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Abstract Book

THURSDAY 13 OCTOBER 2016

11.30 Registration, Poster viewing and light lunch

12.30 **Welcome address**

12.45 **Opening Lecture**

Remodelling small arteries and PhD training: a journey

Professor Michael J Mulvany, *Department of Biomedicine, Aarhus University, Aarhus, Denmark*

Biomedical research is increasingly based on the efforts of PhD students. This talk will trace the development of the author's research, and show how this experience can be used to optimize PhD training. The basis of the research has been that essential hypertension is associated with increased peripheral resistance due to narrowing of the small arteries and arterioles. The author's PhD training ended in 1978 with development of a technique that enabled accurate measurement of the structure and function of small arteries. The technique was adopted by many laboratories world-wide, and also formed the basis for the author to establish a research group (with 22 PhD students over the years) that elucidated excitation-contraction properties and the morphology of small arteries, and how these were altered in essential hypertension. Vessels showed increased media:lumen ratio with inward eutrophic remodelling and limited functional changes. The remodelling was found to have prognostic consequences. The inward remodelling was found to be due to the vasoconstriction itself, mediated through multiple cellular pathways. The remodelling can be prevented by vasodilators and the results have had clinical effect. While this career path points to some success, it would unlikely happen in today's academic environment in that the author's PhD training took about 10 years. Through being head of the faculty graduate school and vice-president of the organization ORPHEUS (Organization for PhD education in Biomedicine and Health Sciences in the European System), the author has sought to establish procedures to ensure that today's PhD students are able to prepare for successful careers – within or outside of academia – even within the normal 3-4 year time constraints.

13.15 **Special Guest Lecture**

Stem cell therapy for cardiovascular diseases

Professor Jean Sebastien Silvestre, *INSERM, Paris, France*

Stem cell-based therapies for vascular regeneration in patients with cardiovascular ischemic diseases initially relied on a very simple concept: therapeutic stem/progenitor cells might differentiate into vascular cells, mainly of endothelial phenotype, increasing new vessel formation and tissue perfusion in the ischemic milieu. This exciting notion challenged the scientific community to start the quest for the Holy Grail in vascular regenerative medicine: the search for the ideal source of endothelial stem/progenitor cells. This concept leads to the development of salutary approaches based on the use of therapeutic autologous adult stem cells thought to contain such bona-fide endothelial progenitor cells such as bone marrow- or peripheral blood-derived mononuclear cells. Beside the classical technical caveats including modalities of cell transfer and optimization of cell engraftment, the negative impact of cardiovascular risk factors as well as the low rate of incorporation of adult stem cells in the targeted vasculature likely explain the mixed results obtained in numerous phase I-II clinical trials incorporating patients with peripheral artery or cardiac diseases. Hence, alternative sources of stem cells have been considered to leverage their intrinsic pluripotentiality and drive them towards a vascular lineage. Both embryonic stem cells and induced pluripotent stem cells have then been tested in various experimental models of post-ischemic vascularization. However, as for their adult counterpart, these "embryonic" cells do not structurally integrate within the recipient vascular network but likely release biomolecules that fine-tune endogenous repair processes. A precise characterization of the cell-released factors purportedly accounting for their benefits still remains elusive. However, there are mounting evidences to suggest that stem cells can release extracellular membrane vesicles that may contain vascular regenerative entities. Hence, the natural evolution of the stem cell theory for vascular regeneration may end with the development of cell-free strategies with multiple cellular targets including vascular cells but also other infiltrating or resident cells.

13.45 **Oral Session I**

1.1 Diabetes and central blood pressure in coronary patients

Professor Piotr Jankowski, Dorota Debicka-Dabrowska, Malgorzata Kloch-Badelek, Leszek Bryniarski, Kalina Kawecka-Jaszcz, Danuta Czarnecka
Department of Cardiology, Interventional Electrocardiology and Hypertension, Jagiellonian University Medical College, Krakow, Poland

Background

Relative (represented by pulsatility) as well as absolute (pulse pressure) changes of central blood pressure (BP) were shown to predict cardiovascular (CV) complications in coronary patients. However, the influence of diabetes (a major CV risk factor) on the values of BP-derived indices is unknown.

Methods
The study group consisted of 1239 patients with coronary artery disease (988 men and 251 women mean age: 58.6±10.1 years) undergoing coronary angiography. Demographic and clinical information as well as cuff brachial and invasive ascending aortic BP during catheterization were obtained. Diabetes was defined as being treated for diabetes or having fasting glucose ≥ 7.0mmol/l. We defined pulsatility as the ratio of pulse pressure (PP) to mean BP and pulsatility index as the ratio of PP to diastolic BP. Multivariate regression analysis was used to assess the effect of diabetes on the values of BP-derived indices.

Results
Diabetes was present in 222 (17.9%) patients. Among them 84 (37.8%) were prescribed insulin, 96 (43.2%) oral drugs, and 42 (18.9%) only diet. β-blockers were prescribed to 82.4% vs 87.2% (p=NS), ACE-inhibitors/sartans to 75.2% vs 57.6% (p<0.05), Ca blockers to 21.2% vs 15.7% (p<0.05), diuretics to 41.0% vs 20.1% (p<0.05), for diabetics and non-diabetics respectively. The effect of diabetes on central pressure is presented in the table. Diabetes was not independently related to the value of peripheral BP-derived indices.

Conclusion
Diabetes is independently related to the higher values of central PP, pulsatility and pulsatility index. This may contribute to higher CV risk in diabetics.

BP – related variables	The mean difference between diabetics and non-diabetics (95% CI)	
	Univariate	Multivariate *
Systolic blood pressure [mmHg]	4.37 (1.03 - 7.70)	2.28 (-1.22 - 5.78)
Diastolic blood pressure [mmHg]	-1.16 (-2.82 - 0.50)	-1.11 (-2.98 - 0.76)
Mean blood pressure [mmHg]	0.66 (-1.34 - 2.66)	0.01 (-2.22 - 2.23)
Pulse pressure [mmHg]	5.53 (2.89 - 8.17)	3.39 (0.80 - 5.99)
Pulsatility	0.05 (0.03 - 0.08)	0.03 (0.01 - 0.06)
Pulsatility index	0.09 (0.05 - 0.13)	0.06 (0.02 - 0.10)

* Age, sex, brachial systolic and diastolic BP, ejection fraction, extent of coronary atherosclerosis, NYHA class, heart rate, creatinine level, risk factors and treatment are included in the model.

1.2 How does obesity influence arterial stiffness in asymptomatic adults?

Dr Bela Benczur[1], Dr Renata Bocskei[2], Professor Attila Cziraki[3]
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Central obesity is an important cause of cardiovascular disease. It's well-known that aortic pulse wave velocity (aoPWV) is a strong predictor of cardiovascular events. However the potential correlation between fat accumulation and increased arterial stiffness is poorly investigated. The aim of this study was to assess the association between obesity and aortic stiffness in normotensive adults.

Patients and methods
AoPWV was assessed in apparently healthy, asymptomatic patient population using an invasively validated oscillometric device (TensioMed Arteriograph). AoPWV-values were stratified according to their BMI-values into three categories: normal weight (BMI<25), overweight (BMI: 25-30) and obese (BMI>30). Data are reported as mean and SD for continuous variables. For data comparison, a Student's t-test was used with a significance level of 0.05. Statistical analysis was carried out with IBM SPSS 20 statistical software.

Results
9076 normotensive individuals (3749 male – 41.3%, and 5327 female – 58.7%) without any antihypertensive, antidiabetic or antilipemic medication were included into the analysis with a mean age of 48.2±14.1 yrs. 4374 individuals were lean (48%), 3346 were overweight (37%) and 1353 were obese (15%) according to BMI-values. Mean aoPWV of lean subjects was significantly better than overweight or obese individuals (8.6±2.41 m/s, 9.3±2.43 m/s ill. 9.8±2.52 m/s respectively p<0.05).

Conclusions
This is the first population-based study to report the effect of weight on vascular stiffness measured by oscillometric method in adults with wide age range. Our results confirmed that overweight and obesity are major determinants of arterial stiffness. The revealed association suggests that weight gain begins to influence on the

vascular system at a very early stage of vascular aging. Nevertheless the effect of weight loss on arterial function needs to be further investigated.

1.3 Central pressures and wave reflections are independently associated with major adverse cardiovascular events in men with erectile dysfunction

Mr Nikitas Skliros, Dr Nikolaos Ioakeimidis, Professor Charalambos Vlachopoulos, Dr Dimitrios Terentes-Printzios, Mr Athanasios Aggelis, Professor Dimitrios Toulousis
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Purpose
Erectile dysfunction (ED) confers an independent risk for cardiovascular events and total mortality. Central pressures and wave reflection indices independently predict cardiovascular events. Aim of this study is to investigate whether central haemodynamics predict major adverse cardiovascular events (MACEs) in ED patients beyond traditional risk factors.

Methods
MACEs in relation to aortic pressures and Augmentation index (AIx) were analyzed with proportional hazards models in 398 patients (mean age, 56 years) without established cardiovascular disease (CVD).

Results
During the mean follow-up period of 6.5 years, a total of 29 (6.5%) MACEs occurred. The adjusted relative risk (RR) of MACEs was 1.062 (95% CI 1.016–1.117) for a 10-mmHg increase of aortic systolic pressure, 1.117 (95% CI 1.038–1.153) for a 10-mmHg increase of aortic pulse pressure (PP), and 1.191 (95% CI 1.056–1.372) for a 10% absolute increase of AIx. The based on categories for 10-year coronary heart disease risk and adapted at 6.5 years overall net reclassification index (NRI) showed marginal and indicative risk reclassification for AIx (15.7%, P=0.12) and aortic PP (7.2%, P=0.20) respectively.

Conclusions
Our results show for the first time that higher central pressures and wave reflections indices are associated with increased risk for a MACE in patients with ED without known cardiovascular disease. Considering the adverse prognostic role of central haemodynamics on outcomes, the present findings may explain part of the increased cardiovascular risk associated with ED.

14.15 Refreshments, Poster and Exhibition viewing

14.45 **Invited Lecture**
Arterial proteomics: Lessons in relation to stiffness, aneurysms, diabetes and other conditions

Professor Lars Melholt Rasmussen, *Odense University Hospital, Odense, Denmark*

Proteins are the main molecular components of the arterial wall. Alterations in the amounts of specific proteins in both the extracellular matrix and in vascular cells are believed to be associated with different arterial pathologies, however only sparse data is currently available, particularly in relation to human arteries.

Proteome analysis is large scale analysis of the quantity of many proteins in a single analytical run from biological samples. Combining “state of the art” proteome analysis by LC-MS (liquid chromatography-mass spectrometry) with access to samples from a large human artery biobank, we have obtained knowledge about protein changes in arteries from patients with various cardiovascular conditions. Specific alterations in matrix proteins are for example present in relation to increased arterial stiffness and to diabetes, whereas alterations in non-matrix proteins are associated with the growth rate of aortic aneurysms.

Such new knowledge about changes of arterial proteins in specific vascular conditions can direct our attention towards pathophysiological understandings and display routes to new potential treatment targets and novel biomarkers for arterial diseases.

15.15 **Career Development Lectures**
Wave potential: a unified model of arterial waves, reservoir phenomena and their interaction

Dr Jonathan Mynard, *Murdoch Childrens Research Institute, Victoria, Australia*

Models of haemodynamics play a central role in current research directed to understanding and addressing cardiovascular disease. Although conventional windkessel and wave models are very useful, they are

incompatible due to conflicting assumptions and neither comprehensively explain the basis and interdependencies of pressure/flow waves, mean pressure and reservoir filling/discharge phenomena. The hybrid reservoir-wave model was proposed to address this gap, but is not widely accepted due to theoretical inconsistencies and negative results from validation studies. We recently described a unified model of haemodynamics based on the concept of 'wave potential', which identifies physically meaningful information from the absolute values of the forward/backward components of pressure and flow. Within this paradigm, hydraulic power may also be separated into forward/backward components, thus allowing study of time-dependent cardiac and vascular effects that influence hydraulic power output and efficiency. Based on in vivo and numerical experiments, it has been shown that 1) absolute values of the pressure/flow/power components represent wave potential, spatial gradients of which produce waves that transfer hydraulic energy, 2) mean pressure is generated by waves, 3) wave potential is a measure of local conduit arterial reservoir function and stored hydraulic energy, and 4) the diastolic pressure decay and associated 'self-cancelling' diastolic waves can be explained purely on the basis of wave reflection and distal leakage of wave potential. Wave potential provides a unified and analytically simple paradigm of arterial haemodynamics that extends and is fully compatible with conventional wave separation, while overcoming the difficulties encountered with the reservoir-wave paradigm.

Vascular dysfunction: at the heart of cardiovascular disease, cognitive impairment and depressive symptoms

Dr Thomas van Sloten, *Maastricht University, Maastricht, The Netherlands*

Vascular dysfunction may be an important pathway through which ageing and other factors, such as diabetes and obesity, can cause diseases of the heart and brain. Vascular dysfunction includes dysfunction of large arteries (due to arterial stiffness), the microcirculation (microvascular dysfunction) and endothelium (endothelial dysfunction). We have investigated, in a series of epidemiological studies, the role of vascular dysfunction in the pathogenesis of cardiovascular disease, dementia and depression. Data were used of The Hoorn Study, The AGES-Reykjavik Study, The Maastricht Study and The SUVIMAX2 Study. In addition, we did two systematic reviews and an individual participant data meta-analysis.

We found that stiffening of the carotid artery is independently associated with incident stroke, but not with coronary heart disease. Furthermore, carotid stiffness improved stroke risk prediction beyond Framingham and cfPWV. In addition, femoral artery stiffening was independently associated with incident cardiovascular disease. Brain MRI studies showed that cerebral small vessel disease is associated with cognitive decline and incident depressive symptoms. In addition, arterial stiffening was associated with cognitive impairment and depressive symptoms, and this association was mediated by cerebral small vessel disease. We also found that endothelial dysfunction is associated with more depressive symptoms. Finally, we showed the presence of interaction (synergy) with regard to cardiovascular risk, between endothelial dysfunction and type 2 diabetes.

From a clinical point of view, these associations are important as they suggest that efforts at favourably influencing vascular dysfunction can have significant public health implications via prevention of cardiovascular disease, dementia and depression.

Arterial inflammation, blood pressure and central hemodynamics – the ABC of diabetic angiopathy

Dr Simone Theilade, *Steno Diabetes Center, Gentofte, Denmark*

Aim

In diabetes patients, we explored relationships between markers of diabetic angiopathy, diabetic complications and adverse outcome.

Methods

Patients were recruited from 3 observational studies from Steno Diabetes Center, Denmark and one randomized, double-blind, international, multicentre study.

We investigated inflammatory proteins, blood pressure (BP) and central hemodynamics as markers of diabetic angiopathy.

Inflammatory proteins were soluble urokinase plasminogen activator receptor and placental growth factor, measured from frozen blood samples (suPARnostic®, ViroGates, Denmark and Elecsys®, Roche, Germany). Sphygmomanometry and/or tonometry measured BPs.

PWV and PWA recordings were obtained with SphygmoCor (Atcor, Sydney, Australia) and Bpro (HealthStats, Singapore) (only PWA). PWA recordings included central BPs, augmentation pressure, augmentation index and subendocardial viability ratio.

Results
We demonstrated increased arterial inflammation and arterial stiffness, and altered central hemodynamics in diabetes. These changes were augmented with longer diabetes duration. Furthermore, diabetic angiopathy measures were related to diabetic complications and predictive of adverse outcome.

We demonstrated significant discrepancies between office and 24-hour BPs, documenting considerable undertreatment of patients and a substantiated need for 24-hour BP recordings.

We demonstrated significant differences in central and brachial BPs, and proposed reference values for central BP in diabetes patients.

Conclusions
Our data show added diagnostic and prognostic value of measurements of diabetic angiopathy evaluated as measures of arterial inflammation, 24-hour ambulatory BP, central BP, arterial stiffness and pulse wave reflection.

Perspectives
Evaluating markers of diabetic angiopathy, may help identify patients at higher risk for development of diabetic complications. These patients may be suited for advanced and earlier medical treatment.

16.15 Refreshments, Poster and Exhibition viewing

16.45 **Oral Session II**

2.1 The relative importance of central and brachial blood pressure in predicting cardiovascular events: an individual participant meta-analysis of prospective observational data from 22,433 subjects

Dr Carmel McEniery[1], Professor Yoav Ben-Shlomo[2], Professor Margaret May[2], Dr Melissa Spears[2], Dr Lyndia Brumback[3], Dr James Cameron[4], Dr Chen-Huan Chen[5], Dr Julio Chirinos[6], Dr Danuta Czarnecka[7], Professor Anthony Dart[4], Professor Richard Devereux[8], Dr Neeraj Dhaun[9], Dr Daniel Duprez[10], Dr Shih-Jen Hwang[11], Dr David Jacobs[10], Professor Piotr Jankowski[7], Dr Julie Janner[12], Dr Peter Lacy[13], Dr Gary Mitchell[14], Professor Riccardo Pini15
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Systolic blood pressure (SBP) differs between the brachial artery and aorta. Prospective data suggest that central pressure predicts future cardiovascular events, but it is unclear if it is superior to brachial pressure.

Methods and Results
A systematic review and individual participant data meta-analysis from 15 studies was undertaken. Study-specific associations of central and brachial pressure with cardiovascular outcomes, with and without mutual adjustment, were determined using Cox proportional hazard models, and random effect models to estimate pooled estimates. Of 22,433 participants, 908 had a myocardial infarction (MI) and 641 a stroke. The pooled age, sex, height and heart rate adjusted hazard ratio (HR) [95% CI] per SD increase in brachial SBP was 1.17 [1.03, 1.32] for MI and 1.28 [1.13, 1.46] for stroke and 1.16 [1.02, 1.33] and 1.33 [1.15, 1.53] for central SBP, respectively. Mutual adjustment attenuated the HRs for MI: brachial SBP (1.16 [0.90, 1.48]), central SBP (1.09 [0.87, 1.38]) and stroke: brachial SBP (1.18 [0.97, 1.42]), central SBP (1.19 [0.99, 1.44]). However, associations between central SBP and stroke, after adjustment for brachial SBP, were higher in those aged <61 years than in older individuals (1.83 versus 1.08 p-interaction <0.001).

Conclusion
Brachial and central SBP have similar associations with future CV events. Larger studies are required to test whether central SBP may be a more powerful predictor of stroke risk in younger individuals.

2.2 Central-to-peripheral diastolic blood pressure attenuation in healthy adolescent and the effects of heart rate. The MACISTE study

Dr Giacomo Pucci, Dr Francesca Battista, Dr Leandro Sanesi, Dr Sara Alessio, Professor Giuseppe Schillaci
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Background
Heart rate (HR) is directly associated to central-to-peripheral pulse wave amplification. We aimed at evaluating the associations between heart rate and each BP component in a cohort of healthy adolescents.

Objective
470 healthy adolescents (17±1.4 years, 56% boys, brachial BP 123/67±11/7 mmHg, HR 72±12 bpm) were enrolled in the present study. Brachial BP was measured on 3 occasions by validated devices. Central BP was estimated by radial and brachial applanation tonometries, and calibrated to brachial MAP/DBP (SphygmoCor).

Results
Brachial and central BP were 123/67±11/7 mmHg and 105/69±9/8 mmHg. SBPamp was 1.17±0.04, PPamp was 1.57±0.13, while DBP amplification was 0.97±0.01 (DBP attenuation). HR had a direct correlation with brachial and central DBP (r=0.38 and r=0.46, both p<0.01) and central SBP (r=0.09, p=0.04), but not with peripheral SBP (p=0.59), and a negative one with brachial and central PP (r=-0.24 and r=-0.37, both p<0.01). HR had a positive association with PPamp (r=0.38, p<0.01), and a negative one with SBPamp (r=-0.14, p<0.01) and DBPamp (r=-0.55, p<0.01). The slope of BP change for each 10-bpm HR increase was steeper for central DBP (2.8±0.3 mmHg), than for peripheral DBP (2.2±0.3 mmHg, p for difference between regression coefficients <0.01), and for central and brachial DBP than for central SBP (0.7±0.3 mmHg, both p<0.01).

Conclusions
HR is associated with more pronounced changes in DBP than in SBP, and in central than peripheral DBP. Increasing HR may attenuate DBP from centre to periphery. The assumption that DBP is constant along the arterial tree may not be valid during dynamic conditions.

2.3 Determinants of inappropriately high pulse wave velocity in hypertensive patients: a retrospective cross-sectional cohort study

Dr Marina Di Pilla[1], Dr Rosa Maria Bruno[1,] Dr Simona Buralli[1], Dr Melania Sgro'[1], Professor Piero Amedeo Modesti[2], Professor Stefano Taddei[1], Professor Lorenzo Ghiadoni1
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Background
Age and blood pressure (BP) are known to be the main determinants of large artery stiffness. However other factors may lead to an inappropriately high pulse wave velocity (PWV). We investigated the determinants of inappropriately high PWV in hypertensive patients and their possible role in causing organ damage accrual.

Methods
Hypertensive patients were selected among those attending a visit in our Hypertension Outpatient Clinic and undergoing carotid-femoral PWV by applanation tonometry, and cardiac and carotid ultrasound during a 5-year period (2006-2011). Inappropriately high pulse wave velocity (PWV) was calculated as the ratio between the observed value and the values predicted according to the formula derived from international reference values stratified by age and mean BP (oPWV/pPWV)1,2.

Results
731 hypertensive patients were selected (age 30-88 years, 42% women, 57% taking BP-lowering drugs). Median oPWV/pPWV was 10±2% (range 6±1-19±6%). In a multiple linear regression model, independent determinants of oPWV/pPWV were: daylight hours (β -1.59, SE 0.33), age (β -0.65, SE 0.08), BMI (β 0.64, SE 0.20), blood glucose (β 0.19, SE 0.05), carotid atherosclerosis (β 2.48, SE 1.20). Though oPWV/pPWV was significantly higher in men and current smokers, the association disappeared in the multiple regression model. There was no association between oPWV/pPWV and any antihypertensive drugs.

Conclusion
Younger age, obesity, dysglicemia are associated with inappropriately elevated PWV in hypertensive patients. A more advanced atherosclerotic process might also contribute to excess aortic stiffness. Whether an inappropriately high PWV translates into an increased cardiovascular risk should be determined in longitudinal studies.

References
1. Determinants of pulse wave velocity in healthy people and in the presence of cardiovascular risk factors: 'establishing normal and reference values'. European Heart Journal 2010; 31(19): 2338-50.

2. http://www.biommeda.ugent.be/research/multiphysics-modeling-and-cardiovascular-imaging/calculator-assessment-measurements-carotid

2.4 Sodium consumption, central and peripheral blood pressure, and food habits in a population of healthy adolescents. The MACISTE study

Dr Giacomo Pucci, Dr Francesca Battista, Dr Marco D'Abbondanza, Dr Leandro Sanesi, Professor Giuseppe Schillaci
Department of Medicine, University of Perugia, Perugia, Italy

Objective
The relationship between sodium consumption, central BP and the main dietary sources of daily sodium intake in adolescence has been poorly explored. We have evaluated sodium intake, central and peripheral BP in a population of Italian adolescents.

Methods
401 healthy adolescents aged 17±1 years (58% boys, average brachial/central BP: 124/67±11/7 mmHg, and 105/69±9/8 mmHg), attending a High School, Terni, Italy, were evaluated. Daily sodium intake was estimated from a single fasting urine by a validated formula. Sources of daily sodium intake were investigated by a self-administered food frequency questionnaire. Central BP was estimated by radial and brachial applanation tonometries, and calibrated to brachial MAP/DBP (SphygmoCor).

Results
24-h estimated urinary sodium (24-hUNa) was 13530 mmol/d (3.116 g/d). The 89% of the population showed excess sodium intake. 24-hUNa was directly correlated to brachial and central SBP (r=0.14 and r=0.15, both p<0.01), to brachial and central PP (r=0.19 and r=0.24, both p<0.01), and to central-to-peripheral PP amplification (r=-0.13, p<0.01), but not to central-to-peripheral SBP amplification (r=-0.01, p=0.85). In a fully-adjusted multivariate regression model, 24-hUNa (b=0.10, p=0.04) was independently related to central-to-peripheral PP amplification, but not to other measures of both peripheral and central BP. In a factorial analysis, the main daily dietary sources of sodium were bread, biscuits, and salt added to foods.

Conclusions
Sodium intake has a direct relationship with both central and peripheral SBP and PP, and shows an independent association with central-to-peripheral PP amplification. The adverse effects of an excess of sodium intake are more pronounced in central than in peripheral PP.

2.5 The effect of renal denervation on central blood pressure and arterial stiffness in treatment resistant essential hypertension: a substudy of a randomized sham-controlled double-blinded trial (the ReSET trial)

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Background
A recent sham-controlled trial (ReSET) showed no sustained effect of renal denervation (RDN) on 24-hour ambulatory blood pressure (24hA-BP) measurements in patients with treatment resistant hypertension.1 The aim of this substudy was to investigate, whether RDN affects central blood pressure (C-BP) and arterial stiffness independently of brachial artery BP-levels.

Methods
ReSET was a randomized, sham-controlled, double-blinded single-center trial. Main inclusion criteria were: daytime systolic 24hA-BP ≥145mmHg following 1 month of stable medication and 2 weeks of compliance registration. RDN was performed by a single experienced operator using the unipolar Medtronic Flex catheter1. C-BP and carotid-femoral pulse wave velocity (PWV) were obtained at baseline and after 6 months with the SphygmoCor®-device.

Results
Fifty-three patients (77% of the ReSET cohort) were included in this substudy. The groups were similar at baseline (SHAM/RDN): n=27/n=26; 78/65% males; age 59±9/54±8 years (mean±SD); systolic brachial BP 158±18/154±17 mmHg; systolic 24hA-BP 153±14/151±13 mmHg; systolic C-BP 146±20/143±17 mmHg; diastolic C-BP 92±14/94±10 mmHg; augmentation index (AIx) 26±9/28±13 %; PWV 10.7±2.1/10.1±2.2 m/s. Changes in systolic C-BP (-2±17 (SHAM) vs. -8±16 (RDN) mmHg), diastolic C-BP (-2±9 (SHAM) vs. -5±9 (RDN) mmHg), AIx (0.7±7.0 (SHAM) vs. 1.0±7.4 (RDN) %), and PWV (0.1±1.9 (SHAM) vs. -0.6±1.3 (RDN) m/s) were not significantly different after six months (P>0.13 in all tests). Changes in brachial BP and 24hA-BP were also not significantly different.

Conclusions
In a sham-controlled setting, there were no significant effects of RDN on C-BP or arterial stiffness. Thus, the idea of BP-independent effects of RDN on large arteries is not supported.

References
1. Mathiassen et al. J Hypertens 2016, E-pub May 24.

2.6 Withdrawn by author

2.7 Non-invasive evaluation of end systolic left ventricular elastane according to pressure-volume curve modelling during ejection in arterial hypertension

Mr Benjamin Bonnet[2], Mr Frank Jourdan[2], Dr Guilhem du Cailar[1], Professor Pierre Fesler[1]
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Objective
Non invasive methods have been proposed to assess end systolic left ventricular (LV) elastance (Ees), but clinical application remains complex. The aim of the present study was to 1) estimate Ees according to modeling of LV pressure-volume (P-V) curve during ejection and validate our method with existing published LV P-V loop data 2) test clinical applicability to detect a difference in Ees between normotensive and hypertensive subjects.

Methods
Based on P-V curve and a linear relationship between LV elastance and time during ejection, we fitted the systolic pressure curve (non linear least square method). We then computed slope and intercept of time varying elastance, and calculated Ees as LV elastance at the end of ejection. As a validation, 22 P-V loops obtained from previous invasive studies were digitized and analyzed with our method. To test clinical applicability, P-V curve was obtained from 32 normotensive and 33 hypertensive subjects, using carotid tonometry and real-time 3D echocardiography.

Results
A strong univariate relationship (r^2=0.92, p<0.005) and good limits of agreement were found between previous invasive measurement of Ees and our new proposed Ejection P-V Curve method. In hypertensives, when compared to normotensives, the increase in arterial elastance (Ea, 1.83±0.80 vs 1.45±0.41 mmHg/mL, p<0.001) was compensated by an increase in Ees (2.65±1.07 vs 1.88±0.54 mmHg/mL, p<0.001) without change in Ea/Ees (0.76±0.19 vs 0.85±0.23, p=0.09).

Conclusions
Ees can be estimated non invasively from modeling of P-V curve during ejection. This approach was found sensitive enough to detect an expected difference in LV contractility in hypertensive patients.

POSTER SESSION I – SPECIAL POPULATIONS I

6.1 Peripheral artery disease and central hemodynamic modification

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Peripheral arterial disease (PAD) affects the hemodynamics of the lower limbs1 and is associated with increased cardiovascular risk and mortality2. The aim of this study was to evaluate central hemodynamics and to test the relationships between lower ankle-pressure index (ABI) and Augmentation index (Aix)3,4.In 242 PAD patients (mean age 67±9.8years),Augmentation index (Aix) carotid-femoral pulse wave velocity (c-fPWV), pulse pressure amplification (PPA) aortic pulse pressure (aPP) and subendocardial viability ratio (SEVR) weremeasured using applanation tonometry5,6.The ABI values were obtained using an 8-mHz Doppler probe7.c-fPWVwas similar (0.164) in both sexes, AIx was higher (p <.0001), aPPwas marginally higher (p=0.062) PPA and SEVR were lower (p= 0.013), (p<.0001) in women with PAD In the multiple regression model Aix was associated with MAP (p<.0001), age (p=0.0003), smoking history (p=0.013), cfPWV (p=0.016) diabetes (p=0.039) and female sex (p =

0.050). In this large PAD populationAix is increased in women with PAD but is not associated with a lower ABI. Furthermore, it remains uncertain whether Aix in women with PAD provides more information concerning the prognosis of these high-risk patients.

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6.2 Impact of diabetes on arterial stiffness

Professor Rogerio Toshiro Passos Okawa, Professor Jorge Juarez Vieira Teixeira, Mr Alex Cardoso Perez, Mr Eigi Wilton de Souza, Miss Giovanna Chiqueto Duarte, Mr Guilherme Norio Hayakawa, Miss Lorena Lima Gargaro, Miss Marina Franciscon Gomes da Cruz, Mr Michel Lima Moro Alves, Miss Milene Cripa Pizatto de Araujo, Mr Patrick Sadao Nishikawa, Miss Rafaela Pelisson Regla, Mr Rafael Campos do Nascimento

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Objectives/ Background

The purpose of our study was to examine the impact of diabetes on arterial stiffness.

A systematic review, published by Cecelja and Chowienczyk (1), describes that pulse wave velocity (PWV), is highly predictive of cardiovascular events, and PWV is associated with age and blood-pressure, but other pressure- independent risk factors including: dyslipidemia, smoking, diabetes, obesity remain inconsistent in many studies.

Methods

We included 796 patients, 398 of whom had diabetes. Patients were separated according to age, and we used the normal values for PWV described by Boutouyrie et al (2) .We analyzed time of disease, diabetes control, and their impact on PWV.

A Mobil- o -Graph device was used to analyze the PWV, and a Stata 9.0 software was used for the statistics analysis.

Results

We found that diabetes is associated with an increase in PWV (OR: 1.6 $p<0.01$) and the diabetes control also had influence in the PWV increase, which means that an glycated hemoglobin above 7.0 % had an OR: 2.4, $p< 0,001$.

When we analysed the time of diabetes diagnosis, the longer duration of disease (> 120 months) had thirty-eight times more risk to increase the PWV, and those that had been diagnosed between 61 to 119 months had approximately three times more risk to increase the PWV.

Conclusions

In our study we found that diabetes had increased the pulse wave velocity.

Diabetes control and duration of disease also had impact on arterial stiffness.

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6.3 Arterial stiffness is associated with low-density non-calcified coronary plaques in patients with type 2 diabetes and healthy controls

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Background

Arterial stiffness may provide non-invasive information about cardiovascular risk in patients with type 2 diabetes. We investigated the association between arterial stiffness and subclinical coronary atherosclerosis in patients with type 2 diabetes and healthy controls.

Methods

Patients with type 2 diabetes and controls were recruited from an on-going study on diabetes complications. Arterial stiffness (carotid-femoral pulse wave velocity [PWV]) was obtained by applanation tonometry (SphygmoCor®, Australia) whereas volumes [mm3] of total [TP], calcified [CP], non-calcified [NCP], and low density non-calcified coronary plaques [LD-NCP]) were obtained by coronary CT-angiography and analyzed by semi-automative software (Autoplaq®, USA). A two-part model was used to describe the association between PWV and 1) the presence of plaques in all participants and 2) the extent of plaques in participants with coronary atherosclerosis.

Results

PWV and coronary atherosclerosis data were available for 49 patients and 63 controls (age 63±10 years, 49% males, diabetes duration 7.7±1.5 years). Patients had higher PWV than controls (9.6±2.4m/s vs. 8.4±1.8m/s, p<0.01). PWV was associated with the presence of plaques in crude analysis (odds ratio per 1m/s increase in PWV: TP 1.5, p<0.01, CP 1.4 p<0.01, NCP 1.4 p<0.01 and LD-NCP 1.3 p=0.03) but not in analysis adjusted for age, sex, blood pressure, and diabetes. In the presence of coronary plaques, PWV was associated with the extent of LDNCP (crude: 1.2 mm3/m/s, p<0.01 adjusted: 1.2mm3/m/s, p=0.02).

Conclusion

The presence and the extent of coronary atherosclerosis is associated with PWV in patients with type 2 diabetes and healthy controls.

6.4 Large and small artery crosstalk in patients with type 2 diabetes

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Background

Vascular complications to diabetes mellitus have, traditionally, been divided in to micro- and macroangiopathy. However, a growing body of evidence has put this categorical division into question, as large artery stiffness has been associated with microvascular complications in diabetics, e.g. diabetic retinopathy. The pathophysiology behind this association is poorly understood. The retinal arterioles lack sympathetic innervation and blood supply is autoregulated to accommodate changes in blood pressure and metabolic demand. Recently, dynamic vessel analysis of the retina, has made direct observation of the dynamic function of the microvascular bed of the retina feasible (spontaneous vessel oscillations). However, the crosstalk between dynamic retinal arteriole functioning and large artery stiffness remains to be elucidated.

