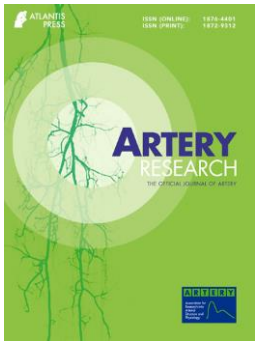

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1.6: PERIPHERAL AND CENTRAL AMBULATORY BLOOD PRESSURE IN RELATION TO ECG VOLTAGE

Wen-Yi Yang, Blerim Mujaj, Ljupcho Efremov, Zhen-Yu Zhang, Lutgarde Thijs, Fang-Fei Wei, Qi-Fang Huang, Aernout Luttun, Peter Verhamme, Tim Nawrot, Jose Boggia, 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

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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

in systolic/diastolic BPs and pulse pressure averaged 11.8/−1.6, 12.7/−1.8 and 10.3/−1.2 mmHg and 13.4, 14.4 and 11.5 mmHg, respectively ($P < 0.0001$). Cornel voltage and index averaged 1.18 mV and 114.8 mV × ms. The Cornell voltages were 0.104/0.086 and 0.082/0.105 mV higher in relation to brachial 24-h and asleep systolic/diastolic BP (per 1-SD), respectively, and 0.088/0.90 mV and 0.087/0.107 mV higher in relation to central BP. The corresponding estimates for the Cornel indexes were 9.6/8.6 and 8.2/105 mV × ms peripherally and 8.6/8.9 and 8.8/10.7 mV × ms centrally. The regression slopes were similar for brachial and central BP ($P \geq 0.054$). Associations of the ECG measurements with awake BP, PP, the augmentation ratio and pressure amplification did not reach significance.

Results: NIAGEN® safely and effectively raised circulating levels of NAD^+ and related metabolites. Although no effect was observed on endothelial function, NIAGEN® significantly lowered PWV as well as systolic (SBP) and diastolic blood pressure (DBP) in all subjects ($P < 0.05$). When separated by baseline BP status, the BP-lowering effect of NIAGEN® was observed in pre-hypertensive (pHTN, n = 13) but not normotensive (N = 11) individuals ($P < 0.01$). Interestingly, NIAGEN® was lowered in all subjects regardless of baseline BP status.

Conclusion: Chronic NIAGEN® supplementation lowers SBP in pHTN older adults and reduces aortic stiffness, independent of baseline blood pressure status.

Table Association of ECG Cornell voltage and indexes with peripheral and central BP.

	Cornell voltage ($S_{V3} + R_{aVL}$, mV)				Cornell index (Cornell voltage × QRS duration, mV·ms)			
	Peripheral BP		Central BP		Peripheral BP		Central BP	
	Estimate (95% CI)	*P*	Estimate (95% CI)	*P*	Estimate (95% CI)	*P*	Estimate (95% CI)	*P*
Systolic BP								
24-h	0.104 (0.016 to 0.191)	0.021	0.088 (0.0003 to 0.177)	0.049	9.61 (0.65 to 18.57)	0.036	8.58 (−0.40 to 17.56)	0.061
Awake	0.086 (−0.001 to 0.175)	0.054	0.062 (−0.026 to 0.151)	0.17	7.69 (−1.30 to 16.69)	0.093	5.80 (−3.23 to 14.82)	0.21
Asleep	0.082 (−0.006 to 0.170)	0.068	0.087 (−0.001 to 0.175)	0.053	8.17 (−0.82 to 17.16)	0.075	8.76 (−0.217 to 17.74)	0.056
Diastolic BP								
24-h	0.086 (−0.002 to 0.174)	0.056	0.090 (0.002 to 0.178)	0.045	8.57 (−0.41 to 17.55)	0.061	8.93 (−0.04 to 17.90)	0.051
Awake	0.056 (−0.032 to 0.145)	0.21	0.060 (−0.029 to 0.149)	0.18	5.62 (−3.42 to 14.65)	0.22	5.97 (−3.06 to 15.00)	0.19
Asleep BP	0.105 (0.017 to 0.192)	0.020	0.107 (0.019 to 0.194)	0.017	10.53 (1.60 to 19.47)	0.021	10.71 (1.78 to 19.64)	0.019
Pulse pressure								
24-h	0.040 (−0.049 to 0.129)	0.38	0.016 (−0.073 to 0.105)	0.72	3.07 (−5.99 to 12.13)	0.50	1.31 (−7.76 to 10.38)	0.77
Awake	0.048 (−0.041 to 0.137)	0.29	0.012 (−0.077 to 0.101)	0.78	3.63 (−5.43 to 12.68)	0.43	0.68 (−8.40 to 9.74)	0.88
Asleep	0.001 (−0.091 to 0.088)	0.98	0.001 (−0.087 to 0.090)	0.98	−0.29 (−9.37 to 8.78)	0.95	0.21 (−8.86 to 9.28)	0.96

