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### **P.030: COFFEE HAS A MORE POTENT UNFAVORABLE ACUTE EFFECT ON WAVE REFLECTIONS THAN CAFFEINE IN NONHABITUAL COMPARED WITH HABITUAL DRINKERS.**

N. Ioakeimidis\*, C. Vlachopoulos, N. Alexopoulos, I. Dima, C. Masoura, P. Margioleas, D. Tousoulis, C. Stefanadis

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## P.027

## AORTIC STIFFNESS IS INCREASED IN PATIENTS WITH HEPATITIS C VIRUS SEROPOSITIVITY

K. Baou\*, C. Vlachopoulos, E. Manesis, N. Ioakeimidis, J. Koskinas, G. Antoniou, A. Archimandritis, C. Stefanadis. <sup>1</sup>1st Department of Cardiology, Athens Medical School, Hippokraton Hospital, Athens, Greece, <sup>2</sup>2nd Department of Medicine, Athens Medical School, Hippokraton Hospital, Athens, Greece

**Background:** Recent data suggest that chronic systemic inflammation impairs vascular function and plays a critical role in cardiovascular disease. Aortic stiffness and wave reflections are independent markers and prognosticators of cardiovascular risk. The present study was undertaken to assess whether chronic infection with hepatitis B virus (HBV) or hepatitis C virus (HCV) affects aortic stiffness and wave reflections.

**Methods:** We determined aortic stiffness and wave reflections in 26 consecutive patients (mean age:  $49 \pm 16$  yrs, 9M/17F) positive for HCV infection and 14 patients (mean age:  $52 \pm 11$  yrs, 9M/5F) with HBV infection, who had never been treated with interferon. 40 healthy individuals were recruited to compare each of the two subgroups and they were matched for age, gender, body-mass index and risk factors. Aortic stiffness was evaluated with carotid-femoral pulse wave velocity (PWV) and wave reflections with augmentation index (Alx) of the aortic pressure waveform.

**Results:** Patients with HCV infection had higher carotid-femoral PWV than controls, indicating increased aortic stiffness ( $7.5 \pm 1.3$  vs.  $6.7 \pm 1.3$  m/s,  $P < 0.05$ ), while Alx did not differ ( $25 \pm 15$  vs.  $27 \pm 15\%$ ,  $P = NS$ ). Carotid-femoral PWV and Alx in the subjects with HBV infection were similar to those in the control subjects. There were no differences as regard systolic, diastolic pressures and heart rate between patients with hepatitis and controls.

**Conclusions:** Patients with HCV have impaired aortic elastic properties, whereas HBV does not influence aortic stiffness. These findings are important to further characterize the increase of cardiovascular risk in patients with hepatitis C virus seropositivity.

## P.028

## NON-ALCOHOLIC FATTY LIVER DISEASE IS ASSOCIATED WITH INCREASED AORTIC STIFFNESS AND CAROTID INTIMA MEDIA THICKNESS

K. Baou<sup>1</sup>\*, C. Vlachopoulos<sup>1</sup>, E. Manesis<sup>2</sup>, N. Ioakeimidis<sup>1</sup>, G. Papathodoridis<sup>2</sup>, J. Koskinas<sup>2</sup>, A. Archimandritis<sup>2</sup>, C. Stefanadis<sup>1</sup>. <sup>1</sup>1st Department of Cardiology, Athens Medical School, Hippokraton Hospital, Athens, Greece

<sup>2</sup>2nd Department of Medicine, Athens Medical School, Hippokraton Hospital, Athens, Greece

**Background:** Non-alcoholic fatty liver disease (NAFLD) is closely correlated to metabolic syndrome, which is a marker of increased cardiovascular risk. Aortic stiffness and intima media thickness (IMT) are independent prognostic factors of cardiovascular risk. We investigated whether NAFLD is associated with increased atherosclerotic damage.

