

Vascular calcification – Impact of PRRG1-4

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Introduction and Aim

Pathophysiological calcification in the vasculature favours cardiovascular and cerebrovascular diseases. In patients with chronic kidney disease vitamin K metabolites are associated with decreased vascular calcification.

In addition to classical Vitamin K binding proteins (VKDPs), known for a long time, essential in blood coagulation or calcification of bone, exists also a group of "new" VKDPs where little information is available about active forms, systemic or tissue specific functions and associations with disease are missing. To this group of VKDPs belong the membrane bound proteins PRRG1-4.

We investigated the expression of the vitamin K dependent proteins PRRG1-4 in vessels and bone to identify differences in expression pattern during atherosclerosis (AS) stages and compare the 2 tissue profiles.

Materials and Methods

Gene expression levels of PRRG 1-4 were examined with predesigned TaqMan gene expression assays on a LC480 system in vessels (external iliac artery and aorta) and bone of 26 brain dead organ donors. Since gene expression in external iliac artery and aorta did not differ, both vessels were combined in the analysis. Beta actin was used as a reference gene and relative Cp values were obtained by division.

Determination of calcification stages was done histologically: unaffected vessels :no changes in the vessel wall, intima thickening: more than one-fold thickening of the intima without calcification, intima calcification: one or more calcification spots.

Statistics: *p<0.05; **p>0.01; *** p>0.001

Results

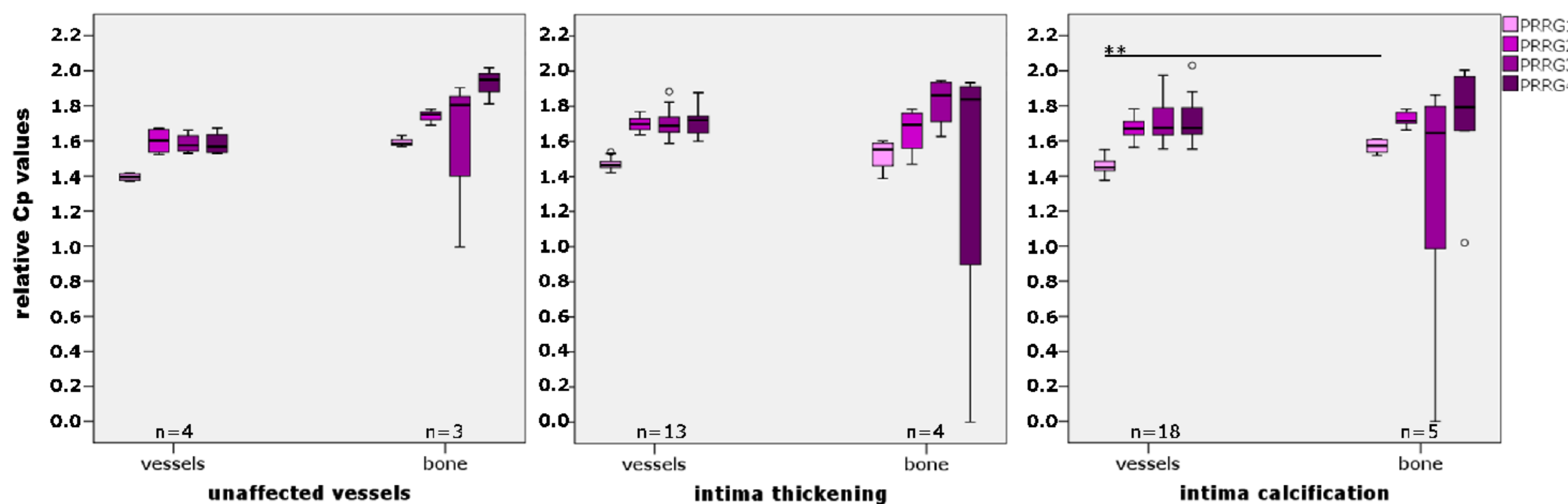


Fig.1: Comparison of gene expression of PRRG1-4 in vessels and bone in three stages of atherosclerosis: No differences in gene expression of PRRG1-4 are seen in unaffected vessels and in intima thickening, in intima calcification PRRG1 show different gene expression in bone and vessels (p=0.001).

