ARTERY 17

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Pisa, Italy
www.arterysociety.org

Programme and Book of Abstracts

ARTERY
Association for Research into Arterial Structure and Physiology

THURSDAY 12 OCTOBER 2017

11:00 Registration

11:45 Welcome address
K Cruickshank, *President, ARTERY*; L Ghiadoni, *Chair, Local Organising Committee, ARTERY 17*

12.00 Opening Lecture
Chair: K Cruickshank, C Vlachopoulos

Endothelial function: from bench to bedside
Professor Stefano Taddei*, University of Pisa, Italy*

12.30 Oral Session I
Chair: M Salvetti, P Chowienczyk

1.1 Central Blood Pressure, Statins and LDL-cholesterol: A Mediation Analysis

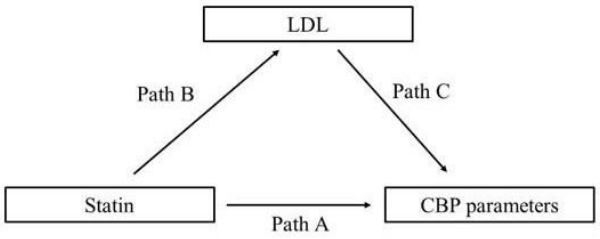
Lamarche, Florence[1]; Agharazii, Mohsen[2]; Madore, Francois[1]; Goupil, Remi[1]
[1]Hôpital du Sacré-Coeur de Montréal, Montréal, QC, Canada, [2]CHU de Québec, Hôtel-Dieu de Québec, Québec, Qc, Canada

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).

Huang, Zhengzheng[1]; Sharman, James[1]; Park, Chloe[2]; Deanfield, John[2]; Charakida, Marietta[3]; Fraser, Abigail[4]; Howe, Laura[4]; Lawlor, Debbie[4]; Chaturvedi, Nish[2]; Smith, George[3]; Hughes, Alun[2]; Schultz, Martin[5]

[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, [4]MRC Integrative Epidemiology Unit, University of Bristol, Bristol, UK., [5]Menzies Institute for Medical Research, University of Tasmania, Hobart, Australia.

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 24h 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]; Battista, Francesca[1]; D'Abbondanza, Marco[1]; Papi, Francesco[1]; Schillaci, Giuseppe[1]

[1]Department of Medicine, University of Perugia, Perugia, Italy; 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 explaied). 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.

Anthopometric 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.

	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

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

1.4 A Proteomic Marker of Diabetic Nephropathy is Associated with Mortality in Patients with Type 2 Diabetes

Currie, Gemma[1]; Mary, Sheon[1]; von Scholten, Bernt Johan[2]; Lindhardt, Morten Kofod[2]; Mischak, Harald[3]; Mullen, William[1]; Rossing, Peter[2]; Delles, Christian[1]

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

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/24hrs), controlled blood pressure (129±16/74±11 mmHg) and preserved renal function (eGFR 88±17 ml/min/1.73m^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 (β=0.402, p<0.001) and eGFR (β=-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

Wei, Fangfei[1]; Trenson, Sander[1]; Thijs, Lutgarde[1]; Huang, Qi-Fang[1]; Zhang, Zhen- Yu[1]; Yang, Wen-Yi[1]; Moliterno, Paula[2]; Allegaert, Karel[3]; Boggia, José[4]; Janssens, Stefan[1]; Verhamme, Peter[1]; Vermeer, Cees[5]; Staessen, Jan[1]

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

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

Yang, Wen-Yi[1]; Mujaj, Blerim[1]; Efremov, Ljupcho[1]; Zhang, Zhen-Yu[1]; Thijs, Lutgarde[1]; Wei, Fang-Fei[1]; Huang, Qi-Fang[1]; Luttun, Aernout[2]; Verhamme, Peter[2]; Nawrot, Tim[3]; Boggia, Jose[4]; Staessen, Jan[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.

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 24h 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 mm Hg peripherally and by 9.3/13.6 mm Hg centrally, whereas pulse pressure (PP) increased by 4.3 mm Hg. 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 mm Hg and 13.4, 14.4 and 11.5 mm Hg, 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*≥0.054). Associations of the ECG measurements with awake BP, PP, the augmentation ratio and pressure amplification did not reach significance.

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_{aVL}), 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.

13.30 Lunch, Poster and Exhibition viewing

14.30 Special Guest Lecture
Chair: F Faita, A Avolio

Imaging the mechanical properties of arteries using their intrinsic pulsation: from the theory to the clinic
Professor Elisa Konofagou, *Columbia University, New York, USA*

15.00 Career Development Lectures
Chair: C Vlachopoulos, T Hansen

The clinical importance of exercise blood pressure
Dr Martin Schultz, *Menzies Institute for Medical Research, University of Tasmania, Hobart, Australia*

Clinical exercise stress testing is a common medical test performed in cardiology and exercise physiology clinics the world over. Measurement of blood pressure (BP) during testing is mandated. Whilst systolic BP should normally rise with incremental exercise, and diastolic BP remain relatively stable, abnormal responses can occur. Low BP or 'exercise hypotension' is a known signal of underlying cardiovascular disease and sign of poor prognosis. On the other hand, observational evidence suggests an exaggerated BP response is also associated with heightened cardiovascular disease risk. Historically, research has focused on the BP response to peak or maximum exercise intensities. However, exaggerated BP during submaximal exercise (light-to-moderate intensity) may expose the presence of high BP otherwise not detected by traditional resting measurement in the clinic. Exaggerated exercise BP is related to subclinical cardiovascular disease risk markers such as raised arterial stiffness and impaired cardiac structure and function. The mechanisms underlying such associations are complex, but physiological insight has been gained from studying changes in arterial haemodynamics in response to dynamic exercise. Similarly, there are several known modifiers of the exercise BP response, including age, disease status and aerobic capacity. An area of continued

focus is to establish if modifiers, such as aerobic capacity, also modify associations between exercise BP and clinical outcomes throughout the life-course. Future work is also directed towards filling a crucial evidence gap, providing population-based thresholds of exercise BP that are associated with acute and longer-term outcomes. This should pave the way for pragmatic research aimed towards enhancing the clinical use of exercise BP.

The centrality of the heart in its relationship with the arterial system: where it all starts and ends

Dr Giacomo Pucci, *Department of Medicine, University of Perugia, Perugia, Italy*
Unit of Internal Medicine, Terni University Hospital, Terni, Italy

The interaction between the heart and large arteries represent a not fully understood process, which results from the integration of pressure wave generation, flow ejection, wave travel and reflection, and geometric mismatch between structures. Left ventricular (LV) mass and geometry, two independent predictors of worse cardiac outcomes, are modelled by changes in cardiac afterload. Central pulse pressure (cPP) itself, a marker of LV afterload, is generated from heart contraction and pressure/flow propagation into the arterial system. As such, increased cPP may be viewed as both the cause and the consequence of an increased LV work.
Our research group first described an inverse, age-dependent, relationship between aortic PWV, relative wall thickness, and the velocity of LV circumferential fiber shortening. We also showed that the relationship between cPP and stroke volume is progressively lost at increasing age. Finally, we found, in a cohort of untreated hypertensives, a pressure-independent relationship between aortic characteristic impedance, LV mass and geometry. Taken together, these results suggest that changes in LV structure and function occur as part of the compensatory response of the LV to unfavourable ventricular-vascular coupling and increased aortic stiffness.
Heart rate (HR) is another relevant effect-modifier of the interconnection between cardiac and arterial function. HR is a independently associated with cardiac index, PP amplification, and aortic stiffness. Pharmacological BP-lowering interventions combined with HR-lowering effect, such as beta-blockers, are ineffective in reducing LV mass. Moreover, HR changes are positively related to DBP changes. Therefore, anti-hypertensive drugs with associated HR-lowering effect only spuriously affect the ventricular-vascular coupling. More research is needed in order to find new targets of treatment able to prevent the occurrence of structural LV remodeling.

Stiff vessels approached in a flexible way: Advancing quantification and interpretation of arterial stiffness

Dr Bart Spronck, *Yale University, School of Engineering & Applied Science, New Haven, USA*

Introduction
Although pulse wave velocity (PWV), a proxy of arterial stiffness, is a strong predictor of cardiovascular complications, it is confounded by blood pressure (BP) and heart rate at the time of examination. Furthermore, establishing whether an artery is stiffened or not does not inform a clinician on the *cause* of the stiffening

Quantification of PWV's confounders
This talk will focus on BP as a confounder of PWV. We developed a method to patient-specifically determine the dependence of PWV on BP —on average 1 m/s per 10 mmHg diastolic BP— and used it to disentangle BP-dependent and -independent stiffening in hypertension and cancer patients. We furthermore showed that cardio-ankle vascular index (CAVI) —a measure that is often presented as BP-independent— shows a residual BP dependence that can be readily corrected using a modified equation ($CAVI_0$). Both developed methods are directly applicable to clinical measurement data from individual patients.

Interpretation of changes in PWV
We developed a computer modelling procedure to disentangle contributions of the individual wall components —collagen, elastin, and smooth muscle— to arterial stiffening in patient data. We used this approach to show that with ageing, the biomechanical phenotype shifted from elastin-dominated to collagen-dominated load bearing.

Outlook
Model-based interpretation of arterial mechanics provides a promising tool to further improve understanding of arterial stiffening. In my future career, I will use such methodology to study stiffening

in various mouse models. The results of these studies can potentially be used to further improve understanding and interpretation of arterial stiffening in patients.

16.00 Refreshments, Poster and Exhibition viewing
Young Investigator Business Meeting (Room D)

16.50 Joint Session with LATAM and North American Artery
Chair: B Fernhall, K Cruickshank

North American Artery 2017 Meeting Update

B Fernhall, *Chicago, USA*; G Pierce, *Iowa City, USA*

NAA1 Nicotinamide Riboside Supplementation Reduces Aortic Stiffness and Blood Pressure in Middle-Aged and Older Adults

Martens, Christopher[1]; Denman, Blair[1]; Mazzo, Melissa[1]; Armstrong, Michael[2]; Reisdorph, Nichole[2]; McQueen, Matthew[1]; Chonchol, Michel[3]; Seals, Douglas[1]

[1]Department of Integrative Physiology, University of Colorado Boulder, Boulder CO, USA, [2]Department of Pharmaceutical Sciences, Skaggs School of Pharmacy and Pharmaceutical Sciences, University of Colorado Anschutz Medical Campus, Denver CO, USA, [3]Division of Renal Diseases and Hypertension, University of Colorado Anschutz Medical Campus, Denver CO, USA

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® (500mg, 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.

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.

LATAM Artery 2017 Meeting Update

L Pupi, *Buenos Aires, Argentina*; P Forcada, *Buenos Aires, Argentina*

LAA1 Hemodynamic and structural arterial parameters´ asociation with interindividual variations of Body mass index in childhood and adolescence

Garcia, Victoria[1]; Curcio, Santiago[1]; Zinoveev, Agustina[1]; Giachetto, Gustavo[2]; Chiesa, Pedro[3]; Bia, Daniel[1]; Zócalo, Yanina[1]

[1]Physiology Department, School of Medicine, Centro Universitario de Investigación, Innovación y Diagnóstico Arterial (CUiiDARTE), [2]Clínica Pediátrica "C", Centro Hospitalario Pereira Rossell, ASSE, [3]Pediatric Cardiology Center, Centro Hospitalario Pereira Rossell

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 (β=0.210), pPP (β=0.150), cSBP (β=0.204) and cPP (β=0.188), CCA DD (β=0.145), FCA (β=0.143), BA (β=0.210), cIMT (β=0.135), and CCA EM (β=0.117).

Conclusions
Higher zBMI associated higher standardized arterial blood pressure, stiffness levels, diameters and thickness. Hemodynamic parameters presented the stronger associations with zBMI variations.

17.30 Invited Lecture

Chair: L Van Bortel, A Paini

Plaque mechanics and effects of the shear stress

Dr Jolanda Wentzel*, ErasmusMC, Rotterdam, The Netherlands*

18.00 Poster Session I and Welcome Networking Reception

M = Moderated poster

Poster Session I – Basic

Chair: P Lacolley, J Baulmann

P1 – Withdrawn by author

P2 Local abdominal versus thoracic aorta stiffening in hypertensive rats under either NO restriction or salted diet M

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Background
Hypertensive humans exhibit reduced nitric oxide bioavailability and increased salt sensitivity, both of which are related to central artery stiffening. We studied the effect of 5 week NO restriction via L-NAME treatment in spontaneously hypertensive rats (SHR) and 5 % salted diet in salt-sensitive SHR (SHRSP), on the thoracic (TA) and abdominal (AA) aorta.

Methods
Ultrasonic recording of the pulsatile aortic diameter together with blood pressure allowed the measurement of diameter distension and ß-stiffness index. SHRLN and SHRSPsalt were compared to their respective control normotensive rats WKY and two measurements were performed in each rat for TA and AA: at operating basal pressure and at reduced WKY matched pressure, n=6-8. Aortic structure was then characterized by immunohistochemical analysis.

Results
At basal blood pressure, stiffness was greatly increased (range 263-330 %) and distension decreased at both TA and AA in both models. At WKY-matched blood pressure and pulse pressure, AA parameters remained significantly altered whereas TA recovered to values not significantly different from WKY values.
Immunohistochemistry evaluation showed similar increases of markers of fibrosis and remodeling for AA and TA in the two models (fibronectin and its integrin alpha5-beta1 receptor, Focal Adhesion Kinase).

Conclusions
This study confirms the potency of ultrasonic derived stiffness measurements and that aortic remodeling is non-uniform along the aortic trunk. The thoracic aorta, which has an important role in dampening cardiac output appears less sensitive to salt loading and NO reduction induced stiffening. Surprisingly, fibrosis does not appear to account for these dynamic differences.

P3 The extent of endothelial dysfunction in the femoral artery is similar in the juvenile male and female spontaneously hypertensive rats

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Objectives
Endothelial dysfunction (ED) plays an important role in the pathogenesis of hypertension. In this work, we studied sex differences in the endothelium-dependent relaxation (EDR) of the femoral artery (FA) and its nitric oxide (NO)-dependent and NO-independent components in peri-pubertal (7-week-old) spontaneously hypertensive male and female rats (SHR). Age-matched Wistar-Kyoto

(WKY) rats served as the control groups.

Method
Systolic blood pressure (sBP) was measured non-invasively by tail-cuff. Vascular studies were conducted using the wire myograph at isometric conditions. EDR was determined using acetylcholine test. Biochemical parameters (lipid profile, uric acid) were determined in plasma.

Results
We found a significant increase in sBP of SHR vs. WKY, however, there were no sex-dependent differences in sBP. Significantly reduced EDR was found in both male and female SHR and the extent of ED was similar in males and females. ED in SHR of both sexes was associated with a reduced NO-independent component, while NO- dependent component was reduced only in females. Concentrations of high-density lipoproteins were significantly increased in females vs. males in both WKY and SHR. Uric acid concentration was decreased only in male SHR vs. male WKY.

Conclusion
In conclusion, we did not find differences in sBP and overall endothelial function between juvenile SHR males and females. ED in both young SHR males and females was NO-independent. In addition, results suggested the association between low serum uric acid concentrations and ED in male SHRs.
Supported by the grants VEGA No. 2/0190/17, APVV-16-0263 and Slovak Society of Cardiology.

P4 Social stress-induced blood pressure increase in borderline hypertensive rats is associated with endothelial dysfunction in the resistant arteries M

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Objectives
Several studies have observed that altered endothelial function is involved in the development of stress-induced hypertension. The aim of this study was to investigate the effects of chronic social stress (crowding) on endothelium-dependent relaxation (EDR) of the superior mesenteric artery (SMA) and of small resistant mesenteric arteries (MA) as well as on neurogenic contractions of SMA in adult borderline hypertensive rats (BHR).

Methods
Twelve-week-old BHR (offspring of spontaneously hypertensive dams and Wistar- Kyoto sires) males were exposed to crowding (living space: 200 cm^2/rat) for eight weeks. Control BHR were kept in the groups of four rats per cage (living space: 480 cm^2/rat). Systolic blood pressure (sBP) was determined by the tail-cuff method.
Vascular function was investigated in the isolated arteries at isometric conditions.
EDR was assessed using acetylcholine test.

Results
Crowding significantly increased sBP of BHR to the hypertensive values. Results showed that stress did not affect total acetylcholine-induced relaxation and its nitric oxide (NO)-dependent and NO-independent components in the SMA. In the resistant MA, stress reduced total acetylcholine-induced relaxation by reducing NO- independent component, without the alterations of its NO-dependent component.
However, stress failed to affect significantly neurogenic contractions of SMA elicited by electrical stimulation of perivascular sympathetic nerves and vasoconstriction induced by exogenous noradrenaline in SMA.

Conclusion
In conclusion, chronic social stress can accelerate the development of hypertension in BHR, which seems to be associated with NO-independent endothelial dysfunction in small resistant arteries.
Supported by the grants VEGA No. 2/0190/17 and APVV-16-0263.

P5 Erythrocyte deformability and nitric oxide production in animal model of primary hypertension and their age-dependent changes.

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Objectives
Reduced deformability of red blood cells (RBC) plays an important role in etiology of various diseases including cardiovascular. The nitric oxide (NO) was identified as one of factors responsible for maintenance of RBC deformability. Reduced bioavailability of NO might be important in the pathogenesis of hypertension. The aim of present study was to determine the effect of hypertension and aging on RBC deformability and NO production of experimental animals.

Methods
Spontaneously hypertensive rats (SHR) and normotensive Wistar-Kyoto (WKY) rats were divided into 6 groups according to age (7, 20 and 52 weeks) and strain: SHR-7, SHR-20, SHR-52 and WKY-7, WKY-20, WKY-52. Blood was used for determination of RBC deformability using filtration method and NO production in RBCs using fluorescent NO probe DAF-2 DA.

Results
We found reduced deformability at WKY-52 and SHR-52 as compared to strain- matched 20-week-old animals. Strain-related differences in deformability were observed at 7 and 52 weeks of age, where the SHR-7 had reduced deformability and the SHR-52 had increased deformability as compared to age-matched WKY. We have found that at younger age, deformability and NO production in RBCs was able to increase, while in the older age there was a decrease in both parameters.

Conclusions
Changes in the RBC deformability under hypertensive conditions are unlikely to be related to changes in NO production. On the other hand, age-related changes in deformability of both, WKY and SHR are at least partially associated with changes in NO production. Supported by grants VEGA 1/0032/14 and Slovak Society of Cardiology.

P6 Angiotensin AT2 receptor agonist, compound 21, maintains vascular integrity and prevents abdominal aortic aneurysm progression in the rat M

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The effects of the selective angiotensin AT2 receptor agonist, compound 21 (C21), on abdominal aortic aneurysm (AAA) formation were investigated in normotensive Wistar rats.

AAA was induced by perfusion of isolated aortic segments with elastase (Anidjar/Dobrin model). Treatment with C21 (0.03 and 0.3 mg/kg daily) was started after surgery and continued for 14 days. Sham operated animals and vehicle-treated animals after aneurysm induction (AI) served as controls. Aortic diameter and wall properties (distensibility, pulse propagation velocity) were measured infrarenally via ultrasound. Hemodynamic parameters, aortic tissue protein expression and serum cytokines were analysed.

On day 14 post AI, aortic diameter of vehicle-treated animals was increased 1,6-fold compared to sham operated rats (p<0.0001). C21 (0.03 mg/kg) decreased aortic diameter in comparison to vehicle (1.9 mm ± 0.06 vs. 2.65 mm ± 0.06; p<0.0001).
Infrarenal blood velocity and aortic distensibility were reduced, whereas aortic wall stiffness was increased post AI. These alterations were significantly ameliorated by treatment with C21 (p<0.0001; p<0.0001; p<0.05). Blood pressure and cardiac contractility were not altered. Protein expression of IL1 beta, NF kappa B, MMP9, TGF-beta1 and MLKL in the aorta was significantly (p<0.05) down-regulated in the C21 group compared with vehicle. In primary rat vascular smooth muscle cells, the release of MMP9, TGF-beta1 and MLKL was significantly diminished after C21 (1µM) treatment. Serum concentration of TGF-beta1 was also decreased by C21 in comparison to vehicle (p <0.01).

In conclusion, AT2 receptor stimulation with C21 prevented extracellular matrix degradation, maintained vascular integrity of the aorta and prevented AAA progression.

P7 The Urinary Peptidomic Signature of Aortic Stiffness Reveals Molecular Pathways and Drug Targets M

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Background
Molecular pathways leading to stiffening of the central arteries are poorly understood. We searched for differentially expressed proteins by urinary peptidomic analysis in patients with arterial stiffness and healthy controls in a case–control study.

Methods
To identify urinary peptides associated with aortic stiffening, we applied capillary electrophoresis coupled to mass spectrometry. We compared 18 cardiovarscular disease-free patients with carotid-femoral pulse wave velocity (PWV >10 m/s standardised to a heart rate of 75/minute as measured by the SphygmoCor method) with 18 controls matched for sex, age and mean arterial pressure.

Results
69 urinary peptides had a different signal amplitude between cases and controls (P≤ 0.049). Among 33 peptides with known sequence, 26 were members of the extracellular matrix family, including collagen type I α-1 and α-2, collagen type III α-1, collagen type IV α-5, collagens IX, XXI and XXVII. Collagen type I was down- regulated, whereas collagen type III was up-regulated. Epidermal growth factor receptor (EGFR), a key regulator of myoblast differentiation, and interactions of laminin with other proteins were down-regulated. Atherosclerosis signalling pathways and intrinsic prothrombin activation were the top pathways associated with increased PWV. Potential drug targets included collagen type IV α 3 and transforming growth factor β 3. Angiotensin-converting enzyme inhibitors, which are widely used for vascular protection, were among the possible therapeutic agents.

Conclusions
We suggest that stiffening of large elastic arteries involves changes of the extracellular matrix, as reflected by collagen turnover and regulation of myoblast differentiation. Pathway analysis identified potential drug targets, possibly amenable by angiotensin-converting enzyme inhibition.

P8 Proprotein convertase subtilisin/kexin type 9 levels and arterial function M

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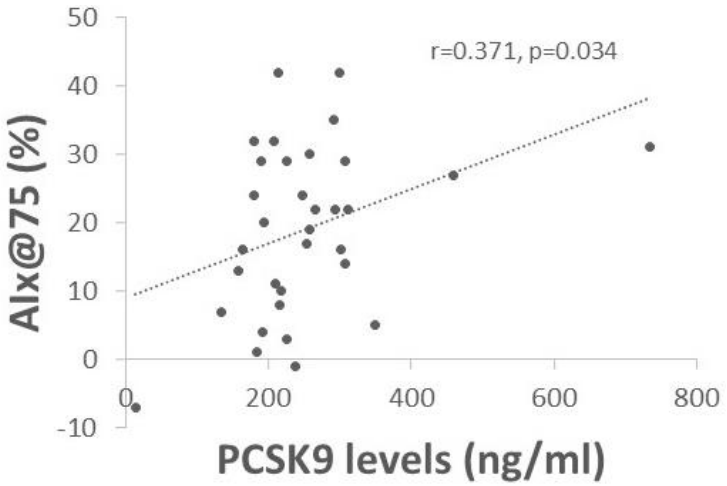
Purpose/Background/Objectives
Proprotein convertase subtilisin/kexin type 9 (PCSK9) levels are modestly but significantly associated with increased risk of total cardiovascular events. Aortic stiffness and wave reflections are also important predictors of cardiovascular events. The aim of this pilot study was to determine if PCSK9 levels are associated with aortic elastic properties in patients with familial dyslipidemia.

Methods
Thirty-three patients with familial dyslipidemia (mean age 45±12 years, 21 men, 14 with heterozygous familial hypercholesterolemia and 19 with familial combined hyperlipidemia) without known cardiovascular disease were enrolled. PCSK9 levels were measured with ELISA. Aortic stiffness was assessed with carotid-femoral pulse wave velocity (cfPWV) and wave reflections were assessed with aortic augmentation index corrected for heart rate (AIx@75). High-sensitivity C-reactive protein (hsCRP) levels were determined as a marker of subclinical inflammation.

Results
There was a positive correlation between AIx@75 and PCSK9 levels (r=0.371, p=0.034). (Figure) No association was found between levels PCSK9 and cfPWV (r=0.043, p=0.813) or hsCRP (r=0.199, p=0.274). In multivariate regression analysis, after adjustment for potential confounders such as age and sex, AIx@75 showed a significant positive correlation with PCSK9 levels (Adjusted R2=0.23, p=0.007). Even after further adjustment for possible confounders such as the type of familial dyslipidemia, low-density lipoprotein levels, cfPWV and hsCRP this association remained statistically significant (Adjusted R2=0.16, p=0.03). Gender was also significantly associated with levels of PCSK9 (p=0.029).



Conclusions
In a group of patients with familial dyslipidemia PCSK9 levels were positively associated with wave reflections but not aortic stiffness.

P9 The participation of nitric oxide and hydrogen sulphide signalisation in vasoactive responses of rat thoracic aorta in condition of developed spontaneous hypertension

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Our previous study in young spontaneously hypertensive rats (SHR) confirmed a participation of nitric oxide (NO) and hydrogen sulphide (H_2S) in probably inherent adaptive strategy of conduit arteries in condition of sustained hypertension. The aim
of study was to confirm or refuse the compensatory mechanisms in developed phase of hypertension in SHR with an emphasis on manifestation of the NO and H_2S
signalisations.
In the experiments 17-20-weeks-old normotensive Wistar rats and SHR were included. Systolic blood pressure (sBP) was measured by plethysmographic method and vasoactivity of isolated thoracic aorta (TA) was recorded by sensors of changes of isometric tension.

We observed an increased sBP and hypertrophy of myocardium in SHR. The contractile response of TA to exogenous noradrenaline was reduced in SHR due to inhibition effect of endogenous NO. In SHR impaired endothelial functions were confirmed, however through a prevalence of vasoconstrictors produced by cyclooxygenase but not as a result of reduced NO synthesis. Dual effect of H_2S
donor (Na_2S) was showed in both strains; however an increased maximal vasorelaxation was proved in SHR. Moreover, acute inhibition of NO production increased the relaxant phase of Na_2S effects. On the other hand, application of Na_2S
modulatory dose increased the release of NO from exogenous NO donor, nitrosogluthation in Wistar rats but not in SHR.

The data confirmed that SHR disposed with adaptive mechanisms including NO and H_2S systems and their interaction (acute NO deficiency potentiated vasorelaxant effect of H_2S). These effects could provide compensation of the increased vascular tone in adulthood.

References

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P10 Loss of endothelium-dependent regulation of arterial wall viscosity in essential hypertension

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Background

Nitric oxide (NO) and epoxyeicosatrienoic acids (EETs) regulate arterial wall viscosity (AWV) in young

subjects (1). During hypertension, characterised by a decrease in endothelium-derived NO and an early disappearance of EETs, AWV is not modified (2,3). We compared the role of NO and EETs in the regulation of AWV in 18 middle- age untreated hypertensive patients (HT) vs. 14 matched normotensive controls (NT).

Methods
Radial artery diameter and pressure were measured before and after infusion of L- NMMA, fluconazole or both. AWV was estimated by the ratio of the area of the hysteresis loop of the pressure-diameter relationship (W_V, viscous energy dissipated) to the area under the loading phase, bounded by pulse pressure and diameter (W_E, elastic energy stored).

Results
At baseline, W_V and W_E were higher in HT than in NT (W_V: 0.71[0.65-1.19] vs. 0.45[0.40-0.62] mmHg.mm², p<0.05; W_E: 1.99[1.45-2.61] vs. 1.09[0.96-1.54] mmHg.mm², p<0.01) but W_V/W_E were similar (40.3±7.1% vs. 40.5±5.9%). In NT, fluconazole and L-NMMA decreased diameter, but did not modify W_V, W_E and W_V/W_E. L-NMMA+fluconazole decreased diameter and increased W_V/W_E (38.9±8.5% to 47.5±8.9%, p<0.05) due to an increase in W_V (+27.1±57.5%) as compared to W_E (- 1.3±27.8%) (p<0.05). In HT, whereas fluconazole had no effect on diameter, W_V and W_E, LNMMA and LNMMA+fluconazole decreased these parameters (p<0.05) without change in W_V/W_E.

Conclusion
In NT, NO and EETs regulate AWV of conduit arteries. Conversely, in HT associated to an increased elastic energy stored, NO regulates elastic work but not AWV that remains stable. Whether this represents an optimal adaptation remains to be investigated.

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R. Impaired regulation of arterial wall viscosity during changes in blood flow in essential hypertensive patients. Artery Research. 2016 Dec 1;16:77–8.

P11 Withdrawn by author

P12 Withdrawn by author

P13 Arhgef1/RhoA signaling participate in ageing-induced arterial stiffness and hypercoagulability

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The RhoA signaling pathway is a master regulator of mechanostransduction and plasticity of vascular smooth muscle cells (VSMCs) that controls arterial stiffening. The RhoA exchange factor Arhgef1 is causally involved in the development of angiotensin II-dependent hypertension.

Our aim was to determine whether Arhgef1 plays a key role in age-associated arterial stiffness and the coupling with modifications of the procoagulant properties of blood and VSMCs. We used 65 week-old

transgenic mice invalidated for Arhgef1 (Arhgef1$^{-/-}$) and age-matched controls (Arhgef1$^{+/+}$). In vivo arterial diameter pressure, distensibility/arterial pressure and elastic modulus/circumferential stress curves at the level of carotid artery were recorded using an echotracking system (VEVO 770 Visualsonics Imaging) in anesthetized animals.

Systolic blood pressure, pulse pressure and heart rate were not different between mutant and control mice. Isobaric carotid distensibility was increased in Arhgef1$^{-/-}$ mice compared to Arhgef1$^{+/+}$ mice. The elastic modulus/circumferential stress curves
were shifted significantly rightwards in Arhgef1$^{-/-}$ mice compared to Arhgef1$^{+/+}$ mice. Thrombin generation in blood and at the surface of VSMCs cultured from aorta was reduced in Arhgef1$^{-/-}$ mice. Anticoagulant markers secreted by the vascular wall (tissue factor pathway inhibitor and thrombomodulin) were increased in plasma of Arhgef1$^{-/-}$ mice.

The time of formation of an occlusive thrombus induced by FeCl3 in the carotid artery was prolonged in Arhgef1$^{-/-}$ mice.

In conclusion, the Arhgef1/RhoA contractile pathway contributes to arterial stiffening
and VSMC procoagulant properties in aging. Whether this reduced procoagulant properties of the vascular wall is a cause or consequence of arterial stiffness remains to be elucidated.

Poster Session I – Epidemiology
Chair: J Staessen, G Pucci

P35 Soluble receptor for advanced glycation end-products and age-dependent arterial stiffening in general population based prospective study M

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Background
Accumulation of advanced glycation end-products (AGEs) is one of pathophysiological processes, responsible for progressive stiffening of vessel
wall. In contrast, soluble isoform of receptor for AGEs (sRAGE) act as “decoy” and physiological defense against circulating AGEs. We hypothesized that low levels of sRAGE might be associated with accelerated age-dependent arterial stiffening.

Methods
We followed 429 population-based subjects (mean age 50.8 (±11.7) years, 41.5% males) in prospective study. Aortic pulse wave velocity (aPWV) was measured using a Sphygmocor device. sRAGE concentrations were assessed in frozen samples by ELISA methods (R&D Systems). Baseline examination was done in 2008/9, while follow-up visit in 2016/17 (median time of follow-up was 7.,6 years)

Results
Mean intra-individual increase of aPWV during follow-up was 1.37 (±1.88) m/sec and was inversely associated with baseline sRAGE concentration- the aPWVV difference [follow-up *minus* baseline] across its quintiles was 2.08((±1.89), 1.51(±2.16), 1.20(±2.10), 0.99(±1.70), 1.13(±1.21) in 1st-5th quintiles of sRAGE, resp.; p=0.003 (adjusted for age, gender and baseline mean arterial pressure) Baseline concentration of sRAGE <917 pg/mL (1st quintile) was associated with about two-fold higher risk, that aPWV increased by more than 0.8 m/sec (expectable “secular“ age- dependent increase) even if adjusted for baseline risk profile and pharmacotherapy [fully adjusted odds ratio was 1.95 (95%CI: 1.12-3.39, p=0.018].

Conclusions
Low concentration of circulating sRAGE was in our sample of generally healthy subjects

associated with markedly accelerated age-dependent arterial stiffening, probably as a consequence of higher deposition of AGEs in vessel wall. *(supported by SVV 02684, PROGRES Q39 and AZV 15-27109 grants)*

P36 Pulse pressure amplification and its relationship with age in young, apparently healthy black and white adults: The African-PREDICT study M

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Background
Pulse pressure amplification (PPA), i.e. the amplification from central arteries to the periphery, is inversely related to arterial stiffness, organ damage and mortality. It is known that arterial stiffness is higher in black than white populations, but it is unclear if this is due to early vascular aging. We therefore investigated whether PPA declines earlier in young normotensive black South Africans, when compared to their white counterparts.

Methods
We included 875 black and white men and women from the African-PREDICT study (55% black, 41% men), aged 20–30 years, with no prior diagnosis of chronic disease, screened for normotensive clinic blood pressure (BP). We determined supine central PP (cPP), and supine brachial systolic– and diastolic BP, from which brachial PP (bPP) was calculated. PPA was defined as the ratio of the amplitude of the PP between these distal and proximal locations (bPP/cPP).

Results
We found the mean PPA to be lower in black compared to white participants (1.43 vs. 1.46; P = 0.013). In black adults PPA declined earlier with increasing age (P– trend < 0.001), with a weak trend in whites (P = 0.063) after adjustment for sex, socio-economic status, height and mean arterial pressure. In multivariable-adjusted regression, we found an independent inverse association between PPA and age only in the black group (β = –0.22, P < 0.001).

Conclusion
PPA declines earlier with age in normotensive black adults younger than 30 years, exemplifying early vascular aging which may predispose black individuals to future cardiovascular outcomes.

P37 Reference values of cardio-ankle vascular index in a random sample of a Caucasian population M

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Objectives
Cardio-ankle vascular index (CAVI), a parameter of arterial stiffness, has been increasingly used for cardiovascular risk estimation. Currently used CAVI reference values are derived from the Japanese population. It is not clear whether the same reference values can be used in the Caucasian population. The aim of the present study was to describe cardiovascular risk factors influencing CAVI and to establish CAVI reference values.

Methods
2160 individuals randomly selected from the Brno city population aged 25–65 years were examined. Of these, 1347 subjects were free from cardiovascular disease, non- diabetic and untreated by antihypertensive or lipid-lowering drugs, forming the reference value population. CAVI was measured using the VaSera VS-1000 device.

Results
At each blood pressure (BP) level, there was a quadratic association between CAVI and age, except for a linear association in the optimal BP group. While there was no association between BP and CAVI in younger subjects, there was a linear association between CAVI and BP after 40 years of age. Reference values by age and gender were established. In each age group, except for the male 60–65 group, reference values in our population were lower than in the Japanese one with the difference ranging from -0.29 to 0.21 for males, and from -0.38 to -0.03 for females.

Conclusion
This is the first study providing CAVI reference values in a random sample of the Caucasian population. Our results suggest that the currently used values slightly overestimate CAVI in younger Caucasian, possibly underestimating cardiovascular risk.

P38 Ascending aorta dimensions and clinic and 24 hours blood pressure in a general population in Northern Italy: the Vobarno Study M

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Background
Epidemiological studies have suggested that even mild enlargement of the ascending aorta may have independent prognostic significance for cardiovascular events.
Therefore, some Authors have proposed that dilatation of the ascending aorta could be considered as a form of preclinical vascular damage in hypertensive patients.

Aim
To assess the correlation between clinic and 24 hours BP values and the dimensions of the aorta, measured at level of the sinuses of Valsalva (Val), at the left ventricular outflow tract(LVOT), and at the level of the proximal ascending aorta(AscAO) in subjects from a general population.

Methods
250 subjects (43% males, mean age56±4years,42%hypertensives-HT) underwent laboratory examinations, clinic and 24 hours BP measurement, cardiac and carotid ultrasound, carotid-femoral pulse wave velocity measurement (AoPWV).

Results
aortic diameters were greater HT as compared to NT (Val:3.41±0.54vs3.25±0.41cm,

LVOT2.10±0.28vs2.04±0.26,AscAo3.39±0.45vs3.18±0.38,all p <0.05).Aortic diameters were all correlated to clinic and 24 hours BP values. The coefficients of correlation were greater for 24 hours BP (Tab). Val, AscAo, LVOT were also significantly correlated with left ventricular mass (r=0.61,r=0.48,and r=0.43,all p <0.001),meanmax intima media thickness (r=0.13, r=0.24, and r=0.13, all p<0.05) and with AoPWV (r=0.16, p<0.05, r=0.28 p<0.001, r=0.08 p=ns).

	Ao Valsalva		Asc		LVOT	
	r	p	r	p	r	p
SBP	0.148*	0.019	0.161*	0.016	0.135*	0.037
DBP	0.253**	0.0001	0.223**	0.001	0.189**	0.003
MBP	0.220**	0.0001	0.175**	0.006	0.208**	0.002
PP	-0.046	0.470	0.004	0.948	0.003	0.968
HR	-0.005	0.933	-0.028	0.687	-0.004	0.949
SBP 24 hrs	0.231**	0.0001	0.162*	0.017	0.108	0.097
DBP 24 hrs	0.346**	0.0001	0.264**	0.0001	0.234**	0.0001
MBP 24 hrs	0.267**	0.0001	0.214**	0.002	0.164*	0.011
PP 24 hrs	-0.003	0.962	-0.031	0.645	-0.082	0.209
HR 24 hrs	-0.058	0.370	-0.051	0.454	-0.026	0.687

Conclusions
The dimensions of the proximal ascending aorta are significantly related to BP values in normotensive subjects and in hypertensive patients. Aortic dimension are more strictly related to twenty-four hours BP values than to clinic BP values. In this sample of general population, a significant correlation between aortic dimensions and measures of cardiac and vascular organ damage was also observed, confirming the parallelism between different forms of organ damage.

P39 Left ventricular structure and function in relation to peripheral and central blood pressure in a general population M

Yang, Wenyi[1]; Efremov, Ljupcho[1]; Zhang, Zhen-Yu[1]; Cauwenberghs, Nicholas[1]; Thijs, Lutgarde[1]; Wei, Fang-Fei[1]; Huang, Qi-Fang[1]; Mujaj, Blerim[1]; Luttun, Aernout[2]; Verhamme, Peter[2]; Kuznetsova, Tatiana[1]; Staessen, Jan[1]

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Background
Central blood pressure (BP) is a predictor of target organ damage. No previous study addressed the question to what extent central compared with peripheral is related to left ventricular (LV) structure and function in a general population.

Methods
In 577 Flemish recruited from the general population (47.8% women; mean age 50.5 years), we assessed the multivariable-adjusted associations of echocardiographic LV structure and systolic and diastolic LV function (Vivid7 Pro device; EchoPac software, version 4.0.4; GE Vingmed, Horten, Norway) with peripheral and central pressure, as recorded by radial applanation tonometry

(SphygmoCor software, version
9.0). Association sizes were expressed per 15/10 mmHg increment in peripheral or central systolic/diastolic BP.

Results
Peripheral compared with central systolic BP was 10.2 mm Hg higher (*P*<0.0001), whereas diastolic BP was similar peripherally and centrally (*P*=0.50). Associations were closer (*P*≤0.020) with central than peripheral systolic BP for LV mass (+0.59 g/m2) and left atrial volume (+0.29 ml/m2) indexed to body surface area, peak A transmitral flow (+0.12 cm/s), peak e' mitral annular movement (–0.18 cm/s) and the E/A ratio (–0.017). Associations were closer (*P*≤0.038) with central than peripheral diastolic BP for left atrial volume index (+0.289 ml/m2), e' (–0.123 cm/s) and E/e' (+0.094). Ejection fraction and global longitudinal strain were similarly associated with central and peripheral systolic (*P*≥0.62) and diastolic (*P*≥0.18) BP.

Conclusions
In asymptomatic people recruited from the general population, LV mass and atrial volume indexes and selected haemodynamic measurements reflecting diastolic LV function are slightly but significantly closer associated with central than peripheral BP.

P40 Does arterial ageing differ between Europeans and Japanese and Korean patient samples? Results from current UK studies M

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Objective
Vascular stiffness has long been linked with the ageing process. However, it is only since the development of accurate methods for measuring arterial compliance that unravelling this relationship has become possible. Arterial stiffening over time appears to differ between ethnic groups and/or geographic areas. We investigated how the cardio-ankle vascular index (CAVI) varied with chronological age to make initial comparisons of its change with age between this European study and published data from Japanese and Korean patient populations.

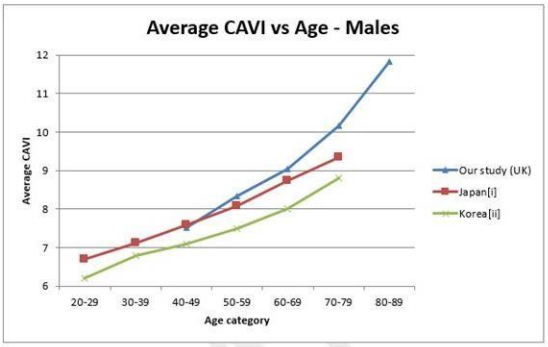
Method
312 participants (180 men, 132 women), age 63.7±12.9 (mean±SD), range 25-92 years. The following were measured: CAVI using VaSera VS-1500N® (Fukuda Denshi, Japan); brachial BP using OMRON705-IT; baseline characteristics and physical examination of cardiovascular health. These data are from current UK studies of healthy volunteers with approximately 20% having two or more cardiovascular risk factors.

Results
CAVI was significantly correlated with age (r=0.63, p<0.001), more closely in men (r=0.71, p<0.001) than women (r=0.54, p<0.001). These data were used to create a preliminary set of 'usual' average CAVI values for each age category (Table) and compared against data from Japan [1] and Korea [2] (plot 1 & 2). Korean men had lower CAVI values at each age.

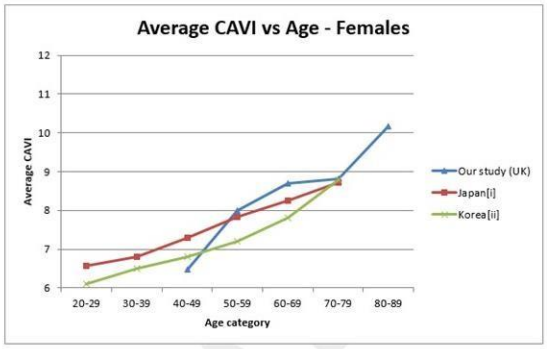
Table

Age category (years)	CAVI Mean (SD)
<40	6.83 (0.76)
40-49	7.22 (0.86)
50-59	8.20 (1.29)
60-69	8.87 (1.24)
70-79	9.60 (1.36)
80-89	11.11 (1.60)

Plot 1



Plot 2



Conclusions

This suggests CAVI is closely related to ageing and may be a useful indicator of vascular age. In initial comparisons, the slope of arterial 'ageing' may be steeper for Europeans, especially men over 60 years, than for Japanese and particularly Koreans, but detailed analysis has not yet been done due to lack of raw data.

References

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P41 Myocardial Mechanoenergetic Efficiency Index (MMEI) and arterial stiffness: Association in a general population in northern Italy M

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A non-invasive approach for the estimation of mechanical efficiency through the calculation of the ratio between stroke work and HR–pressure product has been recently proposed by de Simone et al. This index, which expresses the amount of blood pumped in a single beat in 1 second by the heart, may be easily obtained by echocardiography. The aim of our study was to evaluate the determinants of myocardial mechanoenergetic efficiency index (MEEi), calculated as as stroke volume/heart rate and indexed to LV mass(MEEi=MEE/LVM)in a large general population sample in Northern Italy.

Design and methods

We evaluated 478 subjects participating in a general population study in Northern Italy (Studio Vobarno). All subjects underwent a physical examination with measurement of clinic blood pressure (BP). In all subjects laboratory examinations, 24 hours blood pressure measurement, echocardiography, and assessment of carotid-femoral pulse wave velocity (PWV) were performed.

Results
Subjects had a mean age of 58±10 years, a BMI of 26±4, 44% were males, 69% had arterial hypertension (55 % treated). MEEi was lower in males and in patients with increased PWV. MEEi was inversely correlated with age, BMI, waist circumference, clinic and 24 hours BP, glucose, uric acid, triglycerides and directly correlated with HDL. MEEI was also inversely correlated with relative wall thickness (RWT) and PWV. At linear regression multivariate (?) analysis MEEi remained independently related to male gender(β=0.16,p<0.001),BMI (β=-0.13,p<0.005), RWT (β=-0.56, p<0.001) and PWV(β=-0.10, p<0.05).

Conclusions
In a large sample of general population in Northern Italy myocardial mechanoenergetic efficiency was inversely correlated with arterial stiffness, independently of multiple possible confounders.

P42 24-hour central blood pressure is more strongly associated to target organ damage than brachial blood pressure: first results of the VASOTENS Registry

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Objective
In the present analysis of the VASOTENS study [1] baseline data, we checked whether organ damage of hypertension (TOD) i) is better associated with 24-hour central than peripheral BP and ii) is related to ambulatory arterial stiffness, estimated by pulse wave velocity (PWV) and augmentation index (AIx).

Methods
TOD in 334 hypertensive patients (mean age 53±15, 52% males, 45% treated) was estimated by calculation of left ventricular mass index (LVMI), intima-media thickness (IMT) and creatinine clearance (CC). 24-hour indices were estimated through the Vasotens technology [2]. 24-hour brachial (bSBP) and aortic systolic BP (aSBP), standard deviation of bSBP, PWV and AIx were obtained. Bivariate and multivariate analysis (stepwise linear regression) was used.

Results
A significant relation was found for age, bSBP and aSBP vs. LVMI and IMT (see table). IMT was also significantly related to SBP variability and arterial stiffness, whereas age, SBP variability and AIx were significantly associated with CC. In the multivariate analysis, including all ••••variables entered in the bivariate model, adjusted by sex, statistically significant (p<0.001) association was observed for aSBP and age with LVMI (standardized regression coefficient 0.25 and 0.18, respectively), and for age with IMT (0.56) and CC (-0.53).

Conclusions
In hypertensive patients age appears to be the major determinant of TOD, with central SBP, and marginally peripheral SBP, PWV and AIx, also playing a significant role. Our results suggest that estimation of 24-hour central hemodynamics and arterial stiffness in ambulatory conditions may help improve the individualized assessment of the BP-associated TOD.

Correlation coefficients	LVMI (g/m²)	IMT (mm)	CC (ml/min)
Age (years)	0.25 ***	0.56 **	-0.53 **
bSBP (mmHg)	0.23 ***	0.24 **	-0.01
aSBP (mmHg)	0.28 ***	0.26 **	-0.05
SD bSBP (mmHg)	0.01	0.24 **	-0.19 *
PWV (m/s)	0.09	0.17 *	-0.14
AI (%)	0.07	0.22 **	-0.18 *

*** p<0.001; ** p<0.01; * p<0.05

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P43 Withdrawn by author

P44 Withdrawn by author

P45 Renin at different physical activity levels in a bi-ethnic population: The African-PREDICT study

van Rooyen, Johannes[1]; Huisman, Hugo[2]; Malan, Leonè[2]; Mels, Catharina[2]; Kruger, Ruan[2]; Gafane-Matemane, Lebo[2]; Botha, Shani[2]; Schutte, Alta[2]

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Background and objectives
It is widely accepted that regular physical exercise reduces the BP, particularly in hypertensive individuals. It is recommended in the prevention of hypertension to assist in BP control. The BP lowering mechanisms of exercise remain largely elusive, we therefore evaluated the RAAS as a regulator of arterial BP.

Methods
The sub-study was embedded in the African Prospective study on the Early Detection and Identification of Cardiovascular disease and Hypertension (African- PREDICT) and included 111 white and 99 black participants aged 20-30 years.

Office- and central blood pressure as well as other cardiovascular variables were measured. Renin was analysed with an ELISA- and aldosterone with a RIA kit.

Results
The BP decreased significantly in the white but not in the black participants when tertiles for physical activity levels were compared. The total renin (renin + prorenin) level decreased significantly from 789.2 to 700.0 pg/ml (p=0.04) in the white but not in the black participants (821.6 to 806.6 pg/ml; p=0.84) with high physical activity level. In multiple regression analysis, in the white participants, MAP and aldosterone contributed significantly and independently to the low renin in the third percentile for physical activity level. This was not evident in the black participants.

Conclusion
Only in white participants high physical activity levels were associated with decreased blood pressure and the RAAS may be an important mechanism in this regard.

P46 Arterial stiffness in in relation to birth characteristics in the Jamaican 1986 birth cohort

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Background
We tested the association between birthweight and arterial stiffness measured by aortic pulse wave velocity (PWV) and cardio-ankle vascular index (CAVI) in a birth cohort of 30 year old Jamaicans.

Methods
Participants were from the 1986 Jamaica Birth Cohort. Arterial stiffness was measured as PWV using Arteriograph 24h™ and CAVI with VaSera™ devices. Current anthropometry (height, weight, waist and hip circumference), and brachial blood pressure measures were linked to birthweight and other early life markers of
CVD risk (birth-length and maternal height). Linear regression models were used for analysis.

Results
Analyses included 235 participants 44% male, with mean±SD age 29.8±0.7years, birthweight 3.1±0.0kg, PWV 6.3±0.1m/s and CAVI 6.3±0.1. Bivariate models showed men had higher arterial stiffness (p<0.001). Maternal height (p=0.031), waist/hip ratio (p=0.019), BMI (p=<0.001) and blood pressure (systolic and diastolic) (p<0.001) were associated with PWV, but only BMI (p<0.001) was associated with CAVI. There was no association between birthweight and PWV or CAVI, p=0.38 and p=0.41 respectively. In multivariable models, associations between birthweight and PWV and CAVI did not change after controlling for gender, BMI, and SBP. Positive associations (coef±SE) between PWV and BMI (0.03 ± 0.01 p=<0.01) and SBP (0.03
± 0.01 p=0.001) remained significant; as did the negative associations for BMI and CAVI (-0.04 ± 0.01 p<0.001).

Conclusion
Men had higher arterial stiffness even when controlling for blood pressure and the associations of blood pressure and BMI with PWV were positive whereas and BMI with CAVI was negative. Neither arterial stiffness measure was associated with birthweight.

P47 Tetrahydrobiopterin and markers of oxidative stress in a young bi-ethnic population: The African-PREDICT study

Huisman, Hugo[1,2]; Mels, Carina[3]; Van Rooyen, Johannes[3]; Kruger, Ruan[3]; Fourie, Carla[3]; Gafane, Lebo[3]; Smith, Wayne[3]; Schutte, Alta[3,2]

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Background/Objectives
Tetrahydrobiopterin (BH4) is a cofactor for nitric oxide synthase (NOS). Oxidative stress, reported in black populations (1), may lead to the oxidation of BH4, the uncoupling of eNOS, decreased NO and increased superoxide levels (2,3). We compared BH4 and markers of oxidative stress and their association, between black and white cohorts.

Methods
In the African-PREDICT study, we included black (n=300) and white (N=297) participants (aged 20-30 years). We measured blood pressure, and determined serum levels of BH4 and markers of oxidative stress.

Results
Blacks had higher blood pressure ($p<0.001$). In blacks the following serum levels were lower: BH4 ($p<0.0001$), total antioxidant status (TAS) ($p<0.0001$), glutathione peroxidase (GPx), while reactive oxygen species (ROS) ($p<0.03$) was higher. In blacks BH4 related positively with GPx in single, partial (adjusted for socio-economic status, sex, age, BMI, GGT and cotinine) and multiple regression ($R^2=0.16$, $\beta=0.17$, $p=0.02$) and glutathione reductase (GR) ($R^2=0.16$, $\beta=0.15$, $p=0.05$). We found a negative correlation between BH4 and GPx ($R^2=0.07$, $\beta=-0.26$, $p=0.0006$) in whites.

Conclusions
Higher oxidative stress levels in young blacks (increased ROS, lower TAS and GPx) could explain the low concentrations of BH4, the possible uncoupling of eNOS, resulting in higher blood pressure. The uncoupling of eNOS may explain the production of ROS and peroxinitrite and may be linked to the positive correlation of BH4 with GPx and GR found in blacks, that may lead to early vascular changes.

References

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Poster Session I – Hypertension

Chair: P Boutouyrie, ML Muiesan

P54 Sex differences in ambulatory central blood pressure and pulse wave reflections in untreated patients M

Hametner, Bernhard[1]; Mayer, Christopher Clemens[1]; Whitelegg, Katy[1]; Weber, Thomas[2]; Fitscha, Peter[3]; Wassertheurer, Siegfried[1]

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[2]Cardiology Department, Klinikum Wels-Grieskirchen, Wels, Austria, [3]Practice for Internal Medicine, Vienna, Austria

Objectives
Sex differences for parameters of arterial wave reflection and arterial stiffness were reported from single office measurements, but circadian patterns were not extensively investigated up to now. The aim of this study was to determine sex differences between day and night values of ambulatory central blood pressure as well as ambulatory pulse wave parameters related to arterial wave reflection.

