1D.03 INACTIVE MATRIX GLA PROTEIN IS ASSOCIATED WITH RENAL RESISTIVE INDEX IN A POPULATION-BASED STUDY

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Objective: Renal resistive index (RRI) varies directly with renal vascular stiffness and pulse pressure. RRI correlates positively with arteriolosclerosis in damaged kidneys and predicts progressive renal dysfunction. Matrix Gla-protein (MGP) is a vascular calcification inhibitor that needs vitamin K to be activated. Inactive MGP, known as desphospho-uncarboxylated MGP (dp-ucMGP), can be measured in plasma and has been associated with various cardiovascular (CV) markers, CV outcomes and mortality. In this study we hypothesize that increased RRI is associated with high levels of dp-ucMGP.

Design and method: We recruited participants via a multi-center family-based cross-sectional study in Switzerland exploring the role of genes and kidney hemodynamics in blood pressure regulation. Dp-ucMGP was quantified in plasma samples by sandwich ELISA. Renal doppler sonography was performed using a standardized protocol to measure RRIs on 3 segmental arteries in each kidney. The mean of the 6 measures was reported. Multiple regression analysis was performed to estimate associations between RRI and dp-ucMGP adjusting for sex, age, pulse pressure, mean pressure, renal function and other CV risk factors.

Results: We included 1035 participants in our analyses. Mean values were 0.64 ± 0.06 for RRI and 0.44 ± 0.21 (nmol/L) for dp-ucMGP. RRI was positively associated with dp-ucMGP both before and after adjustment for sex, age, body mass index, pulse pressure, mean pressure, heart rate, renal function, low and high density lipoprotein, smoking status, diabetes, blood pressure and cholesterol lowering drugs, and history of CV disease ($P < 0.001$).

Conclusions: RRI is independently and positively associated with high levels of dp-ucMGP after adjustment for pulse pressure and common CV risk factors. Further studies are needed to determine if vitamin K supplementation can have a positive effect on renal vascular stiffness and kidney function.

1D.04 INVERSE RELATIONSHIP BETWEEN AORTIC ROOT DIAMETER AND RENAL FUNCTION IN HYPERTENSIVE SUBJECTS

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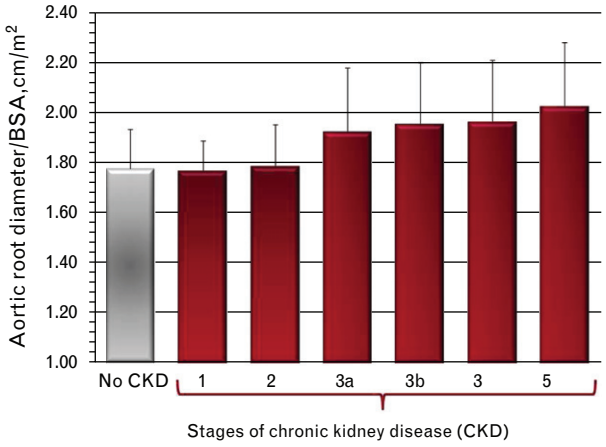
Objective: Recent studies suggest that enlarged aortic root diameter (ARD) may predict cardiovascular events in absence of aneurysmatic alterations. Little is known about the influence of renal function on ARD. Our study was aimed to assess the relationships between glomerular filtration rate (GFR) and ARD in hypertensive subjects.

Design and method: We enrolled 611 hypertensive individuals (mean age: 52 ± 15 years; men 63%) consecutively attending our outpatient unit of Nephrology and Hypertension. Patients on dialysis treatment, with valvulopathy more than mild, bicuspid aortic valve, previous cardiovascular events and genetic aortic diseases were excluded. All the subjects underwent echocardiography. ARD was measured at the level of Valsalva's sinuses by M-mode tracings, under two-dimensional control. In line with the PAMELA study, ARD, ARD indexed to body surface area (ARD/BSA) and to height (ARD/H) were considered increased when they exceeded 3.8 cm, 2.1 cm/m2, 2.3 cm/m in men and 3.4 cm, 2.2 cm/m2, 2.2 cm/m in women, respectively. GFR was estimated by the CKD-EPI equation. The study population was categorized in seven groups: subjects without chronic kidney disease (no CKD) and subjects with increasing severity of CKD (1, 2, 3a, 3b, 4, 5), according to KDIGO classification.

