Warfarin-induced vascular calcification: Underlying cellular mechanisms and effects on bone mineralization

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Background and Aim
Vascular calcification is considered to be an important risk factor for the cardiovascular morbidity and mortality in CKD patients. Loss of calcification inhibitors (such as matrix gla protein, MGP) is one of the mechanisms responsible for the development of vascular calcification in the media of the vessel wall.

Materials and Methods

Rat strains
Wistar rats (n=30)

Sacrifice
At 4, 6, 8 and 10 weeks

Analyses:
• Bulk calcium analysis (by flame atomic absorption spectrometry)
• % calcified area (von Kossa staining)
• Aortic mRNA expression (q-rt PCR)
• Bone histomorphometry

Results

Development of vascular calcifications

Aortic calcium content (calcium bulk analysis)

- Statically significant increase in calcium content at all time-points compared to control.
- 50 fold increase in calcium content in rats treated 10 weeks with warfarin diet, compared to controls.
- Time-dependent increase in severity of vascular calcification

Percentage of calcified tissue (von Kossa staining)

- In line with calcium bulk analysis
- Clear medial localization

Effect on the bone

Bone area (%)
Trabecular number
Trabecular space

Warfarin has a mild impact on bone histomorphometry
• Significant changes in bone area, trabecular number and trabecular space
• Other bone parameters are unchanged (osteoid area, mineral apposition rate, bone formation rate, ...)

Conclusions
Warfarin treatment leads to a time-dependent development of vascular calcification. This is associated with osteochondrogenic transdifferentiation. Warfarin has a mild impact on the bone.

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