Methods

We will include 20 type 2 diabetics and 20 sex- and age-matched controls. Arterial stiffness (carotid-femoral Pulse Wave Velocity) is assessed using applanation tonometry (SphygmoCor). Retinal blood supply regulation is examined using the Dynamic Vessel Analyzer under two conditions: i) during exposure to flickering lights which

increases the metabolism of the retina, and ii) during static exercise (hand-weight lifting) which elevates systemic blood pressure.

Results
Results will be ready for presentation at the congress. Currently, 7 participants have been examined and 16 more participants have been recruited. Study completion September 2016.

Perspectives
This study provides new insight into large-small artery crosstalk. We hypothesize that large artery stiffness is associated with reduced spontaneous vessel oscillations and perturbed retinal blood flow regulation.

6.5 Association between increased arterial stiffness and HbA1c and LDL cholesterol level in type 2 diabetes patients

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Background
In patient with type 2 diabetes mellitus (T2DM) the atherosclerosis apper in younger age, in both gender and the cardiovascular risk is much higher. The aim of our study was to examine the association between pulse wave velocity (PWV) and glycated haemoglobin (HbA1c) and low density lipoprotein (LDL-C) level in patient with T2DM. (1,2)

Methods
We performed a prospective observational study, outpatient measurement included: aorta PWV measured by arteriograph, HbA1c and LDL-C level. The cut off-points are: PWV: 9 m/s, LDL-C: 2,5 mmol/l, HbA1c: 6%. In the first part of the analysis were included 169 patients with T2DM (106 men, 63 women, average age: 59 year), and were 152 patients (99 men, 53 women, average age: 59 year) in the second part. Linear regression analysis was carried using SPSS software.Values of $p<0.05$ were considered to be statistically significant.

Results
In the first investigation we found signicantly higher PWV in 87 patients (51%), mean: 9,27 m/s. The LDL-C level was higher than 2,5 mmol/l in 67% of cases, mean: 2,935 mmol/l. The second investigation underline a strict linear association between PWV and HbA1c (means: PWV: 9,286 m/s, HbA1c: 6,792 %.)

Conclusion
Our studies show parallel association between elevated HbA1c and PWV, as well as between higher LDL-C and PWV, which represent the elevated arterial stiffness (AS). Measurement of arterial stiffness can provide additional information about cardiovascular risk in patient with T2DM, which support the importance of arteriograph the only type of non-invasive method for AS measurement. (3,4)

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6.6 Aortic-brachial stiffness mismatch in patients with arterial hypertension and type 2 diabetes mellitus

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Background
Patients with type 2 diabetes have a high risk of CVD. Arterial stiffness gradient is a new prognostic predictor of mortality previously assessed only in dialysis population1-2.

The aim of the study was to assess arterial stiffness and stiffness gradient in diabetic patients with arterial hypertension (AH).

Methods
The study included 55 patients with AH and DM (38% male, mean age 61.6±12.7 years), mean office BP 142.5±25.5/82.7±10.7mmHg. All patients receive combination antihypertensive therapy, 7.27% of patients received statins. Target BP values (<140/85 mmHg) were achieved in 52.7% of patients. Target HbA1c levels were achieved in 10.9% of patients. Carotid-femoral (CF) and carotid-radial (CR) PWV were assessed and increased arterial stiffness was defined as an elevation of pulse pressure (PP)>60 mmHg,PWV>10 m/s. Stiffness gradient was assessed by CF-PWV/CR-PWV ratio, with values>1 indicating the stiffness mismatch.p<0.05 was considered significant.

Results
Mean PP was 47.6±12.7mmHg. PP>60mmHg was observed in 18,1%.Group with PP>60 mmHg was characterized by higher HbA1c (9.8±1.8vs8.4±2.0%) and stiffness gradient (1.4±0.4vs1.2±0.1)p<0.05 for trend. Mean CR-PWV was 7.7±1.2 m/s, mean CF-PWV was 10.3±2.0 m/s. CF-PWV>10m/s was observed in 27.2% of patients. Groups with PWV above and below 10m/s were similar by age, gender, metabolic risk factors and haemodynamic parameters. Mean stiffness gradient was 1.3±0.4, gradient >1 was observed in 92,7%. Patients with high stiffness gradient were older (63.3±11.6vs54.0±10.2,p<0.05). All other parameters were similar.

Conclusion
Patients with AH and type 2DM are characterized by aortic-brachial stiffness mismatch. Thus it can be used as early marker of vascular ageing in this patients` population.

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6.7 First evidence of pulsatile pressure interaction between the macro-vasculature and micro-vasculature: proof-ofconcept by association with kidney dysfunction among patients with type 2 diabetes
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Objectives
It is widely thought that excess pulsatile pressure energy from increased stiffness of large central arteries (macro-vasculature) is transmitted to capillary networks (micro-vasculature) and causes end-organ damage (i.e. kidneys). However, this hypothesis has never been tested, and we sought to achieve this by examining people with increased macro-vascular stiffness (patients with type 2 diabetes T2DM) compared with non-diabetic controls.

Methods
Among 13 T2DM (68±6 years) and 15 controls (58±11 years) macro-vascular function was measured by aortic stiffness and radial artery waveforms by tonometry. Forearm micro-vascular waveforms were simultaneously measured via low power laser Doppler flowmetry, with augmentation index (AIx) and augmented pressure (AP) derived on all waveforms. Kidney function was assessed by estimated glomerular filtration rate (eGFR).

Results
Aortic stiffness was higher among T2DM (9.3±2.5 vs 7.5±1.4 m/s, p=0.046). There was an obvious pulsatile micro-vascular waveform, with qualitative features similar to radial waveforms. Macro-vasculature AIx and AP were significantly related to micro-vasculature AIx (r=0.428. p=0.005 and r=0.545, p=0.004 respectively). Micro-vascular (but not macro-vascular) AIx was associated with eGFR in T2DM (r=-0.632, p=0.037).

Conclusions
This is the first in-human evidence of pulsatile pressure interaction between the macro-vasculature and micro-vasculature, and provides potential explanation for accelerated kidney dysfunction.

6.8 The relationship between diastolic function and central hemodynamics in diabetic hypertensive patients

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Background
Diabetic hypertensives patients present different hemodynamic pattern than only hypertensive patients. We aimed to investigate the relationship between the diastolic function and the pulse pressure amplification (PPA), an index combining both arterial stiffness and wave reflexion, in diabetic hypertensives subjects compared to hypertensive subjects.

Methods
We examined 123 patients admitted to the one day hospital of the Hotel-Dieu Hospital (Paris, France) for cardiovascular risk assessment. Anthropometric, laboratory and clinical measurements were collected. Hemodynamic parameters (central blood pressure, aortic pulse wave velocity [PWV], augmentation index [AIx] and PPA) were measured using applanation tonometry. Standard ultrasound echocardiography was performed.

Results
Diabetic hypertensive subjects (n=44) were older than hypertensive subjects (n=79) (mean age[SD] 64[9] vs 56[14], p<0.05), and they presented similar cardiovascular risk factors frequencies. Gender was equally distributed. The diastolic function, assessed by the E/E' ratio was significantly positively correlated with PWV in total population (r=0.19, p=0.03), with no differences between the two groups. At the contrary, E/E' ratio was not correlated with PPA in total population, but it was significantly and negatively correlated with PPA only in the diabetic group (p for interaction 0.007, r= - 0.35, p=0.02). The multiregression analysis (containing all the confounding variables) in this group revealed as significant (p value<0.05) determinants of PPA: the diastolic function (partial-R2=0.14), gender (partial-R2=0.27), heart rate (partial-R2=0.26), angiotensin blockers treatement (partial-R2=0.13).

Conclusion
We confirmed that diabetic hypertensive patients have different hemodynamic behaviour than hypertensive non-diabetic patients. The results suggest that the mechanisms linking diastolic function with PPA are more prominent in diabetic patients.

6.9 Antiplatelet and vascular effects of aspirin in healthy persons and patients with type 2 diabetes

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Background
Treatment with aspirin is a cornerstone in the secondary prevention of cardiovascular disease (CVD) in diabetes, whereas its place in primary prevention remains controversial.

The effect of once-daily aspirin on platelet aggregation is unclear in patients with diabetes. Furthermore, the effects of aspirin on endothelial-dependent vasodilation and arterial stiffness, both important predictors of CVD, needs to be clarified.

Our aim is to investigate both the acute and the chronic effects of aspirin on platelet aggregation, endothelial-dependent vasodilation and arterial stiffness during 24 hours in patients with type 2 diabetes without CVD and in healthy controls.

Method
Based on power calculations, we will include 21 patients with type 2 diabetes and 21 sex and age-matched controls. Platelet aggregation is measured by impedance aggregometry, whereas arterial stiffness (carotid-femoral pulse wave velocity) is assessed by applanation tonometry. Endothelial-dependent vasodilation is assessed by peripheral arterial tonometry.

Outcome variables will be obtained at baseline and 1 hour after administration of aspirin. Participants are then treated for 6 days with once-daily aspirin and measurements are performed again 24 hours and 1 hour after aspirin intake.

Results
Preliminary results will be ready for presentation at the congress.

Perspective
This study provides new insight into whether once-daily dosing of aspirin is sufficient for effective platelet inhibition during 24 hours in patients with type 2 diabetes without CVD. Furthermore, this study will clarify if aspirin has positive effects on endothelial-dependent vasodilatation and arterial stiffness and if these effects are obtained effectively using a standard once-daily regimen of aspirin.

6.10 Peripheral sensory neuropathy and vascular angiogenic factors in type 2 diabetes patients in Ghana

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Background
Impaired angiogenesis may be amongst the possible mechanism underlining the development of peripheral sensory neuropathy (PSN) in type 2 diabetes (T2DM) patients.(1) Angiogenesis is regulated by circulating vascular growth factor, notably, angiopoietin (Ang)-1, Ang-2 and vascular endothelial growth factor (VEGF).(2) We studied the relationship between PSN and circulating vascular growth factors, Ang-1, Ang-2 and VEGF in T2DM patients.

Method
PNS was assessed by vibration perception threshold (VPT) using Horwell's neurothesiometer, and serum levels of Ang-1, Ang-2 and VEGF were also measured by Elisa in 107 T2DM patients and 93 nondiabetes subjects (controls). PNS was defined as VPT>25V.

Results
The overall prevalence of PNS was 11.2% higher in T2DM patients (10.1% vs. 1.1%, p=0.012) than controls. T2DM patients had higher mean VPT (12.1±7.8 vs. 7.3±3.8 V, p<0.001) than controls. Compared to those without PNS, PNS patients had lower Ang-2 levels [0.4 (0.2 – 0.8) vs. 0.8 (0.4 – 1.1) nmol/l, p=0.03] and higher VEGF levels [120 (60.8 – 254.4 vs. 59.4 (17.2 – 146.8), p=0.037], but no difference in Ang-1 levels. VPT was associated, positively with VEGF levels (r=0.22, p=0.003), and negatively with Ang-1 (r=-0.17, p=0.024), but not with Ang-2.

Discussion
Diabetes is associated with high prevalence of PNS and elevation of circulating vascular growth factors. PNS patients had imbalanced levels of circulating vascular growth factors, which may indicate impaired angiogenesis.

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POSTER SESSION I – SPECIAL POPULATIONS II

7.1 The detrimental effects of live firefighting on arterial function in firefighters

Mr Alexander Rosenberg[1], Mrs Kanokwan Bunsawat[1], Mr Tommy Wee[1], Dr Tracy Baynard[1], Dr Gavin Horn[2], Dr Denise Smith[3], Dr Bo Fernhall[1]
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Background
Aging is associated with increased arterial stiffness and wave reflection, which is predictive of all-cause cardiovascular (CV) mortality (1-3). Firefighters have the highest cardiovascular mortality of any occupational group (4). High levels of heat stress, physical exertion, and elevated arterial stiffness (5) during/following firefighting provide a susceptible milieu for CV events.

Purpose
To describe the differential effects of age following live firefighting on cardiac, arterial function and wave reflection.

Methods
Firefighters aged 18-37yrs (n=18, YA) or 38-55yrs (n=17, MA) participated in a staged 12-minute live firefighting scenario. Blood pressures (BP), pulse wave analysis, pulse wave velocity (PWV) and hemodynamic measurements were obtained at rest, immediate and 30 minutes post-firefighting using an automated ambulatory blood pressure monitor (Mobil-O-Graph, I.E.M, Germany).

Results
YA increased heart rate and PWV more than MA in response to live firefighting ($p<0.01$). YA also decreased systemic arterial compliance ($p<0.01$) immediately post-firefighting more compared to MA, which returned to baseline values at 30-minutes. MA had higher PWV, total vascular resistance, and diastolic BP than YA ($p<0.01$). Systolic BP, pulse pressure, and reflective magnitude increased immediately post-firefighting for YA ($p<0.01$) but not in MA ($p>0.05$).

Conclusions
Young and MA firefighters exhibit differential cardiovascular responses to live firefighting. Although MA had higher PWV, diastolic BP and higher peripheral resistance they exhibited attenuated changes following live firefighting. Thus, arterial and hemodynamic parameters in younger firefighters appeared to change in a direction associated with increased risk to a greater degree than observed in older firefighters.

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7.2 Poor sleep quality related to worse vascular function in individuals with multiple sclerosis
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Background
Poor sleep quality has been related to poor vascular function and higher risk of cardiovascular disease in the general population. Persons with multiple sclerosis (MS) exhibit a high cardiovascular risk, and report poor sleep quality. To date, the association between sleep quality and vascular health in MS has not been investigated. Objective: To investigate differences in vascular health between good and poor quality sleepers with MS. Methods: After a 10 minute rest in the supine position, resting heart rate (HR) and brachial blood pressure (BP) were collected.Aortic SBP, augmentation index (AIX), HR normalized AIX (AIX@HR75), subendocardial viability ratio (SEVR), end systolic pressure (ESP), and central pulse wave velocity (PWVc) were measured with applanation tonometry in individuals with MS (n=49). Carotid intima-media thickness (IMT) and beta-stiffness were measured with carotid ultrasound, and peak forearm blood flow (FBF Peak) was measured with strain gauge plethysmography. Sleep quality was measured with the Pittsburgh Sleep Quality Index (>5 was categorized as poor sleep quality). Age was used as a covariate.

Results
AIX@HR75 and SEVR were different between groups, even with age as a covariate, suggesting higher vascular risk for the poor quality sleepers with MS.

Conclusions
This study shows that within the MS population, poor quality sleepers have a higher cardiovascular risk than good quality sleepers. Whether poor sleep raises their cardiovascular risk more than in the general population is an area of future investigation.

	Good quality sleepers with MS (n=23)	Poor quality sleepers with MS (n=26)	Effect of sleep quality		Effect of age	
	Mean (SD)	Mean (SD)	p	Partial Eta2	p	Partial Eta2
N Female (%)	18 (75%)	22 (82%)				
PSQI score	2.9 (1.5)	9.7 (3.1)				
Age	44 ±13	52 ±10				
BMI	26.9 ±5.4	28.1± 5.6	.582	0.007	.584	0.007
HR	64 ±10	65± 8	.136	0.048	.014*	0.125
SBP	116 ±14	122 ±14	.384	0.017	.025*	0.105
DBP	72 ±9	74 ±10	.457	0.012	.559	0.007
MAP	86± 10	90 ±11	.403	0.015	.175	0.040
Aortic SBP	106 ±14	114 ±14	.223	0.032	.001**	0.200
AIX	21.1 ±13.7	30.0± 9.0	.082	0.064	<.001**	0.282
AIX@HR75	15.1± 12.0	25.5± 7.6	.007**	0.150	.001**	0.211
SEVR	158± 21	147 ±18	.026*	0.103	.160	0.042
ESP	96 ±12	103± 14	.213	0.034	.007**	0.148
PWVc	6.7± 1.4	7.5± 1.4	.200	0.036	.007**	0.146
PWVc/MAP	0.078± 0.014	0.084 ±0.016	.376	0.017	.063	0.073
IMT	0.51± 0.11	0.53 ±0.12	.571	0.007	<.001**	0.342
Beta	7.3 ±2.3	8.1± 2.7	.785	0.002	.002**	0.193
FBF Peak	17.8 4.4	17.2 6.6	.988	0.000	.185	0.038

* p<0.05**p<0.01

7.3 Assessment of blood pressure and heart rate variability in Multiple Sclerosis

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Background
Reported cardiovascular autonomic dysfunction (CAD) prevalence in Multiple Sclerosis (MS) varies between studies. As CAD lowers quality of life and may contribute to sudden death in MS, early CAD detection may assist treatment and risk identification.

Methods
In 23 MS patients and age and gender matched controls (38±12 years, 15 female), continuous electrocardiogram and finger blood pressure were non-invasively acquired during 5 minutes supine rest. Baroreceptor sensitivity (BRS) was quantified through sequence and coherence analysis. Heart rate variability (HRV) was analysed in the standard manner and systolic blood pressure variability (SBPV) quantified in the very low (0.0033-0.04 Hz), low (0.04-0.15 Hz) and high (0.15-0.5 Hz) frequency ranges.

Results
HRV did not differ between the groups. BRS in the high frequency band was lower in MS than control (22±13 and 39±25 ms/mmHg, p=0.007) as was normalised low frequency SBPV (0.70±0.19 and 0.82±0.14, p=0.006). Normalised high frequency SBPV was greater in MS subjects (0.31±0.19 and 0.18±0.14, p=0.006). Differences in high frequency SBPV indicate differences in respiratory feedback (not directly measured in this study) and in the low frequency range, differences in baroreceptor and/or chemoreceptor cardiovascular control. High frequency coherence in BRS analysis likely indicates reduced BRS control (as suggested by no difference in BRS by the sequence technique), but also respiration derived control of the sinus node.

Conclusions
These results indicate that MS subjects have altered degree of cardiovascular autonomic control compared to healthy subjects and the effect of the respiratory pathway warrants further investigation.

7.4 Higher carotid strain in individuals with Down Syndrome at rest and during hypovolemic sympathoexcitation

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Background
Arterial stiffness and large artery function are independent risk factors for cardiovascular disease.(1) Individuals

with Down Syndrome (DS) have autonomic dysfunction and known to have lower incidence of cardiovascular disease.(2) Limited literatures showed no difference in arterial stiffness in DS compared to a healthy, non-DS population using a longitudinal view of the carotid artery.(3,4) However, it is unknown if individuals with DS exhibit different circumferential strain compared to individuals without DS at rest or during a sympathoexcitation stimulus.

Purpose
To examine the differences in the carotid artery strain and its responsiveness to sympathoexcitation by hypovolemic lower body negative pressure (LBNP) in individuals with and without DS.

Methods
Twenty four volunteers (DS=11, 23 yrs Control=13, 23 yrs) participated in this study. Circumferential strain was measured by ultrasonography B-mode and radial strain from the longitudinal view was calculated using echo tracking analysis at rest, during and after sympathoexcitatory stimulation by LBNP. Changes in hemodynamics (HR, BP) were recorded continuously.

Results
Compared with controls, individuals with DS have significantly higher strain values at all stages ($p < 0.05$) with no group interaction with hypovolemic sympathoexcitation stimulation. However, there were no differences in β-Stiffness or EP, suggesting that the differences in strain were due to differences in blood pressure.

Conclusions
Our results demonstrate significantly higher strain value, which indicates greater arterial movement in individuals with DS. However, these differences were likely due to higher BP in persons with DS.

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7.5 Retinal vessel responses to flickering light provocation in a cohort of black and white teachers: the SABPA study

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Background
Retinal microvascular function can be assessed using flicker light induced provocation (FLIP). Reduced vessel dilation responses to FLIP are noted in various disease conditions. Comparative studies between ethnic groups are scarce, while the importance of different phases of the vessel responses during and following FLIP are not well studied. We compared retinal vessel dilation, constriction and vessel diameter parameters following FLIP in a cohort of black (n=152) and white (n=178) teachers.

Methods
Retinal vessel responses to FLIP were assessed using the Dynamic Vessel Analyzer (IMEDOS Systems, Jena, Germany). Ambulatory blood pressure (BP), anthropometry and blood sampling were performed.

Results
Black participants displayed a better maximum percentage dilation (artery: 4.1±3.5% vs. 3.5±2.0%, $p<0.015$ vein: 4.2 (2.2-8.7)% vs. 3.7 (1.4-8.0)%, $p=0.014$) in response to FLIP. Time to maximum artery constriction (MaxCons) was longer (52.0 (44.0-66.0)s vs. 44.0 (37.0-54.0)s, $p<0.001$), and end FLIP artery diameter was smaller in the black cohort. In linear regression analysis, artery dilation was generally associated with age, BP, BP medication and artery caliber, and mostly in the black cohort. In the black cohort, artery MaxCons was not associated with

selected cardiometabolic variables, but in the white cohort, was related to age, gamma-glutamyltransferase and no BP medication. A smaller artery diameter post FLIP associated with increased C-reactive protein in both ethnicities.

Conclusions
Black and white participants differed in their retinal vessel response to FLIP. Although certain cardiovascular risk markers were associated with these responses, they may not explain all the differences noted between the groups.

7.6 The difference in glutathione peroxidase activity on arteries of a bi-ethnic population: The SABPA study

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Background and objectives
From the literature it is evident that increased oxidative stress is integral in the development of cardiovascular disease. We therefore aimed to compare glutathione peroxidase (GPx) and glutathione reductase (GR) activity between black and white Africans, and to investigate whether the activity of these enzymes are linked with cardiovascular function.

Methods
This sub-study was embedded in the Sympathetic Activity and Ambulatory Blood Pressure in Africans (SABPA) study, included 188 black and 203 white teachers from the Dr Kenneth Kuanda Education District in the North West Province of South Africa. Ambulatory blood pressure (BP) and carotid dorsalis pedis pulse wave velocity (cdPWV) were measured. Biochemical analyses included GPx and GR enzyme activity, serum peroxide and total glutathione levels.

Results
The blacks presented with an unfavourable cardiovascular profile, with systolic- and diastolic BP, pulse pressure and cdPWV being significantly higher ($p \leq 0.006$) when compared to their white counterparts. The black group also displayed significantly higher levels of serum peroxides ($p=0.049$) with concomitant lower GPx activity ($p=0.01$), while their total glutathione levels ($p<0.001$) and GR activity ($p<0.001$) were significantly higher. In single regression analysis, an inverse relationship between GPx activity and cdPWV ($r=-0.16$ $p=0.024$) were indicated, only in the white group. The link between higher GPx activity and lower cdPWV was confirmed to be independent in multiple regression analyses ($R^2= 0.39$ $\beta=-0.18$ $p=0.005$), while it was absent in the black group.

Conclusion
An inverse relationship between GPx activity and cdPWV was encountered, suggesting a protective role of higher GPx activity against arterial stiffening in the white group.

7.7 The effect of marine n-3 polyunsaturated fatty acids on cardiac autonomic and hemodynamic function in patients with psoriatic arthritis: a randomised, double-blind, placebo-controlled trial

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Background
Patients with psoriatic arthritis are at high cardiovascular risk. Marine n-3 polyunsaturated fatty acids (PUFA) may reduce the incidence of cardiovascular disease. The aim of this study was to investigate the effect of marine n-3 PUFA on cardiac autonomic function and vascular function in patients with psoriatic arthritis.

Methods
The study was conducted as a randomized, double-blind, placebo-controlled trial, where 145 patients with psoriatic arthritis were supplemented with 3 g of n-3 PUFA or olive oil (control) daily for 24 weeks. Blood pressure, heart rate, HRV, central blood pressure, pulse wave velocity (PWV) and fatty acid composition of granulocytes, were determined.

Results
At baseline we found a significant difference in the HRV parameter RR when comparing subjects with the highest vs the lowest fish intake ($p = 0.03$).

After supplementation for 24 weeks there was a trend towards an increase in RR ($p= 0.13$) and decrease in heart rate ($p = 0.12$) comparing the n-3 PUFA group with the control group. However, per-protocol analysis (performed on participants who completed the trial with a good compliance) showed significantly increased RR ($p = 0.01$) and lowered heart rate ($p = 0.01$) in the n-3 PUFA supplemented patients compared to controls. Blood pressure, PWV and central blood pressure did not change after supplementation with n-3 PUFA.

Conclusions
Marine n-3 PUFA increased HRV in patients with psoriatic arthritis which may suggest a protective effect of n-3 PUFA against cardiovascular disease in this population.

7.8 Arterial stiffness and systemic inflammation in COPD patients

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Background
COPD is one of the leading causes of mortality worldwide. Systemic low-grade inflammation is a common finding in COPD. Soluble urokinase-type plasminogen activator receptor (suPAR) indicates an inflammatory state and it has an association with atherosclerosis and cardiovascular disease (CVD). ThesuPAR reflects different aspects of inflammation as high sensitive C-reactive protein (hsCRP) and IL-6. Elevated CVD risk is observed in COPD. However the correlation between COPD and arterial stiffness is rarely investigated in the literature.

We investigated the association between some inflammatory biomarkers (suPAR, IL-6, hsCRP) and arterial stiffness in COPD and control patients.

Methods
We measured 45 middle aged individuals (25 COPD and 20 control normotensive patients) without diabetes and cardiovascular disease. IL-6, hsCRP, suPAR were determined in fasting blood samples. Whole body plethysmography, assessment tests and aortic pulse wave velocity (aoPWV), augmentation index (Aix), central systolic blood pressure (cSBP) were determined. COPD patients were categorized according to GOLD-classification.

Results
Patients with COPD have a higher level of IL-6 (5.38 vs 3.63 pg/ml p=0.022), suPAR (2.84 vs 2.41 ng/ml p=0.036), and hsCRP (2.99 vs 1.91 mg/L p=0.068). The patients with COPD have a significant higher aoPWV (p=0.002), and cSBP (p=0.022).

Conclusion
In this study we found elevated inflammatory markers and aoPWV in COPD patients, both of them indicate the presence of earlier atherosclerosis than in controls without COPD.

7.9 Carotid artery stiffness is associated with CT-measured lung air-trapping in COPD patients and controls independent of age, blood pressure and smoking history

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Background
Early stages of chronic obstructive pulmonary disease (COPD) are characterized by loss of the terminal bronchioles and ‘air trapping’ often before overt emphysema manifests (1). COPD patients are also at risk for cardiovascular disease (CVD), therefore, we hypothesized that the degree of air trapping on computed tomography (CT) (2) would be associated with higher aortic (carotid femoral pulse wave velocity, CFPWV) and carotid artery stiffness (β-stiffness), biomarkers of CVD risk.

Methods
Ten adults with COPD but little emphysema (age 66±8 yrs, 5F/5M, GOLD stage 1-3) and 9 adults without COPD (age 59±13 yrs, 5F/4M) that had a research chest CT were recruited.

Results
COPD patients had greater smoking history (45.9 ± 21 vs. 6.4 ± 12.9 pack-years, P<0.001) and air trapping (0.85± 0.07 vs. 0.78 ±0.05 Expiration/Inspiration attenuation ratio, p<0.05) (2) compared with non-COPD subjects, but did not differ by age, BMI, SaO2%, brachial BP or % emphysema (all p>0.05). COPD patients had significantly higher CFPWV (999± 293 vs. 760 ±147 cm/sec, p<0.05) but not carotid β-stiffness (13.3± 5.1 vs. 10.6 ±4.7 U, p=0.26). In the entire cohort (n=19), air trapping was associated with higher CFPWV (r=0.60, p<0.01) and carotid β-stiffness (r=0.75, p<0.001). After adjustment for age, mean BP and pack-years, the correlation between carotid β-stiffness and air-trapping remained significant (r=0.68, p<0.01).

Conclusions
Carotid artery stiffness is significantly associated with air trapping in COPD patients and controls, independent of

age, smoking history and BP. This suggests a link between high CVD risk in COPD patients with small airway disease without predominant emphysema.

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7.10 Aortic stiffness and Body Mass Index (BMI) in Chronic Obstructive Pulmonary Disease (COPD)

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Background

Patients with COPD have increased Cardiovascular (CV) risk and commonly present with altered body composition. Patients with COPD and a low BMI have poorer health outcomes1, while obesity may increase CV risk2. The aim of this analysis was to explore BMI, CV risk, exercise capacity and systemic inflammation in COPD.

Methods

This analysis included 524 stable patients with COPD (confirmed with spirometry) from the ARCADE (Assessment of Risk in Chronic Airways Disease Evaluation) study. Assessments included lung function (forced expiratory volume in 1 second (FEV1)), smoking history, BMI, aortic pulse wave velocity (PWV) (SphygmoCor device), blood pressure (BP), 6-minute walking distance (6MWD). Inflammation was measured by high sensitivity C-reactive protein (HsCRP) and fibrinogen. Patients were classified by BMI as follows: low (<19.9 Kgm2), healthy (20-24.9Kgm2), overweight (25-29.9Kgm2) obese (>30Kg/m2).

Results

There was no difference in gender, age, lung function or smoking history between patients grouped according to BMI. However, there was a difference in PWV, systolic BP, 6MWD and inflammation between the groups ($p<0.05$). The difference in PWV remained after adjustment for age and mean BP (Table 1). Overweight and obese patients (BMI <25) had greater PWV and inflammation, while obese patients had the poorest 6MWD.

Conclusions

The findings suggest obese patients with COPD have greater CV risk which may be a result of poorer physical capacity and greater inflammation. Optimisation of BMI in COPD may improve outcomes further follow-up of this cohort will evaluate the prognostic value of arterial stiffness and possible therapeutic targets.

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POSTER SESSION I – CLINICAL SCIENCE I

8.1 Arterial stiffness, blood pressure and cardiac output study

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We are planning a prospective study in 200 patients with an abdominal artery aneurysm (AAA). Non-invasive measurements will be performed including tonometry-based pulse wave analysis (PWA) and pulse wave velocity (PWV), echocardiography, and 24-hour blood pressure measurements.

This study will provide insight in how PWV/PWA-parameters can help identify characteristics of prostheses used to treat AAA that best match native aortic characteristics and will lead to the best long-term outcome after aneurysm repair. Also the interaction between blood pressure (and control) and cardiac output will be evaluated. These results will form the basis for evidence-based practice for stent choice and lead to better outcomes after

AAA treatment. First we will validate non-invasive against invasive central pressure in 20 patients treated with endovascular aneurysm repair (EVAR).

This study will provide insight if arterial stiffness parameters change over time after treatment of AAA and the possible role of PWV/PWA for the surveillance after treatment. We expect to provide insight in the various determinants of the PWV/PWA-parameters pre- and post-repair of AAA evaluation also includes graft material, intraluminal thrombus, and inflammation. We will study whether the different PWV/PWA parameters predict outcome after AAA repair for different prostheses.

Finally, this study will reveal whether parameters of cardiac output obtained by tonometry correspond with parameters obtained by echocardiography in AAA patients. If so, the PWV/PWA measurement can detect cardiologic problems at an early stage during follow-up. By early treatment, the development of heart failure can be delayed or even prevented. We look forward to input on our study-plan.

8.2 *Withdrawn by author*

8.3 Quantifying heart and arterial contributions to central blood pressure in systole

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Background
A recent study has shown that the central pressure waveform could be determined by a very small set of parameters accounting for the physical properties of the heart and the arteries [1]. Particularly, main pressure features like first systolic shoulder (P1) and systolic (P2) pressures were estimated accurately.

Methods
By combining a numerical virtual population (n=3,325) similar to [2] and experimental data acquired from a pressure/Doppler flow velocity transducer place in the ascending aorta in 18 patients (meanSD: age 63±11 yr, aortic BP 136±23/73±13 mmHg) at the time of cardiac catheterization, we assessed the accuracy of those predictions for magP1 (P1-DBP) and P2 using respectively a water hammer [3] and a 3-element Windkessel models [4]. Contributions of the heart and arterial properties to these estimates though respectively blood velocity, volume and pulse wave velocity, compliance, resistance were then derived from the theoretical models used.

Results
P1 and P2 estimates agreed well with theoretical pressure both in the numerical dataset (mean+/-SD difference, 1.1±3.2 mmHg and -1.6±3.1 mmHg respectively) and the clinical cohort (mean+/-SD difference, -2.4±5.5 mmHg and 1.9±6.5 mmHg respectively). The ratio arterial-to-heart contribution has been shown to be fairly constant as magP1 was increasing.

Conclusions
Arteries and heart contribute as much to rise in P1. More clinical data are being collected to quantify the contributions of the heart and arteries to P2.

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8.4 Diurnal changes in central pressure and pulse wave parameters in healthy subjects

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Purpose
The feasibility of pulse wave analysis (PWA) over 24 hours with oscillometric devices has already been shown and first studies indicate additional information compared to single measurements. Nevertheless, diurnal patterns of PWA parameters in healthy subjects, which can potentially serve as a reference, are currently missing. Therefore, the aim of this study was to perform 24h-PWA measurements in healthy subjects over a wide age range and to analyse day/night differences.

Methods
91 well defined healthy subjects underwent 24h PWA measurements using the Mobil-O-Graph device (IEM, Germany). The subjects were categorized in three age groups (20-29 years, 30-49 years, 50-69 years). Daytime (9-21h) and nighttime (0-6h) averages were calculated.

Results
A significant dipping behaviour in all age groups could be found for diastolic blood pressure (> 14 mmHg in all age groups, p<0.05), peripheral systolic blood pressure (> 15 mmHg, p<0.05) and central systolic blood pressure (> 9 mmHg, p<0.05). A significant rising effect in all age groups was found for the reflection magnitude (> 8 %). In contrast, the day/night difference in augmentation index was age dependent and this dependency remained also for AIx75, see table.

Conclusions
Prominent pressure dipping and a rise in reflection magnitude were present in all age groups during nighttime, while diurnal changes in augmentation index showed an age-dependency. This differing behaviour of PWA parameters should be investigated in further studies. Furthermore, the observed effects of diurnal changes in healthy subjects may provide a basis for reference profiles for future patient evaluation.

