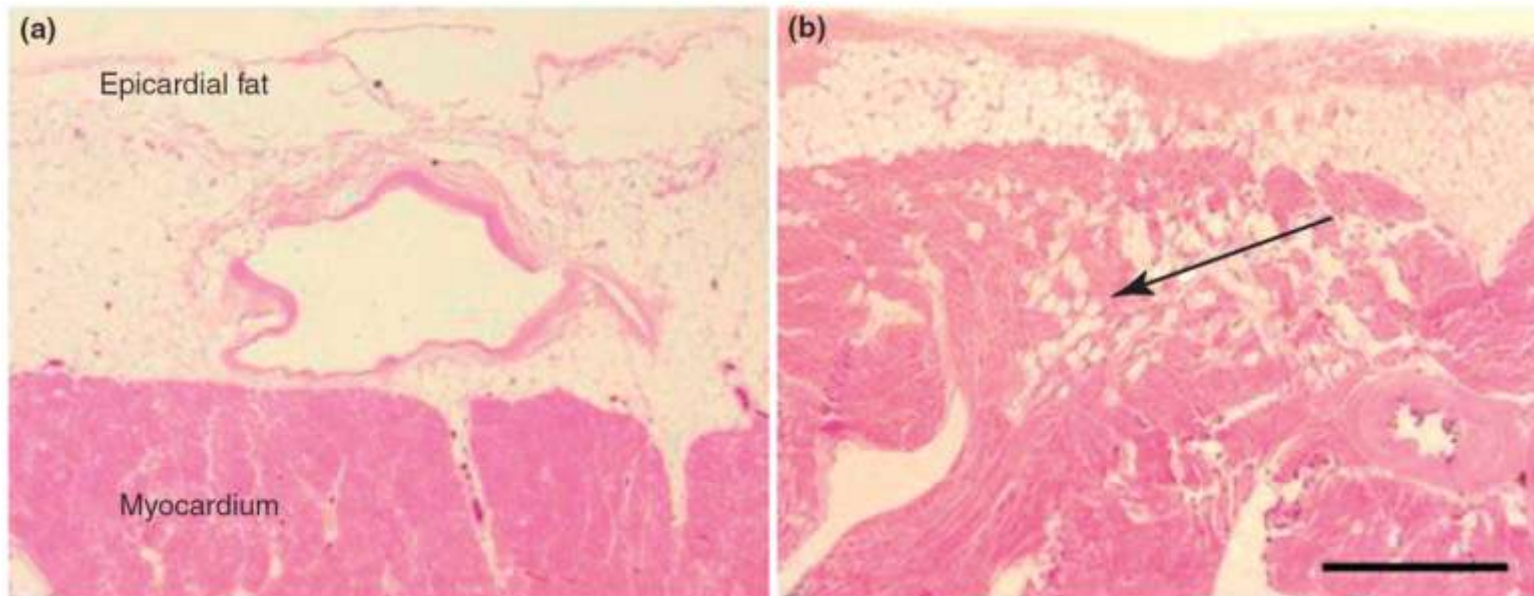
**A role for the pathogenesis of aortic  
stenosis?**