Methods
A Mobil-O-Graph (IEM, Stolberg) with inbuilt PWA technology was used in patients without antihypertensive treatment visiting a doctor's practice for internal medicine. Aortic blood pressure was obtained using a generalized transfer function incorporating mean blood pressure for pressure calibration. Daytime was defined between 9 am and 8 pm and nighttime between 10 pm and 6 am.

Results
In the study 192 men (mean age 50.5 years) and 155 women (57.3 years) were included. Men had higher central systolic (cSBP) and diastolic blood pressures compared to women. In contrast, augmentation index (AIx) and reflection magnitude (RM) were significantly lower in men compared to women both during day and night. For both sexes, AIx and RM were higher during the night, see table for full details (all day-night differences were statistically significant).

	day			night		
	Men		Women	Men		Women
bSBP (mmHg)	134.5	*	130.2	121.5		118.6
bDBP (mmHg)	86.7	*	81.5	74.8	*	70.3
HR (bpm)	75.2		77.1	64.5	*	66.9
cSBP (mmHg)	136.7	*	131.5	131.7	*	125.4
AIx (%)	19.8	*	28.2	25.1	*	35.1
RM	60.5	*	63.4	68.7	*	71.4

Table: Mean values of both sexes during daytime and nighttime; * indicates a significant difference between men and women ($p<0.05$); bSBP... brachial systolic blood pressure, bDBP... brachial diastolic blood pressure, HR... heart rate, cSBP... central systolic blood pressure, AIx... augmentation index, RM... reflection magnitude.

Conclusions
A typical blood pressure dipping during nighttime was found for both sexes. However, an increase in wave reflection parameters was found during nighttime leading to highest values for women during the night. Thus, single measurements have to be interpreted with caution and an ambulatory blood pressure measurement including pulse wave analysis might be beneficial.

P55 Target organ damage and blood pressure variability in hypertension M

Terentes-Printzios, Dimitrios[1]; Vlachopoulos, Charalambos[1]; Angelis, Athanasios[1]; Loakeimidis, Nikolaos[1]; Xaplanteris, Panagiotis[1]; Georgakopoulos, Christos[1]; Sigala, Evangelia[1]; Koutagiar, Losif[1]; Rigatou, Angeliki[1]; Tousoulis, Dimitrios[1]

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Purpose/Background/Objectives
Hypertension is associated with several markers of subclinical target organ damage (TOD). Short-term blood pressure variability (SBPV) is a prognostic factor for cardiovascular events in hypertensives. We hypothesised that there is a relationship between SBPV and TOD in never-treated hypertensives.

Methods
We enrolled 943 consecutive essential hypertensives (mean age 53±12 years, 497 males). Markers of subclinical TOD [left ventricular mass index (LVMI), pulse wave velocity (PWV), total arterial compliance (TAC), aortic augmentation index (AIx@75), ankle-brachial index (ABI) and estimated glomerular filtration rate (eGFR)] and 24-h ambulatory blood pressure were evaluated in all patients. SBPV was calculated as follows: 1) SD of 24-hour, daytime, or nighttime SBP and 2) weighted SD of 24-hour SBP.

Results
In multivariable regression analysis, all four variables of SBPV exhibited significant association with LVMI (p=0.014, p=0.002, p=0.002 and p<0.001, respectively), PWV (p=0.021, p=0.015, p=0.055 and p=0.006, respectively) and TAC (p=0.048, p=0.020, p=0.036 and p=0.006, respectively). In multivariable analysis, ABI and eGFR were not associated with indices of SBPV. We assessed TOD based on 2013 European Guidelines for Hypertension [left ventricular hypertrophy (LVMI>115 g/m2 in men and
>95 g/m2 in women), increased PWV (PWV>10m/s), increased AIx@75 (AIx@75>28%), decreased ABI (ABI<0.9) and decreased renal function (eGFR<60ml/min)]. In multivariable logistic regression analysis, SBPV indices were not associated with markers of TOD (P>0.05).

Conclusions
Our findings support a complex relationship between SBPV and TOD in hypertension. Specifically, SBPV is more closely related to markers of ventricular and vascular compliance than other markers of TOD in hypertension.

P56 Association between Uric Acid and cardiac, vascular and renal Target Organ Damage in Hypertensives subjects M

Maloberti, Alessandro[1,2]; Varrenti, Marisa[3,2]; Triglione, Nicola[1,2]; Occhi, Lucia[1,2]; Panzeri, Francesco[1,2]; Alloni, Marta[2]; Giupponi, Luca[1,2]; Vallerio, Paola[2]; Casati, Matteo[4]; Grassi, Guido[1]; Mancia, Giuseppe[1]; Giannattasio, Cristina[1,2]

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Background
To date no definitive results exist about the relationship of Serum Uric Acid (SUA) and TOD in HT subjects. We sought to determine if such an association exist between SUA and subclinical cardiac, vascular and renal alterations in HT.

Methods
We enrolled 632 consecutive outpatients, followed by the Hypertension Unit of S. Gerardo Hospital (Monza, Italy) affected by essential HT. We evaluated anamnestic data, clinical BP and laboratory data as well as TOD with cardiac echocardiography (both as LMVI and diastolic function – E/A), carotid ultrasound (IMT), arterial stiffness (PWV) and renal function analysis (creatinine and microalbumiuria).

Results
Age was 53.4±12.7 years, SBP/DBP were 140.5±18.8 and 85.1±13.1 mmHg and SUA was 5.2±1.4 mg/dL. Regarding TOD mean LVMI was 109.6±31.4g/m2, IMT 0.71±0.1 mm, PWV 8.5±2.2 m/s, while creatinine and microalbuminuria were 0.8±0.2 mg/dL and 25.4±126.1 mg/24h respectively. When subjects were divided into high and low SUA group (depending on the median SUA of 5.2 mg/dL), with similar age and BP values the first group showed significantly higher values of metabolic index (BMI, HDL chol, triglycerides and glucose, p<0.001), LVMI (117.1±32.8vs102.1±28.1g/m2,p<0.01), IMT (0.73±0.1vs0.70±0.1mm,p=0.04), PWV
(8.8±2.4 vs 8.3±2.1m/s,p=0.01) and creatinine (0.9±0.2vs0.7±0.1mg/dL,p<0.01) and lower E/A (1,0±0.3 vs 1.1±0.3,p<0.01). SUA showed significant correlation with sex, age, BMI, SBP, HDL chol, triglicerides, glucose, creatinine, IMT, LVMI and E/A. Regarding TOD only creatinine presents SUA as as significant determinant in logistic regression analysis.

Conclusion
In HT, SUA values correlate with metabolic derangements and with cardiac, vascular and renal TOD. The most significant correlation is with renal damage.

P57 Assessment of pulse wave velocity and association to target organ damage in treatment-naïve hypertensive patients: a comparison of SphygmoCor and Mobil-O-Graph M

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Introduction
Comparison of Mobil-O-Graph® with SphygmoCor® exclusively in treatment-naïve hypertensives has never been done. Aims of the study were to assess 1) intra- device agreement between both methods, 2) inter-device agreement between two surface measurements of SC (subtracted distance (cfPWVsub)) and direct distance x
0.8 (cfPWV0.8)) with two patient´s positions of MG (supine (supPWVestim)) and sitting (sitPWVestim)), 3) the strength of association between tonometric and oscillometric measures of PWV with target organ damage (TOD).

Methods
Cross-sectional, observational study in 171 consecutive, treatment-naïve subjects derived to a Hypertension Unit with suspected hypertension. Standard echocardiography, ECG, carotid ultrasound and laboratory tests were performed.

Results
Mean age was 49.7 years, 57.3% were women. Reproducibility: Mean differences (±SD of the difference (SDD)) between duplicate SC and MG PWV measurements were non-significant. Agreement: cfPWV0.8 yielded the highest PWV values (8.17 ±1.6 m/s), followed by cfPWVsub (7.98 ±1.7 m/s), supPWVestim (7.83 ±1.7 m/s) and sitPWVestim (7.80 ±1.6 m/s).
We observed significant mean differences only between cfPWV0.8 and all other PWV measures: with cfPWVsub (0.23 m/s, p=0.001), with sitPWVestim (0.39 m/s, p=0.001) and with supPWVestim (0.38 m/s, p=0.002). No significant correlation was found between the mean and the difference for PWV in any comparison.
Association with cardiac damage was highest with cfPWVsub, supPWVestim and sitPWVestim were more closely related to carotid damage, though differences were not significant.

Table 3: Differences between PWV measured by applanation tonometry according to two surface measurements and by brachial oscillometry according to supine or sitting position.

Comparison of PWV	Mean difference	CI	p
cfPWVsub - supPWVestim	0,16	-0,06 / 0,37	0,149
cfPWVsub - sitPWVestim	0,18	-,034 / 0,39	0,098
cfPWV0.8 - supPWVestim	0,38	0,15 / 0,62	0,002
cfPWV0.8 - sitPWVestim	0,39	0,15 / 0,63	0,001
cfPWV0.8 - cfPWVsub	0,23	0,12 / 0,35	0,000
supPWVestim - sitPWVestim	0,02	-0,07 / 0,12	0,635

cfPWV0.8: direct distance x 0.8-based carotid-femoral PWV
cfPWVsub: subtracted distance-based carotid-femoral PWV
sitPWVestim: estimated aortic PWV in sitting position
supPWVestim: estimated aortic PWV in supine position

Conclusions
SC and MG showed similar and acceptable reproducibility. SC and MG were interchangeable only using subtracted distance (cfPWVsub), while direct distance x 0.8 showed significantly higher PWV values. Association to TOD was significant and similar between SC and MG.

P58 Arterial stiffness is associated with lower performance on the cognitive tests at different domains in hypertensive patients M

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Background
Cognitive impairment and elevated arterial stiffness are described in arterial hypertension(AH), but its correlations are not well studied.

Objectives
To study the cognitive function at different domains and arterial properties in patients with AH stage 1 to 3 compared to normotensives and to evaluate the correlations between these variables.

Methods
We evaluated 71 normotensives (52±14yrs,47%male,65%white) and 150 patients with stage 1-3 AH (52±12yrs,45%male,70%white) under treatment. The global cognitive function was assessed by Mini Mental State Examination(MMSE) and Montreal Cognitive Assessment(MoCA).A validated battery of neuropsychological tests(NPE) assessed the main cognitive areas: memory, language, visuospatial ability, executive function, attention. Pulse wave velocity(PWV) was measured by Complior® device. Carotid properties were assessed by radiofrequency ultrasound(WTS®). Central arterial pressure and augmentation index (AIx) were obtained using applanation tonometry(Sphygmocor®).

Results
Mean BP of the normotensive group (122.1±8/76.7±7mmHg) was significantly lower than hypertensive patients (135.2±13/83.3±10 and 149.9±29/91.5±16mmHg). Severe HTN group had worse performance in cognitive evaluation either by MMSE (26.8±2.1 vs 27.4±2.1 vs. 28.0±2.0, p=0.004) or MoCA test (23.4±3.7 vs. 24.9±2.8 vs. 25.5±3.2,
p<0.001). On the neuropsychological tests hypertensive patients had worse performance mainly in visuoperceptual and visuospatial capacities and executive function. On the multivariate regression analysis, the following independent associations were observed: Aix–language, executive function, visuospatial and attention; cSBP–MoCA; IMT–memory and attention; PWV–memory, executive function, visuospatial and attention. Higher PWV group had more cognitive dysfunction.

Conclusions
Cognitive impairment at different domains was more frequent in patients with different stages of AH. Arterial functional and structural properties were diversely associated with cognitive performance at different domains

P59 Arterial stiffness and peripheral vascular resistance in offspring of hypertensive parents - influence of gender and other confounders

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Aim
Established essential hypertension (EH) is associated with increased arterial stiffness and peripheral resistance, but the extent of vascular changes in persons genetically predisposed for EH is uncertain.

Methods
Participants from the Danish Hypertension Prevention Project (DHyPP) (having two hypertensive parents) (n=95, 41±1 years, 53% males) were compared to available spouses (n=45, age 41±1 years, 43% males). The subjects had measurements of ambulatory blood pressure (BP), left ventricular mass (LVM), pulse wave velocity (PWV), central BP and augmentation index (AIx) in addition to forearm resting and minimal resistance (R_{rest} and R_{min}).

Results
DHyPP subjects with and without spouses were comparable and the DHyPP cohort, as compared to spouses, had higher 24-hour mean BP (94±1 vs. 88±1 mmHg, *P*<0.01), LVM (90±2 vs. 80±2 g/m^2, *P*<0.01), central systolic BP (119±2 vs. 111±2 mmHg, *P*<0.01) and AIx (15.1±1.2 vs. 10.5±1.7%, *P*<0.01), but similar values of
carotid-femoral PWV (7.3±0.1 vs. 7.1±0.2 m/s), R_{rest} (51±2 vs. 51±3
mmHg/ml/min/100 ml) and log R_{min} (0.57±0.02 vs. 0.55±0.02 mmHg/ml/min/100 ml). AIx, R_{rest} and R_{min} were higher in female as compared to male DHyPP participants (*P*<0.01 for all) and the same was true for AIx and R_{min} among spouses (*P*<0.05).
Using multiple linear regression analysis adjusting for gender, age, body mass index, 24-hour BP, 24-hour sodium excretion and creatinine clearance, AIx remained elevated in DHyPP subjects (3.4% [0.18; 6.60], *P*=0.039). Furthermore, AIx was linearly associated with R_{rest} and R_{min}.

Conclusion
Young to middle-aged individuals genetically predisposed for EH display increased AIx, while vascular stiffness and peripheral resistance are still normal.

P60 Psychological determinants of target organ damage in hypertensive patients: focus on Pulse Wave Velocity and depression.

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Objective
Prior studies have suggested that the principal determinants of arterial stiffening are age, BP and others CV risk factors such as dyslipidemia and diabetes. However, scanty data are available on the role of psychological factors on arterial stiffness. The aim of the current cross-sectional study was to evaluate the association between depression, anxiety, perceived stress, Type A personality, and Type D personality and Pulse Wave Velocity (PWV) in a cohort of hypertensive patients, using baseline examination data of the TIPICO project.

Methods
A total of 259 outpatients (ages 18-80 years) followed by the Hypertension Unit of S. Gerardo Hospital (Monza, Italy) affected by essential hypertension were recruited.
Aortic stiffness was evaluated by c-f PWV. Moreover, anamnestic data, clinical BP, and laboratory data were evaluated. Patients were asked to complete a battery of psychological questionnaires under the guidance of a psychologist.

Results
At T0 mean age was 55.9±10.1years, SBP/DBP were 135.6±17.7/82.5±9.1mmHg and PWV was 8.6±2.1m/s. The multivariate stepwise linear regression analysis showed that age (beta=0.284,p<0.001), pulse pressure (beta=0.369,p<0.001), dyslipidemia (beta=0.130,p=0.012), family history of CV disease (beta=- 0.123,p=0.017), and depression (beta=0.126,p=0.014) were significantly and independently associated with PWV.

Conclusion
Among psychological factors, higher levels of depression is related to higher PWV, while anxiety, perceived stress, Type-A personality and Type-D personality are not. Depression assessment and target intervention to reduce it should be recommended in hypertensive patients.

P61 Psychological determinants of target organ damage in hypertensive patients: focus on type A Personality and Left Ventricular Mass Index.

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Background
Increased Left Ventricular Mass Index (LVMI) is a well known risk factor for cardiac morbidity and mortality. Furthermore, it is widely recognized that clinical evolution and progression of established CV diseases are related to a range of psychological characteristics, which may partially explain the spread and recurrence of these diseases. Little is known about LVMI and its association with psychological characteristics in arterial Hypertension (HT) patients. The aim of the current cross-sectional study was to evaluate the association between psychological characteristics and LVMI in a cohort of hypertensive patients.

Methods
A total of 244 outpatients (age 18-80 years) followed by the Hypertension Unit of S. Gerardo Hospital (Monza, Italy) affected by essential hypertension were recruited. Anamnestic data, clinical BP, and laboratory data and LVMI were evaluated. Patients were asked to complete a battery of psychological questionnaires under the guidance of a psychologist.

Results
At T0 the mean age was 55.9±10.1years, SBP and DBP were 135.6±17.7 and 82.5±9.1mmHg and PWV was 8.6±2.1m/s. The multivariate stepwise linear regression analysis showed that sex (beta=0.252,p<0.001), age (beta=0.135,p<0.037), mean BP (beta=0.178,p=0.003), family history of CV disease (beta=0.129,p=0.027), and Type-A personality (beta=0.148,p=0.014) were significantly and independently associated with LVMI.

Conclusion
Among psychological factors, higher levels of Type-A personality is related to higher LVMI, while Type-D personality, anxiety, depression and stress are not associated.

P62 Blood pressure lowering halts carotid artery stiffening in hypertensive patients: The CATOD study M

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Background
We anticipate that in vascular outpatients followed over time, measured changes in arterial stiffness will be the multifactorial result of pressure-dependence, ageing- related degeneration, wall stress homeostasis, and medical treatment. Carotid ultrasound enables assessment of carotid pulse wave velocity (cPWV, via Bramwell- Hill), geometry (relative wall thickness, RWT=2*IMT/diameter), and intrinsic material stiffness (Young's-modulus, via Moens-Korteweg). We investigated changes in these carotid properties over time, and their interrelationship. To check whether the change in measured cPWV could be merely due to pressure-dependence, we calculated based on the stiffness index β_0 [2] the theoretical pressure-dependent change in
cPWV [3].

Methods
Hypertensive outpatients (n=147) were assessed at baseline and 3.5±1.1 year follow- up, and were stratified according to baseline-to-follow-up change in diastolic blood pressure (ΔDBP) into three groups: *decreasedDBP* (ΔDBP<-7mmHg), *constantDBP* (-7mmHg≤ΔDBP≤7mmHg) and *increasedDBP* (ΔDBP >7mmHg), with the cut-off being twice the typical DBP measurement error [1].

Results
The theoretical pressure-dependent change in cPWV was 0.4±1.3m/s lower (p<0.001, n=147), corroborating the anticipated multifactorial conditions. Table 1 shows no changes in cPWV, RWT and Young's-modulus for *decreasedDBP*. For *constantDBP*, both cPWV and Young's-modulus were increased at follow-up.
IncreasedDBP showed increases in cPWV and Young's-modulus and a decreased RWT. The latter implies a 9.2±10.7kPa increase in circumferential wall stress (p<0.001), in contrast to a 5.3±6.9kPa decrease (p<0.001) in *decreasedDBP* (p<0.05 for between groups).

Table 1 Changes in measure carotid properties with 3.5-year follow-up

n = 147	ΔcPWV [m/s]		ΔRWT [-]		ΔYoung's-modulus [MPa]	
	mean ± sd	p	mean ± sd	p	mean ± sd	p
decreasedDBP (n = 53)	-0.1 ± 1.4	0.72	0.00 ± 0.04	0.38	-0.01 ± 0.32	0.87
constantDBP (n = 67)	+0.6* ± 1.4	**<0.001**	0.00 ± 0.04	0.18	+0.10* ± 0.26	**<0.001**
increasedDBP (n = 27)	+0.5* ± 1.5	**0.029**	-0.02*,** ± 0.04	**0.002**	+0.19* ± 0.35	**<0.001**

Δs calculated as follow-up – baseline. *: p<0.05 compared to decreasedDBP. **: p<0.05 compared to constantDBP

Conclusions
In this outpatient cohort, with clear DBP reduction, there is a discontinuation of carotid stiffening, but no reversal. In patients with increased DBP, progressive carotid stiffening appears driven by impaired wall stress homeostasis.

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P63 Can braquial oscillometry identify prehypertension among normotensive subjects?

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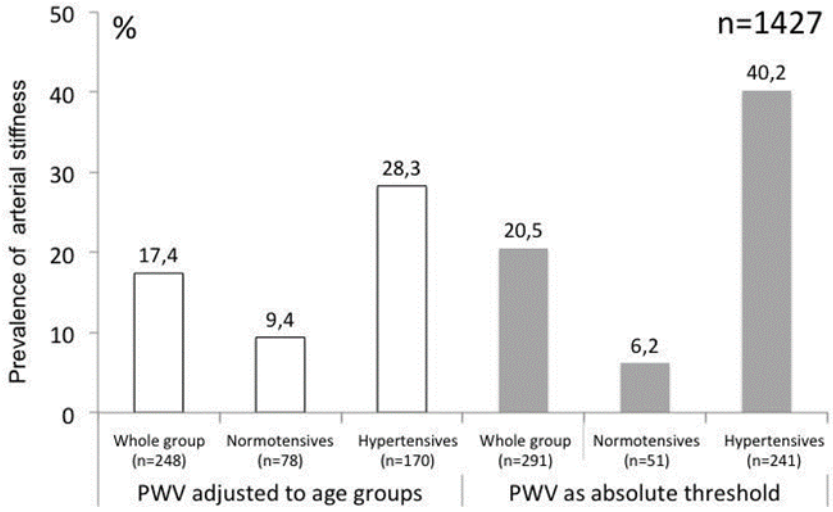
Background and objective
Arterial stiffness (AS) reflects vascular damage. Our objective was to determine 1) the frequency of AS in community pharmacies, 2) if subjects with AS identified by brachial oscillometry have more CV risk factors than normal subjects, and 3) if the prevalence of AS varies upon using either age-adjusted values or a fixed threshold.

Patients and method
Observational, cross-sectional study in 32 community pharmacies of the Valencia Community, between 11/2015 and 4/2016. AS was measured as pulse wave velocity (PWV) with a semi-automatic, validated device (MOBIL-O-GRAPH®, IEM), followed by a 10-item questionnaire.

Results
Mean age of the 1427 consecutive recruited subjects was 56.6 years. Overall prevalence of patients with AS was 17.4% with age-adjusted PWV (9.4% in normotensives, 28.3% in hypertensives). AS showed independent association in normotensives with male gender, obesity, higher pulse pressure and heart rate, in hypertensives, with higher pulse pressure and lower age in multivariate logistic regression. Defining stiffness by PWV > 10 m/s, AS was globally found in 20.5% of subjects, (6.2% in normotensives, 40.2% in hypertensives). It was associated with higher age and pulse pressure in both groups. Concordance in classifying stiffness was 74.6%.



Conclusions
Almost 10% of normotensives showed AS - measured by brachial oscillometry - when adjusting for age-groups. It was associated with male gender, pulse pressure, obesity and heart rate. In hypertensives, AS related to pulse pressure and inversely to age. Stiffness defined by 10 m/s is determined by higher pulse pressure and higher age. Both definitions of PWV are not interchangeable.

P64 Arterial stiffness and pulse pressure amplification in adults with isolated systolic hypertension

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Background/Aim
ISH is usually considered more prevalent in aged individuals and associated to increased large artery stiffness. This study is aimed at identifying determinants of ISH in adult individuals.

Methods: 20 individuals <60 years, referred to the Outpatient Hypertension Unit for high blood pressure (BP) and treatment-naïve, were classified as normotensive (NT), true hypertensives (HT) or isolated systolic hypertensives (ISH) based on office BP. In all individuals the following measurements were obtained: carotid pulse wave velocity (PWV) and aortic BP by applanation tonometry (Sphygmocor CVP, Atcor), 24-h brachial and central BP (Oscar2, SunTech Medical), daily steps by 7-day actigraphy (Fitbit Flex).

Results: the tree groups had similar clinical characteristics, including height and physical activity; only waist circumference was higher in ISH. PWV was normal in ISH and increased in HT. Office brachial and aortic pulse pressure (PP) were greater in ISH than in NT and HT, as well as 24-h brachial and central PP. PP amplification was similar in the three groups either when calculated by tonometry or in 24h.

	ISH (n=7)	NT (n=7)	HT (n=6)
Men	5	5	4
Age (years)	43±15	47±10	41±10
Height (cm)	174±10	171±11	174±11
BMI (kg/mq)	26±2	25±2	24±3
Waist circumference (cm)	93±13*	81±11	81±9
Physical activity (daily steps)	13021±4958	11569±6789	13836±4572
Mean BP (mmHg)	101±9°	90±8	102±13°
Heart rate (bpm)	60±6	61±13	53±10
Office PP (mmHg)	62±9*°	48±7	50±7
Aortic PP (mmHg)	45±8*°	38±4	40±6
24h-brachial PP (mmHg)	55±9*	46±9	51±6
24h-central PP (mmHg)	43±4*	37±4	40±4
24h- PP amplification (mmHg)	12±5	9±2	11±3
Time to reflection (ms)	142±15°	143±13°	161±21*
PWV (m/s)	6.3±1.4°	7.2±2.5°	8.0±2.2*

*: p<0.05 vs NT; ° p<0.05 vs HT

Conclusions
These preliminary data suggest that adults <60 years, newly diagnosed with ISH, present normal PWV and PP amplification from centre to periphery.

P65 Gender differences of aortic wave reflection and influence of menopause on central blood pressure in patients with arterial hypertension

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Background
Evidences suggest that central hemodynamics indexes are independent predictors of future cardiovascular events and all-cause mortality. Multiple factors have been pointed to have potential influence on central aortic function: height, heart rate, left ventricular ejection duration and blood pressure level. Data related to the influence of gender and postmenopausal status on aortic wave form reflection is scarce.

Methods
In a cross sectional study 122 hypertensive patients (52 men and 70 women) were studied. Hypertension was defined as blood pressure (BP) levels ≥140/90 mmHg or use of antihypertensive drugs. Central arterial pressure, augmentation index (AIx) and augmentation index normalized to 75bpm (Alx75) were obtained using applanation tonometry. Menopause and postmenopause history were accessed by a direct questionnaire. Postmenopause was defined as at least one year since last menstruation. Patients were paired by age, gender and menopausal status and 4 groups were compared: group 1 (young men, ≤48y), group 2 (young women, ≤48y), group 3 (older men, >48y) and group 4 (older women, >48y).

Results
Height and weight were significantly lower in women than in men at the same age. Conversely, Alx (32.7±9.8% vs. 20.1±11.7%, p<0.01), Alx75 (29.6±6.7% vs.
18.3±9.4%, p<0.01) and central systolic blood pressure (136±30 vs. 125±23 mmHg, p=0.03) were higher in women than men. The menopausal women had the worst indexes of aortic wave reflection.

Conclusion
Women patients had both higher reflected aortic pressure wave form and central blood pressure indexes and these findings were worsened by the menopausal status.

P66 Association between urinary sodium excretion, endothelial function and arterial stiffness in non-diabetic hypertensive patients

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Background
High salt intake has been associated with structural and functional vascular changes.[1]

Objective
To correlate urinary sodium excretion with endothelial function and arterial stiffness in non-diabetic hypertensive patients.

Methods
Cross-sectional study with non-diabetic hypertensive patients, both genders, aged 45-65 years, submitted to office blood pressure measurement, 24-hour urine sampling, carotid-femoral pulse wave velocity (PWV; Complior Analysis), central hemodynamic parameters by applanation tonometry (SphygmoCor) and microvascular reactivity by Laser Speckle Contrast Analysis (Pericam PSI)[2].

Results
Patients (n=18) were divided according to the urinary sodium excretion (UrNa) median: group 1 (UrNa <165mEq/24h) and group 2 (UrNa ≥165mEq/24h). The mean age was 56 years, 72% were women. Although not statistically significant, group 2 presented higher systolic blood pressure (SBP, 136±12 vs 144±20mmHg, p=0.382) and diastolic blood pressure (84±10 vs 87±10mmHg, p=0.523). Serum insulin (11±5 vs 20±12 mcU/ml, p=0.072), HOMA-IR (2.6±1.2 vs 4.9±3.0, p=0.069), C-Reactive protein (CRP, 0.12±0.35 vs 0.78±0.83 mg/dL, p=0.058) and PWV (8.8±2.1 vs 10.8±2.3 m/s, p=0.093) were also higher in group 2. There were no significant differences in aortic SBP (127±16 vs 132±20mmHg, p=0.556), and in the peak of microvascular reactivity (95.5±24.0 vs 83.4±45.1,

p=0.505). Group 2 presented a higher proportion of patients with HOMA-IR greater than 2.7 (37.5 vs 70.0%, p=0.047), CRP greater than 0.4 mg/dl (12.5 vs 55.6%; p=0.064) and PWV greater than 10m/s (25 vs 80%, p=0.020).

Conclusion
Although without significant differences in blood pressure and endothelial function, hypertensive patients with higher urinary sodium excretion showed changes suggestive of insulin resistance and arterial stiffness.

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Poster Session I – Imaging Technologies

Chair: F Faita, P Segers

P73 The Assessment of Pulmonary Artery Stiffness in COPD using Cardiac MRI the Q/A METHOD M

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Background
Pulmonary artery distensibility and pulsatility has been studied in patients with COPD using cardiac MRI (CMRI) **(1)**. However, pulmonary artery pulse wave velocity (PA- PWV) using 'QA' method **(2)** in CMRI has not been studied in this population. We hypothesized that patients with COPD have a higher PA-PWV compared to healthy individuals.

Methods
This analysis includes 23 COPD and 12 healthy volunteers (current or ex-smokers free from respiratory disease). Cardiac MRI was used to measure PA-PWV using a 3.0T GE Signa HDx MRI scanner (GE Healthcare), phase-contrast cross-sectional images using steady-state free precession sequence were obtained approximately 2 cm above the pulmonary valve, under free-breathing conditions. Aortic PWV was measured using the Sphymocor device along with mean arterial pressure (MAP), heart rate, lung function (forced expiratory volume in 1sec (FEV1) and forced vital capacity (FVC) and their ratio), 6-minute-walk-distance (6MWD) oxygen saturations.

Results
Patients with COPD and the healthy individuals were similar in age, gender and BMI (p>0.05). Patients with COPD had greater PA-PWV and heart rate as well as poorer lung function and oxygen saturations and 6MWD (all p<0.05) (Table-1). PA-PWV did not relate to age, BMI, AoPWV, MAP, heart rate, lung function, oxygen saturations, but PAPWV was greater in males than females (p<0.05).

Conclusions
Patients with COPD have stiffer pulmonary arteries compared to healthy individuals, as measured by PA-PWV using the Q/A method. Further analysis will investigate the association between pulmonary artery stiffness and cardiac function.

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Table 1 Data are Mean ± SD	COPD (n=23)	CONTROLS (n=12)	P-value
AGE (yrs)	65.8 ± 7.3	66.8 ± 7.1	0.713
GENDER (male:female)	11:12	6:6	0.903
BMI Kg/m^2	25.5 ± 3.3	26.6 ± 3.4	0.351
SMOKING (pack years)	39.0 ± 29.9	12.2 ± 8.6	<0.001
PA-PWV (m/s)	3.37 ± 0.6	1.41 ± 0.4	<0.001
AoPWV (m/s)	9.4 ± 2.6	8.5± 1.3	0.316
MAP (mmHg)	97.2 ± 9.5	90.5 ± 11.2	0.088
Resting Heart Rate (bpm)	68 ±9	62 ±7	0.034
FEV_1/FVC (L)	0.55 ± 0.14	0.75 ± 0.06	<0.001
FEV_1 % predicted	59.2 ± 17.6	105.8 ± 12.5	<0.001
6MWD (m)	388.2 ± 127.7	536.8 ± 49.9	<0.001

P74 Wall shear rate and brachial artery flow-mediated dilatory response between healthy young and older populations using multi-gate spectral Doppler ultrasound M

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Background
Ageing is associated with an impaired brachial artery flow-mediated dilatation (FMD) response and a reduced wall shear rate (WSR) stimulus may contribute to this response. However, a detailed analysis of the WSR-FMD response is lacking due to inherent difficulties of WSR estimation near the arterial wall by conventional ultrasound. We have overcome this limitation by using an integrated multi-gate Doppler FMD evaluation system, and in this study, we compared the WSR-FMD relationship between a healthy young and older population.

Methods
Data from 33 young (YNG:27.5±4.9yrs) and 33 older (OLD:64.9±3.6yrs) individuals were analysed. FMD was assessed using Ultrasound Advanced Open Platform (ULA-OP). Acquired raw data were post-processed using custom-designed software to obtain WSR and diameter parameters.

Results
Peak WSR [WSRpk: 635(585-685) vs 424(374-473) s^{-1}] and absolute WSR increase [WSRΔ: 548(504-592) vs 356(313-400) s^{-1}] were greater in YNG than OLD (both p<0.05). WSR area under the curve until its return to baseline value (WSRauc) was also greater in YNG than OLD [18632(16395-20868) vs 13049(10812-15285) au,
p<0.05]. WSRpk, WSRΔ and WSRauc were associated with both absolute and

percentage diameter increases in YNG (all $p<0.05$). However, none of the WSR parameters in OLD were associated with absolute or percentage diameter increases.

Conclusions
These results demonstrate 1) a reduced WSR stimulus during reactive hyperaemia in OLD compared with YNG, and 2) the absence of an association between WSR parameters and FMD response in OLD. These observations suggest that in older adults, diminished WSR together with WSR-independent factors are important determinants of the FMD response.

P75 Signs of Accelerated Carotid Atherosclerosis in early Type 2 Diabetes assessed by Magnetic Resonance Imaging M

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Background
Ischemic stroke from carotid plaque embolism remains a major cause of morbidity and mortality in patients with type 2 diabetes (T2DM). However, the effect of T2DM on early carotid plaque burden and composition is sparsely elucidated. We assessed carotid plaque composition by carotid magnetic resonance imaging (MRI) in short duration T2DM patients compared to a sex- and age-matched control group.

Methods
100 patients with T2DM (duration<5 years) and 100 sex- and age- matched control subjects underwent MRI of the carotid arteries bilaterally in a 1.5 T MRI scanner.
Plaque burden was measured as normalized wall index, maximum wall thickness, maximum wall area, and minimum lumen size. Plaque characteristics were quantified by calcified plaque volume, necrotic core volume, and loose matrix volume.

Results
MRI data were available for 149 and 177 carotid arteries from T2DM patients and control subjects, respectively. T2DM was associated with a higher normalized wall index (ratio 1.03 (1.002; 1.06), p=0.03), a lower minimum lumen area (ratio 0.81
(0.74; 0.89), p<0.001), and lower maximum wall area (ratio 0.94 (0.88; 1.00), p=0.048) compared to controls. Body mass index (BMI) was associated with maximum wall area and all plaque characteristics independently of diabetes status. BMI ≥30 kg/m^2 was associated with an 80% increase in total volume of calcified plaque, and a 44% increase in necrotic core volume compared to BMI<25 kg/m^2.

Conclusions
T2DM patients had increased carotid plaque burden and negative
remodeling. Obesity was associated with increased carotid artery necrotic core volume and calcification independently of diabetes status.

P76 Peripheral blood pressure and stiffness index estimation using the PPG signal measured with the pOpmètre device: Calibration with the cuff blood pressure M

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Arterial stiffness may influence the contour of the peripheral pulse, suggesting that contour analysis of the digital volume pulse (DVP) might be used to estimate peripheral blood pressure and a stiffness index (SI).

The objective is to establish a transfer function that estimates the peripheral blood pressure using the PPG pulse, calibrated with a brachial pressure cuff, and then to deduce a stiffness index using the established parameters.
We positioned the photodiode sensor on the finger. Brachial blood pressure measurement was performed with a cuff adapted to the arm circumference and an oscillometric device (Omron M10 -IT). Pulse wave velocity (PWV) measurements were performed with the pOpmètre® system. DVP waveforms were recorded over a 10 s period and ensemble-averaged to obtain a single waveform from which DT(DVP) was determined as the time between the first systolic peak and the early diastolic peak/inflection point in the waveform. The SI is the ratio of the subject's height to the DT(DVP).

69 subjects were included: 24 healthy subjects and 45 patients with essential hypertension. The correlation between the estimated peripheral diastolic pressure and the brachial one was good and significant ($r^2 = 0.51$; $p<0.001$). A better correlation was found in terms of peripheral systolic pressure ($r^2 = 0.56$; $p<0.001$). The correlation between the SI and the ft-PWV was significant ($r = 0.5$; $p<0.001$) classifying the estimation as good agreement.
The estimation of the peripheral blood pressure and a stiffness index with the PPG signal qualifies as good agreement with the reference technique.

P77 Near Infrared Spectroscopy (NIRS) can detect differences in microvascular reactive hyperaemia in the presence of hypertension

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Background
Hypertension has adverse effects on microvascular function but there are limited methods that permit non-invasive assessment of the microcirculation in man in vivo. We used Near Infrared Spectroscopy (NIRS) to assess microvascular reactive hyperaemia in skeletal muscle following a short period of ischemia. We tested if differences between normotensive and hypertensive individuals could be detected.

Methods
Older adults enrolled in a population-based cohort study underwent measurements of oxy-Hb changes during a 30-second arterial occlusion and hyperaemic response using NIRS (Portamon, Artinis). Time-to-peak hyperaemic response was calculated. Hypertension diagnosis was determined by questionnaire and clinic blood pressure(BP) (diastolic BP>90mmHg or systolic BP>140mmHg). Diabetes diagnosis and information about medication were determined by questionnaire. Data are mean(SD) or adjusted mean±SEM. Multivariable linear regression was used.
Associations with hypertension were adjusted for age, gender, ethnicity and presence of diabetes.

Results
129 participants (99=male, 72(6) years old, 74(57%) hypertensive participated). Time-to-peak hyperaemic response was significantly longer in hypertensive than normotensive participants after

adjustment for age and gender (12.5±0.49 versus 10.5±0.57seconds, p=0.06). This association persisted after adjustment for ethnicity and the presence of diabetes (12.6±0.50 versus 10.5±0.57, p=0.03).

Conclusion
Hypertension is associated with impairment of post-ischemic reactive hyperaemia in skeletal muscle microvasculature. Differences between hypertensive and normotensive older adults can be detected non-invasively using NIRS.

P78 Longitudinal micro-ultrasound assessment of the ob/ob mouse model: evaluation of cardiovascular, renal and hepatic parameters M

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Purpose/Background/Objectives
Obesity is associated with increased risk factors for cardiovascular disease (CVD). Leptin-deficient mice (*ob/ob*) are widely employed to investigate obesity. This study is aimed at providing a micro-ultrasound (mUS) longitudinal evaluation of the *ob/ob* mouse in terms of cardiovascular effects, consequences for renal microcirculation and liver fat accumulation.

Methods
Sixteen wild-type (*wt*) and eleven *ob/ob* male mice were studied at 8 (T_0) and 25 (T_1) weeks of age with a mUS system (Vevo2100). Cardiac output (CO), ejection fraction (EF), stroke volume (SV), fractional shortening (FS) and E/A ratio were measured from cardiac images. Mean diameter (Dm_{abd}, Dm_{car}), relative distension ($relD_{abd}$, $relD_{car}$) and pulse wave velocity (PWV_{abd}, PWV_{car}) were obtained for both abdominal aorta and common carotid. Renal resistivity and pulsatility index (RI, PI) were assessed. The ratio between grey-levels related to liver and kidney (Steato-Score) was used as index of hepatic steatosis.

Results
At T_0, *ob/ob* mice showed reduced SV, EF, CO and $relD_{abd}$ values and increased LVmass, PWV_{abd}, RI, PI and Steato-score. Similar results for SV, EF, CO, RI, PI and Steato-Score were found at T_1; furthermore, obese mice showed reduced Dm_{abd} and Dm_{car} measurements in comparison with lean controls. The longitudinal analysis showed an increase in LVmass and Dm_{abd} and a reduction of FS, EF, CO, $relD_{abd}$ and $relD_{car}$ for *wt* animals and no differences for the *ob/ob* one.

Conclusions
ob/ob mice presented a premature cardiac dysfunction without a further age-related deterioration and a reduction in the abdominal aorta and carotid artery mean diameter in adult age.

P79 Ultrasonographic characterization of the db/db mouse, an animal model of metabolic abnormalities

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Purpose/Background/Objectives
The availability of an animal model that, beside common blood parameters like hyperglycemia or high lipid levels, reliably mirrors organ damage occurring in metabolic diseases, is an urgent need. These

animals have not been fully characterized in terms of cardiovascular, renal and hepatic ultrasound parameters, and only sparse and discordant values can be found in literature. Aim of this paper is to provide a detailed, non invasive description of heart, vessels, liver and kidneys of the *db/db* mouse by ultrasound imaging.

Methods
16 wild type and 34 *db/db* 11 week-old male mice were studied. State of the art ultrasound technology was used to acquire images of cardiovascular, renal and hepatic districts. A full set of parameters describing function of the selected organs was evaluated.

Results
db/db mice are characterized by systolic and diastolic dysfunction, confirmed by strain analysis. On the contrary, abdominal aortic and carotid stiffness seem to be not increased in these diabetic rodents; furthermore, they are characterized by a smaller mean diameter for both vessels. Renal microcirculation is significantly compromised, while liver steatosis is only borderline higher in *db/db* mice than in control animals.

Conclusions
We offer here for the first time an *in vivo* detailed ultrasonographic characterization of the *db/db* mouse model, providing a useful tool for a thoughtful choice of the right rodent model for any experimental design.

P80 Identification of radial vascular wall abnormalities by very-high frequency ultrasound in patients with fibromuscular dysplasia: the FUCHSIA study

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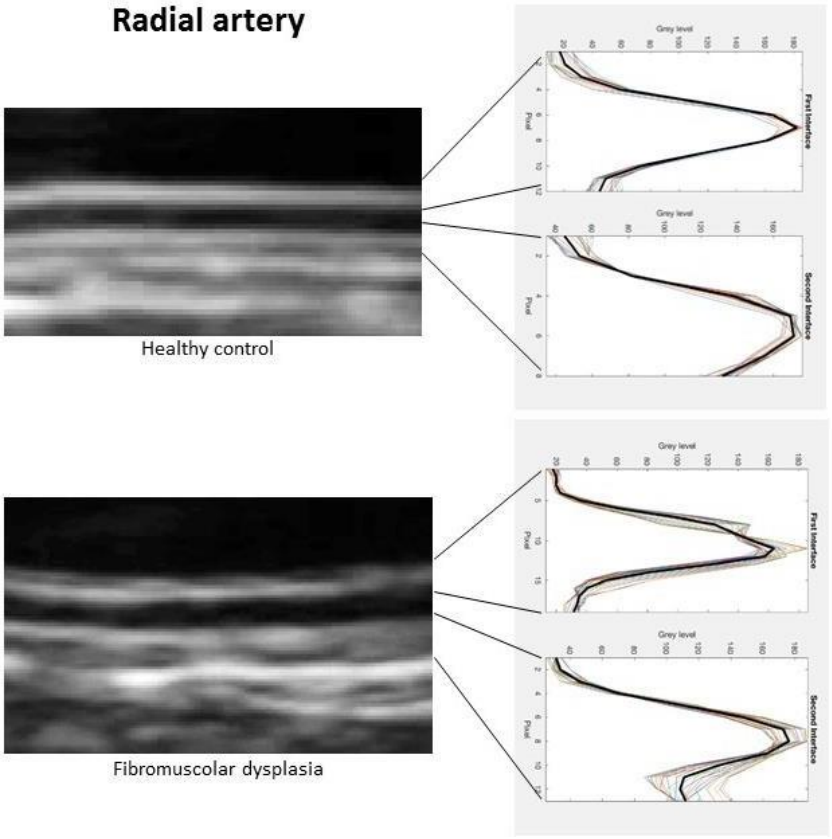
Aim
This case-control study is aimed at identifying radial vascular wall abnormalities in patients with fibromuscular dysplasia (FMD).

Methods
High-frequency ultrasound scans of radial arteries were obtained by VevoMD (70 MHz probe, FUJIFILM, VisualSonics). Radial wall showed two echogenic interfaces: the 1st (lumen-media) and the 2nd (media-adventitia). Intima-media (IMT), adventitia (AT), and global thickness (IMAT) and wall cross-sectional area (WCSA) Measured.
Vascular wall disarray was assessed calculating the root mean square error (RMSE) between 20 gray-level profiles crossing the two interfaces and the profile obtained averaging them, normalized for the maximum value of the corresponding mean profile (RMSE/mean).

Results
11 treated hypertensive female FMD patients and 8 healthy controls (C) were enrolled (age 52±5 vs 45±13years, p=0.51; BMI 26±3 vs 23±3kg/mg, p=0.12; mean BP 97±7 vs 85±10mmHg, p=0.01). Radial lumen was similar; IMT (0.166±0.037 vs 0.128±0.022mm, p=0.03), AT (0.114±0.029 vs 0.083±0.019mm, p=0.008) and IMAT (0.281±0.042 vs 0.211±0.027mm, p=0.003) were higher in FMD. Wall/lumen ratio was similar and WCSA increased in FMD.
The maximum values of 1st (121±43 vs 157±22, p=0.09) and 2nd interface 109 ±44 vs133±18, p=0.09) tended to be lower, whereas RMSE/mean was higher in FMD (1st 1.31±0.24 vs 0.83±0.32, p=0.006; 2nd 1.37±0.38 vs 0.94±0.32, p=0.03). The difference was attenuated for the 1st but not for the 2nd interface when considering age and mean BP as covariates (p=0.054 and p=0.016 respectively).



Conclusions
The radial artery wall of hypertensive FMD patients shows increased thickness and its ultrastructure is characterized of loss of echogenicity and inhomogeneity of the two echogenic layers.

P81 Disarray and remodeling of the radial artery in women with spontaneous coronary artery dissection: the FUCHSIA study

Bruno, Rosa Maria[1]; Di Lascio, Nicole[2]; Al Hussaini, Abtehale[3]; Guarino, Daniela[1]; Vitali, Saverio[1]; Rossi, Piercarlo[1]; Caramella, Davide[1]; Cortese, Bernardo[4]; Faita, Francesco[2]; Taddei, Stefano[1]; Ghiadoni, Lorenzo[1]; Adlam, David[3]

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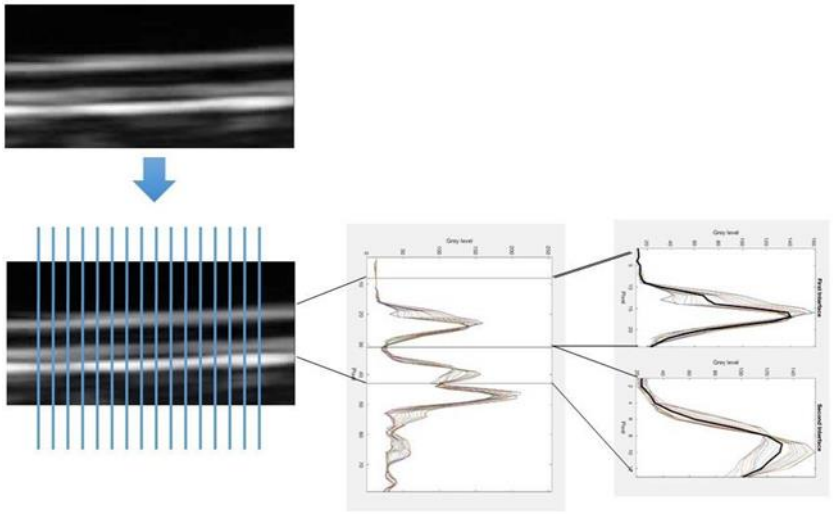
Background
Spontaneous coronary dissection (SCAD) may represent a manifestation of fibromuscular dysplasia (FMD); thus, preclinical lesions might be found in extracoronary vessels with similar size and wall ultrastructure, such as the radial artery.

Methods
Two 5'-clips from the left radial artery were obtained by Vevo MD (70 MHz probe, FUJIFILM, VisualSonics). Radial wall showed two echogenic interfaces: the 1st (lumen-media) and the 2nd (media-adventitia). Intima-media (IMT), adventitia (AT), and global thickness (IMAT) and wall cross-sectional area (WCSA) Measured.

Vascular wall disarray was assessed calculating the root mean square error (RMSE) between 20 gray-level profiles crossing the two interfaces and the profile obtained averaging them, normalized for the maximum value of the corresponding mean profile (RMSE/mean).



Results
5 female SCAD patients and 9 healthy controls (C) were enrolled (age 45±9 vs 45±13years, p=0.95; BMI 21±3 vs 23±kg/mq, p=0.22; mean BP 77±5 vs 85±10mmHg, p=0.053). 2nd interface peak was reduced in the SCAD group (97±29 130±19, p=0.04), whereas RMSE/mean was increased (1.89±0.68 vs 0.97±0.30, p=0.02). Similar values were found for the 1st interface. IMT (0.165±0.031 vs 0.125±0.022mm, p=0.03), but not AT (0.095±0.020 vs 0.081±0.020mm, p=0.20) and IMAT (0.260±0.049 vs 0.206±0.030mm, p=0.053), was significantly higher in SCAD.
Radial internal diameter and wall/lumen ratio were similar: conversely WCSA was increased in SCAD (1.69±0.48 vs 1.07±0.37mm^2, p=0.02).

Conclusions
Radial arteries of SCAD patients were characterized by increased wall thickness. Furthermore, the 2nd echogenic layer exhibited loss of echogenicity and inhomogeneity, features similar to FMD patients.

P82 Image-based characterization of plaque lipid concentration changes in time and the role of statin therapy

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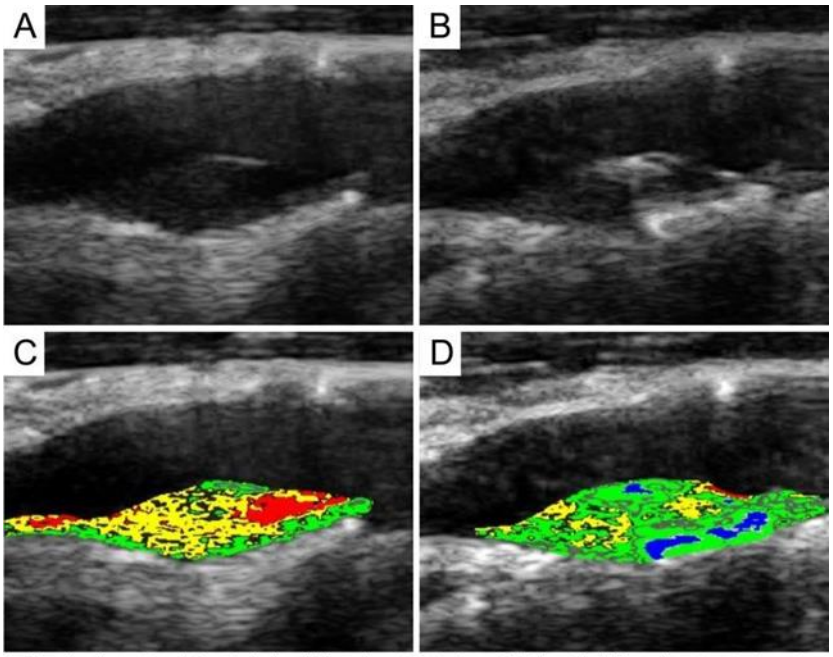
Introduction
Carotid artery atherosclerosis is an established risk factor for cerebrovascular events. Core lipid-rich plaques are considered at a higher risk of embolization compared to fibrous or calcified lesions. Contrast enhanced ultrasound (CEUS) is effective for studying carotid plaques, providing a virtual histology [1]. Here we assess the behavior of non-surgical carotid plaques in terms of lipid variation over time.

Methods
Eleven patients were enrolled (University of Turin) with a 50-69% (ECST) carotid asymptomatic stenosis. Seven patients were on statin therapy. All patients signed an informed consent and underwent standard carotid ultrasound (MyLab25 Gold, Esaote). A 1.5ml bolus of SonoVue (Bracco Spa) was injected; then a 5ml saline flush. Post-contrast Bmode images (180s after injection) were saved and analyzed offline. All patients repeated this protocol after 6 months.
The plaques were segmented, intensity normalized [2], and characterized according to a previous method [3].

Results
We evaluated small cohorts according to lipid concentration changes, identifying four categories. One patient had a plaque showing no lipid variation; four patients showed a slight decrease; four patients a remarkable decrease; two patients an increase.
Seven patients with a decrease in lipid concentration were on statin therapy, while both patients with an increase in lipids were not.



Example of image-based characterization. (A) B-mode post contrast agent injection at t1. (B) B-mode post contrast agent injections at t2, 6 months after t1. (C) Characterization of B-mode image at t1 (40% lipids). (D) Characterization of B-mode image at t2 (13% lipids). Red: blood; Yellow: lipids; Green: fibrous; Blue: Calcified; Black: non-classified.

Conclusions
A method for asymptomatic carotid plaque characterization using CEUS is presented. We focused on plaque lipid variations and the possible influence of statin therapy. We showed that carotid plaques are rarely stable, but rather continuously change composition over time and how statins could play an important role in this process.

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P83 A pilot study to assess peak systolic velocity as a possible marker of atherosclerotic burden using ultrasound

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Introduction
Ischemic heart disease (IHD) has been associated with lower peak systolic velocity (PSV) on penile Doppler measurements [1]. This study establishes whether carotid ultrasound (US) PSV was associated with computational fluid dynamics (CFD) outputs, which in turn may contribute to IHD pathogenesis.