Results: Estimated GFR (eGFR) was lower in subjects with values of ARD, ARD/BSA and ARD/H above the sex-specific cut-offs when compared to those with normal aortic root size (all $p < 0.001$). The analysis of the distribution ARD/BSA in subjects with and in those without CKD, showed a progressive increase of ARD/BSA from the group with normal renal function to the groups with greater severity of CKD (figure).
eGFR correlated significantly with ARD ($r = -0.17$), ARD/BSA ($r = -0.43$) and ARD/H ($r = -0.40$; all $p < 0.001$). The associations of eGFR with ARD/BSA ($\beta = -0.23$) and ARD/H ($\beta = -0.17$; all $p < 0.001$) held in linear multiple regression analyses, after adjustment for various confounding factors.



Conclusions: Our study seems to suggest that a reduced renal function may adversely influence ARD. This may contribute to explain the enhanced cardiovascular risk associated with renal insufficiency.

1D.05 AORTIC-BRACHIAL STIFFNESS MISMATCH IN PRE-DIALYSIS CHRONIC KIDNEY DISEASE

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Objective: The loss of physiological stiffness mismatch between aorta and peripheral arteries was strongly and independently associated with increased mortality in adult dialysis population. The aim of the study was to evaluate if the reversal of arterial stiffness mismatch was present in pre-dialysis patients with chronic kidney disease (CKD).

Design and method: The aortic-brachial arterial stiffness mismatch (pulse wave velocity (PWV ratio) were assessed using carotid-femoral PWV divided by carotid-radial PWV in 112 adult treated hypertensive CKD patients: 54 - with CKD IIIa (age $59,5 \pm 8,4$ years, male 46,3%, brachial blood pressure (BP) $149,6 \pm 10,3/85,8 \pm 9,8$ mmHg), 35 - with CKD IIIb (age $60,2 \pm 7,8$ years, male 45,7%, BP $152,5 \pm 12,5/86,4 \pm 10,2$ mmHg) and 23 with CKD IV (age $57,3 \pm 10,2$, male 43,4%, BP $156,1 \pm 14,3/92,8 \pm 12,4$ mmHg). $P < 0,05$ was considered significant for group comparisons, Spearman correlation test and multivariate regression analysis.

Results: In CKD IIIa aortic PWV was $10,2 \pm 2,0$ m/s, brachial PWV $12,9 \pm 1,6$ m/s, PWV ratio $0,82 \pm 0,25$. In CKD IIIb aortic PWV was $11,3 \pm 2,9$ m/s, brachial PWV $12,2 \pm 1,8$ m/s, PWV ratio $0,90 \pm 0,27$. In CKD IV aortic PWV was $12,7 \pm 3,1$ m/s ($p < 0,05$ vs CKD IIIa), brachial PWV $11,4 \pm 1,6$ m/s ($p < 0,05$ vs CKD IIIa), PWV ratio $1,09 \pm 0,33$ ($p < 0,05$ vs CKD IIIa). Increased aortic stiffness (aortic PWV>10 m/s) was observed in 55,6%, 62,9% and 73,9%, respectively. For the whole study population ($n = 112$) multivariate analysis revealed independent significant correlation between aortic PWV and glomerular filtration rate (GFR) $\beta = -0,36$ ($p < 0,05$), PWV ratio and GFR $\beta = -0,32$ ($p < 0,05$), PWV ratio and age $\beta = 0,44$ ($p < 0,05$).

Conclusions: In the pre-dialysis hypertensive CKD patients worsening of kidney function was associated with discordant changes in aortic and brachial artery stiffness in the reversal of the physiological stiffness mismatch. The loss of this physiological mismatch may promote kidney damage through increased forward pressure wave transmission into the microcirculation. PWV ratio evaluation (in addition to traditional aortic PWV measurement) may be useful for better evaluation of arterial stiffness in pre-dialysis CKD patients.