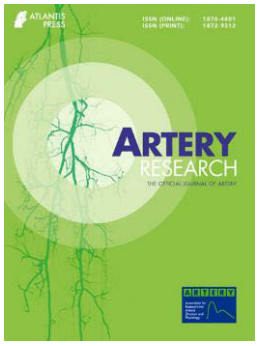

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P4.11: LOWER LIMB VASOMOTOR AND FIBRINOLYTIC EFFECTS OF KININ RECEPTOR AGONISTS IN MAN

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P4.11
LOWER LIMB VASOMOTOR AND FIBRINOLYTIC EFFECTS OF KININ RECEPTOR AGONISTS IN MAN

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Background: Vascular B_1 kinin receptor expression is upregulated in human atheroma and the presence of angiotensin-converting enzyme inhibition (ACEi), but its role in man remains unclear. We examined vasomotor and fibrinolytic responses to selective kinin receptor agonism in the human femoral circulation and correlated responses with femoral arterial plaque load.
Methods: Femoral arterial cross sectional area, blood flow and plaque volume were determined using intravascular ultrasound and a Doppler Flowire during selective femoral arterial infusion of Lys-des-Arg^9-Bradykinin (B_1 agonist; 3, 10, 30 nmol/min), bradykinin (B_2 agonist; 100, 300, 1000 pmol/min) and sodium nitroprusside (6, 12, 24 mcg/min) in eleven patients undergoing diagnostic coronary angiography, in the presence and absence of ACEi. Tissue plasminogen activator (t-PA) release was measured across the femoral vascular bed.
Results: Mean femoral arterial plaque load was 7.0 ± 0.9 mm^3 per mm of vessel. Bradykinin and nitroprusside caused dose-dependent increases in femoral blood flow ($p < 0.05$). Bradykinin alone caused a dose-dependent increase in net t-PA release ($p < 0.05$) that was augmented by ACEi ($p < 0.05$). There were no correlations between femoral plaque load and bradykinin mediated vasodilatation or t-PA release. Lys-des-Arg^9-Bradykinin had no effect on blood flow or t-PA release, irrespective of femoral arterial plaque load or ACEi.
Conclusions: The vasomotor and fibrinolytic actions of bradykinin in the human lower limb are mediated solely by the B_2 kinin receptor, irrespective of the presence of atheroma or ACEi. In keeping with previous data, bradykinin-mediated t-PA release was augmented in the presence of ACEi, consistent with its putative vascular protective effect.

P4.12
EGRESS OF FUNCTIONALLY COMPETENT PROGENITOR CELLS OVER-EXPRESSING CXCR4 FROM THE BONE MARROW FOLLOWING CARDIAC SURGERY WITH THE USE OF CARDIOPULMONARY BYPASS

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Background: The mechanisms of endogenous progenitor cell trafficking in response to tissue injury in humans are poorly understood.
Methods: We based our study on a model of transient myocardial injury, provoked by the use of cardiopulmonary bypass during cardiac surgery in 39 patients. Bone marrow (BM) and blood samples were collected at baseline and after disconnection of bypass machine. CD34+/CD133+ cell numbers (% of 100000 lymphocytes) and stem cell trafficking molecule CXC-chemokine receptor 4 (CXCR4) expression on CD34+ cells were measured by flow cytometry. Hematopoietic colony formation units (CFU) and stromal cell-derived factor-1 alpha dependent chemotaxis were also analyzed.
Results: Increased numbers of circulating progenitor cells after surgery ($1.64 \pm 0.18\%$ vs $1.02 \pm 0.17\%$, $p = 0.003$) directly correlated with baseline BM ($r = 0.7$, $p < 0.0001$) and inversely - with post-bypass BM counts ($r = -0.9$, $p = 0.008$), indicating that circulating cells were mobilized from BM. Following surgery expression of CXCR4 on circulating progenitors increased (88 ± 43 vs 113 ± 72 mean fluorescence intensity (MFI), $p = 0.031$). In post-bypass BM samples CXCR4 expression on CD34+ cells decreased (58 ± 22 MFI vs 44 ± 15 MFI, $p = 0.03$), suggesting that over-expressing CXCR4 cells, being the most suitable for non-marrow tissues migration, were released into circulation. Positive relationship between magnitude of CXCR4 expression on mobilized progenitors and cardiopulmonary bypass time ($r = 0.7$, $p = 0.015$) were shown. Progenitors in post-bypass blood samples compared to baseline had increased chemotactic ($46 \pm 16\%$ vs $59 \pm 22\%$, $p = 0.002$) and clonogenic (70 ± 25 vs 110 ± 70 CFUs) potential.
Conclusion: Increased expression of CXCR4 on mobilised functionally competent progenitors suggests about their ability to migrate towards non-marrow tissues, such as ischemic myocardium.

