



Artery Research

ISSN (Online): 1876-4401

ISSN (Print): 1872-9312

Journal Home Page: <https://www.atlantis-press.com/journals/artres>

6.6: RELATION BETWEEN BLOOD FLOW AND ARTERIOLAR MORPHOLOGY AND REDUCED VASODILATORY CAPACITY IN HYPERTENSIVE PATIENTS WITH INCREASED ARTERIOLAR WALL-TO-LUMEN RATIO IN THE HUMAN RETINAL CIRCULATION IN VIVO

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To cite this article: M. Ritt, J.M. Harazny, C.H. Ott, U. Raff, G. Michelson, R.E. Schmieder (2011) 6.6: RELATION BETWEEN BLOOD FLOW AND ARTERIOLAR MORPHOLOGY AND REDUCED VASODILATORY CAPACITY IN HYPERTENSIVE PATIENTS WITH INCREASED ARTERIOLAR WALL-TO-LUMEN RATIO IN THE HUMAN RETINAL CIRCULATION IN VIVO, Artery Research 5:4, 146–146, DOI: <https://doi.org/10.1016/j.artres.2011.10.230>

To link to this article: <https://doi.org/10.1016/j.artres.2011.10.230>

Published online: 14 December 2019

appears to be mediated by a reduced HR in men, whereas less peripheral β -mediated vasodilation likely contributes in women.

Table 1 Hemodynamic variables before (control) and during systemic β -adrenergic blockade

	Men		Women	
	Control	β -Blockade	Control	β -Blockade
Heart Rate (bpm)	58 \pm 2	50 \pm 1 [†]	62 \pm 2	55 \pm 2 [†]
PSBP (mmHg)	123 \pm 3	119 \pm 3 [†]	125 \pm 3	121 \pm 3 [†]
PDBP (mmHg)	69 \pm 3	70 \pm 2	70 \pm 2	70 \pm 2
PPP (mmHg)	53 \pm 2	48 \pm 2 [†]	55 \pm 2	51 \pm 1 [†]
ASBP (mmHg)	102 \pm 2	101 \pm 2	107 \pm 3	107 \pm 3
ADBP (mmHg)	70 \pm 2	71 \pm 2	71 \pm 2	71 \pm 2
APP (mmHg)	32 \pm 2	30 \pm 0 [†]	37 \pm 2*	37 \pm 2*
MAP (mmHg)	85 \pm 2	85 \pm 2	88 \pm 2	88 \pm 3
PPA	1.69 \pm 0.03	1.62 \pm 0.03 [†]	1.54 \pm 0.05*	1.44 \pm 0.05* [†]
Alx (%)	-2 \pm 3	2 \pm 3 [†]	10 \pm 3*	17 \pm 3* [†]
Alx@75bpm (%)	-10 \pm 3	-10 \pm 3	4 \pm 3*	8 \pm 3* [†]
AG (mmHg)	-0.5 \pm 0.8	0.9 \pm 0.8 [†]	4.3 \pm 1.5*	7.1 \pm 1.6* [†]
Δ tp (msec)	159 \pm 4	163 \pm 3	153 \pm 4	153 \pm 3
E _w (dyne · cm ² · s)	-74 \pm 152	233 \pm 154 [†]	864 \pm 305*	1408 \pm 345* [†]

PSBP, peripheral systolic blood pressure; PDBP, peripheral diastolic blood pressure; PPP, peripheral pulse pressure; ASBP, aortic systolic blood pressure; ADBP, aortic diastolic blood pressure; APP, aortic pulse pressure; MAP, mean arterial pressure; PPA, pulse pressure amplification, Alx, aortic augmentation index; AG, augmented pressure; Δ tp, round trip time of pressure wave to the peripheral reflecting sites and back to heart; E_w, wasted left ventricular pressure energy. * $P < 0.05$ vs. men; [†] $P < 0.05$ vs. control; [‡] $P < 0.05$ Magnitude of change vs. men

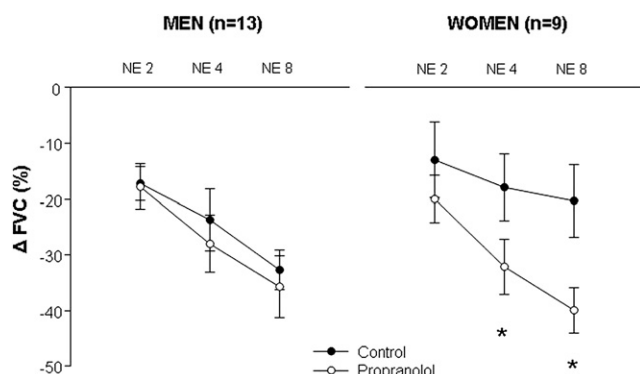


Figure 1 Forearm vasoconstrictor responses to exogenous norepinephrine (2, 4, and 8 ng/100 ml/min) in men and women before (control) and during systemic β -adrenergic blockade. * $P < 0.05$ vs. Control

6.6

RELATION BETWEEN BLOOD FLOW AND ARTERIOLAR MORPHOLOGY AND REDUCED VASODILATORY CAPACITY IN HYPERTENSIVE PATIENTS WITH INCREASED ARTERIOLAR WALL-TO-LUMEN RATIO IN THE HUMAN RETINAL CIRCULATION IN VIVO

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Objective: We hypothesized that blood flow and arteriolar morphological changes are related to each other in the human retinal vascular bed.