Methods
A sample of 57 subjects (with IHD:27, without IHD:30) had US velocity profiles (left- common carotid artery) determined between 10-12 equi-spaced points. Bezier curve fitting was used to fit the profile through the measured velocity points for a normalised diameter. PSV was correlated against CFD results such as wall shear stress (WSS) [2]. Difference in PSV between individuals with/without IHD was studied via t-test. Linear regression was carried out to see if peak systolic velocity was associated with CFD outputs. Any significant associations were analysed within stratified groups (with/without IHD).

Results
PSV was significantly lower ($p=0.042$) in subjects with IHD (with IHD:53.6±17.3 cm/s, without IHD:62.8±16.1 cm/s). PSV was associated with carotid bulb average pressure drop ($p<0.001$), area of average bulb WSS (< 1 Pa: $p=0.016$, < 2 Pa: $p=0.006$, < 3 Pa: $p=0.001$). All the above associations remained significant in individuals with IHD (average bulb pressure drop: $p=0.001$, average bulb WSS (< 1 Pa: $p=0.013$, < 2 Pa: $p=0.008$, < 3 Pa: $p=0.003$). In subjects without IHD, PSV was associated with only average bulb pressure drop ($p=0.016$).

Conclusions
This study suggests that further work on PSV and its associations with CFD outputs is required in individuals with and without IHD in various vascular beds.

References
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P84 High-frame rate vector flow imaging: relationship between carotid bifurcation geometry and flow patterns

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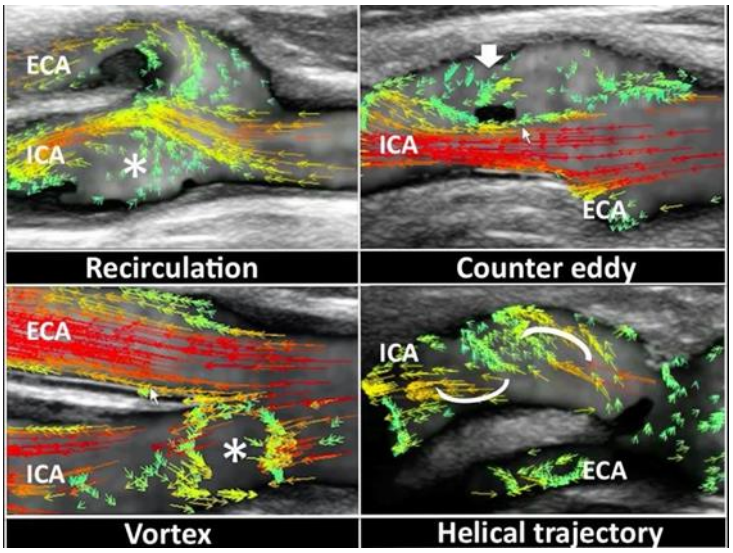
Background
The laminar flow movement in straight arteries is affected by anatomical factors such as bifurcation, lumen diameter changes or plaques. As a consequence of the local deceleration, the detachment of the boundary layer from the wall develops a disturbed flow, which impacts hemodynamics. It results in a non-uniform distribution of wall shear stress (WSS), which is responsible for atherosclerosis [1]. This phenomenon usually occurs in the carotid bifurcation (CB). Computational methods, MRI and conventional Doppler techniques have been used to establish the correlations between flow disturbance and plaque formation. We propose the use of a new method, called high-frame rate Vector Flow imaging (VFI), which dynamically visualises blood flow velocities in all directions, in the evaluation of the flow characteristics in the CB [2,3,4,5].

Methods
CB geometries and flow patterns in 30 healthy subjects of different age were evaluated using a commercial system equipped with high-frame rate VFI based on a frame rate of 600 Hz. The flow is represented by many coloured vectors, displayed as arrows, showing the different velocity, magnitude and direction at each site.

Results
The correlation between flow disturbances and carotid sinus diameter was confirmed: the more relevant the diameter, the more disturbed the flow. Different CB geometries, affecting the flow behaviours and generating complex flow, such as recirculation, counter eddy, vortex and helical trajectory, were identified (Fig 1).



Conclusions
High-frame rate VFI shows in detail the spatiotemporal characteristics of the flow and demonstrates the strong effect of vessel geometries on the flow patterns.

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P85 High frame rate dynamic display ultrasound vector flow imaging for quantitative studies of hemodynamics of carotid arteries

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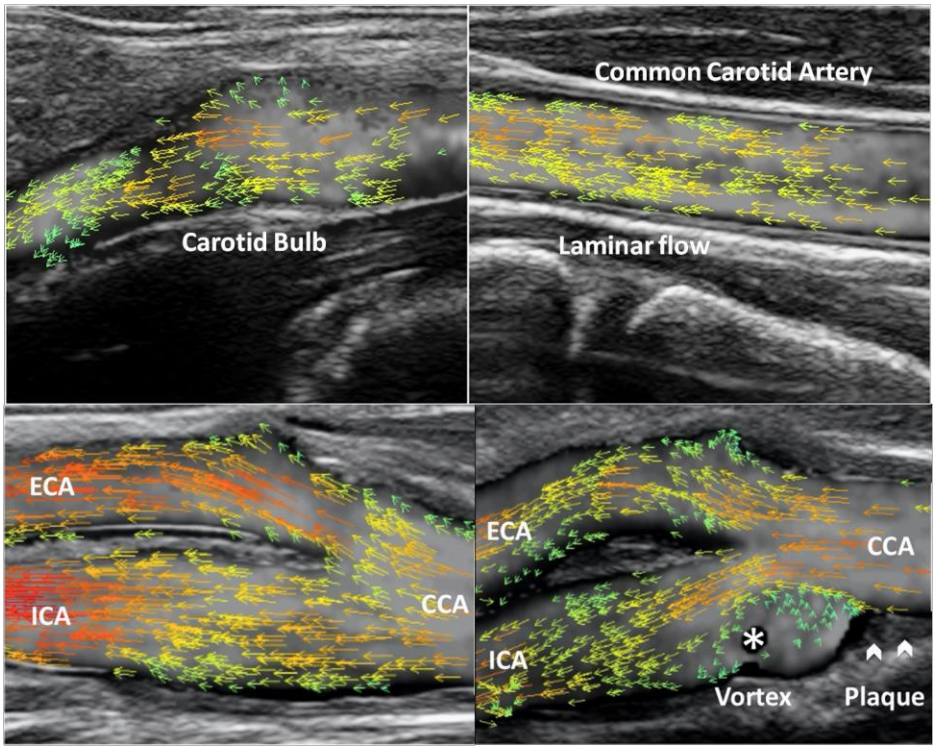
Advanced atherosclerotic patients are faced with significant risks of stroke, which are very likely to cause death or irreversible physical disability. However, the growth of artery stenosis usually needs a very long development. Early diagnosis is necessary and requires detailed and accurate quantitative hemodynamics to be supported. The paper proposes an angle-independent ultrasound flow imaging technique for carotid arteries, which allows true velocity vectors measurement, obtaining both value and direction of blood flow.
The proposed vector flow imaging is implemented based on multi-directional Doppler interleaved transmission [1,2], with high frame rate dynamic display [1] and zone sonography technology [3].

Hemodynamics becomes extremely complicated when plaques develop in the carotid bulb. The dynamic display with velocity vectors assesses flow patterns, e.g. laminar flow, vortex and turbulence (Examples are shown in the figure). The circular variance for the angles of vectors in a desired region of interest can be calculated, allowing disturbance quantification for the non-laminar flow. The method is capable of measuring volume flow (VF) and wall shear stress (WSS) at different locations. To ensure the accuracy both VF and WSS are calculated based on a frame rate of 400- 600 Hz and vector velocities.



The high frame rate vector flow imaging has been implemented in a commercial ultrasound system. It provides various quantitative results such as circular variance, VF and WSS, which are useful for hemodynamics studies of complex flow. This could make the early prevention and diagnosis of carotid disease possible.

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Poster Session I – Models and Methodologies I

Chair: A Avolio, G Gemignani

P120 A Model-Based Study on the Evolution of Blood Pressure During Ageing M

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Background

Hypertension being a major risk factor of cardiovascular mortality, there is a pressing need to understand the ageing mechanisms that lead to the continuous increase of pulse pressure and systolic blood pressure over time. Alterations in both forward and backward waves with age have been widely recognized as key features affecting the development of hypertension, with investigators, however, not reaching a consensus on the relative importance of each wave component (1,2).

Objective

The aim of the current investigation was to examine the wave profile over time after developing an age-adapted, mathematical, one-dimensional model of the cardiovascular system.

Methods

Our state-of-the-art 1-D model (3,4) was extended to include turbulence and inertial effects of the flow exiting the left ventricle. Literature data on the age-associated changes in arterial stiffness, peripheral resistance and cardiac contractility were gathered and used as an input for the simulation.

Results

The predicted evolution of pressure and augmentation index with age followed accurately the curves obtained in a number of large-scale clinical studies. Analysis of the relative contribution of the forward and backward wave components showed that the forward wave becomes the major determinant of the increase in central and peripheral SBP and PP with advancing age.

Conclusions

The 1-D model of the ageing tree and heart captures faithfully and with great accuracy the central pressure evolution with ageing. The stiffening of the proximal aorta and the resulting augmentation of the forward pressure wave is the major contributor of the systolic pressure augmentation with age.

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P121 Identifying haemodynamic determinants of pulse pressure: an integrated numerical and physiological approach M

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Purpose
Hypertension, the single biggest killer worldwide[1], arises mainly as a result of an increase in central pulse pressure (PP)[2], yet haemodynamic basis of that increase is still disputed. We examined the ability of a simple "reduced" model comprising a proximal characteristic impedance linked to a Windkessel element to accurately
predict PP from aortic blood flow and applied the model to examine PP dependence on cardiac and vascular properties.

Method
PP obtained from the model was compared with theoretical values obtained in silico and in vivo. Theoretical values were obtained using a distributed multi-segment model in a population of "virtual" subjects (n=3,095) in which cardiovascular properties were varied over the pathophysiological range. In vivo measurements were in normotensive subject (n=13) during modulation of physiology with vasoactive drugs with divergent actions on cardiac and cascular properties and in hypertensive subjects (n=156).

Results
PP derived from the model agreed with theoretical values (mean difference SD, - 0.09±1.96 mmHg) and with measured values (-1.95±3.74 and -1.18±3.67 mmHg for normotensive and hypertensive subjects respectively). Parameters extracted from the model agreed closely with theoretical and measured physical properties. PP was seen to be determined mainly by total arterial compliance (inversely associated with arterial stiffness) and ventricular dynamics: the volume of blood ejected up to time of pulse pressure and the rate of ventricular ejection up to this point.

Conclusion
Increased flow and/or volume accounted for 20.1 mmHg (52%) of the 39.0 mmHg difference in pulse pressure between the upper and lower tertiles of the hypertensive subjects.

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P122 Calculating Reservoir Pressure With or Without Flow Information: Similarity and Algorithmic Sensitivity at Radial Artery M

Ebner, Michael[1]; Parker, Kim[2]; Vercauteren, Tom[3,1]; Ourselin, Sébastien[3,1]; Wassertheurer, Siegfried[4]; Hughes, Alun[5]; Hametner, Bernhard[4]

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Background
Reservoir pressure is typically estimated from the pressure waveform information only. Comparability with estimates made using pressure and flow depend on assumptions, e.g. a proportional relationship between excess pressure and flow [1]. In this study, we compared (i) results using flow and pressure versus pressure-only at the radial artery, and (ii) two different algorithms used in the literature for pressure- only analysis.

Methods
Reservoir pressure separations were performed on 95 hypertensive individuals where radial pressure and flow velocity waveform measurements were available [2]. Algorithm (F) used flow and pressure information [3]. Algorithms (P1) and (P2) refer to the two different pressure-only implementations as used in [4, 5], and [1, 6], respectively. Reservoir curves characterized by physiologically implausible parameters, i.e. a rate constant $b < 0$ or an asymptotic pressure $P_\infty < 0$, were discarded, leaving 63 subjects with valid reservoir pressure data.

Results
Estimated reservoir parameters are shown in Table 1. Algorithm (F) showed statistically significant differences in most of the parameters compared to (P1) and (P2), although, except time constant τ and asymptotic pressure P_∞, there was a strong correlation between methods. Significant differences were observed in reservoir pulse pressure and area estimates between (P1) and (P2) despite their, in general, high correlation.

Radial Artery	p_{res} (F)	p_{res} (P1)	p_{res} (P2)	*r*(F,P1)	*r*(F,P2)	*r*(P1,P2)
PP [mmHg]	41.5 ± 10.0	36.3 ± 7.2	35.7 ± 7.0	0.82*	0.82*	0.96*
A_p [mmHg s]	17.5 ± 4.3	15.6 ± 3.7	15.5 ± 3.7	0.94*	0.94*	1.00*
τ [s]	0.3 ± 0.1	0.6 ± 0.4	0.6 ± 0.3	0.36*	0.42*	0.88
P_∞ [mmHg]	65.7 ± 10.3	63.9 ± 15.2	64.8 ± 12.6	0.45	0.53	0.79
a [1/s]	----	8.1 ± 5.2	7.4 ± 2.7	----	----	0.93
b [1/s]	----	2.2 ± 1.1	2.1 ± 0.8	----	----	0.84
R [mmHg s/m]	419.0 ± 188.8	453.7 ± 348.2	436.7 ± 302.6	0.68	0.75	0.92
C [mm/mmHg]	0.8 ± 0.3	1.7 ± 1.0	1.7 ± 1.0	0.70*	0.70*	1.00

*Table 1. Quantification of reservoir pressures p_{res} obtained by methods (F), (P1) and (P2) at radial artery in the format of mean ± standard deviation based on 63 subjects whereby PP denotes the reservoir pulse pressure, A_p the area of reservoir pressure above diastolic blood pressure, τ the time constant describing the diastolic pressure decay, P_∞ the asymptotic blood pressure and $a, b = 1/\tau$ the rate constants. Peripheral (area) resistance and compliance, i.e. R and C, were estimated from the rate constants a and b for (P1) and (P2) using flow information. The correlation coefficient r was computed between relevant methods. The statistical significance of the differences between methods was based on a paired t-test with * indicating $p < 0.05$.*

Conclusions:
The discrepancies between (F) and (P1), (P2) raise concerns about the validity of the implicit assumptions in pressure-only reservoir pressure separation at the radial artery. Differences in (P1) and (P2) indicate some sensitivity of derived parameters to the algorithm employed.

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P123 Reservoir pressure is independently associated with 11-12 year old's kidney function: Population-derived study M

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Introduction
Reservoir pressure (RP) and excess pressure (XSP) independently predict cardiovascular events in adults, but have never been investigated as markers of cardiovascular risk among children. This study aimed to determine the association of RP and XSP with end-organ makers of cardiovascular risk related to kidney function and large artery pre-atherosclerosis.

Methods
Participants were 1874 11-12 year-old children (50% male) from the Longitudinal Study of Australian Children's Child Health CheckPoint study. Brachial blood pressure was measured by cuff oscillometric device (SphygmoCor XCEL, AtCor, Sydney). The same device was used to derive reservoir pressure (RP) and excess pressure (XSP) from the brachial pressure waveform. Kidney function was determined from estimated glomerular filtration rate (eGFR, n=926) and large artery pre-atherosclerosis was determined from carotid intima media thickness (cIMT, n=1131) using ultrasound.

Results
The eGFR was significantly correlated with RP peak (r=-0.109, p=0.001), RP integral(r=-0.136, p<0.001), XSP peak (r=0.096, p=0.004) and XSP integral (r=0.102, p=0.002). The RP (whether expressed as peak or integral) was significantly associated with eGFR after adjusting for sex, waist-to-hip ratio, heart rate and
brachial BP indices (RP peak β=-0.079, p=0.02, partial R^2=0.006 and RP integral β=- 0.079, p=0.02, partial R^2=0.007). XSP was not independently associated with eGFR after adjusting for the above variables. Neither RP nor XSP were significantly associated with cIMT.

Conclusion
Independent of conventional risk factors, RP was significantly associated with kidney function among a large population of Australian children. The non-invasive method to derive RP using an oscillometric cuff device could provide useful clinical information in children.

P124 Validity and reliability of Pulse Wave Analisys estimated by a novel wrist- worn tonometer

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Department of Medicine, University of Salamanca, Salamanca, Spain., [10]Primary Care Research Unit, The Alamedilla Health Center. Castilla and León Health Service (SACYL), Biomedical Research Institute of Salamanca (IBSAL)

Objective
To analyze the reliability and validity of Pulse Wave Analysis determined with the new wrist-worn tonometry.

Methods
Cross sectional study including 254 subjects. Aged 51.9 ± 13.4, being women 53%. Main measurements: Peripheral AIx(PAIx) and Central AIx(CAIx) by wrist-worn tonometry and Sphygmocor. Carotid femoral(cf) pulse wave velocity(PWV) by Sphygmocor, Cardio Anckle Vascular index(CAVI), anckle brachial index(ABI) and brachial anckle(ba) PWV by Vasera device. Carotid intima media thickness (IMT) by ultrasonography.

Results
Intra-class correlation coefficient (ICC) intraobserver for the PAIx was 0.886 (95% CI 0.803 to 0.934) and for the CAIx 0.943 (0.901 to 0.968) with a Bland Almant
agreement limit of -0.75 (-23.8 to 21.8) and 0.08 (-15.7 to 15.9) respectively. ICC interobserver for PAIx was 0.952 (95% CI 0.915 to 0.972) and CAIx 0.893 (0.811 to 0.939) with an agreement limit of -0.45 (-13.7 to 12.8) and 0.43 (-17.7 to 1835) respectively.

We found, compared with Sphygmocor, an ICC of 0.849 (0.798 to 0.887) for PAIx, and 0.783 (0.711 to 0.838) for CAIx. The agreement limit for PAIx was -1.03 (-22.73 to 20.67) and CAIx 2.14 (-20.50 to 24.79). We found positive correlation with PAIx, CAIx and CAIx HR75 by Aurora with age, CAVI, ABI, baPWV, cfPWV, IMT and cardiovascular risk and negative with glomerular filtration rate

Conclusions
The wrist-worn tonometry shows an adequate reliability intra and interobserver, and interdevice when compared to Sphygmocor, and an adequate validity when compared with other measures that evaluate arterial stiffness, target organ damage and cardiovascular risk.

P125 Use of vascular adaptation in response to mechanical loading facilitates personalisation of a one-dimensional pulse wave propagation model M

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Background
Mathematical modelling of pressure and flow waveforms in blood vessels using pulse wave propagation (PWP) models could support clinical decision-making. For a personalised model outcome, measurements of all modelled vessel radii and wall thicknesses are required. In clinical practice, however, datasets are often incomplete. To overcome this problem, we hypothesised that the adaptive capacity of blood vessels in response to mechanical load can be utilised to fill in the gaps of incomplete patient-specific datasets.

Methods
We implemented homeostatic feedback loops in a validated PWP model [1] to allow adaptation of vessel geometry to maintain wall stress and wall shear stress. To evaluate our approach, we utilised complete datasets of 10 patients scheduled for vascular access surgery. Datasets comprised of wall thicknesses and radii of 7 central and 11 arm arterial segments.

We simulated reference models (RefModel, n=10) using complete data and adapted models (AdaptModel, n=10) using data of one brachial artery segment only. The remaining AdaptModel geometries were estimated using adaptation. In both models, mean brachial pressure, brachial artery distensibility, heart rate and aortic inflow were prescribed. We evaluated agreement between RefModel and AdaptModel geometries, as well as between pressure and flow waveforms of both models.

Results
Limits of agreement (bias±1.96SD) between AdaptModel and RefModel radii and wall thicknesses were 0.029±1.3mm and 28±230µm, respectively. AdaptModel pressure and flow waveform characteristics across the proximal-to-distal arterial domain were within the uncertainty bounds of the RefModel (Figure 1).

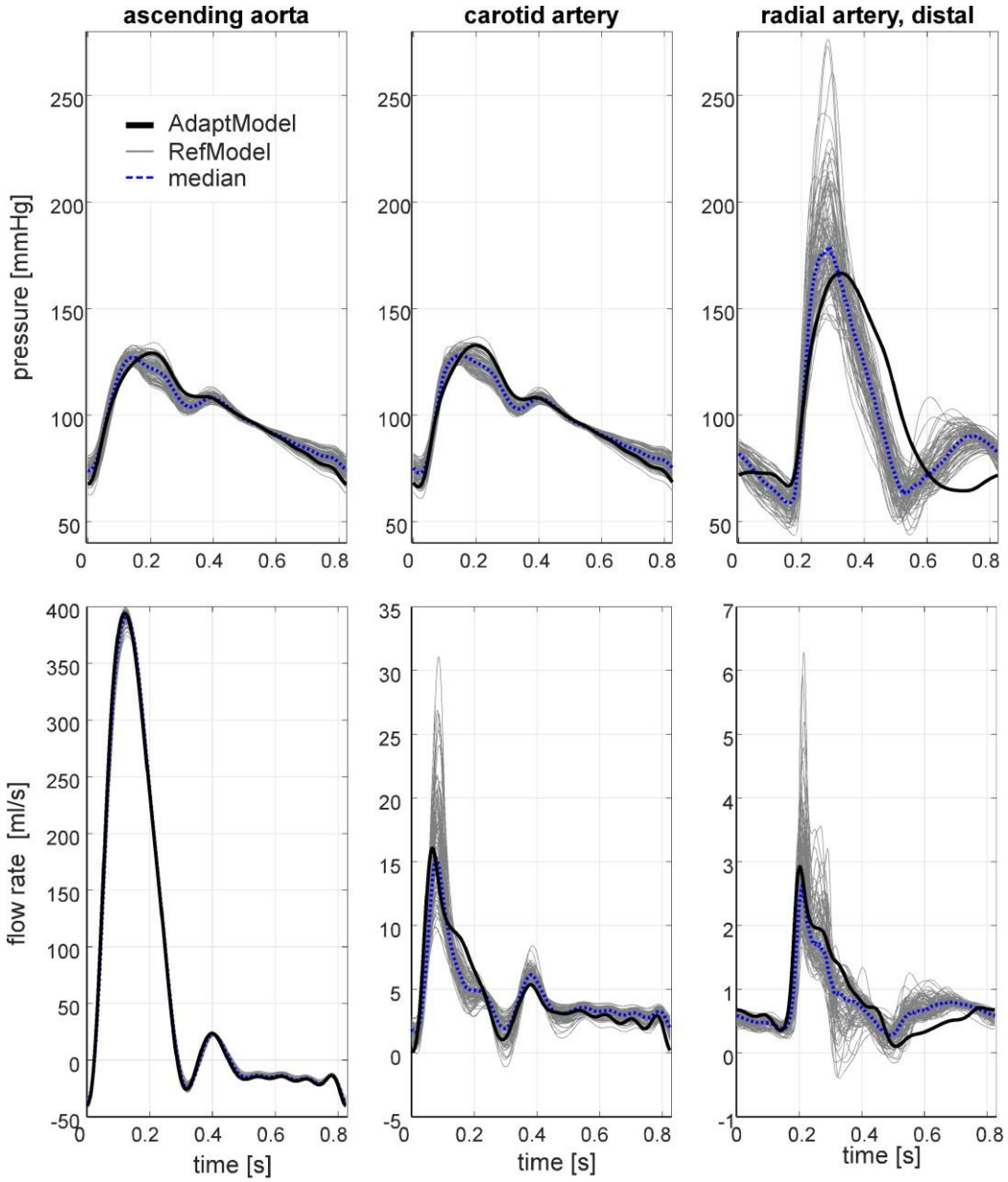

Fig.1: AdaptModel and RefModel pressure and flow waveforms at three arterial locations. For adequate comparison between the AdaptModel and the RefModel, a total of 100 RefModel realisations were generated within the measurement uncertainty. The median RefModel is indicated by the blue dotted curves.

Conclusions

Our adaptation-based PWP model enables personalisation even when not all required data is available.

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P126 Comparison of Pulse Wave Analysis Assessment Methodology in Elderly Men M

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Background
Both the Sphygmocor (S) and Vicorder (V) devices can be used for pulse wave analysis (PWA). However, large studies comparing data from both devices are lacking.

Methods
1,722 men (78.5±4.7yrs) from the British Regional Heart Study underwent PWA with S and V devices. Brachial blood pressure (BP) was assessed by V and by Omron- HEM907 (S). Measures of central Augmentation Pressure (cAP) Augmentation Index (cAIx) and central (c)BP were compared.

Results
Data were successfully obtained in 1,380 (80%) with S and 1,706 (99%) with V. 1,373 men had both S and V data. cAP and cAIx were higher in S than V (17±9vs13±5mmHg and 29±10vs21±6 % respectively, both p<0.001), and were significantly correlated (cAP r =0.65 cAIx r =0.48 p<0.001), but with greater differences at higher values. Brachial BP readings were greater with V vs Omron (mean difference 1.1±9.7/3.7±6.3 mmHg). Mean cBP was higher in V than S (139±17vs131±19mmHg) and despite strong correlation between measures (0.87 p<0.001), cBP was more likely to be greater with S than V cBP at higher cBPs.
These differences between V+S remained directionally consistent even after adjustment for risk factors (with multiple regression analysis) and when S PWA results were recalculated using V BP in a subsample (n=58).

Conclusion
PWA evaluations were more frequently successful with using V than S in elderly men. Differences in cAP, cAIx and cBP found between devices were not due to differences in BP calibration values. Further research is needed to understand the causes and clinical implications of these differences

P127 Flow dynamics and its relation to bicuspid aortopathy assessed by 4D flow CMR

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Purpose
Different altered flow dynamics may influence ascending aorta (AAo) dilation morphotypes in bicuspid aortic valve (BAV) (1). Using 4D-flow CMR, we aimed to identify flow variables related to root or ascending dilation in BAV.

Methods
One-hundred and one BAV patients (no severe valvular disease, aortic diameters <45 mm) underwent 4D-flow on GE 1.5 T Signa scanner (GE Healthcare, Waukesha, USA). Peak velocity, jet angle, normalized flow displacement, in-plane rotational flow (IRF), systolic flow reversal ratio (SFRR) and wall shear stress (WSS) were evaluated at proximal, mid and distal AAo. Dilation morphotypes were classified as non-dilated, ascending and root (2), using z-score>2. Univariate and multivariate linear regression were used to identify factors related to dilation. ROC curves were performed to assess the relationship between variables obtained in the multivariate analysis and dilation morphotypes.

Results

Fusion phenotype was right-left (RL) in 78 patients, and right-non coronary (RN) in 23. Dilation morphotype was non-dilated in 24 patients, root in 11 and ascending in 66. On univariate analysis, BAV phenotype (RN), displacement and circumferential WSS presented the highest odds ratios (Table). On multivariate analysis, sex (male), proximal velocity and axial WSS were related to root morphotype (AUC 0.91, P<0.001), while RN-BAV, distal IRF, and mid-AAo SFRR and circumferential WSS were related to ascending morphotype (AUC 0.81, P<0.001) (Table and Figure).

		Univariate analysis of aortic dilation		Multivariate analysis of aortic dilation			
				Root morphotype		Ascending morphotype	
		Odds Ratio	P-value	Odds Ratio	P-value	Odds Ratio	P-value
	BAV phenotype (RL/RN)	3.23	0.02			1.33	0.008
	Sex (Male)	1.10	0.02	4.67	0.005		
Prox	Peak velocity	1.02	0.028	1.10	0.043		
Prox	Jet angle	1.05	0.037				
Prox	Displacement	3.56	0.001	1.11	0.021		
Prox	IRF	1.01	0.002				
Prox	WSS_{axial}	1.20	0.003	7.64	0.008		
Prox	$WSS_{circumf}$	1.65	0.05				
Mid	Jet angle	1.07	0.006				
Mid	Displacement	2.46	0.002				
Mid	IRF	1.01	0.007				
Mid	SFRR (%)	1.20	0.001			1.2	<0.001
Mid	WSS_{axial}	1.21	0.05				
Mid	$WSS_{circumf}$	2.43	0.02			2.23	0.037
Dist	IRF	1.01	0.026			1.10	0.026
Dist	$WSS_{circumf}$	1.49	0.05				
Dist	SFRR (%)	1.10	0.005				

Table. Univariate and multivariate factors related to of aortic dilation and dilation morphotypes.

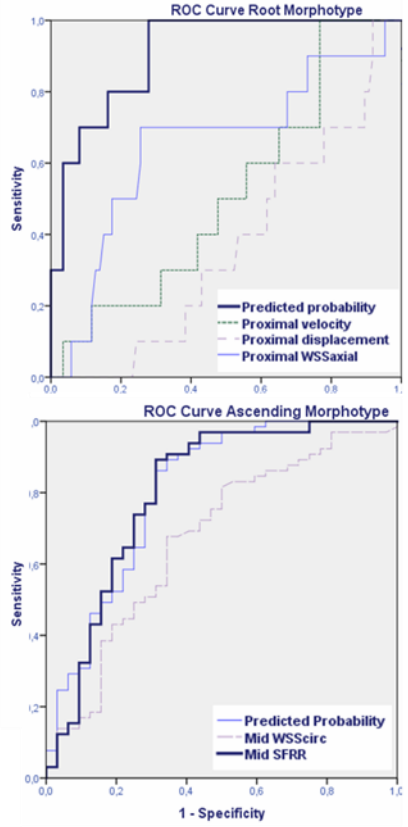

Figure. ROC curves showing flow variables related to aortic dilation morphotypes.

Conclusions

Different altered flow parameters are related to root and ascending morphotypes in BAV. Further longitudinal studies are warranted to evaluate the impact of these flow parameters in determining the risk for aortopathy.

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P128 Comparison of augmentation index obtained from HEM-9000AI and Mobil- O-Graph in Japanese normotensive individuals.

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Background
HEM-9000AI (HEM) is an established device for measurement of radial augmentation index (rAIx) used by applanation tonometry in Japan. Mobil-O-Graph (MOG) is a cuff-based oscillometric device for assessment of central aortic AIx (cAIx) and the usefulness to Europeans has been reported. We compared the AIx between HEM and MOG in Japanese normotensive subjects.

Methods
We enrolled 106 normotensive volunteers (47 male, 21 to 79 years). The left radial arterial waveform was recorded with the HEM. MOG were taken on the left arms, which arm circumferences (ACs) were measured to allow the correct choice of cuff (two sizes available; 20-24 and 24-32 cm). We performed multiple regressions for AIx and key variables in HEM and MOG.

Results
The ACs in M and F were 25.7±1.9 (mean±SD) cm and 23.5±2.1cm, respectively. Both rAIx (70.5±15.3% vs 83.6±11.9%, $p<0.001$) and cAIx (17.2±7.3% vs 29.7±9.8%, $p<0.001$) in M were smaller than those in F. Multiple regression analysis revealed that cAIx in M ($R^2=0.5176$) was significantly associated with age ($\beta=0.17$, $p=0.004$) and cuff size ($p=0.001$). cAIx obtained using the smaller cuff was significantly increased compared to the larger cuff (25.1±5.9% vs 14.8±5.9%). In F, cAIx ($R^2=0.2245$) tended to be associated with age ($\beta=0.16$, $p=0.072$) and was significantly associated with height ($\beta=-0.62$, $p=0.007$) and heart rate ($\beta=-0.26$, $p=0.0029$).

Conclusions
The brachial cuff-based waveform recordings are useful for Japanese normotensive individuals. However, the mean AC is close to the bound of two cuff sizes and the measurement of lower cAx using the larger cuff is less sensitive.

P129 Short-term repeatability of non-invasive aortic pulse wave velocity measures

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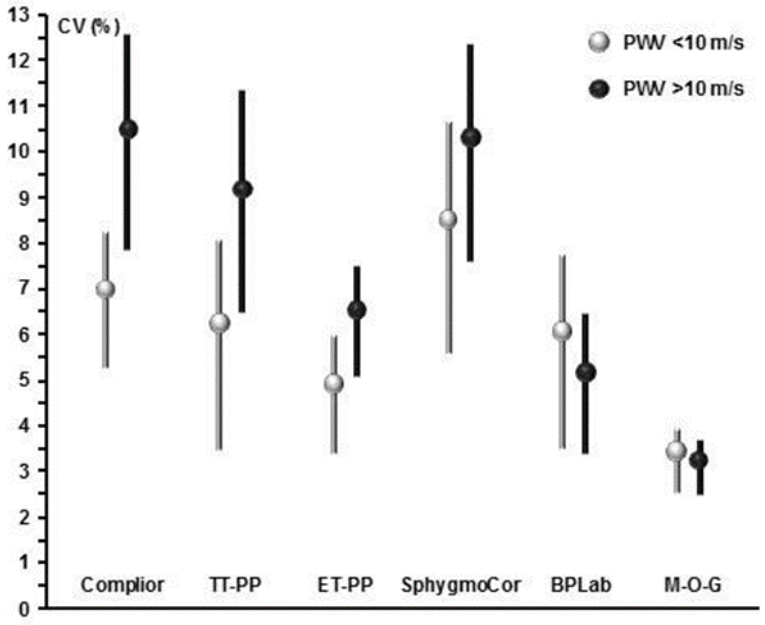
Objective
To compare the short-term repeatability of aortic pulse wave velocity (PWV) measures obtained with non-invasive devices.

Methods
In 102 patients planned to undertake a cardiac catheterization (65±13 years, 70.6% males) duplicate non-invasive measures of PWV, 15-minutes apart, were obtained with 4 devices measuring two-points carotid-femoral PWV and the related pulse transit time (PTT): Complior (AlamMedical), PulsePenETT, PulsePenET (DiaTecne), SphygmoCor(AtCorMedical), and with 2 devices estimating PWV from the oscillometric cuff-derived brachial wave: BPLab (Petr Telegin), Mobil-O-Graph (IEM). PWV and carotid-femoral PTT measurements were compared using coefficients of variation (CV%) and their confidence intervals (CI).

Results
Devices evaluating carotid-femoral PWV showed a good repeatability (CV%[CI]: Complior: 8.8[7.3-10.1]; PulsePen ETT: 8.0[6.2-9.5]; PulsePen ET: 5.8[4.9-6.6]; SphygmoCor: 9.5[7.7-11.0]), whereas the repeatability of PWV estimated by cuff-based devices was for the BPLab=5.5[4.2-6.6] and for the Mobil-O- Graph=3.4[2.9-3.8]). A tendency toward a lower repeatability of carotid-femoral PWV was present for greater arterial stiffness, while repeatability of carotid-femoral PTT was not related to its mean values. Differences between repeated PWV measurements were not correlated with blood pressure (R^2=0.005) or heart rate variations (R^2=0.013).



Conclusions
Short-term repeatability of PWV measures was good, with some differences between different devices. A greater repeatability was observed in devices estimating PTT from a cuff-based measurement, compared to devices measuring carotid-femoral PTT, owing to the algorithm of calculation of PWV (Mobil-O-Graph) or to the procedure of correction which eliminates highly variable PWV values (BPLab).
Repeatability of PWV is not influenced by blood pressure or heart rate variations. For carotid-femoral PWV, the repeatability of measures is lower for higher PWV values.

P130 Test-retest reliability for pulse wave velocity and cardio-ankle vascular index among Afro-Caribbean young adults

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Background
This study evaluated the test-retest reliability of carotid-femoral pulse wave velocity (PWV) and cardio-ankle vascular index (CAVI) among young adults in Jamaica.

Methods
We recruited participants from the Jamaica 1986 Birth Cohort Study. PWV was measured using the Arteriograph device™ (TensioMed, Budapest) and CAVI with the VaSera™ device (Fukuda Denshi, Tokyo). Both measurements were done twice on the same day with a 1-hour interval between measurements. Test-retest reliability was estimated using the intra-class correlation coefficient (ICC) and Bland-Altman plots. Kappa statistic was used to assess agreement between repeated tests in classifying participants as high PWV or CAVI, defined as being in the upper tertile of measurements.

Results
Analyses included 89 participants (43 males; 46 females; mean age 28.4±0.50 years). Mean PWV for first and second readings were 6.56 cm/s and 6.64 cm/s, respectively (mean difference -0.08 [95%CI -0.18, 0.03, p=0.142]). Mean values for first and second CAVI were 6.53 and 6.20, respectively, (mean difference 0.34 [95%CI 0.18, 0.50, p<0.001]). ICC for PWV was 0.88 (95%CI 0.83, 0.92) and for
CAVI 0.57 (95%CI 0.41, 0.69). Bland-Altman plots indicated that measurements taken from both devices were highly reproducible, with most points (85/89 for PWV; 86/89 for CAVI) falling within 2 SD of the mean difference. Kappa statistic was 0.76 for PWV and 0.56 for CAVI.

Conclusion
PWV (Arteriograph™) and CAVI (VaSera™) have good test-retest reliability among Jamaican youth adults; however repeated CAVI values were marginally lower than the first measurement and the ICC and kappa estimates were lower.

P131 Determinants of a new, non-invasive index of ventricular-arterial coupling and myocardial performance in a general population sample.

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Background
The interaction between the heart and arteries (i.e. ventricular-arterial coupling, VAC) is a key determinant of cardiovascular performance. As such, VAC indexes might reflect the interplay between arterial stiffness and left ventricular (LV) dysfunction. In a community-based sample, we assessed the determinants of a new, non-invasive VAC index reflecting myocardial performance.

Methods
In 364 subjects (45.1% women; mean age, 53.8 years; 46.7% hypertensive), we derived echocardiographic indexes of LV structure and function and tonometric measures of central haemodynamics and aortic stiffness. From two-dimensional LV strain curves and simultaneously recorded pressure waveforms, we constructed the pressure-strain loop and calculated ejection work density (EWD), a myocardial performance index, as the area of the pressure-strain loop during LV ejection.

Results
In multivariable-adjusted analysis, EWD increased linearly with age (P<0.0001). While adjusting for age, anthropometric measures and heart rate, EWD was significantly higher in women and patients with hypertension as compared to men and normotensives, respectively (P<0.0001 for all). After full adjustment, EWD increased with higher augmentation pressure, central pulse pressure and carotid-femoral pulse wave velocity in both men and women (P≤0.031). Furthermore, EWD correlated independently and directly with left atrial and LV end-diastolic volumes (P≤0.015) as well as peak early diastolic velocities of transmitral flow and mitral annulus movement (P≤0.025).

Conclusion
Higher age, female sex and hypertension were independent determinants of higher EWD. Being associated with indexes reflecting central haemodynamics, arterial stiffness and LV diastolic function, this myocardial performance index might reflect the interaction between LV performance and arterial properties.

Poster Session I – Pathophysiology

Chair: C Palombo, C Delles

P165 Higher blood pressure in youth is attributable to a combination of higher cardiac output and higher total peripheral resistance M

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Background
It has been proposed that high blood pressure (BP) in young people is due to high cardiac output (CO) with normal total peripheral resistance (TPR) - a hyperkinetic/hyperdynamic circulation. We investigated this in a large, population- based cohort of adolescents.

Methods
The study was conducted on 2091 participants in the Avon Longitudinal Study of Parents and Children (ALSPAC), a prospective population-based birth cohort study, aged 17. BP measurement and echocardiography was performed and heart rate (HR), stroke volume (SV) and TPR calculated. Data are means(SD).

Results
Table 1 shows selected characteristics of the sample. Higher quintiles of systolic BP were associated with higher SV, higher HR and higher TPR. However, the proportional contribution made by SV, HR and TPR to mean arterial pressure differed little by systolic BP quintile (stroke volume (32-34%) heart rate (25-29%) and TPR (39-41%)).

Variable	Males (n=939)	Females (n=1152)	All (n=2091)
, y	(0.3)	(0.3)	(0.3)
, kg/m^2	(3.7)	(4.2)	(4.0)
mmHg	11)/64(8)	9)/65(7)	11)/65(8)
bpm	0)	0)	0)
L/min	1.0)	0.8)	0.9)
ml	3)	1)	3)
, mmHg.ml/min	(5.9)	(6.0)	(6.0)

Conclusions
Higher blood pressure is attributable to a combination of higher cardiac output (i.e. SV x HR) and higher TPR in a population-based sample of adolescents. There is no evidence of a disproportionate contribution from CO at higher BP levels.

P166 Head-down tilt bed-rest significantly increases central arterial stiffness M

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The vascular system is subject to continual variation in mechanical stresses, both physiological and pathological. Vascular remodeling via changes in vessel wall properties, including thickness and stiffness, is a major feature of aging and cardiovascular disease.

A more detailed understanding of the interplay between mechanical stress, aging, CVD and vascular remodeling will aid prevention of increased cardiovascular risk following long term microgravity.
This study aims at assessing vascular remodeling processes resulting from a 60-day head-down-tilt bed-rest period during the European Space Agency Study (Toulouse, France).

We hypothesize that arterial remodeling processes are modified by long term bed- rest and constitute a significant cardiovascular risk in the long term for astronauts. Applanation tonometry is used to assess carotid to femoral pulse wave velocity (PWV) and non-invasive ultrasound imaging are used to assess arterial remodelling processes at the carotid,femoral,brachial and popliteal arteries.Measurements are performed at baseline; at day 29 and 52 of bed-rest; and at day 6 and 30 of the recovery period.

The preliminary results including 10 first subjects, demonstrate a strong effect of bed- rest on arterial PWV.The average PWV at baseline equals 7,6±1.4m/s and is increased to 9.0±1.9m/s after 29 days, and,9.3±1.8m/s after 52 days bed-rest. This increase is significantly different between baseline, and,29 and 52 days bed-rest ($p<0.005$).

Increase in PWV suggests a rapid and significant stiffening of the central arteries, which on healthy subjects corresponds to an aging process wich occurs many years. Low gravity conditions as during bed-rest induce significant arterial stiffening that could be linked to long term CVD risks for either patients in bed-rest or astronauts.

P167 Pulse Pressure Amplification and Augmentation Index change in opposite manner with arterial stiffness independently of systemic resistance M

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Background
Pulse Pressure Amplification (PPA) is the increase in Pulse Pressure (PP) from proximal to distal arteries. The Augmentation Index (AIx) is the secondary increase in aortic pressure in systole relative to PP. With aging and increased arterial stiffness the PPA *de*creases while the AIx *in*creases. Since both depend on the reflection of pressure waves, the finding that PPA and AIx change in opposite ways seems surprising.

Methods
Aortic PPA, AIx and Reflection Magnitude ($RM=P_{reflected}/P_{forward}$) were determined in a multibranched model and during control and Valsalva Maneuver in the human.

Results
During the Valsalva Maneuver reflections decrease: the lower mean arterial pressure results in lower stiffness and Pulse Wave Velocity (PWV) while Systemic Vascular Resistance (SVR) is increased. The model confirms that SVR plays a minimal role in terms of reflections. Reflections result from many reflections sites in the larger arteries. The lower PWV implies shorter wave length and thus artery length/wave length increases. This increase makes the differences in travel times from the many reflection sites to the heart more different resulting in lower total reflection: RM and AIx decrease. The lower PWV, thus the shorter wave length, also implies an increase in travel time over the aorta, and larger amplification. (It has been shown that local reflections change little with changes in stiffness.)

Conclusions
Reflections are mainly determined by travel times of reflected waves of the larger arteries. Mean pressure determines arterial stiffness and the stiffness change, via PWV, results in the opposite changes in RM and PPA.

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P168 Endothelial regulation of AWV is impaired during increase in blood flow in essential hypertension M

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Background
Arterial wall viscosity (AWV) depends on endothelium-derived factors in physiological conditions (1,2). Hypertension is characterized by an altered FMD during sustained flow increase due to endothelial dysfunction (3). Whether NO and EETs regulate change in AWV during increase in flow in hypertensive patients (HT) as compared with normotensive controls (NT) remains to be evaluated.

Methods
Radial artery diameter, wall thickness and arterial pressure were measured in 18 untreated essential HT and 14 frequency matched NT during hand skin heating with saline, L-NMMA, fluconazole, or both inhibitors infusion. AWV was estimated by the ratio of the area of the hysteresis loop of the pressure-diameter relationship (W_V,
viscous energy dissipated) to the area under the loading phase (W_E, elastic energy stored).

Results
During saline infusion, W_V, W_E and W_V/W_E were not modified after heating in NT whereas W_V/W_E increased in HT (39.3±12.0% to 49.9±7.7 %, $p<0.05$) due to a larger increase in W_V than W_E (ΔW_V: +41.5±27.6% vs. ΔW_E: +25.1±28.4%, $p<0.05$). With all inhibition sequences, W_V/W_E increased after heating in NT ($p<0.05$) due to a larger increase in W_V than W_E ($p< 0.05$). In HT with fluconazole, L-NMMA and L- NMMA+fluconazole, W_V/W_E increased after heating ($p<0.05$) due to a larger increase in W_V than W_E ($p< 0.05$), similarly to saline infusion. In all conditions, increase in shear stress was similar between NT and HT.

Conclusion
NO and EETs maintain stable AWV during change in flow in NT, and this regulation is lost in HT resulting in an increased AWV after heating.

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P169 - WITHDRAWN

P170 Short-term effects of transcatheter aortic valve implantation on aortic function and hemodynamics M

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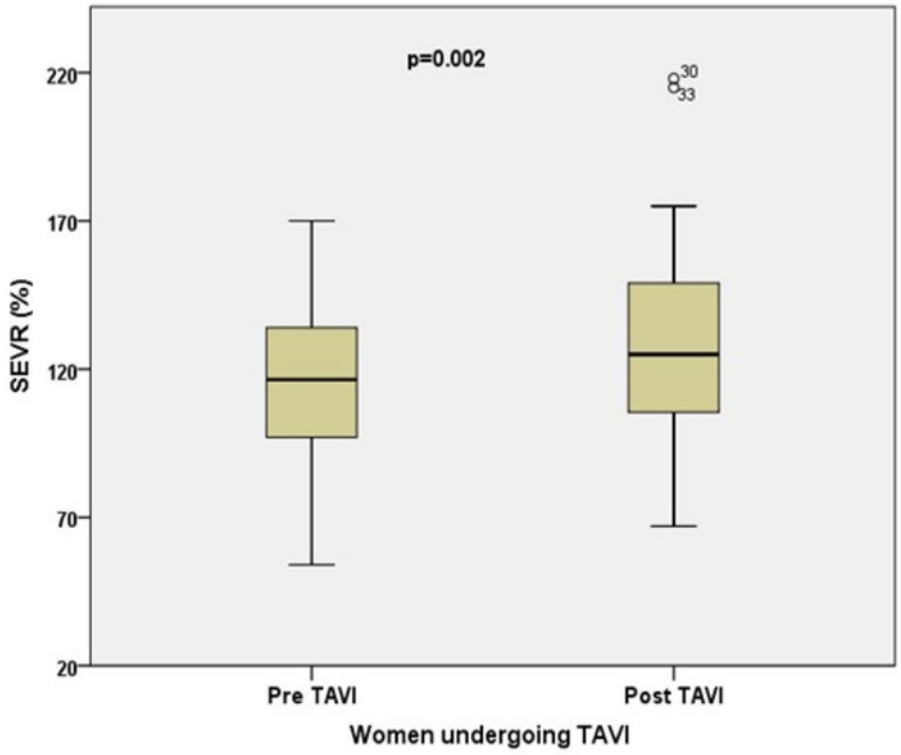
Purpose/Background/Objectives
Aortic stiffness and hemodynamics are independent predictors of adverse cardiovascular events. Transcatheter aortic valve implantation (TAVI) is growingly used in elderly patients with aortic stenosis. We sought to investigate the effect of TAVI upon aortic vascular function and hemodynamics as well as the interplay between genders.

Methods
Twenty high-risk patients (mean age 82.2±5.3 years, 13 female) with severe symptomatic aortic stenosis undergoing TAVI were included. Aortic stiffness was estimated through carotid-femoral pulse wave velocity (PWV). Aortic hemodynamics (aortic pressures, aortic augmentation index [AIx]) and subendocardial viability ratio (SEVR) were measured with Sphygmocor. Measurements were conducted prior to the implantation and at discharge.

Results
PWV prior to the implantation was 8.6±1.5 m/s and aortic AIx=33.0±14.0% for the overall population. There was no statistically significant change in peripheral or aortic pressures as well as on aortic stiffness after implantation of TAVI. However, there was a marginally non-significant trend for an increase in SEVR (116±28 vs 131±40%, p=0.067). Results to the male population were similar to the overall population.
Conversely, in the female population, there was a significant increase in PWV after TAVI (8.4±1.2 m/s vs 8.9±1.3% with p=0.034, respectively). Furthermore, there was a significant increase in SEVR after TAVI (107±28 vs 125±24% with p=0.002, respectively). All other variables did not change significantly in the female population.



Conclusion
Our study shows that shortly after TAVI female subjects experience an increase in aortic stiffness with an improvement of myocardial perfusion. These findings further elucidate the short-term hemodynamic consequences of aortic valve repair.

P171 Compliance of extremely dilated main pulmonary arteries in pulmonary arterial hypertension

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Background
Main pulmonary artery (MPA) dilation is a radiological sign of pulmonary hypertension (PH) and is an independent risk factor of sudden death (Żyłkowska et al, Chest 2012). Extreme MPA dilation is a rare consequence of PH. We hypothesize that the main pulmonary artery compliance is larger and contributes more to total arterial compliance in PH patients with an extremely dilated MPA when compared to patients with a less dilated MPA.

Methods
Cardiac magnetic imaging (CMR) scans of idiopathic and hereditary pulmonary arterial hypertension (PAH) patients were retrospectively analyzed. Six PAH patients with extremely dilated MPAs (≥45 mm diameter on transverse plain CMR images of the MPA) and six PAH patients with MPA diameter <45 mm were included. Total pulmonary arterial compliance (C_{tot}) was calculated by stroke volume (SV) over pulse
pressure (PP) and MPA compliance (C_{MPA}) by (Δarea*length)/PP (length was assumed 5 cm for all MPAs). C_{MPA}/C_{tot} ratio could therefore be calculated by CMR derived flow images alone: $C_{MPA}/C_{tot}=(\Delta area*length)/SV$.

Results
Mean age in both groups was not different, mean pulmonary artery pressure was higher in patients with an extremely dilated MPA (73±9.0mmHg) compared to patients with non-extremely dilated MPA (48±5.4mmHg, p=0.02). A trend toward a higher C_{MPA}/C_{tot} ratio was observed in patients with extremely dilated MPA
(p=0.0534).

Conclusion
In PAH the contribution of the MPA to total compliance tends to be higher in patients with a MPA diameter ≥45 mm then in patients with a diameter <45mm.

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P172 Voluntary liquorice ingestion increases blood pressure via multiple mechanisms: increased volume load, peripheral arterial resistance, and decreased aortic compliance

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Objectives
Liquorice consumption elevates blood pressure [1-3], but the liquorice-induced haemodynamic changes in the upright position are unknown. We investigated haemodynamics after liquorice exposure in healthy volunteers during orthostatic challenge.

Methods
Haemodynamics were recorded from 22 normotensive subjects during passive 10- minute head-up tilt before and after two weeks of liquorice consumption (glycyrrhizin dose 290-370 mg/day) using radial pulse wave analysis, whole-body impedance cardiography, and spectral analysis of heart rate variability. Thirty age-matched healthy subjects maintaining their habitual diet served as controls.

Results
Liquorice ingestion elevated radial systolic (p<0.001) and diastolic (p=0.018) blood pressure and systemic vascular resistance (p=0.037). During orthostatic challenge, heart rate increased less after the liquorice versus control diet (p=0.003) and low frequency power of heart rate variability decreased within the liquorice group (p=0.034). Liquorice intake increased central pulse pressure (p<0.001) and augmentation index (p=0.002) supine and upright, but in the upright position the elevation of augmentation index was accentuated (p=0.007). Liquorice diet also increased extracellular fluid volume (p=0.024) and aortic to popliteal pulse wave velocity (p=0.027), and aortic characteristic impedance in the upright position (p=0.002).

Conclusions
In addition to increased extracellular fluid volume and large arterial stiffness, two weeks of liquorice ingestion elevated systemic vascular resistance and augmentation index. Measurements performed at rest may underestimate the haemodynamic effects of liquorice ingestion, as enhanced central wave reflection and reduced chronotropic response were especially observed in the upright position.

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P173 Coupled nitroso-sulfide signalization triggers specific vasoactive effects in intrarenal arteries of patients with arterial hypertension

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In normotensive conditions, it has been confirmed that S-nitrosothiols, as a source of NO, interact with hydrogen sulfide (H_2S) and create new substance/s with specific vasoactive effects. This interaction could represent new regulator pathway also in hypertension. The aim of the study was to investigate the vasoactive effects of H_2S, GSNO, and products of H_2S/GSNO interaction in lobar arteries isolated from kidney after nephrectomy of patients suffering from arterial hypertension.

Changes in isometric tension after pre-contraction were evaluated. Acetylcholine- induced vasorelaxation was significantly reduced compared to the effect induced by exogenous NO donor, sodium nitroprusside, probably suggesting an endothelium dysfunction. While 1 µmol/l Na_2S had a minimal effect on the vascular tone, 20 µmol/l evoked a slight vasorelaxation. GSNO at 0.1 µmol/l induced vasorelaxation which was significantly smaller compared to the effect induced by 1µmol/l. The mixture of GSNO (0.1 µmol/l) and Na_2S (1 µmol/l) induced significantly higher vasorelaxation compared to GSNO (0.1 µmol/l) alone only in 5th minute without the differences in the speed.

