

Role of Vitamin K in arterial calcifications and cardiovascular diseases

Leon J Schurgers, PhD
Department of Biochemistry
Maastricht University
The Netherlands

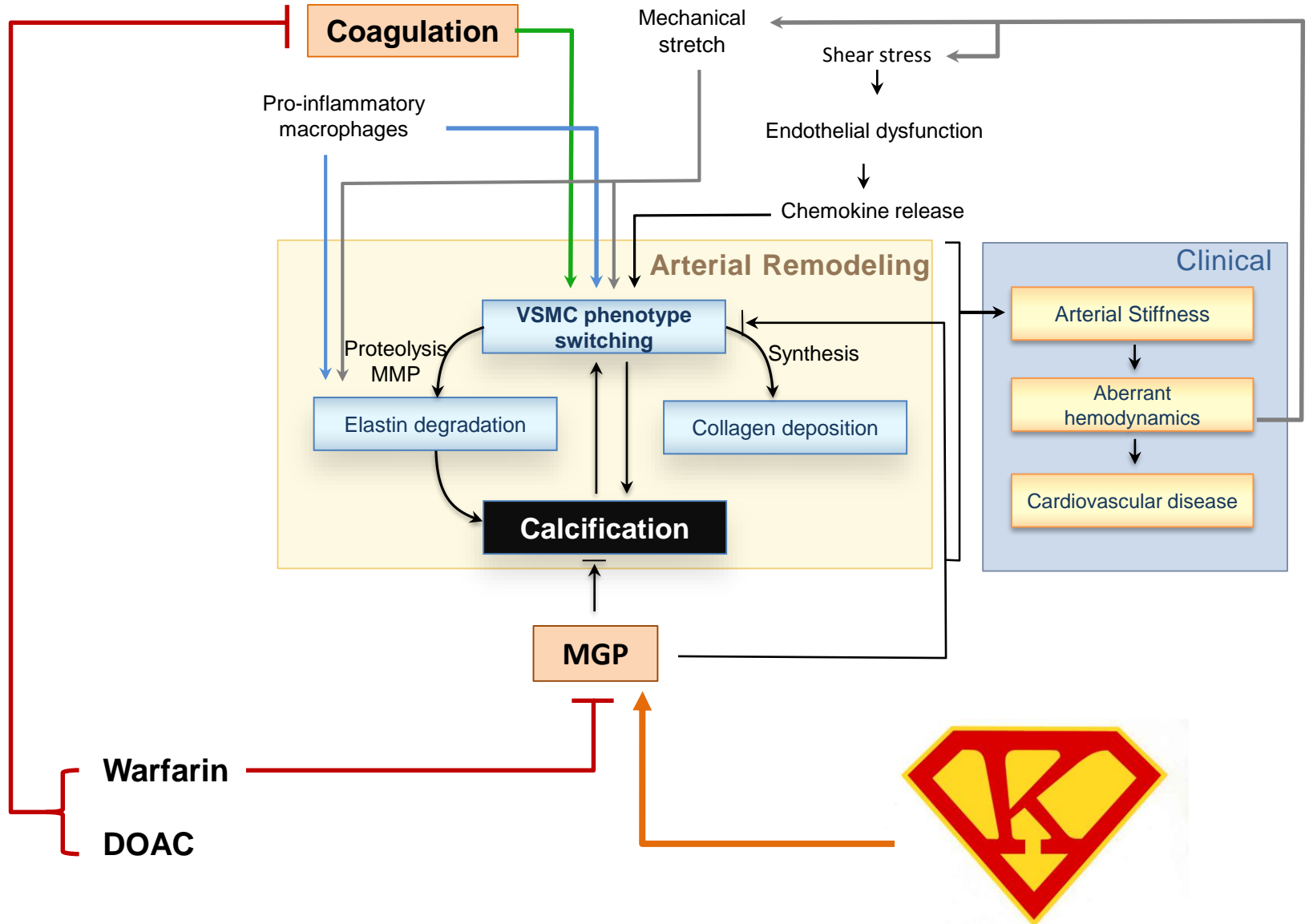
Artery, Pisa, October 13th 2017



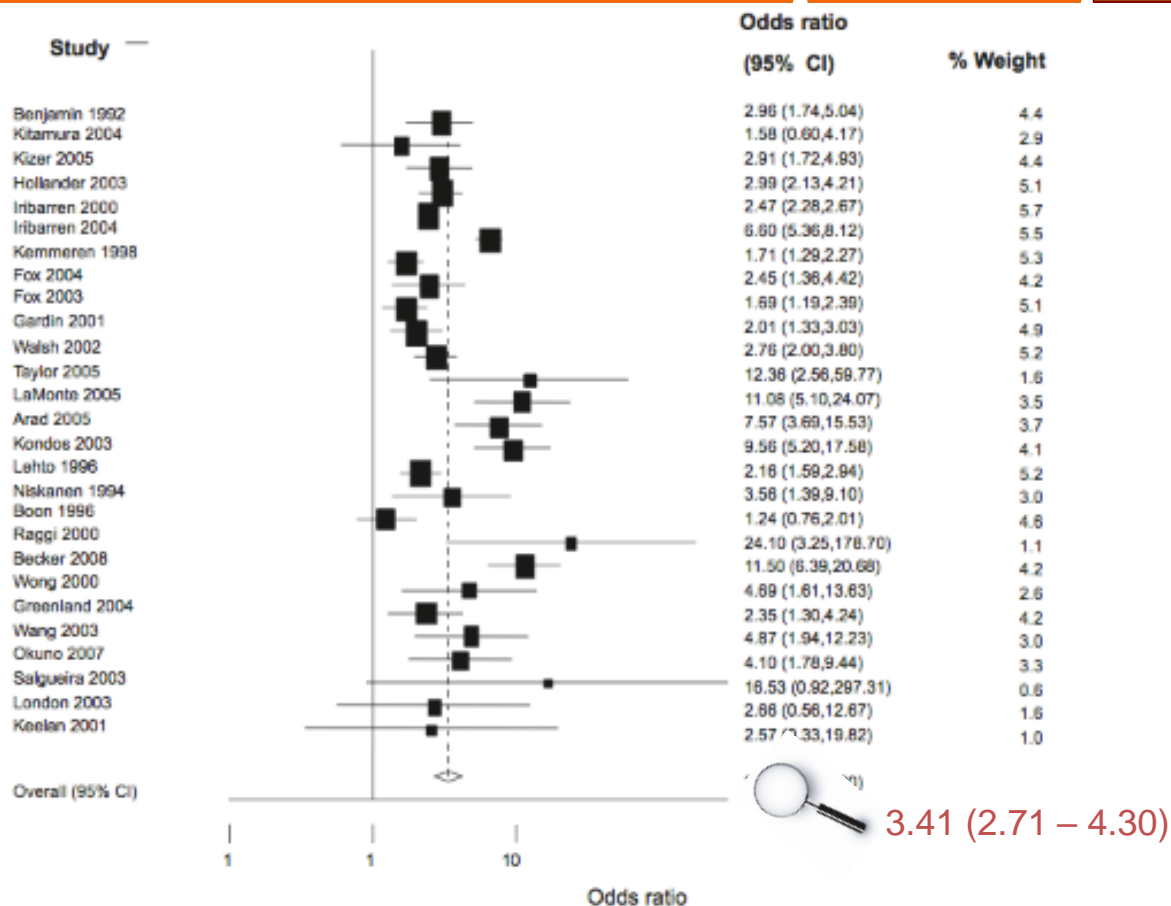
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Conclusions