ECG refers to electrocardiography. BP stands for blood pressure. Cornell voltage is the voltage sum of S wave in precordial V3 lead (S_{V3}) and R wave in limb aVL lead (R_{eVL}), while Cornell index is the product of QRS duration multiplied by the Cornell voltage. The estimate (95% Confidence Interval, CI) of the association was unadjusted and expressed as 1-SD increase of BP. *P* value is for significance of the estimate. The association estimates of Cornell voltage ($P \geq 0.054$) and index ($P \geq 0.079$) with central BP were not significantly different from those estimates with peripheral measurements.

Conclusions: The diurnal rhythm of peripheral and central BP run in parallel. Central BP does not improve the association of Cornell voltage or index with peripheral BP.

Joint Session with LATAM and North American Artery

NAA1
NICOTINAMIDE RIBOSIDE SUPPLEMENTATION REDUCES AORTIC STIFFNESS AND BLOOD PRESSURE IN MIDDLE-AGED AND OLDER ADULTS

Christopher Martens [1], Blair Denman [1], Melissa Mazzo [1], Michael Armstrong [2], Nichole Reisdorph [2], Matthew McQueen [1], Michel Chonchol [3], Douglas Seals [1]
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Purpose: Regular calorie restriction (CR) improves endothelial function and lowers aortic stiffness in older mice and humans; however, adherence to sustained CR remains poor, and possibly unsafe in normal weight older adults. Nicotinamide adenine dinucleotide (NAD^+) is an important signaling molecule involved in the beneficial effects of CR and we have recently demonstrated that boosting NAD^+ reverses these measures of arterial aging in older mice. The purpose of this study was to determine if supplementation with nicotinamide riboside (NIAGEN®; ChromaDex, Inc.), a naturally occurring precursor to NAD^+, would similarly improve vascular function with aging in humans.
Methods: Healthy middle-aged and older adults (65 ± 2 yrs, n = 24) received oral NIAGEN® (500 mg, 2x/day) and placebo capsules for six weeks each in a randomized, placebo-controlled crossover study. Blood pressure (BP), aortic stiffness (carotid-femoral pulse wave velocity [PWV]), and endothelial function, (brachial artery flow-mediated dilation [FMD]), were measured at the end of each intervention phase.

LAA1
HEMODYNAMIC AND STRUCTURAL ARTERIAL PARAMETERS' ASSOCIATION WITH INTERINDIVIDUAL VARIATIONS OF BODY MASS INDEX IN CHILDHOOD AND ADOLESCENCE

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Background: Several works analyze arterial parameters' (stiffness levels, wall thickness, etc.) association with variations of body mass index (BMI) in pediatric populations.
However, none integrate different arterial parameters as comparable continuous (standardized) variables, in order to assess their association with standardized (age- and sex-independent) BMI scores (zBMI).
Aims: To analyze the association of standardized arterial parameters with interindividual variations of zBMI.
Methods: 609 children and adolescents (mean age/range: 12/4−18 years, 45% females) were studied. Body mass index (BMI) was calculated. zBMI scores were derived from population-based tables. Non-invasive arterial assessment was performed: oscillometric measurements of peripheral systolic (pSBP), diastolic (pDBP) and pulse pressure (pPP), and central (applanation tonometry) systolic (cSBP), diastolic (cDBP) and pulse pressure (cPP); ultrasonographic measurements of common carotid (CCA), femoral (CFA) and brachial (BA) diastolic diameters (DD), and CCA intima-media thickness (cIMT). Arterial elastic moduli (EM) were calculated. Arterial parameters were standardized with equations derived from a reference population (no cardiovascular risk factor exposure). Simple linear regression models were obtained for the different standardized arterial parameters with zBMI as the independent variable. Statistical threshold was 0.05.
Results: We found a positive and significant association between zBMI and standardized pSBP ($\beta = 0.210$), pPP ($\beta = 0.150$), cSBP ($\beta = 0.204$) and cPP ($\beta = 0.188$), CCA DD ($\beta = 0.145$), FCA ($\beta = 0.143$), BA ($\beta = 0.210$), cIMT ($\beta = 0.135$), and CCA EM ($\beta = 0.117$).