On the other hand, the mixture prepared from higher concentrations of GSNO (1 µmol/l) and Na_2S (10 µmol/l) induced a significantly higher (in 1st, 2nd, 5th, 10th minute) and faster vasorelaxation compared to the effect induced by GSNO (1 µmol/l) alone.

In conditions of arterial hypertension H_2S in interaction with GSNO regulated a vasoconstrictor-increased arterial tone towards of more pronounced vasorelaxation compared to GSNO alone. We confirmed for the first time that specific vasoactive effects of coupled nitroso-sulfide signalization were triggered also in human arterial tissue.

References

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P174 Hemodynamic and autonomic effects of low-dose glyceryl trinitrate used to test endothelium-independent vasodilation of the brachial artery

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Background/Aim
Smooth muscle function is explored by sublingual glyceryl trinitrate (GTN) administration in vascular function protocols, in order to compare with endothelium- dependent vasodilation of the brachial artery by flow-mediated dilation (FMD). The aim of this study is to evaluate the hemodynamic and autonomic effects of the two most often used GTN dosages.

Methods
In 80 essential hypertensive patients (HT) and 60 normotensive subjects (NT), we evaluated FMD of the brachial artery and endothelium-independent response to 25 and 400 mg of sublingual GTN by high-resolution ultrasound and automated
image analysis. In a subgroup of 10 HT, muscle sympathetic nerve activity (MSNA) was also assessed by microneurography.

Results
NT showed significantly ($p<0.01$) lower FMD (5.5±3.3%) as compared to healthy controls (6.9±2.2%). The response to GTN 25µg also tended to be lower (HT 7.2±3.3%; NT 7.9±2.9%; $p=0.06$), whereas response to GTN 400µg was similar (HT 14.3±4.8%, NT 14.5±54.7%, p=ns). In the whole population, changes in blood pressure (BP) induced by GTN 400µg (systolic BP -3.2±7.7, diastolic BP -4.7±5.0 mmHg) were significantly higher (<0.001) compared to GTN 25µg (systolic BP - 0.7±5.8, diastolic BP -0.7±4.4 mmHg). Changes in heart rate were also higher with GTN 400µg than with 25µg (+5.6±6.4 versus -0.2±5.4 bpm, $p<0.001$). This behavior was similar in HT and NT subgroups. MSNA was significantly increased by GTN
400µg (31±7 to 41±6bursts/min, $p<0.001$) but not by 25µg (33±9 to 37±11bursts/min, $p=0.19$)

Conclusions
The administration of GTN at the dose of 25 µg allows exploring endothelium- independent vasodilation in FMD protocols, inducing only modest hemodynamic and sympathetic responses.

P175 An acute bout of prolonged sitting impairs endothelial function and increases plasma concentrations of endothelin-1 in overweight/obese adults: implications for glucose and insulin metabolism

Grace, Megan[1,2]; Climie, Rachel[1]; Wheeler, Michael[1]; Eikelis, Nina[1,3]; Carr, Joshua[1,2]; Dillon, Francis[1]; Owen, Neville[1,3]; Green, Danny[4]; Kingwell, Bronwyn[1]; Dunstan, David[1,5,2]

[1]Baker Heart and Diabetes Institute, Melbourne, Australia, [2]Monash University, Melbourne, Australia, [3]Swinburne University, Melbourne, Australia, [4]University of Western Australia, Perth, Australia, [5]Australian Catholic University, Melbourne, Australia

Background
Compared to regular active breaks, prolonged uninterrupted sitting amplifies postprandial glucose and insulin in overweight/obese adults with and without type 2 diabetes; and impairs lower limb endothelial function (a predictor of cardiovascular disease) in healthy adults. However, the effects of prolonged sitting on endothelial function in those at heightened risk of cardiometabolic disease have not been investigated.

Methods
Overweight/obese (BMI >25kg/m^2) adults (35-75y) completed two laboratory-based conditions in a random order: (i) 5h prolonged uninterrupted sitting (SIT); and (ii) 5h sitting interrupted with 3min of light-intensity simple resistance activities every 30min (SRA). Femoral artery endothelial function (flow mediated dilation; FMD) and shear rate was assessed at baseline, 1, 2 and 5h. Hourly plasma was

collected for glucose, insulin and endothelin-1 measurement. Muscle sympathetic nervous activity (MSNA) was measured at 5h.

Preliminary Results
In the current sample (n=7), SIT impaired FMD (-2.6±0.9%; p<0.05) and shear rate iAUC (-39±14%; p<0.05), compared to SRA. There was an increase in glucose (40±28%; p=0.18) and insulin (46±25%; p=0.16) iAUC, and mean endothelin-1 plasma concentration (0.28±0.09 pg/ml; p<0.05) in SIT, compared to SRA. MSNA (n=4) was reduced in SIT, compared to SRA (-4±1 bursts/min; p<0.05). Testing and analysis (n=20 participants) is expected to be complete by August, 2017.

Conclusions
These findings are consistent with a potential mechanistic link between sitting- induced endothelial dysfunction, vasoconstriction and insulin resistance, via reduced delivery of glucose and insulin to nutritive vascular beds in muscle. Endothelial dysfunction associated with prolonged sitting may be related to reduced shear rate, and impaired MSNA.

P176 Arterial stiffness as a part of a general abnormality of the fibrous healing process

Forcada, Pedro[1]; Sangiovanni, Miguel[2]; Camino, Alejandra[2]; Pampinella, Wanda[3]; Montaña, Oscar[4]

[1]Cemic, Buenos Aires And Dim Prevencion Cardiovascular Buenos Aires, Argentina, [2]Dim Prevencion Cardiovascular, Buenos Aires Argentina, [3]Dim Prevencion Cardiovascular, Buenos Aires, Argentina, [4]Dim Prevencion Cardiovascular, Buenos Aires, Argentina

Environment
There seems to be a common abnormality of the healing process in several diseases as COPD, liver esteatosis, and arterial stiffening.

Objective
To asses the association of frequency between liver esteatosis and aortic stiffness by means of c-f PWV in patients included in a CV prevention programme.

Methods
43 patients underwent a simultaneous evaluation including antropometry, biochemistry, cardiac, vascular and abdominal ultrasonography.

Results
Mean age was 53,4±11 y.o, 67% male, SBP 137±17, DBP 87 ±10 PP 50,3±11 mmHg, BMi 29± 4. CVRF: HTN 74%, DLP 69%, DBT 7%, TBQ 28%, OBS 42%, OVWT 28%, SED 71%.CV Drugs: 63%.
Nine (21%) presented abnormal PWV and esteatosis and 17 (39,5%) none of them. Whereas 4 (9,5%) presented abnormal PWV with normal liver and 13 (30%) the opposite. (Fisher NS, Cochran´s <.05). More information about LV mass and atherosclerotic burden is presented.

Conclusion
In a group of p. in a Primary CV prevention programme there is a trend to a significative association between the presence or not of liver esteatosis and aortic stiffness.
A wider investigation of fibrosis and the healing process in different tissues should be considered as a future research target.

P177 Associations of ambulatory pulse pressure components with hippocampal volume, white matter hyperintensities and brain infarcts M

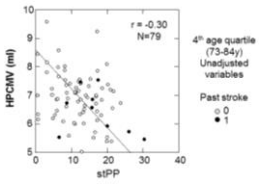
Gavish, Benjamin[1]; Tillin, Therese[2]; Hughes, Alun D[2]; Chaturvedi, Nishi[2]

[1]Yazmonit Ltd., POB 606, ISRAEL, [2]Institute of Cardiovascular Science, Faculty of Population Health Sciences, University College London, London, UK

Background
Arterial stiffness is blood pressure (BP) dependent. Using 24-hour ambulatory BP monitoring (24hABPM) pulse pressure (PP) can be split into an 'elastic' part (elPP: 'diastolic stiffness'), and a 'stiffening' part (stPP: 'stiffness change during systole'). We investigated associations of elPP, stPP and PP with brain MRI measures.

Methods
A community-based sample of 542 individuals (59±6y) with 24hABPM and brain MRI, including hippocampal volume (HPCMV), severity of White Matter Hyperintensities (WMH_SVR), and number of brain infarcts (N_INFRCT). 'High'/'low' (HI/LO) marked variables status (by medians).

Results
elPP and stPP were weakly correlated (r=0.15); stPP-to-PP ratio was 0.21±0.08. Adjusted HPCMV calculated at age quartiles for the HI_PP cohort correlated better with values from HI_stPP than from HI_elPP. For HI_PP and HP_stPP HPCMV reduction between age quartiles 1&4 was similar, but 20% larger than for HI_elPP. In hypertensives at highest age quartile HPCMV correlated negatively with stPP (P<0.05: adjusted for age, sex and diabetes), but not with PP and elPP.
Adjusted WMH_SVR was greater in HI_elPP, HI_PP and HI_elPP comparing diabetics with non-diabetics by 0.38(P=0.001), 0.29(P=0.008) and 0.13 (P=0.25), respectively.
In hypertensives N_INFRCT was greater in past-stroke than no-stroke cohorts in HI&LO elPP, stPP and PP subgroups by 1.96&0.63, 1.48&1.26, and 1.53&1.18 (P<0.0001 for all).



Conclusion
The association of elastic and stiffening components calculated from ambulatory PP differ for different MRI brain measures and may provide a practical tool for associating arterial properties with brain-related pathological changes. Associations with PP may be mainly explained by its relatively-small stiffening component during systole.

21.00 Young Investigator Networking Reception
Modus Bibendi, Via Domenica Cavalca 18, 56126, Pisa

FRIDAY 13 OCTOBER 2017

08.00 Refreshments, Poster and Exhibition viewing

08.30 Oral Session II – Young Investigator Session

Chair: RM Bruno, S Laurent

2.1 Cognition in Relation to the Retinal Microcirculation in Children Born Prematurely or at Term

Wei, Fangfei[1]; Raaijmakers, Anke[2]; Zhang, Zhen-Yu[1]; van Tienoven, Theun Pieter[3]; Huang, Qi-Fang[1]; Yang, Wen-Yi[1]; Thijs, Lutgarde[1]; Struijker-Boudier, Harry[4]; Verhamme, Peter[5]; Allegaert, Karel[2]; Staessen, Jan[1]

[1]Department of Cardiovascular Sciences, University of Leuven, [2]Department of Development and Regeneration, University of Leuven, [3]Department of Sociology, Vrije Universiteit Brussel, [4]Maastricht University, [5]Centre for Molecular and Vascular Biology, KU Leuven Department of Cardiovascular Sciences, University of Leuven

Background
The retinal microvasculature can be visualized noninvasively and mirrors the status of the cerebral vasculature. We therefore investigated in 93 prematurely born infants (birth weight <1000 g) and 87 controls born at term whether neurocognitive performance at ~11 years is associated with the diameter of retinal microvessels.

Methods
We post-processed retinal photographs by a semi-automated software (Singapore I Vessel Assessment, version 3.6) and administered the Wechsler Non-Verbal test, Dutch version (Pearson, The Netherlands) to estimate the intelligence quotient (IQ) by combining matrix reasoning and spatial span.

Results
Compared with the controls, cases had lower IQ (92.5 *vs*. 108.7; *P*<0.001), smaller central retinal arteriolar (CRAE; 162.7 *vs*. 174.0 mm; *P*<0.001) and venular (CRVE;
234.7 *vs*. 242.7 mm; *P*=0.003) diameters and CRAE/CRVE ratio (AVR; 0.70 *vs*. 0.72; *P*=0.002) and lower body mass index (17.0 *vs*. 17.7 kg/m^2; *P*=0.044), but higher mean arterial pressure (82.7 *vs.* 77.7 mm Hg; *P*<0.001). In all children, the effect sizes associated with a 1-SD increase in CRAE were +3.87 (*P*<0.001), +1.80
(*P*=0.004) and +2.26 (*P*=0.003) for total IQ, matrix reasoning, and spatial span, respectively. In models adjusted for body mass index and mean arterial pressure, these estimates were +3.21 (*P*=0.009), +1.57 (*P*=0.020), and +1.84 (*P*=0.024), respectively. The associations of IQ and matrix reasoning with AVR also attained significance (*P*≤0.031).

Conclusions
In conclusion, our findings suggest that underdevelopment of the microcirculation in prematurely born children might have lasting effects on their cognitive performance.

2.2 Heart structure and vascular function in young patients after Endovascular Repair for blunt thoracic aortic injury

Vallerio, Paola[1]; D'Alessio, Ilenia[2]; Maloberti, Alessandro[1]; Varrenti, Marisa[1,2]; Maggioni, Simone[2]; Cantu, Valentina[2]; Carbonaro, Marco[2]; Ferrara, Maria Cristina[2]; Spada, Elisa[2]; Palmieri, Bruno[3]; Lista, Alfredo[3]; Giannattasio, Cristina[1,2]

[1]Cardiology IV, "A. De Gasperis" Department, Ospedale Niguarda Ca' Granda, Milan, Italy, [2]Medicine and Surgery Department, Milano-Bicocca University, Milan, Italy., [3]Vascular Surgery, Ospedale Niguarda Ca' Granda, Milan, Italy.

Objective
Thoracic Endovascular Aortic Repair (TEVAR) currently represents the gold standard of treatment for Blunt Thoracic Aortic Injury (BTAI). Nevertheless, there is an ongoing debate surrounding its safety and efficacy and its subsequent CV effects. The present study is aimed at assessing heart and aortic structure and function after TEVAR in BTAI patients.

Method
In 20 patients (18 men, age 41±14years) treated with TEVAR (11 Gore-CTAG, 9 Medtronic-Valiant) after BTAI, between 2004-2015, after a median follow-up time of 3 years (range 12-1 years; T1) we evaluated BP, cf-PWV (sphygmocor) and Left Ventricular Mass Index (LVMI) on echocardiogrphy.

Results
At baseline, all the patients were normotensive; At T1 despite mean normal BP value (131±12/85±10) 11 patients (55%) were hypertensives. Also LVMI (81,84±28,11 g/m^2) and PWV (7,58±1,48m/s) mean values were within the normal range. When patients were divided accordingly to the used graft patients treated with Medtronic- Valiant showed a significantly higher LVMI (97.17±35.78 vs 69.58±11.24g/m^2;p<0,05) and PWV (7,78±1,74 vs 6,45±1,54m/s;p<0,05) compared with those treated with
Gore-CTAG. Same figures were fouded when patients were divided accordingly to
the treating time with those treated more than 3 years before the evaluation that showed higher LVMI (91,16±34,73 vs 70,20±9,44g/m^2;p<0,01) and PWV (7,50±1,98 vs 6,38±1,04m/s; p<0,05).

Conclusions
TEVAR for BTAI is associated after some years with the development of hypertension and heart and vascular alterations. The presence of TEVAR modify aortic functional properties and induce in young subject an increase in BP and LVMI probably related to the presence of a rigid aorta.

2.3 Biomechanical and structural quantification of vascular damage: A unique investigation of stent implantation

Geith, Markus A.[1,2,3]; Sommer, Gerhard[1]; Schratzenstaller, Thomas[2,3]; Holzapfel, Gerhard A.[1]

[1]Institute of Biomechanics, Graz University of Technology, [2]Laboratory for Medical Devices, OTH Regensburg, [3]Regensburg Center of Biomedical Engineering, OTH & University Regensburg

The most challenging complication after coronary stent implantation is in-stent restenosis [1], which is mainly caused by mechanically induced injuries due to overloading. From a biomechanical point of view, the processes occurring inside the arterial tissues during stent implantation (SI) is rather unknown.

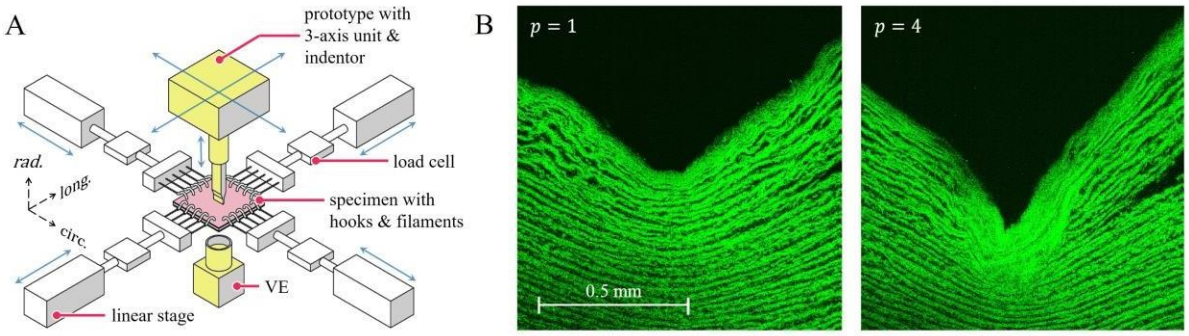
This study shows a novel approach to quantify vascular damage due to SI a multi- scale examination of coronary arteries with generated injuries using a unique experimental *in vitro* setup.

The setup consists of a biaxial tensile testing stage to apply physiological loads on rectangular specimens of coronary arteries and a triple-axis-unit, which allows the indentation of stent struts into arterial tissues under a specified pressure (Fig. A). In addition, the multi-scale investigation of the mechanical and structural responses of the resulting lesion, following the protocol of Sommer et al. [2], is carried out by calculating Cauchy stresses and analyzing healthy and injured specimens with second harmonic generation (Fig. B) and electron microscopy.

The results indicate that the usually wavy collagen fibers straightened, compress and align around the lesion (Fig. B). In addition, the evaluation of the material characteristics reveals a significant softening of injured tissues.

Fig. A: Design of the experimental setup, showing a biaxial tensile testing stage (white parts) and the triple-axis-unit for indentation tests (yellow parts).

Fig. B: Sectional view through the tissue perpendicular to the lesion. The SHG images show collagen fibers of specimens from a 6-months-old porcine descending aorta responding under different pressures (1 and 4 MPa).



References

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2.4 Brachial cuff reservoir characteristics and end-organ markers of cardiovascular risk in Australian adults: a cross-sectional study

Peng, Xiaoqing[1]; Schultz, Martin[2]; Cheung, Michael[3]; Wake, Melissa[4]; Mynard, Jonathan[3]; Burgner, David[5]; Liu, Richard[6]; Sharman, James[2]

[1]Menzies Institute for Medical Research, University of Tasmania, Hobart, TAS, AU, [2]Menzies Institute for Medical Research, University of Tasmania, Hobart, Australia., [3]The University of Melbourne, Parkville, Victoria, Australia; Murdoch Children's Research Institute, Parkville, Victoria, Australia; The Royal Children's Hospital, Melbourne, Victoria, Australia., [4]The University of Melbourne, Parkville, Victoria, Australia; Murdoch Children's Research Institute, Parkville, Victoria, Australia; The University of Auckland, Grafton, Auckland, New Zealand, [5]The University of Melbourne, Parkville, Victoria, Australia; Murdoch Children's Research Institute, Parkville, Victoria, Australia; Monash University, Clayton, Victoria, Australia, [6]Murdoch Children's Research Institute, Parkville, Victoria, Australia.

Objective

Reservoir-excess pressure measured using tonometry methods predicts cardiovascular events, but the operator-dependency of tonometry is an impediment to widespread use. A cuff-based blood pressure device has been developed to derive reservoir-excess pressure from measured brachial

pressure waveforms, but whether this method is independently associated with cardiovascular risk has never been investigated and this was the aim of this study.

Methods
1874 adult participants (age 43.7±5.2 years, 11% male) from the Longitudinal Study of Australian Children's Child Health CheckPoint study had reservoir pressure (RP) and excess pressure (XSP) derived from the brachial pressure waveform measured using cuff oscillometry (SphygmoCor XCEL, AtCor Medical, Sydney).
Central hemodynamics (augmentation index and central blood pressure) were estimated from the central pressure waveform. Carotid intima-media thickness (cIMT, n=1467) and carotid-to-femoral pulse wave velocity (cf-PWV, n=1674) were measured as end-organ markers of cardiovascular risk.

Results
XSP and RP were associated with cIMT after adjusting for age, sex, waist-to-hip ratio, heart rate (HR) and central hemodynamic indices (β=0.070, p=0.027 and β=0.052, p=0.047). RP was also significantly associated with cf-PWV after adjusting for the same variables as above (β=0.128, p<0.001). The additional reservoir-excess pressure variables in a model that originally included the Framingham risk score and HR strengthened the evidence for associations with cIMT and cf-PWV (p<0.001 for
all R^2 changes).

Conclusion
Cuff-based measures of reservoir-excess pressure are significantly associated with end-organ markers of cardiovascular risk independent of traditional risk factors. This cuff method may provide additional information to improve cardiovascular risk stratification.

2.5 Non-invasive Wave Intensity Analysis in the Aorta and Internal Carotid Using Phase-Contrast MR angiography: The effect of Hypertension

Neumann, Sandra[1]; Hamilton, Mark[2]; Paton, Julian[3]; Nightingale, Angus[4]; Brooks, Jonathan[3]; Hart, Emma[3]; Biglino, Giovanni[2]

[1]Clinical Research and Imaging Centre, University of Bristol, [2]University Hospitals Bristol NHS Foundation Trust, [3]University of Bristol, [4]University Hospitals Bristol NHS Foundation Trust and University of Bristol

Introduction
Hypertension is associated with stiffening of blood vessels, reduced arterial lumen and reduced cerebral blood flow; however, it is not known how lower cerebral blood flow relates to arterial structure or impacts on wave dynamics. We hypothesise increased backward wave energy and faster wave speed in the hypertensive internal carotid artery as an indication of increased resistance to flow.

Methods
Normotensive, controlled and uncontrolled hypertensive participants were recruited (daytime ambulatory BP <135/85mmHg and >135/85mmHg, respectively; n=11 per group). Wave intensity analysis was performed on left internal carotid and ascending aorta phase-contrast magnetic resonance angiography.

Results
While ascending aortic wave speed increased significantly in the uncontrolled hypertensive compared to normotensive (p<0.001) and controlled hypertensive participants (p=0.038), no significant difference was observed in the internal carotid. Carotid forward and backward wave intensity increased in uncontrolled hypertensives compared to normotensives (p=0.036 and p=0.033, respectively), and backward wave energy increased in the controlled hypertensives compared to normotensives (p=0.041). There was no significant difference between uncontrolled and controlled hypertensives.

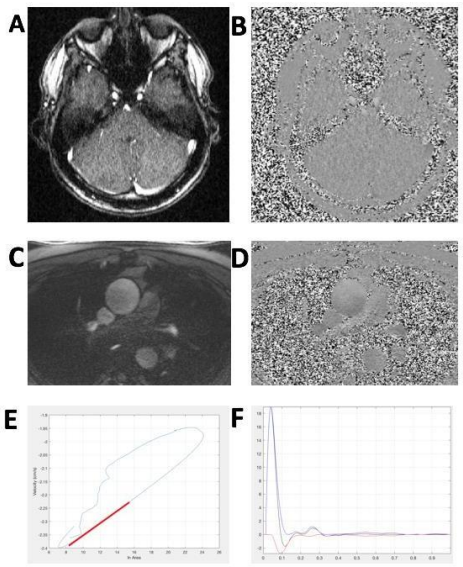


Figure 1: Analysis of the phase contrast MR angiography data. A) Magnitude image B) Phase image of the internal carotid arteries C) Magnitude image and D) Phase image of the ascending aorta E) example of log(Area)-Velocity loop. Red line indicates the slope from which wave speed is calculated in early systole F) Example of the wave Intensity components, where blue is the forward wave energy, red is the backward wave energy and black is the net wave intensity.

Conclusion
Wave intensity in the internal carotid artery is altered in uncontrolled hypertension. This is partly rescued when blood pressure is controlled by medication, although greater backward wave energy persists. This supports the hypothesis of increased resistance to flow in the cerebral circulation of the hypertensives. Whilst increased aortic wave speed confirmed an expected increase in stiffness, this was not observed in the internal carotid. This might suggest a protective mechanism in the cerebral circulation, in conjunction with the effect of vessel tortuosity.

2.6 Blood pressure-independence of aortic-to-brachial artery stiffness ratio is dependent on disease status

Armstrong, Matthew K.[1]; Schultz, Martin G.[1]; Picone, Dean S.[1]; Sharman, James E.[1]

[1]University of Tasmania

Introduction
Aortic stiffness predicts cardiovascular mortality but is limited as a risk marker because it is dependent on blood pressure (BP). A potential solution is provided from the ratio of aortic-to-brachial artery stiffness (ab-ratio), which is purported to be a BP- independent risk marker among patients with renal dysfunction (RD). We sought to determine the BP-independence of the ab-ratio in patients with disease (including RD) and healthy populations.

Methods
The ab-ratio (aortic/brachial pulse wave velocity; PWV) and mean arterial pressure (MAP) were recorded in patients with RD (n=119, aged 65±7years), hypertension (n=140, aged 62±9years), type 2 diabetes (n=77, aged 60±9years) and healthy individuals (n=99, aged 51±8years). Multiple-regression analysis was performed to test the independent association of MAP with the ab-ratio adjusted for age, sex, body-mass index and blood glucose.

Results
There was no significant relationship between the ab-ratio and MAP in patients with RD (β=0.002, 95%CI-0.002, 0.006, p=0.34), hypertension (β=0.001, 95%CI-0.003, 0.006, p=0.62) or diabetes (β=0.006, 95%CI-0.002, 0.014, p=0.11). However, in healthy individuals the ab-ratio was significantly and independently associated with MAP (β=0.008, 95%CI0.003, 0.013, p=0.003). There was a significant difference in the strength of association between the ab-ratio and MAP between patients with disease and healthy individuals ($z>2.2$, $p<0.05$ for all).

Conclusion
Although ab-ratio is purported to be a risk marker that is independent of BP, this was observed only

among patient populations, and not in healthy individuals. Therefore, the ab-ratio is influenced by disease status and may have restricted value as a BP- independent risk marker.

2.7 The gut-derived metabolite trimethylamine N-oxide induces large elastic artery stiffening and endothelial dysfunction in young mice

Brunt, Vienna[1]; Gioscia-Ryan, Rachel[1]; Sapinsley, Zachary[1]; Zigler, Melanie[1]; Richey, James[1]; Seals, Douglas[1]

[1]University of Colorado Boulder

The gut microbiome, an emerging mediator of host physiological function, is adversely altered by aging and many diseases, termed “gut dysbiosis.” One consequence of gut dysbiosis is elevated circulating levels of the gut-derived metabolite trimethlyamine N-oxide (TMAO), which has been directly linked to cardiovascular (CV) risk, including the development of atherosclerosis. However, it is unknown whether TMAO mediates arterial dysfunction that precedes the onset of clinical disease, and if so, the underlying mechanisms.

Purpose
To determine whether TMAO independently induces large elastic artery stiffening and endothelial dysfunction via increased superoxide-related oxidative stress.

Method
Twenty young (6 mo) male C57BL/6 mice were fed a chemically-defined choline (0.08-0.09%) diet supplemented without (Control; N=9) or with (N=11) 0.12% TMAO for 6 months. Arterial stiffness was assessed as aortic pulse wave velocity (aPWV). Endothelial function was evaluated *ex vivo* as carotid artery endothelium-dependent
dilation (EDD) to increasing doses of acetylcholine (10^{-9} to 10^{-4}M) in the absence or presence of the superoxide dismutase mimetic TEMPOL.

Results
TMAO increased aPWV (Control: 392±20 vs. TMAO: 483±32cm/sec, p=0.04) and impaired EDD (peak dilation, Control: 93.7±3.2 vs. TMAO: 79.9±3.4%, p=0.01).
Suppression of oxidative stress with TEMPOL restored EDD in TMAO-treated animals (peak dilation: 92.1±4.7%, p=0.46 vs. Control).

Conclusions
TMAO independently induces large elastic artery stiffening and endothelial dysfunction in mice. Dysfunction appears to occur through increases in oxidative stress. These data may explain, at least in part, why TMAO increases CV risk and provide a potential target for prevention/treatment of arterial dysfunction.
Supported by R01 HL134887 & T32 HL007822

2.8 Invasive study for testing non-invasive methods of aortic pressure estimation

Guala, Andrea[1]; Tosello, F[2]; Leone, D[2]; Sabia, L[2]; D’Ascenzo, F[3]; Crea, T[2]; Moretti, C[3]; Gaita, F[3]; Veglio, F[2]; Ridolfi, L[4]; Milan, A[2]

[1]Vall d'Hebron Institute of Research, Vall d'Hebron Hospital, Autonomous University of Barcelona, [2]Internal and Hypertension Division, Department of Medical Sciences, AOU Citta’ della Salute e della Scienza of Turin, University of Turin, Torino, Italy, [3]Division of Cardiology, Department of Medical Sciences, AOU Citta’ Salute e Scienza of Turin, University of Turin, Torino, Italy, [4]DIATI, Politecnico di Torino, Torino, Italy

Purpose

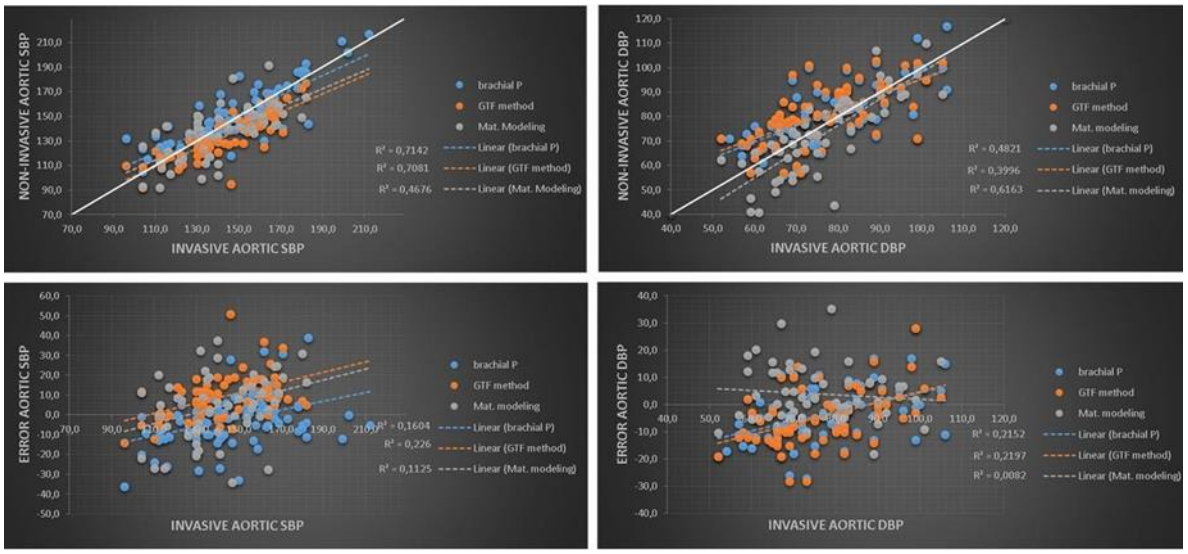
Aortic blood pressure has a superior prognostic value with respect to the brachial pressure [1]. Nonetheless, the low efficacy of the most used non-invasive methods (i.e., approaches based on the generalized transfer function (GTF)) may hamper the detection of this superiority in population studies [2]. In this sense, low-order, patient- specific whole-body mathematical models might help to bridge brachial to aortic pressure waveforms.
We aimed to compare (i) GTF, (ii) a patient-specific 1D-0D mathematical model, and (iii) brachial blood pressure in the estimation of invasive aortic pressure measured through catheter.

Method

One-hundred patients referred to diagnostic coronary angiography were included in this study. Brachial pressure was measured with a validated automatic oscillometric device simultaneously to invasive aortic pressure, which was measured with a calibrated fluid-filled catheter. End-systolic and end-diastolic left ventricular volumes, carotid-femoral pulse wave velocity and tonometric radial waveform were measured immediately prior to the invasive procedure and were used to set GTF and the mathematical model.

Results

Oscillometric brachial pressure overestimated both systolic (2.4±12.6 mmHg, R^2=0.71) and diastolic (3.7±9.8 mmHg, R^2=0.48) aortic pressure. GTF method underestimated systolic (9.4±11 mmHg, R^2=0.71) and overestimated diastolic (4.5±10.2 mmHg, R^2=0.4) aortic pressure. Mathematical model underestimated both
systolic (4±16.5 mmHg, R^2=0.47) and diastolic (3.9±10.4 mmHg, R^2=0.62) aortic pressure. Brachial pressure and GTF methods presented trends toward systolic and diastolic pressure overestimation for higher aortic pressure, while mathematical modeling not.



Conclusions

Systolic and diastolic oscillometric brachial pressures give a better predictor of aortic pressure extremes with respect to both GTF- and mathematical model-based methods.

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10.10 Special Guest Lecture

Chair: C Rajkumar, A Virdis

Estrogen receptors (membrane receptor versus intracellular nuclear factor - endothelium)

Professor Jean Francois Arnal, *INSERM, Toulouse, France*

10.40 Refreshments, Poster and Exhibition viewing

11.10 Oral Session III – Models and Technology

Chair: S Wassertheurer, P Segers

3.1 Integrated central pressure-stiffness risk score: a new opportunity for cardiovascular risk stratification. First results on chronic kidney disease patients

Nemcsik, János[1]; Cseprekál, Orsolya[2]; Tabák, Ádám[3]; Batta, Dóra[1]; Egresits, József[4]; Kiss, István[5]; Tislér, András[3]

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Background

The evaluation of arterial stiffness and central haemodynamics represent a new tool of cardiovascular (CV) risk stratification. Our aim was to create an integrated central pressure-stiffness risk score (ICPS score) which incorporate the predictive potential of identical parameters.

Methods

100 chronic kidney disease patients on conservative therapy (CKD 1-5) were involved in our study. Pulse wave velocity (PWV), augmentation index (Aix), central systolic blood pressure (csys) and central pulse pressure (cPP) were measured.

Patients were followed for 59.7 months and CV morbidity and mortality were registered. Patients were classified into tertiles based on their PWV, Aix, csys and cPP values. After the analysis of the predictive values of the tertiles of the identical parameters, patients were scored. One score was given, when a patient had a third tertile value of PWV, csys or cPP or a second or third tertile value of Aix. Then the CV outcome was analyzed with Cox regression analysis of the groups of patients with different scores.

Results

During follow-up 37 CV events occurred. Compared with the zero-point group (n=21), the one-point group (n=25) did not have significantly increased odds ratio (OR) for CV events (OR:1.10; 95% confidence interval (CI): 0.27-4.44), but the risk has been significantly elevated in the two-point group (n=29, OR:4.59, CI:1.39-15.22) and it increased further in the three-point group (n=16, OR:9.03, CI:2.22-36.65), as well as in the four-point group (n=9, OR:11.84, CI:2.52-55.64).

Conclusion

The ICPS score can help in the identification of chronic kidney disease patients with high CV risk.

3.2 Ascending and descending aorta pulse wave velocity and distensibility in bicuspid aortic valve patients

Guala, Andrea[1]; Rodriguez-Palomares, Jose[2]; Dux-Santoy, Lydia[2]; Teixido-Tura, Gisela[3]; Maldonado, Giuliana[3]; Villalva, Nicolas[2]; Valente, Filipa[2]; Galian, Laura[2]; Huguet, Marina[1]; Gutierrez, Laura[1]; Gonzalez, Teresa[1]; Fernandez, Ruben[1]; Sao- Aviles, Augusto[1]; Garcia-Dorado, David[1]; Evangelista, Artur[2]

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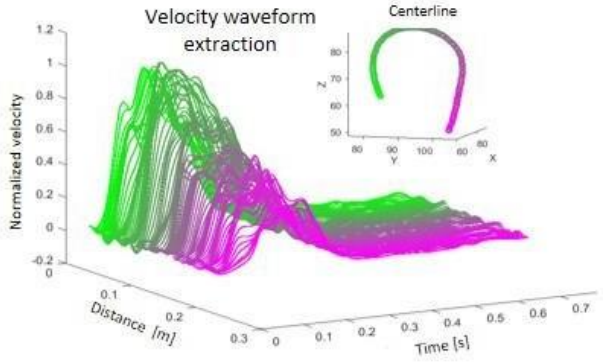
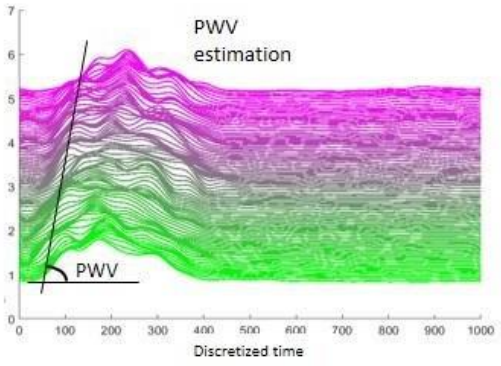
Purpose
Bicuspid aortic valve (BAV) is a cardiac congenital disease associated with ascending aorta (AAo) dilation. The study of the impact of aortic biomechanics in this population has been limited by technical difficulties. Contrasting results have been reported for distensibility while studies including regional pulse wave velocity (PWV) are still lacking. Using 4D-flow MRI, we assessed AAo and descending aortic (DAo) biomechanical properties and determined their association in BAV aortopathy.

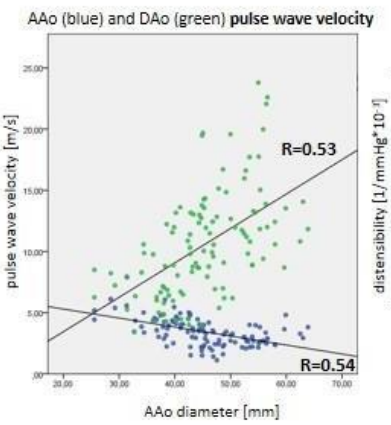
Methods
One-hundred thirty-six BAV patients with no severe valvular disease and 40 healthy volunteers were recruited. The protocol included a 4D-flow acquisition and a set of 2D CINE PC-MRI at 1.5T. Aortic 3D geometry was reconstructed from 4D-flow- derived angiography and at least 100 analysis planes were identified in the thoracic aorta. Transit time was calculated on the velocity upslope through wavelet analysis [1]. CINE PC-MRI were used to compute distensibility. Statistical significance is reported corrected for confounding factors.

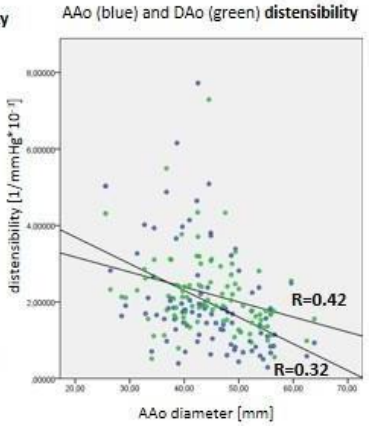
Results
Non-dilated BAV and controls have similar AAo and DAo PWV and distensibility. Dilated patients presented lower AAo PWV and higher DAo PWV compared to non- dilated ($p<0.001$ and $p=0.017$, respectively). Distensibility did not differentiate dilated from non-dilated patients and presented lower association with dilation severity (see Figure).





		CONTROLS	NON DILATED BAV	DILATED BAV
	N	40	30	106
AAo	PWV [m/s]	5.36 [4.02-6.33]	4.35 [3.84- 5.46]	3.02 * [2.43- 3.75]
	Distensibility (*10⁻³) [mmHg⁻¹]	4.21 [3.17-4.87]	1.79 [1.37-3.94]	1.65 [0.97-2.10]
DAo	PWV [m/s]	7.40 [5.92-8.81]	8.23 [6.26- 10.58]	10.87 * [8.37- 13.18]
	Distensibility (*10⁻³) [mmHg⁻¹]	3.09 [2.56-3.71]	2.13 [1.59-2.62]	1.89 [1.46-2.74]





Conclusions

Confirming for the first time previous findings in abdominal aorta aneurysm and fluid- mechanics theory, AAo PWV is reduced in aneurysmatic BAV patients. BAV aortopathy is related to a stiffer DAo. Regional PWV outperforms distensibility as a marker of local aortic biomechanics. These data exclude congenital aortic wall pathology related to BAV

References

[1] Bargiotas I., et al. Estimation of aortic pulse wave transit time in cardiovascular magnetic resonance using complex wavelet cross-spectrum analysis. J Cardiovasc Magn Reson 2015;17(65):1–11.

3.3 How does coarctation influence bicuspid aortic valve disease? Assessment of aortic morphology in a bicuspid aortic valve population

Sophocleous, Froso[1]; Biffi, Benedetta[2]; Milano, Elena Giulia[3,4]; Rajakaruna, Cha[3,4]; Caputo, Massimo[3,4]; Emanueli, Costanza[1,5]; Bucciarelli-Ducci, Chiara[3,4]; Gaunt, Tom[1]; Schievano, Silvia[2]; Biglino, Giovanni[1]

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Background
Bicuspid aortic valve (BAV) is a congenital heart disease associated with aortic wall abnormalities and co-existing with other congenital defects (e.g. aortic coarctation). This study aimed to explore aortic shape features in a BAV population, identifying sub-groups with different aortic morphologies.

Methods
Single-centre retrospective study. Patients with an MRI scan and native BAV diagnosis between 2011-16 were studied (n=525); those with a 3D MRI dataset were included for shape analysis (n=108, 64% males, 38±16.5 years). MRI-derived 3D aortic reconstructions were analysed using a statistical shape modelling framework [1]. A mean aortic shape ('template') was computed and shape deformations were correlated with demographic, volumetric and functional data.

Results
Aortic coarctation (n=71) was significantly associated with a more gothic arch (p=0.02), more tubular ascending aorta and descending aorta dilation (p<0.001). Also, smaller aortic size in patients with coarctation was associated with the younger age of this group (33±13 vs. 47±19, p<0.001), given the overall relationship between aortic size and age (p<0.001). Aortic stenosis (n=30) was also associated with gothic arch (p=0.01), and dilated ascending aorta but with no aortic root dilation (p=0.02).
On multivariate regression analysis, gothic arch was indeed associated with coarctation and stenosis, and also with non-coronary valve fusion pattern (p=0.03). Patients with aortic regurgitation tended to have larger aortas (p=0.005).

Conclusion
The presence of aortic coarctation and stenosis may influence the amount of dilation and the overall arch architecture in BAV patients. Patients with BAV present profoundly different morphological phenotypes depending on the presence/absence of aortic coarctation (Fig.1).

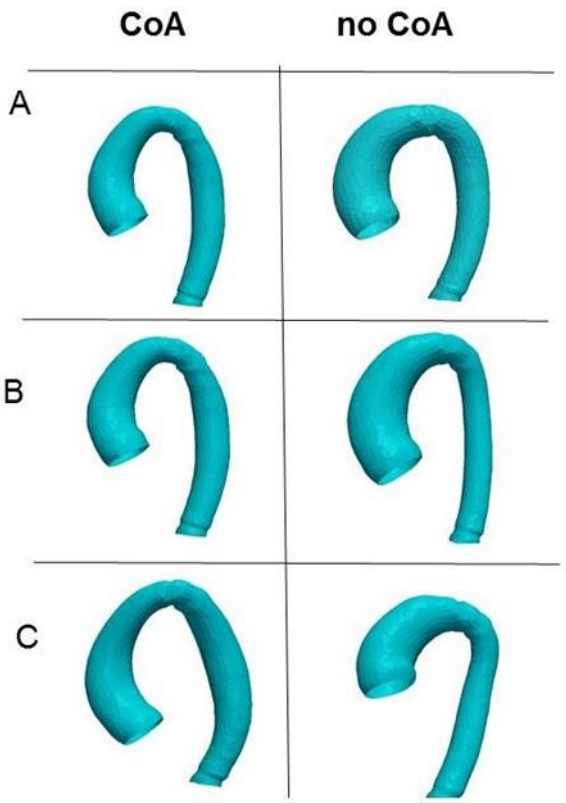

Figure 1: Shape features of coarctation (CoA) vs no CoA in BAV population. A) The 'template' (or average shape) for patients with CoA, on the left, and patients without CoA, on the right. B) Patients with CoA have tubular ascending aortas (left), while patients without CoA tend to have increased ascending aortic dilation (right). C) Patients with CoA have more a gothic arch (left), whereas patients without CoA have a rounder arch (right).

References

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3.4 Reservoir Pressure Separation at Brachial, Carotid and Radial Arteries: A Quantitative Comparison and Evaluation

Ebner, Michael[1]; Parker, Kim[2]; Vercauteren, Tom[3,1]; Ourselin, Sébastien[3,1]; Wassertheurer, Siegfried[4]; Hughes, Alun[5]; Hametner, Bernhard[4]

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Background
At present, reservoir pressure parameters are derived from arterial pressure waveforms regardless of the location of measurement. However, a comparison between sites has not been made, and site-related differences may affect interpretation. In this study, we computed reservoir pressure waveform separations on hypertensive individuals where brachial, carotid and radial pressure measurements were available and quantitatively assessed their results.

Methods
95 participants in the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT) had sequential measurements of pressure and flow velocity waveforms from carotid, brachial and radial arteries [1]. Pre-processing was performed to impose identical diastolic and mean blood pressures at all three arterial locations. Using pressure information only, reservoir pressure separation was performed [2, 3]. Systolic durations were estimated based on minimum pressure waveform derivatives.
Reservoir curves characterized by physiologically implausible parameters, i.e. a rate constant $b < 0$ or an asymptotic pressure $P_\infty < 0$, were discarded, leaving 74 subjects with valid reservoir pressure waveforms at all three arterial locations.

Results
Estimated reservoir parameters are shown in Table 1. We observed significant differences between arteries in almost all parameters. A high correlation was observed between reservoir pulse pressure and reservoir pressure area at all locations, and the correlation between brachial and radial arteries was stronger for all parameters.

Reservoir	**Brachial Artery (B)**	**Carotid Artery (C)**	**Radial Artery (R)**	***r*(B,C)**	***r*(B,R)**	***r*(C,R)**
PP **[mmHg]**	37.1 ± 8.6	41.6 ± 9.0	36.1 ± 8.4	0.84*	0.95*	0.84*
A_p **[mmHg s]**	16.7 ± 5.0	19.0 ± 4.4	16.0 ± 4.3	0.91*	0.96*	0.91*
P_∞ **[mmHg]**	61.6 ± 14.2	66.6 ± 12.8	66.2 ± 11.2	0.50*	0.51*	0.46
a **[1/s]**	8.3 ± 3.7	11.4 ± 2.7	7.0 ± 2.7	0.11*	0.91*	0.18*
b **[1/s]**	1.8 ± 0.6	2.2 ± 0.9	2.1 ± 0.7	0.30*	0.62*	0.40

*Table 1. Quantification of reservoir pressures at three arterial locations in the format of mean ± standard deviation based on 74 subjects whereby PP denotes the reservoir pulse pressure, A_p the area of reservoir pressure above diastolic blood pressure, P_∞ the asymptotic blood pressure and $a, b = 1/\tau$ the rate constants with the time constant τ describing the diastolic pressure decay. The correlation coefficient r is computed between relevant arterial locations. The statistical significance of the differences between locations was based on a paired t-test with * indicating $p < 0.05$.*

Conclusions
The results of this study indicate differences in parameters derived from reservoir pressure separation at different arterial locations. This suggests that interpretations cannot be made agnostic to the location of measurement.

References

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3.5 Heart rate dependence of regional and local aortic pulse wave velocity in rats as a function of blood pressure

Spronck, Bart[1]; Tan, Isabella[2]; Reesink, Koen[1]; Georgevsky, Dana[2]; Delhaas, Tammo[1]; Avolio, Alberto[2]; Butlin, Mark[2]

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Background
Pulse wave velocity (PWV) is quantified by time difference of arrival of the blood pressure (BP) wave at two sites along the arterial bed (transit time; TT-PWV), or by combining measured arterial pressure and diameter using the Bramwell-Hill equation (BH-PWV). Besides the dependence of PWV on BP, TT-PWV also depends on heart rate (HR). The present study aimed to also quantify the dependence of BH-PWV's on HR, as a function of diastolic BP (DBP).

Methods
Adult anaesthetised rats (*n*=24) were randomly paced at 300–500 bpm, at 50-bpm steps. At each step, aortic TT-PWV (two pressure-tip catheters) and BH-PWV (pressure-tip catheter and ultrasound wall-tracking; abdominal aorta) were measured simultaneously, across a pharmacologically induced DBP range of 60–110 mmHg.
Data from 9142 heart beats was analysed using mixed-effects modelling.

Results
HR dependence of TT-PWV increased from 0.03m/s/100bpm at DBP=60mmHg to 0.06m/s/100bpm at DBP=110mmHg (both p≤0.023). HR dependence of BH-PWV was 0.11m/s/100bpm at DBP=60 and 85mmHg, but paradoxically decreased to 0 at DBP=110mmHg (p=0.686). This decrease in dependence is explicable in that standard BH-PWV uses an approximate derivative of pressure to diameter, which overestimates PWV with increasing pulse pressure (PP). PP decreases as HR increases, potentially causing a BH-PWV decrease with HR. This effect can be overcome by estimating the full pressure-diameter curve for each HR, and calculating the true derivative at DBP, yielding a BH-PWV that no longer shows significant HR dependence (p≥0.076 at all DBPs).

Conclusions
BH-PWV and TT-PWV show a different HR dependence, affected by DBP.

3.6 Non-invasive, MRI-based estimation of patient-specific aortic blood pressure using one-dimensional blood flow modelling

Mariscal Harana, Jorge[1]; van Engelen, Arna[1]; Schneider, Torben[2]; Florkow, Mateusz[1,2]; Charlton, Peter[1]; Ruijsink, Bram[1]; De Bliek, Hubrecht[3]; Valverde, Israel[1]; Carakida, Marietta[1]; Pushparajah, Kuberan[1]; Sherwin, Spencer[4]; Botnar, Rene[1]; Alastruey, Jordi[1]

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Background and Objectives
Clinical evidence shows that central (aortic) blood pressure (CBP) is a better marker of cardiovascular risk than brachial pressure [1]. However, CBP can only be accurately measured invasively, through catheterisation. We propose a novel approach to estimate CBP non-invasively from aortic MRI data and a non-invasive peripheral (brachial) pressure measurement, using a one-dimensional (1-D) model

of aortic blood flow.

Methods
We created a population of virtual (computed) subjects, each with distinctive arterial pulse waveforms available at multiple arterial locations, to assess our approach. This was achieved by varying cardiac (stroke volume, cardiac period, time of systole) and arterial (pulse wave velocity, peripheral vascular resistance) parameters of a distributed 1-D model of the larger systemic arteries [2] within a wide range of physiologically plausible values. After optimising our algorithm for the aortic 1-D model *in silico*, we tested its accuracy in a clinical population of 8 post-coarctation repair patients.

Results
Results from our *in silico* study, after varying cardiac and arterial parameters by ± 30%, showed maximum relative errors for systolic, mean and diastolic CBP of 4.5%, 3.6% and 4.2%, respectively. Average relative errors for systolic, mean and diastolic CBP were 2.7%, 0.9% and 1.2%, respectively. Corresponding average relative errors from our clinical study were 5.4%, 1.5% and 8.0%.

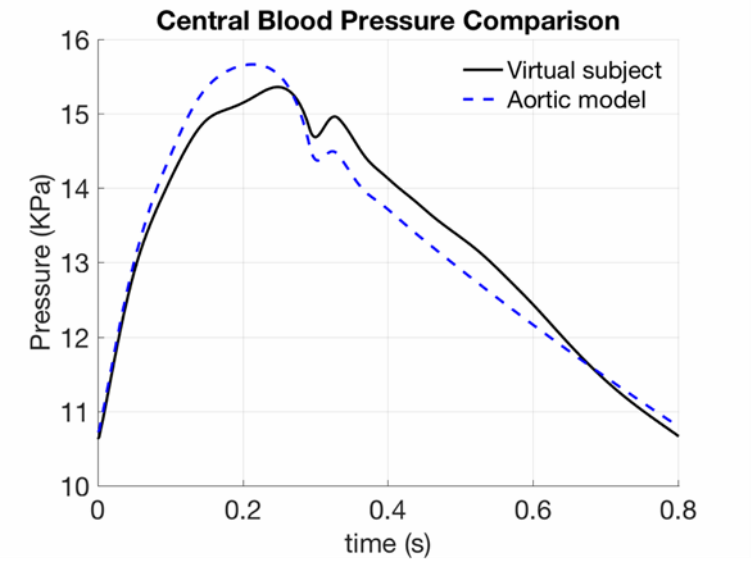

Figure 1: CBP estimation using the aortic 1-D model for a given virtual patient

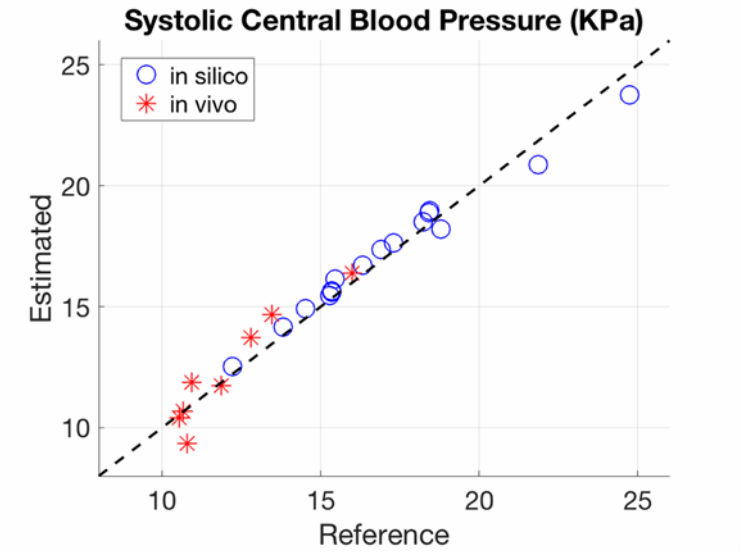

Figure 2: Systolic CBP estimated using the aortic 1-D model against reference systolic CBP values from *in silico* and *in vivo* data

Conclusions
We have provided a proof of concept for the non-invasive estimation of patient- specific central blood pressure using computational aortic blood flow modelling in combination with MRI data and a non-invasive peripheral pressure measurement.