Vascular calcification as marker of increased CVD



Rennenberg et al. Vascular health and risk management 2009

Coronary artery calcium is a better predictor of cardiovascular events than the Framingham risk score and can help to reclassify asymptomatic individuals into high-risk or low-risk categories

Alexopoulos et al. Nature Reviews Cardiology 2009

Calcification is passive process

Calcif Tissue Int (1994) 54:224-230

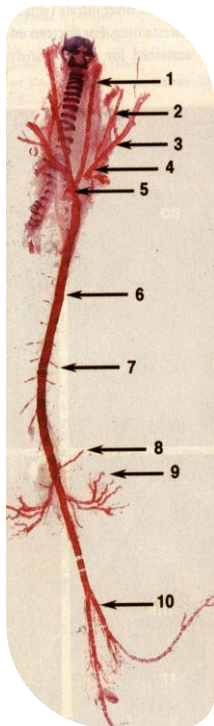
Calcified
Tissue
International
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Coronary Arterial Calcification as an Active Process: A New Perspective on an Old Problem

T. M. Doherty, R. C. Detrano

Division of Cardiology, Harbor-UCLA Medical Center, and Saint John's Cardiovascular Research Center, Torrance, California, USA

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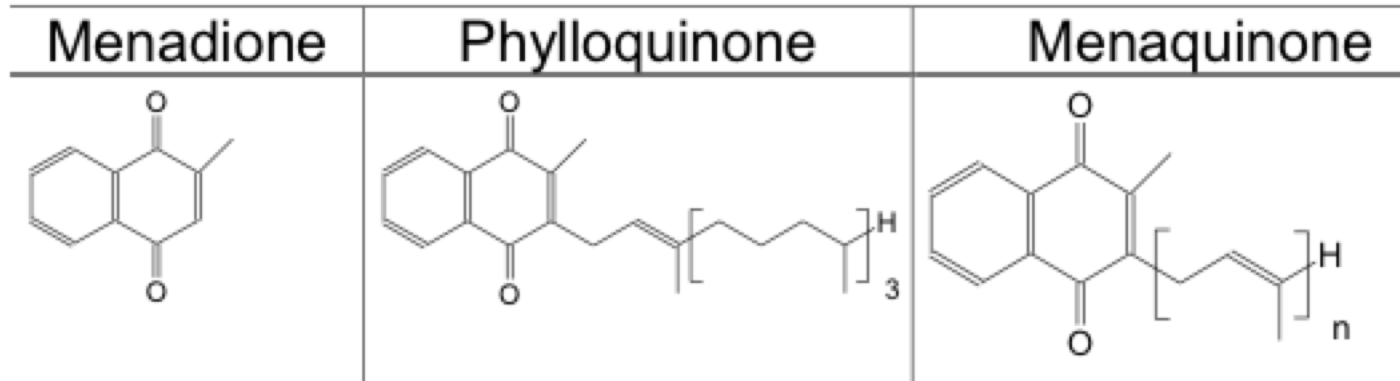
Matrix Gla-protein (MGP)

- Vitamin K-dependent protein
- 84 amino acids (Mw ~11 kD)
- Gla-residues (required for activity)

Abstract. The mechanism and purpose of coronary atherosclerotic calcification remain unknown. However, evidence reviewed here suggests that calcification is not passive precipitation or adsorption, but instead is organized and regulated. Gla containing proteins and other proteins normally associated with bone metabolism appear to play an important role in this process. A variety of studies are currently in progress in our laboratory which we hope will provide a more comprehensive understanding of processes leading to coronary calcification as well as prognostic data useful in clinical cardiology practice. A clearer understanding of the nature and significance of coronary calcification may well pave the way toward new interventions to protect myocardium and minimize the morbidity and mortality associated with coronary artery disease.

