



Artery Research

ISSN (Online): 1876-4401

ISSN (Print): 1872-9312

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

01.05: RESPONSE OF BLOOD FLOW AND VASCULAR RESISTANCE IN COMMON CAROTID ARTERY TO HYPERCAPNIA

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To cite this article: N.P. Saeed, G. Esquivel, I.M. Graf, A.P.G. Hoeks, M.A. van Duinen (2007) 01.05: RESPONSE OF BLOOD FLOW AND VASCULAR RESISTANCE IN COMMON CAROTID ARTERY TO HYPERCAPNIA, Artery Research 1:2, 48–48, DOI: <https://doi.org/10.1016/j.artres.2007.07.040>

To link to this article: <https://doi.org/10.1016/j.artres.2007.07.040>

Published online: 21 December 2019

01.04

NON INVASIVE EVALUATION OF ARTERIAL REMODELING IN PATIENTS WITH FABRY DISEASE AFTER ENZYME REPLACEMENT THERAPY

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Context: Fabry disease (FD) is a deficiency of lysosomal enzyme α -galactosidase A leading to accumulation of glycosphingolipids in vascular and renal tissues. Affected patients exhibit neuropathic pain and premature mortality because of renal failure and cardiovascular diseases. We have already described an accelerated hypertrophy of the arterial wall. Although enzyme replacement therapy (ERT) decreases glycosphingolipids accumulation in tissues, there is no evidence of ERT efficacy on vascular hypertrophy.

Objective: To evaluate efficacy of intravenous ERT at usual dosage on large artery properties.

Design study: Longitudinal follow-up before (23 ± 11 Mo) and after ERT (47 ± 17 Mo). Four to 8 serial measurements of (a) carotid intima-media thickness (IMT) and diameter, obtained with high definition echotracking device, and (b) aortic stiffness, obtained through carotid to femoral pulse wave velocity (PWV).

Patients: 15 patients (12 males and 3 females with clinical manifestations), aged 33 ± 10 years.

Results: Carotid-femoral PWV significantly decreased during follow-up ($P < 0.001$). The slope of PWV changes with time did not differ from zero (-0.16 ± 0.90 m/s/yr, NS) before ERT, but was significantly reduced after ERT (-0.50 ± 0.47 m/s/yr, $P < 0.01$). IMT increased before ERT and kept increasing after ERT (ANOVA). However, individual slopes did not differ from zero (before ERT $+10 \pm 66$ μ m/yr, after ERT: 4 ± 21 μ m/yr ($P = 0.745$)). Diameter, wall-to-lumen ratio and carotid distensibility did not change after ERT ($P = 0.53, 0.20, 0.44$, respectively).

Conclusion: In addition to its effectiveness on pain and glycosphingolipids storage in tissues, ERT with recombinant α -galactosidase-beta proved to decrease aortic stiffness while carotid wall hypertrophy was still progressing.

01.05

RESPONSE OF BLOOD FLOW AND VASCULAR RESISTANCE IN COMMON CAROTID ARTERY TO HYPERCAPNIA

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Background: Although the brachial artery is appreciated as a representative of the arterial tree for endothelial function tests, it would be favourable to estimate flow mediated dilation (FMD) at clinically relevant locations e.g. the common carotid artery (CCA). Hypercapnia strongly stimulates cerebral blood volume flow, with steady state achieved after 2 mins, inducing FMD in the CCA.

Objective: To develop a complete stimulus-response profile (baseline, peak, steady state) of flow velocity, diameter and heart rate during and after hypercapnia, also to evaluate their interrelationships.

Methods: The CCA was visualised with an ultrasound beam at 60° in Doppler-mode with a P350 ultrasound system. Hypercapnia was induced with a 6.8% CO₂ inhalation for a period of 2 mins. Processing of received signals from baseline, during hypercapnia and return to baseline (total 10 mins) clearly revealed in beat-to-beat changes in systolic and end diastolic diameters, blood flow velocity (BFV), blood flow rates, and carotid peripheral resistance.

Results: Continuous long-term measurements indicate a peak at 3 mins, with a steady decay over the remaining follow up time. The BFV (+25%), carotid diameter (+12%), distension and heart rate increase significantly during and post hypercapnia. No significant changes are seen in blood pressure.