# Epicardial adipose tissue

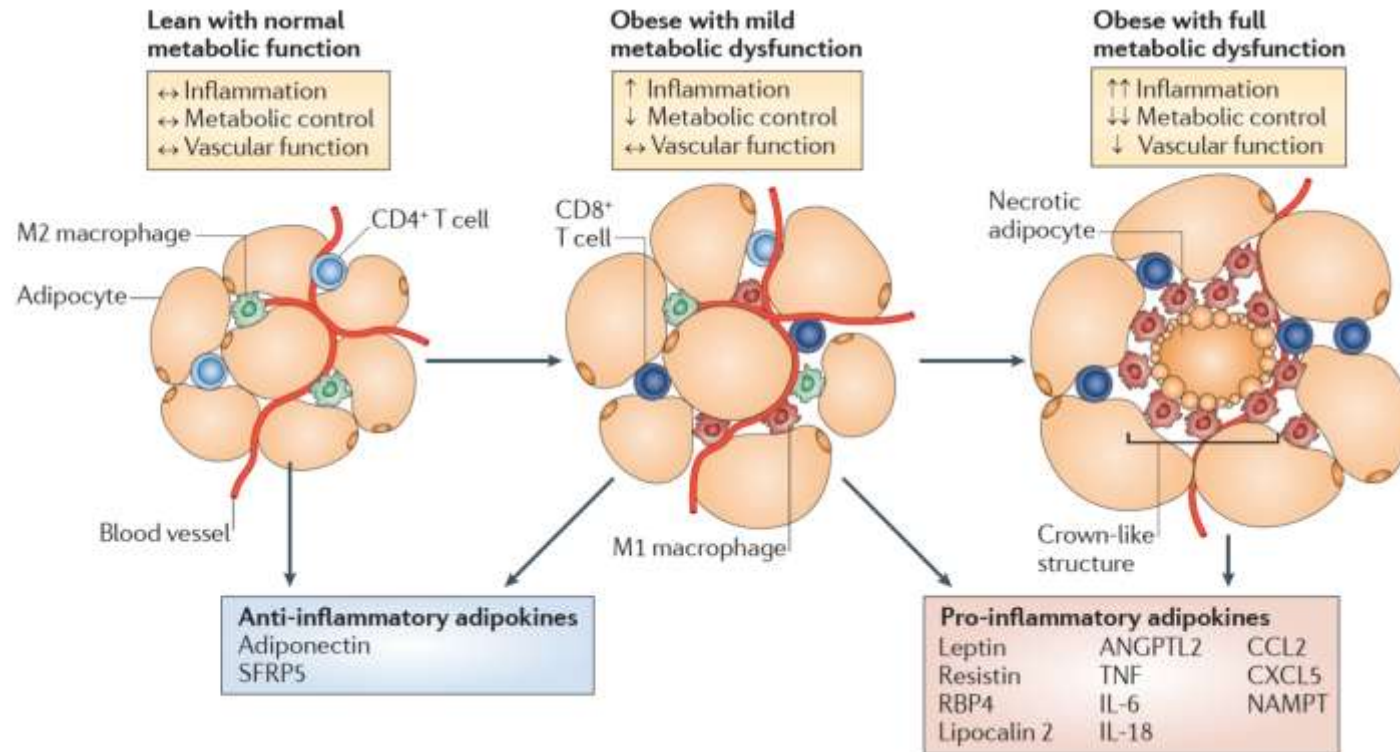
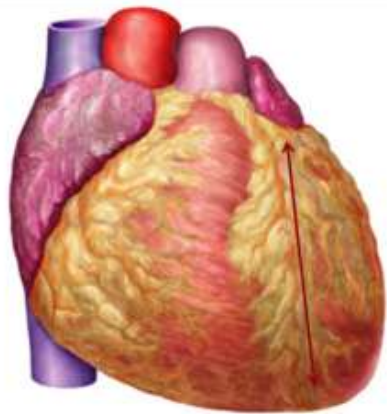