	20-29 years			30-49 years			50-69 years		
	day		night	day		night	day		night
pSBP (mmHg)	118.8	*	103.4	124.8	*	109.0	123.0	*	105.8
pDBP (mmHg)	75.7	*	59.5	81.4	*	64.2	79.6	*	64.8
cSBP (mmHg)	106.3	*	97.1	114.8	*	103.3	114.5	*	100.7
cDBP (mmHg)	77.4	*	60.6	83.1	*	65.3	81.1	*	65.6
HR (bpm)	76.0	*	59.6	77.5	*	64.4	70.4	*	59.8
AIx	18.2		19.0	19.7		22.7	25.9	*	35.0
AIx75	19.3	*	10.4	20.6		15.7	23.4		26.4
RM	55.2	*	63.2	59.7	*	68.8	62.3	*	71.5

Table: Mean day and night values for peripheral systolic blood pressure (pSBP), peripheral diastolic blood pressure (pDBP), central systolic blood pressure (cSBP), central diastolic blood pressure (cDBP), heart rate (HR), augmentation index (AIx, AIx75) and reflection magnitude (RM) * marks a significant difference between day and night (t-test, p<0.05).

8.5 Hemodynamics during intra- and interdialytic periods depend on ultrafiltration volume

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Introduction
Parameters of arterial stiffness are independent cardiovascular risk factors for end-stage renal disease patients. Significant changes of these parameters between intra- and interdialytic periods have been reported previously [1]. The aim of this cross-sectional study is to describe the influence of the ultrafiltration volume on hemodynamic parameters.

Methods
All measurements were obtained with the Mobil-O-Graph 24h PWA (I.E.M. GmbH, Germany) within the ISAR hemodialysis study. Measurement started before the midweek dialysis session and lasted for 24-hours. 348 patients (238 male / 110 female 65 +- 18 years) were included. Intra- and interdialytic parameters were averaged and compared for three subgroups (ultrafiltration volume (UFV) <= 500 ml (N = 50) 500 < UFV< = 2000 ml (N = 159) UFV > 2000 ml (N = 139)) and all subjects.

Results
The results for all patients support the findings of Karpetas et al. [1] (see Table). Beyond [1], the results underpin the differences between subgroups for intra- and interdialytic periods. Furthermore, there are significant differences between intra- and interdialytic periods depending on the ultrafiltration volume (see Table). Exemplarily, there is a significant rise in the augmentation index (26.0 vs. 28.5%, $p < 0.05$) for UFV > 2000 ml and for central pulse pressure (39.6 vs. 43.4 mmHg and 36.0 vs. 38.3, $p < 0.05$) for UFV <= 2000 ml opposed to non-significance for the other subgroups.

Conclusions
Our findings support the hypothesis that hemodynamic parameters depend on ultrafiltration volume. Further studies should investigate their prognostic value considering the ultrafiltration volume.

	UFV <= 500 ml			500 < UFV <= 2000 ml			UFV > 2000 ml			All		
	In		Out	In		Out	In		Out	In		Out
pSBP (mmHg)	128.9		131.0	123.7		122.3	124.5		123.0	124.8		123.8
pDBP (mmHg)	75.9		74.5	74.9		72.3	75.6		73.1	75.3	*	72.9
pPP (mmHg)	53.0		56.5	48.8		50.0	478.8		49.9	49.4		50.9
HR (bpm)	69.4		70.2	68.1	*	70.8	71.8		73.7	69.8	*	71.9
cSBP (mmHg)	116.9		119.3	112.4		111.9	113.4		112.6	113.4		113.2
cDBP (mmHg)	77.3		75.9	76.3		73.6	77.2		74.6	76.8	*	74.3
cPP (mmHg)	39.6	*	43.4	36.0	*	38.3	36.2		38.0	36.6	**	38.9
AIx (%)	29.7		31.8	29.5		30.2	26.0	*	28.5	28.1	*	29.8
AIx75 (%)	26.4		28.8	25.5	*	27.7	24.0	**	27.6	25.1	**	27.8
PWV (m/s)	10.03		10.14	9.88		9.85	9.08		9.07	9.58		9.58

Table: Averaged hemodynamic parameters for intra- and interdialytic periods (In vs. Out) for different subgroups based on ultrafiltration volume (UF) and all subjects. Abbreviations: peripheral diastolic blood pressure (pDBP), peripheral systolic blood pressure (pSBP), peripheral pulse pressure (pPP), heart rate (HR), central diastolic blood pressure (cDBP), central systolic blood pressure (cSBP), peripheral pulse pressure (pPP), augmentation index (AIx, AIx75) and pulse wave velocity (PWV) */** marks a significant difference between intra- and interdialytic periods ($p < 0.05$ and $p < 0.01$, respectively).

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8.6 Aerobic fitness level and peripheral arterial compliance - the role of autonomic nervous system tone
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Physical activity has beneficial effects on prevention of cardiovascular disease. Aerobic fitness is associated with higher central arterial compliance, but its effect on peripheral arterial compliance (pC) is controversial. We aimed to test the hypotheses that aerobic training augments pC at rest and during different autonomic nervous system provocations (ANSP) inyoung healthy men.

We enrolled 44 males, 19-24 years old (22 trained, VO2max=485ml/kg/min - group A, 22 sedentary controls, VO2max=303ml/kg/min - group B). VO2max was determined using cycloergometry (QuarkCPET, Cosmed). On the testing day, ECG, arterial blood pressure (Finapres, Ohmeda) and finger artery compliance at rest, 3 minutes during 0.1Hz breathing and 3 min during mental stress were measured. A noninvasive method was used to determine compliance index (CI), calculated as an average of the pressure dependant compliance curve in the range of arterial pressures from 97 to 105mmHg.

Our results revealed elevated CI in group A compared to group B (4.18±0.38 and 1.28±0.25, p=0.004) at rest and no significant differences in CI between groups during ANSP (1.34±0.20 at 0.1Hz breathing and 0.82±0.18 during mental stress in group A compared to 1.09±0.21, p=0.06, and 0.60±0.12, p=0.08 in group B). A statistically significant positive linear correlation existed between CI and VO2max (P<0.001) at rest in group A, however, no correlation was found at both ANSP.

Regular aerobic training increases pC in healthy young subjects at rest, but not during 0.1Hz breathing or mental stress. Our findings indicate that peripheral and not central autonomic mechanisms govern pC in young healthy males.

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8.7 Changes in cardiac function but not structure in healthy subjects with premature vascular ageing

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Purpose

Changes in myocardial and arterial wall properties/function are consistently reported in patients with established cardiovascular disease1. However, few studies have reported these changes in early subclinical disease. The aim of the present study was to examine cardiac and vascular changes in early subclinical disease and to determine whether these changes occur in parallel.

Methods

For this study, 98 healthy lifelong never smokers were recruited. Subjects were categorised as having normal (Norm, n=71) or abnormal (High. n=27) arterial stiffness (carotid-femoral pulse wave velocity, PWV Vicorder, Skidmore, UK) for their age and blood pressure. M-mode Doppler echocardiography (Vivid 7 Dimension, GE, USA) was used to assess heart structure (interventricular septal thickness, IVSd left ventricular internal diameter, LVIDd left ventricular posterior wall thickness, LVPW left ventricular mass, LV Mass) and function (left ventricular isovolumetric relaxation time, LV IVRT mitral valve early/late filling velocity, MV E/A).

Results

No differences in age (39+/-9 v 39+/-9 years P 0.87) or BMI (24.85+/-3.29 v 25.75+/-3.68 kg.m2 P 0.24) were observed. No differences in IVSd (0.86+/-0.15 v 0.85+/-0.18 cm P 0.64), LVIDd (4.98+/-0.55 v 4.96+/-0.42 cm P 0.95), LVPWd (0.81+/-0.17 v 0.90+/-0.21 cm P 0.05) or LV Mass (168.86+/-56.85 v 182.61+/-61.70 g P 0.43) were observed. However, MV E/A (1.85+/-0.51 v 1.48+/-0.51 P 0.0004), but not LV IVRT (0.09+/-0.02 v 0.09+/-0.01 P 0.25), was different.

Conclusions

Changes in cardiac function are observed before alterations in cardiac structure in healthy subjects with premature vascular stiffening.

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8.8 Sympathetic vasoconstrictor response to lower body negative pressure in young obese adults: the preliminary finding

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Background

Elevations in muscle sympathetic nerve activity (MSNA) and sympathetic vasoconstrictor responsiveness to sympathoexcitation are associated with increased cardiovascular risks, which affect hemodynamics, and have been reported in obese adults with metabolic syndrome (1-3). It remains unclear whether this observation may also be present in young metabolically healthy obese adults.

Purpose

To compare sympathetic vasoconstrictor and hemodynamic responsiveness to lower body negative pressure (LBNP, -20 mmHg) in young normal-weight (NW) vs. obese (OB) adults.

Method
Eleven NW (female=6; 25±2 yrs; 22.4±0.6 kg/m2) and 13 OB adults (female=6; 27±1 yrs; 32.7±0.6 kg/m2) underwent 2-min of LBNP in the supine position. Ultrasonography [brachial diameter, forearm blood flow (FBF), forearm vascular conductance (FVC)], MSNA [burst frequency, total MSNA, sympathetic vascular transduction], and beat-to-beat hemodynamics [heart rate (HR), mean arterial pressure (MAP), total peripheral resistance (TPR), cardiac output (CO), stroke volume (SV), systemic compliance (SC)] were reported. FBF and FVC were normalized to lean forearm mass, and TPR, CO, SV, and SC to body surface area.

Results
Baseline MAP was lower in OB ($P<0.05$). In response to LBNP, normalized FBF, FVC, SV, CO, and SC decreased whereas TPR increased similarly in both groups ($P<0.05$). Brachial diameter and HR did not change in both groups. MAP decreased similarly by ~2-4 mmHg, but the values were lower in the OB group ($P<0.05$). Burst frequency, total MSNA, and sympathetic vascular transduction increased similarly in both groups ($P<0.05$).

Conclusion
Young metabolically healthy obese adults did not exhibit altered sympathetic vasoconstrictor responsiveness under resting condition.

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8.9 Reduction in myocardial wall stress and delayed myocardial relaxation during exercise

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Introduction
Myocardial wall stress (MWS) is thought to be the mechanical stimulus to ventricular hypertrophy (1,2). The objective of this study was to examine the effect of exercise on time-varying MWS (3).

Methods
Twelve subjects, aged 42.0 ± 16.8 (mean ± SD) years, systolic blood pressure (BP) (128 ± 11mmHg), were studied before and during peak bicycle exercise (85% of target heart rate). We estimated MWS from 3D transthoracic echocardiographic imaging of the left ventricle (LV) and LV pressure was derived from carotid tonometry during systole. Carotid pressure calibrated by mean and diastolic BP was used to calculate time-varying LV wall stress from endocardial and epicardial volumes obtained from Philips 3DQ analysis package. Time of onset relaxation (TOR) was defined as percentage of time to peak wall stress to ejection duration.

Results
There was a significant reduction in peak and mean MWS during exercise (rest 435.3±25.3 VS exercise 385.9±22.5, $p=0.001$ and 387.3±24.2 VS 368.7±19.6 kdynes/cm2, $p=0.016$), despite significant increase in systolic BP (128±3 VS 210±6 mmHg, $p<0.001$). LV end-diastolic volume (EDV) (119.3±9.4 VS 95.2±7.8ml, $p<0.001$) and volume at time of peak MWS (86.5±7.0 VS 68.3±6.3ml, $p=0.001$) were reduced significantly during exercise, but TOR was delayed (24.5±1.2 VS 31.0±1.6%, $p=0.003$).

Conclusion
Peak and mean MWS were reduced during peak exercise as a result of reduction in pre-load, despite of significant increase in systolic BP. But there was evidence of delayed myocardial relaxation during exercise.

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8.10 Brachial artery flow-mediated dilatation: different patterns of wall shear rate increase during reactive hyperaemia

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Background
Wall shear rate (WSR) is considered an important stimulus for flow-mediated dilatation (FMD). However, its estimation by conventional ultrasound is challenging due to inherent difficulties of velocity estimation near the arterial wall. To evaluate how WSR influences brachial artery FMD, we used a prototype Doppler ultrasound system which provides simultaneous estimates of WSR at near and far walls and continuous arterial diameter tracking.

Methods
Data from 33 young healthy individuals (27.5±4.9yrs, 19F) were analysed. FMD was assessed with a conventional reactive hyperaemia technique using Ultrasound Advanced Open Platform (ULA-OP). All acquired raw data were post-processed using custom-designed software to obtain WSR and diameter parameters.

Results
Baseline diameter and FMD were 3.29±0.45 mm and 6.54±3.54 %, respectively. During hyperaemia, we observed two distinct patterns of increased WSR: monophasic (MOP, n=15 fast increase reaching peak WSR at once) and biphasic (BIP, n=18 fast followed by slow increase before reaching peak WSR). In BIP, peak WSR (657±153 sec-1 vs 522±132 sec-1) and WSR area under the curve until peak dilation (20398±6265 au vs 13530±5592 au) were significantly greater than in MOP (both $p<0.05$). Absolute diameter increase was significantly greater in BIP (0.24±0.10 mm) than in MOP (0.15±0.09 mm, $p<0.05$). Percentage diameter increase tended to be greater in BIP (7.6±3.3 %) than MOP (5.3±3.5 %, $p=0.08$).

Conclusions
These results demonstrate that there are distinct WSR increase patterns during hyperaemia, and that these patterns are associated with differences in the magnitude of hyperaemic WSR. Our observations suggest that these WSR increase patterns may be associated with the subsequent brachial artery FMD response.

8.11 Cardio-ankle vascular index and carotid-femoral pulse wave velocity are closely associated with chronological age

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Background
Vascular stiffening is part of the ageing process. However, it is not clear which vascular stiffness parameters are closely associated with chronological age.

Methods
Fifty-eight participants (38 men), age 69.57 ± 10.46 (mean ± SD, range = 47-90 years) who have had transient ischaemic attack or lacunar stroke within the last 2 weeks, had vascular stiffness parameters, brachial and central blood pressures measured. Cardio-ankle vascular index (CAVI) was measured with VaSera VS-1500N® (Fukuda Denshi, Japan); carotid-femoral pulse wave velocity (cfPWV) and carotid-radial pulse wave velocity (crPWV) were measured with Complior® (ALAM Medical, France); radial augmentation index (rAIx) and central blood pressure were measured with SphygmoCor® (AtCor, Australia).

Results
The mean and standard error of the mean for each parameter (mean ± SEM) was as follows: CAVI=9.77 ± 0.21, cfPWV = 10.61 ± 0.46 m/s, crPWV = 11.05 ± 0.30 m/s, rAIx = 31.34 ± 1.60 %, and central pulse pressure (cPP) = 50.22 ± 1.81 mmHg. In a bivariate analysis, CAVI ($r = 0.59$, $p<0.01$) and cfPWV ($r = 0.39$, $p<0.01$) were significantly associated with age, but rAIx ($r = 0.12$, $p = 0.371$) and crPWV ($r = 0.06$, $p=0.682$) were not. A multivariate regression analysis, performed with age as the dependent factor and CAVI, cfPWV, crPWV, cPP, and rAIx as independent parameters, showed that CAVI was the only significant parameter ($\beta = 0.49$, $p = 0.002$) associated with age.

Conclusion
CAVI and cfPWV are closely associated with chronological age, whereas crPWV and rAIx are less so. We

suggest that the vascular parameter which best predicts biological age is CAVI, followed closely by cfPWV.

POSTER SESSION I – BASIC SCIENCE AND IMAGING

9.1 Ultrasound characterization of cardiovascular alterations in young ob/ob mice

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Obesity is associated with diabetes and an increased cardiovascular risk. Leptin-deficient mice (ob/ob) are used as model of metabolic disease: they are characterized by obesity and insulin-resistance. Aim of this work is to identify early cardiovascular alterations in young ob/ob mice using micro-ultrasound imaging.

Sixteen wild-type (wt) and eleven ob/ob male mice (8 wo,C57BL6) were studied. B-mode and PW-Doppler images were acquired with a micro-ultrasonographic system (Vevo2100) for assessing cardiovascular biomarkers. Left ventricular mass (LVmass), cardiac output (CO), ejection fraction (EF), stroke volume (SV), fractional shortening (FS) and E/A ratio were measured. Mean diameter (Dm_abd and Dm_car), relative distension (relD_abd and relD_car) and pulse wave velocity (PWVabd and PWVcar) were obtained for both abdominal aorta and common carotid. As regards renal microcirculation, renal resistivity and pulsatility index (RI and PI) were assessed. The ratio between grey-levels related to liver and kidney (HR_ratio) was used as index of hepatic steatosis grade.

ob/ob mice had higher glycemia levels (ob/ob:296±42mg/dl, wt:149±23mg/dl, $p<0.01$) and higher weight (ob/ob: 44.2g, wt: 31.1g, $p<0.01$). relD abd values were lower for ob/ob mice than for wt ones (ob/ob:18.6±4.1%, wt:23.8±3.3%, $p<0.01$) the ob/ob group presented also higher PWV (ob/ob:2.11±0.69m/s, wt:1.73±0.43m/s, $p<0.05$), RI (ob/ob:0.71±0.05, wt:0.64±0.06m/s, $p<0.01$) and PI (ob/ob:1.15±0.17, wt:0.97±0.12m/s, $p<0.01$) values. As concerns hepatic steatosis, there was a difference in HR ratio evaluations (ob/ob:1.27±0.26, wt:0.79±0.17, $p<0.01$).!

Young ob/ob mice have a reduced abdominal aorta distension capability and a higher value of stiffness for this vessel. Moreover, starting from young age, parameters related to renal microcirculation and hepatic fat accumulation are altered.

9.2 Deletion of chromosome 9P21 noncoding cardiovascular risk interval in mice induces a prothrombotic phenotype

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Background
SNPs on chromosome 9p21.3 risk locus have been associated with cardiovascular diseases. We have established a direct mechanistic link between 9p21 noncoding risk interval and susceptibility to aneurysm in a mouse model with a targeted deletion of the 9p21 noncoding cardiovascular disease risk interval.

The deficiency of transcripts encoded by this locus predisposes to a pro-thrombotic phenotype and arterial stiffening in this mouse model and in humans with 9p21 DNA variants.

Methods
Carotid blood flow following FeCl3 application was monitored via Doppler profiles. Results: The deletion of the orthologous 70-kb noncoding interval on mouse chromosome 4 (chr4Δ70kb/Δ70kb), synthetic to human chromosome 9p21, predisposes to arterial thrombosis. The time to occlusion in a FeCl3-induced carotid thrombosis model was significantly decreased by 30% in the absence of the locus and confirmed by a new model of physiological thrombosis. There was no difference between groups in blood pressure, carotid stiffness parameters (diameter and distensibility for a given level of arterial pressure) or in vascular structure. We explored the potential impact of the deletion locus on thrombin generation as well as on platelet aggregation and reactivity all were increased compared to controls. In 100 healthy carriers of the 9p21 risk T allele display an increased aortic arterial stiffness compared with carriers of the C allele.

Conclusion
These results establish a direct link between variants or deletion in the 9p21 non-coding risk interval and increased platelet reactivity and thrombin generation predisposing to thrombosis in mouse and increased arterial stiffness in aged population.

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9.3 Functional aortic changes induced by a high salt diet

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Objective
This study examines effects of high salt diet on arterial blood pressure and aortic function in rats.

Methods
Sprague-Dawley rats were fed either high salt content chow or normal chow from weaning. Weight, tail-cuff systolic blood pressure (SBP), water and food intake, and urine output were measured with age. At 16 weeks, rats were anaesthetised and thoracic and abdominal aortic blood pressure measured across a mean arterial pressure range of 60 to 150 mmHg, induced via intra-venous infusion of phenylephrine and sodium nitroprusside. Aortic pulse wave velocity (aPWV) and thoracic to abdominal aortic pulse pressure amplification (PPA) were calculated. Post-mortem weights of the left ventricle and kidneys were recorded. Statistical comparison between groups across the blood pressure range was by robust analysis of covariance.

Results
Rats on a high salt diet had lower weights ($p=0.04$) but similar body mass index. Food intake was similar whilst water intake was greater on a high salt diet, with correspondingly greater urine output. Tail-cuff SBP was higher in rats on a high salt diet. There was no left ventricular hypertrophy ($p=0.16$) but greater kidney mass in high salt rats ($p=0.01$). High salt diet resulted in higher aPWV ($p<0.001$ at each 5 mmHg interval) and PPA ($p<0.001$ at each 5 mmHg interval).

Conclusions
High salt diet induced a moderate increase in arterial blood pressure, increased aortic stiffness, and higher PPA, indicating marked changes in transmission characteristics of the aorta including altered stiffness gradient and changed peripheral wave reflection characteristics.

9.4 Evolution of cardiac function and metabolism during aging in a murine animal model of obesity

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Purpose/Background/Objectives
Obesity is a well-known risk factor of cardiovascular diseases and a potentially modifiable determinant of arterial ageing. The objectives of this experimental study were to assess the effects of a long-term high fat diet (HFD) on metabolism, adipose tissues and phenotypes of cardiovascular aging.

Methods
Murine model chosen was C57BL/6J mice receiving during one year HFD or control diet (CD). Longitudinal follow-up of weight, systolic bloodpressure, heart rate and metabolic parameters was performed. An echocardiographic system was used to study cardiac function. Metabolism at the level of the adipose tissues was studied with FDG positron emission tomography (PET).

Results
After 12 months of diet the whole mice showed a positive correlation between plasma leptin level and left ventricular thickness and mass (both $p<0.05$).

As compared with the CD, the HFD was associated with metabolic disorders: higher body weight, hyperglycemia (both $p<0.01$) and increase in heart rate ($p<0.05$). Despite lack of modification of the systolic blood pressure, the HFD over 12 months increased left ventricular mass ($p<0.01$) and thickness of the inter-ventricular septum ($p<0.05$). Moreover, this parameter was positively correlated to leptin level ($p<0.05$). Finally, we observed in HFD mice a decrease of glucose metabolism in white fat after 6 months and 12 months and in brown fat only after 12 months (both $p<0.01$).

Conclusions
A long term HFD leads to metabolic disorders and to left ventricular morphological changes. The decrease of glucose metabolism observed in brown fat is compatible with an accelerate process of aging by the HFD.

9.5 Coagulation control by the RhoA pathway and the exchange factor Arhgef1

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Platelet activation by thrombin is an auto-amplification loop of thrombin generation, a major factor in the formation of atherosclerotic plaques. The small G protein RhoA, under the direct control of the exchange factor Arhgef1, modulates several cellular functions in inflammation. The objective was to study the RhoA pathway and its control by Arhgef1 in platelet aggregation and thrombin generation due to PAR receptor activation by thrombin.

We used a knockout mouse model for the exchange factor Arhgef1 (Arhgef1 -/-). In response to an agonist (collagen, ADP and thrombin), the expression of surface glycoproteins and the aggregation of washed platelets were not altered in the Arhgef1 -/- mice compared to Argef1 +/+ mice. In contrast, platelet activation studied by the secretion of granules a, exposure to phosphatidylserine and release of microparticles were decreased in the Arhgef1 -/- mice. Thrombin generation in whole platelet-rich blood was also reduced by 25%. These changes result in a lengthening of the time of occurrence of an occlusive thrombus in the carotid induced by FeCl3.

In conclusion, the results confirm the involvement of the RhoA pathway in platelet activation and demonstrate an Arhgef1-dependent mechanism. The results in mice show a new auto-amplification mechanism of thrombin generation by platelets through PAR and membrane phospholipids. Redistribution of phospholipid linked rearrangements of the membrane complex induced by inflammation suggests that the RhoA pathway potentiates the deleterious effects of thrombin in atherothrombosis.

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9.6 Ventricular volume and arterial flow during preload reduction: an MRI study

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Lower body negative pressure (LBNP) has been used to assess the cardiovascular effect of preload reduction. We are the first to use MRI to investigate ventricular volumes and great vessel flow during LBNP.

13 volunteers (23-47years) underwent LBNP at 0, -5 and -20mmHg. We acquired contiguous short axis steady state free precession cine images (8mm slices) of both ventricles during relaxed expiratory breath hold, and flow images with free breathing phase contrast MR angiography of the ascending aorta (Ao) and main pulmonary trunk (MPA).

Analysis was performed using Argus software (Siemens Medical Solutions), statistical assessment by one-way ANOVA and Bonferroni post hoc tests with p-values adjusted for multiple comparisons.

At 5mmHg, no change in Ao flow, velocity or left ventricular (LV) volumes was seen. Diastolic blood pressure (DBP) increased (p=0.04). Right ventricular (RV) output (p=0.01) and MPA flow (p=0.03) was decreased.

At 20mmHg, Ao flow (p<0.0001) and velocity (p=0.0005) were decreased. Ao retrograde flow increased (p=0.04). LV stroke volume (SV, p=0.0005), ejection fraction (EF, p=0.02) and end diastolic volume (EDV, p<0.0001) decreased. DBP increased (p=0.02). MPA flow (p<0.0001) and velocity (p<0.0001) decreased, with no change in retrograde flow. RV EDV (p<0.0001) and ESV (p=0.02) reduced.

Our data implies (1) that at 5 mmHg LBNP there is an increased left to left shunt likely via the bronchial circulation to explain the different LV/Ao and RV/MPA response (2) different vasoconstrictive response in the systemic vs. pulmonary circulation to explain the differences in retrograde flow.

9.7 Thoracic aorta PWV assessment by using 4D flow in MRI

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Purpose
In MRI, thoracic aorta pulse wave velocity (TAPWV) is usually estimated by 2D phase contrast (PC) with either in plane or through plane velocity acquisition. Thanks to technological improvement, 4D PC with full coverage of the TA and 3 dimension velocity encoding thought time can be now achievable in 10min. Our aim was to compare estimation of TAPWV using 4DPC or 2DPC on healthy volunteer.

Methods
Acquisitions were performed on a 3 Tesla scanner (GEHC, 750w). 2DPC was done with through plane velocity encoding on an axial oblique slice perpendicular to ascending and descending TA. 4D acquisition covered the full TA volume from the aortic valve to diaphragm. Segmentation and velocity estimates were done by using cloud computing (Arterys). Optimal data view sharing was applied to obtain 8ms and 16ms temporal resolution for 2DPC and 4DPC, respectively. Flow data curves where further computed on homemade software (artfun) to assess PWV for both 2D and 4D acquisition.

Results
31 healthy volunteers (13 male, age 50.9y ±18.6) were included. Correlation coefficient between 4DPC and 2DPC PWV was 0.69 (p<0.001) with small underestimation of 4D vs 2D (-0.17m/s limits of agreement [-3.85 ; 3.50]). A strong correlation with aging was obtained for both 4D and 2D PWV(r=0.75 p<0.001 and r=0.74 p<0.001 respectively)

Conclusions
TAPWV can be accurately estimated by 4D flow MRI, since close relation with 2DPC and aging have been obtained. By using the same data set, TAPWV should be estimates in association to other stiffness and geometric parameters of the TA.

9.8 Near Infrared Spectroscopy (NIRS) can detect improvements in arterial function following 6-months of marathon training

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Background
Endurance training improves vascular function and skeletal muscle perfusion. NIRS can measure changes in oxygenated haemoglobin (oxy-Hb) in the skeletal muscle microvascular bed. Therefore, combined with arterial occlusion, NIRS has the potential to assess microvascular function within skeletal muscle. However, NIRS measurements are strongly influenced by adipose tissue thickness (ATT) at the measurement site.

Methods
Vascular function was tested in healthy individuals prior to marathon training oxy-Hb changes were measured by NIRS (Portamon, Artinis) during a 30-second arterial occlusion and the subsequent hyperemic response. ATT was assessed at the site of measurement using ultrasound (Vivid I, GE).

Participants underwent the same test after completing the marathon. Post-occlusive time-to-peak oxy-Hb response and Δoxy-Hb concentration were compared pre- and post-marathon and the effect of ATT on each

parameter was assessed. Results are meanSD a paired t-test was used for comparison and β-coefficients used to compare the ATT relationships.

Results
34 participants (18=male, 30±3 years old) completed vascular testing and ATT measurements. The Δoxy-Hb value was more strongly attenuated by ATT than time-to-peak oxy-Hb (β-coefficients: -0.58, p<0.0001 and -0.14, p=0.45, respectively). 27 participants (15=male, 313 years old) completed the marathon and underwent testing at both time points. Time-to-peak hyperemic response was significantly faster post-marathon (Δ1.95±4.07seconds, p=0.01) but there was no difference in Δoxy-Hb(0.83±6.23 μM, p=0.5).

Conclusions
Endurance training has a positive effect on reperfusion rates following short duration ischemia. Improvements can be detected using NIRS to measure oxy-Hb changes. Comparing the time-to-peak response overcomes some of the limitations of ATT on the NIRS measurements.

9.9 Flow-mediated slowing as a novel method for the non-invasive assessment of endothelial function

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Background
Flow-mediated slowing (FMS) assesses the slowing of pulse wave velocity (PWV) in response to reactive hyperaemia, to provide a measure of endothelial function. We assessed the reproducibility of FMS and whether the technique is sensitive to the influence of age. FMS was compared to the commonly used, but technically demanding, alternative measure of endothelial function, flow-mediated dilatation (FMD).

Methods
PWV was measured using the Vicorder device, with cuffs placed around the upper arm and wrist. FMD was assessed in the contralateral arm. The reproducibility of FMS was assessed in 23 subjects on two separate occasions. FMS and FMD were also assessed concurrently in 23 younger subjects (mean age 22±2years, 11 males) and 13 older subjects (mean age 69±6years, 7 males), all of whom were normotensive and not taking vasoactive medication. Response to glyceryl trinitrate (GTN, 25 μg administered sublingually) was also assessed with both techniques.

Results
FMS was reproducible, with positive correlations between repeat visits (r =0.56, P=0.003). FMS and FMD did not correlate (r=0.23, P=0.18) whereas GTN mediated responses did (rho=0.42, P=0.01). Comparisons between younger and older groups demonstrated that FMS, FMD and GTN-mediated slowing were all significantly attenuated in older subjects (P<0.01 for all) but there was no age-related difference in GTN-mediated dilatation (p=0.7).

Conclusions
FMS is a reproducible technique that is sensitive to the influence of age, but does not correlate with FMD. The extent to which FMS represents endothelial function is worthy of further investigation.

9.10 Structural and functional arterial abnormalities in fibromuscular dysplasia are in the continuum of hypertension: an imaging and biomechanical study

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Fibromuscular dysplasia (FMD) is a non-atherosclerotic non-inflammatory arterial disease of unknown origin. We previously showed the presence of triple signal (TS) at ultrasound within common carotid artery (CCA) wall. We aimed at coupling TS presence with microconstituents of the vessel wall.

We included 50 patients with multifocal FMD, 50 essential hypertensive (HT) patients and 50 healthy subjects (HS) matched for age, sex, ethnicity and BP (HT and FMD). TS score from the right and left CCA were assessed from 15-MHz echotracking system coupled with aplanation tonometry. 14 microconstituents of the CCA, representing geometry, perivascular tethering, and wall material coefficients were derived from fitting of the pressure-diameter curve.

In multivariate analysis, age, hypercholesterolemia and IMT were significantly associated with TS, explaining 9.5% of its variance. TS was more frequent in FMD than HS (49% vs 16%, p<0.01), and HT (32%, p=0.08). When considering the whole population (n=150), several microconstituents appeared correlated with age and BP: particularly, residual stress was higher, and collagen fibers were stiffer with increasing age and BP (p<0.01). TS was positively associated with circular collagen mediated-stiffness (p<0.01), independently of age and BP.

We confirmed that FMD is associated with higher frequency of TS, but with overlap with matched HT and HS. The strong association between TS and carotid remodeling, independently of age and BP, suggests that it corresponds to the muscular transition of an elastic artery [1]. The association of TS with circular collagen stiffness suggests that TS has subtle but measurable mechanical consequences.

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9.11 Vascular phenotyping by means of very high-resolution ultrasound imaging: a feasibility analysis

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Background

The study of medium and small-size arteries might be useful in the characterization of vascular adaptation, remodeling and wall ultrastructure modifications occurring with aging and in the presence of cardiovascular risk factors. However, to date, these districts have not been extensively explored non-invasively, due to limited spatial resolution power of standard ultrasound (US) machines.

Methods

High-frequency US examination by Vevo MD (FUJIFILM, VisualSonics, Toronto, Canada) was performed in 5 healthy volunteers (2 men, mean age: 26.4±3.3 years). Images were obtained at the carotid, brachial and radial artery level, using the 48 MHz (for carotid and brachial) and 70 MHz (for radial) US probes. Mean diameter, relative distension and intima-media thickness (IMT) were obtained using edge detection and contour tracking techniques. Texture analysis was performed on carotid, brachial and radial US images. Contrast, correlation, energy and homogeneity were evaluated from the grey-level co-occurrence matrix calculated on the pixels belonging to the IMT.

Results

IMT and relative distension, as well as texture analysis, could be successfully assessed in all the arterial districts evaluated. Correspondent results are reported in Table 1.

Conclusions

The multidistrict assessment of wall ultrastructure and mechanics in medium- and small-size arteries is highly feasible in healthy individuals. This kind of analysis might provide novel insight on the development of vascular alterations in previously neglected arterial districts, as well as their clinical significance.

	Carotid artery	Brachial Artery	Radial Artery
Mean Diameter (mm)	5.9±0.74	3.22±0.65	2.03±0.24
IMT (mm)	0.42±0.05	0.14±0.02	0.12±0.01
Relative distension (%)	10.6±1.8	4±1.7	7.4±2.5
Contrast	0.05±0.008	0.04±0.01	0.05±0.01
Correlation	0.99±0.001	0.99±0.003	0.99±0.001
Energy	0.19±0.05	0.33±0.17	0.23±0.07
Homogeneity	0.97±0.004	0.97±0.005	0.97±0.005

POSTER SESSION I – MODELLING, SPECIAL TECHNIQUES AND INTERVENTIONS I

10.1 Optimal automated unobserved office blood pressure protocol to detect hypertension: only 10-minutes and four readings may be needed

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Background
Automated office blood pressure (AutoBP) involving repeated, unobserved blood pressure (BP) readings during one clinic visit provides a practical alternative to daytime ambulatory blood pressure (ABP). However, the number of reading taken and measurement duration have varied across previously used AutoBP protocols. Therefore, the optimal AutoBP protocol taken in the least amount of time with the fewest BP readings is yet to be determined and was the aim of this study.