Key words: Coronary calcification — Bone proteins

Vitamin K



Vitamin K1



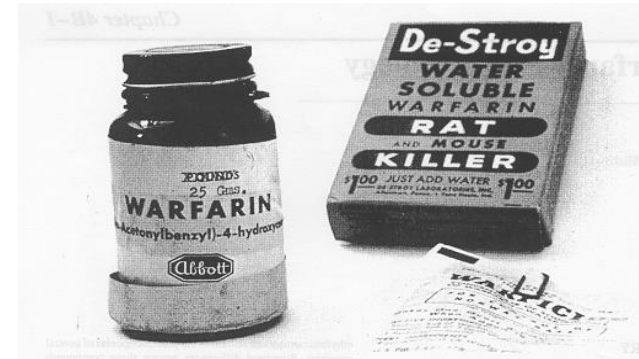
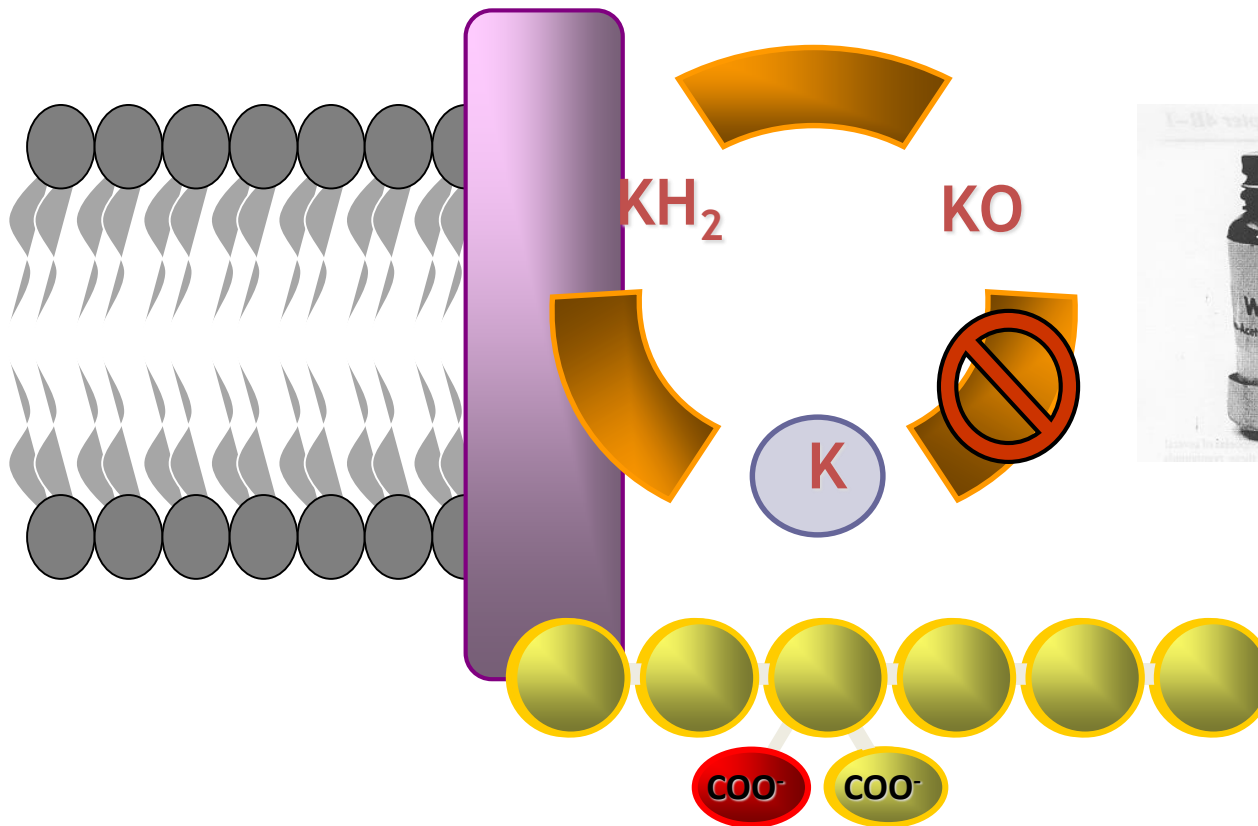
Vitamin K2

THE FRENCH PARADOX
what is the secret?

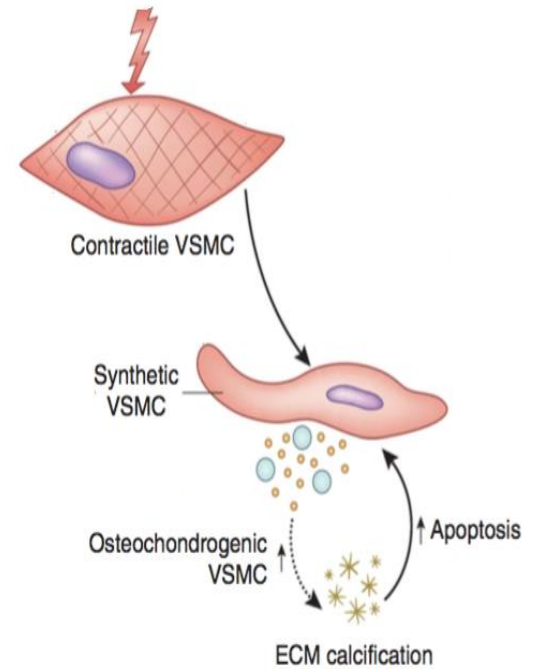
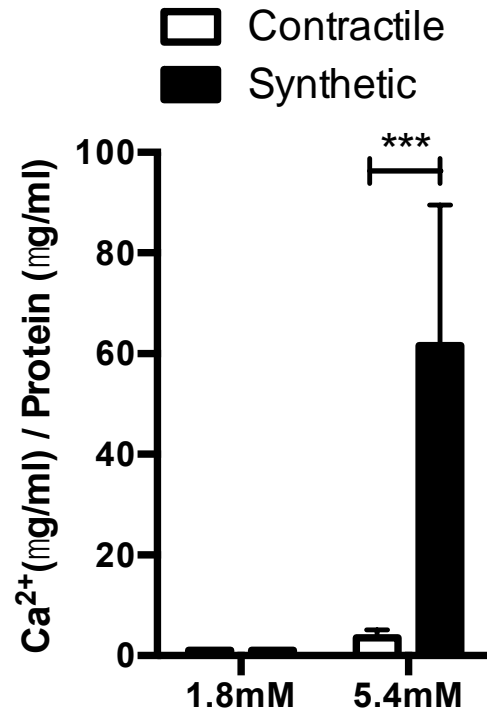
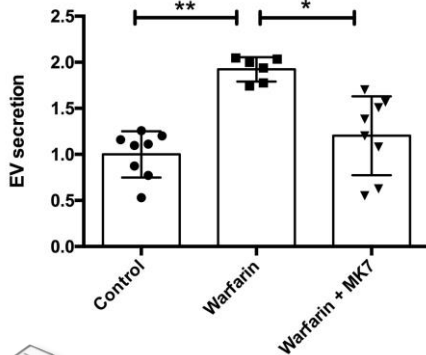
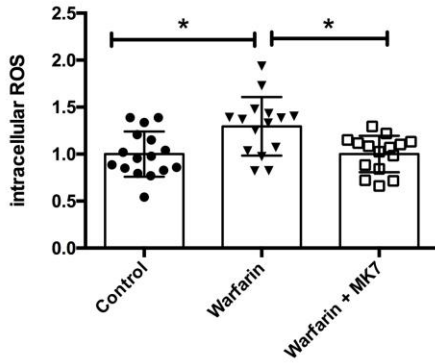
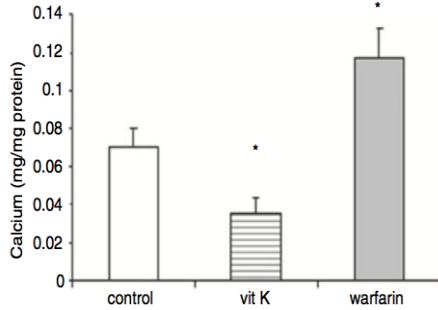


