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### **P4.07: INFLUENCE OF LONG-ACTING ISOSORBIDE-5-MONONITRATE ADMINISTRATION ON LARGE ARTERIAL STIFFNESS IN PATIENTS WITH ESSENTIAL HYPERTENSION**

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disease and have different effects on the lumen diameter (LD) of the carotid artery. We hypothesised that changes in flow and shear stress in the common carotid artery may contribute to these differences in remodelling.

**Methods:** 10 treatment naive hypertensive subjects were recruited into a double blind, placebo controlled, randomised 3-way cross-over study comparing the effects of 7 days treatment with amlodipine or lisinopril. Brachial and carotid blood pressure (BP), common carotid artery (CCA) flow rate, IMT and LD were measured at the end of each treatment period. Magnetic resonance imaging-based computational fluid dynamics was used to calculate time averaged wall shear stress (WSS) in the carotid artery bifurcation.

There were significant reductions in brachial and carotid BP with both active treatments compared to placebo, but brachial and carotid BP did not differ significantly between the antihypertensive agents. CCA flow rate was significantly lower and distal vascular resistance was higher following lisinopril treatment compared with amlodipine. WSS on the inner wall of the CCA was significantly lower after lisinopril treatment compared with amlodipine.

**Conclusion:** Amlodipine causes increased carotid blood flow and increased WSS compared with lisinopril, probably as a result of greater cerebrovascular vasodilatation. These effects could account for differences in arterial remodelling caused by these agents.

#### P4.04

##### LONG-TERM REDUCTION IN AORTIC STIFFNESS IN HYPERTENSIVE PATIENTS IS PARTLY INDEPENDENT OF MBP REDUCTION

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**Purpose:** A decrease in aortic stiffness could theoretically occur after several years of treatment but reduction has never been unequivocally demonstrated in clinical practice. Association with changes in blood pressure remained unclear.

**Methods:** This longitudinal observational study was conducted in 97 patients (63 ± 1 yrs, 47 women) with treated essential hypertension attending the outpatient hypertension clinic at Pompidou Hospital. Aortic stiffness and carotid pulse pressure (CPP) were determined through carotid-femoral PWV and applanation tonometry. The first measurement of PWV was performed when brachial SBP was lowered below 140 mmHg under treatment. 66 patients had 3 PWV measurements, and 31 patients had 2 measurements during an extended follow-up (5.3 ± 1.2 yrs).

**Results:** The reduction in PWV (from 14.2 ± 4.2 to 11.1 ± 2.4 m/s, linear mixed model,  $P < 0.0001$ ) was associated with a reduction in central SBP (from 132 ± 2 to 122 ± 2 mmHg,  $P < 0.0001$ ) and central PP (from 59 ± 2 to 54 ± 2,  $P < 0.001$ ), whereas brachial SBP and PP did not significantly change. In multivariate analysis, the decrease in PWV was significantly associated with age ( $P < 0.005$ ), duration of follow-up ( $P < 0.0001$ ), presence of diabetes ( $P < 0.005$ ) and reduction in brachial MBP ( $P < 0.005$ ), independently of gender, changes in brachial PP, glomerular filtration rate and hypercholesterolemia.

**Conclusion:** These results indicate that a large decrease in aortic stiffness (-22%) can be observed in the long term when hypertensive patients were treated under conditions of routine clinical practice. This reduction of aortic stiffness was associated with a reduction in central SBP and PP contrasting with no change in brachial SBP and PP.

#### P4.05

##### NONINVASIVE PULSE WAVE ANALYSIS FOR MONITORING THE CARDIOVASCULAR EFFECTS OF PNEUMOPERITONEUM DURING LAPAROSCOPIC CHOLECYSTECTOMY

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**Aim of Study:** Due to absorption of carbon dioxide and elevated intraabdominal pressure, pneumoperitoneum during laparoscopic cholecystectomy has potentially harmful intraoperative cardiovascular effects. Our aim was to test the usefulness of a non-invasive method for detecting these hemodynamic parameters.

**Methods:** A total of 35 patients, with low anaesthesia risk (ASA 1 and 2) who underwent laparoscopic cholecystectomy were investigated using SphigmoCor

arterial wave analyzing system. Conventional pneumoperitoneum was performed, insufflation using carbon dioxide to an intraabdominal pressure of 8-12 mmHg. We determined the estimated central aortic pressure, augmentation pressure, augmentation index, ejection duration and subendocardial viability ratio throughout the surgery. These parameters were recorded after induction of anaesthesia and during the inflation period of surgery.

**Results:** A significant increase in mean arterial blood pressure (84.5 ± 22.1 vs. 94.0 ± 14.4 mmHg,  $p = 0.04$ ), aortic pulse pressure (29.5 ± 9.2 vs. 32.7 ± 11.5 mmHg,  $p = 0.04$ ), augmented pressure (5.9 ± 4.1 vs. 11.0 ± 6.9 mmHg,  $p < 0.001$ ) and corrugated augmentation index (20.1 ± 13.3 vs. 32.8 ± 12.9,  $p < 0.001$ ) were recorded after insufflating the abdomen. After deflating the abdomen the measured parameters tended toward normalization.

