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### **6.6: COMPARING THE EFFECTS OF NEBIVOLOL VERSUS METOPROLOL SUCCINATE ON CENTRAL HAEMODYNAMICS, FUNCTIONAL-STRUCTURAL CHANGES OF ARTERIES, AND LEFT VENTRICULAR WALL THICKNESS: THE NEMENDAS STUDY**

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pressure ( $p\text{-}R^2 = 0.066$ ,  $p < 0.001$ ), independently of gender ( $p\text{-}R^2 = 0.048$ ,  $p < 0.001$ ) triglyceride ( $p\text{-}R^2 = 0.044$ ,  $p < 0.001$ ), whereas CS is associated with MBP ( $p\text{-}R^2 = 0.093$ ,  $p < 0.001$ ) and age ( $p\text{-}R^2 = 0.043$ ,  $p < 0.001$ ). CV drugs were associated with ASI (RAAS antagonists decreasing, calcium antagonists increasing), but not with CS.

**Conclusion:** ASI and CS are weakly correlated. Pressure and age, usually strong determinants of CS were modestly associated with ASI which appeared more sensitive to metabolic factors and drug treatments. Both techniques measure differently arterial stiffness and are not exchangeable.

### 6.3

#### ASSESSING VENTRICULAR-VASCULAR INTERACTIONS IN OVERWEIGHT ADOLESCENTS

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**Introduction:** Overweight is associated with changes in vascular and myocardial structure and function. This study compared non-invasively determined ventricular-vascular interactions in overweight adolescents with healthy controls.

**Methods:** Ventricular assessment included M-mode, B-mode, pulse and tissue Doppler echocardiography. Vascular assessment included carotid ultrasound, brachial artery reactivity, applanation tonometry and echo-Doppler assessment of the biophysical properties of the aorta. Ventricular-arterial coupling assessed as the ratio between arterial elastance (Ea) and end-systolic ventricular elastance (Ees), was calculated using SBP, DBP, echo-derived stroke volume and the ratio between aortic pre-ejection time and total systolic time. Between groups comparisons were performed using parametric methods with  $p\text{-}values > 0.05$  considered significant.

**Results:** Twenty-one overweight (BMI  $\geq 85^{\text{th}}$  percentile) adolescents (4 females; median age 14.6 years) and 27 healthy controls (4 females; median age 14.2 years) were studied. Resting heart rate, peripheral and centrally derived SBP, CIMT, aortic PWV, and radial augmentation index were higher in overweight adolescents compared with controls; carotid and aortic distensibility were lower; and flow-mediated endothelial dependent vasodilation was similar. LV mass was higher and diastolic parameters suggested abnormal relaxation in overweight adolescents. Ea was similar, but Ees and the ventricular-arterial coupling ratio Ea/Ees were both reduced in overweight adolescents.

**Conclusion:** Increased arterial stiffness, LV mass and abnormal ventricular relaxation in association with elevated resting heart rate and systolic blood pressure are already present in overweight adolescents. Lower end-systolic ventricular elastance may suggest an adaptive response of the ventricular-arterial coupling.

### 6.4

#### SIMULTANEOUS MEASUREMENT OF WALL SHEAR RATE AND ARTERIAL DISTENSION IN FMD STUDIES BY MEANS OF A MULTIGATE DOPPLER SPECTRAL APPROACH

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Flow-mediated dilation (FMD) estimates endothelial function under the assumption that post-ischemic dilation represents a nitric-oxide mediated response to increase in wall shear stress, i.e. wall shear rate (WSR) times blood viscosity. Implementation of WSR measurements would expand the informative value of this technique.

Aim of the study was to provide preliminary clinical evaluation of a new Ultrasound Advanced Open Platform (ULA-OP, University of Florence) capable to record simultaneously arterial diameter and WSR based on a Multigate Spectral Doppler approach (Tortoli et al, UMB 2006).

**Methods:** The response of brachial artery diameter (FMD) and WSR to different forearm occlusion times was assessed by ULA-OP in twelve volunteers (age 25–29) undergoing two sequential exams (3 and 5-min occlusion) 30 min apart each other in random order. Time variant arterial distension curves and WSR were obtained at baseline and during post-ischemic reflow.

