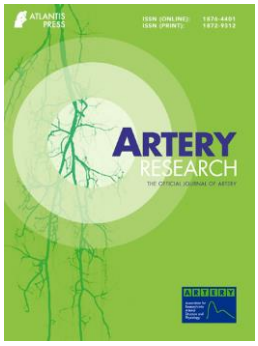

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13.11: EFFECTS OF DAPAGLIFLOZIN ON EARLY ALTERATIONS OF THE MICRO- AND MACROCIRCULATION

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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.