Methods: The study cohort comprised 141 non-diabetic untreated male patients with or without arterial hypertension but without evidence for cardiovascular disease. Retinal capillary blood flow (RCF) before and after

exposure to flicker light and to infusion of nitric oxide (NO) synthase inhibitor N-monomethyl-L-arginine (L-NMMA), and parameters of retinal arteriolar morphology, e.g. wall-to-lumen ratio, were assessed non-invasively and *in vivo* by scanning laser Doppler flowmetry.

Results: Patients were grouped according to their median RCF into two groups. Patients with RCF above the median revealed lower wall-to-lumen ratio compared to patients with RCF equal or below the median (0.30 \pm 0.1 vs 0.34 \pm 0.1 (-), P adjusted = 0.023). In addition, RCF was inversely related to wall-to-lumen ratio independently of major cardiovascular risk factors ($\beta = -0.224$, $P = 0.026$). In parallel, the change of RCF to L-NMMA was greater in patients with RCF above the median compared to the counter group (-8.95 \pm 11 vs. 0.35 \pm 15 (%), P adjusted < 0.001). The increase in RCF to flicker light, was inversely related to wall-to-lumen ratio in hypertensive but not in normotensive or all patients ($r = -0.292$, $P = 0.047$, $r = -0.035$, $P = 0.746$ and $r = -0.126$; $P = 0.144$, respectively).

Conclusions: In the retinal circulation blood flow and arteriolar morphology are related to each other. Basal NO activity might impact on blood flow and arteriolar remodeling. In hypertensive, but not in normotensive patients, the vasodilatory capacity is inversely related to arteriolar wall-to-lumen ratio in the human retinal vascular bed.

Oral Session 7 Free Oral Communications In association with the 'European Society of Hypertension'

7.1

IMPACT OF 3D CULTURE OF MESENCHYMAL STEM CELLS TO REPAIR EXPANDING AAAS

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Abdominal aortic aneurysms (AAAs) are characterized by extracellular matrix degradation and mesenchymal cells rarefaction. In this context, the use of mesenchymal stem cells (MSCs) opens the way for the cell therapy to repair the damaged arterial wall. This study proposes to investigate a cellular therapy by using a 3D structure of MSCs encapsulated in a hyaluronic acid (HA) hydrogel. We show that the morphological remodeling is induced when the MSC is seeded in the hydrogel. The expression marker is not modified and the cell plasticity is better preserved in 3D culture in comparison with the 2D case. The comparison also shows that the ratio of apoptosis cell is reduced when physiological environment is mimicked by applying dynamical strain. Based on these results, the Xenograft model of AAA on the rat [1] is used to test the capability of the MSC to repair the aneurysm. Thus, after 7 days, the endovascular injection in rats tends to stabilize the diameter of AAAs. In summary, preliminary results indicate that (i) the proposed 3D HA hydrogel preserves most of MSC properties, (ii) the 3D culture may allow understanding better MSC stabilizing properties in AAAs, (iii) the investigation of the stresses in the artery wall would be necessary [2].

[1] E. Allaire, E. Guettier, C. Bruneval, P. Plissonnier, JB. Michel, *Cell-free arterial grafts: morphologic characteristics of aortic isografts, allografts, and xenografts in rats*, Journal of Vascular Surgery 19, 446-456, 1994.

[2] F. Mohand-Kaci, A. Eddahak-Ouni, J. Dai, E. Allaire, M. Zidi, *Stochastic Modelling of Wall Stresses in Abdominal Aortic Aneurysms Treated by a Gene Therapy*, Computer Methods in Biomechanics and Biomedical Engineering, (doi:10.1080/10255842.2010.540759).

7.2

IN WHICH EXTENT GAMMA-GLUTAMYLTRANSFERASE CONTRIBUTES TO THE VASORELAXANT EFFECT OF S-NITROSOGUTHATHIONE?

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S-nitrosoglutathione (GSNO) exhibits higher stability than nitric oxide (*NO) and plays an important role in vasoreactivity as it serves as *NO storage and transport, and is a source for protein nitrosation. As gamma-glutamyltransferase (GGT) is involved in *NO release from GSNO, we investigated whether GGT influences the vasorelaxant effect of GSNO in the rat aorta.

We measured specific GGT activity in homogenates from thoracic aortic rings isolated from male adult Wistar rats (mean \pm S.E.M., 3 experiments,