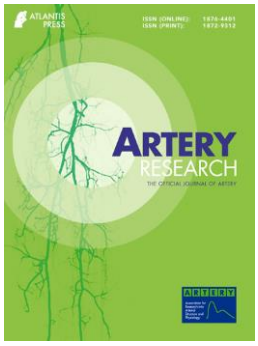

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14.1: MECHANISM OF AGE-RELATED INCREASES IN PULSE PRESSURE: LONGITUDINAL FOLLOW-UP OF THE TWINS UK COHORT

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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.

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 10^6dynes/cm^2, 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.