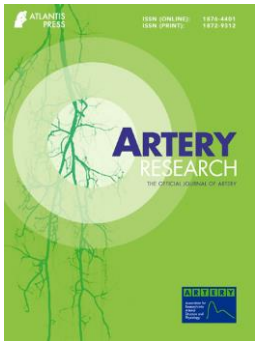

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13.1: THE EFFECTS OF ALPHA 1-ADRENOCEPTOR-BLOCKADE AND ANGIOTENSIN CONVERTING ENZYME-INHIBITION ON INDICES OF AORTIC STIFFNESS MEASURED BY AN OSCILLOMETRIC SINGLE CUFF METHOD IN HYPERTENSION: THE DOXAZOSIN RAMIPRIL STUDY

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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/m^2 ($p<0.001$), Ea (from 1.87±0.29 to 1.64±0.17 mmHg/ml/m^2, $p<0.001$) 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=ESPчSV, PVA=SW+PE (ESPчESV/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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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/m^2 (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/m^2, p>0.05). LCZ696 therapy was associated with potential energy decrease (8049±2846 vs 5037±2492 mmHg*ml/m^2, 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/1.73m^2, 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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