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### 7.10: AORTIC STIFFNESS AND BODY MASS INDEX (BMI) IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

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## 7.7

### THE EFFECT OF MARINE N-3 POLYUNSATURATED FATTY ACIDS ON CARDIAC AUTONOMIC AND HEMODYNAMIC FUNCTION IN PATIENTS WITH PSORIATIC ARTHRITIS: A RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

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**Background:** Patients with psoriatic arthritis are at high cardiovascular risk. Marine n-3 polyunsaturated fatty acids (PUFA) may reduce the incidence of cardiovascular disease. The aim of this study was to investigate the effect of marine n-3 PUFA on cardiac autonomic function and vascular function in patients with psoriatic arthritis.

**Methods:** The study was conducted as a randomized, double-blind, placebo-controlled trial, where 145 patients with psoriatic arthritis were supplemented with 3 g of n-3 PUFA or olive oil (control) daily for 24 weeks. Blood pressure, heart rate, HRV, central blood pressure, pulse wave velocity (PWV) and fatty acid composition of granulocytes, were determined.

**Results:** At baseline we found a significant difference in the HRV parameter RR when comparing subjects with the highest vs the lowest fish intake ( $p = 0.03$ ). After supplementation for 24 weeks there was a trend towards an increase in RR ( $p = 0.13$ ) and decrease in heart rate ( $p = 0.12$ ) comparing the n-3 PUFA group with the control group. However, per-protocol analysis (performed on participants who completed the trial with a good compliance) showed significantly increased RR ( $p = 0.01$ ) and lowered heart rate ( $p = 0.01$ ) in the n-3 PUFA supplemented patients compared to controls. Blood pressure, PWV and central blood pressure did not change after supplementation with n-3 PUFA.

**Conclusions:** Marine n-3 PUFA increased HRV in patients with psoriatic arthritis which may suggest a protective effect of n-3 PUFA against cardiovascular disease in this population.

## 7.8

### ARTERIAL STIFFNESS AND SYSTEMIC INFLAMMATION IN COPD PATIENTS

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**Background:** COPD is one of the leading causes of mortality worldwide. Systemic low-grade inflammation is a common finding in COPD. Soluble urokinase-type plasminogen activator receptor (suPAR) indicates an inflammatory state and it has an association with atherosclerosis and cardiovascular disease (CVD). ThesuPAR reflects different aspects of inflammation as high sensitive C-reactive protein (hsCRP) and IL-6. Elevated CVD risk is observed in COPD. However the correlation between COPD and arterial stiffness is rarely investigated in the literature.

We investigated the association between some inflammatory biomarkers (suPAR, IL-6, hsCRP) and arterial stiffness in COPD and control patients.

**Methods:** We measured 45 middle aged individuals (25 COPD and 20 control normotensive patients) without diabetes and cardiovascular disease. IL-6, hsCRP, suPAR were determined in fasting blood samples. Whole body plethysmography, assessment tests and aortic pulse wave velocity (aoPWV), augmentation index (Aix), central systolic blood pressure (cSBP) were determined. COPD patients were categorized according to GOLD-classification.

**Results:** Patients with COPD have a higher level of IL-6 (5.38 vs 3.63 pg/ml  $p = 0.022$ ), suPAR (2.84 vs 2.41 ng/ml  $p = 0.036$ ), and hsCRP (2.99 vs 1.91 mg/L  $p = 0.068$ ). The patients with COPD have a significant higher aoPWV ( $p = 0.002$ ), and cSBP ( $p = 0.022$ ).

**Conclusion:** In this study we found elevated inflammatory markers and aoPWV in COPD patients, both of them indicate the presence of earlier atherosclerosis than in controls without COPD.

## 7.9

### CAROTID ARTERY STIFFNESS IS ASSOCIATED WITH CT-MEASURED LUNG AIR-TRAPPING IN COPD PATIENTS AND CONTROLS INDEPENDENT OF AGE, BLOOD PRESSURE AND SMOKING HISTORY

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**Background:** Early stages of chronic obstructive pulmonary disease (COPD) are characterized by loss of the terminal bronchioles and 'air trapping' often before overt emphysema manifests (1). COPD patients are also at risk for cardiovascular disease (CVD), therefore, we hypothesized that the degree of air trapping on computed tomography (CT) (2) would be associated with higher aortic (carotid femoral pulse wave velocity, CFPWV) and carotid artery stiffness ( $\beta$ -stiffness), biomarkers of CVD risk.

**Methods:** Ten adults with COPD but little emphysema (age  $66 \pm 8$  yrs, 5F/5M, GOLD stage 1-3) and 9 adults without COPD (age  $59 \pm 13$  yrs, 5F/4M) that had a research chest CT were recruited.