Jean vs. Joe

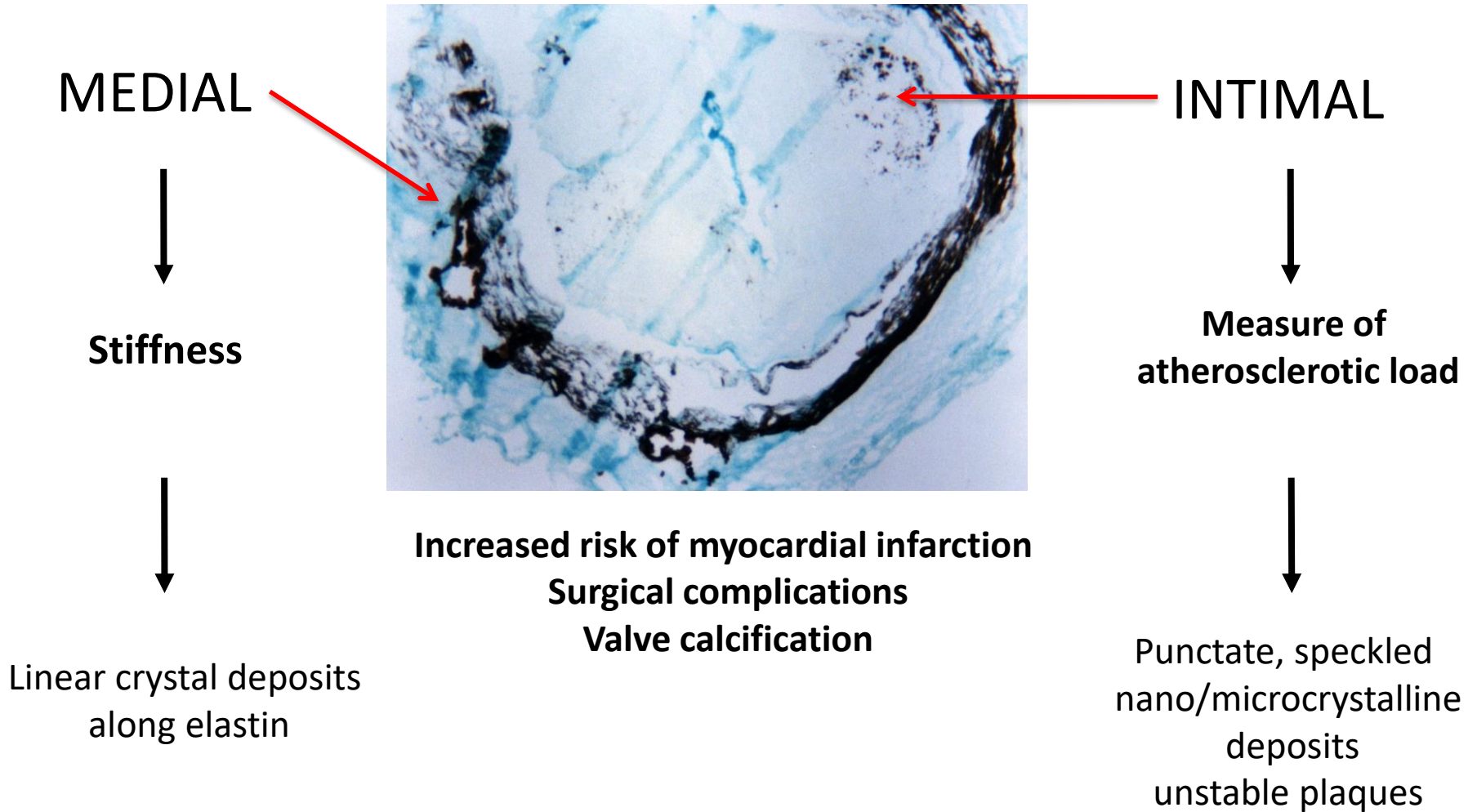
Vitamin K-metabolism



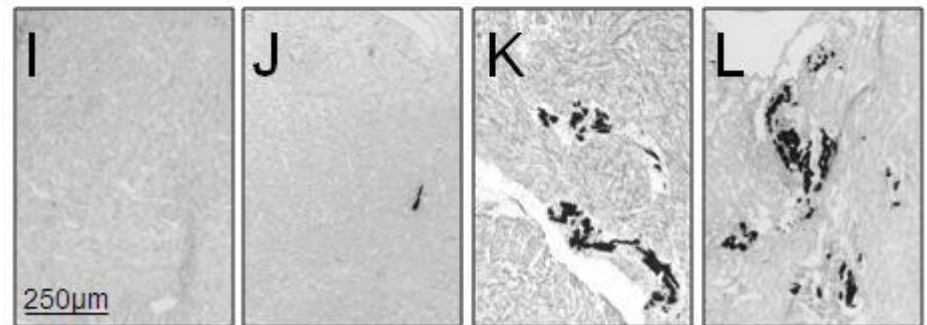
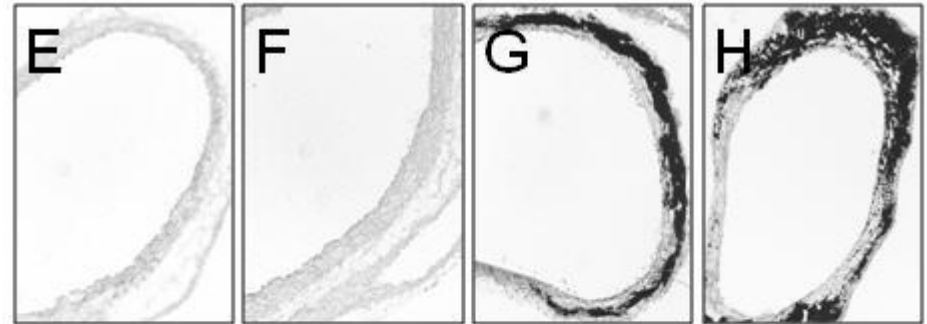
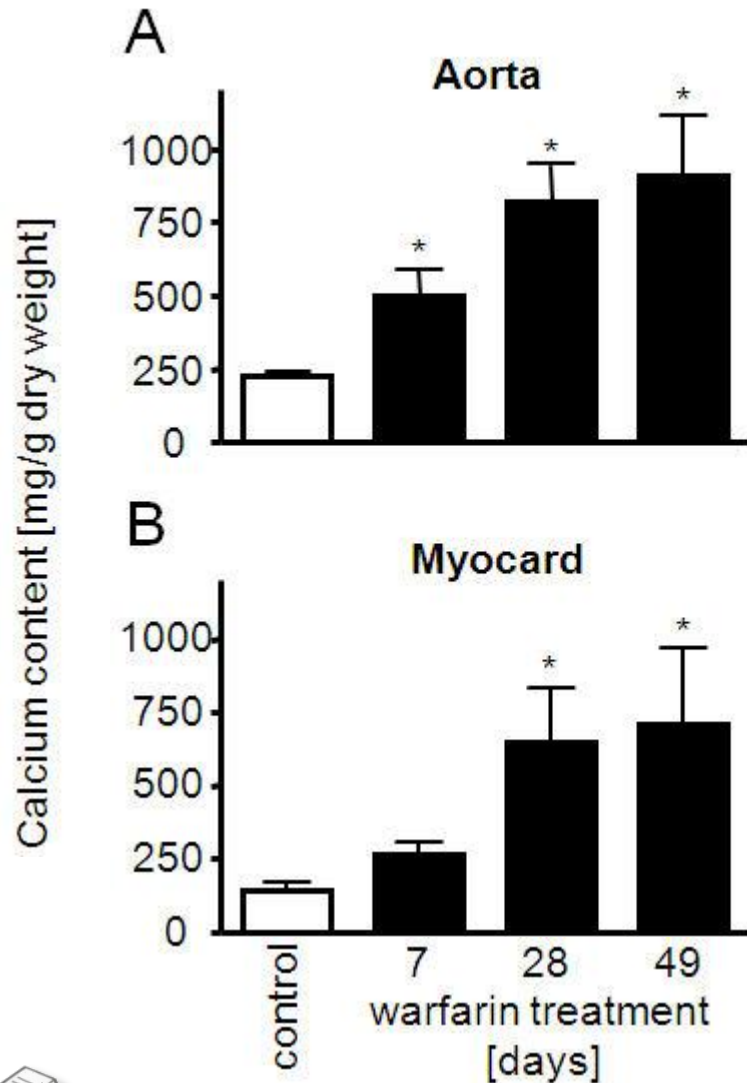
