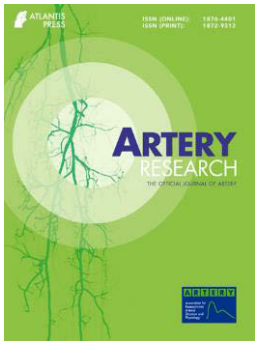

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1.5: DESPHOSPHO-UNCARBOXYLATED MATRIX GLA PROTEIN IS A NOVEL CIRCULATING BIOMARKER PREDICTING DETERIORATION OF RENAL FUNCTION IN THE GENERAL POPULATION

Fangfei Wei, Sander Trenson, Lutgarde Thijs, Qi-Fang Huang, Zhen-Yu Zhang, Wen-Yi Yang, Paula Moliterno, Karel Allegaert, José Boggia, Stefan Janssens, Peter Verhamme, Cees Vermeer, Jan Staessen

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Average cPP was 36 ± 7 mmHg, PPamp 1.57 ± 0.13. cPP was positively associated with male sex, BSA, MAP, SI, and negatively with HR (47% of cPP variance explained). pPP was positively associated with male sex, BSA and SI (44% of pPP variance explained). PPamp was positively associated with age, HR and cf-PWV (17% of PPamp variance explained). Results did not change when BMI and height replaced BSA, iLVM replaced SI, and cr-PWV or PWV ratio (cfPWV/crPWV) replaced cf-PWV.
Anthropometric and hemodynamic factors differently impact on cPP, pPP and PPamp. HR and MAP are related to cPP, but not to pPP. HR, cf-PWV and age are all positively related to PPamp. These results could help in better elucidate the clinical relevance of some BP patterns frequently observed in adolescence.

Table independent determinants of cPP, pPP and PPamp. All the showed coefficients had $p < 0.05$.

	cPP	pPP	PPamp
	Standardized β	Standardized β	Standardized β
Male sex	0.33	0.40	–
BSA, m^2	0.28	0.32	–
Heart rate, bpm	−0.21	–	0.32
Mean arterial pressure, mmHg	0.11	–	–
Stroke index, ml/m^2	0.09	0.09	–
Carotid-femoral PWV, m/s	–	–	0.11
Age, years	–	–	0.10

1.4
A PROTEOMIC MARKER OF DIABETIC NEPHROPATHY IS ASSOCIATED WITH MORTALITY IN PATIENTS WITH TYPE 2 DIABETES

Gemma Currie [1], Sheon Mary [1], Bernt Johan von Scholten [2], Morten Kofod Lindhardt [2], Harald Mischak [3], William Mullen [1], Peter Rossing [2], Christian Delles [1]
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Background: The urinary proteomic classifier CKD273 has been found to predict diabetic nephropathy development in advance of microalbuminuria. Whether it is also a determinant of mortality and cardiovascular disease in patients with established albuminuria is unknown.
Methods: We studied 155 subjects with T2D, albuminuria (geometrical mean [IQR]: 85 [34;194] mg/24 hrs), controlled blood pressure (129 ± 16/74 ± 11 mmHg) and preserved renal function (eGFR 88 ± 17 ml/min/1.73 m^2). Blood and urine samples were collected for measurement of estimated glomerular filtration rate (eGFR), urine albumin excretion (UAE), N-terminal pro-brain natriuretic peptide (NT-proBNP) and urinary proteomics (capillary electrophoresis coupled to mass spectrometry). Computed tomography imaging was performed to assess coronary artery calcium (CAC) score. Outcome data were collected through national disease registries over a 6 year follow up period.
Results: CKD273 correlated with UAE ($r = 0.481$, $p = <0.001$), age ($r = 0.238$, $p = 0.003$), CAC score ($r = 0.236$, $p = 0.003$), NT-proBNP ($r = 0.190$, $p = 0.018$) and eGFR ($r = 0.265$, $p = 0.001$). On multiple regression only UAE ($\beta = 0.402$, $p < 0.001$) and eGFR ($\beta = -0.184$, $p = 0.039$) were statistically significant determinants. Twenty participants died during follow-up. CKD273 was a determinant of mortality (log rank [Mantel-Cox] $p = 0.004$), and retained significance ($p = 0.050$) after adjustment for age, sex, blood pressure, NT-proBNP and CAC score in a Cox regression model. Neither eGFR nor UAE were determinants of mortality in this cohort.
Conclusions: A multidimensional biomarker can provide information on outcomes associated with its primary diagnostic purpose. Here we demonstrate that the peptidomics-based classifier CKD273 is associated with mortality in albuminuric people with T2D in even when adjusted for other established cardiovascular and renal biomarkers.