**Conclusions:** The derived parameters suggested an increased mechanical cardiac activity and a raised peripheral vascular resistance along with increases in left ventricular end-systolic wall stress. SphigmoCor arterial wave analysis successfully documented hemodynamic changes occurring during laparoscopic surgery. Our results from this non-invasive technique correspond to data reported previously, using invasive hemodynamic monitoring.

#### P4.06

##### DIFFERENTIAL EFFECTS OF NEBIVOLOL AND ATENOLOL ON CAROTID ARTERIAL WAVE INTENSITY

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**Background** The hemodynamic effects of the vasodilator  $\beta$ -blocker nebivolol may differ from those of a conventional agent. Wave intensity analysis can describe the energy transported by wavefronts in the arterial system in the direction of wave propagation. A non-invasive ultrasound-based technique [1] was used to compare the effects of nebivolol and atenolol on carotid arterial wave intensity in patients participating in a hypertension treatment study.

**Methods** 38 hypertensive patients (age 63 ± 11yrs, 21 female) took part in a double-blind randomised cross-over study. All received bendroflumethazide 2.5 mg for 6 weeks in advance, and throughout the study. We compared effects of nebivolol 5 mg and atenolol 50 mg on the magnitude of the initial systolic forward compression wave (S), the protodiastolic forward decompression wave (D) (both generated by the heart), the reflected compression wave ( $c_r$ ) and local wave speed.

**Results.** The S and D waves were significantly smaller with atenolol than with nebivolol treatment but wave reflection and wave speed did not differ.

Wave parameter	Nebivolol (n = 38)	Atenolol (n = 38)	p
S wave, kW m <sup>-2</sup> s <sup>-2</sup>	735 (586, 1049)	612 (443, 885)	0.007
D wave, kW m <sup>-2</sup> s <sup>-2</sup>	220 (183, 284)	164 (106, 225)	0.001
$c_r$ wave, kW m <sup>-2</sup> s <sup>-2</sup>	122 (74, 168)	97 (76, 150)	0.4
Wave speed, ms <sup>-1</sup>	6.67 (5.70, 9.28)	6.61 (5.22, 8.40)	0.4

Medians (25<sup>th</sup>, 75<sup>th</sup> percentiles), \* Wilcoxon's signed rank test

**Conclusions:** In hypertensive patients nebivolol has a more favourable effect than atenolol on left ventricular wave generation without increasing wave reflection.

1. Niki K, et al., Heart Vessels 2002; 17:12-21.

#### P4.07

##### INFLUENCE OF LONG-ACTING ISOSORBIDE-5-MONONITRATE ADMINISTRATION ON LARGE ARTERIAL STIFFNESS IN PATIENTS WITH ESSENTIAL HYPERTENSION

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AIM of this study was to evaluate the clinical efficacy of long-acting nitrates, isosorbide-5-mononitrate (ISMN), in addition to ACE inhibitor on artery stiffness in patients with essential hypertension. MATERIALS AND METHODS. 40 hypertensive patients (mean age 61.3 ± 7.4 years, 9 male, 31 female, mean SBP/DBP = 158,1 ± 17,9/91,7 ± 9 mmHg) received moexipril in individual titrated doses (mean dose 11,7 ± 4,8 mg daily) for 3 months. 20 patients, which retained SBP > 140 and/or DBP > 90 mmHg, received additional ISMN (50 mg daily) for 4 weeks. Other patients formed the control

group. Large arterial stiffness was assessed by automatic noninvasive measurement of the brachial-ankle pulse wave velocity (baPWV). Endothelial function was calculated based on flow-mediated dilatation (FMD) parameters. RESULTS. The 3 months treatment of ACE inhibitor produced a significant reduction in systolic (-26,6 mmHg) and diastolic BP (-10,2 mmHg), baPWV (-1,1 m/s) and increase of FMD (+1,5%). Administration with ISMN of 20 pts, without reaching BP target level on treatment of ACE inhibitor, did not lead to significant decreasing of SBP(-1,3 mmHg), DBP(-2,1mmHg) and baPWV (+0,3 m/s). There was no difference in BP and baPWV in ISMN+ACEI treatment group compared with control group (ACEI only). CONCLUSION. Addition of ISMN to ACE inhibitor has no beneficial impact on BP and improvement of arterial stiffness in patient with essential hypertension.

#### P4.08

##### ARTERIAL HYPERTENSION AND CORONARY REVASCULARIZATION SURGERY: A CLINICAL CHARACTERIZATION OF 90 PATIENTS

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**Objectives:** evolution of hypertensive patients during their stay in the CCU after myocardial revascularization surgery (MRS).