Conclusions: Inhalation of CO₂ for 2mins increases blood flow and induces carotid artery dilatation. CCA FMD exposes the dynamic interrelationship between blood flow and CCA diameter and is a good tool to test directly endothelial function in atherosclerotic prone arteries.

01.06

BIOMECHANICAL ANALYSIS OF HUMAN COMMON CAROTID ARTERIES BY SEGMENTED APPROACH ON NON-INVASIVE ECHOTRACKING SYSTEMS

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Background: In addition to measurement of diameter, intima-media thickness (IMT) and stiffness, the high resolution of non-invasive

echotracking systems (Wall Track System® ArtLab®) permits to have insights in new parameters. First we can study longitudinal segmental inhomogeneities of strain defining gradients of strain and layer-by-layer changes in strain within the arterial wall, defining inhomogeneities in compressibility. The aim of the present report is to present feasibility data and first results for these two parameters.

Methods and results: Multidirectional segmentations of radio-frequency matrix recordings were applied to different diseases. First, longitudinal gradient of strain were measured in 92 patients with plaques, either hypertensive or not. Second, strain gradient within the wall (hence estimated compressibility), was tested in 46 patients with vascular Ehlers-Danlos Syndrome (vEDS) and 72 controls. Different conceptual and operational tools were developed under Matlab® software for these purposes. We observed that remodeling at the level of the plaque deeply influenced the segmental behavior of strain, inward remodeling being associated with exaggerated strain, and outward remodeling with reduced strain. We showed that both vEDS and control subjects exhibited marked excess of compressibility within IMT, and that this highly compressible zone was closer to the lumen and accentuated in vEDS than in controls.

Conclusion: It is possible to make segmental analysis of segmental properties of remodelling and bending stress. In addition, apparently homogeneous arterial walls exhibited mechanical interfaces which exaggerated compressibility and local stresses between different sub-layers within the wall.

05.01

CAN WAVE INTENSITY HELP EXPLAIN THE DIFFERENT VELOCITY FLOW PROFILES IN THE CORONARY ARTERIES?

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Background: In the left coronary arteries, coronary flow is said to occur mainly in diastole, but this is not the case in the right coronary artery (RCA). Since the pressure being applied at the aortic end is identical for both arteries, we hypothesised that differences from the microcirculatory end account for the differences in the flow velocity waveform. We apply a new technique, wave intensity analysis, to explain the differences in these velocity waveforms.

Methods: In 10 subjects sensor-tipped intra-arterial wires were used to measure simultaneous pressure and Doppler velocity in the proximal left main stem (LMS), the left anterior descending (LAD), the left circumflex arteries (LCX) and RCA. Wave intensity analysis was applied to derive proximal- and distal-originating waves.

Results: In all three left coronary artery positions, the systolic-diastolic ratio of peak velocity was significantly lower than the corresponding ratio in the RCA (LMS 0.58 ± 0.13 , LAD 0.47 ± 0.12 , LCX 0.57 ± 0.15 versus RCA 1.09 ± 0.48 , $p < 0.03$ for each). The cause was a lower diastolic flow velocity in the RCA than the left coronary arteries (RCA 0.37 ± 0.28 m/s versus LMS 0.58 ± 0.30 m/s, LAD 0.58 ± 0.44 m/s $p < 0.05$ for each, LCX 0.46 ± 0.33 m/s $p = NS$), which is explicable by the lower distal-originating suction wave (RCA $16.6 \pm 5.4\%$ versus LMS $27.6 \pm 7.6\%$, LAD $28.8 \pm 6.3\%$, LCX $26.0 \pm 6.6\%$, $p < 0.02$).

Conclusion: The RCA has a flow velocity waveform which is evenly distributed between systole and diastole, in contrast to the diastolic dominant waveform seen in the left coronary arteries. The reason for this difference is the lower diastolic velocity of the RCA which is due to a smaller distally-originating diastolic "suck" from its microcirculation.

05.02

HERITABILITY AND INTRAFAMILIAL AGGREGATION OF ARTERIAL CHARACTERISTICS

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