**Results:** COPD patients had greater smoking history ( $45.9 \pm 21$  vs.  $6.4 \pm 12.9$  pack-years,  $P < 0.001$ ) and air trapping ( $0.85 \pm 0.07$  vs.  $0.78 \pm 0.05$  Expiration/Inspiration attenuation ratio,  $p < 0.05$ ) (2) compared with non-COPD subjects, but did not differ by age, BMI, SaO<sub>2</sub>%, brachial BP or % emphysema (all  $p > 0.05$ ). COPD patients had significantly higher CFPWV ( $999 \pm 293$  vs.  $760 \pm 147$  cm/sec,  $p < 0.05$ ) but not carotid  $\beta$ -stiffness ( $13.3 \pm 5.1$  vs.  $10.6 \pm 4.7$  U,  $p = 0.26$ ). In the entire cohort ( $n = 19$ ), air trapping was associated with higher CFPWV ( $r = 0.60$ ,  $p < 0.01$ ) and carotid  $\beta$ -stiffness ( $r = 0.75$ ,  $p < 0.001$ ). After adjustment for age, mean BP and pack-years, the correlation between carotid  $\beta$ -stiffness and air-trapping remained significant ( $r = 0.68$ ,  $p < 0.01$ ).

**Conclusions:** Carotid artery stiffness is significantly associated with air trapping in COPD patients and controls, independent of age, smoking history and BP. This suggests a link between high CVD risk in COPD patients with small airway disease without predominant emphysema.

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## 7.10

### AORTIC STIFFNESS AND BODY MASS INDEX (BMI) IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

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**Background:** Patients with COPD have increased Cardiovascular (CV) risk and commonly present with altered body composition. Patients with COPD and a low BMI have poorer health outcomes<sup>1</sup>, while obesity may increase CV risk<sup>2</sup>. The aim of this analysis was to explore BMI, CV risk, exercise capacity and systemic inflammation in COPD.

**Methods:** This analysis included 524 stable patients with COPD (confirmed with spirometry) from the ARCADE (Assessment of Risk in Chronic Airways Disease Evaluation) study. Assessments included lung function (forced expiratory volume in 1 second (FEV<sub>1</sub>)), smoking history, BMI, aortic pulse wave velocity (PWV) (SphygmoCor device), blood pressure (BP), 6-minute walking distance (6MWD). Inflammation was measured by high sensitivity C-reactive protein (hsCRP) and fibrinogen. Patients were classified by BMI as follows: low ( $< 19.9$  Kg/m<sup>2</sup>), healthy (20-24.9 Kg/m<sup>2</sup>), overweight (25-29.9 Kg/m<sup>2</sup>) obese ( $> 30$  Kg/m<sup>2</sup>).

**Results:** There was no difference in gender, age, lung function or smoking history between patients grouped according to BMI. However, there was a difference in PWV, systolic BP, 6MWD and inflammation between the groups ( $p < 0.05$ ). The difference in PWV remained after adjustment for age and mean BP (Table 1). Overweight and obese patients (BMI  $< 25$ ) had greater PWV and inflammation, while obese patients had the poorest 6MWD.

**Conclusions:** The findings suggest obese patients with COPD have greater CV risk which may be a result of poorer physical capacity and greater inflammation. Optimisation of BMI in COPD may improve outcomes further follow-up of this cohort will evaluate the prognostic value of arterial stiffness and possible therapeutic targets.

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## 8.1

## ARTERIAL STIFFNESS, BLOOD PRESSURE AND CARDIAC OUTPUT STUDY

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We are planning a prospective study in 200 patients with an abdominal artery aneurysm (AAA). Non-invasive measurements will be performed including tonometry-based pulse wave analysis (PWA) and pulse wave velocity (PWV), echocardiography, and 24-hour blood pressure measurements.

This study will provide insight in how PWV/PWA-parameters can help identify characteristics of prostheses used to treat AAA that best match native aortic characteristics and will lead to the best long-term outcome after aneurysm repair. Also the interaction between blood pressure (and control) and cardiac output will be evaluated. These results will form the basis for evidence-based practice for stent choice and lead to better outcomes after AAA treatment. First we will validate non-invasive against invasive central pressure in 20 patients treated with endovascular aneurysm repair (EVAR).

This study will provide insight if arterial stiffness parameters change over time after treatment of AAA and the possible role of PWV/PWA for the surveillance after treatment. We expect to provide insight in the various determinants of the PWV/PWA-parameters pre- and post-repair of AAA evaluation also includes graft material, intraluminal thrombus, and inflammation. We will study whether the different PWV/PWA parameters predict outcome after AAA repair for different prostheses.

Finally, this study will reveal whether parameters of cardiac output obtained by tonometry correspond with parameters obtained by echocardiography in AAA patients. If so, the PWV/PWA measurement can detect cardiologic problems at an early stage during follow-up. By early treatment, the development of heart failure can be delayed or even prevented. We look forward to input on our study-plan.