Methods
117 patients (mean age 61.5±12.5 years) referred to a specialist BP clinic underwent AutoBP in a quiet room alone. Eight BP measurements were taken at 2-minute intervals immediately after sitting. The optimal AutoBP protocol with the highest concordance to daytime ABP was defined by smallest mean difference and highest intra-class correlation coefficient (ICC). The same BP device (Mobil-o-graph, IEM) was used for both AutoBP and daytime ABP.

Results
Average 15-minute AutoBP and daytime ABP were 138.4±18.1/84.8±12.2 mmHg and 140.9±15.2/86.2±10.6 mmHg, respectively. The AutoBP protocol with the highest concordance to daytime ABP was the average of two measures taken between two and six minutes of seated rest (systolic BP: mean difference = 0.3 (95%CI -3.0,2.4) mmHg, p=0.84; ICC=0.80; diastolic BP: mean difference = -0.42 (95%CI -2.0,1.1) mmHg, p=0.60; ICC=0.85). Daytime ABP tended to be overestimated by individual and the average of more than one AutoBP recorded before six minutes, however daytime ABP was underestimated after this time.

Conclusion
Only six minutes and two AutoBP readings may be needed to be comparable with daytime ABP.

10.2 Effects of inter-arm differences of brachial systolic blood pressure on the derivation of aortic systolic pressure

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Background
Inter-arm differences in brachial systolic blood pressure (SBP) should not theoretically translate to differences in calculated aortic SBP, there being only a single value of aortic blood pressure (BP) at any time.

Methods
This study assessed seated brachial and derived aortic SBP in 79 subjects (36±16 years, 40 male) using oscillometric brachial BP measurement and cuff volumetric displacement waveform recording. Measurements were taken simultaneously in left and right arm using identical SphygmoCor XCEL units (AtCor Medical, Sydney). Measurements were taken four times in each subject, swapping BP devices between arms.

Results
Brachial SBP was significantly higher in 11 subjects (average difference 5.4±0.7 mmHg) and in 18 subjects for aortic SBP (average difference 3.1±0.6 mmHg). Across all subjects, absolute inter-arm brachial difference in SBP, irrespective of direction, was 3.2±0.3 mmHg ($p<0.001$) and inter-arm aortic SBP difference 2.1±0.3 mmHg ($p<0.001$). Inter-arm SBP differences for brachial and aortic sites were correlated ($r2=0.74$, $p<0.001$). Arm dominance accounted for 1.1±0.5 mmHg of inter-arm brachial SBP difference ($p=0.032$) but did not account for inter-arm aortic SBP difference ($p=0.163$). Average left arm SBP was not different to average right arm SBP for the whole cohort for brachial ($p=0.083$) or aortic ($p=0.789$) measurement.

Conclusions
The inter-arm absolute difference in brachial SBP translates to a significant but small (2.1 mmHg) difference in derived aortic SBP. Further studies are required to establish if this artefactual difference in derived aortic SBP is predominantly due to arm dominance or other factors associated with left/right difference in vascular properties.

10.3 Use of MicroLife BP watch is a feasible approach to determine inter-arm blood pressure differences in a clinical setting

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Aim
The aim of this study is to evaluate the feasibility of Microlife Watch BP for measuring bilateral blood pressure (BP) in a clinical setting.

Method
339 patients (85% diabetic) scheduled for ambulatory blood pressure monitoring at the outpatient clinic for endocrinology, Silkeborg Regional Hospital, were examined with simultaneously bilateral BP measurements. A fully automatic, oscillometric device was used and two successive measurements were made.

Results
9,1% of the patients had a clinically significant inter-arm blood pressure difference (IAD) of ≥10mmHg in the first set of measurements. Mean IAD in the first measurement was -0,3mmHg 6.6. Twenty-three patients had a normal IAD in the first set of measurements but IAD ≥10mmHg in the second set of measurements. Only one of the patients with an IAD ≥10mmHg had a change in the arm with the highest blood pressure. The 95 % Limits of Agreement (LoA) for the mean interarm difference for a single measurement was 13.2 mmHg.

Conclusion
Microlife WatchBP measurement is a feasible method to determine IAD in a clinical setting. Bilateral BP measurements should be performed at first visit to help the clinician choose the right arm for further BP evaluations.

10.4 Comparison of blood pressure variability calculated from peripheral and derived aortic blood pressure

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Background
Systolic blood pressure variability (SBPV), conventionally calculated from peripheral sites such as the arm or finger, may be of more utility when computed from central aortic values, as this has greater applicability to the heart and the baroreceptor function, due to central location of baroreceptors. As the relationship between aortic and peripheral blood pressure is frequency dependent, particularly in the range of physiological heart rate frequencies, peripheral and aortic SBPV may not be identical. Differences between peripheral and aortic SBPV have not been previously quantified.

Methods
In this study, peripheral and derived aortic SBPV was calculated in 30 healthy subjects (25- 62 years). Continuous finger blood pressure was measured for 10 minutes in each subject (Finapres) and aortic blood pressure derived using a general transfer function. SBPV was quantified using a Short Time Fourier Transform in a time-frequency method to calculate the ratio of average power across the low frequency power band (0.05-0.15 Hz) to the high frequency power band (0.15-0.4 Hz).

Results
Aortic SBPV (power band ratio) was correlated with peripheral SBPV ($r^2=0.961$, $p<0.001$) with a mean difference of -0.67±2.07. However, there was a bias toward peripheral SBPV overestimation compared to aortic SBPV for higher values of SBPV.

Conclusions
This study demonstrates that peripheral SBPV cannot be taken as equivalent to aortic SBPV, particularly where the low frequency to high frequency power ratio of SBPV is of higher magnitude.

10.5 Comparison of arterial stiffness assessed by popmetre with arterial stiffness assessed by applanation tonometry: a clinical study

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Background
Large artery stiffness is recognized as a strong, independent marker of cardiovascular risk, mainly through aortic

pulse wave velocity (PWV). pOpmètre® is a new non-invasive method, which estimates aortic PWV through finger-toe (FT) wave analysis. In a previous study, Alivon et al. have shown an acceptable correlation ($r^2 = 0.43$ for PWV) between pOpmètre® and the reference method Sphygmocor. However this study led to the necessity to optimize the algorithm and the procedures because of the presence of several outliers involving mainly obese and elderly subjects.

Materials and Methods
The pOpmètre® has 2 photodiodes sensors, positioned on the finger and on the toe. A particular attention was drawn on positioning of the toe sensor so that the pulp was in contact with the photodiode. Different signal processing chains were applied and no cut-off value was used for pulse height. Applanation tonometry was performed for CF PWV measurements.

Results
45 subjects were included: 18 healthy subjects and 27 patients with essential hypertension aged 32± 7 years and 58 ±18 years respectively. The correlation between FT PWV and CF PWV was good and significant ($r^2 = 0.77$ $p<0.0001$). A better correlation was found in terms of transit time ($r^2 = 0.83$ $p<0.0001$). The standard deviation of the difference was 0.87 m/s versus 6.73 ms, classifying the device as good agreement with reference (Wilkinson, ARTERY RES 2010).

Conclusion
pOpmètre® with optimized algorithm and procedure qualifies as excellent agreement with the reference technique for PWV assessment, however, outcome studies must confirm the value of this new device.

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10.6 Variation of the asymptotic diastolic pressure with different fitting techniques in healthy humans

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Background
Reservoir-wave model assumes the measured pressure (Pm) consists of two additive components: reservoir (Pr) and excess pressure (Pex)1-2. Calculation of Pr requires fitting the diastolic decay of Pm for calculating parameters P_∞ (asymptotical value) and b (time constant)1. However, there is no consensus over the value of these parameters1-3-4. Although many investigators use free-fitting, different degrees of freedom (dof) could be used1-2-5. The aim of this study was to examine the effect of varying fitting method on P_∞ ,b and calculate the peaks of Pr and Pex.

Methods
Pressure data from common carotid artery of 505 middle-aged healthy subjects were selected from the Asklepios dataset. Free-fitting methods with 3 dof (dicrotic notch not fixed) and 2 dof (dicrotic notch fixed) were used to obtain P_∞ , b and calculate Pr and Pex.

Results
Mean value of P_∞ change significantly between 3 dof and 2 dof (58 vs. 50 mmHg $p<0.01$) as well as b (2.3 vs. 1.9 s-1 $p<0.01$). Pr- and Pex- peaks didn't significantly change (Pr= 105 mmHg for 3 dof and 2 dof $p>0.05$ Pex = 30 mmHg and 31 mmHg for 3 dof and 2 dof, respectively $p>0.05$).

Conclusions
P_∞ and b values are method-dependent with a large variation between methods. P_∞ values in our study are higher than previously reported in literature, and variation in P_∞ and b values don't affect Pr- and Pex- peaks. Given the variability in the combination of P_∞ ,b in different subjects, the use of free-fitting is more appropriate.

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10.7 Non-invasive estimation of central systolic pressure: a comparison between radial artery tonometry and a new direct central blood pressure estimation method (DCBP)

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Background
We have developed a new proprietary method (DCBP® Direct Central Blood Pressure) to estimate central systolic blood pressure (cSBP) directly from peripheral pressure. In a previous meta-analysis of published high-fidelity pressure studies with simultaneous aortic and brachial pressure recordings, negligible mean difference between DCBP and cSBP has been documented (1). The accuracy and precision of DCBP against arterial tonometry measurements remain to be documented.

Methods
The cSBP was estimated from radial artery tonometry and a transfer function using a SphygmoCor® system (AtCor Medical, Australia) in 100 subjects (mean age+/-SD = 57+/-10 years). Pressure waveforms were calibrated from the brachial systolic and diastolic pressures, measured just prior to tonometric measurement with an oscillometric cuff system (Omron 705CP Omron, Japan). DCBP and cSBP were compared using the Bland and Altman method and subgroups were compared using unpaired Student's t test.

Results
The difference between DCBP (129.2+/-16.8 mmHg) and cSBP (129.4+/-16.4 mmHg) was -0.2+/-2.6 mmHg. The difference was not influenced by the mean (DCBP + cSBP / 2). Similar results were obtained in men (n=60) and women (n=40), and in subjects with/without hypertension (n=51/49), with/without diabetes (26/74), and with/without dyslipidemia (36/64).

Conclusions
The new DCBP® method and the transfer function applied to radial tonometry method were interchangeable in estimating central SBP. These results pertained strictly to the studied population (patients aged 57 years on average, and displaying a high percentage of cardiovascular risk factors). Further studies are needed to confirm our results.

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10.8 Systolic aortic pressure derived from different calibration methods in the general population

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Background
There is recent evidence from different research groups that accuracy [1] and prognostic value [2,3,4] of systolic aortic pressure significantly depends on the method of calibration. Although these results consistently show superiority of mean pressure calibration (aSBP2) over both, traditional calibrated aortic systolic (aSBP1) and brachial systolic pressure (bSBP), the investigated cohorts were relatively small and it is still unclear whether the observed associations between pressures are preserved in the general population.

Objective
Therefore the objective of this work is the investigation of associations between different methods of systolic pressure assessment it a large cohort and its comparison to reported outcome.

Methods
During a public health campaign cardiovascular hemodynamic data was assessed using the Mobil-O-Graph® device and ARCSolver® algorithms in a kiosk like setting. Systolic aortic pressure was derived from two different calibrations: systolic and diastolic pressure and mean and diastolic pressure. Furthermore brachial pressures, age, sex and anthropometric data were recorded and regression analysis was performed to investigate associations.

Results
Summary statistics of 7409 valid measurements are reported in Table 1. Systolic and subsequent pulse pressures significantly differed from bSPB for aSBP1 but not for aSBP2. Regression analysis unveiled that aSBP2 (R^2=0.853) is significantly (p<0.00001) less associated with bSBP than aSBP1 (R^2=0.937), see Figure 1.

Conclusions
Comparison of our data with literature suggests that unlike aSBP1 [5] the association between bSBP and aSBP2 is only slightly influenced by increased sample size [2] and therefore prognostic superiority over bSBP is likely to be sustainable and warrants further investigation.

Summary statistics

	Male			Female		
	N	Median	2.5 - 97.5 P	N	Median	2.5 - 97.5 P
Age	2276	54,000	24,000 to 83,000	5133	54,000	20,000 to 81,000
aSBP1	2276	120,803	98,754 to 153,254	5133	114,872	91,723 to 152,578
aSBP2	2276	133,102	108,651 to 172,962	5133	124,914	100,692 to 167,257
SBP	2276	131,000	107,000 to 168,000	5133	124,000	100,000 to 165,000
MBP	2276	106,000	85,000 to 133,000	5133	99,000	79,000 to 129,000
DBP	2276	84,000	63,000 to 109,000	5133	77,000	58,000 to 102,175
BMI	2276	26,219	20,065 to 35,774	5133	23,875	18,218 to 36,634

Regression between bSBP, aSBP1 and aSBP2 respectively.

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10.9 Arterial stiffness index beta and cardio-ankle vascular index inherently depend on blood pressure, but can be readily corrected

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Objectives
Arterial stiffness index β and cardio-ankle vascular index (CAVI) are widely accepted to quantify the blood pressure (BP)-independent, intrinsic exponent (β0) of the BP-diameter relationship. CAVI and β assume an exponential relationship between pressure (P) and diameter (d). We aim (1) to demonstrate that, under this assumption, β and CAVI as currently implemented are inherently BP-dependent and (2) to provide corrected, BP-independent forms of CAVI and β.

Methods and results
In P=Pref*exp[β0(d/dref-1)], usually reference pressure (Pref) and reference diameter (dref) are substituted with diastolic BP and diameter to accommodate measurements. Consequently, the resulting exponent is not equal to the pressure-independent β0. CAVI does not only suffer from this reference pressure effect, but also from the approximation of dP/dd.

For example, assuming β0=7, an increase of systolic/diastolic BP from 110/70 to 170/120 mmHg increased β by 8.1% and CAVI by 14.3%. We derived corrected forms of β and of CAVI (CAVI0) that did not change with BP and represent the pressure-independent β0.

To substantiate the BP effect on CAVI in a typical follow-up study, we realistically simulated patients (n=161) before and following BP-lowering treatment (assuming no follow-up change in intrinsic β0 and therefore in actual P-d relationship). Lowering BP from 160±14/111±11 to 120±15/79±11 mmHg ($p<0.001$) resulted in a significant CAVI decrease (8.1±2.0 to 7.7±2.1, $p=0.008$) CAVI0 did not change (9.8±2.4 and 9.9±2.6, $p=0.499$).

Conclusions
β and CAVI as currently implemented are inherently BP-dependent, potentially leading to erroneous conclusions in arterial stiffness research. BP-independent forms were derived to overcome this problem.

10.10 Hemodynamic correlates of the left ventricular mean ejection pressure: a carotid tonometry study

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Background
The systemic arterial load imposed to the left ventricle (LV) is a major determinant of normal/abnormal cardiovascular function. The LV mean ejection pressure (LVMEP) is the best estimate of load faced by the LV throughout ejection. The contribution of the steady and pulsatile blood pressure (BP) component of arterial load to LVMEP is debated. We studied the hemodynamic correlates of LVMEP using carotid tonometry. Intensive care unit patients equipped with an indwelling catheter were studied, thus allowing precise calibration of the tonometer.

Methods
Carotid tonometry (Complior Analyse ® ALAM Medical, France) was prospectively performed on 28 hemodynamically stable, spontaneously breathing patients (12F, mean age+/-SD = 64+/-18 years). Carotid waveforms were calibrated from diastolic BP and time-averaged mean BP invasively obtained at the radial (n=18) and femoral (n=10) artery. All patients were free of aortic stenosis. LVMEP was the area under the systolic part of the carotid pressure waveform divided by ejection time.

Results
LVMEP (111+/-17 mmHg) was strongly related to central systolic BP (126+/-21 mmHg $r^2=0.97$) and was also related to mean BP ($r^2=0.82$), peripheral systolic BP ($r^2=0.83$), peripheral ($r^2=0.35$) and central ($r^2=0.50$) pulse pressure (each $P<0.05$). The LVEMP was not related to age, heart rate and stroke volume. Systolic pulse wave amplification ratio from carotid to periphery was 1.07+/-0.08.

Conclusions
Central systolic BP was strongly related to LVMEP, a measure of the load faced by the LV throughout ejection ($r^2=0.97$). Peripheral systolic BP may be less informative given variable systolic pulse wave amplification across patients.

FRIDAY 14 OCTOBER 2016

08.00 Refreshments, Poster and Exhibition viewing

08.30 **Special Guest Lecture**
Why does non-alcoholic fatty liver disease (NAFLD) contribute to cardiovascular outcomes?
Professor Hannele Yki-Järvinen, *University of Helsinki, Helsinki, Finland*

Take home messages

1. Both 'Metabolic NAFLD' and the features of insulin resistance/the metabolic syndrome (MetS) increase the risk of cardiovascular disease (CVD), even independent of obesity
2. 'Metabolic NAFLD' and insulin resistance share common pathophysiology, which may explain their link with CVD
3. 'Metabolic NAFLD' may be even a better predictor of CVD as it measures more directly abnormal metabolism than the MetS
4. Carriers of the I148M gene variant in PNPLA3 with NAFLD have steatosis but not features of insulin resistance implying that steatosis and insulin resistance and the risk for CVD dissociate

Features of insulin resistance/the metabolic syndrome (MetS) predict cardiovascular disease (CVD), even independent of obesity. NAFLD, diagnosed by liver enzymes, ultrasound or a liver biopsy, has also been shown in at least 14 prospective studies to predict CVD independent of obesity.

The MetS and NAFLD share common pathophysiology. The liver is the site of production of two of the key components of the MetS, fasting serum glucose and very-low density lipoprotein. In subjects with NAFLD, the ability of insulin to normally suppress production of glucose and VLDL is impaired resulting in hyperglycemia and hyperinsulinemia and hypertriglyceridemia combined with low HDL cholesterol. The liver, once fatty, also overproduces many other markers of cardiovascular risk such as C-reactive protein, fibrinogen, coagulation factors and plasminogen activator inhibitor-1.

The increases in markers of insulin resistance and of cardiovascular risk in NAFLD are associated with endothelial vascular dysfunction and could in part explain why NAFLD predicts CVD. NAFLD may be an even better predictor of the risk of CVD than the MetS. Whether this is because measurement of liver fat content provides a more direct estimate of the risk of CVD than the MetS, which can be diagnosed using 10 different combinations of its 5 components or other mechanisms is unclear.

Common genetic forms of NAFLD such as the I148M variant in PNPLA3 ('PNPLA3 NAFLD') are characterized by steatosis but not insulin resistance or an increased risk of CVD or diabetes. The molecular mechanisms underlying this dissociation in the human liver and its implications for CVD will be discussed.

09.00 **Oral Session III – Young Investigator**
3.1 Reducing arterial stiffness independently of BP: Proof of concept? CAVI, PWV and cardiac data in the 6-month VaSera trial
Dr Charlotte Mills[1], Dr Luca Faconti[1], Ms Virginia Govoni[1], Dr Steve Morant[2], Dr Maria-Linda Casagrande[1], Dr Haotian Gu[1], Dr Benyu Jiang[1], Dr Andrew Webb[1], Professor Kennedy Cruickshank[1]
[1.]King's College London, UK; [2.]University of Dundee, UK

Purpose/ background/ objectives
People with or at risk of Type II diabetes (T2DM) are at increased risk of vascular disease and arterial stiffness (AS). We hypothesized that spironolactone and dietary nitrate (beetroot juice) separately and together would reduce AS, measured as cardiac-ankle vascular index (CAVI Fukuda Denshi, Japan mainly BP-independent) or aortic pulse wave velocity (PWV).

Methods
126 (60% T2DM) were randomized, double-blind to spironolactone (≤50mg) or doxazosin (control ≤16mg) and active/ placebo juice (≤9/0mmol) daily. AS and echocardiographic measures (on a subgroup) were performed. Intention-to-treat analysis adjusted for between-group blood pressure (BP) change over time was performed using SAS.

Results
Change in (Δ)BP was not different between spironolactone and doxazosin (mean -6.7mmHg), nor between the juices. ΔCAVI was marginally reduced on doxazosin compared to spironolactone (-0.11[-0.30,0.08] vs. 0.14[-0.06,0.34] units, p=0.080) but more for aortic PWV (-0.44 [-0.69,-0.20] vs. -0.07 [-0.32,0.18]ms-2, p=0.04). Dietary nitrate had no impact, but did rise in plasma.

Spironolactone improved Δrelative wall thickness vs. doxazosin (0.01[-0.02,-0.0], p<0.01). Dietary nitrate decreased left ventricular (LV) end diastolic and systolic volume (-6.3[-11.1,-1.6]mL and -3.2[-5.9,-0.5]mL, p<0.05) and increased end diastolic mass/volume (EDMV) ratio (0.04 [0,0.7] g/mL, p<0.05) vs. placebo. There were no drug–juice interactions.

Conclusions
Contrary to our hypothesis, spironolactone did not reduce AS, rather central PWV declined on doxazosin. Spironolactone enhanced LV remodelling, while dietary nitrate improved LV volumes and the EDMV ratio, perhaps indicating improved LV strain.

3.2 Variability in mean arterial pressure and diastolic blood pressure from central to peripheral large arteries: relevance to arterial physiology and estimated central blood pressure

Dr Martin Schultz[1], Mr Dean Picone[1], Miss Xiaoqing Peng[1], Dr Andrew Black[1,2], Dr Nathan Dwyer[1,2], Dr Phillip Roberts-Thomson[1,2], Dr James Sharman[1]
[1.]Menzies Institute for Medical Research, University of Tasmania, Hobart, Australia; [2.]Royal Hobart Hospital, Hobart, Australia

Background
Mean arterial pressure (MAP) and diastolic blood pressure (DBP) are thought to consistently decline approximately 1-3 mmHg from the aorta to peripheral large arteries, thus providing a small pressure gradient to aid blood flow. The magnitude of this gradient is important for correct waveform calibration and central BP estimation. However, there is little invasive data determining the variability in MAP and DBP from central to peripheral arteries, which was the goal of this study.

Methods
52 patients (mean age 62±11 years) undergoing cardiac angiography had intra-arterial BP measured via catheter in the ascending aorta, brachial and radial arteries by sequential pull-back. MAP was calculated by integration of ensemble averaged waveforms, and DBP from the foot of the waveforms.

Results
On average, MAP and DBP decreased from the aorta-to-brachial (MAP -1.5±3.9 mmHg DBP -2.7±4.1 mmHg) and brachial-to-radial (MAP -2.0±4.4 mmHg DBP -1.8±3.3 mmHg) arteries. However, changes in aortic-to-radial MAP (range -14.9 to 6.8 mmHg) and DBP (range -13.1 to 2.1 mmHg) were highly variable, including increases in MAP among 23% of patients. Importantly, the relationship between MAP and DBP changes were synergistic, with DBP decreasing if MAP increased and vice versa. The magnitude of aorta-to-radial MAP and DBP differences were significantly related to height and age.

Conclusions
Although MAP and DBP are reduced on average from central to peripheral large arteries, the magnitude of change is variable and related to patient characteristics. These new observations are highly relevant to understanding arterial hemodynamic (patho)physiology and accurate non-invasive estimates of central BP.

3.3 Discovery of a new blood pressure phenotype from invasive central-to-peripheral recordings: implications for brachial cuff accuracy and cardiovascular risk assessment

Mr Dean Picone[1], Dr Martin Schultz[1], Miss Xiaoqing Peng[1], Dr Andrew Black[1,2], Dr Nathan Dwyer[1,2], Dr Phil Roberts-Thomson[1,2], Professor Velandai Srikanth[1], Professor James Sharman[1]
[1.]Menzies Institute for Medical Research, University of Tasmania, Hobart, Australia; [2.]Royal Hobart Hospital, Hobart, Australia; [3.]Stroke and Ageing Research Centre, Department of Medicine, School of Clinical Sciences at Monash Health, Monash University, Melbourne, Australia

Background
Accuracy of brachial cuff blood pressure (BP) may be influenced by individual variability in central-to-peripheral systolic BP (SBP)-amplification, but this has never been determined. We aimed to achieve this by characterising SBP-amplification phenotypes and examining associations with cuff BP accuracy.

Methods
Intra-arterial BP was measured at the ascending aorta, brachial and radial arteries in 77 patients (aged 61.5±10.3 years 68% male) following coronary angiography. Cuff BP was measured bilaterally by oscillometric devices before catheterisation, and then simultaneously with intra-arterial brachial BP. SBP-amplification was defined by ≥5 mmHg SBP increase between the aorta-to-brachial or brachial-to-radial arteries.

Results
Average aortic-to-brachial and brachial-to-radial SBP-amplification were 8.5±9.5 mmHg and 6.4±9.4 mmHg respectively. However, four distinct SBP-amplification phenotypes were observed: 1) both aortic-to-brachial and brachial-to-radial SBP-amplification (n=24) 2) only aortic-to-brachial SBP-amplification (n=24) 3) only brachial-to-radial SBP-amplification (n=16) 4) no aortic-to-brachial or brachial-to-radial SBP-amplification (n=13). Compared

with the first three phenotypes, patients with no SBP-amplification had elevated aortic SBP (143.1±23.0 mmHg versus 122.4±18.3 126.0±19.5 and 134.8±12 mmHg respectively p=0.0066) that was significantly underestimated by brachial cuff BP (-11.7±8.7 mmHg, p=0.004), despite no differences in clinical characteristics or cuff BP between phenotypes (p>0.1 all).

Conclusions
These are the first data to describe distinctive central-to-peripheral SBP-amplification phenotypes, and includes discovery of a phenotype in which cardiovascular risk is likely to be elevated because of significantly increased aortic SBP that is not detected by conventional cuff BP methods.

3.4 Wave intensity analysis provides novel insights into pulmonary hypertension

Dr Junjing Su[1], Dr Charlotte Manisty[2], Professor Kim H Parker[3], Dr Soren Mellemkjaer[4], Dr Luke Howard[5], Professor Ulf Simonsen[1], Professor Alun Hughes[2]
[1.]Department of Biomedicine, Aarhus University, Denmark; [2.]Institute of Cardiovascular Science, University College London, UK; [3.]Department of Bioengineering, Imperial College London, UK; [4.]Department of Cardiology, Aarhus University Hospital, Aarhus, Denmark; [5.]National Heart and Lung Institute, Imperial College London, UK

Background
The objective of the study was to apply wave intensity analysis (WIA) in the pulmonary artery to characterise the magnitude, origin, type and timing of arterial waves in individuals with and without pulmonary hypertension (PH).

Methods
Right heart catheterisation was performed using a pressure and Doppler flow sensor tipped catheter to obtain simultaneous pressure and flow velocity measurements in the pulmonary artery. WIA was applied to the acquired data (1).

Results
In controls (n = 10), the wave speed in the pulmonary artery was 3.03 m/s (2.69 – 3.91 m/s) and this increased in pulmonary arterial hypertension (PAH, n = 11, 11.9 m/s [10.5 – 16.4 m/s]) and chronic thromboembolic pulmonary hypertension patients (CTEPH, n = 10, 15.1 m/s [11.5 – 16.8 m/s]). Wave intensity was significantly greater in PH patients compared to controls. Wave reflection index (WRI) was 3.81 % (3.58 – 6.24 %) in controls, 23.4 % (17.5 – 29.7 %) in PAH and 30.4 % (11.9 – 35.6 %) in CTEPH patients. WRI was not related to pulmonary vascular resistance or right ventricular fractional area change and patients with mildly and severely elevated pulmonary pressure had similar WRI.

Conclusions
Wave speed, wave intensity and wave reflection in the pulmonary artery was higher in PH patients indicating increased arterial stiffness, right ventricular work and vascular impedance mismatch, respectively. While WRI does not reflect the severity of PH in established disease, the presence of increased wave reflection could be a novel early marker of pulmonary vascular disease.

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3.5 Non-invasive us-based wave intensity analysis in mice

Dr Nicole Di Lascio[1], Dr Claudia Kusmic[2], Dr Francesco Stea[3], Dr Francesca Lenzarini[2], Dr Francesco Faita[2]
[1.]Institute of Life Science, Scuola Superiore Sant'Anna, Pisa, Italy; [2.]Institute of Clinical Physiology, National Research Council, Pisa, Italy; [3.]Department of Clinical and Experimental Medicine, University of Pisa, Italy

Wave Intensity Analysis (WIA) can provide information about the interaction between vascular and cardiac system. WIA-derived indexes have quantitative physiological meaning. We investigated age-associated changes in WIA-derived parameters in mice and correlated them with biomarkers of cardiac function.

Sixteen wild-type male mice (strain C57BL6) were imaged with high-resolution ultrasound (Vevo 2100) at 8 weeks (T0) and 25 weeks (T1) of age. Carotid pulse wave velocity (PWV) was calculated from B-Mode and PW-Doppler images using the lnD-V loop and employed to evaluate WIA: amplitudes of the first (W1) and the second (W2) local maxima and minimum (Wb) were assessed. Reflection index (RI) was assessed as Wb/W1. Cardiac output (CO), ejection fraction (EF) fractional shortening (FS) and stroke volume (SV) were evaluated strain analysis provided strain and strain rate values for longitudinal, radial and circumferential directions (LS, LSR, RS, RSR, CS, CSR). Isovolumetric relaxation time (IVRT) was calculated from mitral inflow PW-Doppler images and normalized for cardiac cycle length.

W1(T0:4.42e-07±2.32e-07m2/s T1:2.21e-07±9.77e-08m2/s), W2(T0:2.45e-08±9.63e-09m2/s T1:1.78e-08±7.82e-09m2/s), Wb(T0:-8.75e-08±5.45e-08m2/sT1:-4.28e-08±2.22e-08m2/s), CO(T0:19.27±4.33ml/min T1:16.71±2.88ml/min), LS(T0:17.55±3.67% T1:15.05±2.89%), LSR(T0:6.02±1.39s-1 T1:5.02±1.25s-1), CS(T0:27.5±5.18% T1:22.66±3.09%) and CSR(T0:10.03±2.55s-1 T1:7.50±1.84s1) significantly reduced with age. W1 was significantly correlated with CO(R=0.58), EF(R=0.72), LS(R=0.65), LSR(R=0.89), CS(R=0.61), CSR(R=0.70) at T0; correlations were not significant at T1.!

The decrease in W1 and W2 suggests a reduction in cardiac performance, while that in Wb, in view of unchanged RI, can be associated with a reduction in the total energy carried by the wave. The loss of correlation between WIA-derived parameters and cardiac biomarkers might reflect an age-associated alteration in cardio-vascular coupling.

3.6 Longitudinal changes in aortic reservoir function independently predict declining renal function among healthy individuals

Dr Rachel Climie, Mr Dean Picone, Dr James Sharman
Menzies Institute for Medical Research, Hobart, Australia

Objectives
Aortic reservoir function independently predicts end organ damage in cross sectional analyses. However, longitudinal associations are more important regarding causation, but this has never been examined and was the goal of this study.

Methods
Aortic reservoir function (excess pressure integral [xsP] and aortic reservoir pressure), aortic stiffness, brachial and central blood pressure (BP), and renal function (estimated glomerular filtration rate [eGFR]) were recorded among 33 healthy individuals (57±9 years 55% male) at baseline and after an average 3.0±0.3 years.

Results
Over the follow up period there was no significant change in brachial BP ($p>0.05$), whereas there was a trend for xsP ($p=0.061$) and central BP ($p=0.068$) to increase. On the other hand, aortic stiffness and blood glucose increased significantly ($p<0.05$ both). The change over time in xsP (but not aortic stiffness) was significantly related to the change in eGFR ($r=-0.370$, $p=0.044$) and this remained independent age, 24 hour systolic BP and body mass index ($\beta=-0.031$, $p=0.045$), but not blood glucose ($\beta=-0.031$, $p=0.053$). There was no interaction between the change in glucose and change in xsP.

Conclusions
Aortic reservoir function, as determined by excess pressure, is independently associated with a decline in renal function among healthy people followed over 3 years. These novel findings indicate the need to determine the underlying physiological determinants of aortic reservoir function.

3.7 Arterial stiffness for the early prediction of pre-eclampsia compared with clinical characteristics, uterine artery Doppler indices, and angiogenic biomarkers

Ms Kim Phan, Ms Yessica Haydee Gomez, Ms Jessica Gorgui, Dr Amira El-Messidi, Dr Robert Gagnon, Dr Stella Daskalopoulou
McGill University, Montreal, Canada

Objective
To develop a model for the 1st trimester prediction of pre-eclampsia.

Methods
In this prospective longitudinal study, women with high-risk singleton pregnancies were recruited and arterial stiffness was measured using applanation tonometry (SphygmoCor, AtCor) and compared between women who developed PE and those who had a normotensive pregnancy. Arterial stiffness and hemodynamics were assessed, in the 1st trimester, every 4 weeks thereafter, and at 6 weeks postpartum. Angiogenic biomarker concentrations (Quantikine, R&D Systems) were measured at each trimester and at 6 weeks postpartum, and a bilateral uterine artery Doppler (UAD) was performed in the 2nd trimester.

Results
Of the 155 women recruited, 13 developed pre-eclampsia. Analyses adjusted for both maternal age and body mass index showed women who developed pre-eclampsia had significantly increased wave reflection and carotid-femoral pulse wave velocity (cfPWV) from the 1st trimester, throughout pregnancy, and at 6 weeks post-partum with a cfPWV:carotid-radial PWV mistmatch seen in the 1st and 3rd trimester (all p-values<0.05). Arterial stiffness (AUC: 0.80) was a better predictive tool than angiogenic biomarkers (AUC: 0.60; $p=0.04$) or UAD (AUC: 0.53; $p<0.001$) and improved detection of pre-eclampsia when combined with all other predictions (AS sensitivity: 79.8% vs other combinations' sensitivity: 69.2%).