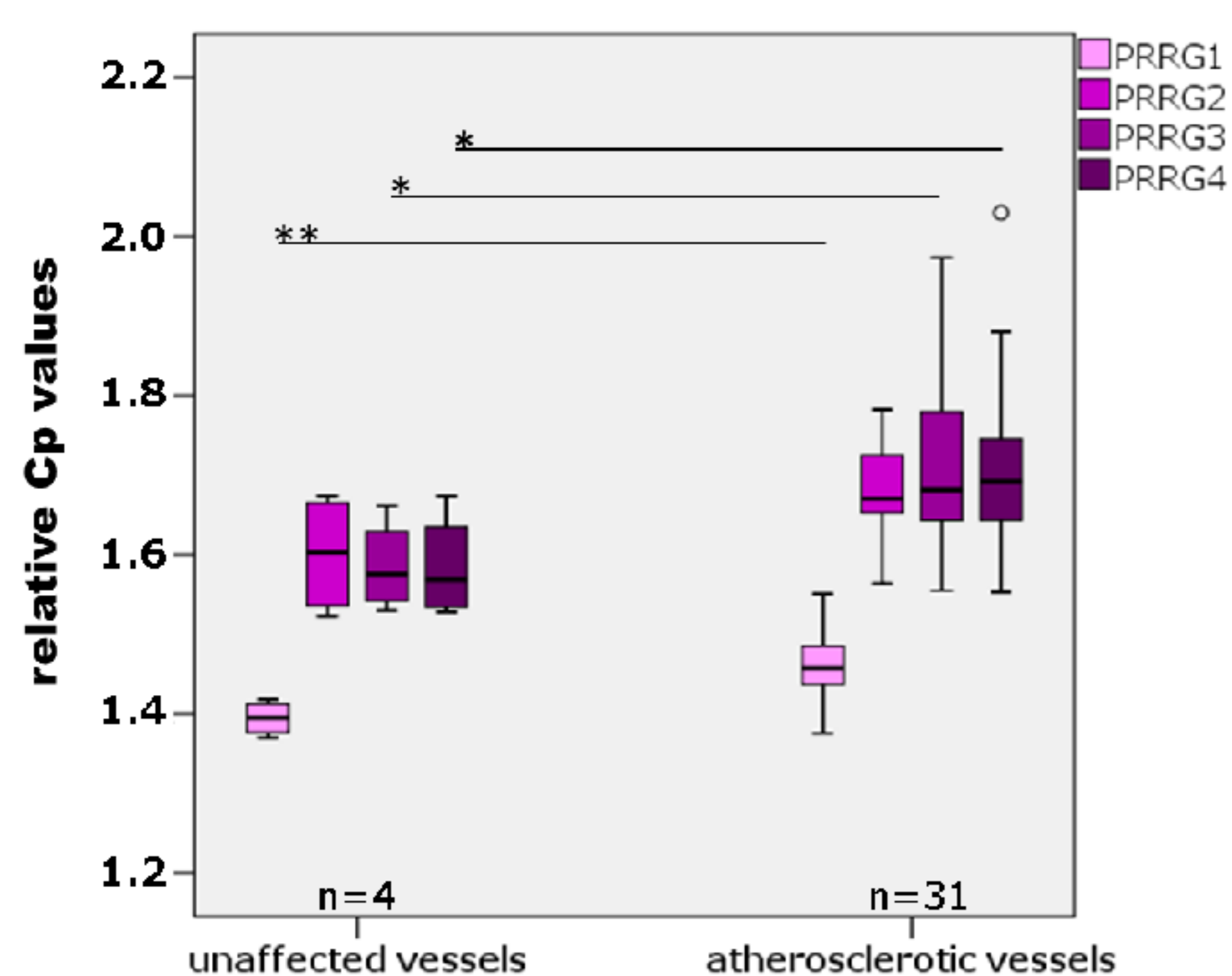


Fig.2: Gene expression of PRRG1-4 in vessels in 2 AS stages: Gene expression of PRRG1, 3 and 4 are significantly decreased in atherosclerosis compared to normal state (p=0.002, p=0.011, p=0.011, respectively).

