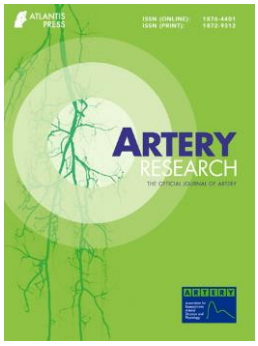

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1.3: DETERMINANTS OF CENTRAL AND PERIPHERAL PULSE PRESSURE IN A POPULATION OF HEALTHY ADOLESCENTS. THE MACISTE STUDY

Pucci Giacomo, Battista Francesca, D'Abbondanza Marco, Papi Francesco, Schillaci Giuseppe

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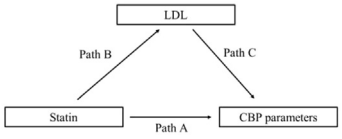
Oral presentation abstracts

Oral session I – Epidemiology

1.1
CENTRAL BLOOD PRESSURE, STATINS AND LDL-CHOLESTEROL: A MEDIATION ANALYSIS

Florence Lamarche [1], Mohsen Agharazii [2], Francois Madore [1], Remi Goupil [1]
[1]*Hôpital du Sacré-Coeur de Montréal, Montréal, QC, Canada*
[2]*CHU de Québec, Hôtel-Dieu de Québec, Québec, QC, Canada*

Background: Central blood pressure (CBP) is a better predictor of cardiovascular burden than peripheral blood pressure (BP). While studies have suggested a reduction in peripheral BP with statins, it remains uncertain to what extent statins reduce CBP and whether this reduction is mediated through a decrease in LDL-cholesterol (LDL).
Methods: Of the 20,004 CARTaGENE participants, 17,011 had CBP and LDL measurements (n = 13,439 without, n = 3,133 with statins). Linear and logistic regression analyses were used to evaluate the association between CBP, LDL and statin use (after stratification for treatment indication for the latter). The impact of LDL on the association between statin use and CBP was determined by mediation analyses. All analyses were adjusted for age, sex, diabetes, cardiovascular disease, smoking, eGFR, BMI, uric acid, heart rate, anti-hypertensive agents and aspirin.
Results: Lower levels of LDL were associated with lower systolic and diastolic CBP in participants treated with (b = 0.098 and 0.125; p < 0.001) and without statins (b = 0.089 and 0.105; p < 0.001). Statin use as primary prevention (per ACC/AHA guidelines; n = 8,865) was also associated with lower systolic CBP, diastolic CBP and central pulse pressure (b = −0.091, −0.073 and −0.055; p < 0,001). Mediation analyses demonstrated that 15%, 46% and -22% of these effects were achieved through the concomitant changes in LDL (Table 1). In secondary prevention (n = 995), statins use was not associated with lower CBP, although the small sample size may lack power.
Conclusion: In this populational cohort, statin use as primary prevention is associated with lower CBP. These changes are mediated directly by statins but also indirectly through effects on LDL.



	Path A (total effect)	Path A (direct effect)	Path BC (indirect effect)	Percent mediation
Systolic CBP	-3.0 (-3.8, -2.3)	-2.6 (-3.4, -1.7)	-0.5 (-0.2, -0.0)	15%
Diastolic CBP	-1.7 (-2.2, -1.2)	-1.0 (-1.5, -0.4)	-0.8 (-1.0, -0.5)	44%
Central pulse pressure	-1.3 (-1.8, -0.9)	-1.6 (-2.2, -1.1)	0.3 (0.0, 0.6)	-22%

Effects represent changes of CBP parameter per 1 standard deviation of LDL (95% CI).

1.2
MASKED HYPERTENSION IS REVEALED BY EXAGGERATED SUBMAXIMAL EXERCISE BLOOD PRESSURE AMONG ADOLESCENTS FROM THE AVON LONGITUDINAL STUDY OF PARENTS AND CHILDREN (ALSPAC)

Zhengzheng Huang [1], James Sharman [1], Chloe Park [2], John Deanfield [2], Marietta Charakida [3], Abigail Fraser [3], Laura Howe [3], Debbie Lawlor [3], Nish Chaturvedi [2], George Smith [3], Alun Hughes [2], Martin Schultz [1]
[1]*Menzies Institute for Medical Research, University of Tasmania, Hobart, Australia*
[2]*The UCL Institute of Cardiovascular Science, University College London, London, UK*
[3]*MRC Integrative Epidemiology Unit, University of Bristol, Bristol, UK*