Conclusions
Arterial stiffness and wave reflection is higher in the 1st trimester, throughout pregnancy, and does not resolve 6 weeks after pregnancy in women who develop pre-eclampsia. It also had superior preeclampsia predictive value over angiogenic biomarkers and UAD alone and improved detection rates when combined with all predictors including clinical characteristics.

3.8 Can arterial wave augmentation in young adults explain variability of cardiovascular risk in ethnic minorities?

Dr Luca Faconti
[1.]Cardiovascular and Social Epidemiology Groups, Diabetes and Nutritional Sciences Division, King's College, London, UK; [2.]Social and Public Health Sciences Unit, University of Glasgow, UK; [3.]Institute for Applied Health Research, Glasgow Caledonian University, Glasgow, UK

Objective
Traditional cardiovascular (CV) risk factors do not fully explain ethnic differences in CV disease [1,2]. We tested if pulse wave velocity (PWV) and Augmentation Index (AIx) and their determinants from childhood may underlie ethnic variability in CV risk as young adults in the 'DASH' longitudinal study.

Methods
DASH, at http://dash.sphsu.mrc.ac.uk/, includes representative samples of 6 main UK ethnic groups [3]. PWV and AIx were recorded using Arteriograph device at ages 21-23y in a sub-sample (n=666) psychosocial, anthropometric and blood pressure (BP) measures were collected then and in 2 previous surveys at the age of 11-13y and 14-16y. For n=334, physical activity (PA) was measured over 5 days (ActivPal).

Results
Unadjusted values and regression models for PWVs were similar or lower in ethnic minority than in White UK young adults [4], while AIx was higher - Caribbean (14.9, 95%CI 12.3-17.0, %), West African (15.3, 12.9-17.7, %), Indian (15.1, 13.0-17.2, %) and Pakistani/Bangladeshi (15.7, 13.7-17.7, %), compared with White UK (11.9, 10.2-13.6, %). In multivariate models, adjusted for gender, central sysBP, height and heart rate, Indian and Pakistani/Bangladeshi young adults had higher AIx (β=3.35, 4.20 respectively, p<0.01) than White UK with a similar trend for West Africans and Caribbeans but not statistically significant. Unlike PWV, PA, psychosocial or deprivation measures were not associated with AIx, with borderline associations from brachial BP but no other childhood variables.

Conclusion
Early adult AIx, but not arterial stiffness, may be a useful tool for testing components of excess CV risk in some ethnic minority groups.

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3.9 Associations of blood pressure throughout childhood with left ventricle mass in adolescence

Dr Chloe Park, Professor Nish Chaturvedi, Professor Alun Hughes
University College London, London, UK

Background
High blood pressure (BP) is a major risk factor for elevated LV mass (LVM) in adults. Evidence suggests that BP tracks from childhood into adolescence and adulthood, however findings on the association between childhood BP and LVM are inconsistent and the temporal relationship between BP in childhood and elevated LVM in adolescence is unknown.

Methods
Echocardiography and sitting brachial systolic BP (SBP) measurements were performed on 2065 17yr olds. 1377

participants (742 females, 635 males) had complete BP data measured at age 7yrs, 9yrs, 11yrs and 15yrs. LVM was calculated and indexed to height2.7 (LVMI). Linear regression was used to investigate associations.

Results
Elevated LVMI at 17yrs was associated with increased SBP at all ages in females and in males at 9yrs, 11yrs, 15yrs and 17yrs (Table 1). Adjustment for cardiometabolic risk factors at age 17 (age, free-fat mass, height, height2 and smoking (Model 1)) did not substantially attenuate all LVMI and BP associations and associations at earlier ages remained significant after further adjustment for SBP at age 17.

Table 1:	Unadjusted		Model 1		Model 1+ SBP at 17yrs	
Age (yrs)	Male	Female	Male	Female	Male	Female
7	0.01±0.03	0.09±0.02**	0.02±0.03	0.06±0.02**	-0.02±0.03	0.07±0.02**
9	0.06±0.03*	0.06±0.02*	0.02±0.02	-0.007±0.02	0.02±0.02	-0.006±0.8
11	0.15±0.03**	0.06±0.02**	0.09±0.03**	0.008±0.02	0.09±0.03**	0.009±0.02
15	0.05±0.02*	0.06±0.02**	0.02±0.02	0.04±0.02*	0.02±0.02	0.03±0.02*
17	0.16±0.03**	0.14±0.02**	0.13±0.03**	0.09±0.02**		
Data are β±SE(g/m 2.7)* = p<0.05 **p<0.0001						

Conclusion
These results show that high antecedent childhood BP from as early as age 7 is associated with higher LVMI in adolescence independent of current BP.

10.30 Refreshments, Poster and Exhibition viewing

11.05 **Invited Lecture**
Constituent based modelling of arterial wall mechanics
Professor Nikos Stergiopulos, *École Polytechnique Fédérale De Lausanne, Lausanne, Switzerland*

In the preclinical setting, Angiotensin-II infusion has been the most popular model for mouse aneurysm research in the last 15 years. Nonetheless, little is known about the ascending aortic aneurysm pathobiology of this model and several lingering questions regarding the abdominal aortic aneurysm pathology (AAA) have long remained unaddressed, namely the suprarenal location of the murine AAA, the large morphological variation of the lesions and the presence of intramural thrombus. Technological advancements in both in vivo and ex vivo imaging techniques have significantly enhanced our understanding of the mechanisms driving the Angiotensin-II mouse model pathology. Our implementation of the groundbreaking PCXTM imaging modality has challenged the existing paradigm on this model while yielding unprecedented insight into previous observations on murine dissecting AAA. The detailed 3D PCXTM images have unveiled a previously unknown pivotal role for small, supraceliac and thoracic side branches to the onset of the disease. Mural ruptures in the vicinity of small side branches lead to apparent luminal dilatation and intramural hematoma. The PCXTM-based observations are in line with -seemingly incongruous- previous findings obtained with other imaging techniques, thereby raising a point on the importance of the implemented imaging modality when characterizing this aneurysm model.

11.35 **Focused Update**
Validation of non-invasive central blood pressure devices: a consensus approach
Dr James Sharman, *Menzies Institute for Medical Research, University of Tasmania, Hobart, Australia*

11.50 **Satellite Symposia** organised in collaboration with **Servier**
Protecting arteries against hypertension and dyslipidemia

12.50 Lunch, Poster and Exhibition viewing

14.00 **Focus Lectures**
Molecular imaging in arterial disease
Professor Andreas Kjær, *University of Copenhagen and Rigshospitalet, Copenhagen, Denmark*

Arterial stiffness in inflammatory disease
Professor Ian Wilkinson, *University of Cambridge, Cambridge, UK*

Many inflammatory conditions are associated with an increased risk of cardiovascular disease (CVD) and mortality. As well as accelerated atherosclerosis, increased plaque instability and endothelial dysfunction; arterial stiffness has been proposed as one of the potential mechanisms underlying the increased CVD in these patients. Indeed, patients with chronic inflammatory conditions such as rheumatoid arthritis (RA), lupus erythematosus, human immunodeficiency virus, chronic obstructive pulmonary disease (COPD), and inflammatory bowel disease

have been shown to have increased arterial stiffness. This appears to correlate with the level of inflammation, suggesting that arterial stiffness may be reversible with anti-inflammatory treatment. Numerous small-scale interventional studies have demonstrated that anti-inflammatory and cholesterol-reduction therapies with pleiotropic effects can reduce arterial stiffness in certain inflammatory conditions.

The association between increased arterial stiffness and inflammation appears obvious, yet the mechanism is poorly understood. One of the proposed mechanisms is arterial inflammation. In FDG PET/CT studies, patients with psoriasis, COPD and RA have been shown to have sub-clinical aortic inflammation. Arterial inflammation can subsequently lead to changes in the hydration state of the arterial wall and the composition of extracellular matrix, such as changes in glycosaminoglycan (GAG) synthesis. Indeed, animal studies have shown that overproduction of GAGs in the aorta resulted in thinning of the elastic lamellae and therefore aortic stiffening. Also, inflammatory cytokines can cause vascular smooth muscle cell proliferation, and phenotypic transformation resulting in an increased bioapatite formation, which can lead to calcification and stiffening. Furthermore, the release of matrix metalloproteinases from leukocytes can degrade elastin fibres within the arterial media.

15.00 Comfort Break

15.05 **Oral Session IV**

4.1 TNF- antagonists improve arterial stiffness in patients with rheumatoid arthritis: a meta-analysis

Dr Georgios Georgiopoulos[2], Dr Dimitrios Terentes-Printzios[2], Dr Charalambos Vlachopoulos[2], Dr Athanasios Gravos[2], Dr Panagiota Pietri[2], Dr Christos Georgakopoulos[2], Dr Kimon Stamatelopoulos[1], Professor Dimitrios Tousoulis[2]

[1.]Department of Therapeutics, Alexandra Hospital, University of Athens, Greece; [2.]Peripheral Vessels Units, 1st Cardiology Department, Hippokration Hospital, Athens Medical School, Athens, Greece

Purpose/Background/Objectives

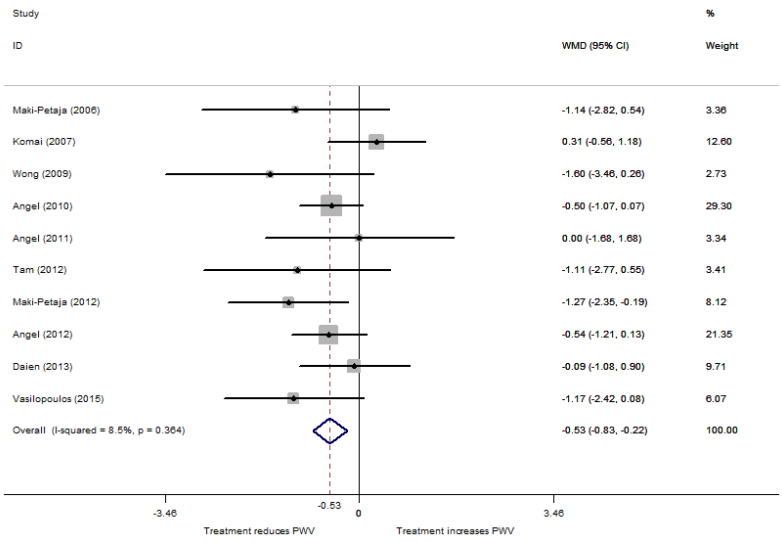
Patients with rheumatoid arthritis (RA) have a higher arterial stiffness than their age-matched healthy counterparts and an increased inflammatory burden that might be associated with their increased cardiovascular risk. Tumor necrosis factor alpha (TNF)-antagonists have been found to reduce inflammatory markers in RA however it is debatable if they have favorable effects on surrogate markers of cardiovascular outcomes. We conducted a meta-analysis to assess the effect of TNF-antagonists on arterial stiffness, a predictor of cardiovascular events and mortality, in RA patients.

Methods

A search of PUBMED was conducted to identify studies into the effect of TNF-antagonists on arterial stiffness in RA patients. Data were available on 3 TNF-antagonists: infliximab, adalimumab, and etanercept.

Results

10 studies (n=208 patients) out of 14 eligible studies in total, measured changes in carotid-femoral PWV after treatment with anti-TNFs. Subjects under therapy with anti-TNFs significantly decreased their arterial stiffness (mean change in PWV: -0.53 m/s, p=0.001)(Figure). No significant heterogeneity was observed across the studies (I2=8.5%, p=0.364). By subgroup analysis, improvement in PWV after therapy was independent of age, sex, nationality and clinical response to treatment and dependent of the type of the TNF- antagonist used.



Conclusions
The balance of evidence suggests that TNF-antagonists may have a beneficial effect on arterial stiffness in RA patients. Given the predictive role of aortic stiffness for adverse cardiovascular outcomes, TNF-antagonists might confer reduction of the cardiovascular risk of these patients beyond their anti-inflammatory effect. However, larger longitudinal studies are warranted to confirm recent findings.

4.2 Withdrawal of statins therapy in patients after carotid endarterectomy associated with increasing risk of significant restenosis

Ms Olga Tereshina, Professor Alexcey Vachev, *Samara State Medical University, Samara, Russia*

Background
The benefit of carotid revascularization is decreased by the occurrence of restenosis at the site of surgery, which is associated with a modestly increased risk of stroke. Preventing restenosis plays pivotal role in the overall treatment and prevention of stroke in patients with carotid artery disease.

Purpose
To evaluate influence of discontinuing of statins therapy on occurrence of restenosis in patients after carotid endarterectomy.

Methods
We studied 240 patients after carotid endarterectomy, mean age – 64.4±6.8 years. All the patients were divided into two groups: 1 group comprised 124 patients, who had taken atorvastatin in dose 10-40 mg daily and 2 group – 116 patients who discontinued statins therapy due complication 3 %, poor tolerance 9% or personal reluctance 88%. All the patients also underwent serial standardized ultrasound examination on 1, 3, 6, 12 month during first year after operation and then annually. Mean observation time was 5.6±2.1 years. Significant restenosis carotid artery (more than 70%) was established by standard Doppler velocity criteria.

Results
The significant restenosis of internal carotid artery was found in 2,4% patients with statins therapy and in 7,8% patients without statins. Statins withdrawal increased the incidence of late significant restenosis of internal carotid artery (odd ratio: 3.393 95% confidence interval: 0.895–12.857). Patients with withdrawal of statins had higher wall thickness: 4.3±0.8 against 2.9±0.9 (#1088 p<0,05).

Conclusion
Withdrawal of statins therapy in patients after carotid endarterectomy associated with increasing risk of significant restenosis carotid artery.

4.3 Electronic cigarette smoking increases aortic stiffness in young smokers

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Purpose/Background/Objectives
Smoking increases aortic stiffness which is an important predictor of cardiovascular risk. Electronic cigarettes (EC) simulate tobacco cigarette (TC) and have been advocated as a less harmful alternative. We investigated the acute effect of EC smoking on aortic stiffness compared to the effect of TC smoking.

Methods
We studied 24 healthy smokers (mean age 30±8 years, 13 females), who were free of risk factors X from smoking. Each participant visited our unit on four separate occasions (96 in total) and smoked: a) TC over 5 minutes b) EC over 5 minutes c) EC for a period of 30 minutes. During the sham procedure, participants did not smoke anything. Carotid-femoral pulse wave velocity (PWV) was used to assess aortic stiffness.

Results
Both TC and EC smoking increased systolic and diastolic BP, and the differences in changes of BP responses between the two smoking forms were not significant. Compared to TC, EC5 min smoking resulted in a less potent PWV increase throughout the study (F=4.425, P=0.005). On the other hand, EC30min resulted in a PWV increase similar to that of TC smoking throughout the study period (F=0.268, P=0.615). EC30 min smoking resulted in a more potent effect on PWV compared to EC5 min smoking (F=3.167, P=0.030).

Conclusions
EC over 30 minutes induces an unfavorable effect on aortic stiffness similar to TC smoking. The influence of EC smoking over 5 minutes on aortic stiffness is not as prompt and is less potent compared to the effect of TC smoking.

4.4 Arterial phenotype modulation and regulation of vascular fibrosis in mice by conditional inactivation of integrin av subunit in vascular smooth muscle cells

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Integrin αv functions as a receptor for adhesion proteins and is expressed at high density in vascular smooth muscle cells (VSMC)1,2,3,4,5 whose phenotypic modulation plays a crucial role in arterial ageing and atherosclerosis.6,7.

Our aim was to define the arterial phenotype in mice conditionally inactivated for the integrin αv subunit in VSMC8,9,10(αv SMKO) and its role in angiotensin II (AngII)-induced arterial fibrosis. Transgenic mice αv SMKO and their control littermates (WT) were treated with two doses of AngII, low (0.3 mg/kg/day) and high (1.5 mg/kg/day), for 4 weeks.

At baseline, blood pressure was lower in αvSMKO compared to WT mice. Carotid distensibility was increased in αv SMKO mice (13.3±0.7 vs 10.3±0.6 mmHg-1.10-3). With low dose AngII isobaric distensibility remained higher in αvSMKOmice (12.4±1.2 vs 10.7±1.0 mmHg-1.10-3).With high dose AngII the increase in collagen content in carotid media was lower in αvSMKOthan in WT (19 vs 35%) for a similar increase in blood pressure (30 mmHg) and arterial wall hypertrophy. Collagen immunostaining and fluorescence measurements (multiphoton microscopy second harmonic generation) confirmed that high dose AngII induced lower increases in collagen content in αvSMKO mice versus WT (8.9±1.7 vs 14.2±1.4 greyscale mean/pixel). The combination of similar arterial wall hypertrophy with less fibrosis in mutant mice explains an increased distensibility in response to AngII.

The αv subunit regulates AngII-induced arterial fibrosis as determined by collagen staining, immunostaining and fluorescence. Pharmacological targeting of vascular αv integrin may have clinical applications in the treatment of patients with fibrosis associated with hypertension and atherosclerosis.

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4.5 U-shaped relationship of reservoir pressure to cardiovascular events in patients with heart failure with reduced ejection fraction

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Objectives
Parameters of aortic stiffness are considered important indicators of cardiovascular risk. However, in heart failure with reduced ejection fraction (HFrEF), their association to outcome was found to be inversed. The aim of this work was to analyze the relationship of the amplitude of reservoir pressure (PresAmp) to cardiovascular events in HFrEF.

Methods
Patients with HFrEF were collected from a cohort undergoing coronary angiography at the hospital Wels-Grieskirchen, Austria. PresAmp was computed from central pressure obtained from radial readings by a generalized transfer function. A combination of myocardial infarction, death, stroke and cardiovascular revascularization served as primary endpoint. Cox-regression analysis and Kaplan-Meier estimates were used for survival analysis.

Results
83 (9 female) patients were included with a mean age of 61 years. During a median follow-up of 1272 days, 30 patients suffered from the combined endpoint. No significant linear association to outcome was found for PresAmp, brachial or central pulse pressure in Cox-analysis. In all three cases, Kaplan-Meier analysis comparing the respective quartiles indicated a nonlinear, U-shaped relation, but only for PresAmp the increase in risk was significant (P<0.05) in both directions. Although patients with low (16.6 (2.8 SD) mmHg) and high (26.1 (3.2 SD) mmHg) PresAmp showed similar risk, they differed in blood pressure, age, presence of hypertension, presence of coronary artery disease, ventricular dimensions, ejection fraction and diastolic function (table).

Conclusion
We found a U-shaped relation of reservoir pressure to outcome in our population. Pulsatile hemodynamics seem to separate patients with HFrEF into different phenotypes with different prognosis.

Parameter	1st quartile PresAmp	4th quartile PresAmp	P-value
N patients	21 (19m/2f)	21 (19m/2f)	
Age, years	57.1 (9.68 SD)	69.4 (9.24 SD)	<0.001
Hypertension	6 (29 %)	19 (90 %)	<0.001
Coronary artery disease	8 (38 %)	14 (67 %)	0.06
Brachial PP, mmHg	31.0 (6.87 SD)	63.0 (8.32 SD)	<0.001
Central PP, mmHg	20.4 (4.08 SD)	48.6 (9.33 SD)	<0.001
E/E'medial	30.8 (15.8 SD)	19.3 (10.0 SD)	0.008
EF, %	22.5 (7.33 SD)	31.6 (7.49 SD)	<0.001
LVEDV, ml	253 (91.3 SD)	162 (64.5 SD)	<0.001
LVESV, ml	199 (75.8 SD)	112 (50.8 SD)	<0.001

Table: Comparison of patients with low (1st quartile) and high (4th quartile) PresAmp. PP, pulse pressure. EF, ejection fraction. LVEDV, left ventricular end-diastolic volume. LVESV, left ventricular end-systolic volume. Values are presented as mean (standard deviation).

4.6 Beat-by-beat assessment of cardiac afterload using aortic PU loop - a pilot study

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Purpose/Background/Objectives
Cardiac afterload evaluation is crucial during general anesthesia (GA) especially during hypotension episode. Using beat to beat aortic pressure (P) / flow velocity (U) loop constructed from routine signals recorded during GA might allow to track afterload changes.

Methods
We defined 3 angles characterizing the PU loop (alpha, beta and Global After-Load Angle (GALA) angles). Augmentation index (AIx) and total arterial compliance (Ctot) were also measured via radial tonometry and transfer function. Twenty patients were recruited and classified into low and high cardiovascular (CV) risk group. Vasopressors were administered, when baseline mean arterial pressure (MAP) fell by 20%.

Results
We studied 118 pairs of pre/post bolus measurements. At baseline, patients in the lower CV risk group had higher cardiac output (6.1±1.7 vs 4.2±0.6 L/min meanSD p<0.001), higher Ctot (2.7±1.0 vs 2.0±0.4 ml/mmHg p<0.001), lower AIx (13±10 vs 32±11 % p<0.001) and lower GALA (41±15 vs 68±6 ° p<0.001). GALA was associated with Ctot and AIx. After vasopressors, MAP increase was associated with a decrease in Ctot (2.4±0.9 vs 1.7±0.7 ml/mmHg p<0.001), and an increase in AIx (21±14 vs 25±14 % p<0.001) and GALA (53±18 vs 61±16 ° p<0.001). Changes in GALA and Ctot after vasopressors were strongly associated (p=0.004).

Conclusions
PU Loop assessment from routine hemodynamic optimization management during GA and especially our novel GALA parameter could monitor cardiac afterload continuously in anesthetized patients, and may help clinicians to titrate vasopressor therapy**.**

4.7 Measurement of arterial stiffness using a connected bathroom scale: calibration against Sphygmocor

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Background
Measurement of arterial stiffness (AS) is still considered difficult. We developed a non-invasive technique to assess AS from a connected bathroom scale, based on ballistocardiography (BCG) and impedance plethysmography (IPG).

Methods
We included 198 subjects and patients, 111 for calibration study (cal), 88 for validation study (val), 34% hypertensives, mean age 48±17 years, 50% women. The scale pulse transit time (WS-PTT) was calculated as the difference between BCG systolic signals and IPG blood flow in the foot. Distance was estimated from body height and PWV was calculated. Carotid to femoral transit time (CF-PTT) was measured using Sphygmocor. Spearman and robust multivariate regressions were used.

Results
The WS-PTT correlated well with CF-PTT with R=0.69 in pooled population (cal 0.73, val 0.60). WS-PWV correlated with CF-PWV with R=0.73 (cal 0.67, val 0.59). The standard deviation of difference was 1.19 m/s with no significant bias compared with CF-PWV. Correlations of WS-PWV with age and blood pressure were similar (R= 0.69 and 0.60, resp.) to those of CF-PWV (R=0.67 and 0.60, resp.). These good correlations were non-trivial given the differences in wave paths, the fact that measurements are made in orthostatic position and totally investigator-free.

Conclusion
We show in two distinct populations that a simple user-oriented instrument such as a connected bathroom scale can estimate arterial stiffness with accuracy close to healthcare-oriented systems. Because these devices will be used by the general population, the availability of arterial stiffness data on very large, non-medicalized populations will change our management of well-being and health.

4.8 Increased cardiac workload in the upright posture in male subjects: non-invasive hemodynamics in men versus women

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Background
Men and women differ in the risk of cardiovascular disease, but the underlying mechanisms are not completely understood. We examined possible sex-related differences in supine and upright cardiovascular regulation.

Methods
Hemodynamics were recorded from 167 men and 167 women of matching age (~45 years) and body mass index (~26.5 kg/m2) during passive head-up tilt. None had diabetes, cardiovascular disease other than hypertension, or

antihypertensive medication. Whole-body impedance cardiography, tonometric radial blood pressure, and heart rate variability were analyzed. Results were adjusted for height, smoking, alcohol intake, mean arterial pressure, plasma lipids and glucose.

Results
Supine hemodynamic differences were minor: lower heart rate (-4%) and higher stroke volume (+7.5%) in men than women ($p<0.05$ for both). Upright systemic vascular resistance was lower (-10%), but stroke volume (+15%), cardiac output (+16%), and left cardiac work were clearly higher (+20%) in men than women ($p<0.001$ for all). Corresponding results were observed in a subgroup of men and postmenopausal women (n=76, age >55 years). Heart rate variability analyses showed higher low frequency to high frequency ratio in supine ($p<0.001$) and upright ($p=0.003$) positions in men.

Conclusions
The foremost difference in cardiovascular regulation between sexes was higher upright hemodynamic workload of the heart in men, a finding not explained by known cardiovascular risk factors or hormonal differences before menopause. Heart rate variability analyses indicated higher sympathovagal balance in men regardless of body position. The deviations in upright hemodynamics could play a role in the differences of cardiovascular risk between men and women.

4.9 Proportional pressure relations in the pulmonary arterial system

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Background – Objectives
The pulmonary arterial system can be characterized by:

1. A constant product of Pulmonary Vascular Resistance (PVR) and Total Arterial Compliance (TAC) with Tau=PVRxTAC≈0.7 seconds (1).

2. A proportional relation exits between systolic and diastolic pulmonary artery pressure, sPAP, dPAP, with mean pulmonary artery pressure mPAP (2). Recently it was shown that the time constant Tau is affected by Pulmonary Arterial Wedge Pressure (PAWP), and thus not constant under all conditions (3).

We therefore questioned how the product PVRxTAC = Tau depends on PAWP.

Methods
We have studied proportionality of pressures in a group of patients (n=1054) and determined the contribution of Pulmonary Arterial Wedge Pressure.

Results
We found that sPAP=1.61mPAP and dPAP =0.62mPAP, for all PAWP between 1 and 31 mmHg. Calculating PVR and TAC in the standard way as PVR=(mPAP-PAWP)/CO and TAC=PP/SV, with CO: Cardiac Output, PP: Pulse Pressure, SV: Stroke Volume, and HR: Heart Rate, it follows that: PVRxTAC=(1-PAWP/mPAP)/HReq. 1

Comparison with Tedford's data (their fig 3C) is as follows:

PAWP Tau-TedfordTau-Eq. 1
6 mmHg 0.43s 0.48s
45 mmHg 0.18s 0.18s

Conclusions
These findings imply that for a certain PAWP and Heart Rate a hyperbolic relation remains, but the time constant Tau depends on the ratio of PAWP/mPAP and Heart Rate. A clinically measured low Tau could suggest a high PAWP.

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16.35 **Poster Session II**

POSTER SESSION II – SPECIAL POPULATIONS III

11.1 Endothelial function is impaired in women who had pre-eclampsia

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Background
Women with a history of pre-eclampsia (PE) are at higher risk of cardiovascular disease later in life. We evaluated the cardiovascular health of women who had PE in comparison with women who had normotensive pregnancies.

Methods
We assessed heart rate-adjusted augmentation index (AIx SphygmoCor), carotid-femoral pulse wave velocity (PWV SphygmoCor), carotid intima-media thickness (CIMT ultrasound) and brachial flow-mediated dilatation (FMD ultrasound) in women who were pregnant 1-30 years ago.

Results
A total of 166 women (86 cases, 80 controls) attended for vascular studies. Women with a history of PE had higher systolic blood pressure (SBP) (130±14 vs 122±10 mmHg P<0.001) and diastolic blood pressure (DBP) (82±9 vs 78±7 mmHg P=0.001) compared with controls. They also had a higher BMI (29.4±6.1 vs 26.6±4.5 kg/m² P=0.002). We found impaired endothelial function (FMD 5.9±3.3 vs 7.0±3.3 %, P=0.017) and greater PWV (7.8±1.6 vs 7.1±1.1 m/s, P=0.002) and heart rate-adjusted AIx (25.7±11.0 vs 22.5± 9.6 %, P=0.023) in cases compared with controls. There was no difference in CIMT (P=0.110). After adjustment for age, BMI and SBP the difference in endothelial function remained statistically significant (P=0.014).

Conclusions
Women who had PE have higher blood pressure and BMI compared to women at similar age who had normotensive pregnancies. A history of PE is also associated with impaired endothelial function which could explain the higher cardiovascular risk in this group.

11.2 Coronary artery disease topography in relation to rheology of the peripheral small arteries in middle aged erectile dysfunction men

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Background
Middle age represents a life period where incidence of cardiovascular events typically augments. Our aim is to investigate any association between peripheral vascular rheology and distribution of coronary artery disease (CAD) in middle aged erectile dysfunction (ED) population.

Methods
146 ED patients (46-61 y/o) with a coronary angiography documented single vessel CAD (> 50% of luminal narrowing) enrolled the study and divided into two subgroups according to the coronary lesions allocation. Patients with left main (LM), proximal or mid-left anterior descending artery (LAD) disease consisted Group 1. Group 2 included the rest of participants. All underwent carotid-femoral pulse wave velocity (PWV) augmentation index (AIx), carotid intima- media thickness (IMT) and peak systolic penile Doppler velocity (PSV) evaluation. Low PSV (< 25cm/sec) implies an impaired physiology of the peripheral small arteries network.

Results
Mean penile PSV was significantly lower in Group 1 compering to Group 2. ROC curve analysis revealed a cut-off value of 22.5 cm/s on PSV for detecting LM, proximal or mid-LAD coronary lesions (sensitivity of 79% and positive predictive value of 86 %). PWV, AIx and IMT did not differ statistically between two groups.

Conclusions
In middle aged ED patients, low penile arterial Doppler flow associates to an increased probability of CAD of the left main and left anterior descending arteries resulting in a theoretically larger jeopardized myocardial ischemic area. Our data may offer non- invasive clinical information on coronary artery disease topography of that special population suggesting further profound diagnostic and follow up strategies.

11.3 Atheromatosis and endothelial response of the small peripheral arteries: a peritoneal dialysis versus hemodialysis patients mismatch

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Background

Peritoneal dialysis (PD) and hemodialysis (HD) are treatment options for end stage renal disease (ESRD). However, few are known on the cardiovascular impose of those therapeutic modalities. Our aim is to uncover endothelial damage and subclinical atheromatous process in male patients on chronic ESRD treated by either of those methods.

Methods

84 male ESRD patients, 46 on HD and the rest 38 on PD without apparent cardiovascular disease enrolled the study. The two groups did not differ statistically in age, (64,9 vs 64) prevalence of hypertension, diabetes mellitus, smoking and lipid profile. All underwent common carotid ultrasound intima –media thickness (cIMT) evaluation to uncover subclinical atheromatosis. Endothelial function was estimated by the SHIM-5 score (theoretical range 0-25) that grades erectile potency, a nitric oxide depended phenomenon based on vasodilator ability of the penile vasculature. Higher grading indicates a healthier endothelial vascular status.

Results

HD patients had statistically higher cIMT (1.5 vs 0.85) and lower SHIM-5 score grading (8.8 vs 12.8) compering to PD patients. Statistics remained significant after adjustment for age, body mass index, presence of hypertension, diabetes mellitus, tobacco use and statin therapy.

Conclusion

Peritoneal dialysis ESRD male patients appear to have a favorable endothelial function and a mild atheromatous load as compared to hemodialysis patients. Our data may offer clinical information guiding further therapeutic efforts in patients with end stage renal disease, a special population where cardiovascular morbidity remains typically high.

11.4 Relationship between inflammatory cytokines and aortic stiffness in patients with chronic kidney disease

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Introduction

Cardiovascular diseases are the primary cause of morbidity and mortality in patients with chronic kidney disease (CKD). Aortic stiffness is a non-traditional risk factor in these patients. Using an animal model of CKD with vascular calcification, we reported that inflammation is involved in the development of aortic calcification and stiffness. Hence, increased vascular production of IL-1β, IL-6 and TNFα was associated with aortic calcification. Therefore, we investigated the impact of the latter cytokines on aortic stiffness and determined the profile of inflammatory cytokines in a cohort of CKD patients.

Methods

This is a transversal study involving 196 CKD patients on dialysis, in which aortic stiffness was determined non-invasively by the assessment of carotid-femoral pulse wave velocity (cf-PWV) using Complior SP (Artech Medical, Pantin, France). The profile of inflammatory cytokines (IFNv, IL-1α, IL-1β, IL-2, IL-4, IL-6, IL-8, IL-10, IL-12 and TNF α) was determined in plasma by ELISA using a Multiplex (Aushon, Maine, USA).

Results

Mean cf-PWV of the cohort was 12.8±3.9 m/s. Median plasma levels of IL-1β, IL-6 and TNFα were 1.01 pg/ml, 4.26 pg/ml and 3.33 pg/ml, respectively. IL-6 levels positively correlated with cf-PWV (β = 0.218, P = 0.006, R = 0.129), suggesting a role in aortic stiffness. In contrast, no correlation between PWV and plasma levels of IL-1β or TNFα was established.

Conclusion

This study reveals a relationship between an inflammatory cytokine, Il-6, and aortic stiffness in patients with CKD. Our results, together with our previous findings in an experimental animal model, indicate that IL-6 may represent a novel therapeutic target of cardiovascular diseases in CKD.

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11.5 Differences of heart rate variability and augmentation index between dialysis and post-dialysis periods in patients with end-stage renal disease

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Introduction
Heart rate variability (HRV) analysis is a non-invasive tool for assessing the cardiac health. There is evidence that the cardiac autonomic system and central hemodynamics respond to hemodialysis. The aim of this work is to compare HRV parameters and augmentation index (AIx) between intra- and interdialytic periods in patients with end-stage renal disease.

Methods
All 24-h electrocardiogram data were obtained using the Lifecard CF digital Holter recorder (Delmar Reynolds/Spacelabs, Germany) and 24-h pulse wave analysis (PWA) measurements were taken with the Mobil-O-Graph 24h PWA (I.E.M. GmbH, Germany) within the ISAR hemodialysis study. Two-hundred patients (132 men / 68 women: 61+-16 years) were included. HRV was analyzed in the time- and frequency-domain in 5-min segments. AIx values and HRV parameters were averaged for intra- and interdialytic periods.