1.5
DESPHOSPHO-UNCARBOXYLATED MATRIX GLA PROTEIN IS A NOVEL CIRCULATING BIOMARKER PREDICTING DETERIORATION OF RENAL FUNCTION IN THE GENERAL POPULATION

Fangfei Wei [1], Sander Trenson [1], Lutgarde Thijs [1], Qi-Fang Huang [1], Zhen-Yu Zhang [1], Wen-Yi Yang [1], Paula Moliterno [2], Karel Allegaert [3], José Boggia [4], Stefan Janssens [1], Peter Verhamme [1], Cees Vermeer [5], Jan Staessen [1]
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Background: Recent studies showing an inverse association between estimated glomerular filtration rate (eGFR), a microvascular trait, and inactive desphospho-uncarboxylated matrix Gla protein (dp-ucMGP) support the hypothesis that after vitamin K dependent activation MGP is renoprotective, but were limited by their cross-sectional design.
Methods: In 1009 randomly recruited Flemish (50.6% women), we assessed the association between eGFR and plasma dp-ucMGP, using multivariable-adjusted analyses.
Results: From baseline to follow-up 8.9 years later (median), dp-ucMGP increased by 3.7%, whereas eGFR decreased by 4.05 ml/min/1.73 m^2 ($P < 0.001$). In 938 participants with baseline eGFR ≥ 60 ml/min/1.73 m^2, incidence of eGFR < 60 ml/min/1.73 m^2 at follow-up was 8.0% *vs.* 4.1% in the top *vs.* the bottom halve of baseline dp-ucMGP. For each doubling of baseline dp-ucMGP, eGFR at follow-up decreased by 1.36 ml/min/1.73 m^2 [95% confidence interval (CI) 0.55−2.17 ml/min/1.73 m^2; $P = 0.001$]. The hazard ratio expressing the risk of progression to eGFR < 60 ml/min/1.73 m^2 was 1.67 (95% CI 1.16−2.41; $P = 0.006$). The hazard ratio relating the presence of microalbuminuria at follow-up to baseline dp-ucMGP was 1.96 (95% CI 1.22−3.12; $P = 0.005$).
Conclusions: In conclusion, circulating inactive dp-ucMGP, a biomarker of poor vitamin K status, predicts renal dysfunction. Possible underlying mechanisms include protection by activated MGP against calcification and inhibition of bone morphogenetic protein signaling pathway.

1.6
PERIPHERAL AND CENTRAL AMBULATORY BLOOD PRESSURE IN RELATION TO ECG VOLTAGE

Wen-Yi Yang [1], Blerim Mujaj [1], Ljupcho Efremov [1], Zhen-Yu Zhang [1], Lutgarde Thijs [1], Fang-Fei Wei [1], Qi-Fang Huang [1], Aernout Luttun [2], Peter Verhamme [2], Tim Nawrot [3], Jose Boggia [4], Jan Staessen [1]
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Background: The heart ejects in the central elastic arteries. No previous study addressed the question whether ECG voltages are more closely associated with central than with peripheral blood pressure (BP).
Methods: Using the oscillometric Mobil-O-Graph 24 h PWA monitor, we measured brachial, central BP and central hemodynamics over 24 hours in 177 men (mean age, 29.1 years), and linked to ECG voltages.
Results: From wakefulness to sleep, as documented by diaries, systolic/diastolic BP decreased by 11.7/13.1 mmHg peripherally and by 9.3/13.6 mmHg centrally, whereas pulse pressure (PP) increased by 4.3 mmHg. Over 24 hours and the awake and asleep periods, the peripheral-minus-central differences