References
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3.7 Changes of intrinsic stiffness of the carotid arterial wall during the cardiac cycle measured by shear wave elastography in hypertensives compared to normotensives

Marais, Louise[1,2]; Pernot, Mathieu[3]; Khettab, Hakim[1]; Tanter, Michael[3]; Messas, Emmanuel[1]; Zidi, Mustapha[4]; Laurent, Stéphane[1]; Boutouyrie, Pierre[1]

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Objective
Because measurement of arterial stiffness is highly dependent on blood pressure (BP), methods independent of BP are required. Shear wave elastography (SWE, Supersonic Imagine, Aix-en-Provence, France) enables to assess local tissue stiffness by tracking the propagation of shear waves generated into the tissue using ultrafast imaging. This method has never been tested against classical Echotracking (Artlab, Esaote, Maastricht, NL) and carotid to femoral pulse wave velocity (cf-PWV, Sphygmocor, AtCor, Sydney, Australia).

Methods
We included 25 subjects, 14 normotensives (NT) and 11 essential hypertensives (HT), matched for age and sex. We optimized SWE algorithms for carotid wall tracking and shear wave group velocity calculation for the anterior (a-SWV) and posterior wall (p-SWV). 8 ultrasonic pushes were triggered at intervals of 200 ms to study the variations of stiffness during the cardiac cycle.

Results
p-SWV showed no association with carotid PWV, cf-PWV nor BP. Mean a-SWV over the cardiac cycle was strongly associated with carotid PWV measured by Echotracking ($r=0.56$, $p=0.003$) and cf•PWV ($r=0.66$, $p<0.001$). a-SWV strongly increased with BP level during the cardiac cycle ($p<10^{-6}$). Similar associations
between a-SWV and BP were found in NT and HT although HT had higher values of a-SWV throughout all BP levels. However, when a common BP value (100 mmHg) was considered, no significant difference was found between NT and HT.

Conclusion
We have demonstrated with a method independent of BP that the increased arterial stiffness in HT is entirely due to the BP increase. SWE seams a promising technique for assessing arterial stiffness.

3.8 Implementing Fluid-Structure Interaction Computational and Empirical Techniques to Assess Hemodynamics of Abdominal Aortic Aneurysms

Safi, Hannah[1]; Phillips, Nathan[1]; Ventikos, Yiannis[2]; Bomphrey, Richard[1] [1]Royal Veterinary College, [2]University College London

An Abdominal Aortic Aneurysm (AAA) represents a degenerative disease process of the abdominal aorta that leads to a focal dilation and irreversible remodeling of the arterial wall [1].

The reliable assessment of AAA rupture risk in a clinical setting is crucial in decreasing related mortality without needlessly increasing the rate of surgical repair. Currently there is no accepted technique to quantify the risk of rupture for individual AAAs. Elective repair decisions are generally founded on the “maximum diameter criterion”[2].
A multi-disciplinary approach including constitutive modeling and vascular biomechanics is required to increase the effectiveness in assessing and treating the disease.

Guidelines for treatment of AAAs from the Society for Vascular Surgery indicate computationally acquired rupture predictors need additional validation prior to their implementation in clinics. For this purpose, silicone replicas of anatomically realistic geometries of AAAs are fabricated and the flow field in the aneurysmal region is experimentally measured *in vitro*, using time-resolved volumetric Particle Image Velocimetry (PIV) [3-4]. Furthermore, the experimental setup allows for strain measurements of the aneurysmal wall to be taken simultaneously using Digital Image Correlation (DIC).

These data are used to validate concurrent computational simulation results and FSI analyses. The results demonstrate that the FSI computational approach can predict the patterns of flow from the PIV measurements, which arise from the geometry of the AAA. This work highlights that empirical and computational modelling can complement each other to investigate AAA development towards our goal of producing validated computational simulations that can be used for diagnostic purposes.

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12.30 Invited Lecture

Chair: J Cockcroft, E Agabiti-Rosei

Fetal programming and vascular dysfunction

Professor Claudio Sartori, *University Hospital, Lausanne, Switzerland*

Authors: Meister TA, Rexhaj E, Rimoldi SF, Scherrer U, Sartori C.

Cardiovascular diseases are the main cause of mortality and morbidity in Western countries, but the underlying mechanisms are still poorly understood. Genetic polymorphisms, once thought to represent a major determinant of cardiovascular risk, individually and collectively, only explain a tiny fraction of phenotypic variation and disease risk in humans. It is now clear that non-genetic factors, i.e., factors that modify gene activity without changing the DNA sequence and that are sensitive to the environment can cause important alterations of the cardiovascular phenotype in experimental animal models and humans. Here, we will review recent studies demonstrating that distinct pathological events during the perinatal (transient perinatal hypoxemia), late foetal (preeclampsia), and early embryonic (assisted reproductive technologies) periods induce profound alterations of the cardiovascular phenotype in humans and experimental animals. Moreover, we will provide evidence that epigenetic modifications are contributing importantly to this problem and are conferring the potential for its transmission to subsequent generations.

13.00 Poster Session II and Lunch and Exhibition viewing

Poster Session II – Interventions

Chair: RM Bruno, P Jankowski

P89 Upright posture enhances the unfavourable influences of bisoprolol on central blood pressure in hypertensive middle aged men: a double-blinded randomized placebo-controlled cross-over study M

Pörsti, Ilkka[1]; Suojanen, Lauri[1]; Haring, Antti[1]; Tikkakoski, Antti[1]; Eräranta, Arttu[1]; Huhtala, Heini[2]; Kähönen, Mika[1]; Kivistö, Kari[1]; Mustonen, Jukka[1]

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Objective
Treatment with beta-blockers is characterised by inferior reduction of central versus peripheral blood pressure. We examined changes in central and peripheral blood pressure, cardiac function, and vascular resistance during beta-blockade.

Methods
Haemodynamics were investigated after 3 weeks of bisoprolol treatment (5 mg/d) in a double-blinded, randomized, placebo-controlled cross-over trial in never-treated 16 Caucasian males with grade I-II primary hypertension using continuous tonometric pulse wave analysis and whole-body impedance cardiography.

Results
Bisoprolol decreased blood pressure in the aorta (~8/10 mmHg) and radial artery (~10/9 mmHg), reduced heart rate and left cardiac work, and increased subendocardial viability index in supine and upright positions ($p<0.01$ for all). Stroke volume was increased in the supine (~11 ml, $p<0.01$) but not in the upright position, while upright (~1 l/min, $p<0.01$) but not supine cardiac output was significantly reduced. Upright increase in systemic vascular resistance was amplified after bisoprolol ($p<0.05$). Pulse pressure amplification was reduced especially in the upright position (supine reduction 10%, upright reduction 20%). Aortic augmentation index, augmentation pressure and pulse pressure were not changed in the supine position, but were increased in the upright position (from 7 to 20%, 3 to 7 mmHg, 28 to 35 mmHg, respectively, $p<0.01$ for all).

Conclusions
Bisoprolol decreased central and peripheral blood pressure in male subjects with grade I to grade II hypertension, but central blood pressure was reduced less efficiently than peripheral blood pressure. Importantly, the harmful influences of bisoprolol on central pulse pressure and pressure wave reflection were especially observed in the upright position.

P90 Positive effects of antihypertensive treatment on aortic stiffness in the general population M

Mateřánková, Markéta

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Aortic stiffness is strongly related to age and mean arterial pressure (MAP). We investigated whether antihypertensive treatment modulates the association of the aortic pulse wave velocity (PWV) with age and with MAP in the general population. In the Czech post-MONICA, we measured the PWV in 735 subjects (mean age 61.2±7.8 years, 54.1% women, 44.3% on antihypertensive medication). We used a linear regression model to assess the effect of treatment on the PWV.

The independent covariates in our analysis included sex, age, MAP, body mass index, plasma glucose, low-density lipoprotein cholesterol, smoking and observer. The patients receiving treatment were older (64.1±6.7 vs. 58.9±7.8 years), had higher systolic blood pressure (135.9±16.2 vs. 130.1±16.5 mm Hg) and had higher pulse wave velocity (9.1±2.2 vs. 8.2±2.1 m s 1; P for all o0.0001) than untreated subjects.

After adjustment for MAP, the use of treatment modified the association between age and the PWV (regression equations, treated patients 9.68–0.009 age vs. untreated subjects 6.98 þ 0.020 age, difference of regression slopes, F ¼ 11.2; P ¼ 0.0009). In analyses adjusted for age, treatment was associated with a smaller increase of the PWV with MAP (treated patients 9.63–0.006 MAP vs. untreated subjects 7.18 þ
0.010 MAP, F ¼ 10.70; P ¼ 0.0001). These results were driven primarily by subjects whose blood pressure was below 140/90 mm Hg.

In the cross-sectional analysis from a random sample of the general population, antihypertensive treatment was associated with a less steep increase in the PWV with age and the mean arterial pressure.

P91 Green Tea Extract reduces lipid profile, percentage of aortic augmentation index and increases soluble RAGE concentrations in normotensive Patients with Type 2 Diabetes Mellitus: A Randomized, Double-Blinded, and Placebo- Controlled Trial M

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Background
Type 2 diabetes mellitus is associated with premature atherosclerosis and arterial stiffening by an accumulation of advanced glycation end-products in vessel wall (1). Green tea polyphenols are considered a cardioprotective substance and may be used as an adjuvant for diabetes treatment, because its ability to stimulates the soluble RAGE secretion (2). There is no clinical evidence of the effect of green tea extract administration on metabolic parameters, arterial stiffness and the soluble RAGE expression.

Material and methods
A double-blind, placebo-controlled, randomized clinical trial in normotensive patients with type 2 diabetes mellitus was conducted to identify the effect of green tea extract on arterial stiffness, metabolic and anthropometric parameters and on soluble RAGE (sRAGE) with the S100A1 ligand.

Results
We included 20 subjects, there was no difference between groups at baseline. There was a decrease in the green tea extract group on aortic augmentation index (21.12 ± 8.9 to 18.07±9.7, p=0.045), total cholesterol (203.9 ± 37.6 to 176.9±25.9 mg/dl, p=0.019) triglycerides (202.6±146.9 to 123.2±64.8 mg/dl, p=0.023) and an increase in sRAGE (1358.5 ± 390.0 to 1281.1± 369.7 p=0.052).

Table 1. Effect of 12 weeks of Green tea extract intervention or placebo on circulating parameters

	GTE		PLACEBO		
	Basal n= 10	Final n = 10	Basal n= 10	Final n = 10	P
Fasting Glucose, mg/dl	169.9 ± 92.3	123.9 ± 69.8	168.1 ± 49.7	171.3 ± 39.8	0.089
Creatinin, mg/dl	0.75 ± 0.2	0.81 ± 0.14	0.7 ± 0.2	0.78 ± 0.14	0.853
Total Cholesterol, mg/dl	203.9 ± 37.6	176.9 ± 25.9	187.9 ± 44.6	216.1 ± 48.2	0.019*
Triglycerids, mg/dl	202.6 ± 146.3	123.9 ± 64.8	159.9 ± 57.0	184.3 ± 93.9	0.023*
HDLc, mg/dl	47.9 ± 7.8	44.9 ± 5.2	48 ± 8.9	46.9 ± 10.2	0.529
LDLc, mg/dl	123 ± 32.8	109.4 ± 25.1	92.3 ± 30.2	111.2 ± 53.3	0.436
TGO, U/ml	25.6 ± 10.1	25.3 ± 7.08	40.7 ± 13.8	44.4 ± 26.8	0.971
TGP, U/ml	23.8 ± 13.6	28.9 ± 11.9	35.4 ± 14.5	44.7 ± 25.4	0.912
TFG, mL/min	119.9 ± 56.3	101.8 ± 23.9	120.6 ± 50.2	102.3 ± 22.7	0.739

Values are arithmetic means ± SE except for mean differences between groups, which have been adjusted for baseline values. Between-group P values reflect the between-group comparison change-scores from Man Whitney U statistic methodology. *Significant (p<0.05) within-group change.

Conclusions
Green tea extract reduces lipid levels, percentage of aortic augmentation index and increases soluble RAGE concentrations in normotensive patients with Type 2 Diabetes.

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P92 Simultaneous invasive and noninvasive monitoring of central blood pressure on critically ill patients suffering from cardiogenic shock treated with IABP M

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Intraaortic balloon counterpulsation (IABP) is a method of temporary mechanical circulatory support in patients suffering from cardiogenic shock to improves the balance of myocardial oxygen supply and demand by using systolic unloading and diastolic augmentation. Arteriograph is an invasively validated oscillometric device which measures central blood pressure (SBPao) noninvasively.

The recently developed Arteriograph24 is a combination of a 24-hour BP-monitor and a single-measurement Arteriograph which provides both 24-hour peripherial and central BP profile. Comparison of simultaneous invasive measurements by IABP and noninvasive ones by Arteriograph of SBPao was never published yet.

Aim
The aim of this work was to compare the SBPao values measured with these two modalities.

Subjects and method
11 severely ill patients placed on IABP were included into this study. Noninvasive monitoring of SBPao was carried out by Arteriograph24 simultaneously with IABP. Descriptive statistics were calculated for both measurements and the variables were indicated as means and standard deviations. Linear regression analysis was carried out to define the relationship between the invasive and noninvasive variables.

Results
A strong and linear correlation was found between the invasive and non- invasive SBPao values, Pearson's correlation coefficient was $R=0.76$; $p<0.001$.

The diastolic counterpulsation pressure waves could be correctly identified on Arteriograph-registrations. Furthermore, the onset and the end of counterpulsation were also exactly defined noninvasively.

Conclusions
The noninvasive SBPao values showed strong correlation with invasive values. Our results confirm that the SBPao values, measured by Arteriograph, are close to the true aortic SBP. This is the first investigation when Arteriograph24 is validated againts invasive SBPao measurement by IABP.

P93 Are hemodynamic measures associated with frailty in elderly patients undergoing Transcatheter Aortic Valve Implantation? M

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Background
Aortic valve stenosis (AS) is common in the elderly and is associated with high morbidity and mortality, and leads to functional decline. The aim of this study was to investigate the possible relation between aortic stiffness, AS and frailty in older patients undergoing Transcatheter Aortic Valve Implantation (TAVI).

Methods
TAVI Care&Cure is an observational ongoing study including consecutive patients undergoing TAVI procedure at the Erasmus University Medical Center. Prior to TAVI echocardiography was performed and aortic stiffness was measured non-invasively by the Mobil-O-Graph. The frailty status was assessed including 5 domains. Primary outcome was to investigate the relationship between structural and functional cardiovascular parameters and frailty status. Linear regression was used.

Results
A total of 212 patients were included for analysis. Mean age was 79,2 years (±7,8), 52,7% men, mean Aortic Valve Area (AVA) was 0,73 (± 0,3), mean Pulse Wave Velocity was 12,6 (±1,5). Frailty was found in 57,8%. Peripheral pulse pressure (p=0.04) and central pulse pressure (p=0.02) but not aortic stiffness were associated with AS severity. AVA was associated with frailty (p=0.02) whereas measures of aortic stiffness were not.

Conclusion
Aortic valve area but not measures of aortic stiffness is associated with frailty status in elderly patients with AS undergoing a TAVI procedure.

P94 Dapagliflozin acutely restores endothelial dysfunction, reduces aortic stiffness and renal resistive index in type 2 diabetic patients: a pilot study

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Objective
Sodium-glucose co-transporter-2 inhibitors reduce blood pressure and renal and cardiovascular events in patients with type 2 diabetes through not fully elucidated mechanisms. Aim of this study was to investigate whether dapagliflozin is able to acutely modify systemic and renal vascular function.

Methods
Neuro-hormonal and vascular variables, together with 24h-urinary sodium, glucose, isoprostanes, diuresis and free-water clearance, were assessed before and after a 2- day treatment with dapagliflozin 10 mg/die in 16 type 2 diabetic patients. Brachial artery endothelium-dependent and independent vasodilation (by flow-mediated dilation) and pulse wave velocity were assessed. Renal resistive index was obtained at rest and after glyceril trinitrate administration.

Results
Dapagliflozin decreased systolic blood pressure and urinary isoprostanes and induced an increase in 24h-diuresis, 24h-urinary glucose and serum magnesium; 24h-urinary Na and fasting blood glucose were unchanged; serum magnesium slightly increased. Flow-mediated dilation was significantly increased (2.8±2.2 to 4.0±2.1%, $p<0.05$), and pulse-wave-velocity was reduced (10.1±1.6 to 8.9±1.6 m/s, $p<0.05$), even after correction for mean blood pressure. Renal resistive index was reduced (0.62±0.04 to 0.59±0.05, $p<0.05$), as well as its response to nitrates.

Conclusions
An acute treatment with Dapagliflozin significantly improves systemic endothelial function, arterial stiffness and renal resistive index; this effect is independent of changes in blood pressure and occurs in the presence of stable natriuresis, suggesting a fast, direct beneficial effect on the vasculature, possibly mediated by oxidative stress reduction.

P95 Effect of Chronic Inflammation Inhibition with Salsalate on Aortic Stiffness and Vascular Endothelial Function in Older Adults: A Randomized Controlled Study M

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Chronic activation of the proinflammatory transcription factor nuclear factor kappa-B (NFkB) is linked to age-associated vascular dysfunction. Acute inhibition of NFkB with high-dose salsalate (>4g), a non-acetylated salicylate known to block NFkB activation, improves aortic stiffness and endothelial function in aged rodents and humans.

Therefore, we hypothesized that chronic salsalate therapy at the US FDA approved starting dose (3 g/day) would improve age-associated aortic stiffness and endothelial dysfunction in older adults. A total of 28 normotensive older adults (57.4 ± 1.3 yrs; 11M/13F) were randomized to salsalate 3 g/day (n=14) or placebo (n=14) for 4 weeks and had assessments of aortic stiffness (carotid-femoral pulse wave velocity, CFPWV) and endothelial function (brachial artery flow-mediated dilation, FMD).

A group of 17 young adults (age 26 ± 1 yrs) were not randomized. As expected, baseline CFPWV was higher (8.1 ± 0.3 vs 5.3 ± 0.2 m/sec, P<0.01) and FMD was lower (3.4 ± 0.8 vs. 5.9 ± 1.0%, P=0.03) in the older vs. young. In the older adults, neither FMD (SALS: 3.5 ± 1.4 to 4.6 ± 1.2%; PLAC: 3.4 ± 1.2 to 2.5 ± 1.3%, ANOVA
P=0.98) nor CFPWV (SALS: 8.1 ± 0.5 to 8.4 ± 0.6 m/sec; PLAC: 7.6 ± 0.5 to 7.6 ± 0.4 m/sec, ANOVA P=0.41) was altered after 4 weeks of salsalate vs. placebo.

These data fail to demonstrate that chronic salsalate timproves age-associated aortic stiffness or endothelial dysfunction in older adults. Future studies should test longer duration therapy or more selective inflammatory inhibitors on vascular aging in humans.

P96 Acute effect of electronic cigarette smoking on pulse pressure amplification in young smokers

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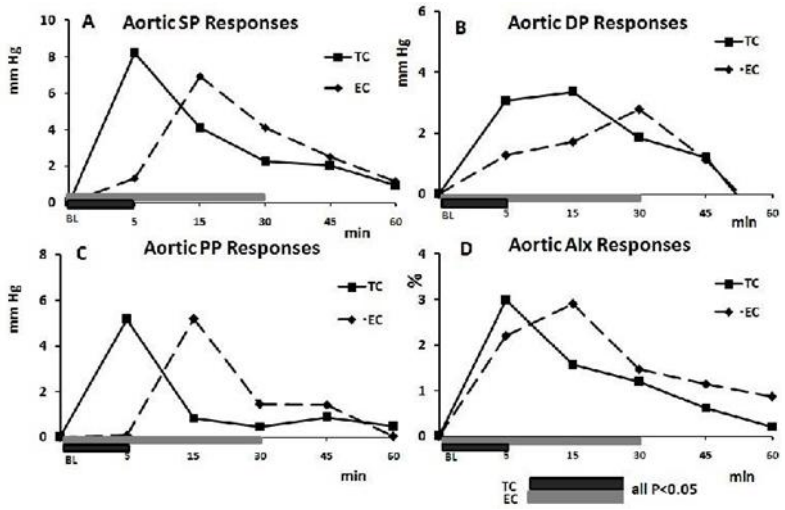
Purpose/Background/Objectives
We investigated the acute effect of electronic cigarette (EC) smoking on the aortic pressure waveform amplification. We also sought to compare the effect of EC and combustible cigarette (TC) smoking on central haemodynamics.

Methods
We studied 24 smokers (age: 30±8 years) on 3 separate occasions: a) tobacco cigarette (nicotine content, 1.2 mg) over 5 minutes, b) EC (18 mg E-liquid) for a period of 30 minutes, and c) nothing (sham procedure) for 60 minutes. Smoking EC for 30 min (15 puffs) was chosen to mimic the common pattern of EC smoking.
Results: Both TC and EC smoking caused a significant increase in brachial pressures and heart rate (HR), and the differences in blood pressure (BP) and HR responses between the two smoking forms were not significant. The aortic pressures also increased significantly after smoking both TC and EC, with the greatest changes seen in the first 5 minutes after TC smoking and 15 minutes EC smoking

(figures 1A- C, all P<0.05). Although AIx, decreased in both two smoking forms, by applying a correction factor for changes in HR, the AIx increased significantly after TC (by 3.0 % at 5 minutes, P<0.05) and EC (by 2.9% at 15 minutes, P<0.05) (figure 1D).



Conclusions
Electronic cigarette smoking exerts an unfavourable and comparable to that of TC smoking acute effect on aortic pressure waveform amplification. Given the prognostic role of central haemodynamics on cardiovascular disease risk, EC may still be considered a hazardous smoking method.

P98 Effect of long-term androgenic treatment on the structural and functional properties of the great arteries of female transsexuals

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Background
Androgens act directly on the vasculature through your connection to the androgen receptor in the vascular wall, and can promote changes in structural and functional vascular properties.

Objective
To evaluate the structural and functional properties of large arteries in TF in prolonged use of testosterone esters and compare them with those of a control group men and women.

Patients and methods
42 patients with diagnosis of TF (42±10 years) in treatment with testosterone esters for at least 1 year (1-38 years) and 147 healthy controls matched for age and BMI were submitted to evaluation of carotid parameters by radiofrequency ultrasound(WTS®): intima media thickness(IMT), diameter and relative distension. The carotid-femoral pulse wave velocity(PWVcf) was measured by Complior® device.

Results
The TF showed higher (p<0.01) PWVcf (7.2±0.8 m/s) than the male controls (6.6±0.9 m/s), but not than female controls (7±1 m/s). When categorized by age, considering median values of age, TF ≥ 42 years showed higher PWVcf than male and female controls, independently of BP values. There is no diferences in carotid parameters between TF and control groups, but obese TF presented higher carotid diameter (6944±527 vs. 6438±555 µm and IMT (691±72 vs. 601±126 µm), and lower carotid distension (4,8±1,5 vs. 6,5±2,1 %) than lean TF. The PWVcf was significantly correlated to age (r=0.63), time of androgenic treatment (r=0.37) and waist-hip ratio (0.39) in TF.

Conclusion
Older TF subjects and TF with prolonged treatment had higher aortic stiffness. Obese TF presented worst carotid structural and functional markers

P99 The effect of L-arginine on the vascular function in healthy trained and sedentary subjects

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Background
The aim of our study was to determine whether the use of food supplement L- arginine improves vascular function, which could be beneficial in preventing the formation and development of cardiovascular diseases. We investigated differences between trained and sedentary subjects.

Method
Measurements were performed in healthy normotensive men, divided into four groups, according to age and physical activity: 12 young sedentary (YS) (mean age 23,5 ± 2,4) and age matched trained (YT) (N=18); 11 elder sedentary (ES) (mean age 45,7 ± 7,5) and age matched trained (ET) (N=12) subjects. Parameters were measured at rest with the Task Force Monitor device (CNSystems Medizintechnik, Austria) before and after administration of 0.9 g L-arginine.

Results
After ingestion of L-arginine the heart rate in all groups statistically significantly decreased (YS 70.4 ± 4.2 vs. 66.3 ± 3.3; YT 62.1 ± 2.7 vs. 58.3 ± 2.0; ES 69.6 ± 3.2 vs. 62.7 ± 2.7; ET 58.0 ± 1.8 vs. 53.6 ± 1.2 beats/min) (paired t-test, $p<0.05$). The cardiac output decreased in three groups (YT 7.04 ± 0.4 vs. 6.32 ± 0.3; ES 6.95 ± 0.5 vs. 5.9 ± 0.4; ET 7.08 ± 0.6 vs. 6.58 ± 0.4 L/min) (paired t-test, $p<0.05$). The systolic (126.3 ± 4.1 vs. 120.0 ± 3.2 mmHg) and diastolic pressure (77.6 ± 2.5 vs. 74.3 ± 1.9 mmHg) (paired t-test, $p<0.05$) decreased in the ES group.

Conclusions
The systemic effect of L-arginine was observed. Improved cardiovascular function in response to L-arginine could justify the use of dietary L-arginine supplementation.

P100 Trial of Exercise to Prevent Hypertension in Young Adults (TEPHRA): Rationale and Protocol

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Background
Hypertension or pre-hypertension in young adults is unusual and more often linked with an adverse family or pregnancy history, such as preterm birth, than hypertension which develops later in life[1-4]. Surprisingly, no trials have investigated whether lifestyle advice developed for blood pressure control in older adults is effective in these young populations[5].

Methods
TEPHRA is a randomised control trial of a 16 week physical activity intervention including behaviour change and structured exercise in young adults with pre- and stage 1 hypertension. On-line recruitment is used with targeting to ensure inclusion of a proportion born preterm. Primary outcome is 24 hr ambulatory blood pressure at 4 months. Subjects undergo additional multimodal assessments including vascular stiffness, blood sampling, microvascular assessment, echocardiography, remote activity monitoring and multi-organ magnetic resonance imaging to identify potential predictors of blood pressure change.

Results
Recruitment started in April 2016 and currently (June 2017) 344 potential participants have been screened with 103 progressing to a baseline visit, of which 91 have been randomized. Two participants have completed their 12 month follow up. Recruitment is predicted to be completed by February 2018 with data reporting of four months outcomes in late 2018.

Conclusion
TEPHRA aims to deliver the most in-depth investigation to date on the effects of physical exercise on the cardiovascular system and health of young adults at risk of early hypertension and cardiovascular disease.

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Poster Session II – Kidney
Chair: L Ghiadoni, B Pannier

P106 Aortic stiffness and central systolic pressure are associated with orthostatic hypotension in patients with chronic kidney disease M

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Objective
Orthostatic hypotension (OH) is common cardiovascular problem affecting older adults, and is associated with falls, stroke and chronic kidney disease (CKD). This postural drop (PD) in blood pressure (BP) has been independently associated with increased aortic stiffness in older adults. Aortic stiffness is a modifiable cardiovascular risk factor, and measureable non-invasively. We investigated the association between OH, aortic stiffness and central aortic systolic pressure (CSP) in CKD patients (ACADEMIC cohort).

Design and method
Postural BP changes were measured in one-hundred and forty-six patients (mean age 68.6 SD±11.4, 75% male, 21% diabetic) using 24-hour-ambulatory blood pressure monitoring with postural sensing (Diasys Integra II®, Novacor, France). Patients were divided into those with systolic postural drop (SPD, n=23, mean standing systolic BP<mean lying systolic BP) versus those without (n=123).
Complior® (Artech Medical, France) measured aortic stiffness as carotid-femoral pulse wave velocity (cf-PWV) and peripheral arterial stiffness as carotid-radial PWV (cr-PWV). Sphygmocor® (Atcor, Australia) measured CSP and augmentation index (AI) from the radial artery.

Results
Cf-PWV and CSP were significantly higher in CKD patients with SPD versus those without (15.2m/s vs 12.7m/s, p<0.001, 148mmHg vs 136mmHg, p=0.012).
Multivariate logistic regression showed SBP remained significantly associated with aortic stiffness (p=0.002, OR=1.45 95%CI=1.15-1.77) and CSP (p=0.026, OR=1.031, 95%CI=1.00-1.06), independent of age, eGFR, diabetes, smoking pack-years, cholesterol, height and weight. RAI (32.1%vs28.9%, p=0.093) and cr-PWV (11.0m/s vs 11.2m/s, p=0.62) were not significantly different between groups.

Conclusion
Increased aortic stiffness and CSP are independently associated with OH. Stiff central arteries, rather than peripheral, contribute more to OH.

P107 Oscillometric measurement of 24-hour pulse wave velocity predicts all-cause mortality in patients with end-stage renal disease: The ISAR-Study M

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Objectives
Mortality rate in end-stage renal disease (ESRD) are still at a high level. Sarafidis et al. showed the predictive value of 48h PWV in patients undergoing hemodialysis [1], although recent studies using office measurement showed controversial predictive results. Aim of the present study was to confirm the predictive value of a novel oscillometric measurement of pulse wave velocity on mortality in an elderly cohort of patients with ESRD.

Methods
The ISAR study is a prospective and longitudinal study targeting patients with ESRD undergoing hemodialysis. Oscillometric measurement of 24-hour PWV was performed at baseline. Survival analysis included Kaplan-Meier analysis, logrank test and Cox regression.

Results
A total of 350 patients had a median age of 69.3 [55.8;77.3] years. Mean PWV was 9.6 (2.2) m/s and 120 patients died during the mean follow-up of 45 months. PWV was significantly higher in the deceased (10.6 +/- 1.9 m/s) than in surviving patients (9.0 +/- 2.2 m/s). Kaplan-Meier analysis showed differences in dichotomized PWV (cut-off 10 m/s [2]; Logrank test: p=0.001). For results of univariate Cox regression, see Figure. Adjusted Cox regression analysis showed a significant risk prediction for all-cause mortality (HR 2.322; p=0.011). Patients older than 50 years

showed even higher predictive values (HR 2.442; p=0.008) as well as patients with PWV values of at least 10 m/s (HR 3.300; p=0.006).

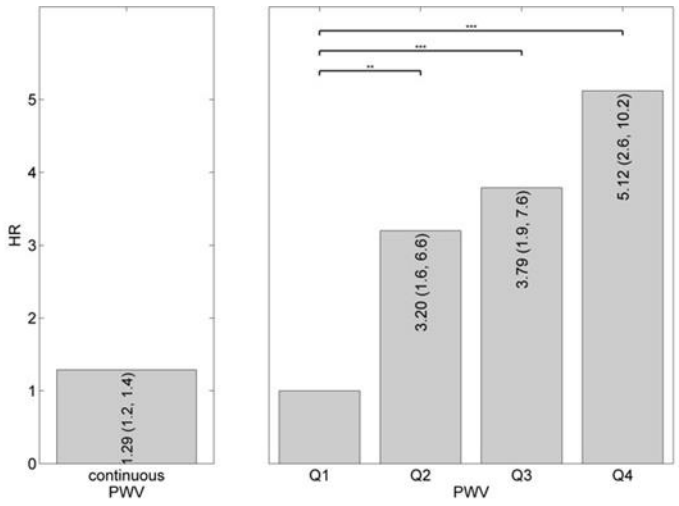

Figure: Univariate hazard-ratios and their 95%-confidence intervals for continuous PWV and PWV quartiles (Q1 as reference; ** p=0.002; *** p < 0.001). Q1: <=7.92 m/s; Q2: 7.92-9.83 m/s; Q3: 9.83-11.23 m/s; Q4: >11.23 m/s.

Conclusion
Oscillometric measurement of 24-hour pulse wave velocity is a simple and valid method and has an additional predictive value for all-cause mortality in elderly patients with end-stage renal disease.

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P108 Impact of kidney transplantation on aortic stiffness index β0 M

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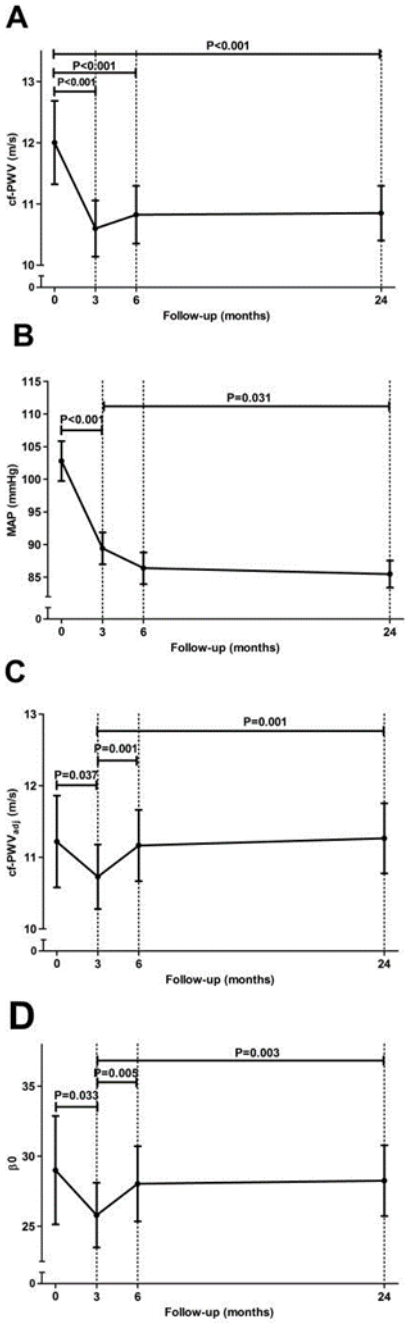
Purpose/ Background/ Objectives
We have shown that aortic stiffness improves as early as 3 months post-kidney transplantation (KTx). Aortic stiffness index β0, a blood pressure independent parameter, has been proposed to be a better indicator of vascular wall property. This study was designed to examine 1) the early versus late changes in aortic stiffness index β0 and 2) to define the characteristics of patients with favourable and unfavourable trajectories of aortic stiffness index β0 after KTx.

Methods

In 79 patients who underwent KTx, aortic stiffness was assessed before, 3, 6 and 24 months after KTx. Aortic stiffness was determined by carotid-femoral pulse wave velocity (cf-PWV), while aortic stiffness index β0 was obtained using a formulae proposed by Spronck and colleagues. Cytokines profile was measured in plasma by ELISA.

Results

There was a reduction of β0 3 months after KTx (29.0±2.0 to 25.8±1.2,P=0.033). Then, aortic stiffness index β0 gradually increased at 6 (28.0±1.4,P=0.005 vs 3 months) and 24 months (28.3±1.3,P=0.003 vs 3 months). Unfavourable progression of β0 was not related to renal function, age, comorbidities or kidney donor characteristics. However, the unfavourable progression of β0 was associated with higher levels of interleukin-6 (P=0.029).



Conclusions
The improvement of aortic stiffness index β0 3 months after KTx suggests that KTx leads to an early improvement of the intrinsic mechanical properties of aorta.
However, this improvement is followed by a late progression of β0, which is associated with increased pro-inflammatory cytokine, suggesting that activation of immune system may be involved in arterial wall remodeling in kidney transplant recipients.

P109 Progression of aortic arch calcification after kidney transplant and its importance in predicting cardiovascular risk: single-center 2-year follow-up study M

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Vascular calcification (VC) is linked to post-transplant cardiovascular events in the long term. We aimed to evaluate whether pretransplant chest X-ray based aortic arch calcification (AoAC) or pulse wave velocity measurement can better predict post- transplant cardiovascular or cerebrovascular events, and to assess the progression of calcification within 2 years.

Methods
Our single-center observational longitudinal study enrolled 40 kidney transplant recipients (KTR) without previous history of vascular events (no cardiovascular, cerebrovascular events, no peripheral artery disease). Two radiologists evaluated pretransplant and postransplant (after 2 years) AoAC on chest X-ray by using two different AoAC scales: AoAC grade evaluation [1] and AoAC score as suggested by Ogawa et al. in 2009 [2]. Cohen's kappa coefficient was 0.75. The mismatching results were repeatedly reviewed and resulted in consensus. Carotid-femoral (cfPWV) and carotid-radial pulse wave velocity (crPWV) was measured using applanation tonometry and the PWV ratio (cfPWV/rPWV) was calculated. Patient clinical, biochemical data and cardiovascular/cerebrovascular event rate were monitored within 2 years.

Results
During 2-year follow-up 5 patients experienced cardiovascular events, which were predicted by PWV ratio, but not related to AoAC. In 3 patients, we observed progression of AoAC, in others – AoAC was less evident or remained unchanged in 2-years follow-up. AoAC score [2] could better describe the extent of vascular calcification in KTR.

Conclusions
KTR without previous vascular events have quite low cardiovascular/ cerebrovascular event rate within 2-year follow-up, which are better predicted by pretransplant PWV ratio. AoAC postransplant regression is evident even when using simplified chest X- ray scales.

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P110 Differences in arterial stiffness measured by cardio-ankle vascular index in patients with normal and decreased renal function M

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Background
Arterial stiffness (AS) is a highly prognostic risk factor of cardiovascular diseases. The aim of this study was to investigate the relationships between cardio-ankle vascular index (CAVI) and eGFR in patients under the risk of cardiovascular disease.

Methods
This was a retrospective study of Lithuania High cardiovascular risk patients' database. Demographic, renal function and AS data was gathered. Patients were divided into groups by gender and age by intervals of 5 years. Mean values of CAVI were further investigated according to the patients' eGFR. ANOVA was used to compare mean values of CAVI.

Results
This study included data of 2070 patients aged from 40 to 65 years. The mean eGFR of the patients was 100.13 ml/min/1.73m2, 58.7% were women. The increase in CAVI was observed with age in overall population, with mean values in different age groups of 6.55±1.28, 7.13±1.84, 7.71±1.92, 7.79±1.95, 7.73±1.98, 8.06±1.79,
p<0.001. Calculation of the mean CAVI in different age and gender groups of eGFR are presented in Table 1. Further comparison of mean values of CAVI did not yield statistically significant results.

Table 1. Mean values of CAVI

	Men						Women					
eGFR	40-45	p	45-50	p	50-55	p	50-55	p	55-60	p	60-65	p
<60	5,80	0,159	8,58	0,610	7,74	0,150	7,70	0,948	6,34	0,172	7,33	0,068
60-90	6,63		7,80		7,71		7,54		7,73		8,23	
>90	7,17		7,67		8,32		7,49		7,78		7,92	

Conclusions
Arterial stiffness increases with age in overall population. There was no statistically significant difference between mean values of CAVI in groups divided by age and gender according to eGFR.

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P111 Association and Clinical Relevance of Absence of Lower Limb Arterial Pulse and Coronary Artery Disease in Hemodialysis Patients

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Objectives
To determine the association between PAD and DAC in patients treated by haemodialysis in the waiting list for renal transplantation and to assert the influence of that association on prognosis and clinical management.

Methods
1246 renal transplant candidates underwent coronary angiography. Peripheral artery disease was defined as either absence of pulse in the lower limb or a history of gangrene, amputation, or vascular intervention.

Results
The prevalence of peripheral artery disease and coronary artery disease were 34% and 52%, respectively. The association of peripheral artery disease with coronary artery disease was significant (68% versus 32%, OR=2.60, 95% CI 2.03–3.32, P = .0001). The specificity, sensitivity, positive predictive value, and negative predictive value were 77%, 44%, 67%, and 56%, respectively. Peripheral artery disease predicted the indication of coronary intervention. Patients lacking peripheral artery disease and coronary artery disease enjoyed higher event-free survival. Peripheral artery disease and coronary artery disease together did not add to the very high cardiovascular risk associated with each isolated condition. Death by any cause was influenced by peripheral artery disease independently of coronary artery disease.

Conclusions
A safe and inexpensive clinical method was useful to assess the association between PAD and CAD and may be useful to select patients for invasive studies. PAD was equivalent to CAD as a predictor of cardiovascular prognosis. Combining coronary and PAD evaluation helps to assess the prognosis of patients with CKD with reasonable accuracy.

P112 Central pulse wave parameters are associated with valve calcification in patients with end-stage renal disease on maintenance hemodialysis

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Background
Arterial stiffness is known marker of poor cardiovascular prognosis. The aim if the study was to assess the incidence of valve calcification (VC) in patients with end- stage renal disease (ESRD) and its associations with clinical parameters of arterial stiffness.

Methods
In 68 adults with ESRD on maintenance hemodialysis for >3 months (45.6% males, median age 58.3 (interquartile range (IQR) 54.6; 61.6) years, dialysis duration 62.7 (47.8;77) months, echocardiography and applanation tonometry was performed.

Results
Calcification of the aortic, mitral and both valves was revealed in 46 (67.6%), 34 (50%) and 33 (48.5%) of patients. 20 (29%) patients had no signs of VC. Patients with vs without AVC were older (65.1±9.5 vs 41.4±11,9 years, p<0.001), had higher dialysis duration (51 (8;252) vs 21 (10;38) months, p<0.01), lower peripheral diastolic blood pressure (DBP) (76±17 vs 84±12 mmHg, p<0.05), central DBP (75±15 vs 82±11 mmHg, p<0.05), reflected wave transit time (RWTT) (131±17 vs 137±15 ms, p<0.05). Patients with vs without MVC were older (67.8±8.2 vs 47.9±13,5 years, p<0.001), had higher dialysis duration (51 (34;111) vs 36 (14;57) months, p<0.01), carotid-femoral pulse wave velocity (10.1±2.7 vs 8.9±3.5 m/s, p<0.05), lower peripheral DBP (73±17 vs 84±14 mmHg, p<0.01), central DBP (72±13 vs 83±13 mmHg, p<0.001), higher central pulse pressure (52±13 vs 45±16 mmHg, p<0.05), lower RWTT (133 (120;130) vs 135 (132;142) ms, p<0.05).

Conclusion
High prevalence of VC (71%) was revealed in patients with ESRD on maintenance hemodialysis. Patients with vs without VC were older, had higher duration of dialysis and more pronounced arterial stiffness.

P113 Diastolic ambulatory blood pressure parameters are associated with valve calcification in patients with end-stage renal disease on maintenance hemodialysis

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Objective
valve calcification (VC) is common in patients on hemodialysis and increases the risk of cardiovascular morbidity and mortality. The aim if the study was to evaluate the association between VC and 44-hour ambulatory blood pressure (ABP) variables.

Materials and Methods
In 68 patients with end-stage renal disease (ESRD) on maintenance hemodialysis (45.6% males, median age 58.3 (interquartile range (IQR) 54.6;61.6) years, dialysis duration 62.7 (47.8;77) months, arterial hypertension 94%, heart failure 28%,
diabetes mellitus 21%, glomerulonephritis 35%, pyelonephritis 25%, multicystic dysplastic kidney 13%) echocardiography and 44-hour ABP monitoring was performed. Mann-Whitney test was considered significant if p<0.05.

Results
Calcification of the aortic (AVC), mitral (MVC) and both valves was revealed in 46 (67.6%), 34 (50%) and 33 (48.5%) of patients. 20 (29%) patients had no signs of VC. Patients with vs without AVC had lower daytime diastolic BP (DBP) (79±13 vs 89±12 mmHg, p<0.01), nighttime DBP (75±13 vs 83±13 mmHg, p<0.05), day one DBP (77±13 vs 89±15 mmHg, p<0.01), day two DBP (79±14 vs 88±10 mmHg, p<0.01),
44-hour DBP (78±13 vs 88±12 mmHg, p<0.01).
Patients with vs without MVC had lower daytime DBP (78±15 vs 86±11 mmHg, p<0.01), nighttime DBP (74±14 vs 81±12 mmHg, p<0.05), 44-hour DBP (77±15 vs 85±11 mmHg, p<0.01), higher daytime DBP variability (10±3 vs 9±3 mmHg, p<0.01).

Conclusion
High prevalence of valve calcification (71%) was revealed in patients with ESRD on hemodialysis. Patients with VC were older, had higher duration of dialysis, lower values of ambulatory DBP.

P114 Arterial Stiffness is associated with ambulatory blood pressure parameters in patients on maintenance hemodialisys

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Introduction
Arterial stiffness is a principal pathogenetic mechanism of aortic systolic blood pressure (SBP) augmentation, left ventricular hypertrophy and sudden cardiac death. The aim of the study was to evaluate the association between parameters of pulse wave and 44-hour ambulatory blood pressure (ABP) variables in patients with end- stage renal disease.

Methods
In 68 patients with ESRD on maintenance hemodialysis (45.6% males, median age 58.3(interquartile range (IQR) 54.6;61.6) years, dialysis duration 62.7(47.8;77) months applanation tonometry and 44-hour ABP monitoring was performed.

Results
Carotid-femoral pulse wave velocity (PWV)<10 vs PWV≥10m/s was revealed in 52(76.5%) of patients respectively. Patients with PWV≥10 vs <10 m/s had higher dialysis duration (median 60; IQR 36;84) vs 28; IQR 11;50.5) months, p<0.05), peripheral SBP (148.1±24,8 vs 140.7±23,6 mmHg, p<0.05); diastolic blood pressure (DBP) (85.7±15,2 vs 83.3±12,7 mmHg, p<0.05); 48-hour heart rate (HR) (74.7±13,0
vs 72±8,7 bpm, p<0.05), mean day one HR (78.7±7,5 vs 72.5±9,7 bpm, p<0.05), 48- hour DBP variability (DBPV) (78±13 vs 88±12 mmHg, p<0.01), day two SBP variability (13.5±4,4 vs 13.1±4,1) mmHg, p<0.05), mean day two BD variability (12±3,9 vs median 11; 11.8±3,6) mmHg, p<0.05). Patients with PWV≥10 vs <10 m/s had lower daytime DBPV (median 8.5; IQR 7;9) vs IQR 10 (8;11) mmHg, p<0.05), day one DBPV (median 8; IQR 8;9) vs 9 IQR
8;10 mmHg, p<0.01).

Conclusions
Patients with PWV≥10 m/s had higher duration of dialysis, higher values of ambulatory DBP and higher – of HR. These findings may have implications in gaining further insights into the mechanism of arterial stiffness.

P115 Albumin-to-creatinine ratio is associated with target organ damage in hypertension

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Purpose/Background/Objectives
Hypertension is associated with higher cardiovascular risk as well as several markers of subclinical target organ damage (TOD). Albumin to creatinine ratio (ACR) in urine has been recognised as an independent risk factor for cardiovascular events. We hypothesised that there is a relationship between ACR and markers of TOD in never- treated hypertensives.

Methods
We enrolled 924 consecutive essential hypertensives (mean age 53±12 years, 486 males) without known cardiovascular disease (CVD). Markers of subclinical TOD [left ventricular mass index (LVMI),

pulse wave velocity (PWV), ankle-brachial index (ABI) and estimated glomerular filtration rate (eGFR)] were evaluated in all patients. LVMI was assessed echocardiographically using the Devereux formula. Carotid-femoral PWV was estimated with the Complior device. eGFR was calculated by the Cockcroft-Gault formula. ABI was calculated by dividing the highest ankle systolic blood pressure by the highest brachial systolic blood pressure.

Results
ACR exhibited significant association with LVMI (r=0.277, p<0.001), PWV (r=0.277, p<0.001) ABI (r=-0.078, p=0.018) and eGFR (r=-0.100, p=0.002). In further analysis, ACR was associated with TOD as suggested by the 2013 European Guidelines for Hypertension [left ventricular hypertrophy (LVMI>115 g/m2 in men and >95 g/m2 in women), increased PWV (PWV>10m/s), decreased ABI (ABI<0.9) and decreased renal function (eGFR<60ml/min)]. Specifically, ACR exhibited a significant association with the number of TOD and this association was independent of age and gender (p<0.05).

Conclusions
Our findings support the close relationship between ACR and TOD in hypertension, as well as, the predictive ability of ACR for TOD.

Poster Session II – Models and Methodologies II

Chair: S Wassertheurer, E Bianchini

P135 Precision calibration of peripheral pressure waveforms using intra- arterial blood pressure reveals the need for improved ways to accurately estimate aortic blood pressure M

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Background
Estimating aortic blood pressure (BP) non-invasively requires peripheral waveform calibration using cuff systolic (SBP) and diastolic (DBP). Accuracy of estimated aortic BP has never been determined when peripheral waveforms are precision calibrated using peripheral intra-arterial SBP/DBP. This is relevant to understanding the best methods to estimate aortic BP accurately and was the aim of this study. We also determined how other calibrations influence estimated aortic BP accuracy.

Methods
Ascending aortic, brachial and radial artery intra-arterial BP was measured among 104 patients (61.8±10 years, 66% male) undergoing coronary angiography. Intra- arterial aortic SBP was compared with estimated aortic SBP by generalised transfer function (SphygmoCor) using: (1) intra-arterial brachial pressure waveforms calibrated with intra-arterial brachial SBP/DBP; (2) intra-arterial radial pressure waveforms calibrated with intra-arterial brachial SBP/DBP and (3) radial SBP/DBP and; (4) intra-arterial aortic mean arterial pressure (MAP)/DBP.

Results
All intra-arterial SBP/DBP peripheral waveform calibrations significantly underestimated intra-arterial aortic SBP ((1) -4.5±7.0 mmHg; (2) -8.8±8.0 mmHg and
(3) -5.4±7.6 mmHg; p<0.0001 all). Conversely, intra-arterial aortic MAP/DBP calibration (4) accurately estimated aortic SBP (0.03±4.6 mmHg, p=0.95). Underestimation of intra-arterial aortic SBP was related to lower aortic-to-brachial SBP amplification (r>0.25, p<0.009 all calibrations).

Conclusion
Even when using accurate (intra-arterial) SBP/DBP for precision peripheral waveform calibration, aortic SBP was significantly underestimated. Intra-arterial aortic MAP/DBP was the most accurate

calibration, but is not feasible for non-invasive use. These findings highlight the need for improved ways to accurately estimate aortic SBP.

P136 Altered adventitial collagen fibril mechanics and morphology with high pulse wave velocity M

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Background
Arterial stiffening, occurring as part of the natural aging process of the artery, is well- established as a powerful predictor of cardiovascular disease. However, little is known about how localised changes in the extracellular matrix and mechanical properties of arterial tissue contribute to gross stiffening in the vasculature, particularly in the adventitia. The mechanical properties of the adventitia are attributed to the collagen fibrils which exhibit high tensile strength when an axial load is placed on the vessel.

Objective
To determine the relationship between the adventitial collagen fibril properties and carotid-femoral pulse wave velocity (PWV).

Methods
16 patients were split into high PWV (13.6 ± 1.1ms^{-1}) and low (8.5 ± 0.3ms^{-1}) PWV groups (t-test, *P* <0.001). Internal mammary arteries (IMAs) which were collected during coronary artery bypass grafting (CABG) were used to nano-scale characterisation of the tissue with atomic force microscopy (AFM). AFM was used to determine nanomechanical properties and collagen fibril morphology.

Results
Abundant, highly oriented collagen fibrils were observed in the adventitial layer in both groups. The adventitia had high elastic modulus values in the high PWV group (Low PWV= 2298.64±75.38MPa; High PWV=2734.63±95.52MPa, *P*<0.001). The
collagen fibril diameters were found to be higher in patients with high PWV (Low PWV=117.23±22.19nm, High PWV=119.18±21.96nm, *P*<0.001).

Conclusion
Nanomechanical properties and collagen fibril morphology in arterial tissue associated with carotid-femoral PWV. Nano-scale changes in the IMA are therefore indicative of systematic changes in arterial stiffness in the vasculature.

P137 Numerical assessment and comparison of pulse wave velocity methods presuming to measure aortic stiffness M

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Recently several methods have been proposed as tools to measure aortic pulse wave velocity (aPWV). The carotid-femoral pulse wave velocity (cf-PWV), the current clinical gold standard method for the noninvasive assessment of aPWV, uses the carotid–femoral pulse transit time (cf-PTT) to derive cf-PWV. The heart-ankle PWV (ha-PWV), brachial-ankle PWV (ba-PWV) and finger-toe (ft-PWV) are also methods presuming to approximate aPWV based on time delays between physiological signals at two locations (~heart-ankle PTT, ha-PTT; ~brachial-ankle PTT, ba-PTT; ~finger-toe PTT, ft-PTT). To test the validity of these methods, we used a 1D arterial network model

(143 segments) including the foot and hand circulation.
The arterial tree dimensions and properties were taken from the literature and completed with CT-scans data. We calculated PTT's with all the methods above.