Vascular calcification is mediated by VSMC phenotypic switching



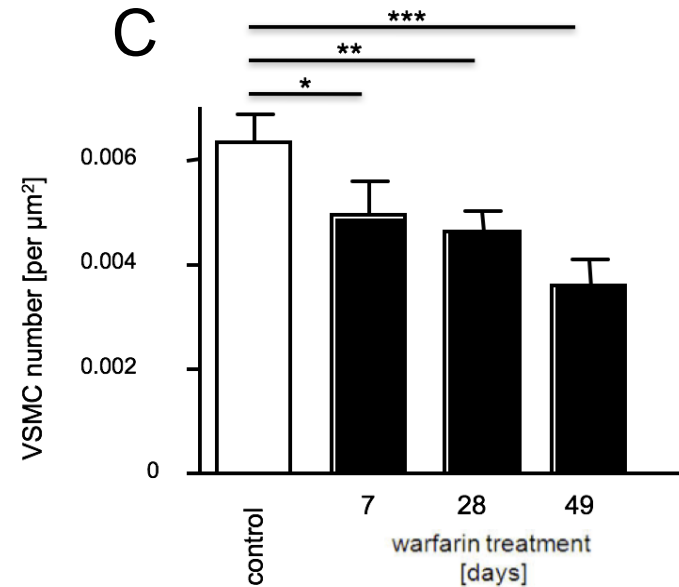
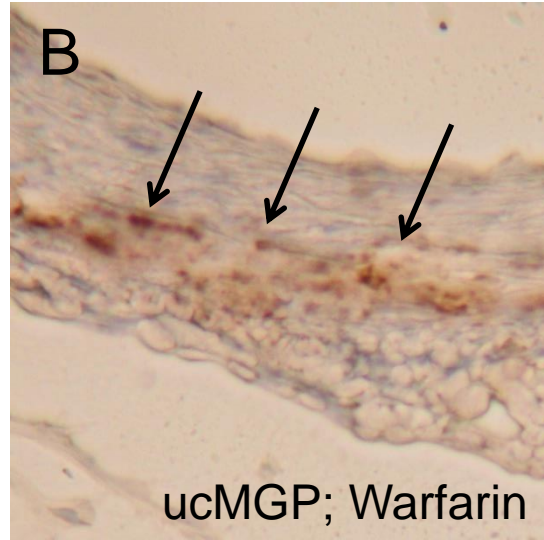
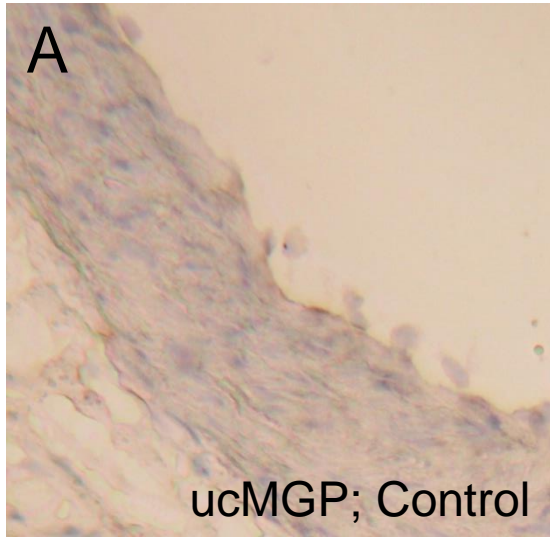
Medial vs intimal calcification



