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**CELIPROLOL INCREASES THE ELASTICITY OF THE RADIAL ARTERY IN VASCULAR EHLERS-DANLOS SYNDROME: A RANDOMIZED CONTROLLED CLINICAL TRIAL**

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**Introduction** — Vascular Ehlers-Danlos syndrome (vEDS) is an autosomal dominant inherited disorder of connective tissue. This syndrome results from mutations in the gene encoding type III procollagen. The patients can present with spontaneous arterial rupture or dissection. We had previously described that celiprolol stiffened large-sized elastic artery (common carotid artery) in vEDS. We tested the effects of celiprolol, a beta1-adrenoceptor antagonist with a beta2-adrenoceptor agonist action in small-sized muscular artery (radial artery) in vEDS.

**Methods** — 47 vEDS patients with no previous beta-blocker were randomized to 5 years treatment. According to a PROBE design, they were allocated either to celiprolol (50 to 200 mg once a day, n=23) or no treatment (n=24). Radial internal diameter, intima-media thickness (IMT) and distension were measured on the right arm with a 10-MHz ultrasound system analyzing the radiofrequency signal. Radial blood pressures were obtained with applanation tonometry. Other radial parameters (wall cross-sectional area, wall-to-lumen ratio, distensibility, Young’s elastic modulus and circumferential wall stress) were calculated from radial internal wall-to-lumen ratio, distensibility, Young’s elastic modulus and tonometry. Other radial parameters (wall cross-sectional area, wall-to-lumen ratio, distensibility, Young’s elastic modulus and circumferential wall stress) were calculated from radial internal wall-to-lumen ratio, distensibility, Young’s elastic modulus and circumferential wall stress did not change in both groups. Radial blood pressure, pulse pressure, IMT, Young’s elastic modulus and wall-to-lumen ratio decreased significantly (p=0.03) and to the same extent in both groups (-5% in the celiprolol group and -6% in the control group) (period effect). Radial internal diameter, wall cross-sectional area increased significantly (+5%, p=0.04 and +12%, p=0.04 respectively) and wall-to-lumen ratio decreased significantly (-2%, p=0.04) in celiprolol group but not in control group (period-by-group interaction). Significant increase in distensibility was observed in celiprolol group (+18%, p=0.04) but not in control group (group effect).

**Conclusions** — compared to no treatment, celiprolol induced a moderate dilation and an important augmentation of elasticity of the radial artery with no change in radial blood pressure. The results proposed the pleiotropic effect of celiprolol in small-sized muscular artery.

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**MECHANICAL MODELING OF IN VIVO HUMAN CAROTID ARTERIES FROM NON-INVASIVE CLINICAL DATA, APPLICATION TO NORMAL SUBJECTS**

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**Background** — For mechanical modeling, in vivo data are relatively incomplete in comparison to in vitro results. However, identification of mechanical properties from human clinical data to compute wall stress fields can play an important role in understanding better pathological evolutions.

**Aim** — Demonstrate the feasibility of material identification and stress computation from clinical data for normal subjects.

**Methods** — In vivo human common carotid arteries (CCAs) were explored non-invasively for 16 normal subjects. During several cardiac cycles, medial diameter, intimal-medial thickness and blood pressure were measured by a high-resolution echotracking (Art. Lab®) and applanation tonometry (SphygmoCor®), respectively. To study the wall mechanical behavior, the CCA was assumed to be a 3D hollow cylinder subjected to dynamical intraluminal pressure and perivascular constraints. We also assumed that the arterial wall is made of hyperelastic, fibrous, and incompressible material with smooth muscle activity and residual stresses. We included wall mechanical contributions by microconstituents: an elastin-dominated matrix, collagen fibers, and vascular smooth muscle (VSM). We solved the in vivo boundary value problem semi-analytically to compute the intraluminal pressure during a cardiac cycle. Minimizing the difference between computed and measured inner pressures over the cardiac cycle provided the identification of optimal model parameters employing a nonlinear regression.

**Results** — The fit-to-data gave very good results and was possible in all cases. There was a convergence of parameters for major constituents such as collagen, elastin and VSM tone. Age was correlated with collagen content and residual stresses. The predicted radial, circumferential, and axial stretches and stresses within the wall during the cardiac cycle were sensible.

**Conclusion** — We were able to reproduce the evolution of inner blood pressure identifying experimentally unknown geometric and material parameters directly from in vivo human data, in order to compute wall stresses and stretches over a cardiac cycle. We can extend the proposed approach to pathological cases such as hypertension.