The calculated PTT's were compared with the aortic PTT (aPTT), considered as the absolute reference method in this study. The correlation between methods and aPTT was good and significant, cf-PTT (R^2 = 0.97; P<0.001; mean difference 5 ± 2 ms), ha- PTT (R^2 = 0.96; P<0.001; 150 ± 23 ms), ba-PTT (R^2 = 0.96; P<0.001; 70 ± 13 ms) and ft-PTT (R^2 = 0.95; P<0.001; 14 ± 10 ms).

Consequently, good correlation was also observed for the PWV values derived with the tested methods, but absolute values differed because of different path lengths used. In conclusion, our computer model based analyses demonstrate that for PWV methods based on peripheral signals, PTT's closely correlate with the aPTT, supporting the use of these methods in clinical practice.

P138 Can pulse wave velocity be measured in the fetal ascending aorta? M

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Background
Routine ultrasound exams are conducted to assess fetus development. Heart defects and cardiac function are the main areas investigated in an ultrasound assessment.
However, prenatal assessment of the fetal arterial stiffness is yet to be established in the ascending aorta.

Aim
To investigate whether pulse wave velocity (PWV) can be determined in the fetus ascending aorta using ultrasound examination.

Methods
35 fetuses (19 normal, 16 growth restricted) were included in the study. High quality recordings were achieved in 6 normal and 8 fetuses diagnosed with fetal growth restriction (FGR). Images of the diameter and blood velocity in the ascending aorta were recorded (Voluson, GE and Samsung) with a curvilinear probe 2-8MHz/1- 7MHz. The diameter and velocity waveforms were extracted from DICOM images, offline, using in-house developed codes in Matlab. The extraction was based on thresholding of the grey-scale images. Local PWV was determined using the ln(D)U- loop method [1].

Results
PWV in the fetal ascending aorta increased with gestational age in both normal (r^2=0.77) and FGR (r^2=0.55) fetuses. Mean PWV in the fetal ascending aorta per gestational week was 0.045m/s in normal and 0.066m/s in FGR fetuses, with a percentage difference of 32%.

Conclusions
Despite the challenging ultrasound images of the fetal ascending aorta, local PWV measurement has proven to be possible through recordings of diameter and blood velocity. PWV increases with gestational age and it is higher in FGR than normal fetuses. Further studies are needed to determine the potential clinical predictive value of fetus PWV.

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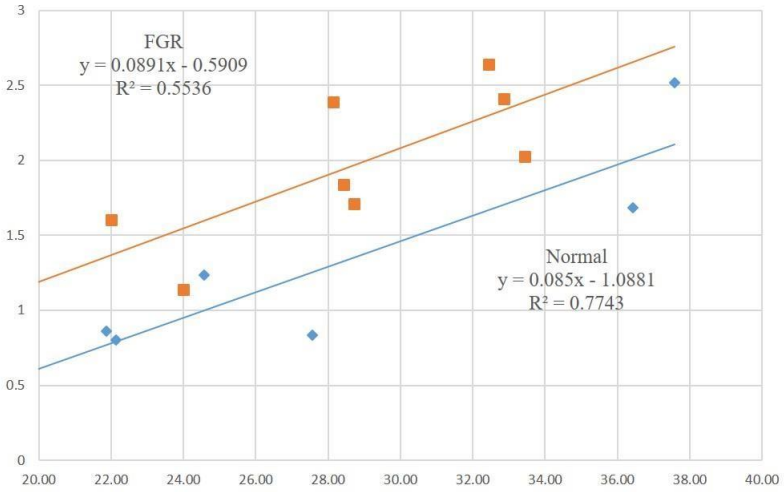

Figure 1. PWV vs gestational age in weeks for normal (blue diamond ♦) and FGR (red squares ■) fetuses and the trendlines with equations describing them and their r^2 values.

P139 Comparison of ejection durations derived from radial and brachial pressure waves M

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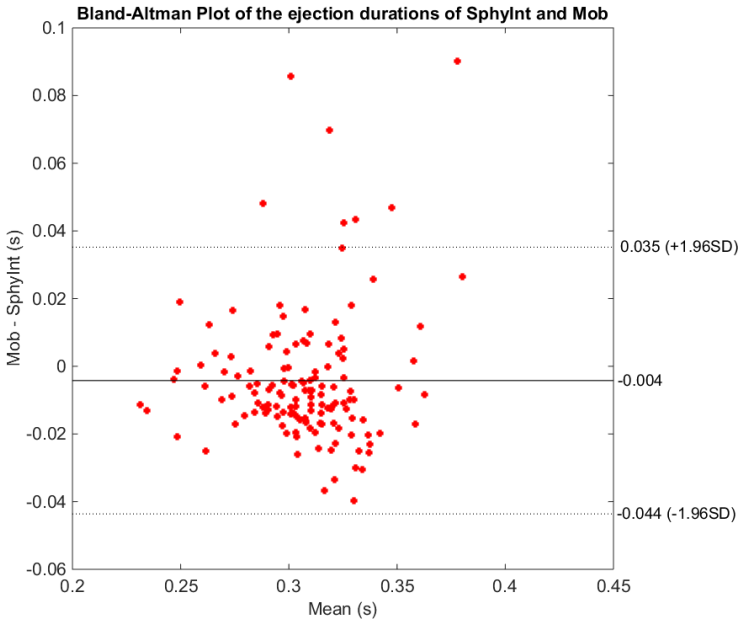
Purpose
The ejection duration (ED) is an important indicator of ventricular function as well as ventriculo-arterial coupling. Thus, the non-invasive oscillometric determination of ED from arterial pressure waves could enhance methods of pulse wave analysis. The aim of this work was to test and to validate the calculation of ED based on measurements from two different devices (brachial oscillometry and radial tonometry).

Methods
138 pulse wave measurements from 79 patients were obtained in direct succession with the Mobil-O-Graph (IEM, Germany) and with the Sphygmocor device (At Cor Medical Pty. Ltd., Australia) in a comparative study. An algorithm based on numerical derivatives was developed to determine the ejection duration from the arterial pulse wave. For both measurements, the ED was calculated and the ED from the internal algorithm of the Sphygmocor was obtained.

Results
The mean ED of the internal Sphymocor algorithm (SphyInt) is 309+-27 ms, of the calculated ED from the Mobil-O-graph measurements (Mob) 304+-29 ms and of the calculated ED from the Sphygmocor recordings (Sphy) 308+-30 ms. So, the mean differences between Mob and SphyInt are -4+-20ms, see figure, and between Mob and Sphy are -3+-26ms. The sampling rates of Sphymocor and Mobil-O-Graph are 128 respectively 100 Hz, so the mean errors are below the particular step sizes.



Conclusion
The algorithm for calculation of the ED was tested successfully on radial and brachial recordings. As the differences between locations as well as between algorithms are sufficiently small, the determination of ejection duration from brachial oscillometric pulse waves seems feasible.

P140 Comparison of Doppler and oscillometric methods of assessing ankle- brachial index in patients with systemic lupus erythematosus

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Objective
Peripheral arterial disease (PAD) is a common cardiovascular complication in systemic lupus erythematosus (SLE) patients [1]. PAD is objectively diagnosed with ankle-brachial index (ABI), which can be measured by the Doppler method, or oscillometric technique [2]. In Ghanaian SLE patients, we compared the utility of oscillometric ABI to Doppler ABI, which is the 'gold standard'.

Method
ABI was measured using 8 MHz hand-held Doppler (LifeDop 250, Summit Doppler) and oscillometric technique (Vasera 1500N, Fukuda Denshi) in 80 SLE patients (160 legs). PAD was defined as ABI<0.9 in at least one leg.

Results
There prevalence of PAD by oscillometric technique was higher than that of Doppler technique (32.5% vs 23.8%, p=0.004). There was fair level of agreement between PAD by Doppler and oscillometric techniques (κ=0.36, p=0.003). Doppler ABI correlated with oscillomteric ABI in the right leg (r=0.34, p=0.005), but not in the left leg (r=0.18, p=0.127). Reliability analysis showed that Doppler-ABI does not agree with oscillometric ABI in both right (intraclass r=0.23, p=0.13) and left (intraclass r=0.31, p=0.061) legs.

Conclusion
In Ghanaian SLE patients with high prevalence of PAD, measurement of ABI using oscillometric technique does not agree with Doppler-based ABI.

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P141 Comparison between techniques of evaluation microvascular morphology: the gold-standard locally invasive micromyography vs. three non- invasive techniques. Preliminary data

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Objective
The gold standard technique of evaluation microvascular morphology in human is generally considered the measure of media to lumen ratio (M/L) of subcutaneous small vessels obtained by local biopsies and evaluated by wire or pressure micromyography. However, non-invasive techniques for the evaluation of retinal arterioles were recently proposed, in particular two approaches seem to provide interesting information: Scanning Laser Doppler Flowmetry (SLDF) and adaptive optics (AO); both of them provide an estimation of the wall to lumen ratio (WLR) of retinal arterioles. A non-invasive measurement of basal and total capillary density may be obtained by videomicroscopy/capillaroscopy. No direct comparison of the non-invasive techniques in the same population was previously performed, in particular AO was never validated against micromyography.

Methods
In the present study, we enrolled 12 normotensive subjects and 8 hypertensive patients undergoing an election surgical intervention;(11/20 were severely obese). All patients underwent a biopsy of subcutaneous fat during surgery. Subcutaneous small resistance artery structure was assessed by wire myography and the M/L was calculated. WLR of retinal arterioles was obtained by SLDF and AO (SLDF, Heidelberg Engineering, Heidelberg, Germany and RTX-1, Imagine Eyes, Orsay, France). Functional (basal) and structural (total) microvascular density were evaluated by capillaroscopy before and after venous congestion.

Results
The results are summarized in the Table (slope of the relation: $p<0.01$ RTX-1 vs. SLDF).

	Basal capillary density in the nailfold / M/L	Total capillary density in the forearm / ML	Basal capillary density in the dorsum of the finger / M/L	Total capillary density in the dorsum of the finger / ML
Correlation coefficients (n=20)	0.53, r^2=0.28, p<0.05	0.50, r^2=0.25, p<0.05	0.17, r^2=0.29, P=NS	0.34, r^2=0.12, P=NS
	W/L retinal arterioles (SLDF) / M/L	W/L retinal arterioles (RTX-1) / M/L	W/L retinal arterioles (SLDF) / W/L retinal arterioles (RTX-1)	
Correlation coefficients (n=20)	0.54, r^2=0.29, p<0.01	0.90, r^2=0.81, p<0.001	0.71, r^2=0.50, p<0.001	

Conclusions
Our data suggest that AO has a substantial advantage over SLDF in terms of evaluation of microvascular morphology, since it is more closely correlated with the M/L of subcutaneous small arteries, considered a gold-standard approach.

P142 Aortic Root Stiffness and Mechanical Properties of Healthy Adults

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Background
Arterial stiffness, often expressed in terms of pulse wave velocity (PWV), is an important risk factor for cardiovascular disease. PWV can be determined locally and non-invasively, by means of ultrasound.

Aim:
To assess PWV, local compliance (Cs), distensibility (Ds) and Young's modulus of the aortic root using non-invasive ultrasound measurements.

Methods
10 healthy volunteers aged 21-39, 1 male, were scanned using ultrasound (GE, Vivid E95) with a phased array transducer 1.5-4.5MHz. DICOM images were recorded from the parasternal long axis: M-mode for diameter measurements, and apical 5- chamber view for blood Doppler velocity, sequentially. Each measurement was repeated 3 times for 20s. Velocity and diameter waveforms were extracted offline in Matlab based on grey-scale thresholding. PWV was determined using the ln(D)U- loop method [1]. Wall thickness was extracted from the B-mode images used to measure the diameter. Distensibility and compliance were calculated as $Ds=1/(\rho \cdot PWV^2)$, $Cs=dA/dP=Ds \cdot A$, where $\rho=1050 kg/m^3$ blood density, A is the cross- sectional area, and Young's modulus was calculated as previously described [2] using the Bramwell-Hill and Moens-Kortweg equations.)

Results

Across all patients mean PWV was 3±0.8m/s, mean distensibility was $1.3 \cdot 10^{-4} \pm 0.61 \cdot 10^{-4} Pa^{-1}$, and mean compliance was $0.6 \pm 0.31 m^2 Pa^{-1}$. The average wall thickness was 0.4±0.06cm while Young's modulus was 63.6±40.4kPa. These results are comparable to corresponding values reported in the literature using other techniques.

Conclusions
Aortic root PWV, distensibility, compliance and Young's modulus can be determined using ultrasound measurements of diameter and velocity. Further studies are required to investigate the potential clinical utility of aortic root parameters.

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P143 Validity of pulse wave velocity and augmentation index measurements in patients with atrial fibrillation M

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Background

Individualized weighing of the risk-benefit of anticoagulation is recommended in patients with atrial fibrillation (AF) that have low established risk scores or, conversely, are at increased risk for bleeding[1]. Parameters of arterial stiffness and wave reflection could improve risk stratification, but their use has not been validated in arrhythmia[2-3].

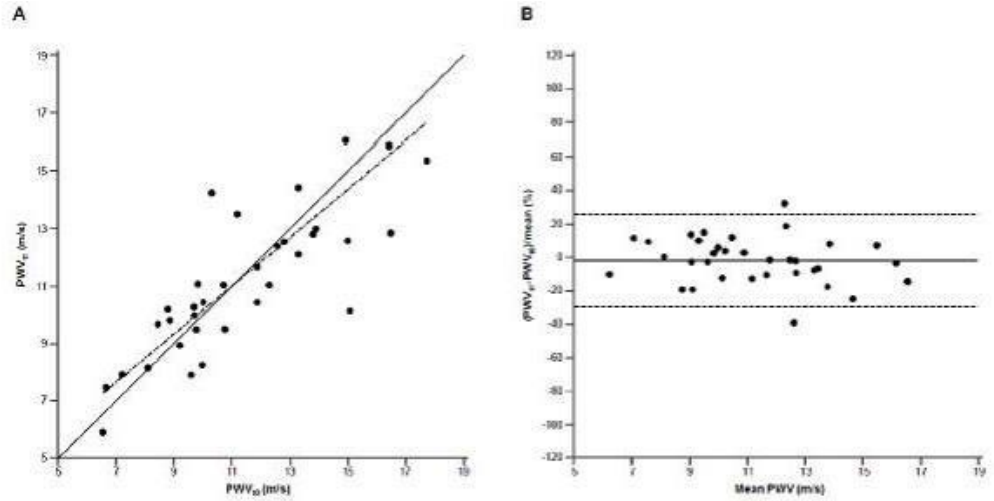
Methods

We measured carotid-femoral pulse wave velocity (PWV), central augmentation index (AI) and central pulse pressure (CPP) using the SphygmoCor (AtCor Medical, Sydney, Australia) system in 34 patients (53 to 85 years; 25 males) with AF before and after elective electrical cardioversion. Agreement was assessed using the intraclass correlation coefficient (ICC) and the coefficient of variation, completed with Bland-Altman plots.

Results

Following cardioversion, mean arterial blood pressure (MAP) and heart rate (HR) decreased significantly by 7 mmHg and 18 bpm respectively. PWV decreased from 11.8 m/s to 10.7 m/s, AI increased from 24% to 29%, and CPP rose from 45 mmHg to 50 mmHg. The decrease in PWV was related to the decrease in MAP (beta=0.57; R^2=0.33; P<0.001) whereas changes in AI and CPP were related to the decrease in HR (AI: beta=-0.59; R^2=0.35; P<0.001, CPP: beta=-0.52; R^2=0.26; P=0.001).

After adjustment for changes in MAP and HR, reliability analysis showed an excellent agreement for PWV (ICC=0.89; 95%CI: 0.79-0.95) but moderate agreement for AI (ICC=0.59; 95%CI: 0.17-0.80). Excellent agreement was also found for CPP (ICC=0.89; 95%CI: 0.78-0.94).



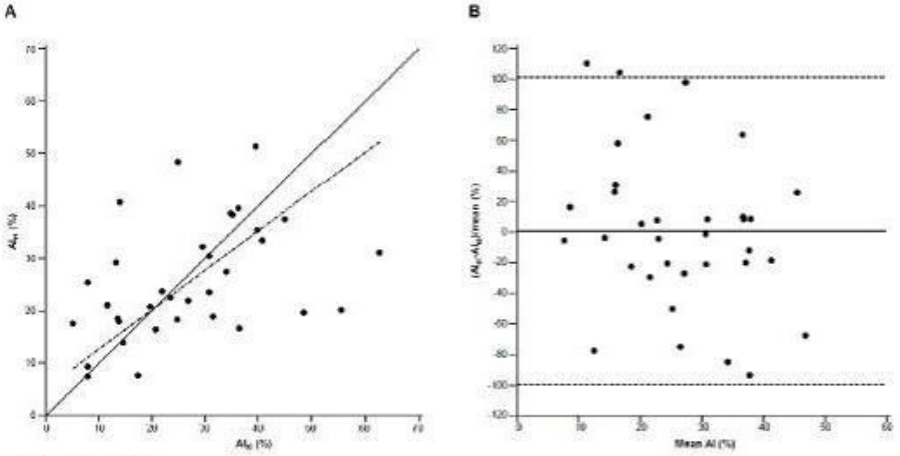


FIGURE LEGENDS

Figure 1

A. Scatter plot showing PWV before (PWV_{t0}) and after (PWV_{t1}) cardioversion. The solid line is the line of identity, the broken line the regression line for PWV_{t1} vs PWV_{t0} (Passing & Bablok regression).
B. Bland–Altman plot showing the proportional difference (%) between PWV after (PWV_{t1}) and PWV before (PWV_{t0}) cardioversion. The solid line represents the mean value of PWV and the dotted lines mean±2 SD.

Figure 2

A. Scatter plot showing AI before (AI_{t0}) and after (AI_{t1}) cardioversion. The solid line is the line of identity, the broken line the regression line for AI_{t1} vs AI_{t0} (Passing & Bablok regression).
B. Bland–Altman plot showing the proportional difference (%) between AI after (AI_{t1}) and AI before (AI_{t0}) cardioversion. The solid line represents the mean value of AI and the dotted lines mean±2 SD.

Conclusions

Measurement of PWV and CPP is reliable in patients with AF, as they appear unaffected by the presence of arrhythmia.

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P144 Ascending and descending thoracic aorta PU-loops for the estimation of left ventricular afterload.

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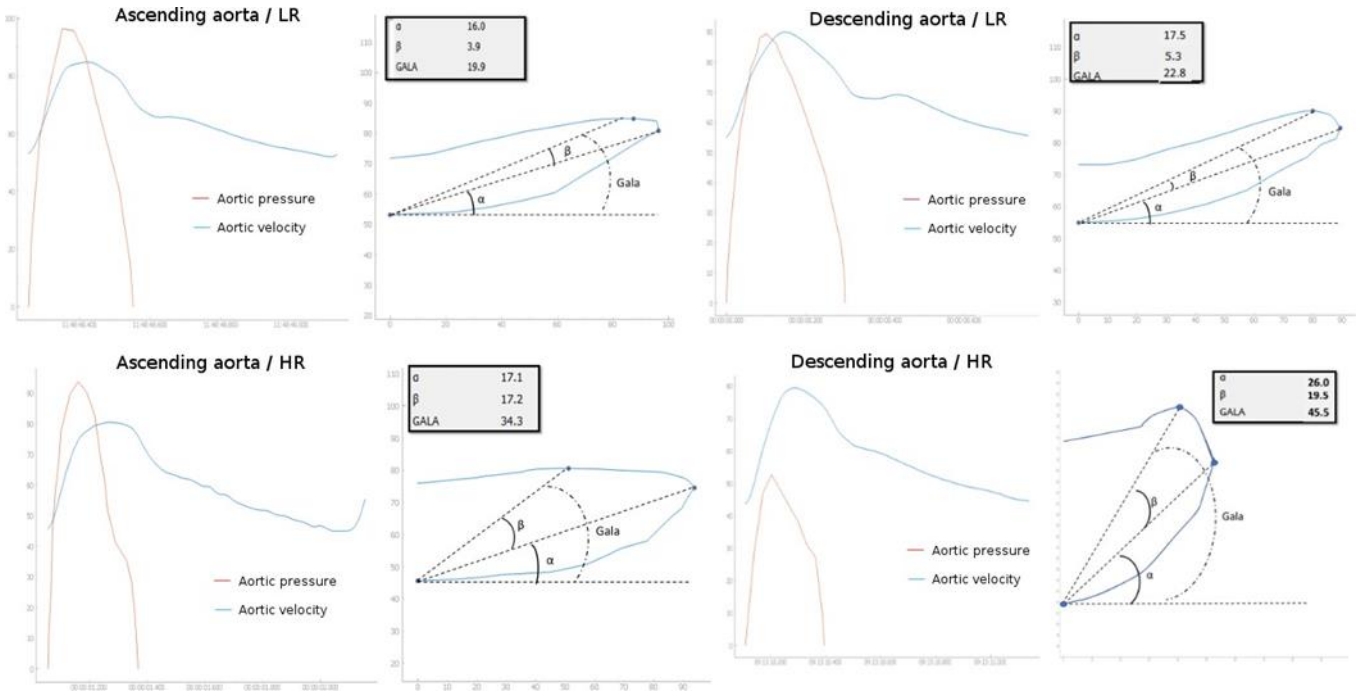
Introduction
Pressure-Velocity (PU) loops obtained in the descending thoracic aorta (PU-loops$_{des}$) could estimate left ventricular afterload with two remarkable angles: β and GALA *(Global Afterload Angle)* [1] .The aim of this study is to compare PU-loops measured in the ascending aorta (PU-loops$_{asc}$) versus PU-loops$_{des}$.

Methods
This study was conducted in patients scheduled for elective interventional neuroradiology. During the procedure, we measured pressures at two different sites:
(1) in the ascending aorta where we obtained a transthoracic echocardiogram (TEE) concomitantly to measure ascending aortic blood velocity, (2) in the descending thoracic aorta where blood velocity was obtained using a trans-esophageal Doppler probe. Patients were divided into high risk (HR) and low risk (LR) groups based on their cardiovascular risk factors.

Results
Twenty five patients were included (13 HR, 12 LR). We observed a significant increase in both β and GALA angles between PU-loops$_{asc}$ and PU-loops$_{des}$ (from 7° [0-15] to 13° [5-20] and from 30° [23-37] to 41° [29-54], $p < 0.01$ respectively). This
increase was more marked in the HR group compared to the LR group ($p < 0.05$) (Fig 1). Just like in PU-loops$_{des}$, we found that β and GALA angles in PU-loops$_{asc}$ could also discriminate between LR and HR patients (3° [0.4 - 6] vs 17° [9-25] and 24° [22-26] vs 38° [34-43], $p < 0.01$ respectively).

Conclusion
PU-loops$_{asc}$ had lower β and GALA angles compared to PU-loops$_{des}$. However, GALA could discriminate between high and low cardiovascular risk patients in both sites.



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P145 Measurement of blood pressure dependency of carotid-femoral pulse wave velocity

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Background
Carotid-femoral pulse wave velocity (cfPWV) is predictive of cardiovascular outcomes but clinical interpretation is confounded by blood pressure (BP) interaction. This study proposes a method for PWV pressure dependency measurement suitable for routine clinical or research use.

Methods
Carotid tonometry and thigh-cuff volumetric displacement allowed cfPWV measurement in the seated and supine position. Brachial oscillometry gave systemic BP. Solving simultaneous equations describing the seated and supine measurement gave hydrostatic BP change across the carotid-femoral arterial path and the pressure dependency of cfPWV. Stepwise multiple linear regression quantified the association of pressure dependency of cfPWV with demographic and cardiovascular parameters.

Results
Of 88 subjects (19 to 91 years, 41 female), 4 (4.5%) had an unexpected increase in cfPWV with decreased BP from seated to supine position. Cross-sectional analysis in the remaining cohort showed blood pressure dependency of cfPWV correlated with brachial pulse pressure (β=0.40, p<0.001), diastolic pressure (β=-0.33, p<0.001), gender (β=0.25 for female/male=1/0, p=0.010), and heart rate (β=0.23, p=0.033).
There was no correlation with supine cfPWV nor age. Average pressure dependency of cfPWV was 0.6±0.3 m/s per 10 mmHg (range of 0.09 to 1.5 m/s per 10
mmHg). Average change in transmural BP across the carotid-femoral arterial path was 20±7 mmHg (diastolic BP change 4±7 mmHg; hydrostatic BP change 16±2 mmHg).

Conclusions
Changing from seated to supine position imparts a BP change across the carotid- femoral arterial path, the majority of the effect being hydrostatic. Measuring cfPWV in these two stable BP positions allows calculation of the BP dependency of cfPWV.

P146 Methodological aspects and determinants of hyperemia-mediated slowing in pulse wave velocity: a general population study.

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Background
Recent studies proposed that deceleration in pulse wave velocity (PWV) following hyperemia might reflect arterial distensibility and endothelial function. We therefore investigated methodological aspects and clinical determinants of newly proposed indexes of such flow-mediated slowing (FMS) in a community-based sample.

Methods
In 71 subjects (60.3±13.7 years; 50.7% women), we continuously assessed brachial- radial pulse wave velocity (PWV) using Vicorder® equipment at rest and after 3 or 5 minutes suprasystolic occlusion to induce reactive hyperemia. We calculated the relative change (Δ) in PWV per 30s post-occlusion intervals. We performed stepwise
regression analyses to assess determinants of the PWV response.

Results
The decline in PWV during hyperemia was significantly stronger after 5 minutes of occlusion as compared to 3 minutes (effect sizes for 0-180s intervals: -3.58% to - 10.1%; $P \leq 0.0019$). PWV declined significantly less with higher age during the 0-90s post-occlusion intervals (+1.61 to +3.99%; $P \leq 0.023$). On the other hand, we observed that, after 120s of hyperemic response, ΔPWV remained significantly lower in smokers (-4.28% to -5.37%) and subjects with high mean arterial pressure (-2.14% to -2.23%) and low pulse pressure (+2.06% to +2.07%; $P \leq 0.046$ for all). Hence, compared to non-smoking normotensives, subjects with cardiovascular risk factors exhibited a delayed age-adjusted recovery of PWV after 5 minutes of occlusion ($P \leq 0.039$).

Conclusions
Our findings confirm an occlusion time of 5 minutes for assessment of endothelial function by FMS. Whereas early FMS response might deteriorate with ageing, cardiovascular risk factors such as smoking and hypertension might impair the late recovery of PWV following reactive hyperemia.

Poster Session II – Clinical Aspects

Chair: F Mattace Raso, A Paini

P18 The Association between Metabolic Syndrome components, Arterial Markers of early Atherosclerosis and Left Ventricular Diastolic Dysfunction M

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Background
The aim of the study was to evaluate the relationship between MetS components and arterial stiffness in concert with left ventricular diastolic dysfunction(LVDD) in patients with high risk of cardiovascular disease.

Methods
A study was carried among 436 subjects (aged 53,8±6, 37,2% men) without overt atherosclerotic disease and systolic LV dysfunction. The average of observations was 4,4 years. According to the MetS components (pathologically increased waist circumference– W, increased triglyceride– T, increased fasting plasma glucose– G, low high-density lipoprotein level- H, arterial hypertension– B) patients were divided into the metabolic phenotypes. Arterial stiffness parameters (carotid to femoral pulse wave velocity(cfPW), aortic augmentation index(AIxHR75) were assessed by applanation tonometry. Cardioankle vascular index(CAVI) was calculated using the VaSera VS-1000. Impaired relaxation was described as E/A<1,0 and E/e‘ mean<13. Participants were considered as having pseudonorma/restrictive LVDD if the E/e‘mean ratio was≥13. In case of E/A>1,0 and e‘ septal≥8cm/s and e‘ lateral≥10cm/s diastolic function was interpreted as normal.

Results
Most of study subjects had LVDD at the first visit (n=358, n=171 with relaxation abnormalities and n=187 with pseudonormalisation). In presented cohort the most common metabolic phenotypes were: WTGHB(n=70), WGB(n=66), WTGB(n=61), WTB(n=46), WTHB(n=30), WGHB(n=27). During the observation period we found significant changes of LV diastolic function distribution between metabolic phenotypes(p<0,001). All patients with WGHB phenotype at first visit had LVDD comparing with other groups. We found significant differences of arterial markers between first and follow up visits- in women (cfPWV 8,70vs 8,94m/s, p<0,001), in man(CAVI 8,05vs 8,45, p<0,001) and in whol cohort (AIxHR75 23,1vs 24,1, p>0,001).

Conclusion
Metabolic phenotype is closely associated with the development of LVDD. Some metabolic phenotypes promote early arterial aging.

P19 Influence of brachial artery stiffness on flow-mediated dilatation in healthy young and older populations M

Aizawa, Kunihiko[1]; Sbragi, Sara[2]; Ramalli, Alessandro[3]; Tortoli, Piero[4]; Casanova, Francesco[1]; Morizzo, Carmela[2]; Thorn, Clare[1]; Shore, Angela[1]; Gates, Phillip[1]; Palombo, Carlo[2]

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Background
Increased brachial artery (BA) stiffness has previously been shown to affect the magnitude of FMD response in patients with high cardiovascular risk. However, it is unclear whether increased BA stiffness explains the diminished FMD response typically observed in a healthy older population. We determined whether BA stiffness would be greater in the older than the young population, and whether it would influence FMD responses in the former.

Methods
Data from 33 young (YNG: 27.5±4.9yrs) and 33 older (OLD: 64.9±3.6yrs) individuals were analysed. FMD was assessed with reactive hyperaemia using Ultrasound Advanced Open Platform (ULA-OP). All acquired raw data were post-processed using custom-designed software to obtain parameters of WSR and diameter. BA stiffness was calculated from BA systolic and diastolic diameters with simultaneous contra-lateral BA blood pressure measurements, and was expressed as pulse wave velocity (PWV) and β-stiffness index.

Results
Both PWV [YNG: 9.5(8.7-10.3) vs OLD: 9.4(8.6-10.2) m/s] and β-stiffness index [YNG: 17.5(14.7-20.2) vs OLD: 16.7(13.9-19.4) au] were similar between populations. In YNG, there was no association between BA stiffness parameters and diameter changes obtained during FMD and nitroglycerin-mediated dilatation assessments. The association was also absent in OLD during either assessment.

Conclusions
These results demonstrate that BA stiffness is not increased in the healthy older population compared to the young counterpart. Furthermore, there is no association between BA stiffness parameters and the FMD response in either population, suggesting that BA stiffness may not influence BA vasodilatory response in healthy adults.

P20 Augmentation index associates with impaired early ventricular ejection M

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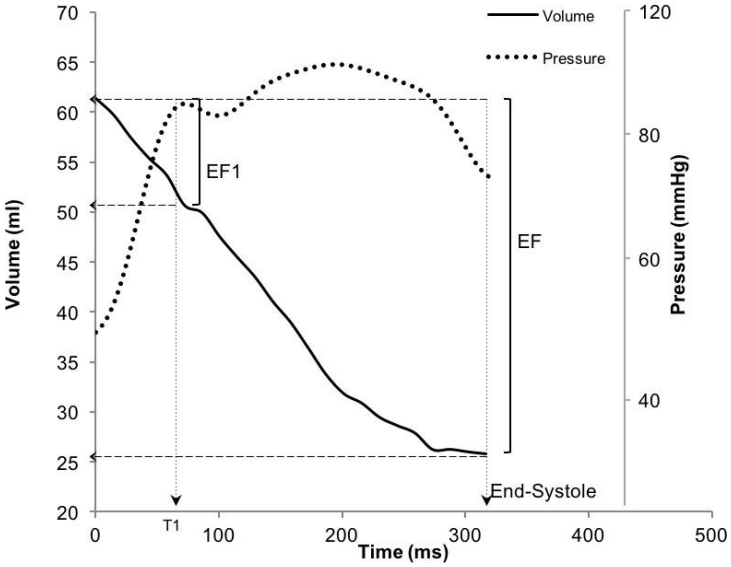
Background
Previously regarded as a measure of pressure wave reflection, central augmentation index (cAI) may be influenced by the pattern of early ventricular ejection. We examined the relationship of cAI to first-phase ejection-fraction (EF1), a measure of ventricular ejection up to the time of the first systolic peak in central pressure in patients with a wide range of cardiac and arterial phenotypes.

Methods
Carotid pressure, obtained by tonometry calibrated from peripheral mean and diastolic blood pressure, was used to calculate augmentation pressure (difference between the second and first systolic peaks of the aortic waveform) and index. Time- resolved LV volumes were obtained by 2D echocardiography. EF1 was defined as the fraction of LV volume ejected from the start of systole to the time of the first systolic peak (T1) on the carotid pressure waveform(Figure1). Aortic arch to abdominal aorta pulse wave velocity (aPWV) was measured by pulsed wave Doppler.



Results
We studied 127 subjects, including healthy subjects (n=44, aged 51.5±13.6years) and patients with hypertension (n=52, 53.6±12.9), severe aortic stenosis (AS, n=10, 73.5±9.6) and Hypertrophic Obstructive Cardiomyopathy (HOCM, n=21, 54.2±12.7). Ejection-fraction (58.7±5.3%) was preserved in all subjects. There was a graded inverse relationship between EF1 and cAI across different disease groups (healthy:

EF1=21.0±1.3%, cAI=22.6±2.5%; hypertension: EF1=17.4±1.0%, cAI=31.7±1.5%; AS: EF1=15.9±2.7%, cAI=36.0±3.8%; HOCM: EF1=23.7±1.3, cAI=-1.4±4.2%). In a multiple linear regression model, cAI was negatively associated with EF1 independent of age, gender, mean arterial pressure, aPWV and disease group (standardized regression coefficient β=-0.422, p=0.003).

Conclusion
In patients with preserved EF, an impairment of early ejection is associated with greater augmentation pressure.

P21 Reduction of cardiac pre-load has antithetical effects on blood pressure and arterial stiffness: is blood pressure the main determinant of within-subject variation in pulse wave velocity? M

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Objective
Blood pressure (BP) is considered the most important determinant of within-subject variation in pulse wave velocity (PWV) and the possibility of altering arterial stiffness independently of BP is still a matter of debate. When investigating acute effects of a reduction in cardiac pre-load, we hypothesised that this would decrease BP and PWV.

Design and methods
Hypertensive patients (mean±SD age 44 ±14 years, n=45) had brachial BP measurements (OMRON), central BP recorded by radial pulse wave analysis (SphygmoCor) and estimation of aortic PWV (aoPWV) by trans-thoracic echocardiography. Carotid-femoral PWV (cfPWV) was also evaluated by SphygmoCor in n=17. Measurements were performed before and after (>5 minutes) supra-diastolic, sub-systolic pressure inflation of thigh cuffs in order to decrease venous return from the lower limbs. Evaluation of inferior vena cava (IVC) diameter was used to assess pre-load.

Results
Leg cuff-inflation was effective in reducing cardiac pre-load (change in IVC diameter (mean±SE) from 1.6±0.4 cm to 1.3±0.4 cm, $p<0.01$) and decreased both brachial and central SBP (-3±0.9 mmHg and -3.6±1.2 mmHg respectively, both $p<0.05$) while change in DBP (0.8±0.9 mmHg) and heart rate (-0.1±0.6 bpm) were not significant.
By contrast, aoPWV increased by 0.8±0.35 m/s ($p<0.01$) and cfPWV by 1.05 ±0.33 m/s ($p=0.014$).

Conclusions
Contrary to our hypothesis, acute reduction of cardiac pre-load significantly decreased BP but had an opposite effect on PWV. This could be mediated by an increase in sympathetic tone triggered by reduction in circulating blood volume; sympathetic tone might affect PWV independently of BP.

P22 Circadian variations in the cardiovascular system M

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Background
Comprehensive information on 24-hour profiles of pulsatile as well as steady-state hemodynamics in humans is not available yet.

Methods
In 693 healthy individuals (352 men) free from antihypertensive drugs, we performed 24-hour blood pressure (BP) monitoring with a validated oscillometric brachial cuff (mobilograph, i.e.m., Stolberg, Germany). Brachial waveforms were acquired and processed with ARCSolver algorithms to derive information on central pressures, wave reflections, stroke volume and systemic vascular resistance. Nighttime/daytime difference (N/D) was defined as nighttime (01.00 - 06.00) minus daytime (09.00 -

21.00) values / daytime values. Patients were categorized as young (Y: 15-40 years; n=187), middle-aged (M: 41-70 years; n=446), and old (O: 71-94 years; n=60).

Results
Averaged 24-hour brachial BP was 123/78 (Y), 127/82 (M), and 126/74 (O) mm Hg. N/D for brachial SBP was -13% (Y), -12% (M), and -5% (O). N/D for heart rate was - 20% (Y), -17% (M), and -15% (O). N/D for central SBP was less pronounced: -4% (Y), -6% (M), and -0% (O).
Brachial pulse pressure (PP) displayed small circadian variations, whereas central PP was higher at nighttime: N/D was 25% (Y), 14% (M), and 17% (O). Consequently, PP amplification was higher at daytime (N/D was -21% (Y), -16% (M), and -12% (O)), and was related to heart rate, age, and gender. Measures of wave reflections were higher at nighttime, with N/D related to age, heart rate, mean pressure, systemic vascular resistance and stroke volume.

Conclusion
The circadian profiles we provide may serve as reference for cardiovascular diseases and drug studies.

P23 Prediction of total and cause-specific mortality incidence as well as cardiovascular morbidity by use of non-invasive measurement of carotid- femoral pulse wave velocity as a measure of arterial stiffness M

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Objective
Arterial stiffness (AS) increases with age and predicts total mortality and total cardiovascular (CV) events. It has also been shown that positive family history (FH+) of cardiometabolic disease influences AS. We aimed to: 1) examine if AS predicts total mortality among elderly subjects, as well as total, fatal, and non-fatal CV events; and 2) to assess if FH+ influences the prediction of AS.

Methods
Participants from the Malmö Diet Cancer CV cohort (MDC-CV; n=3,056, mean age 71 years, 40% men) in Sweden were examined during 2007-2012. AS was measured with carotid-femoral pulse wave velocity (c-f PWV; Sphygmocor®). Follow-up started from date of measurement and ended at death, emigration or on 31st December
2014. Hazard ratios (HRs) with 95% confidence intervals were computed using multivariable Cox and competing risks regression (sub-hazard ratio, SHR) adjusting for age, sex, cardiovascular risk factors, prevalent cardiometabolic diseases and FH+.

Results
c-f PWV (per log-unit) significantly predicted total mortality, HR 2.57 (95%CI: 1.28– 5.16, p=0.008), after full adjustment for risk factors, and HR 3.01 (95%CI: 1.41-6.42) after adding FH. The prediction of CV events was of borderline significance, HR 1.85 (95%CI: 0.91–3.78, p=0.09). FH+ contribution to c-f PWV prediction of non-CV mortality was of borderline significance SHR 2.30 (95%CI: 0.89-5.95, p=0.085).

Conclusion
Arterial stiffness (c-f PWV) predicts total mortality, even adjusted for family history. Thus c-f PWV is a promising risk marker for total mortality, beyond the prediction offered by conventional risk factors.

P24 Sex-specific pulse wave velocity cut-offs improve survival analysis in patients with suspected coronary artery disease

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Objectives
There is evidence for sex and age influences on pulse wave velocity (PWV). Guidelines suggest a sex-independent cut-off for PWV. It is not obvious that an age- and blood-pressure-independent cut-off is suitable in different populations [1, 2].
Thus, the aim is to investigate the suitability of sex-independent cut-offs for risk prediction in a high-risk cohort.

Methods
PWV was measured invasively (invPWV; catheter pullback) and non-invasively (non- invPWV; ARCSolver PWV) for patients with suspected CAD at the hospital in Wels- Grieskirchen (Austria). Patients were grouped in four subgroups based on sex and PWV cut-offs (guidelines and sex-specific ones). A combination of myocardial infarction, death, stroke and cardiovascular revascularization served as primary endpoint. Kaplan-Meier curves, logrank test and hazard-ratios were used for survival analysis and receiver-operating-characteristics (ROC) to determine sex-specific cut- offs.

Results
604 male (61 (11 SD) years) and 324 female (65 (11 SD) years) with a median follow-up of 1576 days and 215 events were included. Logrank test revealed significant differences between Kaplan-Meier curves ($p < 0.001$), but dichotomized PWV remained just discriminative in women, but not men, for invasive and non- invasive recordings. ROC analysis revealed sex-specific cut-offs of 8.5 m/s (men) or
9.6 m/s (women) for invasive and 8.9 m/s (men) or 10.0 m/s (women) for non- invasive recordings. When using these cut-offs, PWV turned out to be discriminative in both sexes (table).

	HR (<=10m/s vs. > 10m/s)	Sex-specific cut-off	HR (<= sex-specific cut-off vs. > sex-specific cut-off)
invPWV			
Male	1.41 [0.94; 2.11]	8.5 m/s	1.64 [1.15; 2.34]
Female	2.46 [1.58; 3.84]	9.6 m/s	3.28 [2.14; 5.03]
non-invPWV			
Male	1.46 [0.99; 2.16]	8.9 m/s	1.73 [1.22; 2.46]
Female	3.20 [2.11; 4.85]	10.0 m/s	3.20 [2.11; 4.85]

Table: Results of survival and ROC analysis for invasive and non-invasive PWV for male and female. Hazard-ratios (HR) are presented with their 95% confidence intervals.

Conclusion
Sex-specific PWV cut-offs improve survival analysis in patients with suspected CAD. Cut-offs seem to be directly dependent on the prevalence of CAD and thus need further investigation.

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P25 Vascular aging is associated with the severity of cerebral white matter lesion load

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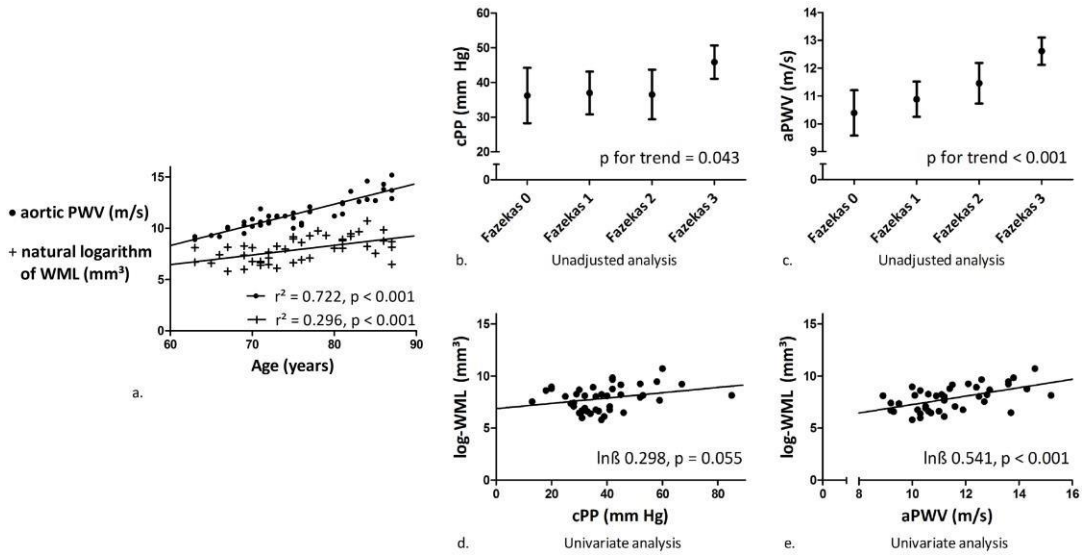
Background
Blood pressure (BP) levels and aortic stiffness are associated with the presence of cerebal small vessel disease, whereas little is known on the possible association of BP levels, aortic stiffness and the severity of cerebral small vessel disease. In a pilot study we investigated whether hemodynamic measures are associated with the presence and severity of cerebral white matter lesion load (WML).

Methods
Fazekas score was used to analyse WML on neuroimaging of 84 persons visiting the Outpatient Geriatric Clinic; an automatic white matter hyperintensity segmentation method was used in a subgroup of 44 MRI-scans to determine the exact volume of WML. Aortic stiffness, measured as aortic pulse wave velocity (aPWV), and BP levels were non-invasively measured by Mobil-o-Graph.

Results
Mean age was 76.6 years. Age was correlated with aPWV ($r^2 = 0.722$, $p<0.001$) and volume of WML ($r^2 = 0.296$, $p<0.001$). aPWV and central pulse pressure levels (cPP) increased with increasing Fazekas score (p for trend <0.001 and 0.043, respectively). After adjustment, higher aPWV was observed in the highest Fazekas category compared to the lowest, although not statically significant (p for trend = 0.151). Both cPP and aPWV were associated with WML volumes in univariate analyses (*ln*β 0.298, p=0.055 and *ln*β 0.541, p<0.001, respectively); in multivariate analyses, estimates were less consistent.



Conclusion
Increased pulse pressure and increased aortic stiffness were associated with the severity of WML, assessed with both Fazekas score and a quantative hyperintenstity segmentation method. Age is highly associated with aortic stiffness and cerebral small vessel disease.

P26 Withdrawn by author

P27 Replaced right hepatic artery and interlobar bridge of liver with unusual arterial supply of IVth segment

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A replaced right hepatic artery (rRHA) arising from the superior mesenteric artery and an interlobar parenchymal bridge over the sagittal fissure of liver have been observed on a 64 year old formalin-fixed male cadaver in the anatomy laboratory.

As we followed a detailed segmental anatomy, encountered an arterial distribution on the segment IV featuring a different pattern from the literature so far. According to our observations, the segment I is supplied by both left (LHA) and middle (MHA) hepatic arteries; the segments II and III are supplied by the LHA while the segment IV is supplied by both the MHA and rRHA.

The segments V-VIII are supplied only by the rRHA. Our case emphasizes the importance of arterial variations of liver once again in terms of the surgical procedures during the liver transplantation, hepatic tumors, and etc.
Our discussion particularly focuses to the arterial supply of the segment IV and possible complications it may cause during/after the liver operations.

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P28 Determinants of arterial stiffness as marker of early vascular aging in physicians population

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Objective
To analyze determinants of arterial stiffness in physician's population.

Methods
Observational multicenter study of doctor's vascular health conducted in 12 Russian cities (VICTORIA study). Demographics; smoking status; anamnesis of arterial hypertension (AH) with/without therapy, medications, established CV, renal diseases, diabetes mellitus; cholesterol and glucose level were registered. Arterial stiffness and vascular age was assessed using BPLab® device with Vasotens® technology (Petr Telegin Company, Nizhny Novgorod, Russia). Arterial stiffness was defined as an elevation of pulse pressure (PP)>60 mmHg, PWV>10 m/s.

Results
464 individuals were included (247 normotensives (mean age 44 yrs) and 237 with AH (mean age 58 yrs)). Mean PP was 46.0± 9.8 mm Hg in normotensive group and
58.6 ± 17.4 mm Hg in group with AH ($p<0.001$). Mean PWVao was 10.9±2.0 m/s and 12.5±2.5 m/s in groups without and with AH, respectively ($p<0.001$). PP>60 mm Hg had 11% subjects without AH and 43% with elevated blood pressure (BP) ($p<0.001$). PWVao >10 m/s had 68% of normotensive subjects and 92% of hypertensive patients ($p<0.001$). PWVao correlated with brachial systolic ($r=0,42$, $p<0.05$) and diastolic BP ($r=0,38$; $p<0.05$), central systolic ($r=0,45$, $p<0.05$) and diastolic BP ($r=0,41$; $p<0.05$), age ($r=0,37$, $p<0.05$), heart rate ($r=0,41$, $p<0.05$). There was association between elevated PWVao and body mass index ($r=0,39$, $p<0.05$). In a multiple linear regression model, independent determinants of PWV were systolic BP ($\beta=0,29$, $p<0.001$), body mass index ($\beta=0,19$, $p<0.001$).

Conclusions
High PWVao measured by BPLab® device with Vasotens® technology is characterized physician's population with and without AH. The main determinants of PWVao are systolic BP and body mass index.

P29 Total longitudinal displacement (tLoD) of the common carotid artery (CCA) does not differ between patients with moderate or high cardiovascular risk (CV) and patients after acute myocardial infarction (AMI)

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Background
Total longitudinal displacement (tLoD) of the common carotid artery (CCA) wall is a novel ultrasound marker of vascular function that can be evaluated using modified speckle tracking techniques. Decreased CCA tLoD has already been shown to be associated with diabetes and was shown to predict one year cardiovascular outcome in patients with suspected coronary artery disease (CAD). The aim of our study was to evaluate if CCA tLoD differ between patients with moderate or high cardiovascular (CV) risk and patients after recent acute myocardial infarction (AMI).

Methods
49 patients (54±6 years) with moderate or high CV risk and 42 patients (58±7 years) after recent AMI were included. All patients were non-diabetic. CCA tLoD was evaluated using GE EchoPAC speckle tracking software and expressed as mean of both sides. Data on systolic blood pressure, total and high density lipoprotein (HDL) cholesterol levels, high sensitivity C-reactive protein (hsCRP) level, smoking status and family history of early CV events was evaluated and assessed for association with CCA tLoD.

Results
tLoD of CCA did not differ between patients with moderate or high CV risk and patients with very high CV risk after MI (0.265±0.128 mm vs. 0.237±0.103 mm, p>0.05). Lower tLoD was associated with lower HDL cholesterol levels (r=0.211, p=0.04) and male gender (0.228±0.1 vs. 0.297±0.134, p=0.01).

Conclusions
tLoD of CCA did not differ between patients with moderate or high CV risk and patients with very high CV risk after AMI. However, lower CCA tLoD was significantly associated with low HDL cholesterol levels and male gender.

P30 The role of novel biomarkers in arterial stiffness, and in predicting further vascular events after TIA and lacunar stroke

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Objective
To explore the role of biomarkers (hsCRP, sRANKL, PRDX1 and EPO) in arterial stiffness and in predicting further vascular events.

Methods
Patients from the ongoing ASIST study each attended a laboratory visit within fourteen days of their diagnosed TIA or lacunar stroke. Arterial stiffness was calculated using cfPWV (carotid-femoral pulse wave velocity) measured with Complior ®Artech, France, and with the CAVI ®Fukuda, Japan (cardio-ankle vascular index) method. Blood samples were taken for ELISA assays. Analysis was completed with SPSS software.

Results
Forty patients were evaluated in this preliminary project (29 male/11 female, mean age 70.7 ± 11.99), with four experiencing a further event during the six month follow up (10%).

All biomarkers and both measurements for arterial stiffness had a higher mean value in patients with a further event (hsCRP 3.89 vs 1.42, P=0.08; EPO 9.06 vs 9.01, P=0.85; sRANKL 0.05 vs 0.03, P=0.31; PRDX1 6.27 vs 6.21, P=0.95; CAVI 11.13 vs
9.69, P=0.15; cfPWV 10.82 vs 10.2, P=0.55), however none were statistically significant.

Levels of PRDX1 were elevated acutely post-event before falling significantly (R=- 0.475, P=0.002), while hsCRP and EPO continued to be elevated at >10 days post- event. In addition, CAVI

correlated closely with hsCRP (R=0.28, P=0.09) and EPO (R=0.29, P=0.08), but cfPWV was not closely related to any of the biomarkers.

Conclusions
This preliminary data suggests that biomarkers, particularly EPO and hsCRP, are more closely related to CAVI than cfPWV. hsCRP was the most relevant as an independent predictive factor for further vascular events.

Poster Session II – Obesity and Diabetes

Chair: P Nilsson, A Solini

P150 Arterial stiffness and progression of cerebral white matter lesions in asymptomatic patients with type 2 diabetes and matched controls: a 5-year cohort study M

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Aim
Stroke is a frequent and feared complication in patients with type 2 diabetes. Arterial stiffness may improve current suboptimal risk prediction of stroke. However, studies in diabetes populations are lacking. We investigated the association between arterial stiffness progression (carotid-femoral pulse wave velocity [PWV]) and the progression of cerebral white matter lesions (WML), a marker of stroke risk, in patients with type 2 diabetes and matched controls.

Methods
In a 5-year follow-up study, data from 49 patients and 58 controls were available for analysis. At baseline, participants had a mean (±SD) age of 59±10 years and patients had a median (range) diabetes duration of 1.8 (1.0-3.2) years. Fifty-two (49%) were males. At both baseline and follow-up, PWV was obtained by tonometry and WML by cerebral T2-FLAIR MRI. WML was assessed by Breteler score, and progression was defined as an upward change in category during follow-up.

Results
Patients with type 2 diabetes had a higher PWV than controls at both baseline (9.2±2.2 vs. 7.9±1.4m/s, p<0.01) and follow-up (9.8±2.4 vs. 8.6±1.9m/s, p=0.01). Breteler scores and WML progression were similar in the two groups (p>0.05). PWV progression was associated with WML progression in the total cohort (adjusted for age, sex, diabetes, baseline PWV and systolic blood pressure progression: OR 1.58 [95%CI: 1.09-2.28], p=0.02). We found no interaction between diabetes and PWV progression on WML progression.