Influence of VKA on medial calcification



Influence of VKA on medial calcification



Control

28 days warfarin

49 days warfarin

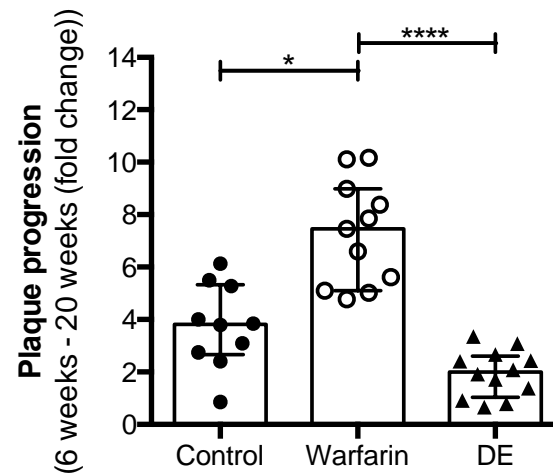
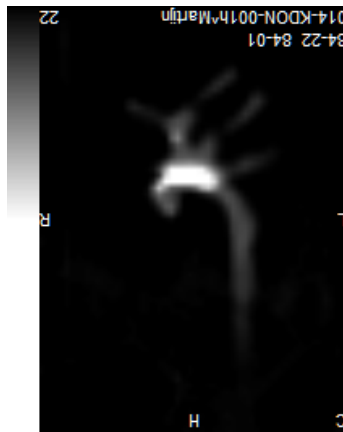
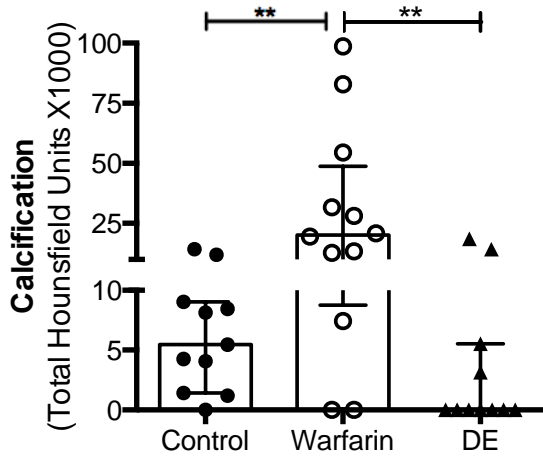
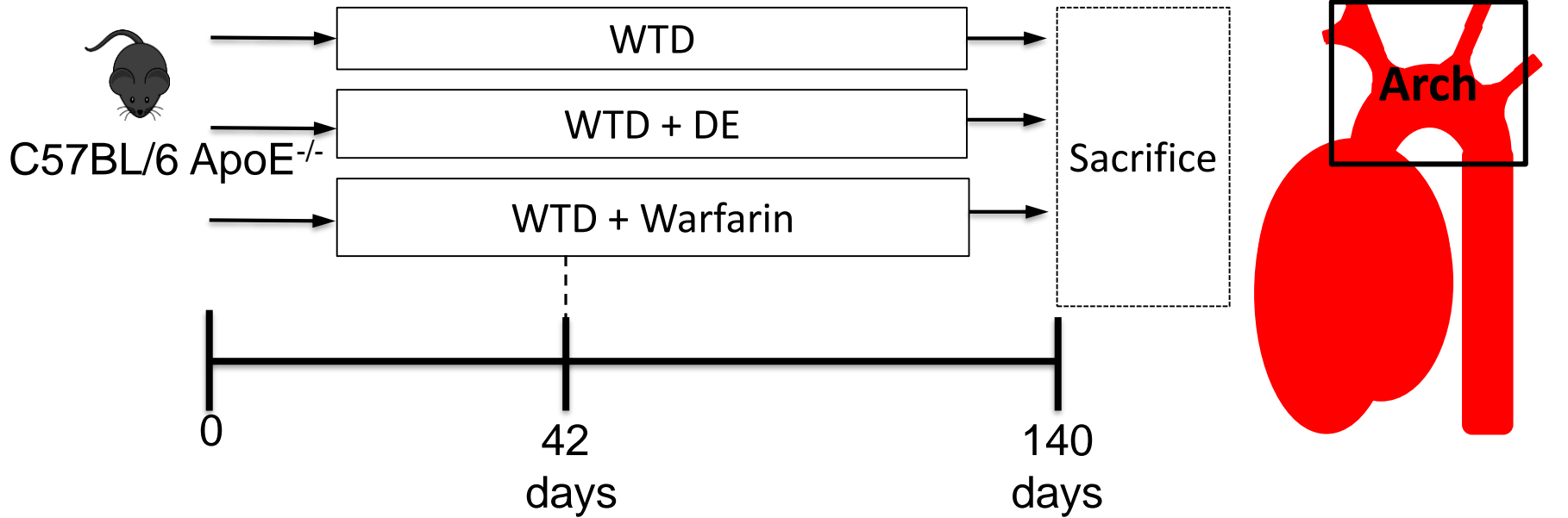
Aortic valve

Oral anticoagulation results in medial vascular calcification, associated with vascular smooth muscle cell loss and parameters of vascular stiffening

pulse wave velocity [m/s]