Objectives: Masked hypertension (MH) is associated with hypertension-related markers of organ damage, but is undetectable by clinic (resting) BP. Exaggerated systolic BP response to submaximal exercise reveals MH in adults, but it is unknown whether this is the case during adolescence. We aimed to determine if exercise BP was raised in adolescents with MH, and associations with markers of organ damage.
Methods: 585 adolescents (aged 17.7 ± 0.3 years; 41.9% male) from the Avon longitudinal study of parents and children (ALSPAC), completed a step-exercise test with post-exercise BP, resting (clinic) BP and 24-hour ambulatory BP (ABP). MH was defined on the basis of guideline adult thresholds as clinic BP ≤ 140/90 mmHg and 24 h ABP ≥ 130/80 mmHg, or paediatric thresholds (age, sex and height percentiles). Assessment of markers of organ damage including left-ventricular mass (LVM) and carotid-femoral pulse wave velocity (PWV) was also undertaken.
Results: 45 (7.7%) participants were classified with MH. Resting and post-exercise SBP were higher in those with MH vs. normotensives (126.1 ± 7.3 mmHg vs. 114.7 ± 10.0 mmHg, $p < 0.001$; 152.2 ± 17.3 vs 141.1 ± 15.1 mmHg, $p = 0.001$). A post-exercise SBP threshold of 150 mmHg revealed MH (AUC = 0.69, 95% CI: 0.61–0.76, $p < 0.001$) and was associated with greater LVM index (30.2 ± 6.5 vs. 27.6 ± 5.8 g/m$^{2.7}$, $p < 0.001$) and PWV (5.9 ± 0.6 vs. 5.7 ± 0.7 m/s, $p = 0.01$).
Conclusions: This is the first study within adolescents demonstrating post-exercise SBP can reveal MH and an association with markers of organ damage. Exaggerated exercise BP might be a warning signal of underlying high BP and increased cardiovascular risk undetected by clinic BP.

1.3
DETERMINANTS OF CENTRAL AND PERIPHERAL PULSE PRESSURE IN A POPULATION OF HEALTHY ADOLESCENTS. THE MACISTE STUDY

Pucci Giacomo [1,2], Battista Francesca [1,2], D'Abbondanza Marco [1,2], Papi Francesco [1,2], Schillaci Giuseppe [1,2]
[1]*Department of Medicine, University of Perugia, Perugia, Italy*
[2]*Unit of Internal Medicine, Terni University Hospital, Terni, Italy*

We aimed at evaluating the anthropometric and hemodynamic factors associated with central pulse pressure (cPP), peripheral pulse pressure (pPP) and central-to-peripheral PP amplification (PPamp) in healthy adolescents.
We studied 459 subjects (boys 57%, 16.8 ± 1.5 y) attending the Liceo Donatelli High School in Terni, Italy. cPP was estimated from radial applanation tonometry (SphygmoCor GTF) calibrated to brachial MAP/DBP. Indexed left ventricular mass (iLVM = LVM/BSA) and stroke index (SI = stroke volume/BSA) were derived from 2D-echocardiography (Teicholz's formula, Devereux correction). Carotid-femoral (cf-PWV) and carotid-radial (cr-PWV) pulse wave velocities were measured by SphygmoCor. cPP, pPP and PPamp were introduced as dependent variables in three separate stepwise multivariate regression models. Age, male sex, BSA, heart rate (HR), MAP, stroke index (SI: stroke volume/BSA) and cf-PWV were included in each model as independent factors.

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]
[1]*University of Glasgow, UK*
[2]*Steno Diabetes Center Copenhagen, Denmark*
[3]*Mosaiques, Diagnostics GmbH, Germany*

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]
[1]*Department of Cardiovascular Sciences, University of Leuven, Belgium*
[2]*Escuela de Nutrición, Universidad de la República, Uruguay*
[3]*Department of Development and Regeneration, University of Leuven, Belgium*
[4]*Centro de Nefrología and Departamento de Fisiopatología, Hospital de Clínicas, Universidad de la República, Uruguay*
[5]*R&D Group VitaK, Maastricht University, Netherlands*

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]
[1]*Studies Coordinating Centre, Research Unit Hypertension and Cardiovascular Epidemiology, KU Leuven Department of Cardiovascular Sciences, Faculty of Medicine, University of Leuven, Leuven, Belgium*
[2]*Centre for Molecular and Vascular Biology, KU Leuven Department of Cardiovascular Sciences, Faculty of Medicine, University of Leuven, Leuven, Belgium*
[3]*Centre for Environmental Sciences, Hasselt University, Diepenbeek, Belgium*
[4]*Unidad de Hipertensión Arterial, Departamento de Fisiopatología, Centro de Nefrología, Hospital de Clínicas, Universidad de la República, Montevideo Uruguay, Uruguay*

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