Conclusions
PWV progression is associated with WML progression in patients with type 2 diabetes and healthy controls. PWV candidates as a new risk marker for stroke.

P151 Central pulse pressure is associated with aortic-brachial stiffness mismatch in patients with arterial hypertension and diabetes mellitus M

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[1]RUDN University

Background
Central pulse pressure (PP) is a surrogate measure of arterial stiffness (AS) and a predictor of cardiovascular events in type 2 diabetes mellitus (T2DM). AS gradient reflects the vascular ageing.

The aim of the study
To evaluate the associations between 24-h central PP and parameters of AS in patients with arterial hypertension (AH) and T2DM.

Materials and methods
90 patients with AH and T2DM were included (39%males, mean age 63,8±11,6). Mean office BP was 146±23/86±10mmHg. Median duration of DM was 8,5 years. 24- h peripheral and central BP monitoring was performed (BPLab Vasotens). AS parameters were assessed by applanation tonometry (Sphygmocor, AtCor). AS gradient was calculated as cfPWV/crPWV and its elevation ≥1 was considered as AS mismatch. p<0,05 was considered significant.

Results
Mean central BP was 132±18/79±12 mmHg,cfPWV–10,5±2,4 m/s,crPWV– 8,5±1,4m/s,AS gradient–1,2±0,3. 24-h central BP levels were as follows:132±18/79±12mmHg for 24hBP, 132±18/81±13mmHg for daytime and 129±20/75±11mmHg for nighttime. Mean PP levels were 53±14, 52±14 and 56±15mmHg, respectively. 24-h central PP increase>50 mmHg was observed in 30% patients. These patients were older (67,1±10,5 vs 61,8±11,9 years), had higher median duration of DM (10;IQR 7-15vs5;IQR 0,9-12 years), cfPWV (11,4±1,9vs10,0±2,6 m/s) and stiffness gradient (1,4±0,3 vs 1,2±0,2), p<0,05 for trend. There were significant correlations between 24-h central PP and age (r=0,27) and AS gradient (r=0,32), p<0,05 for trend. No predictors of PP elevation were found.

Conclusions
In diabetic patients with AH increase of central PP is associated with aortic-brachial stiffness mismatch. This finding confirms its importance as a marker of vascular ageing in this patient population.

P152 Microalbuminuria in newly diagnosed diabetes mellitus: not only about blood pressure or arterial stiffness M

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Background
Diabetes mellitus (DM) and hypertension (EH) are both associated with micro- and macro-vascular damage. Microalbuminuria is a recognized marker of sub-clinical target organ damage in both DM and EH. However, it's determinants in newly diagnosed DM with or without EH remain unclear.

Methods
We enrolled consecutive newly diagnosed DM patients, recording history, demographics, renal, lipid and glycemic profile, office and ambulatory blood pressure, macro-(pulse-wave velocity/PWV) and micro-vascular (microalbuminuria in 24-hour urine) damage and subclinical atherosclerosis (intima-media thickness).

Results
We studied 65 DM patients (40 male: 25 female, aged 57±11 years), with a median duration from diagnosis of 2 weeks. Their fasting glucose was 121.5 (IR: 36) mg/dl, HbA1c: 7.47 (IR:2)%. Among them, 26 had already been diagnosed with EH (median duration of 8 (IR: 8) years), while 17 were diagnosed with EH at the time of DM diagnosis. No difference was observed between the two groups, except for significantly higher office and ambulatory BP and PWV in the newly diagnosed EH patients. Microalbuminuria was associated with fasting glucose (p=0.04), HbA1c (p=0.002), serum creatinine

(p=0.035), glomerular filtration rate (GFR) (p=0.002), office systolic (p=0.009) and diastolic (p=0.026) BP and PWV (p=0.031). In the multivariate analysis, HbA1c (beta=0.351, p=0.015) was the only determinant of microalbuminuria.

Conclusions
Our study indicates that hyperglycaemia has a significant impact on microalbuminuria even in patients with newly diagnosed DM and EH (either newly diagnosed with high BP values or longer lasting), emphasizing on the need of early and effective glycemic control.

P153 Marker of type VI collagen formation (Pro-C6) is associated with higher arterial stiffness in type 1 diabetes M

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Aim
Arterial stiffening reflects fragmentation and loss of elastin fibers and accumulation of stiffer collagen fibers in the media of large arteries. We evaluated associations between carotid-femoral pulse wave velocity (cfPWV) and a marker of collagen type VI formation (Pro-C6) and a marker of collagen type III degradation (C3M) in type 1 diabetes.

Methods
Serum and urinary level of Pro-C6 and C3M was measured with ELISA in 634 patients with type 1 diabetes. cfPWV was assessed by the SphygmoCor device. We applied unadjusted and adjusted linear regression analyses. Adjustment included sex, age, mean arterial pressure, LDL cholesterol, smoking, HbA_{1c}, eGFR and
urinary albumin excretion rate. To adjust for urine output levels, the urinary markers were normalized for urinary creatinine.

Results
Of the 634 patients, 349 (55%) were male, mean±SD age was 54.6±12.6 years and cfPWV 10.4±3.3 m/s.
Higher serum and urinary level of Pro-C6 was associated with higher cfPWV in unadjusted models (p≤0.039), after adjustment only higher serum level remained significantly associated with higher cfPWV (β estimate per doubling: 0.47±0.21; p=0.028).
Lower urinary level of C3M was associated with higher cfPWV in the unadjusted model (p<0.001), but significance was lost after adjustment (p=0.44). Higher serum level of C3M was associated with higher cfPWV in the unadjusted model (p=0.002), but significance was lost after adjustment (p=0.34).

Conclusion
In type 1 diabetes, higher serum levels of Pro-C6, a marker of collagen type VI formation, was associated with increased arterial stiffness. This observation could introduce a new target for therapeutic intervention.

P154 Vascular structure and function in relation to weight excess and blood pressure in a sample of obese children M

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Objective
To investigate the influence of weight excess and blood pressure (BP) on vascular structure and function in a sample of obese children.

Methods
We measured office and ambulatory BP (ABPM), carotid intima-media thickness (cIMT), endothelial function by the Flow Mediated Dilation (FMD) technique, carotid distensibility (cDC) (ultrasonograph: LogiQ P5 Pro; software: Multimedia Video Engine II, DSP Lab, Pisa CNR, Italy) (1) and stiffness index (SI) by photopletismography (Pulce Trace PT1000, MicroMedical Ltd, UK) (2) in overweight and obese children (BMI>90th percentile for sex and age).

Results
Seventy children with weight excess were enrolled (age 11.5 ± 2.4 years; female n: 30). cDC showed inverse correlation with BMI and waist circumference ($r_{Spearman}$= -0.403 and r_s= -0.346, respectively), 24h-SBP (r_s=-0.449) and nighttime-SBP (r_s=- 0.490). SI inversely correlated with BMI (r_s=-0.359) and waist/height ratio (r_s=-0.303). When comparing normotensive and hypertensive children, as defined on the basis of the ABPM, no significant differences in vascular tests were found, although cDC tended to be lower in hypertensive. In normotensive subjects (n: 53) cIMT directly correlated with nighttime-SBP and DBP. Most of the correlations remained significant after adjustment for age, sex, BMI and BP.

Conclusions
These data suggest that arterial elasticity is negatively affected by weight excess and 24h-BP levels even in childhood. In the normotensive subgroup it is detectable an effect of BP also on arterial structure

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P155 Correlation of soluble receptor for advanced glycation end products and S100-A1 on Arterial stiffness in normotensive patients with diabetes

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Background

Accumulation of advanced glycation end products (AGEs) are involved in several pathophysiological processes in the vessel wall, that may cause premature atherosclerosis and arterial stiffening (1). A soluble form of RAGE (sRAGE), which is a splice variant of full-length RAGE has been considered to be protective against diseases originating from RAGE activation since sRAGE can bind and sequester RAGE ligands and reduce RAGE activation (2). S100A1 is the most abundant calcium-binding protein in myocardial tissue and is a major determinant of cardiac function. This circulating ligand of the RAGE is known as a pro-inflammatory factor in diabetes. Aberrant expression levels of S100A1 surfaced as molecular key defects, driving the pathogenesis of cardiovascular diseases (3).

Objective

This study was design to explore the relationship between serum levels of sRAGE and S100A1 on arterial stiffness in non-hypertensive patients with diabetes.

Methods

Using a cross-sectional design, a total of 20 non-hypertensive patients with diabetes were recruited. A fasting blood sample, medical history and arterial stiffness parameters were collected.

Results

In bivariate analysis, sRAGE positively correlated with time evolution of diabetes ($r=0.503$, $p<0.024$) and negatively correlated with systolic ($r=-0.457$, $p=0.043$) and diastolic blood pressure ($r=-0.527$, $p=0.017$). S100A1 positively correlated with creatinine ($r=0.724$, $p<0.000$) and negatively correlated with peripheral and central hemodynamics, including augmentation index ($r=-0.469$, $p=0.037$), as shown in table 2.

Table 2. Correlation of sRAGE with metabolic, hemodynamic and arterial stiffening variables

Variables	r Spearman	p- value
T2DM time evolution	-0.203	0.309
HbA1c	-0.082	0.780
Creatinine	0.724	0.000*
Systolic Blood pressure	-0.487	0.029*
Diastolic Blood pressure	-0.456	0.043*
Pulse pressure	-0.476	0.034*
Arterial Mean Pressure	-0.437	0.054*
Central Systolic Blood Pressure	-0.452	0.045*
Central Diastolic Blood pressure	-0.448	0.047*
Aortic Pulse Wave velocity	-0.361	0.118
Central pulse pressure	-0.035	0.041*
Aortic Augmentation Index	-0.469	0.037*

Abreviation: sRAGE, soluble receptor for advanced glycation end products; T2DM, type 2 diabetes mellitus

Conclusion

This study shows a significant correlation of serum sRAGE and S100-A1 on peripheral and central hemodynamics in non-hypertensive diabetic patients.

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P156 Duration of diabetes mellitus is a significant predictor of arterial stiffness in patients with arterial hypertension and type 2 diabetes mellitus

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Background
Diabetic complications increase with disease duration but little is known about the relationships between aortic stiffness and diabetes duration.
Aim: to assess associations of diabetes mellitus (DM) duration and parameters of arterial stiffness in patients with arterial hypertension (AH) and T2DM.

Methods
90 patients with AH and T2DM were included (39%males, mean age63,8±11,6 years, 44%smokers). Mean office BP was 146±23/86±10mmHg. All patients received combined AHT, target BP<140/85 mmHg was achieved in 52,7% of patients. Median duration of DM was 8,5 years (IQR 2;13 years), mean glucose was 8,0±2,4 mmol/l, mean HbA1c 9,2±2,0%. BP was measured with a validated oscillometric device.
Parameters of arterial stiffness were assessed by applanation tonometry, cardio- ankle vascular index (CAVI) and vascular age were measured (VaSera 1500). p<0,05 was considered significant.

Results
Mean central BP was 132±18/79±12 mmHg, mean cfPWV–10,5±2,4 m/s, mean R- CAVI-8,8±1,9, L-CAVI-8,9±1,8. Further analysis was performed in subgroups according to tertiles of DM duration (G1<4 years (n=31), G2–4-10 years (n=30), G3>10 years (n=29)). Patients in G3 were older (69,5±11,1vs62,1±11,2vs 60,0±10,8 years), had higher vascular age (73,8±9,0vs68,6±11,8vs64,5±13,4 years) and R- CAVI (9,3±1,9vs9,0±1,8vs8,1±1,9); p<0,05 for trend. Patients from G3 and G2 had the highest level of cfPWV compared to G1 (11,0±2,0 and 11,4±2,4vs9,1±2,4 m/s,p=0,0009). There were significant correlations between duration of DM and age (r=0,35), vascular age (r=0,30), creatinine (r=0,23), cfPWV (r=0,34), and R-CAVI (r=0,3). Only age and DM duration were predictors of PWV increase (β=0,3,p=0,02 and β=0,2,p=0,04,respectively).

Conclusions
In diabetic patients, aortic stiffness is strictly correlated with diabetes duration, independently of blood pressure level and diabetes control.

P157 Retinal arteriolar function, endothelial dysfunction and arterial stiffness in patients with type 2 diabetes M

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Background
Crosstalk between large and small arteries has been suggested to partake in the microvascular complication development in patients with type 2 diabetes mellitus (T2DM). Yet, data are scarce. In the present study, we aimed to elucidate the crosstalk between large and small arteries in T2DM.

Methods
Twenty patients with T2DM and 20 sex- and age matched controls were included. Arterial stiffness was assessed by carotid-femoral Pulse Wave Velocity (cfPWV) using the SphygmoCor. Endothelial

function was assessed using EndoPAT. Retinal blood supply regulation was examined by retinal arteriolar diameter change during i) exposure to flickering lights, ii) isometric exercise (hand-weight lifting), and iii) a combined stimulus of i)+ii) using the Retinal Vessel Analyzer (RVA).

Results
T2DM patients had higher cfPWV than controls (9.3 ± 1.8 m/s vs. 8.3 ± 2.2 m/s, p = .049). No group difference was observed in endothelial function (0.71 ± 0.30 vs. 0.81 ± 0.30, p = .32) or in response to intervention with flicker, exercise or the combination (all p > 0.05). Endothelial function was associated with mean arteriolar diameter change for the combination intervention (Beta = 0.033 [0.0013;0.064], p = .042) in patients and controls.
No association was observed between cfPWV and retinal arteriolar %-diameter change in patients or controls.

Conclusion
Peripheral endothelial function was associated with retinal arteriolar diameter change. Our findings may indicate a contribution of macro-microvascular crosstalk in diabetes complication development.

P158 Association between ambulatory arterial stiffness index, markers of blood pressure variability and indices of subclinical vascular damage in obese children

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Objective
Ambulatory Arterial Stiffness Index (AASI) and symmetric AASI (sAASI) have been proposed as indices of arterial stiffness obtained by 24-hour ambulatory blood pressure monitoring (ABPM). ABPM allows the analysis of indices of BP variability like day and night SD, BP dipping, weighted 24-h SD (wSD), average real variability (ARV). Aim of the present study was to address the relationship between these indices and other markers of vascular subclinical damage in children.

Design and method
45 obese children were included. Children underwent vascular measurements, including: (i) office and 24-hour ambulatory BP; (ii) brachial flow-mediated dilatation (FMD), carotid intima media thickness (cIMT), and distensibility (cDC); (iii) systemic arterial stiffness (SIDVP). From ABPM we calculate AASI, sAASI, ARV, SD, SD, systolic and diastolic dipping and wSD.

Results
ARV showed a significant correlation with SIDVP (r=0.379; p=0.023). AASI but not sAASI correlated with FMD (r=0.361; p=0.031). In the population divided in hypertensive (n=11)/normotensive (n=34), ARV was associated with SIDVP only in normotensive (r=0.446; p=0.015). In normotensive, z score-BMI was correlated with both sAASI and wSD (respectively 0.340; p=0.049 and 0.423; p=0.014), wSD correlated with FMD (r=0.384; p=0.048); in hypertensive children, ARV correlated with FMD (r=0.828; p=0.011; rspearman=0.738; p=0.037). No indices of BP variability correlated with cIMT or cDC.

Conclusions
BP variability, in particular ARV, shows a correlation with systemic but not local vascular stiffness in a sample of obese children, suggesting a relation between daily BP variability and arterial elastic properties. Further studies, especially perspective ones, are needed to clarify the pathophysiological significance of these relations.

P159 Association between pulse wave velocity and apnea-hyoppnea index in patients with type 2 diabetes and obstructive sleep apnea

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Introduction
Obstructive sleep apnea (OSA) is associated with increased cardiovascular (CV) risk. OSA is highly prevalent among patients with type-2 diabetes (T2D).
Patients with T2D have increased risk of cardiovascular events, and have an increased aortic stiffness.
Continuous Positive Airway Pressure (CPAP) treatment reduces severity of OSA, but whether it reduces CV risk remains unclear. One randomized trial with CPAP intervention and pulse wave velocity (PWV) as endpoint has shown a significant reduction in PWV after four months, in non-diabetic patients. The effect on patients with diabetes remains unknown.

Aim
Investigate the effects of CPAP treatment on PWV in patients with T2D and newly diagnosed OSA. Furthermore, investigate the relationship between PWV and severity of OSA.

Method
A randomized, controlled, multicenter study. 70 patients with T2D and newly diagnosed OSA randomized to: CPAP treatment or a control group. Data will be collected at baseline, 4 and 12 weeks. PWV was measured using SphygmoCor (AtCor Medical, Sydney, Australia) and AHI measured using ApneaLink (ResMed, Poway, CA, USA). Relationship between PWV and AHI was evaluated at baseline.

Results
Baseline data from the first 21 patients showed mean age 63 years (±8.1), mean systolic blood pressure (BP) was 134 (±12.5) mmHg, mean AHI was 30.2 (±12.4) and mean PWV was 11.6 (±1.9) m/s.
AHI was associated with PWV in multivariate analysis with adjustment for age and systolic BP, beta-coefficient 0.08, p=0.029.

Conclusion
At baseline PWV and AHI were correlated. Progression of the study will reveal if CPAP treatment can lower PWV in this cohort.

P160 Vascular abnormalities and haemodynamic pattern in obese young adults

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Background
Obesity is linked to a higher prevalence of risk factors, metabolic and inflammatory pathways conducting to increased vascular disease and CV risk.

Objective
To assess vascular disarrangements and haemodynamic patterns in obese young subjects (O) compared with matched lean (L) controls, using non invasive methods.

Methods
From the database of our Non Invasive Vascular Lab with 3964 first evaluated patients, we performed a case control study with 363 sujects, 268 obese and 95 lean, age and sex matched controls. We measured IMT, Plaque analysis, PWV, Endothelial Function (EF) and arterial stiffness (CAP and Aix) (AS) using an oscillometric device (Arteriograph, Tensiomed. Hungary®) and non invasive haemodynamic evaluation using impedance cardiography (Z Logic Exxer®).

Results
Age(O 42.5+5; L 43.5+11) and sex %(O 80.6%;L 78%) were matched.

BMI (O 33.5+3.3 L 25+1.1Kg/m2), waist (O110.4+7.5; L 91.2+6.1cm) and BP (SBP O 139.8+16.8; L119+8.8 and DBP O 89+3.9; L 74.3+8 mmHg) were higher in O ($p<0.001$).CV Risk Factors in O: HTN 68% DLP 59.7% SMKG 24.2% DBT2 7.8%
SED 72.4%.The % of abnormalities in IMT (O/L : 65.8/25.3%), Plaques (75.6/38.9%), EF (57.5/33.7%)and PWV (41.4/17.9%) were higher in O ($p<0.001$). Central and Peripheral PP were higher in O but not Aix. CI was significantly lower and PVRI and Thoracic Fluid content higher in O.

Conclusion
Young obese patients present a higher prevalence of vascular disarrangements either structural and functional and a haemodynamic pattern of high peripheral resistance with volume expansion that may explain the role of this condition as a CV risk factor.

P161 Roles of angiopoietins 1 and 2 on arterial function during a treatment trial in people with or at risk of diabetes

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Background/ Objective
Vascular growth factors angiopoietin-1 (Ang1) and -2 (Ang2) regulate vascular permeability and inflammation, Ang2 likely as Ang1's selective antagonist. Their role before or in type 2 diabetes (pre-&T2D) is unknown. We hypothesised that higher circulating Ang1 and lower Ang2 (=lower Ang2/1 ratios) would be linked to increased arterial stiffness *and its change* over the trial, independent of blood pressure (BP).

Methods
ELISA assays were performed from 60 participants with all time-points of plasma samples from 'VaSera', a trial of single-centre, double-blind, parallel, randomised, controlled, 2x2 factorial design. Interventions were spironolactone and beetroot juice, a NO^{3-} donor, with doxazosin and placebo juice respectively to control for BP change (Δ) over the trial. Vascular measurements were aortic pulse wave velocity (aPWV), cardiac-ankle pulse wave velocity (CAVI), analysed by multiple regression adjusted for baseline BP and ΔBP over 6 months.

Results
Baseline Ang1 was positively while higher baseline Ang2 was negatively associated with baseline aoPWV at (ß=0.37, p=0.01; ß=-0.27, p=0.047, respectively), independent of BP, BMI and DM status, so baseline r= -0.45 for the Ang2:1 ratio with aPWV, and r=0.39 for ΔaPWV over the trial. Higher baseline Ang1 independently predicted decreased aoPWV over 6 months (ß=- 0.44m/sec per ng/ml,

p=0.006). Angiopoietin concentrations were not associated with CAVI or BP.

Conclusions
Angiopoietins were related to baseline aPWV, independently of BP, and to ΔaPWV over the trial, also independent of BP change, but were unrelated to CAVI or BP. Monitoring and manipulating Angiopoietins may help arterial health in pre-&T2DM.

Poster Session II – Special Populations

Chair: L Van Bortel, J Sharman

P182 Arteries in patients with Huntington's disease M

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Background
Huntington's disease (HD) is a neurodegenerative disorder leading to the progressive death of neurons in various brain regions. Although it is a disease of the central nervous system (CNS), mortality surveys indicate that heart disease is one of the mayor causes of death in HD patients. The mechanisms of cardiac pathophysiology of the disease remain unknown. It might be a consequence of altered activity of autonomic nervous system as part of the CNS.

Methods
Our study evaluated global risk factors for coronary heart disease (CHD), structure and function of precerebral arteries in 41 HD subjects and 41 matched controls. HD subjects were divided into groups by the United Huntington disease rating scale (presymptomatic-PHD, early-EHD, midstage-MHD and late-LHD). CHD risk factors assessment and Doppler examination of precerebral arteries were performed, including measurements of the carotid artery intima-media thickness (IMT), and parameters indicating local carotid artery distensibility (stiffness index β, pulse wave velocity, pressure strain elasticity module and carotid artery compliance).

Results
In the HD and controls we identified a comparable number of non-obstructive plaques (<50% lumen narrowing). No obstructive plaques (>50% lumen narrowing) were found in patients or controls. There was significantly increased IMT in MHD patients. In PHD and EHD the parameters of arterial stiffness were significantly higher and the carotid artery compliance was significantly lower.

Conclusions
Our results reveal functional vascular pathology in PHD, EHD, and MHD. Precerebral arteries dysfunction in HD therefore appears to be mostly functional and in agreement with autonomic nervous system dysfunction in HD.

P183 Increased arterial stiffness is associated with poorer left ventricular structure and function in adolescence M

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Introduction
Increased arterial stiffness (AS) in adults causes increased left ventricular (LV) afterload, putting additional strain on the heart. Long-term, this can lead to an adverse cardiovascular phenotype and AS has been found to be a determinant of CVD, independent of traditional cardiovascular risk factors. However, limited evidence exists for this association in children and adolescents.

Methods
1625 young adults (age 17y; 46% male) from the Avon Longitudinal Study of Parents and Children (ALSPAC), a UK based birth cohort, underwent echocardiography and carotid-to-femoral pulse wave velocity (PWV) measures. Linear regression was used to investigate associations between PWV and LV structure and function, including LV mass, relative wall thickness (RWT), left atrial diameter (LAD), mitral inflow (E:A), midwall fractional shortening (MFS) and tissue Doppler peak systolic velocity (s').

Results
Elevated PWV was associated with increased LV mass and RWT and inversely associated with E:A and MFS (Table 1). Adjustment for age and sex attenuated the association with LV mass. Further adjustment for body mass index (BMI), systolic blood pressure (SBP), alcohol, smoking and socioeconomic status (SES) attenuated the association with RWT, whilst the associations with E:A and MFS remained.

Table 1	Unadjusted		Age and sex adjusted		Age, sex, BMI, SBP, alcohol, smoking, SES adjusted	
	Coefficient±SE	P value	Coefficient±SE	P value	Coefficient±SE	P value
LV mass$^{2.7}$ (g/m$^{2.7}$)	0.55±0.21	0.009	-0.066±0.225	0.768	-0.123±0.225	0.584
RWT	0.007±0.002	<0.001	0.008±0.002	<0.001	0.005±0.00	0.069
LAD (cm)	-0.004±0.015	0.784	-0.017±0.015	0.268	-0.010±0.016	0.516
E:A	-0.054±0.014	<0.001	-0.073±0.015	<0.001	-0.067±0.019	<0.001
MFS (%)	-0.40±0.079	<0.001	-0.246±0.085	0.004	-0.232±0.1	0.022
s' (cm/s)	0.078±0.05	0.138	0.004±0.057	0.937	-0.038±0.067	0.567

Conclusion
Increased AS is already associated with poorer measures of LV structure and function in adolescence. Adjustment for potential confounders did not substantially attenuate these associations with LV function.

P184 Increased arterial stiffness is associated with high inflammatory activity in rheumatoid arthritis M

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Background
Patients with rheumatoid arthritis (RA) have a high cardiovascular (CV) risk. Relationships between inflammation and arterial stiffness (AS) in patients with RA are not well understood.

Aim
To evaluate parameters of AS and their associations with inflammation in patients with RA.

Methods
62 patients with RA without known CVD were examined (73%females, age 58,5±15,4 years,13%smokers, 61%with AH). Median duration of RA was 8 years (IQR 3-17).
Median hsCRP 12,1 mg/dl (IQR 2,2;23,4), median rheumatoid factor (RF) 32,5 IU/ml (IQR 8,3;173 IU/ml). All patients received disease-modifying antirheumatic drugs.
Median duration of AH 6,1 years (IQR 0-10 years). Parameters of AS were assessed by applanation tonometry. Cardio-ankle vascular index (CAVI) and vascular age were measured by VaSera 1500. PWV>10,0 m/s and CAVI>9,0 were considered as AS increase. $p<0.05$ was considered significant.

Results
Mean PWV was 9,3±3,2 m/s. PWV>10m/s was observed in 32,3% patients, CAVI>9,0 in 25,8%. Patients with PWV>10m/s were older (69,8±8,5vs53,2±15,1 years), had higher BMI (29,3±6,5vs24,7±4,8 kg/m^2), duration of AH (median 11,5 [IQR 5,5;17] vs 0 [IQR 0;5] years), higher SBP levels (144±20vs123±14mmHg),
higher levels of hs-CRP (median 22 [IQR 13,3;60] vs 6,7 [IQR 1,6;17,2]mg/dl), higher CAVI (9,5±1,1 vs 7,6±1,4), vascular age (71±8,4 vs 53,4±17,5 years). There were positive correlations between PWV and age (r=0,7), BMI (r=0,4), SBP (r=0,6), hs- CRP (r=0,3), vascular age (r=0,6). Multiple regression analysis confirmed that AH duration (β=0,2,p=0.03), SBP (β=0,6,p<0.0001) and hs-CRP (β=0,3,p=0.000009)
were independent predictors of AS increase.

Conclusion
Elevation of hsCRP as well as other traditional risk factors is an independent predictor of PWV increase in patients with RA.

P185 Cardio-ankle vascular index and plasma levels of leptin and adiponectin in patients with systemic lupus erythematosus

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Objective
Systemic lupus erythematosus (SLE) is a chronic inflammatory disease associated with vascular derangement [1]. Leptin and adiponectin are adipokines with immunomodulatory and vascular functions [2]. We studied the association between arterial stiffness and plasma leptin and adiponectin levels in SLE patients in Ghana.

Methods
In a case control design involving 80 SLE patients and 90 non-SLE controls, arterial stiffness was assessed by cardio-ankle vascular index (CAVI) and heart-ankle pulse wave velocity (haPWV) using Vasera 1500N. Circulating levels of leptin, adiponectin, insulin and C-reactive protein (CRP) were measured by ELISA.

Results
Compared to non-SLE controls, SLE patients had higher levels of CAVI (7.3±1.1 vs 6.1±1, p<0.001), haPWV (7.7±1.3 vs 6.5±0.8 m/s, p=<0.001), insulin [76.8 (45.9 – 184.8) vs 39.8 (22.9 – 86.3) pmol/ml, p=0.007], leptin [856.1 (364.8 – 1509.3) vs 426.7 (426.8 (84.7 – 1178.7) ng/ml, p=0.039], adiponectin [1.1 (0.8 – 2.3) vs 1.6 (1.3 – 2.6) ng/ml, p=0.039] and CRP [1.6 (0.8 – 2.2) vs 0.9 (0.6 – 1.2) mg/ml, p=0.021]. In a partial correlation analysis with adjustment for age and BMI, CAVI was associated with leptin (r=0.21, p=0.031), CRP (r=2.9, p<0.001) and insulin (r=0.18, p=0.04), but not adiponectin (r=-0.15, p=0.068).

Conclusion
In our study population, SLE patients have higher arterial stiffness, associated with low-grade inflammation and deranged circulating adipokine levels.

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P186 Impact of Obesity on Vascular Structure and Function in Individuals with Multiple Sclerosis M

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Background
Cardiovascular disease is a leading cause of disease progression and death in multiple sclerosis (MS). Obesity has a negative impact on vascular structure and function, but whether this contributes to worse vascular function similarly in individuals with MS and controls is unknown.

Aim
To investigate the impact of obesity on vascular function and structure in a group with MS.

Methods
In a sample of n=133 participants (MS: n=89, control n=44), height and weight were measured to calculate BMI. After a 10 minute rest in the supine position, resting heart rate (HR) and brachial blood pressure (BP) were collected. Augmentation index (AIX), HR normalized AIX (AIX@HR75) and pulse wave velocity (PWV) and subendocardial viability ratio (SEVR) were measured with applanation tonometry.
Carotid intima-media thickness (IMT) and beta-stiffness (beta) were measured with carotid ultrasound, and Forearm Blood Flow (FBF Baseline, Peak and Area Under the Curve (AUC)) was measured with strain gauge plethysmography. Data were analyzed with multiple linear regression analyses with group, sex, BMI and GroupxBMI as independent variables.

Results
Higher BMI correlated with higher HR and PWV in both groups. In the MS group however, a higher BMI was also correlated with worse outcomes on the SEVR, FBF Baseline, Peak and AUC.

Outcome variables	Standardized beta[1]				Adjusted R^2
	Group	Sex	BMI	Grp x BMI	
HR rest	**1.081***	0.005	**0.520***	-0.944	0.11
AIX	-0.019	**-0.523***	0.040	0.045	0.26
AIX@HR75	0.341	**-0.536***	0.235	-0.270	0.32
SEVR	**-1.292***	**0.175***	**-0.565***	**1.090***	0.22
PWVc	0.001	-0.003	**0.321***	0.120	0.12
PWVc/MAP	0.324	-0.126	0.278	-0.122	0.11
IMT	0.715	0.164	0.385	-0.511	0.12
FBF Baseline	0.432	0.070	**0.326***	**-1.090***	0.33
FBF Peak	0.580	**0.318***	0.152	**-1.035***	0.35
FBF AUC	0.746	**0.230***	0.316	**-1.174***	0.21

[1] Group (0=control, 1=multiple sclerosis), Sex (1=Female, 2=Male)

* ($p<0.05$)

Conclusions

Having a higher BMI contributes even more to a worse vascular profile in MS patients than in controls, suggesting that reducing overweight and obesity in the MS population will benefit their vascular structure and function.

P187 In severe aortic stenosis, decreased systemic vascular resistance is associated with a larger, thicker walled ventricle except for the septum M

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Background

The ventricle in aortic stenosis (AS) is influenced by both valvular and vascular factors. The importance of afterload on left ventricular (LV) remodeling is not completely understood. Traditional imaging techniques which rely on geometric assumptions may not assess regional remodeling accurately.

Aim

To understand the influence of systemic vascular resistance (SVR), systemic arterial compliance (SAC), valvulo-arterial impedance (Zva) on LV remodeling using a cardiac atlas technique.

Methods

109 patients with symptomatic severe AS awaiting surgical valve replacement (age 69±10y, 60% male, aortic valve area 0.7±0.3cm^2, mean gradient 48±15mmHg) underwent comprehensive clinical, echocardiographic and cardiovascular magnetic resonance (CMR) examinations. SVR, SAC and Zva were calculated as previously published (1)**.** CMR LV short axis steady-state free precession cine images were segmented and co-registered using a cardiac atlas technique (2). Data were extracted and analysed using mass-univariate 3D regression modeling adjusted for age, sex, and height and accounting for multiple testing, presented as standardized *ß.*

Results

Lower SVR correlated with increased wall thickness and larger cavity volume. SVR related changes were more prominent in the lateral wall (*ß* -0.3 to -0.6, *p=0.04*), with no discernable influence on the septum (Figure 1). With lower SVR, LV cavity enlargement was directed away from the septum (*ß* -0.17 to -0.56*, p=0.002)*. There was no influence of SAC or Zva on 3D parameters.

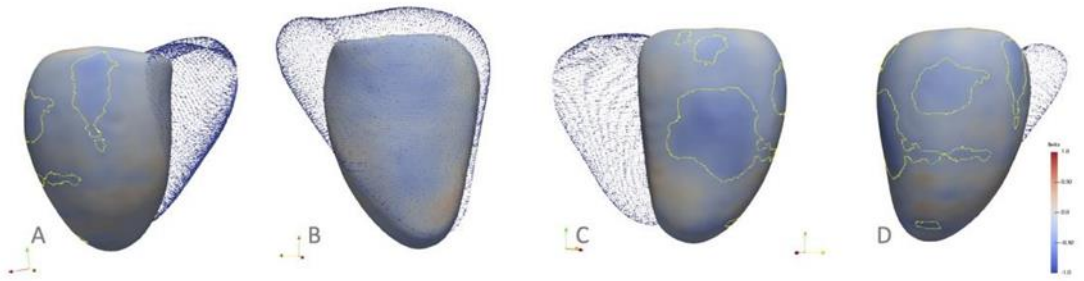

Figure 1 Mass-univariate 3D regression maps relating wall thickness and systemic vascular resistance over the left ventricle, adjusted for age, sex and height. Yellow line encloses areas with p values < 0.05. There is a negative correlation between SVR and wall thickness, sparing the septum(B). SVR= (80 * Mean Arterial Pressure(MAP))/Cardiac Output.

Conclusion

In severe AS there is an association between lower SVR and a larger, thicker walled ventricle except for the septum. The use of a cardiac atlas in aortic stenosis may offer new insights into regional LV remodeling.

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P188 Effects of radiotherapy on large vessels in hodgkin lymphoma survivors M

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New chemotherapeutic drugs and radiation therapy have significantly improved cancer patient's survival, although the cardiovascular(CV)side effects of cancer treatment are increasingly important. In previous studies, an increased risk of cerebrovascular complications such as stroke and transient ischemic attack was described in patients undergoing neck radiotherapy.

Aim

To evaluate vascular carotid structural (IMT, plaque) and functional (carotid stiffness) damage, and changes in arterial stiffness (Carotido-femoral pulse wave velocity;cf- PWV)in Hodgkin Lymphoma survivors previously treated with radiotherapy.

Patients and Methods

We enrolled206 Hodgkin lymphoma survivors(mean age 54±14years, 51%males,mean follow-up of9±6years).CV risk factors were investigated and atherosclerotic carotid damage was assessed by standard carotid ultrasound evaluation for intima-media thickness(IMT)measurement(MeanMax-IMT,CBMax,Tmax;n=167);in141 patienys radiofrequency-based carotid stiffness analysis(distensibility;distensibility coefficient,DC;compliance coefficient;CC)was also performed.Cf-PWV measurement were obtained in 154 patients.

Results

A significant correlation between radiotherapy dose and: MeanMax-IMT(r=0.20; p<0.05),Tmax(r=0.20;p<0.05),distensibility (r=0.24; p<0.05),DC(r=0.24; p<0.05),CC(r=0.24;p<0.05)was observed.Patients were divided into 4groups according to radiotherapy dose(Dose:20-30;31-36;37-42;>42Gy).An increase inTmax (1.27±0.61,1.35±0.59,1.46±0.69,1.76±1.12 mm,pfor trend<0.05)and in the

prevalence of carotid plaque(29%,31%,47%and55%,pfortrend<0.05)was observed as related to dose-category. One-hundred-seventeen patients received neck irradiation (67bilateral;50 unilateral).In unilaterally irradiated patients,MeanMaxIMT was greater in the irradiated side as compared to unirradiated carotid artery and the difference reached statistical significance in the group of patients who received a high radiotherapy dose (0.97±0.35 vs 0.92±0.34 p<0.05).Cf-PWVwas significantly greater only in patients that received high dose(>42Gy),as compared to all the other dose groups(9.7±2.3vs8.3±2.2,8.0±1.5and8.3±1.4,p<0.05).

Conclusions
In this large number ofHL survivors, carotid IMT, plaque prevalence and aortic and carotid stiffness were significantly related with radiotherapy doses. Carotid IMT, carotid and aortic stiffness were significantly higher in the irradiated carotid arteries,but only at doses >42Gy,suggesting that there may be a dose threshold for radiotherapy-induced carotid wall damage.

P189 Identifying PTPN14-dependent mechanisms that influence clinical manifestations of Hereditary Hemorrhagic Telangiectasia

Mamai, Ons

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Hereditary Hemorrhagic Telangiectasia (HHT) is a genetic disorder caused predominantly by loss of a single allele of *ENG* (HHT1) or *ACVRL1* (HHT2). Global incidence is about 1 in 5,000. Clinical manifestations include cutaneous, mucosal and/or gastrointestinal (GI) tract telangiectases that can cause severe epistaxis or GI bleeding. Some patients (10-50%) develop arteriovenous malformations (AVMs) in the lung, brain or liver. We previously showed that genetic variants of *PTPN14* (Phospho-Tyrosine Phosphatase Non-Receptor Type 14) genetically associate with the presence of lung AVMs. Homozygous loss of *PTPN14* has also been reported to cause lymphedema due to lymph EC hyperplasia.

Other studies, in tumor epithelial cells, show that PTPN14 can dephosphorylate b- catenin, modulate HIPPO signaling and regulate tyrosine kinase receptor turnover through endosomal pathways.
To investigate its role in ECs and its interactions with the endoglin/ACVRL1 axis, we studied the effect of *PTPN14* knock down on differential expression of components of BMP9 and TGF-b signaling pathways in primary human umbilical artery ECs (HUAEC). *PTPN14* expression had no effect on pSmad2/3 or pSmad1/5/8 activation but affected protein levels of VEGFR2 and EphrinB2. PTPN14 may thus act on a network of interacting signaling pathways, including endoglin and ACVRL1, by regulating cell surface receptor presentation and endocytic turnover.

Studies are ongoing to address this issue in greater molecular detail. Elucidating the molecular mechanisms involved should contribute to a better understanding of the molecular pathology of HHT, and the regulation of angiogenesis versus stabilization of the vascular bed.

P190 Cardiovascular disease in axial spondyloarthritis.

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Objectives
To estimate the state of the brachiocephalic trunk in patients with axial spondyloarthritis (SpA) and the relationship of changes with the clinical manifestations of the underlying disease.

Material and methods
55 patients with a diagnosis of axial spondyloarthritis were examined. The average age was 35 ± 0.8 years, the duration of the disease was 5 ± 0.45 years. The criterion for exclusion was the presence of clinical manifestations of diseases of the cardiovascular system (CVS). Control group in the amount

of 20 people, corresponding to the sex and age, without clinical manifestations of diseases from the musculoskeletal system and CVS. All patients underwent a duplex study of the brachiocephalic trunk.

Results
Investigation of the intima-media vessel complex (IMC) as an indicator of the thickness of the subendothelial layers of the intima and / or muscle layer of the media is an early marker of the atherosclerotic process. The thickness of IMC was higher in patients with axial SpA (0.75 ± 0.05 mm) compared with the control group (0.68 ± 0.08 mm). The incidence of carotid plaque was higher than in the control group (40% vs. 28%, p <0.05). The presence of plaque was most often observed in patients with a longer duration of the disease, with hip joint damage, syndesmophytes, a higher limited functional capacity of the joints in the BASFI and BASMI indices.

Conclusion
The asymptomatic course of cardiovascular damage justifies the need for mandatory duplex research of the brachiocephalic trunk patients with axial spondyloarthritis.

P191 Aortic stiffness and inflammation in Inflammatory Bowel Diseases: an individual participant data meta-analysis

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Importance
The finding that aortic pulse wave velocity (aPWV) is increased may explain why patients with inflammatory bowel disease (IBD) have an increased cardiovascular risk despite the low prevalence of classic cardiovascular risk factors.

Objective
To determine why these patients have an increased aPWV.

Data sources
A systematic literature search for aPWV in IBD was performed using PubMed, Scopus, Web of Science, and Google Scholar databases.

Study selection
Inclusion criterion was peer-reviewed publications on clinical studies reporting original data.

Data extraction and synthesis
This study followed PRISMA-IPD 2015 guidelines. Data were provided for 4 cohorts in 3 countries (151 participants with ulcerative colitis [UC], 159 with Crohn disease [CD], and 227 controls). Using aPWV, cohort-specific z-scores were calculated after $\log_e$-transform and combined in meta-analysis to form pooled effects using a random-effects model.

Main outcome and measures
The aPWV, a reference measure of aortic stiffness, after adjusting for age, sex, mean blood pressure, known cardiovascular risk factors, and study of origin.

Results
The pooled z-score was 1.2 m/s. The aPWV was dependent on CD (β 0.80 z-score [1.0 m/s], 95% confidence interval 0.61-1.00 z-score, *P*<0.001) and UC (β 0.69 z- score [0.8 m/s], 95% confidence interval 0.49-0.88 z-score, *P*<0.001). In patients with IBD, the aPWV was dependent on disease duration (square root [years], β 0.15 z- score, 95% confidence interval 0.02-0.29 z-score, *P*=0.03) and white blood cell count (Log_e [billion cells/L], β 0.48 z-score, 95% confidence interval 0.12-0.84 z-score,

P=0.01) but not on cardiovascular risk factors and therapy.

Conclusions
The increased aPWV reported in this patient population is dependent on inflammation.

P192 Endothelial dysfunction, arterial stiffness in lung transplanted individuals

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Background
The immunosuppressive treatment after organ transplantation highly contribute to evolve cardiovascular comorbidities like hypertension, hyperlipidemia, diabetes and kidney diseases. The effect of hypertriglyceridemia could cause accelerated atherosclerosis. Previous smoking and excessive inflammatory response could increase the cardiovascular risk on those patients who were transplanted because of end-staged chronic obstructive pulmonary disease. Long term follow up needed on lung transplanted (LuTx) patient with cardiovascular risk assessment and to screen patients with vulnerable cardiovascular diseases. However, the correlation between LuTx patients and arterial stiffness is not investigated in the literature.

Method
We investigated the arterial stiffness parameters in 51 LuTx and 49 healthy individuals. The arterial stiffness parameters were measured with oscillometric method (Tensiomed Arteriograph). Aortic pulse wave velocity (aoPWV), augmentation index (Aix), central systolic blood pressure (cSBP) and aortic pulse wave reflection time (RT) were determined.

Results
We found increased aoPWV and Aix values in lung transplanted (LuTx) patients than in the healthy individuals. Significant higher aoPWV (8.45 vs 7.49 m/s; p=0.045), and RT (120 vs 134 ms; p=0,0004) were found. Patients who were transplanted because of COPD and lung fibrosis the aoPWV were significantly higher versus the patient who were transplanted because of cystic fibrosis or pulmonary hypertension.

Conclusion
We strongly recommend the long term cardiovascular follow up on lung transplanted patient, because of the common systemic atherogen effect of the frequent infection and immunsupressive therapy.

P193 Carotid atherosclerosis, aortic stiffness and penile vascular damage in patients with erectile dysfunction: Relation to low density lipoprotein levels and statin therapy

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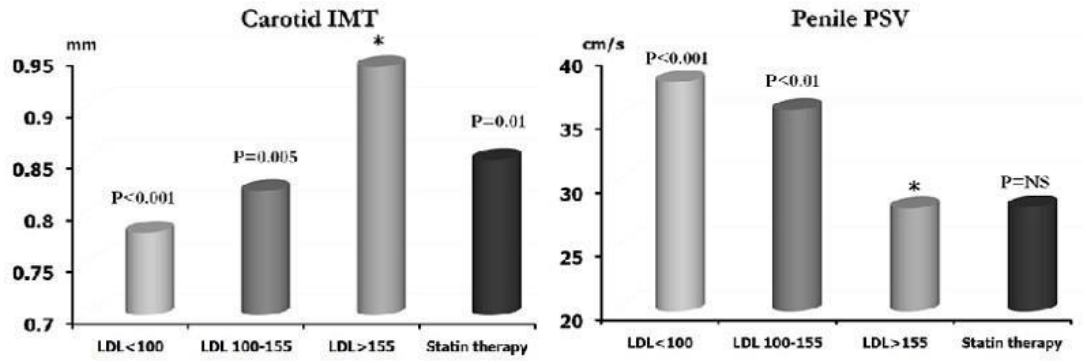
Purpose/Background/Objectives
Aim of the study is to examine the possible differentiation of aortic stiffness, carotid atherosclerosis and penile vascular function among patients with erectile dysfunction (ED) according to cholesterol level and statin therapy.

Methods
We measured carotid intima-media thickness (IMT), carotid-femoral pulse wave velocity (PWV) and penile peak systolic velocity (PSV) 20 min after intracavernous injection of prostaglandin E1 in 356 consecutive ED patients (mean age 57±9 years). Lipid parameters and total testosterone were measured in all patients.

Results
95 (26.7%) ED patients are treated with statins. The patients not receiving statin therapy (n=261) were subsequently divided into three groups according to LDL level (group 1: LDL<100 mg/dl, group 2: LDL: 100-155 mg/dl, group 3: LDL >155 mg/dl).
Patients with statin therapy and subjects in group 2 have similar mean LDL
level. Carotid IMT was higher in patients with LDL >155 mg/dl (group 3) compared to patients treated with statins (P=0.01) and subjects with LDL:100-155 mg/dl (P=0.005) and LDL<100 mg/dl (left plot, P<0.001). Post hoc analysis showed that patients treated with a statin and subjects in group 3 had comparable penile PSV and lower mean value compared to that of patients in group 1 and group 2 (right plot).
Carotid-femoral PWV was similar between the studied groups. Testosterone levels were similar between patients treated with a statin and males not receiving hypolipidemic therapy (groups 2 and 3).



Conclusions
Although treated hypercholesterolemic patients exhibited lower atherosclerotic burden compared to untreated individuals with high LDL levels, penile blood inflow remains significantly impaired.

P194 Cardiovascular responses to increased pressure during healthy pregnancy

Meah, Victoria L[1]; Shave, Rob E[1]; Backx, Karianne[1]; Stöhr, Eric[1,2]

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A long-standing question is whether pregnant females, who bear an increased biological stress, experience exacerbated cardiovascular responses during physiological challenge. At rest, pregnant females have reduced blood pressure, increased cardiac output, heart rate and stroke volume (1), with reported reductions in cardiac contraction and relaxation (2). Increased cardiac work may potentially exasperate impairments in function observed at rest. The aim of this study was to investigate the cardiovascular responses to an isolated increase in pressure in healthy nulliparous non-pregnant, primiparous pregnant (22 - 26 weeks gestation; *n* =
14) and primiparous postpartum (12 - 16 weeks after delivery; *n* = 13) females.

The pressure challenge was elicited through a sustained isometric hold for approximately 5 minutes at 30% of maximum using an externally loaded handgrip dynamometer. Echocardiographic images were collected to measure cardiac volumes and mechanics. Blood pressure was monitored continuously using finger photoplethysmography. Analyses of covariance, with baseline measures as

covariate, were completed to determine differences between groups (P=<0.05). *Post hoc* analyses were performed with a Bonferroni adjustment.

There were no significant differences between groups in cardiac volumes or blood pressure during the challenge however; pregnant females had a greater heart rate (68±2 *versus* 62±2 beats·min^{-1}) and longitudinal strain (-20.6±1.0% *versus* - 17.1±0.7%) than non-pregnant females.

Increased longitudinal strain and heart rate are likely result of increased contractility mediated by greater myocardial sympathetic innervation (3). In healthy pregnant females, increased pressure does not result in impaired cardiovascular function, however dysfunctional responses may predict hypertensive disorders of pregnancy.

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14.30 Satellite Symposia organised in collaboration with **Servier**

New pathways for targeting Early Vascular Aging
Chair: P Boutouyrie, K Cruickshank

Autophagy as a key mechanism in cardiovascular diseases
Dr Pierre-Louis Tharaux, *INSERM, Paris, France*
Paris Cardiovascular Center - PARCC, INSERM

Blood flow imposes shear stress on endothelial cells (ECs). ECs are able to convert these mechanical stimuli into intracellular signals that affect cellular function. As deregulated autophagy is associated with an acceleration of a variety of cardiovascular and metabolic diseases where impaired flow-mediated EC responses promote cardiovascular risk, we hypothesized that endothelial autophagy and endothelial function interact.
We found that defective endothelial autophagy, caused by targeted deletion of the *Atg5* gene in ECs alone, results in selective loss of flow-induced vasodilation in mesenteric arteries and in kidneys *ex vivo*; this leads to increased cerebral and renal vascular resistance *in vivo*. Furthermore, we find a crucial pathophysiological role for endothelial autophagy in flow-mediated outward arterial remodelling, prevention of neointima formation following wire injury and recovery after myocardial infarction. Together, these findings unravel a fundamental role for autophagy in endothelial function, linking cell proteostasis to mechanosensing signaling that will be discussed. These findings also open new questions regarding the potential role of endothelial proteostasis in arterial diseases.

Role of Vitamin K in arterial calcifications and cardiovascular diseases
Professor Leon J Schurgers, *Cardiovascular Research Institute Maastricht, Maastricht, The Netherlands*

Vascular calcification: from innocent bystander to culprit risk factor

Vascular calcification was regarded as an innocent bystander in cardiovascular disease. It was considered to be the passive chemical nucleation of calcium and phosphate ions on cellular debris and therefore the end-stage of atherosclerosis. Currently, vascular calcification is understood to be an actively regulated process involving cellular and humoral contributions that may offer targets for diagnosis and intervention. Vascular calcification is clearly associated with poor cardiovascular outcome, and may result in stiffened vessels and unstable lesions that can rupture and cause acute ischaemic events such as acute myocardial infarction and stroke. In

atherosclerotic disease research, calcification is commonly used as a measure of atherosclerotic burden. However, recent data suggest that especially microcalcification have destabilising effects on atherosclerotic plaques. Therefore, the development of novel imaging solutions for early detection of initiation events resulting in microcalcification are of utmost importance. Phenotypic switching of VSMCs plays a key role in vascular disease and is a precondition for vascular calcification, possibly via oxidative stress and shedding of extracellular vesicles. The discovery that vitamin K-dependent processes are involved in the inhibition of vascular calcification has further boosted our mechanistic understanding of the vascular calcification process and has opened up novel avenues. Indeed, the current thrombosis treatment using vitamin-K antagonists (VKAs) paradoxically leads to a high risk of calcification. The treatment of vascular calcification and stiffness using vitamin K supplements is currently under investigation.

Targeting vascular smooth muscle cell to improve arterial stiffness

Professor Patrick Lacolley, *INSERM, Cedex, France*

Hypertension and arterial aging engage a plethora of key signaling pathways that act in concert to induce vascular smooth muscle cell (VSMC) phenotypic changes leading to vascular degeneration and extracellular matrix (ECM) changes responsible for alterations of the mechanical properties of the vascular wall. This review highlights proof-of-concept examples of components of the extracellular matrix, VSMC receptors which connect extracellular and intracellular structures and signaling pathways regulating changes in mechanotransduction and vascular homeostasis. This presentation presents new directions in the role of vascular smooth muscle cells VSMCs traditionally limited to regulation of contractile properties and synthesis of ECM proteins. VSMCs may exert negative feedback or positive feedback on ECM stiffness and mechanical load via stabilized focal adhesions, activated Rho-ROCK signaling pathways or actomyosin contraction. Understanding the mechanisms of cellular stiffness are also important to appreciate its contribution to mechanical properties at the tissue-level. Many other cell types, including macrophages, could participate to inflammation and VSMC stiffness leading to fibrosis of the arterial wall. In view of the multitude roles of VSMCs and feedback controls, only omic approaches and computational models may extrapolate the overall effects on the vascular wall in light of hemodynamics and complex interactions amongst differentially sized vessels. The use of novel animal models with multiple genetic manipulations of VSMC signaling pathways can provide further insight into the link between large vessel stiffness and small vessel dysfunction.

15.30 Oral Session IV – Clinical Aspects

Chair: ML Muiesan, P Cunha

4.1 Pilot study on the preclinical vascular damage in bolivian patients with chagas indeterminate chronic phase

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Background

In Italy, the prevalence of seropositivity for Trypanosoma Cruzi in immigrants from endemic countries is about 11.3% (30.7% for Bolivian immigrants).