Results
The low to high frequency ratio (LF/HF) as a representative of sympathovagal balance (2.85 vs 3.36, $p<0.01$) and the augmentation index (AIx) (26.9 vs 28.5 %, $p<0.01$) were significantly decreased during dialysis. Whereas, the root mean square of successive differences (RMSSD) reflecting the parasympathetic cardiovascular modulation was significantly increased during hemodialysis session (13.9 vs 13.7 ms, $p<0.05$) (see Table).

Conclusions
The present work confirms previous findings of changes in HRV and AIx between intra- and interdialytic periods in a larger cohort [1,2]. The data suggests a reduced arterial stiffness in the context of a reduced sympathetic and increased parasympathetic activity during dialysis. Further studies should investigate the prognostic value of HRV changes in dependency of ultrafiltration volume in patients on dialysis.

	In	Out	p-value
AVNN (ms) **	836 [750,939]	819 [759,902]	<0.01
SDNN (ms) **	27.8 [21.4,39.2]	31.2 [24.2,42.3]	<0.01
RMSSD (ms) *	13.9 [9.35,22.9]	13.7 [10,20.3]	<0.05
pNN50 (%)	0.81 [0.19,4.87]	0.91 [0.25,3.97]	0.476
HRVIdx	6.88 [5.45,9.22]	7.03 [5.84,8.92]	0.920
TINN (ms)	102 [79,137]	104 [83.5,132]	0.713
LF (nu) **	68.8 [49.5,80.6]	70.6 [55.4,81.4]	<0.01
HF (nu) **	31.2 [19.4,50.5]	29.4 [18.6,44.6]	<0.01
LF/HF **	2.84 [1.31,5.63]	3.38 [2,6.58]	<0.01
Aix (%) **	26.9 [20.4,34.2]	28.5 [21.6,36.4]	<0.01
AIx75 (%) **	25.4 [20.3,31.6]	28.8 [22.9,33.6]	<0.01

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11.6 The aortic-to-brachial stiffness gradient and aortic reservoir-excess pressure in a dialysis population

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Background
Aortic reservoir function is associated with increased cardiovascular events. Patients with chronic kidney disease in need of dialysis have increased aortic stiffness and reversal of the aortic-to-brachial stiffness gradient, which could impair aortic reservoir function. The aim of this study was to determine the relationship between the aortic-to-brachial stiffness gradient and aortic reservoir function.

Methods
Among 310 patients with chronic kidney disease on dialysis, aortic and brachial stiffness were measured by pulse wave velocity (PWV), with the aortic-to-brachial stiffness gradient calculated by the ratio of aortic and brachial PWV (PWV ratio). Aortic reservoir function was measured by radial tonometry-derived reservoir pressure (RP) and excess pressure (XSP) integrals.

Results
RP was significantly and positively associated with PWV ratio (Standardized β=0.168 $p<0.001$) independent from age, sex, height, mean blood pressure, heart rate, treatment by hemodialysis and diabetes status (Model adjusted $R2=0.68$ $p<0.001$). On the other hand, XSP, which was significantly correlated to PWV ratio (Standardized β=0.20 $p<0.001$), lost its relation in multivariable adjusted model, and instead was predicted by age, heart rate, mean blood pressure and diabetes status, but this was only a weak model (Adjusted $R2=0.15$ $p<0.001$).

Conclusion
Among patients with chronic kidney disease on dialysis, the aortic-to-brachial stiffness gradient is an independent predictor of adverse aortic reservoir function.

11.7 Aortic calcium score affects non-invasively obtained estimates of central blood pressure in patients with advanced chronic kidney disease

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Background
We recently reported that central blood pressure (BP) obtained non-invasively in chronic kidney disease (CKD) patients significantly underestimated the central BP with decreasing eGFR in comparison with invasively measured true central BP in the aorta. This post-hoc analysis investigated whether the presence of aortic calcification affected non-invasive estimates of central BP.

Methods
CKD stage 4-5 patients undergoing coronary angiography were included. Invasive aortic BP was measured through angiography catheters. Non-invasive central BP was obtained with the SphygmoCor device. Calcium score (CS) in the aorta was quantified using CT.

Results
Twenty-four patients were enrolled (meanSD): 63% males, age 53±11 years, and eGFR 95 ml/min/1.73 m2. Invasive aortic SBP was 152±23 mmHg. Estimated central SBP was 133±20 mmHg. Ten patients had a CS=0 in both ascending and descending aorta, 2 patients had ascending aortic CS>0 while 8 patients had descending aortic CS>0 and 4 patients had both ascending and descending aortic CS>0. In patients with CS>0 in the descending aorta, central SBP was underestimated by 4(117) mmHg (P=0.02) compared to patients with CS=0. No significant difference was found between patients with and without calcium in the ascending aorta (P=0.13). In patients with CS>0 in both descending and ascending aorta central SBP was underestimated by 14(326) mmHg (P=0.02) compared to patients with CS=0 in both segments.

Conclusion
In advanced CKD, aortic calcification significantly affected the difference between estimated and invasively measured central BP. This may question the usefulness of non-invasive estimates of central BP in high-risk patients with severe aortic calcification.

11.8 Aortic systolic blood pressure is no longer marker of the arterial stiffness in stable patients with heart failure with reduced ejection fraction

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The aim of the study was to assess arterial stiffness and its diagnostic and prognostic value in patients with arterial hypertension (AH) and heart failure with reduced ejection fraction (HFrEF).

Methods
In 93 stable patients (75% male, age 64±9 years (MSD), history of myocardial infarction 67%, diabetes mellitus 32%, blood pressure (BP) 131±14/80±10 mmHg with AH, symptoms and signs of HF, LV EF <40% and NT-proBNP >100 pg/ml applanation tonometry and 2-dimentional echocardiography were performed. Mann-Whitney and Spearman tests were considered significant if $p<0.05$.

Results
Patients with NYHA III compared with patients NYHA II class had lower central systolic (118±12 vs 134±10 mmHg, $p<0.001$), diastolic (82±10 vs 87±15 mmHg, $p<0.05$) and pulse BP (36±7 vs 46±6 mmHg, $p<0.001$), time to reflected wave (Tr) (131±15 vs 145±21 ms, $p<0.05$), higher augmentation index (AI) (26±7 vs 16±8%, $p<0.001$), carotid-femoral pulse wave velocity (PWV) (13.5±4.1 vs 9.2±1.5 m/s, $p<0.001$). Central systolic and pulse BP positively correlated with EF and paradoxically negatively correlated with PWV. In prospective study AI ≥25, Tr <135 ms were associated with adverse outcomes. PWV ≥15 m/s increased risk of HF hospitalizations. AI ≥35%, Tr <116 ms increased risk of all-cause death.

Conclusions
In patients with AH and HFrEF dissociation between central systolic and pulse BP and arterial stiffness markers was revealed. Patients with more severe HF/ poor prognosis had lower systolic and pulse PP but higher PVW and AI. In this population central systolic and pulse BP were more dependent on LV systolic function and were no longer markers of aortic elasticity.

11.9 Parameters of arterial stiffness have independent prognostic value in stable patients with heart failure with reduced ejection fraction

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The purpose of the study was to determine the prognostic value of ventricular-arterial coupling (VAC) in patients with arterial hypertension (AH) and stable heart failure with reduced ejection fraction (HFrEF).

Methods
In prospective study (follow-up 12-24 months, median 18 months) prognosis of 93 stable patients with controlled hypertension and HFrEF was evaluated. Adverse outcomes included all cause death or first HF hospitalization. 2-dimentional echocardiography was used to assess arterial elastance (Ea) and end-systolicLV elastance (Ees). VAC was assessed as the ratio Ea/Ees. Arterial stiffness was assessed using applanation tonometry. Clinical and demographic parameters, parameters of LV function, VAC and arterial stiffness were included in multivariate analysis. $P<0.05$ was considered significant.

Results
Adverse outcomes were revealed in 39% of patients (15% deaths, 24% HF hospitalizations). The following factors increased the risk of adverse outcomes: LVEF <25%, index of VAC ³3.3, stroke work (SW)/pressure volume area (PVA) (LV work efficiency) <38%, augmentation index (AI) ≥25%, time to reflected wave(Tr) <135. Pulse wave velocity ≥15 m/s, office systolic BP <120 mmHg were associated with increased risk of HF hospitalizations. AI >35%, office systolic BP <120 and diastolic BP <70, Tr <116, SW/PVA <48% were associated with increased risk of all-cause death.

Conclusions
Parameters of VAC and arterial stiffness have independent prognostic value as well as LVEF and BP in patients with AH and HFrEF. Assessment of VAC via Ea/Elv, an additional noninvasively derived metric, can be used for risk stratification of patients with HFrEF.

11.10 Arterial elastance is associated with central blood pressure and arterial peripheral resistance in patients with heart failure with reduced ejection fraction

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Objective of the study was to assess ventricular-arterial coupling (VAC), parameters of left ventricular (LV) work efficiency and their determinants in patients with arterial hypertension (HTN) and stable heart failure with reduced ejection fraction (HFrEF).

Methods
In 93 stable patients with HTN and HFrEF 2-dimentional echocardiography was used to assess arterial elastance (Ea) and end systolic LV elastance (Ees). VAC was assessed as the ratio Ea/Ees. Mann-Witney test and multivariate analysis was performed. P<0.05 was considered significant.

Results
The range of VAC was 0.9-4.7. VAC >1.2 (upper optimal level) was revealed in 87%. Ea positively correlated with aortic systolic BP, office diastolic BP, arterial peripheral resistance, systole duration, negatively – with body mass index (BMI). Ees positively correlated with EF, office systolic and diastolic BP, negatively – with LV mass index (LVMI). Increased VAC was associated with decrease of office and aortic systolic BP, BMI, LV EF, increase of LVMI and NT-proBNP.

Conclusions
Impairment of functioning of cardio-vascular system assessed by increased value of VAC> 1.2 was revealed in 87% of patients with HTN and stable HFrEF. Increase of VAC was associated predominantly with decrease of Ees and LV work efficiency (SW/PVA). In HFrEF LV and arterial system matched to maximize SW. VAC and its components are associated with echocardiographic parameters and markers of arterial stiffness.

POSTER SESSION II – CLINICAL SCIENCE II

12.1 Evaluation of acute effects of coffee consumption on arterial stiffness in healthy adult people using an oscillometric device

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Environment / Objectives
Several studies in different populations and conditions shown contradictory results about the effect of coffee on arterial stiffness (AS). Coffee consumption is high around the world and it is very important to define its CV effects.

To evaluate the acute effects on haemodynamic parameters and AS, after consumption of regular coffee or, decaffeinated coffee.

Methods
In a prospective, self controlled cohort study we included 32 healthy p. (46.2±10.4y.o., 16 men (53.5±18) and 16 women (43.0±21)(p=0,186)). Fourteen regular coffee consumers (87.5%) (p=NS). Haemodynamic parameters and AS were assessed non invasively using oscilometric Arteriograph® (TensioMed Budapest, Hungary Ltd.). Each subject received 14 gr. of excelso coffee (151.2 mg caffeine) and two weeks apart, 14 gr of decaf coffee (3.92 mg) in random order. Baseline, 30 and 60 min parameters are reported.

Results
SBP increased at 30 and 60 min 3.9 mmHg (p=0.013) y 3.8 mmHg (p=0.002) respectively, la DBP increased 4.1 mmHg (p=0.001) y 3.2 mmHg (p=0.003), MAP 4.0 mmHg (p<0.001) y 3.3 mmHg (p=0.001), Heart rate decreased 3.2 (p=0.002) and 5 latidos/minuto (p<0.001) and aortic SBP increased 5.8 mmHg (p=0.002) and 7.6 mmHg (p=0.003) only with caffeine. Brachial Aix increased 19.9% at 30 (p<0.001) and 20.0% at 60 minutes (p<0.001). Aortic Aix increased 10.05% (p<0.001) y 10.2% (p<0.001) only with caffeine. PWV was not affected by caffeine (p=0.861). The shift of these parameters was mainly driven by changes in women.

Conclusions
Caffeine at usual doses (two expresos) increased peripheral AS but not aortic PWV, specially in women.

12.2 High pulse wave velocity is associated with increased visit-to-visit systolic blood pressure variability in controlled arterial hypertension

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Background
Visit-to-visit blood pressure variability (BPV) is associated with adverse cardiovascular outcomes in different patients' populations1-2. Arterial stiffness is a potential mechanism of increased visit-to-visit BPV3. Carotid–femoral PWV has become increasingly important for total cardiovascular risk estimation.

Materials and Methods
52 pts (20 men, age 58.9±9.0 yrs 4 smokers 6 diabetics) were treated to target BP<140/90mmHg with a RAAS-inhibitor/amlodipine combination for 14 months. Baseline brachial BP was 163.4±8.1/100.9±4.2mmHg achieved-123.7±9.7/76.8±6.7mmHg. Central BP and PWV were measured at baseline and after 14 months. Individual values of PWV were assessed according to age and BP categories4. BPV was calculated as SD for 5 visits during 8 months after target BP achievement.$p<0.05$ was considered significant.

Results
Baseline central BP was 137.8±17.3/86.6±12.0mmHg, achieved 125.2±13.5/80.3±6.6mmHg ($p<0.05$). Baseline PWV varied from 7.6 to 19.2 m/s (median 12.2 m/s), achieved – from 9.9 to 17.4 m/s (median 13.4 m/s),$p>0.05$. Normal values of PWV according to individual reference values were observed in 25.5% of patients (group1, mean PWV 10.0±1.5 m/s), increased – in 74.5% (group2, mean PWV 13.8±2.4 m/s). Groups were similar by age, gender, metabolic risk factors, baseline and achieved BP and visit-to-visit BPV. SBPV range was 1.79-16.79 mmHg (tertile I<5.38 II 5.38 – 7.78 III>7.78 mmHg). Increased PWV value was more often observed in the III tercile of visit-to-visit SBPV (90.3% comparing to 58.8% in tercile I and 73.3% in tercile II, Pearson $(\chi 2)=5.9$,$p<0.05$).

Conclusion
Elevation of PWV above individual reference values in patients with uncomplicated AH is associated with higher visit-to-visit SBPV. This finding confirms role of arterial stiffness in visit-to-visit BPV increase.

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12.3 24 hour ambulatory blood pressure monitoring and pulse wave velocity patterns in Kenyan adolescents

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Background
There are no data on ambulatory blood pressure monitoring (ABPM) and arterial stiffness parameters in sub-Saharan African children. We performed 24-hour ABPM and pulse wave velocity (PWV) measurements in adolescents living in 2 slums in Nairobi, Kenya.

Methods
We selected 1,100 11-17 year olds who from birth had been continuous residents of the Nairobi Urban Health and Demographic Surveillance System (NUHDSS) to participate in the study. Participants underwent anthropometric measurements (weight, height, mid-upper arm circumference [MUAC]) and answered questions on their socioeconomic status (SES). A clinic BP measurement was then taken using an automated Omron ™ M10-IT monitor (mean of 2 from 3 readings). Participants then underwent 24-hr ABPM and PWV measurement using an Arteriograph ™24 monitor.

Results
500 (90%) of 558 children recruited between December 2015 and June 2016 had acceptable ABPM readings (≥ 20 daytime and ≥7 nighttime readings). Mean (SD) clinic BP, and 24 hour-ABPM values were 98(11) and 117(12) systolic and 63(8) and 64(7) mmHg diastolic respectively. Mean clinic PWV and 24 hour-PWV were 7.3(1.5) ms-1 and 7(0.8) ms-1respectively. In multivariate regression analyses age (p=0.004), BMI (p=0.033) and PWV (p<0.001) were strong independent predictors of 24-hour BP values. Blood indices (hemoglobin, white cell and platelet count), gender, MUAC and SES had no independent influence on 24hr BP and PWV.

Conclusions
These are to our knowledge the first 24hr ABPM and PWV data generated from sSA adolescents. Long-term cardiovascular outcome studies are needed to determine the predictive ability of ABPM and PWV measurements.

12.4 Withdrawn by author

12.5 Impaired regulation of arterial wall viscosity during changes in blood flow in essential hypertensive patients

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Background
Arterial wall viscosity (AWV) is a major source of cardiac energy dissipation along the arterial tree. Evolution of AWV during increase in blood flow and the impact of essential hypertension on this evolution have never been studied.

Methods
Radial artery diameter, wall thickness and arterial pressure were simultaneous measured in 18 untreated essential hypertensive (HT) subjects and 14 frequency matched normotensive (NT) controls at baseline and during a sustained blood flow increase induced by hand skin heating. AWV was estimated by the ratio of the area of the hysteresis loop of the pressure-diameter relationship (viscous energy dissipated, WV) to the area under the loading phase of this relationship (elastic energy stored during the cardiac cycle, WE).

Results
At baseline, WV and WE were higher in HT than in NT subjects (WV: 1.06±0.78 versus 0.66±0.49mmHg.mm², p<0.01 WE: 2.33±1.47 versus 1.69±1.15mmHg.mm², p<0.05) but WV/WE was similar (43.0%±10. 1% versus 39.4%±11.8%). Heating did not modify significantly WE in both groups but induced an increase in WV only in HT patients (HT: +0.39±0.67mmHg.mm², p<0.05 NT: +0.24±0.43mmHg.mm², p=0.14 HT versus NT: p=0.09). Subsequently, WV/WE increased in HT but not in NT subjects (HT: +9.2%±9.1%, p<0.01 NT: +3.9%±9.9%, p=0.22 HT versus NT: p<0.01). Midwall stress, used as index of wall loading conditions, similarly increased in both groups (HT: +19.0±7.8 kPa, p<0.001 NT: +28.1±7.7 kPa, p<0.01 HT versus NT: p=0.13).

Conclusions
AWV is maintained during flow increase in NT subjects but increases in HT subjects. Excessive loss of energy may contribute to impair cardiovascular coupling during hypertension.

12.6 The role of neuronal nitric oxide synthase in young adults

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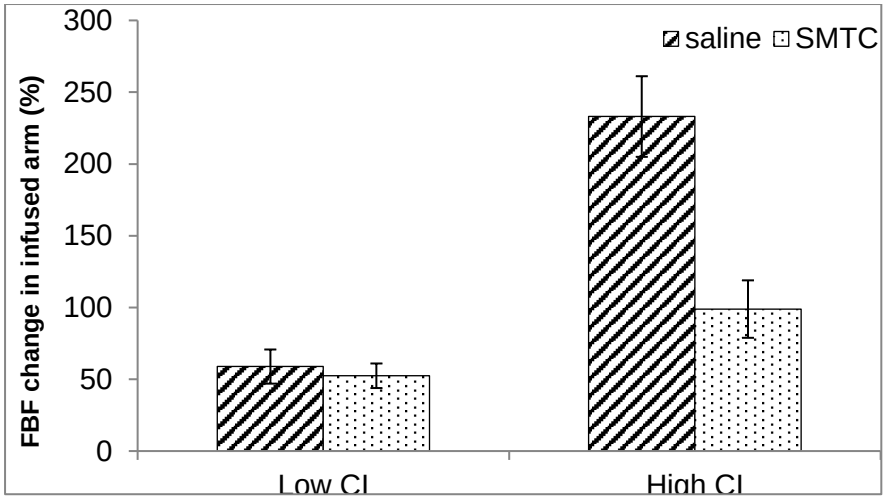
Background
Early elevation in blood pressure are characterised by a hyperkinetic circulation, with an elevated cardiac index (CI) being the dominant feature. Neuronal NOS is a key regulator of vascular tone during mental stress and is attenuated in patients with established hypertension. However, the role of nNOS has not yet been examined in young adults with a hyperactive response to stress.

Methods
20 subjects (M:11, 28±6 years) were dichotomised into high and low CI. Forearm blood flow (FBF) was measured using strain gauge plethysmography at rest and during a word interference test (Stroop); before and after the infusion of the nNOS-specific inhibitor, S-methyl-l-citrulline (SMTC).

Results
Cardiac index was 2.88±0.7 versus 4.32±0.9 L/min/m2 in the low and high groups, respectively. Mental stress induced a marked increase in FBF in subjects with high CI versus low CI, which was signficantly blunted after infusion of SMTC (P<0.05 for Two-way repeated measures ANOVA).

Figure 1: FBF response to mental stress during saline or SMTC in subjects with low versus high CI



Conclusions
The vasodilatory response to mental stress is enhanced in individuals with elevated cardiac index and nNOS appears to play a key role in this response. This may be a protective response in individuals in whom sympathetic activity may be high.

12.7 The relationship between functional arterial response and circulating biomarkers of patients with fibromuscular dysplasia

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Background
Fibromuscular dysplasia (FMD) is a rare idiopathic, non-atherosclerotic non-inflammatory vascular disease. This work represents the first study of the pathophysiology of FMD. We investigated the relationships between circulating biomarkers and the non-invasive vascular parameters.

Methods
We included 50 patients with FMD, 50 essential hypertensive patients (HT) and 50 healthy subjects (NT) matched for age, sex, ethnicity and blood pressure. We determined circulating levels of total microparticles (MPs) (annexinV+MPs), endothelial MPs (CD144+MPs, CD62E+MPs and CD31+CD41-MPs) and SMC-MPs by flow cytometry analysis. We measured forearm endothelial function by post-ischemic flow dependent vasodilation. Shear stress was estimated using the formula of Weaver (1-3). Aortic stiffness was assessed by measuring carotid-femoral pulse wave velocity. Triple signal score was assessed from 15-MHz echotracking system.

Results
There are no significant differences between rates of total MPs, endothelial MPs (CD144+MPs, CD62E+MPs and CD31+CD41-MPs) and SMC-MPs between 3 groups (with p-value 0.38 0.52 0.65 0.17 and 0.25 respectively). Endothelial MPs were not correlated with the endothelial dysfunction, nor with the shear stress, whether in FMD, NT or HT. We observed a strong negative correlation between aortic stiffness and nitroglycerin-mediated dilation in the group NT, HT and whole population (r= -0.43, p= 0.001 r= -0.29, p= 0.03 r = -0.35, p<0.001 respectively), but not in FD (p=0.5). SMC-MPs were not associated with the triple signal or any arterial parameter in the group FMD nor in the whole population.

Conclusions
The number of MPs was not correlated with large artery properties. Arterial stiffness is negatively related to endothelium-independent dilatation.

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12.8 Ventricular-arterial uncoupling does not depend on arterial elastance after myocardial infarction

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Objective
Ventricular remodeling may occur following myocardial infarction (MI) of the left ventricle (LV) and such remodeling has been shown to be correlated with increased patient morbidity and mortality. It is important to estimate the likelihood of remodeling from the state of the infarcted LV. The aim of the study was to assess the ventricular-arterial coupling (VAC) in patients with ST segment elevation (STEMI) and non ST segment elevation MI (NSTEMI) treated with percutaneous coronary intervention (PCI).

Methods
In 93 patients with acute coronary syndrome and PCI (70% male, age 61.5±10.1 years (M±SD), 57 (61.3%) with STEMI, smokers 25%, arterial hypertension 20.4%, blood pressure 129±6/82±7 mmHg) 2-dimentional echocardiography was performed to assess arterial elastance (Ea) and end-systolic LV elastance (Ees) on admission and in 4 weeks. VAC was assessed as the ratio Ea/Ees.

Results
Baseline LV ejection fraction (LVEF) was 47.4±4.3%, E/A 0.95±0.18, Ea 1.9±0.3 mmHg/ml/m2, Ees 2.1±0.4 mmHg/ml/m2, VAC 0.89±0.1. At baseline all patients had LVEF >40% and VAC in optimal range. In 4 weeks after PCI VAC >1.2 (upper optimal level) was revealed in 19% of patients with STEMI and 44% with NSTEMI. In patients with achieved VAC >1.2 Ees (from 2.1±0.4 to 1.5 ±0.3 mmHg/ml/m2, p <0.001), stroke work (SW) (from 6585±1059 to 6919±2131 mmHg*ml/m2, p <0.05), potential energy (PE) (from 1976±371 to 3025±1127 mmHg*ml/m2, p <0.001), pressure-volume area (PVA) (from 6647±1060 to 6977±2136 mmHg*ml/m2, p <0.001), LV work efficiency (SW/PVA) (from 78 to 89% , p<0.001) significantly decreased while Ea (1.9±0.3 and 2.1±0.4 mmHg/ml/m2, p >0.05) did not change. In patients with VAC in optimal range in 4 weeks Ees decreased from 2.3±0.3 to 2.1±0.4 mmHg/ml/m2 (p<0.001), Ea (from 1.87±0.29 to 1.64±0.17 mmHg/ml/m2, p<0.001) and VAC (from 0.82±0.12 to 0.81±0.19, p<0.04) did not change.

Conclusions
Impairment of functioning of cardio-vascular system assessed by increased value of VAC >1.2 was revealed in 30% of patients with acute coronary syndrome. Increase of VAC is associated predominantly with decrease of Ees and LV work efficiency (SW/PVA). Increased VAC index >1.2 indicating LV-arterial uncoupling may be an early marker of unfavorable cardiac remodeling.

12.9 Ventricular arterial coupling in isometric handgrip test in untreated hypertensive patients

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Aim
To evaluate cardiovascular adaptation to increased afterload during handgrip isometric exercise (HIE) in untreated hypertensive patients.

Methods
75 untreated hypertensive patients (age 54±7years, 44 males, BP 153/93 mmHg) underwent simultaneous EchoCG and blood pressure (BP) acquisition at rest and during HIE. End-systolic pressure was determined as 0,9 x brachial systolic BP (SBP). Arterial elastance (Ea) and LV elastance (Ees) were calculated as end-systolic pressure (ESP) /stroke volume (SV) and ESP/end-systolic volume (ESV). Ventricular-arterial coupling index was assessed as Ea/Ees. Efficiency of left ventricle (ELV) was evaluated by stroke work (SW)/pressure-volume area (PVA) ratio. SW=ESPxSV, PVA=SW+PE (ESPxESV/2-end diastolic pressure xESP/4). p<0,05 was considered significant.

Results
Ea/Ees<0,5 was found in 76% (n=57, 18 female) before HIE. In 38% (n=22, 4 (23%) female) Ea, Ees, Ea/Ees and SW/PVA did not change significantly. In 11% there was further decrease of Ea/Ees associated with significant increase of ELV. In 51% (n=29, 14 (49%) female) Ea/Ees increased due to increase of Ea from 1,98±0,32 to 2,35±0,41 (p<0,05) while Ees increased from 5,95±2,2 to 4,58±1,0 (p<0,05). Ea/Ees increase was associated with decrease of ELV from 0,89±0,02 to 0,84±0,02 (p<0,05) indicating cardiovascular misadaptation to HIE.

In subjects (n=18, 3 female) with normal Ea/Ees 0,5-1,2 before HIE Ea/Ees and ELV did not change in 8 (49%, all males). In 10 subjects (3 female) Ea/Ees decreased due to significant increase of Ees (from 3,15±0,68 to 5,02±1,34 (p<0,05), and ELV increased from 0,81±0,03 to 0,88±0,01 (p<0,05).

Conclusion
Cardiovascular misadaptation to afterload is the most prevalent type of reaction to HIE in subjects with decreased baseline Ea/Ees and may be also observed in subjects with normal baseline ventricular-arterial coupling. This misadaptation in subjects with baseline ventricular arterial uncoupling is associated with female gender.

12.10 Reduced ventricular-arterial coupling as an early marker of cardiovascular remodeling in hypertensive men

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Objective
To evaluate ventricular-arterial coupling (VAC), left ventricular hypertrophy (LVH), diastolic function and arterial stiffness in young and middle-aged men with uncomplicated arterial hypertension

Methods
97 young men aged 18-27 years (21,2±1,9 years, BP 156,5±14,0/98,5±9,1 mmHg) and 68 middle-aged men aged 40-60 years (n=68, age 53,9±7,2 years, BP 152,7±9,6/94,8±7,8 mmHg) (M) underwent simultaneous EchoCG, blood pressure (BP) and pulse wave velocity measurement. VAC index was calculated arterial elastance (Ea) and left ventricular elastance (Ees) ratio. Ea=end-systolic pressure/stroke volume, Ees=end-systolic pressure/end-systolic volume. LVH was diagnosed if LV mass index was >115 g/m2, Increased arterial stiffness -if PWV >10 m/s, diastolic dysfunction – if E/A <1,0 and E/E'<7 m/s.

Results
In young men Eea 1,86±0,32 and index VAC (0,52±0,10) was similar to that in middle-aged (1,9±0,47 and 0,48±0,19, respectively), despite that Ees in young men was significantly lower (3,67±0,85) than in middle-aged men (4,6±2,1, p<0,01). VAC index <0,5 was found in 34% young men and in 57% middle-aged men (p<0,05), LVH in 7,4% and 67% (p<0,05), diastolic dysfunction 4,1% and 62%, respectively. VAC index was similar in those with and without LVH or diastolic dysfunction in the both age groups. In young men with LVH VAC index was 0,63±0,26, without LVH 0,54±0,12, in middle-aged patients with LVH - 0,45±0,16, without LVH - 0,49±0,21. In young men with diastolic dysfunction VAC index was 0,61±0,13, without diastolic dysfunction - 0,58±0,16. In middle-aged men 0,45±0,14 and 0,48±0,16, respectively. PWV>10 m/s was found in 22,7% of young men and in 80,1% of middle-aged (p<0,05). No significant correlation between VAC index and BP, LVMI, PWV, E/A, E/E' was found.

Conclusion
Decrease in the VAC index<0,5 indicating LV-arterial uncoupling may be an early marker of cardiovascular remodeling in hypertensive men that may be observed before development of LVH, diastolic dysfunction or increased arterial stiffness.

12.11 Sarcopenia and Vascular Risk in a Healthy Elderly UK Population (BRAVES study)

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Introduction
Sarcopenia, the loss of skeletal muscle mass and strength that occurs with advancing age [1] is correlated with functional decline and disability but little is known about its relationship with cardiovascular risk. Bioimpedence analysis (BIA) is a validated technique for measuring muscle mass, convenient for use in large cohort studies. Arterial stiffness (compliance) is an independent predictor of cardiovascular events.

Methods
The BRAVES study was designed to compare cardiovascular risk between two healthy elderly cohorts in the UK and in Italy. We used data from the UK cohort to investigate the relationship between sarcopenia and vascular compliance.

Participants were eligible if aged 65-85 years, lived within the Brighton area and had weight loss of no more than 5% in the last month. All underwent physical exam, BIA assessment of skeletal mass index (SMI) and two measures of arterial compliance. Pulse wave velocity (PWV) was measured between carotid-femoral and carotid-radial arteries and the augmentation index (AIx) derived from carotid and radial arteries. A bivariate correlation was performed.

Results
Ninety patients (64 female; 26 male) had mean age 73, mean FFM 46.84kg (range 34.7-74.7) and mean SMI 6.77 (range 4.84-10.09). There was a negative relationship between SMI and Radial AIx (R=0.-542, p=0.000) as well as Carotid AIx (R=-0.391, p=0.002) but not PWV. Using multiple regression to control for the effects of age and gender, SMI was independently related to radial AIx (p=.013).

Conclusions
Skeletal muscle mass index is strongly negatively correlated with augmentation index, a measure of vascular stiffness. This finding suggests that elderly patients with higher muscle mass have a more compliant aorta and hence lower cardiovascular risk. Whether sarcopenia acts as a marker for CV risk or plays an active role in cardiovascular disease progression is not yet established and deserves further investigation.

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POSTER SESSION II – CLINICAL THERAPEUTICS

13.1 The effects of alpha 1-adrenoceptor-blockade and angiotensin converting enzyme-inhibition on indices of aortic stiffness measured by an oscillometric single cuff method in hypertension: the doxazosin ramipril study

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Objectives
To study whether inhibition of the renin-angiotensin-aldosterone system has effects on arterial stiffness beyond blood pressure (BP) reduction alone.

Methods
Hypertensive patients (age 54±12 years, 34% women) were randomized double-blind to ramipril (10 mg od, n=32) or doxazosin (8 mg od, n=26) for 12 weeks. Central aortic BP and pulse pressure (PP), aortic pulse wave velocity (PWV), and augmentation index (AIx) were assessed by a single cuff oscillometric cuff method (Arteriograph, Tensiomed). With PWV and Aix adjustments were made for potential confounding by height, age, gender, and baseline mean arterial pressure.

Results
Seated office brachial BP on inclusion was (mean values ± SD) 154±10/93±9 mmHg. Baseline central BP was 154±19/93±9 mmHg, central PP was 61±13 mmHg, PWV 9.0±2.1 m/s, AIx 45±13%, and transit time 61±12 ms. Treatment induced changes (mean values ± SEM) in central BP (-8±2/-8±1%; both P<0.01), aortic PP (-9±2 mmHg; P<0.01), PWV (-5.2±2.0%; P<0.05), AIx (-12±3%; P<0.01), and transit time (8±3 ms; P<0.01). Ramipril induced greater changes than doxazosin in central BP (-13±2/-11±2 vs -2±2 /-3±2%; all P<0.01), central PP (-16±3 vs -2±3 mmHg; P<0.01), and AIx (-18±4 vs -5±4%; P<0.05). The reductions in PWV were similar for ramipril and doxazosin (-6±3 vs -4±3%, respectively).

Conclusions
Both ramipril and doxazosin reduce BP and indices of arterial stiffness, with greater effects by ramipril on central BP and AIx. The results suggest that the single cuff oscillometric cuff technique can be used to evaluate effects of antihypertensive treatment on central BP and arterial function.

13.2 Effects on vascular structure and function of single at1r blockade or its combination with CCB, diuretics or their triple association

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Environment/Objectives
The antihypertensive efficacy of Valsartan (VAL) is largely known in monotherapy and combination with CCB and diuretics (D) but there is scarce evidence of its vascular effects in subjects younger than 60 y.o. Otherwise, there is a rationale supporting using combinations in high CV risk or patients with higher BP but vascular findings are not considered still as a reason.

To analyze a population of subjects <60 y.o treated with different regimens of antihypertensive drugs and the vascular patterns in each group.

Methods
From the database of our Non Invasive Vascular lab with 7865 p. first evaluation, we analyzed in a real life case

control, retrospective study 700 control hypertensives, 57 on VAL monotherapy, 28 on VAL+D, 64 on VAL+CCB and 21 on triple combination (VAL+CCB+D). Data of CV RF and Vascular parameters (IMT, Plaques, PWV, Endothelial Function (EF) and Arterial Stiffness (AS) like CAP and Aix) are reported.