# No fascial structure divides the epicardial adipose tissue from the myocardium

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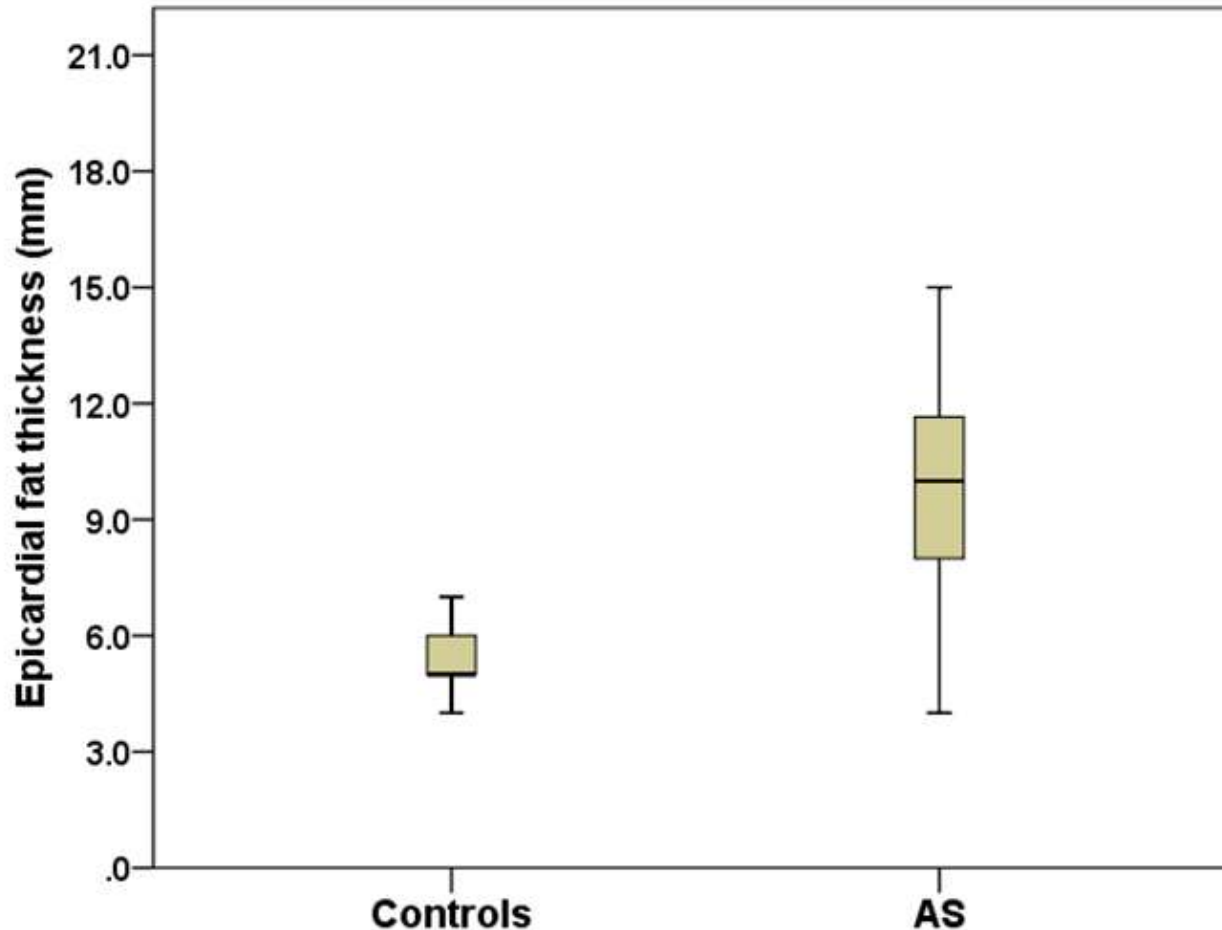