**Methods:** 46 patients (mean age  $55 \pm 13$  yrs, 24M/22F) with increased serum alanine aminotransferase levels and abdominal ultrasound and/or biopsy evidence of NAFLD, and 40 age, gender, body-mass index, and cardiovascular risk factors adjusted controls were studied. Carotid-femoral pulse wave velocity (PWV), an established index of aortic stiffness, was calculated using a validated noninvasive device (Complior®). Higher values of PWV indicate stiffer aorta and vice versa. Mean IMT of common carotid arteries was determined as a marker of generalized early atherosclerosis using B-mode ultrasound imaging.

**Results:** NAFLD subjects had significantly increased carotid-femoral PWV ( $8.5 \pm 1.7$  vs  $7.9 \pm 1.5$  m/s,  $p < 0.05$ ) and mean value of carotid IMT ( $0.98 \pm 0.3$  vs  $0.77 \pm 0.2$  mm,  $p < 0.05$ ) compared to controls. Systolic, diastolic and pulse pressure were not different among the two groups. Interestingly enough, patients with increasing fibrosis stage (ALT/AST ratio of greater than 1,  $n = 21$ ) had increased carotid-femoral PWV and mean carotid IMT compared to patients with ratio lower than 1, after adjusting for age and systolic blood pressure ( $9.2 \pm 1.6$  vs.  $8.2 \pm 1.5$  m/s,  $p < 0.01$  and  $1.08 \pm 0.37$  vs  $0.83 \pm 0.21$  mm,  $p < 0.05$ , respectively).

**Conclusions:** Patients with NAFLD have increased aortic stiffness and IMT, indicating both functional and structural changes in large arteries. These findings are important to further characterize the increase of cardiovascular risk in such patients.

## P.029

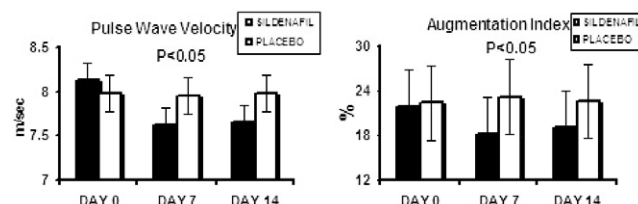
## LONG-TERM SILDENAFIL ADMINISTRATION IMPROVES AORTIC ELASTIC PROPERTIES AND WAVE REFLECTIONS IN PATIENTS WITH ERECTILE DYSFUNCTION OF VASCULAR ORIGIN

N. Ioakeimidis\*, C. Vlachopoulos, K. Aznaouridis, K. Rokkas, G. Antoniou, A. Bratsas, A. Askitis, C. Stefanadis. <sup>1</sup>1st Department of Cardiology, Athens Medical School, Hippokraton Hospital, Athens, Greece

**Background:** Aortic stiffness and wave reflections are independent prognosticators of cardiovascular risk and may be impaired in men with erectile dysfunction (ED) considered as the first clinical manifestation of a generalized vascular disease. We investigated the chronic effect of a long-term daily sildenafil administration on aortic elastic properties and wave reflections.

**Methods:** The chronic effect of a 2-week long treatment with sildenafil on aortic stiffness and wave reflections were studied in 11 men (age  $58 \pm 15$  years) with non-hormonal and non-psychogenic ED. The study was carried out on two separate arms, one with sildenafil (100 mg) and one with placebo according to a randomized, placebo-controlled, double-blind, cross over design. All measurements were performed 24 hours after the last sildenafil or placebo intake. Aortic stiffness was evaluated with carotid-femoral pulse wave velocity (PWV) and wave reflections with augmentation index (Alx) of the aortic pressure waveform using high-fidelity pulse wave analysis.

**Results:** Daily sildenafil intake led to a significant sustained decrease in PWV and Alx, indicating a decrease in aortic stiffness and wave reflections ( $p < 0.05$ , figure). There were no significant changes in systolic and pulse pressure.



**Conclusions:** The present study shows for the first time that chronic treatment with sildenafil has a favourable effect on aortic stiffness and wave reflections in patients with ED. This finding may have important implications in patients with increased cardiovascular risk.

