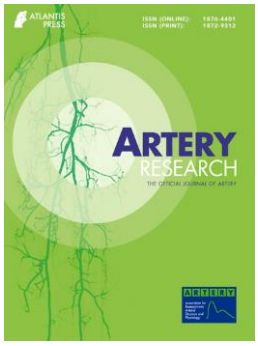

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13.8: VENTRICULO-VASCULAR INTERACTIONS AND THE ARTERIAL WINDKESSEL: NEW INSIGHTS FROM CARDIOVASCULAR MAGNETIC RESONANCE IMAGING BEFORE AND AFTER RENAL DENERVATION

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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 BISOPROLOL/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 ReSET[1] 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/m^2, 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.
1. Mathiassen ON, Vase H, Bech JN, Christensen KL, Buus NH, Schroeder AP *et al*. Renal denervation in treatment-resistant essential hypertension. A randomized, SHAM-controlled, double-blinded 24-h blood pressure-based trial. *Journal of Hypertension* 2016.

13.8
VENTRICULO-VASCULAR INTERACTIONS AND THE ARTERIAL WINDKESSEL: NEW INSIGHTS FROM CARDIOVASCULAR MAGNETIC RESONANCE IMAGING BEFORE AND AFTER RENAL DENERVATION

Giovanni Biglino [1], Amy Burchell [2], Jonathan Rodrigues [2], Robert D. M. Gray [3], Emma C. Hart [2], Julian F. R. Paton [2], Nathan E. Manghat [2], Andreas Baumbach [2], Angus K. Nightingale [2]
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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.

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.