# Physiological, pathophysiological mechanisms and vasocrine/paracrine pathways of epicardial fat



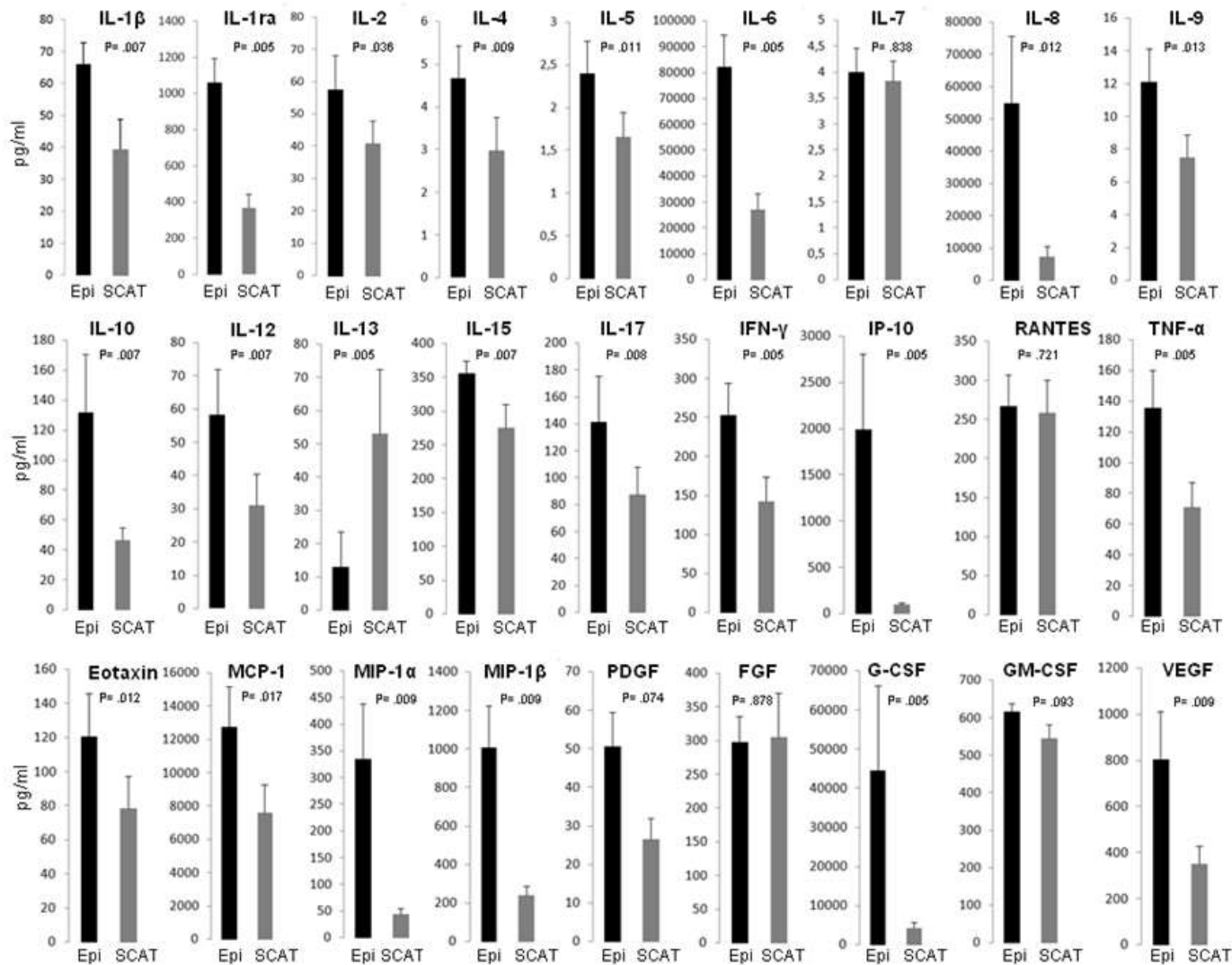
# Epicardial adipose tissue is increased in pts with calcific aortic stenosis