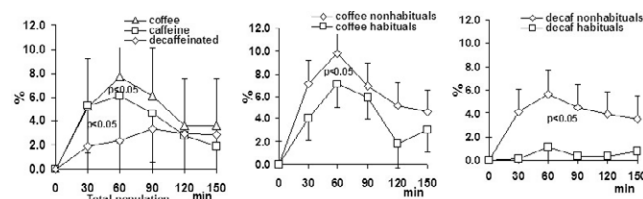
## P.030

## COFFEE HAS A MORE POTENT UNFAVORABLE ACUTE EFFECT ON WAVE REFLECTIONS THAN CAFFEINE IN NONHABITUAL COMPARED WITH HABITUAL DRINKERS.

N. Ioakeimidis<sup>1</sup>\*, C. Vlachopoulos<sup>1</sup>, N. Alexopoulos<sup>1</sup>, I. Dima<sup>1</sup>, C. Masoura<sup>1</sup>, P. Margioleas<sup>2</sup>, D. Tousoulis<sup>1</sup>, C. Stefanadis<sup>1</sup>. <sup>1</sup>1st Department of Cardiology, Athens Medical School, Hippokraton Hospital, Athens, Greece, <sup>2</sup>4th Division of Athens - Section B General Chemical State Laboratory, Athens, Greece

**Background:** Arterial wave reflections (WR) are determinants of cardiovascular performance and predictors of the corresponding risk. The aim of this study was to assess whether there is a differential effect of coffee and caffeine on WR and whether this effect is related to habitual coffee consumption.

**Methods:** We studied 24 healthy volunteers (11 habitual-13 nonhabitual coffee consumers) on 4 separate occasions receiving: (a) triple espresso, (b) decaffeinated triple espresso, (c) 240mg of caffeine alone (amount contained in a triple espresso) and (d) placebo. Augmentation index (Alx) was measured as an index of WR using a validated system (Sphygmocor®). Higher Alx values indicate increased WR and vice versa.



**Results:** The effect of coffee and caffeine on WR is described as response of each variable, where response is defined as net coffee or caffeine minus placebo values at each time point. In the whole population, coffee and caffeine increased Alx, however the effect of coffee was more pronounced

(left figure). Habitual and nonhabitual drinkers demonstrated similar changes with caffeine, whereas the effect of coffee (regular: middle figure; or decaffeinated: right figure) was more potent in nonhabitual compared to habitual drinkers. Pressures also increased, however the increase was more potent in nonhabitual drinkers after both regular ( $p < 0.05$ ) or decaffeinated ( $p < 0.01$ ) coffee intake.

**Conclusions:** Both coffee and caffeine increase WR, however drinking coffee leads to a more potent response in nonhabitual drinkers. These findings indicate that substances other than caffeine are partially responsible for the unfavourable effects of coffee on the cardiovascular system.

#### P.031

##### AORTIC STIFFNESS AND WAVE REFLECTIONS ARE ASSOCIATED WITH PENILE DOPPLER FINDINGS IN PATIENTS WITH VASCULOGENIC ERECTILE DYSFUNCTION

N. Ioakeimidis\*, C. Vlachopoulos, K. Rokkas, D. Tsekoura, A. Tsokanis, K. Aznaouridis, C. Fassoulakis, C. Stefanadis. *1st Department of Cardiology, Athens Medical School, Hippokration Hospital, Athens, Greece*

**Background:** Erectile dysfunction (ED) has been reported as the first sign of a generalized vascular disease. Aortic stiffness and wave reflections are independent markers and prognosticators of cardiovascular risk. The association between ED and measures of aortic stiffness and wave reflections has not been investigated.

**Methods:** A total of 107 men with ED were evaluated for penile vascular disease severity by penile Doppler ultrasound: 40 men (aged  $61 \pm 9$  yrs) with coronary artery disease (CAD) and 67 men (aged  $59 \pm 11$  yrs) without CAD. Aortic stiffness was evaluated with carotid-femoral pulse wave velocity (PWV) and wave reflections with augmentation index (AIx) of the aortic pressure waveform using high-fidelity pulse wave analysis.