P4.13
REDUCTION OF ARTERIAL STIFFNESS AND CENTRAL BP IN PATIENTS WITH ARTERIAL HYPERTENSION AND OBSTRUCTIVE SLEEP APNEA ON CPAP- THERAPY

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Arterial stiffness (AS) and central BP (CBP) are new «target-objects» for Antihypertensive Therapy (AT), but the possibility to correction these parameters on nonmedicament treatment is discussed.
Aim: To research the possibilities of correction of AS and CBP by AT and Continuous Positive Airway Pressure (CPAP) in patients (pts) with severe arterial hypertension (AH) and obstructive sleep apnea (OSA) in prospective, randomized, double-blind, placebo- controlled cross- sectional study.
Methods: Included 44 pts (34men) $55{,}8 \pm 9{,}4$ years with AH II-III *gr.* and OSA index >30, treated with combination of amlodipine 5-10 mg, valsartane 160 mg and HCT 25 mg. After 3-9 week AT pts were randomized into 2 groups: additional effective CPAP (eCPAP) and CPAP-placebo ($P = 4$ mmH_2O). After 3 weeks on CPAP-therapy we carried out the crossover of these groups. At each step of intervention we produced ABPM and CBP measuring (SphygmoCor). AS was estimated by Ambulatory AS Index (AASI) and by carotid-to-femoral pulse wave velocity (PWV).

M ± STD	Initial	AT	AT+ eCPAP
PWVcf (m/s)	$14{,}3 \pm 2{,}7$	$12{,}1 \pm 3{,}2$*	$11{,}8 \pm 2{,}2$*#
AASI	$0{,}55 \pm 0{,}17$	$0{,}48 \pm 0{,}19$ ns	0,41 ± 0,18*ns
24hBPmmHg	$157/96 \pm 21/11$	$139/86 \pm 10/10$*	$137/81 \pm 14/8$*#
CBPmmHg	$154/99 \pm 14/14$	$129/87 \pm 11/9$*	$122/81 \pm 8/7$*#

*- $p < 0{,}05$#vs initial, #- $p < 0{,}05$ vs medication.

Results: PWV demonstrated reduction of AS during AT and additional positive effect of eCPAP. Significant reduction of AASI was demonstrated only in cases of combination of AT and CPAP. We estimate additive decreasing of 24 h-BP and CBP on eCPAP in comparison CPAP- placebo.
Conclusion: Effective CPAP induced only mild reduction in 24-hBP, but significant decreasing in AS and CBP.

Therapeutic Aspects 2

P5.01
THE EFFECT OF PULMONARY REHABILITATION ON ARTERIAL STIFFNESS IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

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Background: We have previously shown increased arterial stiffness using aortic pulse wave velocity (PWV) in patients with COPD. Pulmonary rehabilitation (PR) (exercise, education and nutritional advice) has respiratory and functional benefits, though effects on cardiovascular (CV) risk have not been explored. We hypothesised PWV would improve with PR.
Methods: 22 (8 male) clinically stable patients, free from overt CV disease had BP, PWV, spirometry (FEV_1), shuttle walk (ISWT) and fasting glucose and lipids performed pre and post PR. 20 age and gender matched controls were studied for baseline comparison.
Results: Median (range) age for patients was 62.5 (54-79) years, mean (SD) FEV_1 was 44.9 (15.6)% predicted. Aortic PWV, cholesterol and BP reduced with PR. 3 of 11 patients no longer met the criteria for hypertension. The fall in aortic PWV was attributable to the fall in BP.