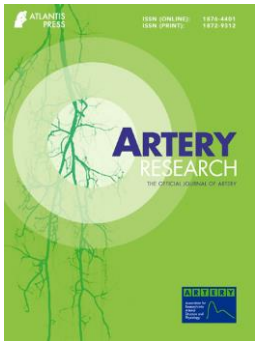

Artery Research

ISSN (Online): 1876-4401 ISSN (Print): 1872-9312
Journal Home Page: https://www.atlantis-press.com/journals/artres

P4.20: SHORT-TERM EFFECT OF ANTI-VEGF DRUGS ON HEART AND VESSELS

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To cite this article: F. Cesana, C. Colombo, C. Valsecchi, M. Stucchi, P. Vallerio, A. Cereda, P. Meani, R. Ricotta, S. Siena, C. Giannattasio (2013) P4.20: SHORT-TERM EFFECT OF ANTI-VEGF DRUGS ON HEART AND VESSELS, Artery Research 7:3_4, 141–141, DOI: https://doi.org/10.1016/j.artres.2013.10.138

To link to this article: https://doi.org/10.1016/j.artres.2013.10.138

Published online: 14 December 2019

index (AIx), aortic-pulse wave velocity (aPWV) and blood samples were obtained at baseline and 8-weeks into the programme. MMP-9 mRNA expression was analysed using real-time PCR, circulating MMP-9 levels assessed via ELISA, and AIx and aPWV were measured via applanation tonometry (SphygmoCor). Participants were split into those who adhered and did not adhere to the exercise programme.
Results: MET-minutes significantly increased; whilst MMP-9 expression, MAP and AIx significantly decreased in the exercise-adherent group compared to the non-adherent group, between baseline and 8-weeks. aPWV did not change significantly between the groups (Table-1). Significant correlations were observed between ΔIPAQ MET-minutes and ΔMMP-9 expression.
Conclusion: Adherence to the exercise programme reduced wave reflection and MAP. These pilot data demonstrate that MMP-9 expression is down-regulated in healthy, sedentary adults after 8-weeks of aerobic, moderate-intensity exercise. Thus suggesting that exercise-induced down-regulation of MMP-9 may result in a reduction in ECM degradation and therefore reduce vascular remodelling. These data provide a biomolecular rationale for how aerobic exercise is effective at delaying age-related increases in aPWV.

Table 1

Parameter	Adherent n=17 (Mean±SE)	Non-Adherent n=19 (Mean±SE)	P Value
Δ IPAQ (MET-minutes)	+2848 ±547	-404 ±267	<0.001
Δ MMP-9 (Ct)	-0.56 ±0.09	+0.42 ±0.44	0.034
Δ Supine MAP (mmHg)	-2.64 ±1.59	+1.45 ±1.16	0.044
Δ Supine AIx@75 (%)	-4.1 ±1.75	+1.9 ±2.23	0.045
Δ CF-PWV (m/s)	+0.3 ±0.2	+0.2 ±0.2	0.854

P4.20
SHORT-TERM EFFECT OF ANTI-VEGF DRUGS ON HEART AND VESSELS

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Objectives: Drugs opposing the effect of vascular endothelial growth factor (anti-VEGF) inhibit angiogenesis slowing down and eventually stopping solid tumors growth. Nevertheless these drugs can cause hypertension (that seems to be correlated with cancer outcome) and cardiac dysfunction. We hypnotize there is a correlation between the early stiffening of cardiovascular system and the drug effectiveness. For this purpose we analyzed the short term changes in cardiovascular structure and function in patients treated with antiVEGF drugs.
Methods: We enrolled 20 patients suffering from metastatic cancer (17 renal, 2 thyroid and 1 GIST), age 64±11 years (mean±SD). We measured blood pressures (BPs), cardiac and vascular parameters at baseline (B) and after two weeks of treatment (T1) (transthoracic echocardiography with 2D strain evaluation, cf-PWV, Aix).
Results: At B our population showed normal BPs (mean±SD:121±17/69±9.5mmHg) and systolic function (EF: 59%,). Global longitudinal strain (GLS) was -21±3%, cf PWV was 12.1±3.3m/sec and Aix was 0.24±0,08%. At T1 we observed a significant increase in BPs (137±16/83±10mmHg, p<0.001 vs B), impaired GLS (-19±3%, p<0.005 vs B), and increased cf-PWV (13.5±3m/sec, p=0.01 vs B) while Aix rise didn't reach statistical significance. Adjusting for PAS only strain impairment remained significative and it was not correlated with BP and PWV modifications.
Conclusions: In the short term anti-VEGF drugs causes an increase of BP and of arterial stiffness, while myocardial deformation is impaired. The increase of PWV, without a significant change in Aix, may suggest that anti-VEGF drugs increase arterial stiffness, and, perhaps, have a less apparent effect on wave reflections.

P4.21
MILD UREMIA INDUCES AORTIC DILATATION AND HEART REMODELLING VIA NF-KB ACTIVATION

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Objectives: The aim of this study was to investigate the effects of mild uremia on aortic and heart remodelling in the rat.
Methods: Mild uremia was induced by reduction of renal mass after 5/6 nephrectomy (NE). Rats with proteinuria >300 mg/24h were included in further investigations. Four weeks after NE, an abdominal aortic aneurysm (AAA) was induced via continuous infusion of an isolated aortic segment with elastase. One group of NE animals was additionally treated with hydralazine (15 mg/kg). Sham operated rats served as controls (n=12). Aortic diameter and heart function were measured by ultrasound biomicroscopy. Aortic tissues, renal functional parameters and serum pro-inflammatory cytokines were investigated.
Results: Uremia induced aortic dilatation (2.1±0.04mm vs. 1.8±0.03mm, p<0.001). Histological analysis revealed an outward aortic remodelling, increased elastin fragmentation (p<0.05), cystic medial degradation, calcification of tunica media and inflammatory infiltrates in the adventitia. After aneurysm induction, aortic diameter was further increased in the NE group as compared to AAA rats without NE (2.6±0.05mm vs 2.3±0.03mm, p<0.05). Hydralazine treatment significantly reduced blood pressure (115±4 vs 160±7mmHg, p<0.05) but did not influence aortic diameter. Protein expression of NF-kB was strongly (3-fold) up-regulated in aortic tissues from NE rats. MMP2, MMP9, cathepsin D and TGF-beta1 were significantly (p<0.05) increased after AAA and further up-regulated in the NE/AAA group. Uremia decreased systolic heart function (p<0.05).
Conclusion: Mild uremia induces aortic dilation and heart remodelling independently of blood pressure elevation. Activation of NFkB by uremic toxins may contribute to remodelling via inhibition of elastin- and collagen gene transcription.

P4.22
THE ROLE OF TESTOSTERONE AND ARTERIAL STIFFNESS IN THE PREDICTION OF RISK FOR CARDIOVASCULAR EVENTS IN HYPERTENSIVE PATIENTS

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Objectives: Androgen deficiency confers an independent risk for cardiovascular events and total mortality. Hypertension, a major contributory factor to the development of cardiovascular disease (CVD), has been associated with increased prevalence of low testosterone. We investigated whether low androgen concentration predicts major adverse cardiovascular events (MACE) in hypertensive patients without clinical atherosclerosis.
Methods: MACE in relation to total testosterone (TT) were analyzed with proportional hazards models in 228 non-diabetic hypertensive patients without a history of known CVD.
Results: The mean follow-up time was 44 months, during which 19 (8.3%) subjects developed MACE. Compared to patients who did not experience MACE, subjects who developed MACE had lower TT (3.9±0.7 ng/ml vs