**Results:** Patients with CAD had decreased peak systolic velocity (PSV) ( $27$  vs  $34$  cm/s,  $p = 0.001$ ), and increased PWV ( $9.0$  vs  $8.4$  m/s,  $p < 0.05$ ) and AIx ( $30$  vs  $24\%$ ,  $p < 0.01$ ) compared with men without CAD. PSV was correlated with age ( $r = -0.24$ ,  $p < 0.05$ ), Framingham risk score ( $r = -0.27$ ,  $p < 0.05$ ), PWV ( $r = -0.31$ ,  $p = 0.001$ ) and AIx ( $r = -0.33$ ,  $p < 0.001$ ). In multivariate linear regression models adjusting for age, height, heart rate, mean pressure and cardiovascular risk factors (BMI, total cholesterol, HDL, logCRP, hypertension, diabetes and intensity of smoking), penile Doppler results were significantly associated with both AIx ( $\beta = -0.265$ ,  $p = 0.004$ ) and PWV ( $\beta = -0.250$ ,  $p = 0.009$ ).

**Conclusions:** Our study shows that aortic stiffness and wave reflections correlate significantly with increasing severity of penile vascular disease as measured by penile Doppler. This finding provides further insights into the pathophysiology of ED and may have implications for the cardiovascular risk in these patients.

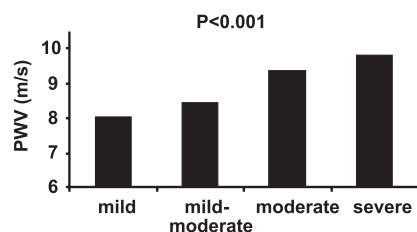
#### P.032

##### CORRELATION OF AORTIC STIFFNESS WITH SEVERITY OF ERECTILE DYSFUNCTION

N. Ioakeimidis\*, C. Vlachopoulos, K. Rokkas, C. Aggeli, D. Tsekoura, N. Alexopoulos, G. Latsios, C. Stefanadis. *1st Department of Cardiology, Athens Medical School, Hippokration Hospital, Athens, Greece*

**Background:** Accumulating evidence suggests that erectile dysfunction (ED) may be an early manifestation of generalized vascular disease. Aortic stiffness is an independent marker and prognosticator of cardiovascular risk. The association of ED with aortic stiffness has not been defined.

**Methods:** A total of 164 men (mean age  $59 \pm 9$  yrs) affected by non-psychogenic and non-hormonal erectile dysfunction for more than 6 months were studied. All participants were invited to complete a 5-item form of the International Index of Erectile Function (IIEF-5) which is a validated and widely applied method for the evaluation of ED. ED was defined as mild (SHIM score 17-21), mild to moderate (11-16), moderate (8-10) and severe (7 or less). Carotid-femoral pulse wave velocity (PWV) was measured as an index of aortic stiffness using an automated non-invasive device (Complior®).



**Results:** There was a stepwise increase in PWV from mild ED, to mild-moderate and moderate ED and to severe ED ( $p < 0.001$ , figure). In univariate analysis, a negative correlation between PWV and IIEF-5 score was observed ( $r = -0.37$ ,  $p < 0.001$ ). Moreover, in separate backward elimination multiple regression model, PWV was significantly associated with IIEF-5 score ( $b = -0.223$ ,  $P = 0.006$ ,  $R^2 = 0.41$ ), after controlling for age, body-mass index, mean pressure, cholesterol, triglycerides, C-reactive protein, hypertension, diabetes, history of smoking, antihypertensive agents and statins.

**Conclusions:** ED is associated with impaired aortic elastic properties. This finding provides further evidence for the potential link between ED and cardiovascular risk.