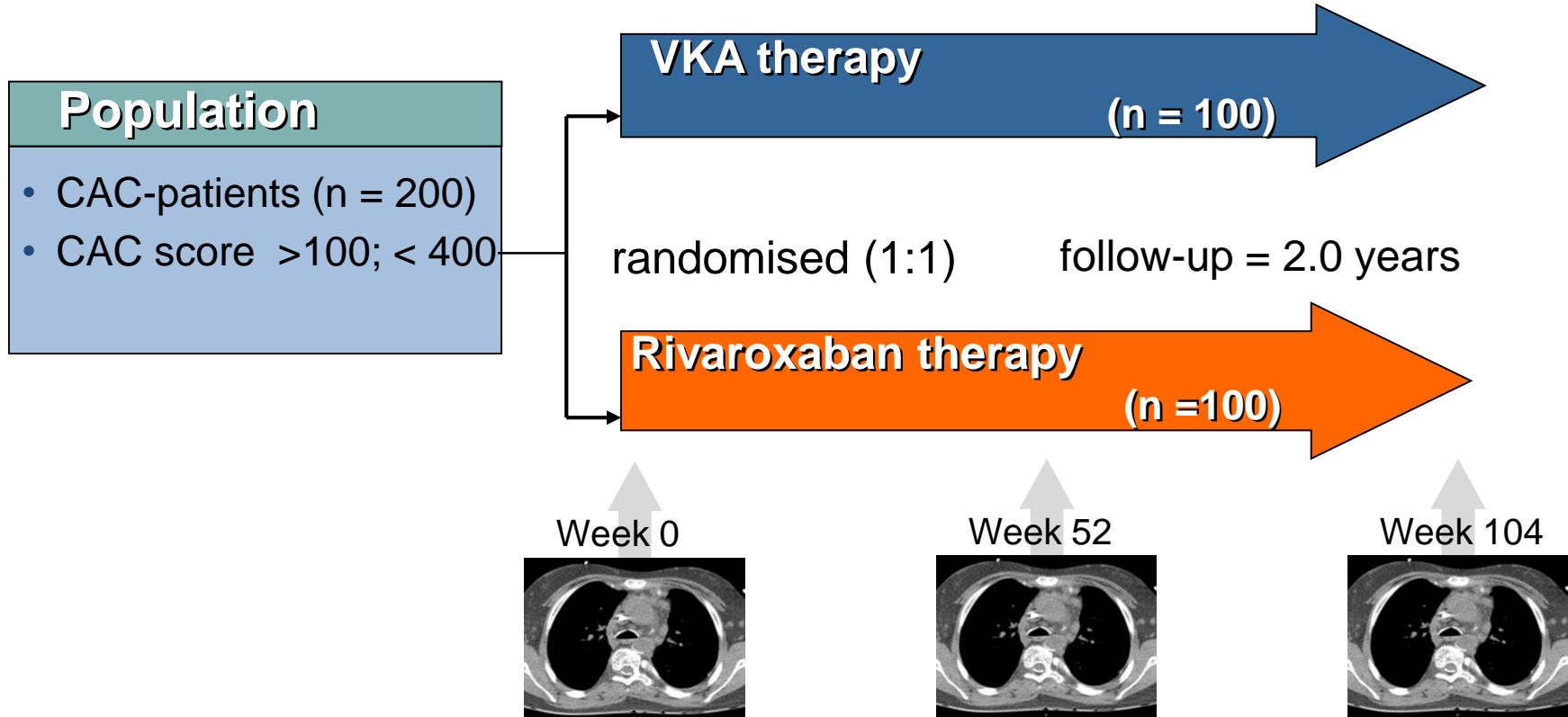


Influence of VKA on atherosclerosis





VKA - Rivaroxaban - Design -



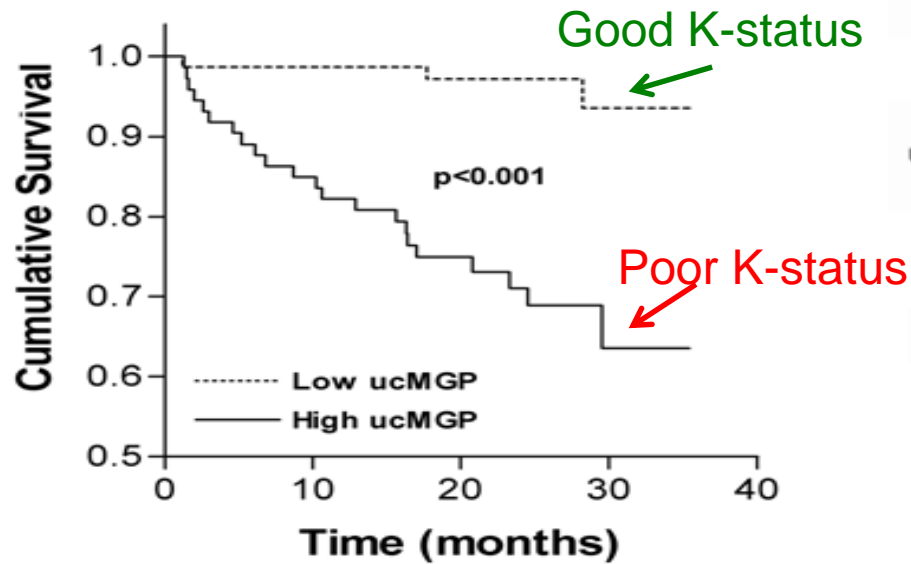
End points:

primary = progress of coronary calcification

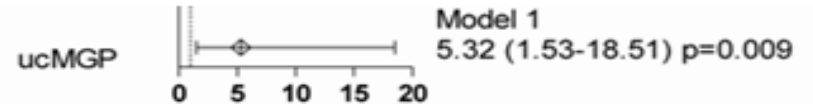
secondary = vascular stiffness and biomarkers