**Results:** Mean percent changes observed in peak WSR (far wall) and diameter (FMD) after 3 and 5 min ischemia are below reported in Table, together with the corresponding time lags between peak WSR and peak diameter (D). The post-ischemic WSR peaks always preceded peak diameter increase.

	FMD (%)	$\Delta$ Peak WSR (%)	Time to peak D (s)
3 min occlusion	6.14 $\pm$ 3.5	80 $\pm$ 28	41 $\pm$ 10
5 min occlusion	7.13 $\pm$ 3.1	101 $\pm$ 31	35 $\pm$ 9

**Conclusions:** WSR and D can be simultaneously measured during FMD studies by ultrasound. Compared to the standard 5-min occlusion, the post-ischemic response to a 3-min occlusion appears slightly delayed and lower, for both diameter and shear. Simultaneous recording of WSR and arterial distension may expand knowledge of the mechanisms regulating vascular responses to hemorheologic changes.

### 6.5

#### HEMOGLOBIN A1C IS ASSOCIATED WITH PULSE WAVE VELOCITY IN NEVER-TREATED HYPERTENSIVES: THE IMPACT OF THE AMERICAN DIABETES ASSOCIATION 2010 POSITION STATEMENT DEFINITIONS

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**Introduction:** Hypertension is associated with increased arterial stiffness. Arterial stiffness, which is a predictor of cardiovascular risk, has been shown to correlate with glycemic control in diabetics. However, it is unclear what is the impact of the recent American Diabetes Association (ADA) 2010 position statement definitions for hemoglobin A1c (HbA1c) on the prediction of arterial stiffness.

**Methods:** We enrolled 1225 consecutive essential hypertensives (mean age 52.9  $\pm$  11.7 years, 728 males, 86 diabetics). Arterial stiffness was determined with carotid-femoral pulse wave velocity (PWV) using the Complior<sup>®</sup> device. HbA1c was measured in venous blood samples.

**Results:** In multivariable regression analysis, HbA1c exhibited significant positive association with PWV, which was independent of age, gender, mean blood pressure, smoking, body-mass index, blood glucose, LDL and CRP ( $p < 0.001$ , adjusted R2 of model = 0.418). In further analyses we employed dichotomous outcome variable (PWV  $\geq 50^{\text{th}}$  percentile [7.8 m/s]). Subjects were divided into 3 groups according to HbA1c levels, based on ADA definitions (Normal group: HbA1c  $< 5.7$ , Pre-diabetes group: 5.7  $\leq$  HbA1c  $\leq 6.4$ , Diabetes group: HbA1c  $\geq 6.5$ ). In multivariable logistic regression models adjusting for the abovementioned confounders, compared to subjects in the normal group, both the subjects in the pre-diabetes and diabetes group had a significantly elevated odds risk of PWV  $\geq 50^{\text{th}}$  percentile (OR = 1.653, 95% CI: 1.215–2.249,  $p = 0.001$  and OR = 6.518, 95% CI: 1.742–24.381,  $p = 0.005$ , respectively).

**Conclusion:** Higher HbA1c is an independent predictor of increased arterial stiffness in never-treated essential hypertensives. Furthermore, our findings support the significance of the cut-off points of the ADA definitions, as they are able to predict increased arterial stiffness and eventually increased cardiovascular risk.

### 6.6

#### COMPARING THE EFFECTS OF NEBIVOLOL VERSUS METOPROLOL SUCCINATE ON CENTRAL HAEMODYNAMICS, FUNCTIONAL-STRUCTURAL CHANGES OF ARTERIES, AND LEFT VENTRICULAR WALL THICKNESS: THE NEMENDAS STUDY

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**Aims:** The vasodilating  $\beta$ -blockers (BB) have several advantages over conventional cardioselective BB atenolol in the treatment of hypertension. However, metoprolol (MET) is the most widely used cardioselective BB in Northern and Eastern European countries. The aim of the present study was to investigate the long-term effects of nebivolol (NEB) and MET on central haemodynamics, structural and functional changes of arteries, and left ventricular wall thickness.