#### P.033

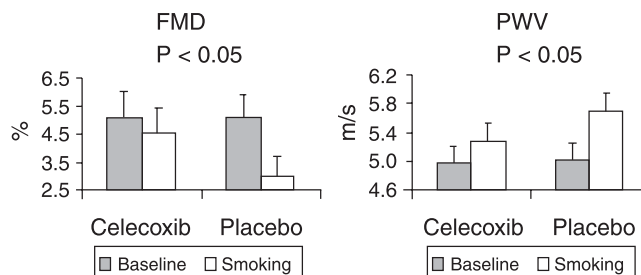
##### SELECTIVE CYCLOOXYGENASE-2 INHIBITION BY CELECOXIB ABROGATES THE ACUTE SMOKING-INDUCED VASCULAR DYSFUNCTION

A. Bratsas\*, C. Vlachopoulos, K. Aznaouridis, N. Ioakeimidis, P. Xaplanteris, N. Alexopoulos, I. Dima, C. Stefanadis. *1st Department of Cardiology, Athens Medical School, Hippokration Hospital, Athens, Greece*

**Background:** The cardiovascular toxicity that is associated with cyclooxygenase-2 (COX-2) inhibitors is perhaps not a class effect, but may be rather limited to certain drugs in the class. Endothelial function and aortic stiffness are predictors of cardiovascular risk. The effect of celecoxib, a selective COX-2 inhibitor on acute smoking-induced vascular impairment is unknown.

**Methods:** We studied the effect of 200 mg of celecoxib in 12 healthy smokers (mean age 29.5 years) according to a randomized, double-blind, crossover fashion. Endothelial function and aortic stiffness were evaluated with flow-mediated dilatation (FMD) of the brachial artery and carotid-femoral pulse wave velocity (PWV) respectively. Measurements were done before celecoxib/placebo and immediately after a regular cigarette (tar 14 mg, nicotine 1 mg) that was smoked 3 hours after drug administration.

**Results:** Celecoxib blunted the smoking-induced increase in systolic BP ( $p < 0.05$ ), but not in diastolic BP ( $p = NS$ ). Celecoxib abrogated the smoking-related decrease in FMD (decrease by  $2.1$  vs  $0.6\%$ ,  $p < 0.05$ , left figure). Moreover, the increase in PWV after smoking was significantly lower with celecoxib (increase by  $0.69$  vs  $0.29$  m/s,  $p < 0.05$ , right figure).



**Conclusion.** Selective COX-2 inhibition by celecoxib abolishes the endothelial dysfunction and aortic stiffening that is induced acutely by smoking. This finding provides further insights into the cardiovascular profile of this drug.

#### P.034

##### ERECTILE DYSFUNCTION IS RELATED TO ARTERIAL STIFFNESS AND MARKERS OF SYSTEMIC VASCULAR INFLAMMATION AND ENDOTHELIAL DYSFUNCTION IN PATIENTS WITH METABOLIC SYNDROME

N. Ioakeimidis\*, C. Vlachopoulos, K. Aznaouridis, C. Vasiladiou, I. Dima, A. Dagre, K. Rokkas, C. Stefanadis. *1st Department of Cardiology, Athens Medical School, Hippokration Hospital, Athens, Greece*

**Background:** Erectile dysfunction (ED) has been reported as the first sign of a generalized vascular disease. Arterial stiffness may be an early marker for vascular changes associated with metabolic syndrome (MetS). We evaluated associations between ED, arterial stiffness and markers of systemic vascular inflammation and endothelial dysfunction in patients with MetS.

**Methods:** Two groups of subjects with MetS were investigated: 39 men (mean age: 59 yrs) with ED of vascular origin and 30 men (mean age: 57 yrs) with normal erectile function. Aortic stiffness was evaluated with carotid-femoral pulse wave velocity (PWV) using high-fidelity pulse wave analysis. Plasma levels of interleukin  $1\beta$  (IL- $1\beta$ ), tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) and soluble vascular cell and intercellular adhesion molecules (sVCAM-1, sICAM-1) were measured with ELISA.

**Results:** The mean erectile function score (IIEF-5) was 13 (range 6-20) in men with MetS and ED and 23 (range 22-25) in men with MetS and normal erectile function. ED patients had increased PWV compared to patients