GENETIC STUDY OF PHACTR1 AND FIBROMUSCULAR DYSPLASIA, META-ANALYSIS AND EFFECTS ON CLINICAL FEATURES OF PATIENTS: THE ARCADIA-POL STUDY

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Objective: We have recently established a complex genetic basis for fibromuscular dysplasia (FMD), a common cause of renovascular hypertension (HTN). Here we aimed to replicate the association between the PHACTR1 locus and FMD in a Polish case control study, and assess the effect of this genetic locus on clinical features of patients.

Design and method: Patients are part of the ARCADIA-POL study (75% women, mean age = 45 ± 11 yrs) with confirmed FMD in at least one vascular bed. All patients underwent detailed clinical evaluation including: ABPM, biochemical evaluation, duplex Doppler and whole-body angio-CT. Controls were randomly ascertained from the WOBASZ study, a population-based Polish cohort. Genotyping for rs9349379 was by direct sequencing. We used logistic regression and global effect estimation using METAL, Mann-Whitney test for continuous traits and Fischer exact test for categories.

Results: We analysed 151 FMD patients and 298 controls, all with European ancestry. We confirmed the association between rs9349379 and FMD in the ARCA-DIA-POL case control study and found 56% increased risk for FMD risk per A allele (OR = 1.56; 95%CI = 1.14-2.13; P = $5.5 \times 10-3$). We now globally update the estimated effect of this risk variant on FMD through meta-analysis of 1,283 FMD cases and 4,193 controls, (OR = 1.40; 95%CI = 1.27-1.55; P = $1.8 \times 10-11$).

Among the 151 Polish patients, we found equal distribution of rs9349379 genotypes in both sexes (P = 0.64), current (P = 0.27) or ex-smokers (P = 0.42) and multifocal and unifocal FMD sub-phenotypes (P = 0.33). Patients with AG/AA genotypes tend to be less likely to present multivessel FMD (19%vs48% in GG patients, P = 0.04). No differences were found between mean age of FMD (P = 0.70) of HTN (0.77) diagnosis. However, patients with AG/AA genotypes tend to have an average of 4.4 years more delay between HTN and FMD diagnosis (P = 0.04).

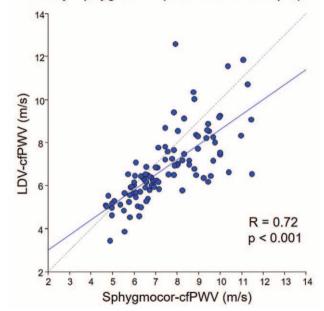
Conclusions: We provide confirmatory association between PHACTR1 locus with FMD in this first genetic study in a Polish population and an updated global effect through the largest existing genetic meta-analysis for this disease. Further confirmation is required for the association we observed among the risk allele carriers with less arterial beds affected and in longer delay of FMD diagnosis.

MEASUREMENT OF AORTIC STIFFNESS BY LASER DOPPLER VIBROMETRY: THE CARDIS STUDY

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Objective: The CARDIS consortium developed a non-contact device for measuring carotid to femoral pulse wave velocity (cfPWV) using a laser doppler vibrometer (LDV). CARDIS-LDV measures skin vibrations induced by large artery pulses. From pulse waveforms, transit time (TT) can be calculated. The aim of the study was to compare LDV-cfPWV with the reference cfPWV measured by applanation tonometry (Sphygmocor).

Association between cfPWV measured by LDV and by Sphygmocor (reference technique)



Design and method: 100 patients with mild to stage 3 hypertension, controlled or not, were tested. LDV-cfPWV was measured 4 times by applying reflective tapes on the carotid and femoral arteries. TT was measured at the foot of the wave from the maximum of 2nd derivative using in-house algorithms not requiring ECG, and compared to Sphygmocor (3 acquisitions).

Results: LDV-cfPWV was obtained in 100% of patients. Mean age was 47 \pm 19 (range 19–85). Hypertensives were well controlled (119/65 mmHg). Mean value of LDV-cfPWV was 6.9 \pm 1.7 m/s, compared to 7.5 \pm 1.7 m/s with Sphygmocor, bias 0.65 \pm 1.27, R value 0.72 (see Figure), which qualifies agreement as acceptable according to the guidelines from the ARTERY Society (Wilkinson et al., Artery Research 2010). Reproducibility was good with a median coefficient of variation of 5.6%. LDV-cfPWV has similar association with age and blood pressure than tonometry (r = 0.68, p < 0.001 and r = 0.44, p < 0.001, respectively).

Conclusions: Non-contact measurement of pulse wave velocity by laser doppler vibrometry is feasible, highly acceptable by patients and provides acceptable agreement with reference technique.

ASSESSMENT OF EFFICACY OF NON-INVASIVE PERIPHERAL TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION FOR CORRECTION OF BLOOD PRESSURE IN PATIENTS WITH ARTERIAL HYPERTENSION

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Objective: To assess efficacy and safety of the non-invasive method for peripheral transcutaneous electrical nerve stimulation (TENS) for blood pressure (BP) correction in patients with arterial hypertension (AH).

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