Vitamin K status in patients having AS

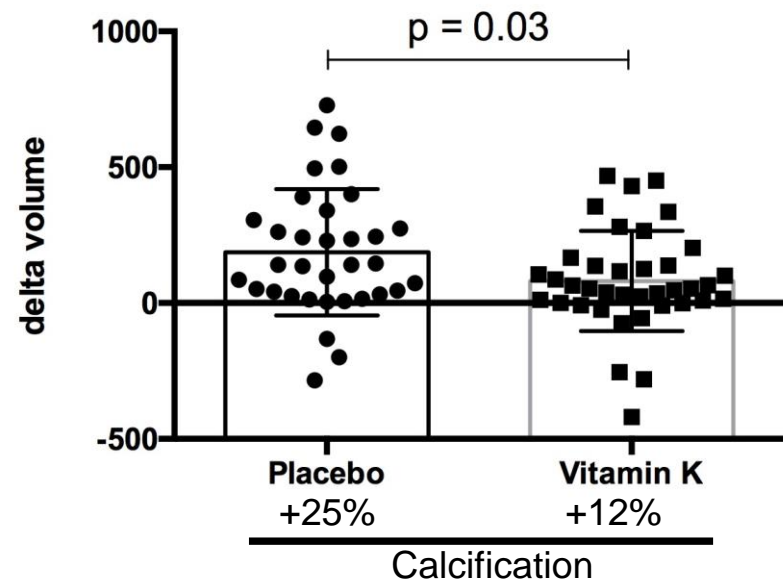
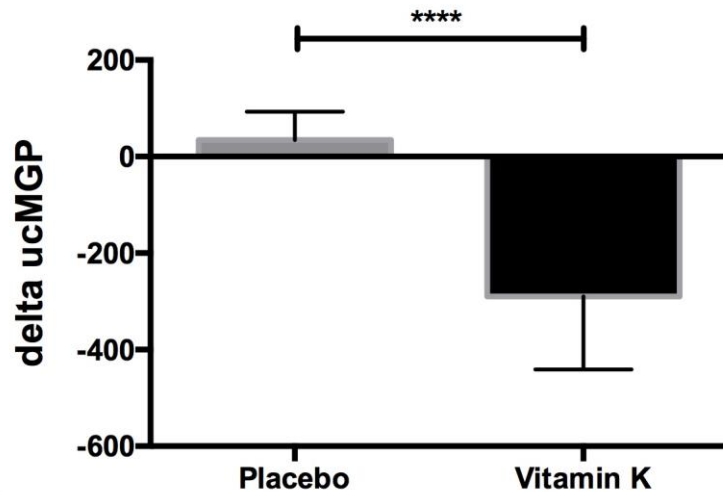
149 aortic stenosis patients
Age 74 years, 55% male
Cardiac index / HF, outcome (death)



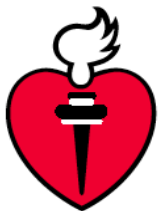
-vitamin K antagonists



Less progression of AVC by vitamin K

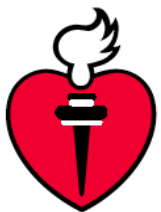


Brandenburg et al. Circulation 2017



**VitaK-CAC
Study**
- Design -

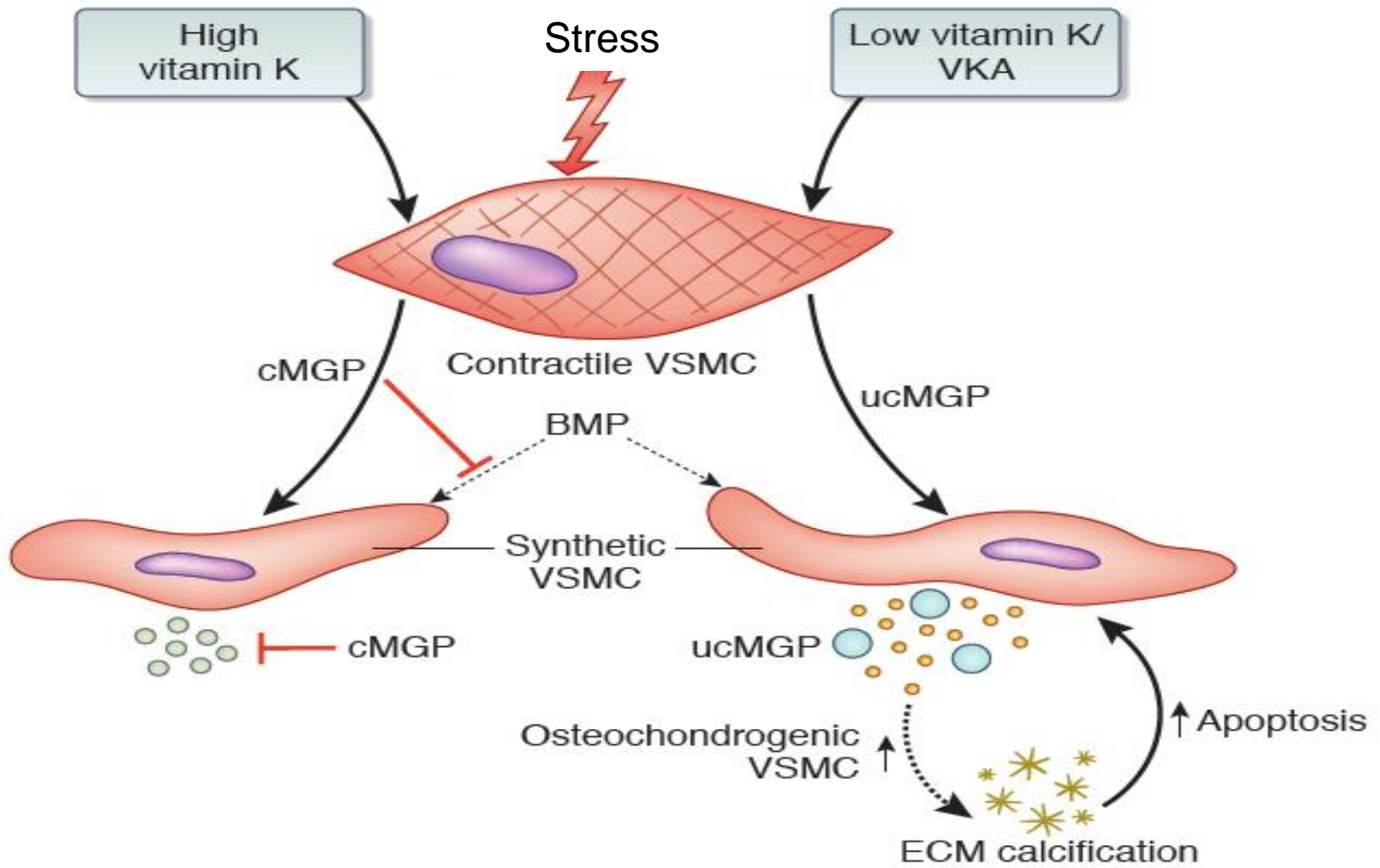
Placebo (n=100) vs Vitamin K2 (n=100)
2 year treatment
Primary readout: **progression calcification**
Measured with CT



BASIK2
- Design -

Placebo (n=20) vs Vitamin K2 (n=20)
1 year treatment
Primary readout: **progression valve calcification**
Measured with PET/MRI en CT

What did Leon say...?





Nederlandse Hartstichting

TRIMBOSESTICHTING
NEDERLAND



Boehringer
Ingelheim



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