## Echocardiographic EAT thickness



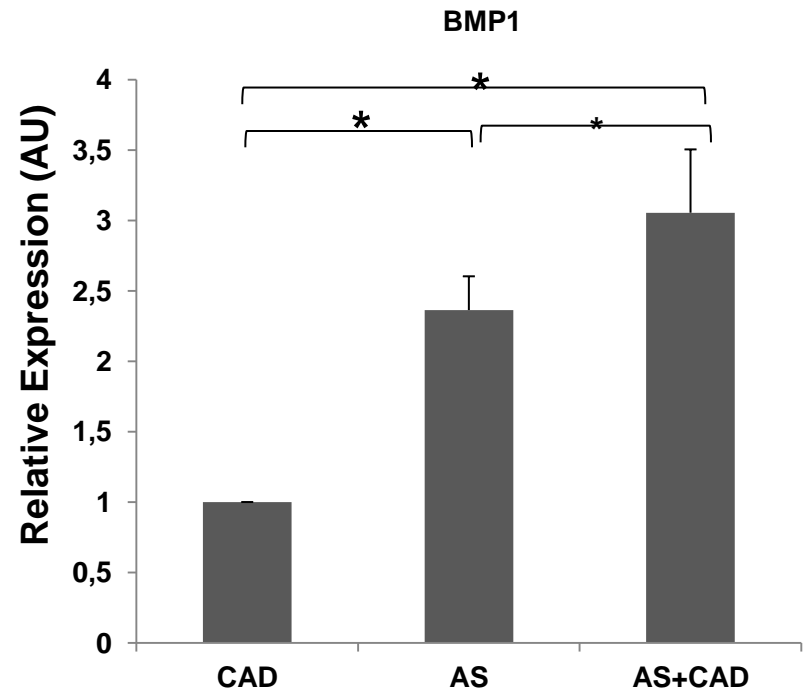
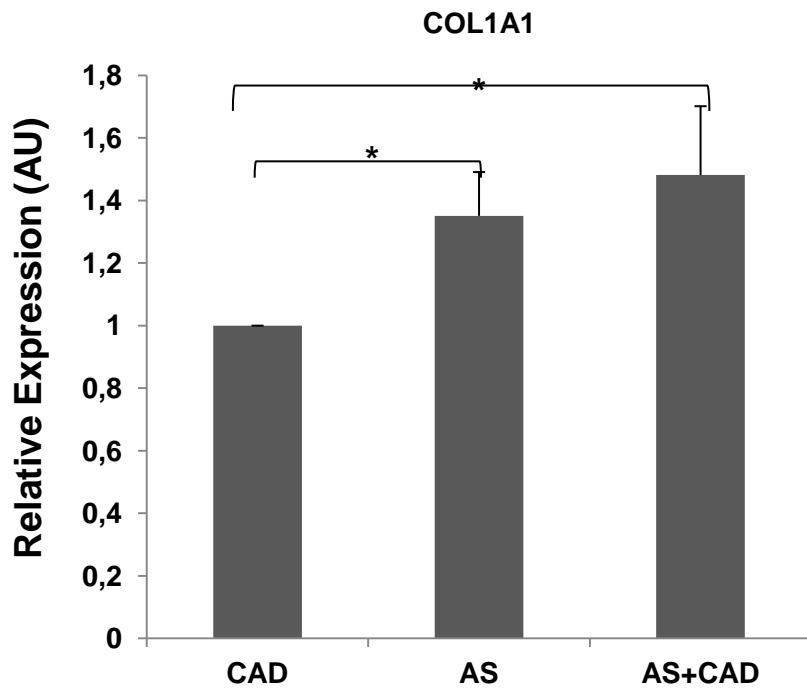
*Personal in progress data*

