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### 3.2: IS AORTIC STIFFNESS READY FOR CLINICAL PRACTICE? RESULTS FROM THE ROTTERDAM STUDY

G.C. Verwoert, S.E. Elias-Smale, D. Rizopoulos, E.W. Steyerberg, A. Hofman, M. Kavousi, E.J.G. Sijbrands, A.P.G. Hoeks, R.S. Reneman, F.U.S. Mattace-Raso, J.C.M. Witteman

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## Oral Presentation Abstracts

### 3.1

#### AORTIC STIFFNESS IN MIDDLE AGED WOMEN IS HERITABLE AND RELATES TO BLOOD PRESSURE AND AORTIC CALCIFICATION: A TWIN STUDY

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**Background:** Pulse wave velocity (PWV), measure of aortic stiffness, is predictive of cardiovascular events. PWV is strongly related to age and blood pressure but its relation to other risk factors and presence of calcification is unclear. We sought to determine the association between PWV and cardiovascular risk factors, aortic calcification and heritability of PWV.

**Methods:** Subjects were 900 female twins (504 dizygotic, 396 monozygotic), 53–63 years (interquartile range), from TwinsUK cohort. PWV was determined over the carotid-femoral region using the SphygmoCor system. Age matched women ( $n = 40$ ) with PWV in the 1<sup>st</sup> and 3<sup>rd</sup> tertiles of the PWV distribution (entire cohort) underwent computed tomography from the carotid to iliac bifurcation to determine calcification. Calcium content was scored using the Agatston method. Heritability of PWV was determined using structural equation modelling.

**Results:** In multivariate regression PWV was significantly correlated with age, mean arterial blood pressure (MAP) and heart rate (standardized regression coefficients,  $\beta = 0.41$ , 0.39 and 0.20 respectively, each  $P < 0.001$ ). PWV was not significantly associated with LDL-cholesterol, HDL-cholesterol, smoking or body mass index. Aortic calcification was greater (median 450 vs. 63 units,  $P = 0.001$ ) in the highest compared to lowest tertile of PWV and was independently associated with PWV in regression analysis ( $\beta = 0.48$ ;  $P < 0.01$ ). Heritability of PWV was 0.54 and when corrected for MAP and heart rate 0.51.

**Conclusion:** In women aortic stiffness is heritable and relates to age, blood pressure and aortic calcification but not to other conventional cardiovascular risk factors. Genes involved in aortic calcification may be important determinants of PWV.

### 3.2

#### IS AORTIC STIFFNESS READY FOR CLINICAL PRACTICE? RESULTS FROM THE ROTTERDAM STUDY

G. C. Verwoert<sup>1</sup>, S. E. Elias-Smale<sup>1</sup>, D. Rizopoulos<sup>1</sup>, E. W. Steyerberg<sup>1</sup>, A. Hofman<sup>1</sup>, M. Kavousi<sup>1</sup>, E. J. G. Sijbrands<sup>1</sup>, A. P. G. Hoeks<sup>2</sup>, R. S. Reneman<sup>2</sup>, F. U. S. Mattace-Raso<sup>1</sup>, J. C. M. Witteman<sup>1</sup>.

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**Background:** It has been demonstrated that aortic stiffness, as determined by the carotid-femoral pulse wave velocity, is an independent predictor of cardiovascular disease. Whether this measure is of use in cardiovascular risk stratification in clinical practice needs to be determined. We investigated whether aortic stiffness had an additional predictive value beyond traditional risk factors in older subjects.

**Methods:** Within the framework of the Rotterdam Study, a population-based prospective study, we stratified subjects free of cardiovascular disease at baseline into categories of low (<10%), intermediate (10–20%) and high (>20%) 10-year risk of cardiovascular disease based on Framingham risk factors. Within each risk category, we determined the percentages of

subjects moving into a higher or lower risk category using a model that included prior risk and pulse wave velocity. Reclassification percentages and corresponding pulse wave velocity cut-off values are presented for the midpoint of prior risk within each risk category.

**Results:** Among 2855 participants, 304 cardiovascular events occurred during a median follow-up of 5.9 years. In subjects in the intermediate risk group (prior 10-year risk probability of 15%), 1.5% was reclassified to the high-risk group. Reclassified subjects had pulse wave velocity levels of above 19.7 m/s. In the low and high-risk groups additional measurements of pulse wave velocity did not result in reclassification to another risk category.

**Conclusion:** In an elderly population, addition of aortic stiffness measurement to traditional cardiovascular risk factors does not seem to be a powerful clinical tool for classification of subjects in 10-year cardiovascular disease risk categories.

### 3.3

#### EFFECT OF CELIPROLOL ON PREVENTION OF CARDIOVASCULAR EVENTS IN VASCULAR EHLERS-DANLOS SYNDROME

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**Background:** Vascular Ehlers-Danlos syndrome (vEDS) is a rare severe genetic disease which results from mutations in the gene encoding type III procollagen (COL3A1), characterized by vascular and/or hollow organic ruptures. No treatment is yet validated. We tested the ability of celiprolol, a beta1-adrenoceptor antagonist with a beta2-adrenoceptor agonist action, for preventing the complications of vEDS in a prospective, randomized, open, blinded endpoints trial.

**Methods:** Fifty three previously untreated vEDS patients were randomized to a 5-year treatment with either celiprolol ( $n = 25$ ) or no treatment ( $n = 28$ ). The two groups were matched for demographic, medical historic and clinical characteristics. Celiprolol was up-titrated from 100 to 400 mg by steps of 100 mg every 6 months. The primary end-point was an arterial event (rupture or dissection, fatal or not) occurring during follow-up. Secondary endpoints were intestinal or uterine rupture or major clinical events, related to vEDS, judged by the event committee.

**Results:** Mean duration of follow-up was 47 ( $\pm 15$ ) months. The study was ended prematurely by the safety monitoring board since significant differences were reached between two groups. The primary endpoint was reached by 5 patients (20%) in the celiprolol group and by 14 patients (50%) in the control group (hazard ratio, 0.36; 95% CI, 0.15 to 0.88;  $P = 0.04$ ). Primary