**Methods:** We conducted a randomized, double-blind study in 80 hypertensive patients, who received either nebivolol 5 mg or metoprolol succinate

50–00 mg daily for one year. Endothelial function (Salbutamol-induced vasodilation), wave reflection (Augmentation index (AI<sub>x</sub>)), carotid-femoral pulse wave velocity (PWV), carotid artery intima-media thickness (IMT) and left ventricular wall thickness were measured at baseline, 6 months, and 12 months of treatment.

**Results:** NEB and MET decreased equally brachial blood pressure (BP), whereas reduction in central pulse pressure and left ventricular wall thickness was significant only in the NEB group. Left ventricular wall thickness change was significantly related to central systolic BP change ( $r = 0.41$ ;  $P = 0.001$ ) and central pulse pressure change ( $r = 0.32$ ;  $P = 0.01$ ). No significant changes in AI<sub>x</sub>, PWV and IMT were detected in either treatment group. Endothelial function improved significantly after 6 months in the NEB treatment group.

**Conclusion:** Our study expands earlier observations with vasodilating BB and shows that nebivolol has a stronger impact on central blood pressure and left ventricular wall thickness reduction than metoprolol. Thus,  $\beta$ -blockers with vasodilating properties may offer a clear advantage over a conventional  $\beta$ -blocker in antihypertensive therapy.

### 8.1

#### BLOOD PRESSURE INCREASE AND DEVELOPMENT OF TARGET ORGAN DAMAGE IN SUBJECTS WITH HIGH NORMAL BLOOD PRESSURE IN A GENERAL POPULATION SAMPLE. A 9 YEARS FOLLOW-UP

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**Background:** Subjects with high-normal (HN) blood pressure (BP) may be at increased risk of progression to hypertension (HT) and of cardiovascular events, in comparison with normotensives (NT). Aim of our study was to evaluate the progression to hypertension and the development of target organ damage in a general population in Northern Italy.

**Methods:** In 585 subjects (age  $50 \pm 8$  years, 46% males) a baseline visit and laboratory examinations were performed. Subjects were divided into 3 groups according to systolic (SBP) and diastolic blood pressure (DBP) values: NT (SBP/DBP < 130/85 mmHg); HN (SBP/DBP > 130/85 and < 140/90 mmHg) and HT (SBP/DBP > 140/90 mmHg). In 478 subjects a follow-up (FU) visit, laboratory examinations, measurement of carotid-femoral PWV and carotid IMT were performed after  $8.7 \pm 2.3$  years.

**Results:** at baseline 30% of patients were NT, 25% were HN and 45% were HT. Among patients classified as HN at baseline, 71% developed hypertension at FU, 18% had HN BP, 11% were NT. Among subjects classified as NT at baseline, 34% developed hypertension at FU, 23% were classified as HN and 43% were NT. Mean BP values at FU were  $129 \pm 13/82 \pm 7$  in NT,  $139 \pm 13/87 \pm 6$  in HN,  $146 \pm 15/89 \pm 8$  mmHg in HT, respectively (ANOVA  $p < 0.001$ ). At FU in HN and in HT, as compared with NT, a significant increase of PWV ( $11.2 \pm 2.1$  and  $12.4 \pm 3.3$  vs  $10.1 \pm 1.9$  m/sec, ANOVA  $p < 0.01$ ) and of common carotid IMT ( $1.00 \pm 0.19$  and  $1.09 \pm 0.27$  vs  $0.93 \pm 0.15$  mm, ANOVA  $p < 0.01$ ) was observed.

**Conclusions:** In a general population in Northern Italy a large proportion of subjects with high normal BP developed hypertension and vascular target organ damage during a 9 years follow up.

### 8.2

#### (SHEAR) STRAIN IMAGING OF THE COMMON CAROTID ARTERY

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The primary trigger for myocardial infarction and stroke is destabilization of atherosclerotic plaques. The chance of a plaque to rupture is related to its composition and geometry. Ultrasound (shear) strain imaging allows assessment of local tissue mechanics and possible risk assessment of vulnerable plaques.

To non-invasively assess the local tissue mechanics of the common carotid artery radiofrequency data were acquired using a linear array ultrasound transducer (Philips 11-3L,  $f_c = 7.5$  MHz) in longitudinal and in transverse direction. In transverse direction we used multiple beam steered angles. Simultaneously the ECG-signal was recorded. Axial and lateral displacement of the local tissue were estimated using a 2D coarse-to-fine cross-correlation based strain algorithm [1]. And from these displacements we derived the radial strain [2] and the longitudinal shear strain [3].