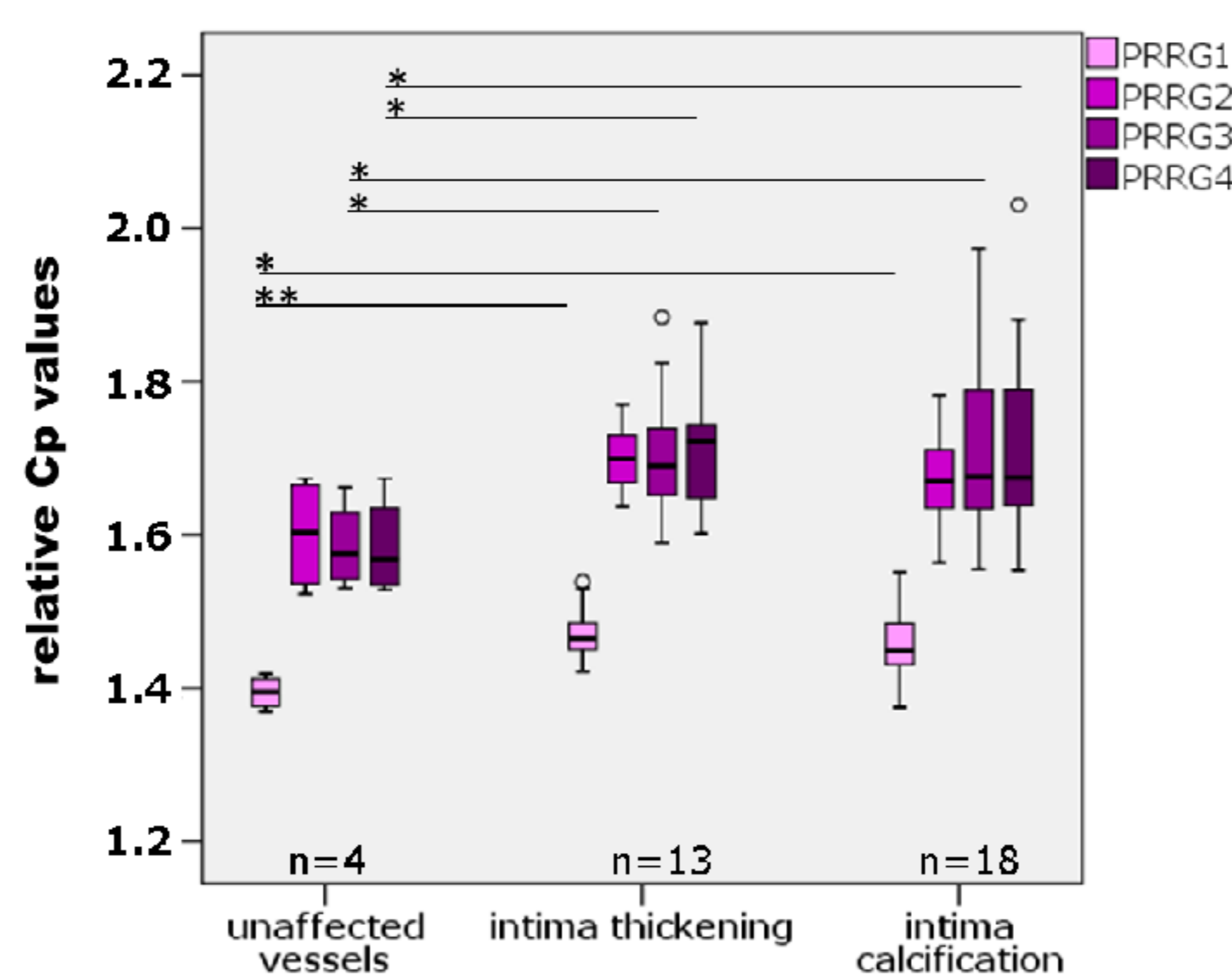


Fig.3: Changes in gene expression of PRRG 1-4 in vessels in 3 AS stages: PRRG1, 3 and 4 gene expression decreased during intima thickening (p=0.013; p=0.048 and p=0.049, respectively) and keeps low in the calcification stage.

Conclusion

- We show that gene expression of PRRGs change in the vessel wall in atherosclerosis development.
- PRRG 1 is differentially expressed in vessels and bone during intima calcification.
- In bone, gene expression of PRRG1-4 did not differ during and during AS progression.
- In vessels, the pattern of gene expression of PRRG 1, 3 and 4 changes during AS progression:
- Gene expression of PRRG1, 3 and 4 decreases in the stage of intima thickening
- and stays low in the stage of intima calcification.

Discussion

Gene expression of the vitamin K dependent proteins PRRG1-4 changes during calcification of the vessel wall.

These data implicate a new role of PRRGs in vascular calcification. Changes in PRRG gene expression already occur in the stage of intima thickening previously to calcification.

Acknowledgments

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