Strategies for prevention and regression of vascular calcification: Vitamin K as novel treatment option?

Leon J Schurgers, PhD
Department of Biochemistry
Maastricht University
The Netherlands
The realm of vitamin K dependent proteins: Shifting from coagulation toward calcification.

Chatrou et al. Blood Reviews 2012; Willems et al. MFNR 2013
Vascular calcification as a marker of increased cardiovascular risk: a meta-analysis

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.
Matrix Gla-protein (MGP)

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

Warfarin causes rapid calcification of the elastic lamellae in rat arteries.

Warfarin induced artery calcification is promoted by increases in serum calcium or phosphate. Strong upregulation of MGP at sites of calcification, though in the inactive uncarboxylated form.
Low-risk AF patients on VKA treatment

Weijs et al. Eur Heart J 2011
If vitamin K-antagonism induces vascular calcification, what about vitamin K-treatment?
Absorption of natural vitamin K1 from spinach and natural vitamin K2 (MK7) from natto

Schurgers, LJ et al. Haemostasis 2000
Influence of VKA on medial calcification: time dependency

Influence of vitamin K status on medial calcification

![Graph showing the influence of vitamin K status on medial calcification. The x-axis represents Warfarin concentration [mg/g] with 0, 0.03, 0.3, and 3 mg/g, and the y-axis represents a unitless scale for Aorta. Different concentrations of Vitamin K1 [mg/g] are shown, with the highest concentration being 1.5 mg/g. The bars indicate a significant increase in calcification with increasing Warfarin concentration.]
Vitamin K-deficiency in dialysis

188 CKD5D patients

PIVKA-II (ng/mL)

Normal range

>80 % deficiency!

Schlieper et al; JASN 2011
VitaK-CAC Study
- Design -

Population
- CAC-patients (n = 200)
- Not on VKA
- CAC score >100; < 400

Standard therapy + placebo (n = 100)
randomised (1:1) follow-up = 2.0 years

Standard therapy + Vitamin K2 – MK7 (360) (n = 100)

Week 0
Week 52
Week 104

- End points: primary = progress of coronary calcification
  secondary = vascular stiffness and biomarkers
Acknowledgements

Chris Reutelingsperger
Roger Rennenberg

Juergen Floege
Willi Jahnen-Dechent
Vincent Brandenburg
Thilo Krueger
Georg Schlieper
Ralf Koos

Catherine Shanahan
Alexander Kapustin
Rukshana Shroff

Martin Shearer

Ralf Westenfeld