Results
Mean age was 52.5 + 4.2 y.o. and males mean 73%. Older subjects, obese, smokers and those presenting Metabolic Syndrome (MS) were predominant in combination groups. (p<0.001) Higher levels of BP and lower levels of BP control were observed in combination groups.(p<.001)

Vascular disease parameters were worse in combination groups (IMT, Plaques, PWV, CAP and Aix) but no EF (p<.001) than in monotherapy.

Conclusion
With limitations of an observational study, we found that doctors use combinations in more sick patients, with high CV risk profile and it is related with more severe vascular compromise deserving more intensive therapeutic regimens.

13.3 Sacubitril/valsartan therapy is associated with decrease of arterial elastance in stable patients with heart failure with reduced ejection fraction

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Objective
Angiotensin receptor-neprilysin inhibition with LCZ696 is a novel approach for the treatment of heart failure with reduced ejection fraction (HFrEF). The aim of the study was to assess the effects of valsartan/sacubitril on parameters of ventricular-arterial coupling and left ventricular (LV) work efficiency in patients with stable HFrEF.

Methods
In the open-label follow-up to PARADIGM HF study 18 patients with stable HFrEF (16 male, 69±9 years (MSD), arterial hypertension 83%, previous myocardial infarction 89%, diabetes mellitus 39%, LVEF 324%) were enrolled. 2-dimentional echocardiography was performed to assess arterial (Ea) and end-systolic LV elastance (Ees) baseline and after 6 month LCZ696 therapy. VAC was assessed as the ratio Ea/Ees. Wilcoxon test was considered significant if p<0.05.

Results
Baseline brachial BP decreased from 137.1±22.0/83.4±11.8 to 120.5±13.5/75.1±9.3 mmHg (Δ -16.6±14.2/-8.3±10.3 mmHg, p<0.05). LCZ696 therapy was associated with significant decrease of VAC (2.10±0.55 vs 1.68±0.32, p<0.05), Ea (2.11±1.04 vs 1.66±0.6 mmHg/ml/m2 (Δ -0,70 (-0.26%)), p<0.05), arterial peripheral resistance (0.029±0.016 vs 0.027±0.011 mmHg/ml/min, p<0.05), increase of stroke volume (63±24 vs 78±26 ml, p<0.05). Ees remained unchanged (1.11±0.42 vs 1.01±0.52 mmHg/ml/m2, p>0.05). LCZ696 therapy was associated with potential energy decrease (8049±2846 vs 5037±2492 mmHg*ml/m2, p<0.05),stroke work/pressure-volume area index (LV work efficiency) increase (0.48±0.09 vs 0.63±0.05, p<0.05). There was no statistically significant correlation between decrease of Ea and brachial BP decrease.

Conclusion
LCZ696 therapy was associated with BP-independent improvement in VAC related with decrease of Ea rather than Ees changes and associated with decrease of arterial peripheral resistance and improvement of LV work efficiency

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13.4 Sacubitril/valsartan therapy is associated with decrease of pulse wave velocity in stable patients with heart failure with reduced ejection fraction

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Objective
Dual neprilysin inhibition and angiotensin receptor blockade with LCZ696 has been shown therapeutic benefits in

chronic heart failure (CHF) patients. The aim of the study was to assess sacubitril/valsartan effects on parameters of arterial stiffness in stable heart failure with reduced ejection fraction (HFrEF).

Methods
In the open-label follow-up to PARADIGM HF study 18 patients with stable HFrEF (16 male, 699 years (MSD), arterial hypertension 83%, previous myocardial infarction 89%, diabetes mellitus 39%, dyslipidemia 56%, LVEF 324%, serum creatinine 11821 µmol/l, eGFR 5613 ml/min/1.73m2, potassium 4.450.35 mmol/l) were enrolled. Patients received a stable background treatment for at least a month (ACEI 94%, beta-blockers 100%, aldosterone receptor antagonists 83.3%, loop diuretics 72.2%). Applanation tonometry was performed baseline and after 6 month LCZ696 therapy. Wilcoxon test was considered significant if $p<0.05$.

Results

Baseline brachial BP decreased from 137.1±22.0/83.4±11.8 to 120.5±13.5/75.1±9.3 mmHg (Δ -16.6±14.2/-8.3±10.3 mmHg, $p<0.05$), heart rate did not change (78±12 vs 75±15 beats/min (Δ -2.7±14.7 beats/min, $p>0.05$). Valsartan/sacubitril therapy was associated with significant decrease of carotid-femoral pulse wave velocity (11.5±2.9 vs 10.2±2.9 m/s, $p<0.05$), central systolic (125±16 vs 116±15 mmHg, $p=0.005$) and diastolic (78±7 vs 74±9 mmHg, $p<0.05$) blood pressure. Central pulse pressure (45±11 vs 41±16 mmHg), augmentation pressure (16±7,1 vs 13,8±8,4 mmHg), augmentation index (29±7 vs 28±11%), time to reflected wave (128±8 vs 132±7 ms) did not change significantly ($p>0.05$ for all comparisons).

Conclusion
6 month sacubitril/valsartan therapy was associated with significant decrease of aortic systolic pressure and pulse wave velocity.

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13.5 Ventricular-arterial coupling during treatment with bisoprolol and bisiprolol/amlodipin in hypertensive patients

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Objective
To evaluate ventricular-arterial coupling in hypertensive patients after therapy with a beta-blocker and its fixed dose combination (FDC) with amlodipine.

Design and method
28 patients (age 53,95±7,2, 20 males, BP 148,7±13,4/96,6±14,1 mmHg, HR 83,2±10,1 bpm) with untreated uncomplicated hypertension underwent simultaneous EchoCG and blood pressure (BP) acquisition at baseline, after 4 weeks of bisoprolol 5-10 mg monotherapy and after 8 weeks after switching to FDC bisoprolol 5-10/amlodipine 5-10 mg. Doses were titrated to reach BP <140/90 mmHg. Arterial elastance (Ea) and LV elastance (Ees) at rest were calculated as end-systolic pressure (ESP)/stroke volume (SV) and ESP/end-systolic volume (ESV). Ventricular-arterial coupling (VAC) was assessed as Ea/Ees. Mechanical efficiency of left ventricle (ELV) and peripheral arterial resistance (PAR) were evaluated also. $p<0,05$ was considered significant.

Results
After monotherapy with bisoprolol BP was 146,1±15,3/85,3±11,3 mmHg ($p>0,05$ vs baseline), HR 59,8±7,7 ($p<0,05$ vs baseline), after FDC 132,1±11,3/76,23±11,1 mmHg and 64,54±7,0 bpm, respectively (all $p<0,05$ vs baseline). Bisoprolol decreased Ees from 4,45±1,9 to 3,67±0,98 ($p<0,05$) whereas Ea, PAR did not change significantly. Ea/Ees increased significantly from 0,47±0,16 to 0,55±0,14 ($p<0,05$). Switching to bisoprolol/amlodipine FDC resulted in decrease of Ea from 1,88±0,39 at baseline and from 1,92±0,38 after bisoprolol monotherapy, PAR from 137,1±35,3 at baseline and from 128,9±36, respectively to 105,6±28. Ees did not change from that on bisoprolol, Ea/Ees (0,45±0,1) returned to baseline values. ELV did not change significantly throughout a study.

Conclusions
In hypertensive patients monotherapy with bisoprolol reduces initially increased Ees without negative effect on Ea

and PAR and switching to bisoprolol/amlodipine FDC results in additional Ea reduction. Thus the study confirms potential benefits of bisoprolol/amlodipine in arterial hypertension in terms of cardiovascular functioning.

13.6 Switching to bisoprolo|/amlodipine fdc eliminates adverse effect of a beta-blocker on aortic pulse pressure augmentation

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Objective
The aim of the study was to evaluate if combination with amlodipine eliminates the adverse effect of beta-blockers on aortic pulse pressure (PP) augmentation.

Methods
28 previously untreated non-diabetic hypertensive subjects (age 53,6±5,7 years, 19 males) where treated bisoprolol 5-10 mg, if in 4 weeks BP >140/90 mmHg amlodipine 5 mg-10 mg was added to therapy to reach BP <140/90 mmHg. Before treatment, after monotherapy and after bisoprolol+amlodipin, applanation tonometry was done. The changes were considered significant if p<0,05.

Results
At the end of the study 23 patients were treated with bisoprolol 5/amlodipine 10 mg fixed dose combination, 5 - 10/10 mg. After 4 weeks of monotherapy brachial BP decreased from 153,9±9,1/83,4±7,5 to 146,7±8,3/85,1±3,4 mmHg, HR from 79,2±4,7 to 63,5±4,7 bpm (p<0,05). At the end of the study BP was 129,1±5,6/74,3±4,9 mmHg (p<0,05 vs baseline and monotherapy period), HR 62,8±4,9 bpm (p<0,05 vs baseline). Baseline central SBP was 143,2±8,2, PP 46,810,4 mmHg, augmentation index (AI)@HR 75 bpm 20±14%, PWV 10,5±2,1 m/s. After bisoprolol monotherapy the values were, respectively, 134±7,6, PP 44,2±7,3 mmHg, 27,1±16,1%, PWV 10,0±1,6 m/s. After further 4 weeks treatment with bisoprolo+amlodipine central SBP was 119,5±5,7 (p<0,05 vs baseline), PP 41,4±6,3 mmHg (p<0,05 vs baseline), AI@HR 75 bpm 21,9±6,5 % (p<0,05 vs baseline), PWV 9,6±1,0 m/s.

Conclusion
Monotherapy with bisoprolol increases central PP augmentation. Combining with amlodipine in a single pill eliminates the adverse effect of a beta-blocker on aortic PP augmentation and results in effective reduction of central SBP.

13.7 Renal denervation in treatment resistant hypertension: effects on coronary flow reserve and forearm dilation capacity. A randomized, double-blinded, SHAM-controlled clinical trial

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Background
Microvascular impairment is well documented in hypertension. In this ReSET1 sub-study we investigated the effects of renal sympathetic denervation (RDN) on coronary flow reserve (CFR) and coronary- and forearm minimum vascular resistance (C-Rmin and F-Rmin) in patients with resistant hypertension.

Methods
A randomised, single centre, double-blind, sham-controlled clinical trial in 58 patients with resistant hypertension randomised to RDN or SHAM. Inclusion criteria: ASBP-day > 145 mmHg following stable antihypertensive treatment and 2 weeks of compliance registration. RDN was performed with the unipolar Medtronic Flex catheter (Medtronic, California, USA). CFR and C-Rmin were determined with transthoracic Doppler echocardiography and F-Rmin with venous occlusion plethysmography at baseline and six-months follow-up.

Results
Baseline mean 24-h ambulatory BP was 111±1 mmHg (RDN, n=29) and 111±2 mmHg (SHAM, n=29). Similar reductions in MAP were seen at six-months follow up (-3.5±2.0 vs -3.2±1.8, p=0.92). Baseline CFR was 2.9±0.1 (RDN) and 2.4±0.1 (SHAM) with no significant change at follow-up (0.2±0.2 vs. -0.1±0.2, P=0.57). C-Rmin was 1.9±0.3 (RDN) and 2.7±0.6 (SHAM) (mmHg min/ml pr. 100 g LVM) and unchanged (0.3±0.5 vs. -0.4±0.8, P=0.48). F-Rmin was 3.6±0.2 (RDN) and 3.6±0.3 (SHAM) (mmHg min/ml pr. 100 ml tissue) and unchanged at

follow-up (0.6±0.3 vs. 0.1±0.2, P=0.17). There was a tendency toward increased baseline LVMI in the SHAM-group (121±7 (SHAM) vs. 108±3 (RDN) g/m2, P=0.08), but with proportional change at follow-up (-4±7 vs. 3±5, P=0.38).

Conclusion
RDN had no significant effect on CFR, C-Rmin and F-Rmin. Thus, data does not support microvascular improvement following RDN in resistant hypertension.

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13.8 Ventriculo-vascular interactions and the arterial Windkessel: new insights from cardiovascular magnetic resonance imaging before and after renal denervation

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Background
Cardiovascular magnetic resonance (CMR) imaging is considered the gold standard for the evaluation of ventricular morphology and function. We implemented wave intensity analysis and the reservoir-wave hypothesis for CMR to assess ventriculo-arterial coupling non-invasively. We present the feasibility of both methods.

Methods
Wave intensity analysis was performed on patients undergoing renal denervation (RDN, Symplicity Flex catheter) for treatment of hypertension (n=9 32-65 years 4 males office blood pressure (BP) 192/104 ±16/14 mmHg). Phase-contrast CMR flow data was acquired in the ascending aortic pre-RDN and at 6 months follow-up. Wave intensity was derived from the product of aortic blood flow velocity differentials and fractional changes of aortic area. The reservoir-hypothesis was implemented for CMR-derived velocity and area data in a Phyton script, using the Levenberg-Marquardt nonlinear fitting algorithm. Feasibility of extracting reservoir-wave parameters (i.e. diastolic time constant, arterial compliance, and asymptotic area value) was tested in an additional cohort of normotensive subjects (n=20 20-74 years 17 males).

Results
Wave intensity analysis was feasible in hypertensive patients, with an increase in peak forward compression wave post-RDN (7.9±3.8 pre-RDN vs. 9.8±2.5 post-RDN, p=0.046), suggesting improved ventricular contractility in response to altered downstream impedance. Systolic BP reduced (-21±26 mmHg, p=0.040) post-RDN, whilst ejection fraction and LV mass were unchanged. Reservoir wave parameters were physically realistic, with a reasonably tight distribution, the fitting algorithm converging robustly in 19/20 test cases.

Conclusion
Routine CMR data can provide valuable insight into ventriculo-arterial coupling and reservoir-wave parameters. Pilot data suggest that RDN improves left ventricular contractility.

13.9 The effect of rosuvastatin added to a standard antihypertensive therapy on arterial stiffness in patients with uncontrolled hypertension

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We studied the influence of rosuvastatin added to a standard therapy on central BP and pulse wave velocity (PWV) in patients with uncontrolled hypertension. 60 patients (31 men and 29 women aged 51.19.1) with uncontrolled hypertension were randomized into two groups. Group 1 included 30 patients who received a fixed combination of 10 mg/day lisinopril and 5 mg/day amlodipine (Ekvator®, Richter Gedeon, Hungary). Group 2 consisted of 30 patients who followed the same regimen of therapy with addition of 20 mg/day of rosuvastatin. The central (aortic) BP, augmentation index (AIx), carotid-femoral and carotid-radial PWV were evaluated before and after a 48-week follow-up period.

Results
The central systolic/diastolic BP decreased in both groups from 153.6±22.1/100.5±13.2 to 121.3±17.6/83.3±10.4 mmHg (p<0.001) in the 1st group and from 157.0±20.3/100.0±10.6 to 119.8±15.8/80.1±9.7 mmHg (p<0.001) in the 2nd one. The extent of central BP decline did not differ. AIx decreased from 30.6±14.0 to 23.5±15.2%

(p=0.001) in the 1st group and from 35.2±8.2% to 24.1±13.0% in the 2nd group (p<0.001) with more prominent AIx decrease in the latter (-6.2% and -9.8% respectively, p=0.15). Mean carotid-femoral PWV decreased statistically only in the 2nd group from 9.5±1.7 to 8.7±1.6 m/s (p=0.04). The carotid-radial PWV did not change in both groups.

Conclusion
Addition of rosuvastatin to a fixed lisinopril/amlodipine combination in the treatment of patients with uncontrolled hypertension resulted in the carotid-femoral pulse wave velocity decline, but was beneficial neither for the decrease of aortic systolic and pulse BP nor of augmentation index.

13.10 Impact of the glycemic control status on the 2-year progression of the arterial stiffness in add-on a dipeptidyl peptidase 4 inhibitor treatment

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Aims
The effect of sitagliptin on the 2-year progression of the arterial stiffness and also to determine the effect of good glycemic control on the rate of progression of the arterial stiffness was examined.

Methods
The study participants were either allocated to add-on sitagliptin treatment or to continued treatment with conventional anti-diabetic agents. We succeeded in measuring the brachial-ankle pulse wave velocity (baPWV) at least two times during the 2-year study period in 96 subjects.

Results
The changes in the baPWV during the study period were similar between the both groups, overall. On the other hand, when the study subjects were divided into two groups according to the glycemic control status during the study period {good glycemic control group (GC) = hemoglobin (Hb)A1c < 7.0 at both 12 and 24 months after the treatment randomization poor glycemic control group (PC) = HbA1c ≥ 7.0 at either 12 months, 24 months, or both}, the 2-year increase of the baPWV was significantly larger in the PC group (144 235 cm/sec) as compared to that the GC group (-10 282 cm/sec) (p = 0.036).

Conclusion
While the present study could not confirm the beneficial effect of sitagliptin per se on the arterial stiffness, the results suggested that good glycemic control may be beneficial for delaying the annual progression of the arterial stiffness.

13.11 Effects of dapagliflozin on early alterations of the micro- and macrocirculation

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Background
Diabetes mellitus, primarily a metabolic disorder, must be considered also as a vascular disease. Early vascular changes are characterized by hyperperfusion (e.g. eye), vascular remodeling of small arteries and increased pulse wave reflection leading to increased (central) aortic pressure. We investigated the effects of the SGLT-2 inhibitor dapagliflozin on parameters of early micro- and macrovascular changes in patients with type-2 diabetes.

Methods
In this prospective, double-blind, placebo-controlled, cross-over trial 59 patients (61+/-7.6 years) with type-2 diabetes were randomly assigned to dapagliflozin 10mg and placebo for 6 weeks. Retinal microvascular structure (wall-to-lumen ratio [WLR]) and retinal capillary flow [RCF]) were non-invasively assessed by scanning laser Doppler flowmetry. In addition, macrovascular parameters (central pulse pressure) were assessed by pulse wave analysis in addition to 24-h ambulatory blood pressure (ABP).

Results
Treatment with dapagliflozin for 6 weeks improved diabetic control (HbA1c, fasting and postprandial blood glucose, all p<0.001) compared to placebo. Compared to placebo treatment with dapagliflozin reduced numerically but not significantly both microvascular parameters (RCF and WLR). When compared to baseline, treatment with dapagliflozin reduced RCF (308+/-78 vs. 324+/-84 AU, p=0.028), indicative of a normalization of retinal hyperperfusion, and prevented vascular remodelling of retinal, which occurred in the placebo group (WLR: 0.356+/-0.1 vs. 0.391+/-0.1, p=0.034). Moreover, compared to placebo, treatment of dapagliflozin reduced systolic and diastolic 24-h ABP (126+/-11/75+/-8 vs. 129+/-12/77+/-7 mmHg, p=0.021/0.027), and central pulse pressure (40.9+/-11 vs. 43.9+/-12 mmHg, p=0.05).

Conclusions
Overall, our data indicate that treatment with the SGLT-2 inhibitor dapagliflozin exerts beneficial effects on vascular parameters of the micro- and macrocirculation, suggesting an improvement of cardiovascular prognosis.

POSTER SESSION II – EPIDEMIOLOGY

14.1 Mechanism of age-related increases in pulse pressure: longitudinal follow-up of the Twins UK Cohort

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Objective
Widening of pulse pressure contributing to increased prevalence of systolic hypertension in older subjects could result from arterial stiffening, increased peripheral pressure wave reflection and/or an altered pattern of ventricular ejection. We evaluated the roles of these factors in determining changes in pulse pressure during longitudinal follow-up of the Twins UK cohort.

Methods
Non-invasive central blood pressure and flow were obtained by carotid tonometry and Doppler sonography respectively in a total of 329 women at first visit (mean SD, age 58± 8 years) and a follow-up visit approximately five years later (mean age 63± 8 years). Aortic root pulse wave velocity and reflection index (the ratio of the peak of the backward pressure wave over that of the forward pressure wave) were computed from the pressure and flow waves.

Results
Over the five year follow-up period, pulse pressure increased by 9.2%, from 43.7±73 to 47.7±0.78 mmHg (means SE, $P < 0.001$), PWV increased by 18.5 % from 4.01±0.08 m/s at first visit ($P<0.001$), the maximum value of flow velocity tended to increase (from 1.13±0.01 to 1.15±0.01 m/s) but reflection index decreased from 0.38±0.01 to 0.32±0.01 ($P<0.001$).

Conclusions
These results suggest that the increase of pulse pressure is related mainly to an increase in arterial stiffening rather than to an increase in pressure wave reflection.

14.2 Longitudinal change in vascular structure and function over a 5 year period in Twins UK Cohort

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Background
Vascular aging is characterised by structural changes: wall thickening and an increase in lumen diameter, together with a functional increase in arterial stiffness. We investigated the longitudinal structural and functional changes that occur in the aortic wall over a 5 year follow-up period.

Methods
Subjects were 472 female twins (mean ageSD, 57.9±8.6 years at baseline). Measures of diameter and intima-media thickness (IMT), averaged from the carotid and femoral artery, and carotid-to-femoral pulse wave velocity (PWV) were made at two time-points, first between 2008-2014 and then on a second occasion an average of 4.7±3.0 years later. Young's incremental elastic modulus was estimated from the simplified Moens-Korteweg equation: $PWV=\sqrt{Eh/D}$, where h is the wall thickness and D is diameter.

Results
There was a significant increase in intima-media thickness (0.064±0.01 cm at baseline and 0.070±0.01 cm at follow-up, $P<0.0001$), diameter (0.75±0.06 cm at baseline and 0.76±0.07 cm at follow-up, $P<0.0001$) and PWV (9.15±1.8 at baseline and 9.75±1.8 m/sec at follow-up, $P<0.0001$), over the five-year follow-up period. The influence of the estimated increase in elastic modulus (10.2±4.0 and 10.7±4.1 106dynes/cm2, at visit one and two respectively, $P=0.001$) on PWV was amplified by intima-media thickness increasing more than arterial diameter (10.5% versus 2.2%).

Conclusion
In our cohort of middle age to older women, increase in aortic wall thickness to lumen diameter was the most marked structural change and could potentially amplify the increase in PWV produced by intrinsic stiffening of the aortic wall.

14.3 Ideal cardiovascular health is inversely associated with increased carotid-femoral pulse wave velocity in Italian adolescents. The Maciste Study

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Objective
Ideal cardiovascular health (ICH) among adolescents is defined as the optimal levels of three CV risk factors (SBP/DBP, fasting glucose, total cholesterol) and four behaviours (BMI, not smoking, healthy diet, physical activity)1. We investigated the burden of ICH among Italian adolescents, and its association with arterial stiffness (carotid-femoral pulse wave velocity,cfPWV).

Methods
307 healthy subjects (mean age 17±2 years, 55% men) attending the High School at Terni, Italy, were evaluated. Physical activity, dietary and smoking were assessed through self-reported questionnaires. Sodium consumption was estimated by second fasting urine. Smoking was confirmed by exhaled carbon-oxyde. cfPWV was evaluated by arterial tonometry (SphygmoCor, subtracted distance). For each ICH metric, a score of 2 was also assigned if levels were ideal, 1 if intermediate, and 0 if poor.

Results
None had all 7 ICH metrics the majority (76%) had 4 or more ICH metrics. An inverse linear trend in cfPWV was observed over the number of ICH (p for linear trend <0.01). According to ICH score, after adjustment for age and sex, subjects in the lower tertile, compared to upper tertile, showed higher values of cf-PWV (5.1±1.3 m/s vs 4.6±1.8 m/s, p<0.01), which remained significant after further adjustment for mean BP and other confounding factors (p=0.02).

Conclusions
ICH is relatively uncommon among Italian adolescents, and is inversely related to cf-PWV in females. The potential adverse effects of CV risk factors and unhealthy behaviours on arterial stiffness, an early marker of vascular damage, begins to develop at an early stage of lifespan.

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14.4 A positive family history of diabetes is associated with arterial stiffness: The Malmo Diet Cancer Study

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Objective
Arterial stiffness (AS) is known to be associated with a number of clinical conditions including hypertension, diabetes and dyslipidemia. AS may also be associated with lifestyle and early life factors, which are greatly affected by family history. The aim of this study was to investigate the association between self-reported family history (FH) and AS.

Design and Method
The study population consists of 3056 individuals (mean age 72 years, 40% men) from the population-based Malmo Diet Cancer study, Sweden. Carotid-femoral pulse wave velocity (c-f PWV), a marker of AS, was measured with Sphygmocor®. Data on FH for diabetes, hypertension and cardiovascular (CV) events was retrieved from a questionnaire. Using multiple regression, adjustments were made for age, sex, mean arterial pressure (MAP) and heart rate (HR) in Model 1, and in Model 2 further adjustment made for diagnosed diabetes or hypertension, respectively.

Results
In an unadjusted model AS was associated with a FH of diabetes and CV events. These associations were significant after adjustment in Model 1 and Model 2.

Conclusion
The results indicate associations between AS and FH of both diabetes and CV-events. This shows that FH is a relevant marker of vascular ageing. There was no clear association between AS and FH for hypertension which could be explained by a lack of knowledge regarding this diagnosis even in close relatives. The associations between AS and FH will be compared to those of AS and Genetic Risk Scores (GRS) for diabetes and hypertension in ongoing analysis.

14.5 Levels of angiopoietin-like-2 are positively associated with aortic stiffness and mortality after kidney transplantation

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Introduction
Angiopoietin-like-2 (angptl2) is a secreted glycoprotein with homology to the angiopoietins. Through an autocrine/paracrine manner, it promotes endothelial dysfunction and atherosclerosis. Angptl2 is increased in chronic kidney disease (CKD), where the risk of cardiovascular disease (CVD) is amplified. The objectives of the present study were to 1) examine whether kidney transplantation (KTx) reduces angptl2 levels, 2) identify the determinants of angptl2 after KTx, 3) study the association of angptl2 with aortic stiffness and 4) assess the impact of angpl2 on mortality of KTx.

Methods
In 75 subjects undergoing KTx, we evaluated clinical, biochemical and aortic stiffness before and 3 months after KTx. Angptl2 levels were determined by Elisa. Aortic stiffness was assessed by carotid-femoral pulse wave velocity (cf-PWV). Logistic and Cox regressions were used for data analysis.

Results
After 3 months of KTx, angptl2 levels decreased from 71 ng/mL (IQR: 53-95) to 11 ng/mL (IQR: 9-15) P<0.001). In multivariate analysis, age, CVD, lower renal function and mean blood pressure were independently associated with higher angptl2 levels. There was a positive relationship between cf-PWV and angptl2 after KTx (r=0.260 P=0.024). After a median follow-up of 89 months, 13 deaths occurred. The group with higher angptl2 levels had a higher mortality rate (HR= 0.249 95% CI: 0.068-0.912, P=0.036).

Conclusion
There is a significant reduction in serum angptl2 levels after KTx however, our data demonstrate that after KTx, there is a positive association between angptl2, aortic stiffness and mortality, suggesting that angptl2 may play a biological role in CKD- related CVD.

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14.6 Relationship between 24-hour blood pressure variability and 24-hour central arterial pressure, pulse wave reflection and stiffness in hypertensive patients

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Objective
Twenty-four-hour blood pressure variability (BPV) predicts cardiovascular complications in hypertension, but its association with pulse wave indices (central arterial systolic pressure or CASP, pulse wave velocity or PWV, and augmentation index or AIx) is poorly understood. In the present study we assessed the degree of the impact of 24-hour BPV on 24-hour pulse wave indices.

Methods
Brachial BP was measured non-invasively over the 24-hours by an electronic, oscillometric, automated device (BPLab) in 661 uncomplicated, treated or untreated, hypertensive patients. Digitalized oscillometric waveforms were analyzed by a validated algorithm in order to obtain pulse wave indices. Twenty-four-hour BPV was calculated as unweighted (SDu) or weighted standard deviation (SDw) of the mean blood pressure, or as average real variability (ARV). Patients were classified in two groups according to whether the 24-hour BPV was below or above the median of the whole group.

Results
Twenty-four-hour systolic blood pressure variability (SBPV) showed a direct and significant relation with CASP (r=0.28 SDu, r=0.40 SDw, r=0.34 ARV), aortic PWV (r=0.10 SDu, r=0.21 SDw, r=0.19 ARV) and AIx (r=0.17 SDu, r=0.27 SDw, r=0.23 ARV). After adjustment for age, gender, body mass index, antihypertensive treatment and

24-hour SBP, the relationship was attenuated, but was still significant for all measures, X for AIx. Pulse wave indices were larger in patients with high than in those with low BPV: after adjustment these differences were abolished for AIx. Diastolic BPV showed a weak association with pulse wave indices.

Conclusions
In hypertensive patients 24-hour SBPV is moderately and independently associated with 24-hour CASP, wave reflection and stiffness.

14.7 Hyaluronan is associated with aortic stiffening in healthy subjects

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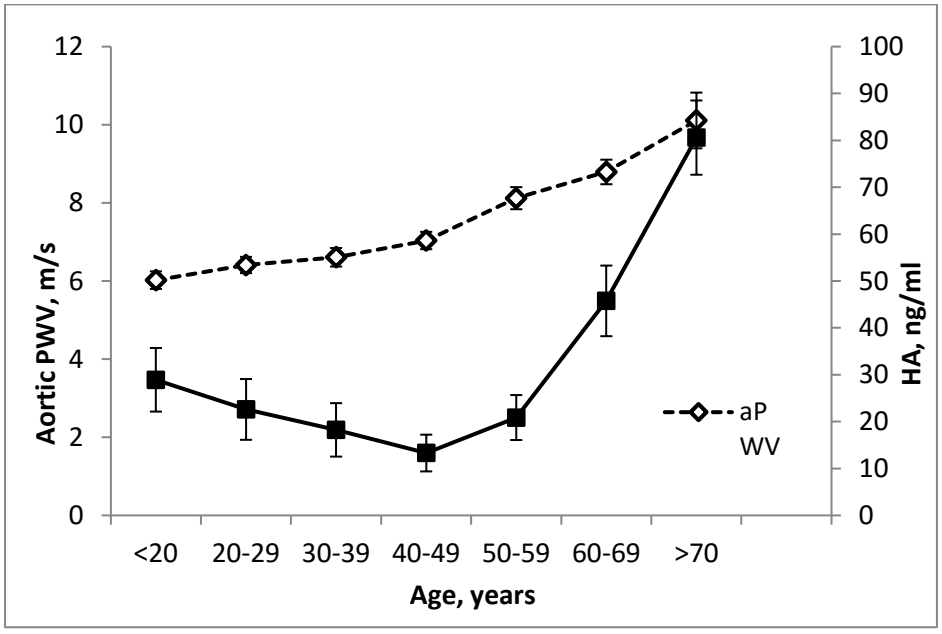
Background
Over-expression of hyaluronan (HA), glycosaminoglycan found in the extracellular matrix, results in the stiffening of the arterial wall by thinning of elastic lamellae in animal models. However, the effect in human arteries is more contentious. We aimed to study the relationship between serum HA and aortic stiffness in a cohort of healthy subjects.

Methods
Subjects were randomly selected from the Anglo-Cardiff Collaborative Trial (ACCT) database. Subjects underwent detailed haemodynamic assessment, including measurements of blood pressure (BP) and aortic pulse wave velocity (aPWV) (SphygmoCor, AtCor, Australia). Serum HA levels were measured by commercially available ELISA kit (DY3614, R&D Systems, U.K).

Results
155 individuals (73 females and 82 males), with a mean age of 44±19 years, and a mean of BP of 134±16/86±11 mmHg were studied. HA and aPWV both increased with aging (P<0.0001 for both see the figure). Subjects were then split into tertiles of serum HA. aPWV was positively associated with HA tertile (7.03±1.42 v. 7.57±1.69 v. 8.10±2.00 m/s P=0.002). In multiple regression analysis, we found that HA remained independently associated with aPWV after adjusting for mean arterial pressure, BMI and gender (model R2=0.233,P<0.001).



Conclusions
Our data suggests that hyaluronan may be one of the factors behind age-related aortic stiffening. However, further studies are needed to establish whether this association is causal and to understand the mechanism behind it.

14.8 Vascular abnormalities related with obesity

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Environment and Objectives
Obesity is linked to a higher prevalence of risk factors, metabolic and inflamatory pathways conducting to increased vascular disease and CV risk.

To assess vascular disarrangements using non invasive methods in obese subjects (O) compared with matched lean (L) controls.

Methods
From the database of our Non Invasive Vascular Lab with 3964 first evaluated patients, we performed a case control study with 363 subjects, 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, Tendiomed. Hungary)

Results
Age (O 42.5+5 L 43.5+11) and sex % (O 80.6% L 78%) were similar. 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 proportion 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.

Conclusion
Obese patients present a higher prevalence of vascular disarrangements although structural and functional explaining the role of this condition as a CV risk factor .

14.9 Increased arterial stiffness predicts less recovery of left ventricular systolic function after myocardial infarction

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Objective
Left ventricular (LV) remodeling may occur following myocardial infarction. Estimate the likelihood of remodeling from the state of the infarcted may with speckle tracking echocardiography (STE). Research powerful predictors of outcomes in patients after myocardial infarction (MI) continue now. Increased pulse wave velocity (PWV), a non-invasive index of arterial stiffness, predicts cardiovascular event in different clinical conditions, but no study on the relationship between PWV and improvement of LV ejection function (EF) in patients with acute MI.

Methods
97 patients with acute MI and primary percutaneous coronary intervention (PCI) (67% male, age 61.5±9.8 years (M±SD), 57 (58.7%) with ST-elevation myocardial infarction (STEMI), smokers 29%, arterial hypertension 80%, blood pressure 129±8/79±8 mmHg, left ventricular ejection fraction (LVEF) 50.6±3.4%. Arterial stiffness was assessed using applanation tonometry. Global longitudinal peak strain (GLPS) by STE was calculated in a 16-segment LV model as the average segmental value on the basis of three apical imaging planes. Mann-Whitney and Spearman tests were considered significant if $p<0.05$.