Both strains showed a cyclic pattern with an increase during the systolic and a decrease during the diastolic phase. The first *in vivo* results of radial strain in a plaque show increased strain values in the core of the plaque that might be related to a fatty composition.

The first results of non-invasive ultrasound strain imaging using radio-frequency ultrasound demonstrate the potential of quantifying plaque mechanics. Further validation of these methods will open the door for clinical screening of vulnerable plaques.

[ 1] Lopata RGP, *et al.* Ultrasound Med. Biol. 2009.

[ 2] Hansen HHG, *et al.* Phys. Med. Biol. 2010.

[ 3] Idzenga T, *et al.* Ultraschall in der Medizin 2010.

### 8.3

#### REDUCED SYSTEMIC ARTERIAL COMPLIANCE IN STABLE HEART TRANSPLANT PATIENTS

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**Purpose:** Despite high prevalence of cardiovascular diseases in heart transplanted patients (HTx), the global systemic arterial properties are not well described. Thus, the aim of this study was to evaluate arterial properties in HTx.

**Methods:** 26 stable heart transplanted patients (age  $50 \pm 17$  years (mean  $\pm$  SD)) with no signs of rejection or cardiac failure were investigated 4.5  $\pm$  1.8 years after HTx and compared with healthy age-matched subjects with either normal blood pressure or similar brachial mean arterial blood pressure (MAP). Aortic root pressure and flow data were obtained by semi-simultaneous recordings of aortic root Doppler flow velocities, brachial arterial blood pressure and calibrated carotid arterial pulse trace. Systemic arterial properties were described by total arterial compliance (C), arterial elastance (Ea), characteristic impedance (Z<sub>0</sub>), and peripheral vascular resistance (TVR). Parameters were estimated by Fourier analysis of central aortic pressure and flow data and methods based on the 2-element Windkessel model (pulse pressure method).

**Results (Table):** HTx patients had significantly higher Ea and lower C compared with the normotensive subjects. However, C tended lower ( $p = 0.07$ ) in the MAP-matching group compared with the normotensive subjects.

**Conclusion:** Systemic arterial properties in HTx differ significantly from normotensive subjects; however only small variations were seen compared to the MAP-control group. Thus, the low compliance is likely due to a pressure-dependent effect.

	TxCor	MAP-control	Normotensive	P-ANOVA
Subjects (men/women)	26 (19/7)	22 (17/5)	24 (16/8)	
MAP (mmHg)	102 $\pm$ 12	103 $\pm$ 7 †	89 $\pm$ 6 **	< 0.001
Heart rate (beats/s)	79 $\pm$ 13	62 $\pm$ 9 **	60 $\pm$ 9 **	< 0.001
Cardiac output (l/min)	5.0 $\pm$ 1.1	5.1 $\pm$ 1.3	4.8 $\pm$ 1.0	0.57
TVR (mmHg/(ml/s))	1.28 $\pm$ 0.4	1.26 $\pm$ 0.3	1.17 $\pm$ 0.3	0.41
Z <sub>0</sub> (103mmHg/(ml/s))	98 $\pm$ 29	104 $\pm$ 25	111 $\pm$ 41	0.36
C (ml/mmHg)	0.88 $\pm$ 0.3	0.95 $\pm$ 0.2	1.12 $\pm$ 0.2 **	0.005
Ea (mmHg/ml)	1.74 $\pm$ 0.5	1.43 $\pm$ 0.3 *	1.27 $\pm$ 0.4 **	0.001

Mean  $\pm$  SD, \*  $p < 0.05$  and \*\*  $p < 0.005$  compared with TxCor. †  $p < 0.005$  compared with normotensive subjects.

### 8.4

#### SYSTEMATIC REVIEW OF THE EFFECT OF ANTI-HYPERTENSIVE DRUG THERAPY ON ARTERIAL STIFFNESS

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**Background:** Since arterial stiffness (AS) is one of the factors influencing prognosis in hypertensive patients, we performed a systematic review of studies testing the effect of anti-hypertensive therapy on AS.

**Methods:** We performed a systematic search of the literature using on-line databases (1966-Dec 2009). We included studies on Pulse Wave Velocity