**Methods:** retrospective study with 90 patients.

**Results:** prevalence of AHT before surgery was 86.7%; 61.3% were treated with BB, 39% received ACEI, 11% calcium antagonists and 14.4% diuretics. From hypertensive patients, 56% presented AHT during the stay in the CCU (65 % of men and 41.3% of women) ( $p < 0.05$ ). In the CCU the patients with AHT were treated with nitroglycerin in the 95.6% of the cases. BB were used in 48% of the patients, and only 13% needed sodium nitroprusside. The most frequent early postoperative complications were taquiarrhythmias and mayor bleedings but we did not find a relation between these complications and AHT in the early postoperative. Bleeding was found in 21 % of the patients that developed AHT postoperatory vs. 10 % of the patients that did not (NS). 21% of the patients that developed AHT presented taquiarrhythmias vs. 16% of the patients that did not (NS). Almost all patients were sent home with BB, 60% of patients with ACEI and 3.3 % with calcium antagonists.

**Conclusions:** 1. AHT was more frequent in previously hypertensive men than in women in the early postoperatory of MRS. 2. AHT was not significantly associated with bleeding or taquiarrhythmias 3. Most of the cases of HTA responded to the treatment with nitroglycerin and BB. 4. BB and ACEI were the drugs more prescribed to patients after acute phase of MRS.

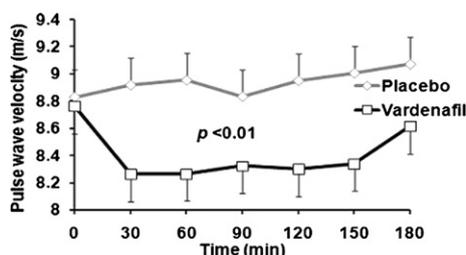
#### P4.09

##### EFFECT OF VARDENAFIL ON ARTERIAL STIFFNESS AND WAVE REFLECTION

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**Introduction:** While vardenafil is widely prescribed for erectile dysfunction, its effect on arterial function is not established. Arterial stiffness and wave reflections are markers of cardiovascular disease and predictors of cardiovascular risk. We assessed the acute effect of vardenafil on arterial stiffness and wave reflections on patients with erectile dysfunction.

**Methods:** Ten patients (mean age  $58 \pm 10$  years) with erectile dysfunction received vardenafil 20 mg in a randomized, placebo-controlled, double-blind, 2-way cross-over design. Aortic elastic properties were evaluated with carotid-femoral pulse wave velocity (cfPWV); wave reflection was evaluated with augmentation index (AIx) of the aortic pressure waveform.



cfPWV and wave reflection indices were measured at baseline and for 3 hours after the vardenafil intake or placebo.

**Results:** cfPWV decreased significantly (by 0.502 m/s,  $p < 0.01$ ), denoting a decrease in aortic stiffness. AIx decreased significantly (by 3.11%,  $p < 0.01$ ), denoting a decreased effect of wave reflection from the periphery. Aortic pulse pressure decreased significantly (by 5.09 mmHg,  $p < 0.01$ ). The effect of vardenafil lasted throughout the study (3 hours), being evident 30 to 60 minutes after drug intake.

**Conclusion:** This study shows, for the first time, that vardenafil has a favorable effect on aortic stiffness and wave reflection in patients with erectile dysfunction.

#### P4.10

##### EFFECT OF SHORT-TERM PERINDOPRIL THERAPY ON ARTERIAL STIFFNESS AND ENDOTHELIAL FUNCTION IN DIASTOLIC HEART FAILURE PATIENTS

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**Background:** Vascular load is an important determinant of ventricular function. Understanding the physiologic basis of vascular load is central to the development of new strategies and drugs to treat HF. Aim: to evaluate arterial stiffness, endothelial function, clinical status at baseline and in 6 months follow-up period of perindopril therapy in diastolic HF.

**Methods:** 40 patients with exertional dyspnea, I-II NYHA, EF > 45%, aged 62(8,4) years, F/M = 27/13, history of CHF 29(16) months, BMI 29,4 kg/m<sup>2</sup>. Arterial stiffness was assessed by measuring carotid-femoral PWV and central: mean BP(MAP), pulse pressure(CPP), AIx using applanation tonometry (Sphygmocor) at the baseline and in 6-months f-up. Endothelial dysfunction using FMD during reactive hyperemia (HDI 5000), clinical status with MQLHF were assessed at the baseline and in 6-months f-up period. All patients were on perindopril therapy, mean dose 8 mg/day.

**Results:**

	Baseline	6months f-up	p
PWV	10(8,6;11,9)	9(8,3;11,5)	=0.06
CSBP	135(123;152)	132(124;140)	ns
CDBP	85(79;93)	82(80,5;90)	ns
SBP	145(134;154)	131(126;142)	<0.05
DBP	85(80;91)	80(76;86)	ns
CPP	52(41,5;59)	44(42;52)	ns
MAP	105,5(97,5;115,5)	104(98;110)	ns
AIx	32,5(27,5;41,5)	38(30,38)	ns
FMD	5,6(3;6,5)	6,5(3,3;7,1)	<0.05
NYHA FC	2(1;2)	1(1;2)	<0.05
MQL	39,5(27;48)	33,5(25;41)	ns

**Conclusions:** The present study demonstrates that short-term perindopril therapy improved endothelial function, led to favourable trends with regard to the reduction of arterial stiffness and resulted in improvement of NYHA functional class in diastolic heart failure patients, that suggests that perindopril is therapeutically useful in the therapy of diastolic HF.