# Inflammatory mediators levels in EAT and SCAT secretomes in pts with aortic stenosis



*Personal in progress data*

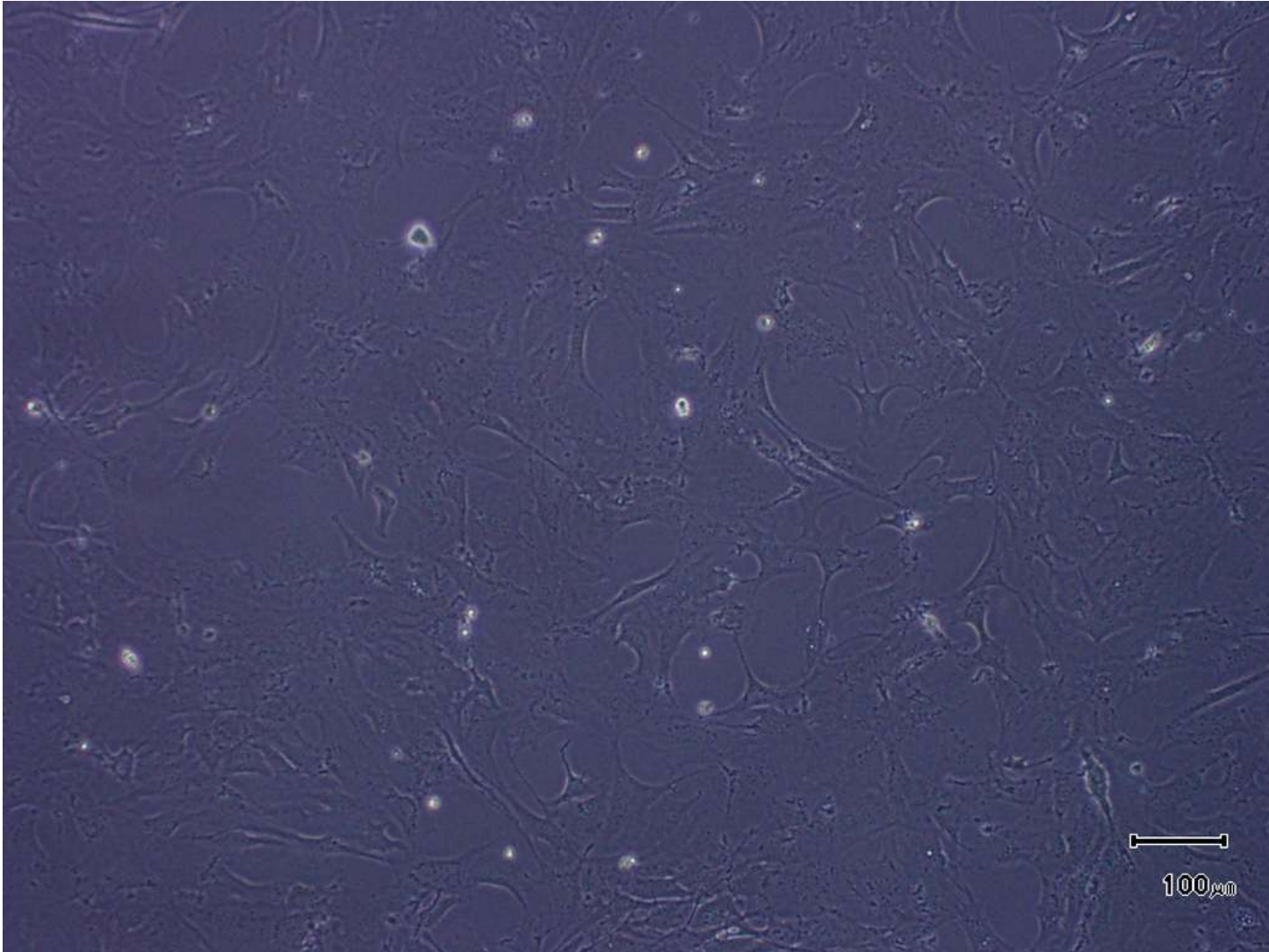
# Expression of osteogenic markers in EAT of pts with calcific AS