Results
Baseline GLPS >18% was not detected in any patient. GLPS increased from 14.3±2.3 to 15.6±2.4%, $p<0.04$ in 4 weeks after PCI. GLPS normalized (>18%) in 24 (25%) patients. Achieved GLPS differed significantly in patients without vs with normalization (14.5±1.8 vs 18.6±0.3%, $p<0.02$). Mean carotid-femoral pulse wave velocity (PWV) decreased from 11.5±1.9 to 10.1±2.3%, $p <0.05$. Patients without vs with GLPS normalization were older (63.2±9.1 vs 56.6±11.4 years, $p <0.04$), more frequent male (71 vs 33%, $\chi2=7.8$; $p <0.01$), smokers (83 vs 50%, $\chi2=6.5$; $p <0.05$), STEMI (60 vs 67%, $\chi2=4.6$; $p <0.03$), had higher diastolic BP (84±7 vs 80±8 mmHg, $p <0.02$), higher baseline PWV (12.9±6.9 vs 9.9±2.1 m/s, $p <0.03$). EF increased non-significant between groups. A significant correlation was found between decreased Δ speckle tracking and higher PWV ($r=-0.21$, $p <0.05$).

Conclusions
Arterial stiffening may result in a less effective recovery of LV function after acute MI. Measuring PWV values after acute MI important information could be obtained about LV function recovery.

14.10 Increased central pressure augmentation is associated with reduced sleep duration in individuals exposed to aircraft noise pollution: the SERA-CV study

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Background
Exposure to environmental noise might exert negative effects on cardiovascular function (1). Aim of the study is to explore whether sleep loss associated with exposure to aircraft noise has a detrimental effect on vascular function.

Methods
22 individuals, heavily exposed (E) to aircraft noise (>50 DbA) were recruited and matched with a group of non-exposed individuals (NE). Pulse wave velocity (PWV), central blood pressure (BP), augmented pressure (AP) and augmentation index (Aix) were performed. 7-day actigraphy was performed for the assessment of total sleep time (TST) and wake after sleep onset (WASO).

Results
E showed similar TST (7.2±1.8 vs 7.1±1.3h, p=0.77) and WASO (50±46 vs 47±30 min, p=0.49) compared to NE. E showed higher Aix (26±12 vs 14±16, p=0.006) and AP (11±7 vs 7±8, p=0.03) than NE, in the presence of similar PWV, mean BP and heart rate (HR).

In E group, Aix was related with height (r= -0.56, p=0,009), TST (r= -0.65, p=0.002), while was not related with age, mean BP, PWV and HR. The association remained significant in a multiple regression model (beta = -2.92, p=0.01), with TST accounting for 12.9% of Aix variance (r2 full model 0.84).

In NE Aix was related with age (r= -0.82, p<0.001), HR (r=0.76, p<0.001), TST (r= -0.49, p=0.01), mean BP (r=0.61, p=0.01), PWV (r=0.57, p=0.004). The only independent determinants of Aix in NE were age (beta=0.64, p=0.02) and HR (beta=-0.37, p=0.03).

Conclusions
Central pressure augmentation is independently affected by sleep duration in individuals exposed to high levels of environmental aircraft noise.

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14.11 Total arterial compliance as a risk factor for organ damage in hypertension

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Purpose/Background/Objectives
Hypertension is associated with several markers of subclinical target organ damage (TOD). Total arterial compliance (TAC) is a prognostic factor for cardiovascular events. We hypothesized that there is a relationship between TAC and TOD in never-treated hypertensives.

Methods
We enrolled 990 consecutive essential hypertensives (mean age 52.6±12.2 years, 526 males). 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. 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. The ratio of stroke volume to pulse pressure was measured echocardiographically as a surrogate of TAC.

Results
In multivariable regression analysis, TAC exhibited significant association with LVMI (p=0.004, adjusted R2 of model=0.400), PWV (p<0.001, adjusted R2 of model=0.298) ABI (p=0.002, adjusted R2 of model=0.009) but not with eGFR. In further analysis, TAC was associated with the number of TOD markers (p<0.001) 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)]. In logistic regression model increasing TAC was associated with a reduction in the likelihood of TOD, similarly to the multivariable regression model. (P<0.05 for all X eGFR).

Conclusions
Our findings support the relationship between TAC and TOD in hypertension.

POSTER SESSION II – MODELLING, SPECIAL TECHNIQUES AND INTERVENTIONS II

15.1 Analysis of three statistical methods to predict the presence of carotid atheromatous plaques

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Background
At least 15-20% of all ischemic strokes are attributable to atherosclerosis [1]. We analyzed three statistical methods for 12 traditional risk factors (TRF) i.e. age, sex, arterial pressure, Intima Media Tickness (IMT), Pulse Wave Velocity (PWV) in order to predict the presence of carotid atherosclerotic plaques.

Methods
We studied 48 patients (27 men, mean age 52+/-10.9) after a vascular screening for atherosclerosis from a metabolic syndrome cohort in a retrospective way. Fourteen patients presented carotid atheromatous plaques confirmed by a trained operator using an ultrasound system. The sensitivity and specificity of the combination of the IMT and the PWV indices with other risk factors were considered using: multiple linear regressions (MLR), support vector machines (SVM) [2] and discriminant analysis (DA). The best combinations of variables were kept for each learning machine.

Results
The best sensibility and specificity were obtained using DA. This method reached a sensitivity of 95+/-7% and a specificity of 73+/-36% with an area under the ROC curve equal to 0.84+/-0.35. The other methods showed a sensitivity of 73+/-13% for the MLR method and 53+/-34% for the SVM method with an area under the ROC curve of 0.72+/-0.07 and 0.74+/-0.18 respectively.

Conclusion
This preliminary study shows that carotid atherosclerotic plaques could be reliably predicted using discriminant analysis method. Additional studies are needed to confirm the statistical differences observed using this method and to predict the severity of carotid atherosclerosis.

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15.2 Estimates of arterial stiffness and central blood pressure in patients with type 2 diabetes: A comparison of SphygmoCor and Arteriograph

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Background
The Arteriograph is a cuff-based oscillometric device for non-invasive assessment of central systolic blood pressure (cSBP), aortic augmentation index (Aix) and aortic pulse wave velocity (PWV). The reproducibility of Arteriograph measurements and the agreement with SphygmoCor measurements in diabetic patients has never been assessed.

Methods
We compared Arteriograph reproducibility and agreement with SphygmoCor with data from two study populations: Study 1 (n=17/mean age 64 years/diabetes duration 9 years) was conducted in a research laboratory and Study 2 (n=19/mean age 67 years/diabetes duration 9 years) in a catheter lab. SphygmoCor PWV data was only available in study 1.

Results
Reproducibility: Mean differences (Standard deviation of the difference (SDD)) between duplicate cSBP, Aix and PWV Arteriograph measurements were -0.6 ± 6.6 mmHg (cSBP), -1.1±3.3% (Aix) and 0.1±0.5 m/s (PWV) in study 1 and -0.01±4.3 mmHg (cSBP), 1.5±3.2% (Aix) and -0.2±0.6 m/s (PWV) in study 2, all differences non-significant.

Agreement
Mean differences between SphygmoCor and Arteriograph were -14±10 mmHg (cSBP), -8±7% (Aix) and 2.4±1.8 m/s (PWV), (p<0.001 for all) in Study 1 and -5±10 mmHg, p=0.04 (cSBP) and -10±8%, p=<0.001 (Aix) in Study 2. In study 1, a significant correlation was observed between the mean and the (SphygmoCor – Arteriograph) difference for cSBP, r=-0.75, p<0.001 and for Aix, r=-0.67, p<0.001.

Conclusion
In patients with type 2 diabetes, Arteriograph data were reproducible yet the device systematically overestimated cSBP, Aix and PWV compared with the SphygmoCor. Hence, the two devices cannot be used interchangeably in patients with type 2 diabetes.

15.3 Arterial stiffness recordings with pOpmetre in a general primary care population: the IPC cohort

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Objectives
Aortic stiffness, best approached by pulse wave velocity (PWV), is a determinant of health. Among the devices measuring PWV, gold standard are pulse transit time recordings. pOpmetre® (P®) measures pulse at finger and toe levels using oximetry clips and adequate algorithm in less than 5 minutes. It showed good agreement against reference techniques, but P® feasibility and relevance were never tested in a large general population.

Population and methods
From September 2015, 527 Normotensives (43.8±13.6 years) had a standard health check-up at the IPC Center (Paris, France) including finger to toe pulse wave velocity recording with pOpmetre®, performed by nurses after 10 minutes supine rest permitting ECG and blood pressure measurements (three values averaged). Data were compared to aortic PWV reference values (Eur Heart J, 2010 31, 2338-2350).

Results
Pre-specified factors for measurement failure were variation coefficient within one record> 30%, and PWV extreme outliers: 13 were excluded. BP and PWV were respectively: 121±10/73±7 mmHg 7.64±2.7 m/sec. 231 had optimal BP, 202 normal and 81 high normal BP. PWV increased with age classes from <30 to >70 years. The P® values fell exactly within the aortic reference ranges for age classes: 6.2±1.2, 7.1±2.1, 7.4±2.2, 8.2±2.8, 10.2±3.6, 9.6±2.6 m/sec.

Conclusion
The simple and quick measurement with pOpmetre® device can be performed by nurses during a tight time schedule. It provides values within aortic Reference value ranges in normal population. It is a promising substitute to reference techniques for assessing PWV during standard health check-up.

15.4 Measuring arterial stiffness with pOpmètre® in cardiac rehabilitation program

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Background and Objectives
Pulse Wave Velocity (PWV) is a good surrogate of the arterial aging. This is an independent biomarker of cardiovascular events (ESH-ESC Guidelines 2013). PWV seems to be reduced with regular exercise. The effect of cardiac rehabilitation (CR) is less known on this biomarker. The aim of this study was to evaluate the impact of a CR program on arterial stiffness measured by pulse wave velocity (PWV).

Patients and Methods
Data from 100 consecutive patients recruited in a French CR centre were analyzed after exclusion for High variability cv > 30 % and aberrant values PWV>30 m/s. The finger-toe PWV was measured with a new validated device (pOpmètre®-AxelifeSAS-France) at the beginning and the end of CR (mean duration =18.3±4 days). They were measured at the same time and under the same recommended conditions.

Results
Patients (Mean age 64±11 years, 84% males), were coronary artery disease (51%), valvular (38%), heart failure (3%) and other (8%). The classical cardio vascular risk factors were the following: 1- current smoking (n=3), 2- Diabetes (n=26), 3- high blood pressure (n=58), 4- high blood cholesterol (n=48), There were also obesity (n=15) coronary heredity (n=19) sedentary lifestyle (n=20). They took part in 155 physical training sessions (mean

duration 120 min/day) The maximal workload (MWL) increased from 94.9±35 to 116±37 Watts and the 6min walking test (6MWT) from 430±113 to 505±106 m (p<0.0001). PWV decreased from 9.16±3.0 to 8.39±2.5 m/s (p<0.008). We found a positive correlation with age (r=0.38 p<0.0003) and inverse correlation with maximal workload (r=-0.34 p<0.001) and 6MWT (r=-0.22 p<0.003).

Conclusion
Maximal physical capacity and 6MWT correlated with PWV measured with pOpmètre, and a current CR program seems to improve the arterial stiffness in a cardiac population.

References
1. Maureen Alivon et al. Archives of Cardiovascular Disease (2015). A novel device for measuring arterialstiffness using finger-toe pulse wavevelocity: Validation study of the pOpmètre.

15.5 Association of a new surrogate of total arterial compliance with left ventricular mass: the SAFAR study
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We investigated the association of total arterial compliance (CT) with left ventricular mass (LVM) and hypertrophy (LVH). The study hypothesis was that CT may be better related with LVM compared to the gold-standard regional aortic stiffness.

Methods
Two hundred twenty six subjects with established hypertension (untreated or treated with antihypertensive drugs) or with suspected hypertension underwent blood pressure (BP) assessment, carotid-to-femoral pulse wave velocity (cf-PWV) and echocardiographic measurement of LVM. LVM index (LVMI) was calculated by the ratio of LVM to body surface area. CT was estimated by a previously proposed and validated formula: CT = 36.7 / PWV2 [ml/mmHg], which is based on Bramwell-Hill equation.

Results
LVMI was significantly associated with age (r=0.207, p=0.002), systolic BP (r=0.248, p<0.001), diastolic BP (r=0.139, p=0.04), mean BP (r=0.212, p=0.002), pulse pressure (r=0.212, p=0.002), heart rate (r=-0.172, p=0.011), cf-PWV (r=0.268, p<0.001) and CT (r=-0.317, p<0.001). The highest correlation was observed for CT which was significantly stronger than the respective correlation of cf-PWV (p<0.001). Multivariate analysis showed that CT was a stronger determinant, compared to cf-PWV, of LVMI and LVH.

Conclusion
Total (systemic) arterial compliance is better associated with left ventricular mass and hypertrophy than the cf-PWV. It remains to be further explored whether CT has also a superior prognostic value beyond and above local or regional (segmental) estimates of pulse wave velocity.

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15.6 Influence of the pressure measuring site for velocity/pressure loops

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Background

Velocity/pressure (Vel/P) loops are obtained by combining aortic blood velocity (measured by esophageal Doppler-ED-, CombiQ™, Deltex Medical, Chichester, UK) and arterial pressure signals. They represent a tool to estimate afterload of the heart and arterial stiffness with at least two remarkable angles: β and γ. Pressure is usually measured in the radial artery (PRad) rather than in the descending thoracic aorta (PAoDesc) where ED measures blood flow. Our aims were to assess the influence of the site of pressure recording on the values of β and γ and to develop a mathematical transfer function (TF) to estimate PAoDesc from PRad and then reconstruct Vel/PTFAoDesc loops.

Methods

After institutional review board approval (CE SRLF n#17611-356), 15 patients scheduled for elective endovascular neuroradiology were included. Pressures were recorded simultaneously in the radial artery and in the aorta. Vel/PRad and Vel/PAoDesc loops were constructed and compared. A transfer function was estimated using an autoregressive-exogenous (ARX)[1] model to obtain a simulated descending thoracic aorta pressure waveform (PTFAoDesc). The estimation was quantified by the normalized root mean squared error (NRMSE).Vel/PTFAoDesc loops were constructed and compared to Vel/PAoDesc loops.

Results

153 loops were analysed. β and γ angles were systematically lower in the Vel/PRad compared to the Vel/PAoDesc loops (36 º [34 º - 40 º] vs. 43 º [38 º - 48 º] for β, 11 º [3 º -15 º] vs 25 º [13 º -30 º] for γ, $p < 0.0001$). The ARX model simulated PTFAoDesc with a NRMSE of 93% [77 - 96]. β and γ obtained with Vel/PAoDesc and Vel/PTFAoDesc were similar and strongly correlated $\rho = 0.96$, $p < 0.0001$) (Fig 1&2)

Conclusions

The location where the arterial pressure is monitored has a huge influence on the Vel/P loop parameters. Using a transfer function improves the estimation of the pressure waveform at the site of the Doppler signal.

References

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15.7 Study of wave dynamics of an extra-aortic counterpulsation device in a one-dimensional computer model of the arterial system

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Background

The C-Pulse heart assist system (Sunshine Heart, Inc., Eden Prairie, Minnesota) is a novel extra-aortic counterpulsation device to unload the heart in heart failure patients. Its impact on overall hemodynamics, however, is not fully understood.

Methods

The function of the C-Pulse device was implemented in a previously published and validated one-dimensional model of the arterial tree (1).Central and peripheral pressure and flow waveforms with the C-Pulse disabled and activated were simulated for different settings. The results were studied using wave intensity analysis and compared with in-vivo data measured non-invasively in three heart failure patients and with invasive data measured in a pig.

Results

In all cases the activation of the C-Pulse showed a diastolic augmentation in the pressure and flow waveforms. The device activation initiates a forward compression wave, whereas a forward expansion wave is associated to the device relaxation, with waves exerting an action in the coronary and the carotid vascular beds. In settings with reduced arterial compliance, the same level of aortic compression demands higher values of external pressure, leading to stronger hemodynamic effects and enhanced perfusion. Computer simulations were in good qualitative agreement with in-vivo observations, but in-vivo effects of the device were stronger. We speculate that besides a direct hemodynamic effect, the C-Pulse action might also induce other adaptive (neuromodulated) mechanisms, not captured by the model.

Conclusions
The one-dimensional model may be used as an efficient tool for predicting the hemodynamic impact of the C-Pulse system in the entire arterial tree, complementing in-vivo observations.

References
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15.8 An extended one-dimensional arterial network model for the simulation of pressure and flow in upper and lower limb extremities

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Background
Arterial pulse wave velocity and pulse waveform analysis have become an established component of cardiovascular research. As validation and assessment of devices is not always trivial in an in vivo setting, arterial network computer models may be useful for that purpose. It is, however, mandatory that the model includes sufficient detail, especially when analysing peripheral waveforms.

Objectives
To extend the existing 1D arterial network model (103 segments) of Reymond et al. to a more detailed model (143 segments) including the foot and hand circulation (radial and tibial arteries). The arterial tree dimensions and properties were taken from the literature and completed with data from patient scans. The model solves the one-dimensional form of the Navier-Stokes equations over each arterial segment. A non-linear viscoelastic constitutive law for the arterial wall was considered.

Results
Comparison of simulations with and without detailed hand and foot circulation demonstrate important differences in waveform morphology in the distal beds. The completed model predicts pressure and flow waves in the hand and foot arteries which are in good qualitative agreement with the published in-vivo measurements. The agreement is especially good for the shape and wave details of the flow wave, where all features are reproduced in a rather faithful manner.

Conclusions
The extended model yields realistic pressure and flow waveforms in arteries of the hand and the foot. After full validation, this extended model will be used to assess the performance of diagnostic and screening devices relying on peripheral hemodynamics signals, such as the pOpmètre®.

References
Philippe Reymond et al. 2009. Am J Physiol Heart Circ Physiol 297: H208–H222. Validation of a one-dimensional model of the systemic arterial tree

15.9 Modelling arterial pulse pressure from heart rate during sympathetic activation

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Background
The duration of the time segment between the systolic (SP) and post-dicrotic notch peak pressures (PDP) of the arterial pressure wave in humans has been proposed to be related to arterial pulse pressure (PP).1,2 We considered an effect of RR-interval length on the diastolic pressure run-off and tested the hypothesis that heart rate (HR) affects the timing of systolic and post-dicrotic notch peak pressures.

Methods
We modelled the effects of sympathetic stimulation by progressive central hypovolemia on PP changes based on morphological features of a peripherally measured arterial blood pressure wave shape and HR, making use of linear mixed effect (LME) models. Changes of the arterial pulse wave were tracked from rest towards central hypovolemia in 44 subjects by exposing them to continuous –50 mmHg lower body negative pressure (LBNP). SP and PDP, and HR were extracted from arterial finger pressure and used as model input to predict PP.

Results
From rest to sympathetic stimulation, HR (30%) and thoracic impedance (15%) increased and systolic (SAP) fell by 10%. Model errors of PP (median, and 1stand 3rd quartiles) were 5.2 [3.3 8.9], 4.9 [3.8 7.7], and 4.9 [3.7 8.6] for LME models of, respectively, SP-PDP, HR and their combination.

Conclusion
Our study highlights that during sympathetic stimulation by progressive central hypervolaemia, HR affects arterial pressure wave characteristics and that linear models from both HR and SP-PDP duration allow for estimating PP.

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15.10 Form factor of the femoral artery: an invasive study

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Background
There is a growing interest in precisely estimating mean blood pressure (MBP) in large arteries. The form factor (FF) is the fraction of pulse pressure that must be added to diastolic pressure to estimate the actual MBP, i.e., the pressure integrated (averaged) over the whole cycle. It is admitted that FF of the radial artery is 0.33, while FF of the aorta and carotid and brachial arteries is in the 0.40-0.45 range. The FF of the femoral artery remains to be determined.

Methods
Sixty-five hemodynamically stable intensive care unit patients equipped with an indwelling femoral catheter were prospectively studied (mean age+/-SD = 64+/-14 years). FF of the femoral artery was calculated as the time-averaged MBP minus diastolic blood pressure difference divided by pulse pressure (FF = (MBP – DBP) / PP).

Results
Form factor of the femoral artery was 0.35+/-0.04 (n=65 range 0.22-0.47). FF was similar in female (n=23) and male (n=42) patients (0.36+/-0.05 vs 0.34+/-0.04, respectively) and in patients receiving vasopressors (n=43) or not (n=22) (0.34+/-0.05 vs 0.35+/-0.03, respectively). FF of the femoral artery was positively related to MBP (r^2=0.11) and DBP (r^2=0.07) (each $P < 0.05$) while it was not related to patient's age, body height, body weight, heart rate, systolic pressure and PP.

Conclusions
The mean form factor of the femoral artery was 0.35, a value closer to the FF of radial artery than to the FF of central and brachial arteries. The implications for pressure wave transmission to the lower limbs remain to be studied.

15.11 Towards noninvasive cardiac catheterization

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Background
Doppler echocardiographic measures of diastolic function, such as E/e' are correlates of left ventricular (LV) end-diastolic pressure (ped) and diastolic compliance (Cd) [1]. We developed a noninvasive computational approach to obtain these essential markers of LV diastolic abnormalities and tested it against the invasive gold standard.

Methods
In patients undergoing coronary angiography (n=8, age 60+/-13yrs, with no atrial fibrillation or other dysrhythmia), we obtained mitral and aortic valve Doppler tracings, LV wall thickness and cavity volumes, brachial systolic and diastolic blood pressure (BP) and, for validation purposes, LV pressure and volume invasively by conductance catheter. Repeated echocardiography and BP measurements were performed at baseline conditions and

averaged. Catheter measurements were performed during baseline and Valsalva manoeuvre. The latter causes a change in LV preload, enabling a robust estimation of Cd. We fitted a computational model describing the cardiovascular circulation (CircAdapt,www.circadapt.org) to the noninvasively measured data. Catheter measurements served as a reference to validate model-predicted ped and Cd.

Results
Catheter-measured ped was found to be 21+/-6mmHg (mean+/-SD, n=8) and Cd was 3.1+/-3.0ml/mmHg (n=6). The bias and limits of agreement between the model-estimated and catheter-measured ped and Cdwere -0.9+/-7.5mmHg and 1.1+/-2.6ml/mmHg, respectively.

Conclusions
We found reasonable agreement between our noninvasive modelling-based method of estimating ped and Cd and catheter measurements. Due to its noninvasiveness, our method could be useful for detection of LV diastolic abnormalities in more patients and settings. Next, we will investigate how measurement errors propagate into the uncertainty of model predictions of ped and Cd.

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17.35 **ARTERY Annual Business Meeting** – *open to all ARTERY Members*

19.30 **Conference Dinner -** Moltkes Palæ

SATURDAY 15 OCTOBER 2016

08.00 Refreshments, Poster and Exhibition viewing

08.30 **Debate**
PRO: Microvascular disease precedes the development of hypertension
Dr Christian Ott, *University of Erlangen, Erlangen, Germany*
CON: Microvascular disease always trails hypertension
Professor Jan A Staessen, *University of Leuven, Leuven, Belgium*

09.30 **Invited Lecture**
Von Willebrand factor and its shear stress-mediated degradation in aortic stenosis and LVAD implantations
Peter Lenting, INSERM, *France*

10.05 **Oral Session V**
5.1 Mild reduction of glomerular filtration rate is associated with increased systemic vascular resistance independent of changes in cardiac autonomic tone
Professor Ilkka Porsti[2], Dr Kati Vaaraniemi[3], Dr Pauliina Kangas[1], Dr Antti Tikkakoski[2], Dr Jenni Koskela[2], Dr Anna Tahvanainen[2], Dr Arttu Eraranta[1], Professor Jukka Mustonen[2]
[1.]University of Tampere, Finland; [2.]Tampere University Hospital, Tampere, Finland; [3.]Central Hospital of Central Finland, Jyvaskyla, Finland

Objective
Our aim was to evaluate the influence of mild impairment in kidney function on hemodynamics and cardiac autonomic tone.

Methods
We studied 561 (50% male) normotensive and hypertensive subjects without kidney or other cardiovascular diseases or antihypertensive treatment. Supine and upright hemodynamics were recorded using continuous pulse wave analysis, whole body impedance cardiography and heart rate variability analysis. Estimated glomerular filtration rate (eGFR) was calculated using the CKD-EPI cystatin C equation.

Results
Mean eGFR was 99 (range 53-152) ml/min/1.73 m2 and one third of the patients had values below 90. After adjustments for age, sex, body mass index and low density lipoprotein cholesterol level, regression analysis indicated significant associations between lower eGFR and higher systolic ($p<0.001$) and diastolic blood pressure ($p<0.001$) and systemic vascular resistance ($p=0.001$) regardless of body position. Lower eGFR was associated with higher low frequency to high frequency ratio of heart rate variability in supine but not in upright position. The level of eGFR was not associated with the level of cardiac output.

Conclusions
Even mild kidney impairment is associated with higher systemic vascular resistance and increased supine sympathovagal balance. However, changes in autonomic tone, as based on analysis of heart rate variability, do not seem to explain the relation between lower eGFR and higher systemic vascular resistance in the upright position. The close relationship between the regulation of GFR and systemic vascular resistance may play a role in the pathogenesis of primary hypertension.

5.2 An associated with Familial Hemiplegic Migraine Type 2 mutation in the alpha-2 isoform Na,KATPase disturbs vascular responses in mouse brain
Mr Christian Staehr, Mrs Lise Hangaard, Dr Karin Lykke-Hartmann, Dr Elena Bouzinova, Professor Christian Aalkjaer, Dr Vladimir Matchkov
Aarhus University, Aarhus, Denmark

Objectives
Migraine attack is associated with severe changes in brain perfusion vasoconstriction-induced hypoxemia during aura and rebound vasodilation in subsequent headache. Familial Hemiplegic Migraine Type 2 is associated with point mutations (including G301R) in the α2 isoform Na,K-ATPase. Heterozygote mice bearing G301R mutation (FHM2) were recently characterized for several behavioral and neuronal abnormalities.

Methods
Vascular function of wild type (WT) and FHM2 mice was compared in vivo (telemetry and Laser Speckle measurements of brain perfusion), in vitro (myography) and in situ (changes in astrocytic [Ca2+]iand parenchymal arteriole diameter in brain slices to electric field stimulation (EFS)).

Results
Vascular abnormalities were shown for cerebral circulation while only minor or no significant changes were found in peripheral arteries. Accordingly, no difference in blood pressure was seen under resting conditions. Middle cerebral artery from FHM2 mice had large inner diameter and constricted stronger to U46619, endothelin and K+-depolarization. This was associated with increased depolarization and Src-kinase-dependent sensitization to [Ca2+]i.

Isolated cerebral arteries from FHM2 mice have exaggerated relaxation to elevated [K+]out(4-12mM) due to increased role of the inward-rectifying K+channels. Repeated EFS (>3 times) reduced the [Ca2+]iresponses in astrocytic endfeet and increased relaxation of parenchymal arterioles in the FHM2 in comparison with WT. Flow responses to whiskers stimulation were also potentiated in FHM2 mice.

Conclusions
A knock-out mutation of the α2 Na,K-ATPase leads to both elevated contractility and increased relaxation of cerebral arteries. These dysfunctions could affect the blood supply to active neurons and thus disturb neurovascular coupling.

5.3 Reversibility of arterial stiffness after kidney transplantation: systematic review and meta-analysis

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Background
Chronic kidney disease is associated with increased arterial stiffness. Correction of the uremic milieu by kidney transplantation (KTx) may be improve arterial stiffness. However, results from clinical studies are not uniformly convincing. This could be related to small sample size of studies, heterogeneity in methods and timing of assessment of arterial stiffness after KTx. We aim to measure the reversibility of arterial stiffness after KTx.

Design and Method
Observational studies and randomized controlled trials with measurements of pulse wave velocity (PWV), pulse pressure (PP) and/or augmentation index (AIx) were extracted from MEDLINE, EMBASE, COCHRANE LIBRARY, and Web of Science from their inception to January 2016. Two reviewers independently identified eligible studies comparing PW, PP and/or AIx pre to post KTx and extracted data including population characteristics, interventions and outcomes.

Results
13 studies of 981 met our inclusion criteria. 11 Studies (408 renal transplant) have been included in meta-analysis. There was a standard mean change of PWV by -0.45 (95% CI: - 0.68 -0.20, I2=58%) post-KTx. Both studies using aortic PWV (5 studies, 160 patients) and those using brachial-ankle PWV, showed a significant decrease of PWV by -1.58 m/s (95% CI: -2.97 - 0.19, I^2= 87%) and by -1.21 m/s (95% CI: - 1.89 – 0.54, I2=0 %) post-KTx, respectively. Analysis of central PP and AIx showed significant reduction post-KTx by -4.77 (95% CI: -9.19 -0.35, I2=55%) and by -11.59 (95% CI:-15.64 -7.53, I2=43%), respectively. Only two studies have reported adjusted parameters for mean arterial pressure.

Conclusions
There is a significant reduction in PWV, central PP and AIx after KTx. Heterogeneity among studies are globally moderate. Further analysis is required to examine the importance of changes in different vascular beds taking into account changes in blood pressure.

5.4 High PWV is associated with nano-scale changes in the medial layer of the internal mammary artery

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Background
Arterial stiffening occurs as part of the natural ageing process. Degradation of the extracellular matrix (ECM) in the medial layer is typically implicated in arterial stiffening. However, little is known about how localised changes in arteries in terms of both structure and mechanical properties contribute to the overall stiffening of arteries.

Aim
To determine localised differences in the nano-structure and mechanical properties in the medial layer of internal mammary arteries (IMA) in patients with high and low pulse wave velocity (PWV).

Methods
IMAs were collected form coronary bypass operations from 7 patients with high (13.8 3.3 m/s) and 7 patients with

low (8.6 0.7 m/s) PWV. The samples were cryo-sectioned to a nominal thickness of 5 µm for atomic force microscopy (AFM) measurement. All the samples were tested hydrated. Histological analysis was used to determine collagen and elastin content. Data are presented as means SEMs.

Results
The medial layers of IMAs in the high PWV group were significant stiffer than in the low PWV group (Low 228.4 15.6 kPa, High 735.8 108.8 kPa,) ($p < 0.0001$). Topographical features as visualised with AFM were similar in both groups but the higher nanomechanical stiffness was found to correlate with histological data.

Conclusions
Nanomechanical properties of the medial layer in the IMA associate with PWV data. Changes in composition in the ECM drive the profound localized changes in tissue stiffness.

5.5 Age-dependent telomere attrition, short telomeres and atherosclerosis

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Background
Short leukocyte telomere length (LTL) is associated with atherosclerosis. The prevailing view is this association exists since LTL is a biomarker of cumulative inflammation and oxidative stress during adult life. However recent studies show that LTL in adults is defined mainly by LTL at birth and attrition during childhood. Therefore we can suggest that short LTL might precede clinical expression of atherosclerosis.

Objectives
To examine the directionality in the relation between carotid atheroma and LTL dynamics.

Methods
LTL was measured by TRF in samples donated 9 years apart on average by 257 men and women aged 41 to 80 at the inclusion.

Results
LTL attrition during follow-up (FU) period was 25±17 bp/year. No relation was observed between LTL attrition and presence of carotid atherosclerotic plaques (PCAP). Baseline (BL)-LTL was highly correlated ($r=0.96$, $p<0.0001$) with FU-LTL. In 87.9%of the subjects LTL ranking by deciles was the same 1 decile at BL and FU. BL- and FU-LTL were inversely associated with PCAP ($p<0.01$). After adjusting for age and gender, BL-LTL was 6.50±0.04 Kb in subjects without PCAP 6.46±0.06 in those with PCAP only at the FU visit and 6.27±0.06 in those with PCAP in both BL and FU visits ($p=0.027$). LTL attrition was the same in these groups.

Conclusions
LTL attrition in adulthood is not influenced by PCAP and does not play a significant role in LTL ranking. By contrast, patients with shorter telomeres present CAP earlier in life. Telomere length could be considered as a bio-determinant for atherosclerosis.

5.6 Cardiovascular consequences of extreme prematurity: a follow-up from the EPICure Study

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Background
Long-term outcomes following extremely preterm (EP) birth are becoming increasingly relevant, given improved survival rates. We previously reported altered arterial haemodynamics in 11 year olds who were <25 weeks gestation. The same individuals have now been re-evaluated in young adulthood.

Methods
EP subjects (n=130) and term-born matched controls (n=64) were seen at age 19 years for detailed hemodynamic assessments including blood pressure (BP), augmentation index (AIx), aortic pulse wave velocity (aPWV), cardiac output (CO) and peripheral vascular resistance (PVR). All subjects were drawn from the UK 1995 EPICure Study cohort.

Results
Brachial diastolic and mean BP was higher in EP versus controls ($P<0.01$ for both). Similar to findings at 11

years, AIx was significantly higher in EP subjects (mean difference 6.1% 95% CI 3.4-8.7%, P<0.001) whereas aPWV was not different. Cardiac index was similar between groups, but stroke volume index was lower and heart rate higher in EP (P<0.05 for both). PVR was also significantly higher in EP (mean difference 96 dynes.sec.cm5, 95% CI 27-165 dynes.sec.cm5, P<0.001).

Conclusions
There remains no difference between groups in aPWV from age 11 years into young adulthood, but significant differences in AIx have persisted from childhood and are associated with significantly elevated PVR. These findings suggest abnormalities in the resistance vasculature, which may be structural or functional in origin. Long-term monitoring of cardiovascular risk is recommended in this population.

11.05 Refreshments, Poster and Exhibition viewing

11.45 **McDonald Lecture**
Forward and Reflected Waves and Cardiovascular Disease
Dr Gary Mitchell, *Cardiovascular Engineering, Inc, Norwood, Massachusetts, USA*

12.15 **Lifetime Achievement Award**
presented to Professor Luc Van Bortel, *Emeritus Professor Clinical Pharmacology and Pharmacotherapy, Heymans Institute of Pharmacology, Ghent University, Belgium*

12.30 **Concluding Remarks and Close of Conference**

12.40 Light lunch