The disease acute phase is usually asymptomatic, often leading to chronic infection that may remain silent for life (chronic indeterminate phase). Chagas heart disease is the most severe and frequent (20-30%) form of chronic phase; its pathophysiology shares similar mechanisms with the arterial impairment associated to other diseases (diabetes, hypertension, aging), leading to chronic

inflammation and stiffening. In literature there are no data about the possible elastic arteries deterioration in Chagas disease. Our hypothesis was that early arterial compliance modifications might be found in the chronic indeterminate phase of Chagas disease.

Methods
35 consecutive Bolivian subjects (21 with indeterminate Chagas disease, mean age[SD] 44.2[8.2], 5 women, and 14 controls, mean age 40.2[8.2], 5 women) accessing the service of Tropical Medicine were enrolled. Staging of the disease, laboratory assay, and hemodynamics (central and peripheral blood pressure [BP], aortic pulse wave velocity [PWV], carotid intima media thickness, cardiac ultrasound) were assessed.

Results
No clinical nor laboratory differences were found between the cases and controls. Peripheral and central BPs components were similar. Chagas patients presented higher PWV than controls (7.87±1.29 vs 6.43±1.12m/s, p=0.002), even when adjusting for age, mean BP, heart rate, body mass index, smoking status (p=0.001).

Conclusion
Patients with Chagas indeterminate chronic phase presented higher arterial stiffness than controls, pointing out an early arterial involvement as the possible etiological mechanism underlying the increased cardiovascular risk in these patients.

4.2 Sex-dependent Effects of Perivascular Adipose Tissue on Vascular Function

Delles, Christian[1]; McNeilly, Sarah[1]; Mary, Sheon[1]; Sheikh, Adam[1]; Small, Heather[1] [1]University of Glasgow

Background
Premenopausal women are relatively protected against hypertension compared to males. Estrogen levels have been identified as a potential underlying cause, but the pathophysiological mechanisms remain incompletely understood. We hypothesised that sex-dependent effects of perivascular adipose tissuePVAT mediate altered vascular function in hypertension.

Methods
The effect of PVAT was investigated on resistance vessels of 16 week old male and female stroke-prone spontaneously hypertensive rats (SHRSP).

Results
Wire-myography was used on 3rd-order mesenteric vessels (maximum contraction: male +PVAT 113.3±1.1 vs. female +PVAT 91.4±11.36 %). Noradrenaline mediated vasoconstriction was increased in SHRSP males compared to females. K_{ATP} channel-mediated vasorelaxation by cromakalim was impaired in males compared to females (maximum relaxation: male +PVAT 46.9±3.9 % vs. female +PVAT 97.3±2.7 %) A cross-over study assessing function of male PVAT on female vessels and vice versa confirmed the reduced K_{ATP} mediated vasorelaxation induced by male PVAT (maximum relaxation: female +$PVAT_{female}$ 90.6±1.4 % vs. female +$PVAT_{male}$ 65.8±3.5 %). An adipokine array with subsequent western blot validation identified resistin as a potential modifier of vascular reactivity. Resistin was increased by approximately 2- fold in SHRSP male PVAT. Male and female vessels pretreated with resistin (40ng/ml) showed no difference in response to noradrenaline. However, vasorelaxation in response to cromakalim was significantly impaired in resistin treated female vessels, similar to levels observed in male vessels (maximum relaxation: female +PVAT 97.3±0.9 % vs. female +PVAT +resistin 36.8 ±2.3 %).

Conclusion
We identified a novel role for resistin in sex-dependent PVAT mediated vascular function in hypertension through a K_{ATP} channel mediated mechanism.

4.3 Abnormal pressure wave reflection accelerates the development of hypertension via the

increase of arterial stiffness

Tomiyama, Hirofumi[1]; Yamashina, Akira[1]; Komatsu, Shunsuke[1]; Shiina, Kazuki[1]; Matsumoto, Chisa[1]; Fujii, Shogen[1]; Chikamori, Taishiro[1]

[1]Tokyo Medical University

Objectives
It is noted that not only arterial stiffness but also abnormal pressure wave reflection are risks for the development of hypertension. However, the association between arterial stiffness and pressure wave reflection in the development of hypertension has not been fully clarified. The present study was conducted to examine whether the abnormal pressure wave reflection accelerates the development of hypertension via the increase of arterial stiffness.

Methods
In 3102 middle-aged healthy Japanese men without hypertension at baseline, systolic/diastolic blood pressures, brachial-ankle pulse wave velocity (baPWV), and radial augmentation index (rAI) were annually measured during a 9-year study period.

Results
In multivariate linear regression analysis and in mixed model linear regression analysis, baPWV was not longitudinally associated with rAI. Linear regression analysis demonstrated that the higher rAI at the baseline was associated with the larger longitudinal increase of baPWV (beta = 0.17, $p<0.01$). At the end of study period, 404 subjects were developed to hypertension. The prevalence rate of the development of hypertension during the study period was higher in subjects with higher baPWV and higher rAI at the baseline (220 in 939 subjects: 23 %) than that in other 3 groups classified by the status of baPWV and rAI at the baseline (e.g. 52 in 942 subjects with low baPWV combined with low rAI: 6%, $p<0.01$).

Conclusion
The abnormal pressure wave reflection, which may be derived from both arterial stiffness and peripheral vascular damages, may be an accelerator for the development of hypertension via the increase of arterial stiffness.

4.4 Middle cerebral artery pulsatility in heart failure and patients with continuous-flow left ventricular assist devices

Stöhr, Eric[1]; Castagna, Francesco[1]; Pearson, James[2]; Watkeys, Laura[3]; Trocio, Samuel[1]; Zatvarska, Oksana[1]; Crimmins, Timothy[1]; Pinsino, Alberto[1]; Colombo, Paolo[1]; Yuzefpolskaya, Melana[1]; Garan, Reshad[1]; Topkara, Veli[1]; Takayama, Hiroo[1]; Takeda, Koji[1]; Naka, Yoshifumi[1]; Cockcroft, John[3]; Willey, Joshua[1]; McDonnell, Barry[3]

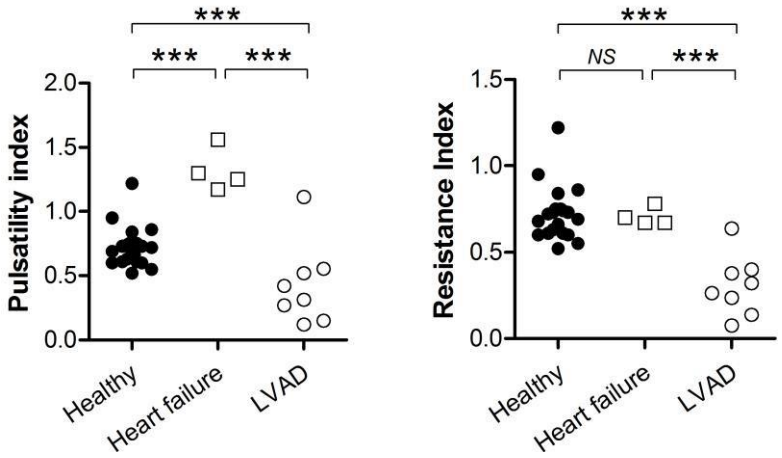
[1]Columbia University Irving Medical Center, [2]University of Colorado at Colorado Springs,

[3]Cardiff Metropolitan University

Background
High pulsatility index (PI) in the cerebral circulation has been associated with increased prevalence of stroke (1). Interestingly, heart failure (HF) patients implanted with continuous-flow left ventricular assist devices (CF-LVADs) have increased rates of stroke despite presenting with dramatically lower pulse pressures compared with healthy individuals (20mmHg *vs*. 30-40mmHg). Characterising and understanding flow velocity profiles of the middle cerebral artery (MCA) may provide a useful and local marker of pulsatile energy transmitted into the brain of HF and CF-LVAD patients.

Methods
PI and resistance index (RI) were quantified from Duplex ultrasound images (2D and pulsed-wave Doppler) of the MCA obtained in four heart failure patients (HF; 68±7 yrs), eight CF-LVAD patients (59±4 yrs) and 20 healthy controls (51±7 yrs).

Results
Compared with healthy controls, PI of the MCA was actually higher in the HF group (0.72±0.16 *vs.* 1.32±0.17, $P < 0.0001$), but markedly lower in patients on CF-LVAD (0.36±0.21, $P < 0.0001$). However, RI was similar between healthy controls and HF patients ($P > 0.05$), and only lower in CF-LVAD patients ($P < 0.0001$).



Conclusions
PI in the MCA is significantly higher in HF but markedly lower in CF-LVAD patients, relative to healthy controls. The higher PI in HF does not appear to be associated with an altered RI. Future work should examine the cerebrovascular outcomes associated with varying levels of pulsatility and resistance in both HF and CF-LVAD patients.

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4.5 The effect of lung function on blood pressure and vascular indices from adolescence to early adulthood in a multi-ethnic cohort

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[1]The Third Xiangya Hospital of Central South University, [2]King's College London

Given the significance of lung function (LF) for vascular health in adulthood, there are surprisingly few studies that have examined the interrelationships of their developmental trajectories. Both develop and decline over the life course, though LF peaks in the 20s, and both predict cardiovascular events and mortality. We used the multi-ethnic Determinants of Adolescent Social well-being and Health (DASH) longitudinal study to test whether lung function (LF) from early adolescence to young adulthood affected vascular indices. In 2002-3, 6643 11-13y olds from 51 London schools participated at baseline, and 4785 were seen again at 14-16y.

Recently 665 participated in pilot follow-up at 21-23y. Regression models examined relationships between Forced Expiratory Volume (z-scores for $zFEV_1$ derived using Global Lung Initiative equations), blood pressure (BP), aortic pulse wave velocity (PWV) and augmentation index (AIx), the latter 2 measured only at 21-23y. At 11-13y, 1z-score zFEV1 was associated with +1.90mmHg (95%CI 1.11-2.68, p<0.001) in systolic BP. In contrast at 21-13y, a relationship between these measures was not evident.

Between 11-13y and 21-23y, 1 z-score change in zFEV1 was associated with +1.38 mmHg (0.25-1.51, p<0.05) SBP, adjusted for age, sex, ethnicity, waist-height ratio, employment, and reported racism, smoking and alcohol use. zFEV1 at 11-13y or 21- 23y was not associated with PWV or central AIx (AIxao) at 21-23y. These findings signal that whilst cross-sectionally LF is differently associated with SBP in early adolescence than in the 20s, longitudinal change in LF is positively associated with changes in SBP during this part of the life course.

4.6 Hippocampal cerebral blood flow depends on systemic endothelial function in individuals with mild cognitive impairment: the Train the Brain-Mind the vessel study

Bruno, Rosa Maria[1]; Pratali, Lorenza[2]; Sicari, Rosa[2]; Stea, Francesco[2]; Berardi, Nicoletta[3]; Tognoni, Gloria[1]; Bonuccelli, Ubaldo[1]; Ghiadoni, Lorenzo[1]; Taddei, Stefano[1]; Scelfo, Danilo[4]; Biagi, Laura[4]; Tosetti, Michela[4]; Maffei, Lamberto[3]; Picano, Eugenio[2]

[1]University of Pisa, Pisa, Italy, [2]Institute of Clinical Physiology - CNR, Pisa, Italy, [3]Institute of Neuroscience - CNR, Pisa, Italy, [4]IRCSS Stella Maris, Pisa, Italy

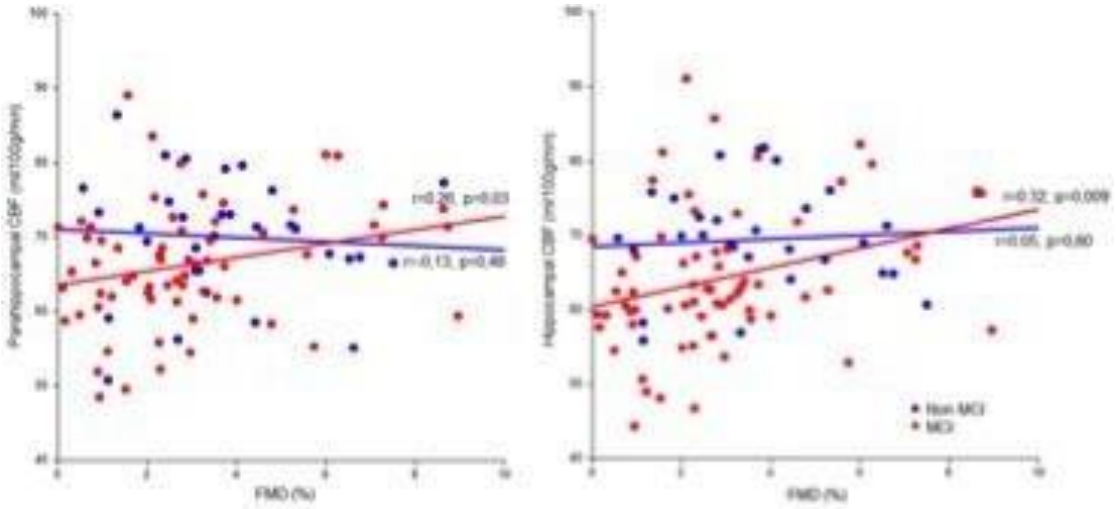
Background
Dementia has been recently viewed as a predominantly vascular disorder. Indeed, reduced brain NO availability causes increased ß-amyloid deposition by several mechanisms, including hypoperfusion.

Purpose
To investigate the relationship between cerebral blood flow in the hippocampal and parahippocampal regions (CBF-hipp and CBF-parahipp), crucial areas for memory and processing of non-verbal/spatial information, and systemic endothelial function in individuals with mild cognitive impairment (MCI), a subclinical condition predisposing to dementia.

Methods
CBF-hipp and CBF-parahipp were evaluated by magnetic resonance imaging (arterial spin labeling, GE HDxt 1.5 T Signa Neuro-optimized System) and systemic endothelial function by flow-mediated dilation (FMD) in the brachial artery.

Results
Complete data about CBF and FMD at enrollment were available for 66 individuals with MCI and 32 without (non-MCI). The two groups were matched for age (75±5 vs 74±5years, p=0.22), sex (men 45 vs 50%, p=0.18) and mean BP (96±10 vs 97±9mmHg, p=0.41). FMD was significantly lower in MCI than in non-MCI (2.93±2.18 vs 3.74±2.03%, p=0.02); CBF-hipp (64.3±9.43 vs 69.5±7.03ml/100 gr/min,

p=0.002)
and CBF-parahipp (66.3±8.02 vs 70.0±8.12ml/100 gr/min, p=0.002) were significantly lower in MCI as well. Among MCI, FMD was significantly correlated with CBF- parahipp (r=0.26,p=0.03) and CBF-hipp (r=0.32,p=0.009). In multiple regression models, including age, sex, mean BP, BMI, brachial artery diameter as confounders, FMD remained an independent determinant of CBF-parahipp (beta=0.93, r2=0.063, p=0.04) and CBF-hipp (beta=1.31, r2=0.089, p=0.01). Nor CBF-parahipp (r=-0.13, p=0.48) neither CBF-hipp (r=0.05, p=0.80) were correlated with FMD in non-MCI group.



Conclusions
An independent association between hippocampal and parahippocampal CBF and systemic endothelial function is present in individuals with MCI.

4.7 Parameters of the reservoir-wave approach and mortality in dialysis population.

Agharazii, Mohsen[1]; Fortier, Catherine[1]; Desjardins, Marie-Pier[1]; Schultz, Martin[2]; Sharman, James[2]

[1]CHU de Québec-Université Laval, [2]Menzies Institute for Medical Research, University of Tasmania

Background
A new model has been proposed to explain hemodynamic consequences of arterial stiffness, which integrates both wave propagation and aortic reservoir function. The aim of this study was to assess the association between parameters of reservoir- wave analysis and all-cause mortality in a population with accelerated vascular ageing.

Methods
Among 311 patients with chronic kidney disease on dialysis, central arterial pressures were derived from applanation tonometry (Sphygmocor) of radial artery. Reservoir wave analysis was applied on radial pressure waveforms (without generalized transfer function) to obtain reservoir pressure (Peak RP), its integral (RP integral), excess pressure parameters (Peak XS, XS integral), and systolic (SC) and diastolic time constant (DC).

Results
During a median follow-up of 33 months, 204 (66%) deaths occurred. In Kaplan- Meier survival curves, only increasing tertiles of DC was associated with a significant decrease in survival time (p<0.001). Amongst all parameters, only DC and XS integral were predictors of all-cause mortality in univariate Cox analysis as shown by hazard ratios for changes in 1-standardized deviation (HR 1-SD, Table 1). However, DC and XS integral were no longer significant when age was introduced in the

model (p-value>0.179).

Continuous variables	HR 1-SD	95% CI	p-value
Peak RP (mm Hg)	1.121	0.987-1.273	0.079
RP integral (mm Hg.sec)	1.050	0.920-1.197	0.470
Peak XS (mm Hg)	1.112	0.966-1.281	0.138
XS integral (mm Hg.sec)	1.217	1.062-1.395	0.005
SC ($x10^{-2}$)	1.099	0.970-1.244	0.138
DC ($x10^{-2}$)	1.186	1.060-1.328	0.003

Conclusions
Amongst all parameters of the reservoir-wave analysis, DC was the most important parameter associated with survival time and mortality. Despite its hypothetically more integrated approach to arterial tree function, none of the derived parameters showed a robust and independent association with mortality in this population. The study shows that despite its simplicity, arterial stiffness gradient remains the best predictor of mortality in this population.

4.8 Arterial stiffness and its relationship to mortality in patients with peripheral artery disease

Dimitrov, Gabriel[1]; Scandale, Giovanni[1]; Recchia, Martino[2]; Perilli, Edoardo[1]; Minola, Marzio[1]; Carzaniga, Gianni[2]; Carotta, Maria[1]; Catalano, Mariella[3]

[1]Research Center on Vascular Diseases and Angiology Unit, University of Milan, [2]Research Center on vascular Diseases-University of Milan-Milan-Italy, [3]Research Center on Vascular Diseases-University of Milan-Milan

Background and aim
Several studies (1,2) suggest that patients with peripheral artery disease (PAD) show an increase in arterial stiffness, nevertheless the impact on mortality is less documented.(3)

Methods
228 PAD patients mean age (68±9 years) were followed-up for 4,8±2 years. Anthropometric and clinical measurements were collected, ankle-brachial index (ABI) was estimated with standard protocol and hemodynamic parameters (central blood pressure, aortic pulse wave velocity [aPWV], augmentation index [Aix]) were measured using applanation tonometry. Prognostic factors of mortality were identified by Cox proportional hazards regression model.

Results
During follow-up 26 (11,6%) deaths occurred. Among them, 5 (19%) were of cardiovascular origin. The Cox analysis applied to data relative to the third tertile of aPWV (11.4-21.4, m/s), is significant for age, (p=0.039), smoking history (p =0.0003) non use of lipid lowering drugs (p=0.026) and lower height (p=0.007) but not for aPWV (p =0.312), Aix (p =0.075) and ABI (p =0.305).

Conclusions
The present study provides further insights into the lack of association between large artery stiffness, pressure wave reflections and mortality in PAD patients.

References
[1] N.M. Van Popele, D.E. Grobbee, M.L. Bots, R. Asmar, J. Topouchian, R. S. Reneman, A.P.G. Hoeks, D.A.M. van der Kuip, A. Hofman, J.C.M. Witteman. Association between arterial stiffness and atherosclerosis. The Rotterdam Study. Stroke. 32 (2001) 454–460. [2] M. Catalano, G. Scandale, G. Carzaniga, M. Cinquini,
M. Minola, G. Dimitrov, M. Carotta. Increased aortic stiffness and related factors in patients with peripheral arterial disease. J. Clin. Hypertens. 15 (2013) 712–716. [3] J. Kals, J. Lieberg, P. Kampus, M. Zagura, J. Eha, M. Zilmer. Prognostic impact of arterial stiffness in patients with symptomatic peripheral arterial disease. Eur. J. Vasc. Endovasc. Surg. 48 (2014) 308–315.

16.50 Refreshments, Poster and Exhibition viewing

17.20 Focus Update
Chair: T Weber, G Mitchell

Central BP measurement and validation: what is still needed?
Professor James Sharman, *Menzies Institute for Medical Research, University of Tasmania, Hobart, Australia*

Accurate measurement of blood pressure (BP) is a critical goal for appropriate diagnosis and management of high BP. The measurement reference standard is brachial cuff BP, but recent large-scale meta-analyses show major deficiencies in the accuracy of this method. Indeed, irrespective of cuff technique (e.g. mercury auscultation or oscillometry) brachial cuff BP measures lack precision for representing the BP within both the brachial artery and the central aorta. These data clearly indicate the need to refine and improve methods to measure BP accurately, whether at the brachial or central aortic level, with preference towards the latter as the best representation of pressure loading experienced by the organs at risk from hypertension. The current focus to improve measurement of central aortic BP is on better calibration methods, with mean arterial pressure (MAP) and diastolic BP (DBP) proposed as the best solution. However, the ability to accurately estimate central aortic BP using this calibration method appears to be device-specific and related to the capacity of different devices to accurately measure MAP/DBP using conventional cuff BP. Beyond this, even if we can accurately measure MAP/DBP using non-invasive cuff methods, this does not necessarily provide a final solution because characteristic waveform features and the level of systolic BP amplification still influence accuracy. Thus, altogether, manufacturers of devices purporting to measure central aortic BP need to provide robust evidence about accuracy performance; preferably according to ARTERY Society recommendations.

Central BP measurement and validation: the engineer's point of view
Professor Siegfried Wassertheurer, *AIT Austrian Institute of Technology GmbH, Vienna, Austria*

The non-invasive assessment of aortic (central) pressure evolved as an emerging clinical research area over the last two decades. Several non-invasive methods and devices were developed to support these investigations. A variety of technical approaches and sites of peripheral signal acquisition have been established to non-invasively estimate aortic pressure, but interchangeability of results was limited due to the lack of standardization. To overcome this threatening situation, an ARTERY Society task force was set up to provide a consensus document with recommendations regarding appropriate protocols to assess and report the evaluation of accuracy of devices measuring aortic pressure.
This presentation aims to provide background information about the genesis of the actual ARTERY consensus document and discusses resulting strengths and opportunities. Furthermore it reviews the document from an engineering viewpoint, focusing on several novel and strong statements that have been proposed in the published consensus document, e.g. for the first time ever invasive (preferably solid state) catheter measurements as the sole reference (gold) standard for comparison have been defined. Amongst other relevant topics, particular focus is brought to issues of waveform calibration and subsequent effects leading to differences between measures of brachial and aortic pressures.

17.45 ARTERY Annual Business Meeting

20.00 Conference Dinner
Arsenali Repubblicani, Via Bonanno Pisano, 56126 Pisa

SATURDAY 14 OCTOBER 2017

08.30 Refreshments, Poster and Exhibition viewing

09.00 Oral Session V – Pathophysiology and Intervention

Chair: F Mattace Raso, H Tomiyama

5.1 Effects of the SGLT-2 inhibitor empagliflozin on vascular function and central hemodynamics in patients with type 2 diabetes

Ott, Christian[1]; Striepe, Kristina[1]; Jumar, Agnes[1]; Karg, Marina[1]; Schneider, Markus[1]; Kannenkeril, Dennis[1]; Schmieder, Roland[1]

[1]Department of Nephrology and Hypertension, Friedrich-Alexander University Erlangen-Nuremberg

Background
The selective sodium-glucose cotransporter 2 (SGLT-2) inhibitor empagliflozin leads to improved cardiovascular, renal and heart failure outcome in secondary prevention. To better understand these effects, we examined vascular function and central hemodynamics.

Methods
In this prospective, double-blind, randomized, placebo-controlled, crossover study 76 patients with untreated type 2 diabetes were randomized to empagliflozin 25mg orally once daily or placebo. After 6 weeks of treatment with either empagliflozin or placebo and 1 week wash-out-phase, patients crossed over to the other treatment. Central hemodynamics and vascular function were assessed by central systolic blood pressure (BP), central pulse pressure, forward and backward wave amplitude under office (Sphygmocor, AtCor, Australia) as well as ambulatory conditions (Mobilograph, IEM, Aachen).

Results
Treatment with empagliflozin reduced central systolic BP (114±12 vs. 119±14mmHg, p<0.001), central diastolic BP (74.4±6.9 vs. 76.8±8.2mmHg, p=0.004) and central pulse pressure (39.5±9.9 vs. 42.2±11mmHg, p=0.012) compared to placebo.
Forward (p=0.006) and backward (p=0.026) reflection amplitude, assessed under office conditions, were also significantly lower with empagliflozin than with placebo. Under ambulatory conditions over 24-hours we also observed lower central systolic (117±9 vs. 119±9mmHg, p=0.059) and diastolic (79±7 vs. 81±7mmHg, p=0.011) BP after 6 weeks treatment with empagliflozin compared to placebo. Pulse wave velocity under ambulatory conditions was also reduced after 6 weeks with empagliflozin (p=0.016).

Conclusions
Our study demonstrated consistent significant improvements of vascular function and central hemodynamics with empagliflozin under office and ambulatory conditions.
Our data support the concept that empagliflozin exerts beneficial effects on cardiovascular and heart failure outcome via improved vascular function.

5.2 Reduced sublingual endothelial glycocalyx in type 1 diabetics with diabetic nephropathy

Winther, Signe Abitz[1]

[1]Steno Diabetes Center Copenhagen and Novo Nordisk A/S

Background
Glycocalyx is a glycoprotein layer protecting the capillary endothelium. An impaired glycocalyx may precede the development of microvascular complications in diabetes. Capillaroscopy is a new method to estimate the dimensions of the glycocalyx by measuring the perfused boundary region (PBR). We evaluated the glycocalyx thickness in type 1 diabetic patients with different levels of historical and current albuminuria.

Methods
Cross-sectional study including 77 type 1 diabetics stratified by history of normoalbuminuria (<30 mg/g;n=26), microalbuminuria (30-299 mg/g;n=27) and macroalbuminuria (>300 mg/g;n=24).
Glycocalyx thickness was assessed by 5 measurements with the GlycoCheck® device, a non-invasive hand-held microscope generating video recordings of the sublingual capillaries. Endothelial glycocalyx thickness was estimated from the PBR in capillaries with a diameter range of 5-25 µm. Higher PBR indicates smaller glycocalyx width. Urinary albumin-to-creatinine ratio (UACR) was measured in 3 morning samples.

Results
In normo-, micro-, and macroalbuminurics PBR was (mean±SD) 2.30±0.22 µm, 2.32±0.25 µm, and 2.49±0.35 µm, respectively. Differences between normo- and macroalbuminurics and micro- and macroalbuminurics were significant ($p<0.05$) in an unadjusted model and remained significant after adjustment for age, sex, HbA_{1c},
diabetes duration and systolic blood pressure. In pooled (n=77) multivariate linear regression, higher level of current UACR was associated with a higher PBR ($p=0.0007$).

Conclusion
In type 1 diabetics with a history of macroalbuminuria, measurements with the non- invasive GlycoCheck® device revealed significantly higher PBR, suggesting an impaired glycocalyx, compared to patients with normo- or microalbuminuria.
Moreover, higher current level of albuminuria was associated with higher PBR.

5.3 High Fit Older Adults Maintain a Similar Endothelial Response to Acute Inflammation as Younger Adults

Schroeder, Elizabeth[1]; Lane-Cordova, Abbi[2]; Ranadive, Sushant[3]; Baynard, Tracy[1]; Fernhall, Bo[1]

[1]University of Illinois at Chicago, Chicago, IL, [2]Northwestern University, Chicago, IL,
[3]Mayo Clinic, Rochester, MN

Inflammation is associated with an increased risk of cardiovascular events and reduced endothelial function. Higher cardiorespiratory fitness is associated with lower risk of cardiovascular events and improved vascular function. Whether fitness plays a role during acute inflammation is unknown.

Purpose
Evaluate the role of fitness in the endothelial response to acute inflammation in younger (YA) and older (OA) adults.

Methods
Acute inflammation was induced using influenza vaccine in 23 YA (12 male, 26±4 yrs, 24.0±3.5 kg/m^2) and 60 OA (20 male, 65±5 yrs, 27.8±5.0 kg/m^2). Blood pressure, flow-mediated dilation (FMD) and inflammatory markers were measured before and 24-hours post-vaccination. VO_2peak was measured via a treadmill test. A VO_2peak
greater than age- and sex-associated 50th percentile according to the American College of Sports Medicine was defined as Fit.

Results
Fit OA reduced FMD more than low fit OA ($p=0.02$) 24h post-vaccination. High and low fit YA similarly decreased FMD at 24h ($p=0.66$). YA and high fit OA had a similar reduction (relative %) in FMD ($p>0.05$). Regression analyses indicated no association between VO_2peak and change in FMD ($\beta=-0.01$, $p=0.98$) in YA, but a significant
association existed in OA ($\beta=-0.36$, $p=0.04$) after adjusting for age, sex, BMI and baseline FMD

	YA – High Fit	YA – Low Fit	OA – High Fit	OA – Low Fit
n	14	9	16	43
VO_2Max, ml/kg/min	48.4 (5.6)*	35.6 (4.9)	32.3 (4.2)*	21.9 (4.3)
Baseline SBP	113 (13)	115 (13)	125 (14)	125 (14)
Baseline PP	47 (8)	47 (11)	54 (10)	53 (11)
Baseline FMD, %	12.4 (2.7)	11.6 (5.5)	7.5 (3.9)*	5.4 (2.5)
Baseline CRP, mg/l	1.1 (0.7)	0.6 (0.6)	2.4 (3.3)	2.5 (2.2)
Baseline IL-6, pg/ml	1.0 (0.7)	0.8 (0.5)	1.7 (1.4)	1.6 (1.1)
Change SBP, mmHg	-3 (6)	2 (8)	-2 (9)	-2 (11)
Change PP, mmHg	2 (6)	5 (7)	0 (7)	0 (8)
Change FMD, %	-3.2 (4.1)	-2.3 (5.5)	-3.7 (3.8)*	-0.2 (3.5)
Change CRP, mg/l	1.0 (1.5)	0.9 (0.8)	1.1 (2.2)	0.9 (1.4)
Change IL-6, pg/ml	1.0 (1.5)	1.6 (2.3)	0.8 (2.6)	0.4 (1.0)

FMD: Flow mediated dilation, CRP: C-reactive protein, IL-6: interleukin-6, SBP: systolic blood pressure, PP: pulse pressure
*p < 0.05 vs. low-fit of same age category

Conclusion
In OA, higher fitness is associated with a greater decrease in endothelial function during acute inflammation; high fit OA had a similar endothelial response compared to YA. This suggests intact reactivity of the vasculature to inflammatory stress in high fit OA, which may indicate a healthier vessel versus low fit OA.

5.4 Effect of Acute Resistance Exercise on Arterial Hemodynamics and Cerebral Blood Flow Dynamics: Does Sex Matter?

Rosenberg, Alexander[1]; Wee, Tommy[1]; Schroeder, Elizabeth[1]; Bunsawat, Kanokwan[1]; Grigoriadis, Georgios[1]; Griffith, Garett[1]; Fernhall, Bo[1]; Baynard, Tracy[1]

[1]Integrative Physiology Laboratory, University of Illinois at Chicago, Chicago, IL

High-intensity resistance exercise (RE) acutely increases arterial stiffness and blood pressure (BP), coupled with reduced cerebral blood flow velocity (CBFv) and greater flow pulsatility in the cerebral circulation, which may be detrimental to cerebral microvasculature. Because females have different CV control mechanisms, it is important to assess potential sex differences in cerebrovascular responses to acute RE.

Purpose
To examine the effect of sex on hemodynamics and cerebral vasculature following acute RE.

Methods
Men (n=18, 27yrs, BMI=24.2) and women (n=14, 25yrs, BMI=23.8) performed RE (3x10, isokinetic knee flexion/extension). Measurements were obtained at baseline and post-exercise (1, 5, 30-minute). Beat-to-beat heart rate (HR), brachial BP, cardiac output (CO), stroke volume and end-tidal CO_2 were collected. CBFv was
measured by transcranial Doppler, carotid BP by applanation tonometry and central pulse wave velocity (PWV) by an automated ambulatory BP monitor.

Results
Table 1. CBFv pulsatility increased following RE at 1-minute post ($p<0.05$) in men and was elevated above baseline 5-minute post-exercise ($p<0.05$) in both groups (Figure 1). Mean CBFv increased 1-min post-exercise and decreased below baseline 5-minute post-exercise ($p<0.05$) in both sexes. PWV increased 1-minute post-exercise ($p<0.05$) in both groups.

Variables		Baseline	1-minute	5-minute	30-minute
Heart Rate (bpm) *†	Men	63 ±9	82 ± 9	71 ± 10	70 ± 8
	Women	70 ± 7	93 ± 13	79 ± 10	76 ± 9
CO (L/min) *	Men	4.9 ± 0.7	7.9 ± 1.3	6.1 ± 1.3	5.2 ± 0.9
	Women	5.4 ± 1.0	8.2 ± 1.4	6.3 ± 1.0	5.7 ± 0.8
SV (ml/min) * ‡	Men	77 ± 16 [ab]	95 ± 17 [bc]	85 ± 17 [c]	72 ± 13
	Women	80 ± 17 [a]	91 ± 20 [bc]	81 ± 14	76 ± 16
bSBP (mmHg) *	Men	124 ± 10	140 ± 12	127 ± 10	127 ± 9
	Women	124 ± 9	136 ± 15	122 ± 13	123 ± 9
bDBP (mmHg) *	Men	72 ± 8	74 ± 7	72 ± 7	76 ± 6
	Women	73 ± 5	76 ± 9	71 ± 7	73 ± 5
bMAP (mmHg) *	Men	92 ± 8	100 ± 8	93 ± 8	96 ± 7
	Women	95 ± 6	101 ± 11	93 ± 8	95 ± 6
cSBP (mmHg) *	Men	120 ± 12	129 ± 18	125 ± 13	126 ± 10
	Women	122 ± 12	124 ± 13	119 ± 18	123 ± 8
cDBP (mmHg) *	Men	75 ± 7	74 ± 7	75 ± 7	79 ± 6
	Women	74 ± 6	73 ± 6	75 ± 7	74 ± 5
cMAP (mmHg) *	Men	93 ± 8	94 ± 8	94 ± 7	97 ± 7
	Women	94 ± 6	93 ± 8	95 ± 9	96 ± 5
PWV (m/s) *	Men	5.2 ± 0.5	5.6 ± 0.5	5.4 ± 0.5	5.2 ± 0.3
	Women	5.0 ± 0.4	5.3 ± 0.5	5.1 ± 0.3	5.0 ± 0.3
CBFv Mean (cm/s) *†	Men	55.8 ± 7.6	63.9 ± 9.6	51.4 ± 6.9	53.7 ± 7.9
	Women	69.8 ± 14.4	81.0 ± 23.1	63.7 ± 12.9	65.8 ± 12.0
CBFv Pulsatility Index *†‡	Men	0.91 ± 0.12 [ab]	1.10 ± 0.16 [c]	1.13 ± 0.17 [c]	0.89 ± 0.13
	Women	0.81 ± 0.09 [b]	0.90 ± 0.18	0.95 ± 0.13 [c]	0.81 ± 0.11
End-Tidal CO2 (%) *	Men	4.86 ± 0.48	5.72 ± 0.66	4.64 ± 0.51	4.51 ± 0.58
	Women	4.41 ± 0.60	5.44 ± 0.65	4.26 ± 0.39	4.24 ± 0.50

Table 1. All Data are mean ± SD, * Exercise effect, p<0.05. † Group effect, p<0.05. ‡ Interaction effect, p<0.05. **a** significantly different from 1-minute, **b** significantly different from 5-minute. **c** significantly different from 30-minute, p<0.05). Brachial systolic BP (bSBP), brachial diastolic BP (bDBP), brachial mean BP (bMAP), Carotid systolic BP (cSBP),carotid diastolic BP (cDBP), cardiac output (CO), stroke volume (SV) and central pulse wave velocity (PWV), cerebral blood flow velocity (CBFv).

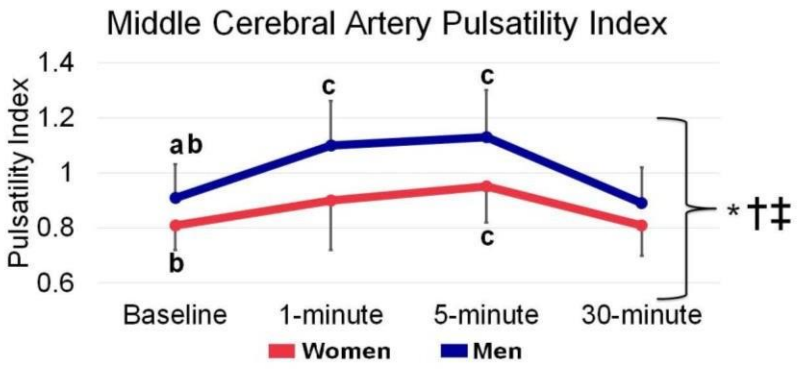


Figure 1. All Data are mean ± SD, * Exercise effect, p<0.05. † Group effect, p<0.05. ‡ Interaction effect, p<0.05. **a** significantly different from 1-minute, **b** significantly different from 5-minute. **c** significantly different from 30-minute, p<0.05).

Conclusion

Men increased CBFv pulsatility at 1-minute post-RE compared to women, demonstrating a sex difference in cerebral vascular reactivity. RE increased central arterial stiffness, mean CBFv, HR, and BP similarly for both sexes. CO was also elevated at 5-minute, but CBFv dropped below baseline and pulsatility continued to rise above baseline. This temporary disruption in cerebral autoregulation may impact brain health in both sexes.

5.5 Impact of pulmonary endarterectomy on pulmonary arterial wave propagation and reservoir function

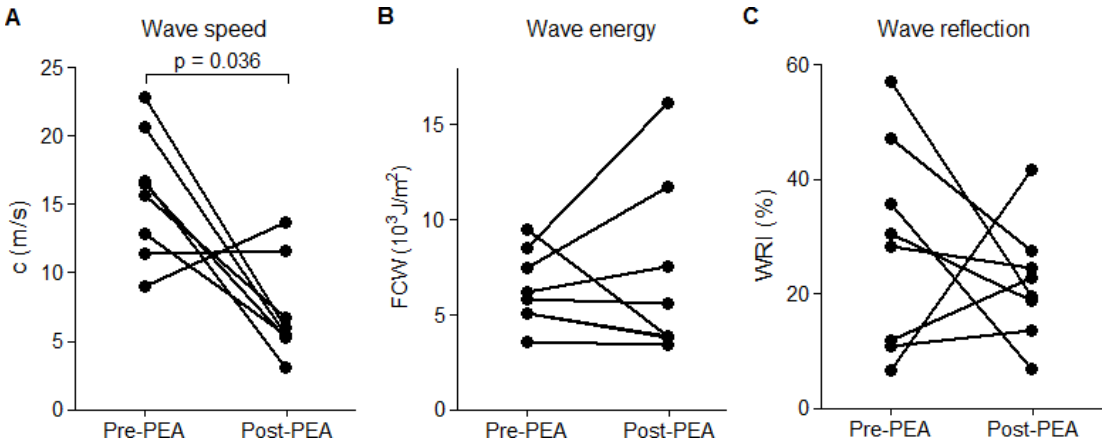
Su, Junjing[1,2]; Hughes, Alun[3,2]; Simonsen, Ulf[1]; Nielsen-Kudsk, Jens Erik[4]; Parker, Kim[5]; Howard, Luke[2]; Mellemkjaer, Søren[4]

[1]Department of Biomedicine, Aarhus University, [2]National Heart and Lung Institute, Imperial College London, [3]Institute of Cardiovascular Science, University College London, [4]Department of Cardiology, Aarhus University Hospital, [5]Department of Bioengineering, Imperial College London

Background
Recent studies have demonstrated distinctive arterial wave characteristics in patients with chronic thromboembolic pulmonary hypertension (CTEPH)[1]. Therefore, we aimed to assess the impact of pulmonary endarterectomy (PEA) on pulmonary arterial wave propagation and reservoir function in CTEPH patients.

Methods
Right heart catheterization was performed using a pressure and Doppler flow sensor tipped guidewire to obtain simultaneous pressure and flow velocity measurements in the pulmonary artery in eight CTEPH patients before and 3 months after PEA. Wave intensity and reservoir-excess pressure analyses[2] were subsequently applied to the
acquired data and the diastolic pressure decay time was estimated.

Results
Following PEA, mean pulmonary pressure (49 ± 10 mmHg versus 32 ± 13 mmHg), pulmonary vascular resistance (PVR) and wave speed, i.e. local arterial stiffness, significantly improved. However, there were no significant changes in arterial wave energy and wave reflection index (29.3 % [11.4 – 41.4 %] versus 21.2 % [16.2 – 25.9
%] post-PEA), even in patients with normalized pulmonary pressure. The RC-time (product of PVR and compliance) decreased post-PEA. Furthermore, the reservoir pressure related to arterial compliance, excess pressure caused by arterial waves and asymptotic pressure at which the flow would cease significantly decreased post- PEA and the changes were associated with improved right ventricular afterload, function and size.



Conclusion
Large wave reflection persisted post-PEA indicating lack of normalization of vascular impedance mismatch. Decreased RC-time suggests structural damage to the pulmonary vasculature. Wave intensity and reservoir-excess pressure analysis may be used as an additional assessment of the hemodynamic outcomes following PEA.

References
(1) Quail MA, Knight DS, Steeden JA, Taelman L, Moledina S, Taylor AM, et al. Noninvasive pulmonary artery wave intensity analysis in pulmonary hypertension. Am J Physiol Heart Circ Physiol 2015 June 15;308(12):H1603-H1611. (2) Parker KH. Arterial reservoir pressure, subservient to the McDonald lecture, Artery 13. Artery Research 2013 September;7(3-4):171-85.

5.6 Longitudinal follow-up of arterial stiffness in patients with severe psoriasis treated by anti-IL12/IL-23 compared to anti-TNF alpha

Khettab, Hakim[1]; Viguier, Manuelle[2]; hamdidouche, Idir[3]; Bachelez, Hervé[4]; Boutouyrie, Pierre[5,1,3]

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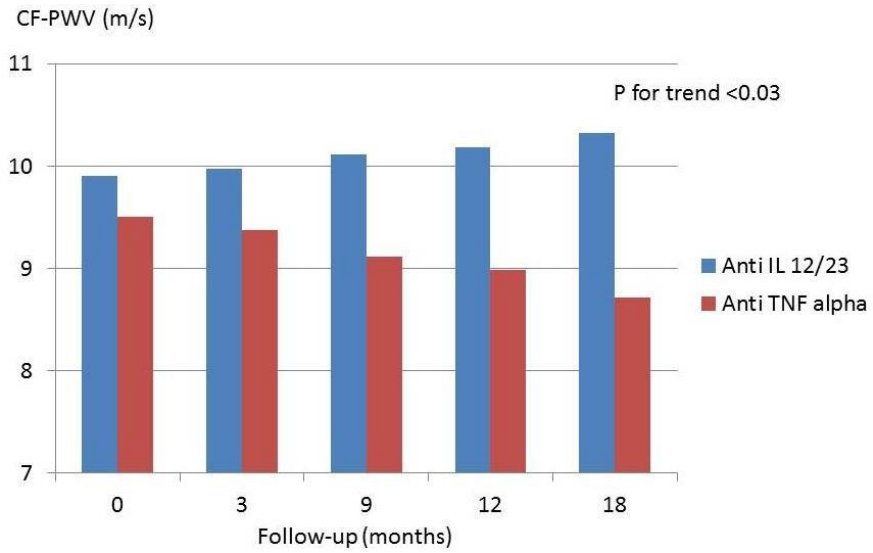
Patients with chronic severe psoriasis are at increased cardiovascular risk (CVR). Modern systemic treatments of psoriasis involve anti-TNF alpha (ATNF) and more recently introduced anti-IL12/IL-23 (ustekinumab, AIL12/23) which, by interfering with IL-17, a possibly vasculoprotective cytokine, may increase CVR. We characterized large arteries remodeling and stiffness during longitudinal follow-up under ATNF and AIL12/23.

We included 31 patients. Followed-up was 13±3 months with a mean number of 3 visits. Patients were treated either by ATNF (n=13) or by AIL12/23 (n=18). Mean age was 49 (27-71) 50% were females, 89% were overweight, 55% smokers and 32% (well controlled) hypertensives. Patients did not differ for severity scores of psoriasis or baseline characteristics. Carotid to femoral pulse wave velocity (PWV) and central pressure (applanation tonometry), carotid PWV and IMT (echotracking) were measured at each visit.

Blood pressure and heart rate did not change with either treatment. Carotid diameter did not change during follow-up, IMT increased more with AIL12/23 than in ATNF group (diff. à 18 months 75 µm, p=0.10). Carotid distension and carotid distensibility decreased significantly under AIL12/23, whereas it increased with ATNF, independently of BP. Carotid PWV and CF-PWV increased independently of BP with AIL12-23 and decreased with ATNF (18 months diff. +1.60 m/s and +1.15 m/s, p<0.05, respectively).



We documented an increased in stiffness and hypertrophy of large arteries during longitudinal follow-up of patients under antiinterleukin 12/23 treatment for psoriasis, compared to antiTNFalpha. Whether this is due to a protective effect of ATNF and/or adverse effect of AIL12-23 remains to be determined.

References

Bachelez H. Interleukin 23 inhibitors for psoriasis: not just another number Lancet. 2017 31474-5. .

5.7 Subpopulations of circulating T lymphocytes in obese patients undergoing bariatric surgery

Agabiti Rosei, C[1]; Rossini, C[1]; Mittempergher, F[2]; Titi A[2]; Portolani, N [2]; De Ciuceis, C[1]; Caletti, S[1]; Coschignano, MA[1]; Trapletti V[1]; Porteri E[1]; Pileri P[1];Agabiti Rosei, E[1], Rizzoni, D[1,3]

[1]Clinica Medica and [2]Clinica Chirurgica, Department of Clinical and Experimental Sciences, University of Brescia, Italy; [3]Istituto Clinico Città di Brescia, Division of Medicine, Brescia, Italy

Objective
It has been previously demonstrated that T lymphocytes may be involved in the development of hypertension and microvascular remodeling, and that circulating T effector lymphocytes may be increased in hypertension. In particular, Th1 and Th17 lymphocytes may contribute to the progression of hypertension and microvascular damage while TREG lymphocytes seem to be protective. However, no data is avaliable about patients with severe obesity, in which pronounced microvascular alterations were observed.

Methods
We have investigated 32 severely obese patients undergoing bariatric surgery, 24 normotensive lean subjects and 11 hypertensive lean subjects undergoing an election surgical intervention. No sign of local or systemic inflammation was present in any subject or patient. A peripheral blood sample was obtained before surgery for assessment of CD4+ T lymphocyte subpopulations. Lymphocyte phenotype was evaluated by flow cytometry after 5 hour in vitro activation in order to assess T- effector and T-regulatory (TREG) lymphocytes. Subsets of TREGS were defined as follows: -TREGS recent thymic emigrants (RTE), directly derived from thymus: CD31+; -TREGS naïve: CCR7+CD45RA+; -TREGS central memory (CM): CCR7+CD45RA-; -TREGS effector memory (EM): CCR7-CD45RA-; -TREGS
terminal differentiated effector memory (TDEM): CCR7-CD45RA+.

Results
The results are summarized in the Table (*p<0.05, **p<0.01, ***p<0.001 vs. lean normotensives; #p<0.05, ##p<0.01, ###p<0.001 vs. lean hypertensives). A marked reduction of several TREG subpopolations was observed in obese patients compared with controls, together with an increased in some T-effector cells.

	Lean normotensives	Lean hypertensives	Obese patients
TREGs (%)	4.11±1.60	4.64±1.66	2.69±1.81 **##
TREGs (abs number)	45.4±24.3	45.4±23.8	27.3±21.1 **#
TREGs naive (%)	22.1±10.1	18.1±13.1	13.34±12.9 **
TREGs naive (abs number)	10.6±7.75	9.71±8.87	3.87±5.28 ***##
TREG CM (%)	32.3±13.8	32.8±17.8	22.7±15.2 *#
TREGs CM (abs number)	14.7±10.2	14.2±9.08	6.10±8.08 ***##
CD4+ EM (%)	24.4±9.96	26.8±12.5	34.1±13.3 **
CD161+CD28+ (%)	86.2±28.5	94.9±5.63	97.2±5.39 *

Conclusion
TREG lymphocytes are clearly reduced in severely obese patients, possibly contributing to the development of marked microvascular alterations previously observed in such a population.

10.10 Focus Update

Chair: J Sharman, C Palombo

Arterial hemodynamics and wave reflections

Professor Patrick Segers, *Ghent University, Belgium*

Professor Alun Hughes, *University College London, UK*

Despite years of research, there are still some contentious aspects of arterial hemodynamics that have remained unresolved. These were discussed during a workshop entitled Arterial hemodynamics: past, present and future held in London on June 14 and 15, 2016, with keynote contributions by Nico Westerhof, Kim Parker and Michael O'Rourke. In follow-up of that meeting, we formulated a list of potential consensus statements informed by discussion at the meeting in London and quantified the degree of agreement and invited comments from the participants of the workshop. The survey was set up making use of Google forms.

Overall the responses and comments show a high measure of quantitative agreement with the various proposed 'consensus' statements. There is a large consensus on the nature and role of wave reflections in arterial hemodynamics, while consensus gets more blunted when it comes to methods and paradigms for the analysis of hemodynamics.

The followed methodology provided an elegant way to collect input from a broad scientific community, but we also learned that statements were too broadly formulated, making it harder to obtain clear-cut positions on specific topics. Also, it is highly unlikely that all participants to the poll had the same degree of expertise on all of the topics. As we did not want to weigh answers according to a presumed level of competence (what may also be another source of bias), all answers were equally valued.

Taken together, these statements seem a useful basis for proceeding with a more detailed and comprehensive consensus document on the current understanding and approaches to analysis of the pulse waveform. Future efforts should be directed at identifying remaining areas of dispute and future topics for research.

10.40 Debate

Chair: A Solini, L Ghiadoni

PRO: Arteries are the most important target for CV prevention in diabetes

Professor Kennedy Cruickshank, *Kings College London, UK*

CON: Glucose is the most important target for CV prevention in diabetes

Professor Francesco Giorgino, *University of Bari, Italy*

The overall impact of glucose-lowering on vascular complications and major clinical outcomes, including mortality, in type 2 diabetes is still an open issue. While intensive glucose control has undoubted benefit for microvascular endpoints, the relationship between glucose-lowering approaches and reduced incidence and/or progression of macrovascular complications is less clear. This presentation will discuss the effect of glucose-lowering per se as well as the effects of specific glucose-lowering therapies on vascular outcomes in type 2 diabetes. Recent analyses from large cardiovascular outcome studies (ACCORD, ADVANCE, VADT) provide new information on factors that modulate the impact of intensive glucose-lowering on outcomes, helping to identify the specific clinical characteristics of the patients receiving the intervention that would show better response. Several studies on cardiovascular outcomes with diabetes drugs are now available, and they highlight cardiovascular benefits from using specific medications, as for the SGLT-2 blockers and some GLP-1 receptor agonists.

11.30 Refreshments, Poster and Exhibition viewing

12.00 McDonald Lecture
Chair: K Cruickshank, L Ghiadoni

The Metabolic-Microvascular Dysregulation Syndrome
Professor Coen Stehouwer, *Maastricht University Medical Centre, Maastricht, The Netherlands*

Microvascular and metabolic physiology are inextricably linked. Thus, metabolic dysfunction impairs microvascular function *and* microvascular dysfunction impairs normal metabolism. The relationship is therefore reciprocal, justifying the concept of a 'Metabolic-Microvascular Dysregulation Syndrome'. For example, metabolic dysregulation (hyperglycaemia) causes microvascular dsyfunction, diabetic retinopathy and diabetic nephropathy. Conversely, microvascular dysregulation impairs insulin-mediated glucose disposal, i.e. causes insulin resistance, impairs insulin secretion, and is associated with onset of type 2 diabetes in prospective studies. Obesity is a key driver of the Metabolic-Microvascular Dysregulation Syndrome, as it impairs insulin signal transduction in endothelial cells through adverse changes in adipokines such as adiponectin, free fatty acids and tumour necrosis factor-α. Microvascular dysfunction in obesity appears reversible by diet-induced weight loss. Next to obesity, other factors are also likely to play a role. Examples are microvascular dysfunction of adipose tissue as a primary cause of adipose tissue dysfunction; early life exposures,both antenatal and postnatal; and large artery stiffening. Large artery stiffening is unquestionably important for microvascular function in susceptible organs such as the brain, the eye and the kidney but whether it can cause microvascular dysfunction in metabolically crucial tissues such as skeletal muscle, pancreas and adipose tissue has not been studied. It is therefore not clear that arterial stiffening in and of itself is sufficient to cause the Metabolic-Microvascular Dysregulation Syndrome.

12.30 Lifetime Achievement Award
Chair: K Cruickshank, L Ghiadoni
posthumously awarded to Professor Guiseppe Schillaci

12.45 Concluding Remarks and Close of Conference

13.00 Light lunch

AUTHOR INDEX-SUBMITTED ABSTRACTS

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