*Personal in progress data*

# Human myofibroblasts isolated from a severely calcified aortic valve

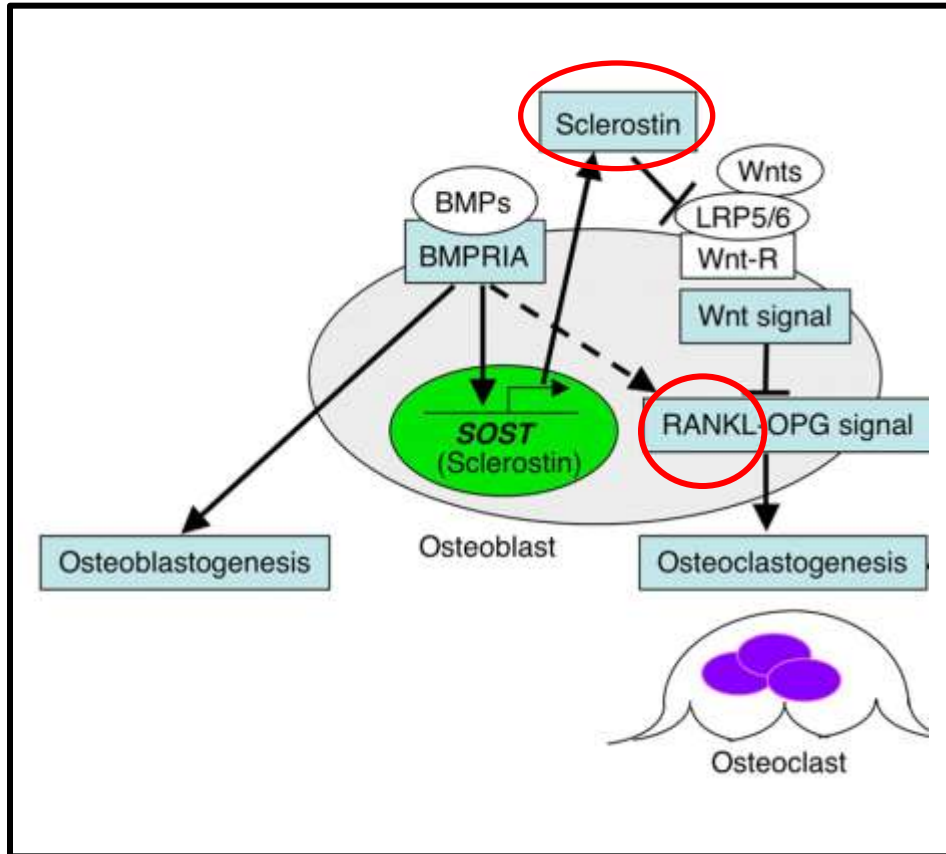
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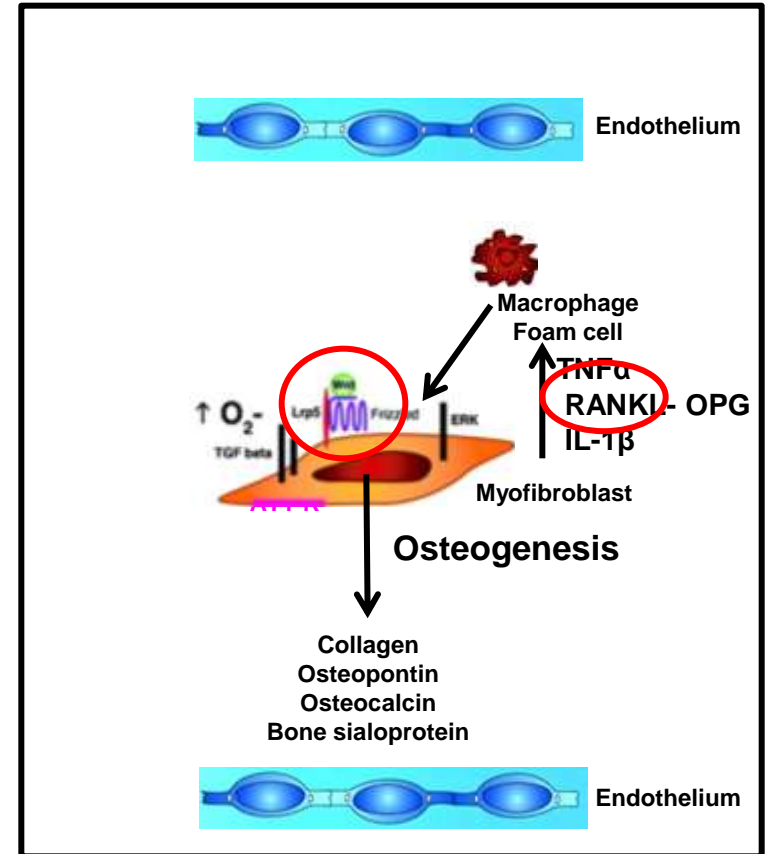
*Personal in progress data*

# Molecular Mechanisms Potentially Involved in the Bone Paradox and Future Molecular Targets

## Bone



## Aortic Valve



# Regular Exercise Training Prevents Aortic Valve Disease