## 8.3

## QUANTIFYING HEART AND ARTERIAL CONTRIBUTIONS TO CENTRAL BLOOD PRESSURE IN SYSTOLE

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**Background:** A recent study has shown that the central pressure waveform could be determined by a very small set of parameters accounting for the physical properties of the heart and the arteries [1]. Particularly, main pressure features like first systolic shoulder (P1) and systolic (P2) pressures were estimated accurately.

**Methods:** By combining a numerical virtual population ( $n=3,325$ ) similar to [2] and experimental data acquired from a pressure/Doppler flow velocity transducer placed in the ascending aorta in 18 patients (meanSD: age  $63\pm 11$  yr, aortic BP  $136\pm 23/73\pm 13$  mmHg) at the time of cardiac catheterization, we assessed the accuracy of those predictions for magP1 (P1-DBP) and P2 using respectively a water hammer [3] and a 3-element Windkessel models [4]. Contributions of the heart and arterial properties to these estimates through respectively blood velocity, volume and pulse wave velocity, compliance, resistance were then derived from the theoretical models used.

**Results:** P1 and P2 estimates agreed well with theoretical pressure both in the numerical dataset (mean+/-SD difference,  $1.1\pm 3.2$  mmHg and  $-1.6\pm 3.1$  mmHg respectively) and the clinical cohort (mean+/-SD difference,  $-2.4\pm 5.5$  mmHg and  $1.9\pm 6.5$  mmHg respectively). The ratio arterial-to-heart contribution has been shown to be fairly constant as magP1 was increasing.

**Conclusions:** Arteries and heart contribute as much to rise in P1. More clinical data are being collected to quantify the contributions of the heart and arteries to P2.

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## 8.4

## DIURNAL CHANGES IN CENTRAL PRESSURE AND PULSE WAVE PARAMETERS IN HEALTHY SUBJECTS

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**Purpose:** The feasibility of pulse wave analysis (PWA) over 24 hours with oscillometric devices has already been shown and first studies indicate additional information compared to single measurements. Nevertheless, diurnal patterns of PWA parameters in healthy subjects, which can potentially serve as a reference, are currently missing. Therefore, the aim of this study was to perform 24h-PWA measurements in healthy subjects over a wide age range and to analyse day/night differences.

**Methods:** 91 well defined healthy subjects underwent 24h PWA measurements using the Mobil-O-Graph device (IEM, Germany). The subjects were categorized in three age groups (20-29 years, 30-49 years, 50-69 years). Day-time (9-21h) and nighttime (0-6h) averages were calculated.

**Results:** A significant dipping behaviour in all age groups could be found for diastolic blood pressure ( $> 14$  mmHg in all age groups,  $p<0.05$ ), peripheral systolic blood pressure ( $> 15$  mmHg,  $p<0.05$ ) and central systolic blood pressure ( $> 9$  mmHg,  $p<0.05$ ). A significant rising effect in all age groups was found for the reflection magnitude ( $> 8\%$ ). In contrast, the day/night difference in augmentation index was age dependent and this dependency remained also for Alx75, see table.

**Conclusions:** Prominent pressure dipping and a rise in reflection magnitude were present in all age groups during nighttime, while diurnal changes in augmentation index showed an age-dependency. This differing behaviour of PWA parameters should be investigated in further studies. Furthermore, the observed effects of diurnal changes in healthy subjects may provide a basis for reference profiles for future patient evaluation.

**Table:** Mean day and night values for peripheral systolic blood pressure (pSBP), peripheral diastolic blood pressure (pDBP), central systolic blood pressure (cSBP), central diastolic blood pressure (cDBP), heart rate (HR), augmentation index (Alx, Alx75) and reflection magnitude (RM) \* marks a significant difference between day and night (t-test,  $p<0.05$ ).

	20–29 years		30–49 years		50–69 years	
	Day	Night	Day	Night	Day	Night
pSBP (mmHg)	118.8 *	103.4	124.8 *	109.0	123.0 *	105.8
pDBP (mmHg)	75.7 *	59.5	81.4 *	64.2	79.6 *	64.8
cSBP (mmHg)	106.3 *	97.1	114.8 *	103.3	114.5 *	100.7
cDBP (mmHg)	77.4 *	60.6	83.1 *	65.3	81.1 *	65.6
HR (bpm)	76.0 *	59.6	77.5 *	64.4	70.4 *	59.8
Alx	18.2	19.0	19.7	22.7	25.9 *	35.0
Alx75	19.3 *	10.4	20.6	15.7	23.4	26.4
RM	55.2 *	63.2	59.7 *	68.8	62.3 *	71.5