

## EPOSTER'S SECTION

### OBESITY, SLEEP APNOEA AND METABOLIC SYNDROME

#### PROLONGED NOCTURNAL HYPOXEMIA PREDICTS WORSE PROGNOSIS IN PATIENTS WITH CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION UNDERGOING PULMONARY ENDARECTOMY

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**Objective:** Obstructive sleep apnea (OSA) and/or nocturnal hypoxemia is prevalent in patients with chronic thromboembolic pulmonary hypertension (CTEPH), yet the pathological determinants of adverse outcomes remain ambiguous. We aimed to investigate the prognostic significance of various sleep parameters for poor prognosis in patients with CTEPH undergoing pulmonary endarterectomy (PEA).

**Design and method:** Consecutive patients diagnosed with CTEPH who underwent overnight cardiorespiratory polygraphy for the assessment of OSA were enrolled. Time-to-event analysis was performed investigating cardiorespiratory indices (eg, apnea-hypopnea index [AHI], time percentage with oxygen saturation below <90% [T90]) and clinical worsening using the log-rank test and multivariable Cox proportional hazard models adjusted for multiple confounders.

**Results:** Of 71 operable CTEPH patients, 36 (50.7%) had OSA (AHI = 5 or above) and 32 (45.1%) had nocturnal hypoxemia (T90 no less than 30%). A 10% increase in T90 was associated with a nearly 27% greater risk of being classified as a high-risk group (odds ratio: 1.27, 95% confidence interval [CI] 1.07-1.50,  $P = 0.006$ ), as quantified by mean pulmonary artery pressure over 46 mmHg. Over a median follow-up of 39.0 months, 19 (26.8%) patients experienced CW events. AHI did not predict a higher risk of incident CW (hazard ratio [HR]: 1.00, 95% CI: 0.93-1.06,  $P = 0.906$ ). By contrast, compared with normoxemic patients, patients with nocturnal hypoxemia had a higher cumulative incidence of CW (43.8% vs. 12.8%, log-rank  $P = 0.017$ ). Notably, nocturnal hypoxemia was associated with an increased risk of CW events (HR: 3.27, 95% CI 1.17-9.13,  $P = 0.024$ ), and these associations persisted even after covariate adjustment.

**Conclusions:** Among patients with operable CTEPH, nocturnal hypoxemia quantified by T90 was a robust risk predictor of both short-term and long-term CW events. Investigation of nocturnal hypoxemic burden in CTEPH may aid in the early risk-stratification.

#### EDUCATION LEVEL AND OBESITY IN WOMEN LIVING IN THE CROATIAN RURAL AREA DAMAGED BY AN EARTHQUAKE. "THE SILENT KILLER HUNT PROJECT"- CROATIAN SOCIETY OF HYPERTENSION PROJECT

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**Objective:** The rates of obesity and the resultant morbidities are rising worldwide, making it a high-priority health issue for the medical community. Obesity prevalence varies depending on several factors, one of which is educational level and stress.

Our goal was to determine the relationship between the level of education and body mass index (BMI), mid-upper arm circumference and visceral fat percentage of women in the Croatian rural area damaged by an earthquake.

**Design and method:** We analyzed the association between the level of education and BMI, mid-upper arm circumference and visceral fat percentage of 170 women (opportunistic screening). A structured questionnaire was prepared, and it included questions about the years of formal education. Weight, BMI, body fat percentage, and visceral fat were measured by using a metabolic scale with a body composition monitor.

**Results:** In our studied female population the average value of BMI was  $29.8 \pm 6.04$  kg/m<sup>2</sup>, mid-upper arm circumference was  $31.6 \pm 3.30$  cm and visceral fat percentage was  $10.5 \pm 3.87$  %. By dividing the observed population into 2

subsets based on educational status (low educated and highly educated) there was a noticeable difference between the measured variables. Mean values of BMI, mid-upper arm circumference and visceral fat percentage in highly educated and low educated categories were  $28.2 \pm 6.25$  kg/m<sup>2</sup>,  $30.5 \pm 4.14$  cm,  $8.88 \pm 3.35$  % and  $30.4 \pm 5.9$  kg/m<sup>2</sup>,  $32.0 \pm 4.32$  cm,  $11.1 \pm 3.89$  %, respectively. Each of these factors had statistical significance with the following p values: BMI  $p < 0.040$ , mid-upper arm circumference  $p < 0.049$ , visceral fat percentage  $p < 0.001$ .

**Conclusions:** Our results have shown that BMI, mid-upper arm circumference, and visceral fat percentage are higher in women with the lower level of education. This observation highlights the role of patient education in our endeavors to improve health and quality of life on a population level. Average values are higher than in other rural parts of Croatia indicating that earthquake stress further contributed to obesity.

#### THE ASSOCIATION OF HYPERTENSION AND OBESITY: WHAT IMPACT ON THE LONGITUDINAL SYSTOLIC FUNCTION OF THE LEFT VENTRICLE

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**Objective:** Hypertension and obesity are well known each result in heart failure with preserved ejection fraction. Indeed, there is ample evidence that the accumulation of adipose tissue in obese subjects negatively affects the left atrial and ventricular structure, as well as diastolic and systolic function. Predisposing factors for heart failure with preserved LVEF are advanced age, hypertension, diabetes, dyslipidemia and obesity.

The development of the 2D strain has made it possible to make an early diagnosis of ventricular dysfunction in patients with cardiovascular risk factors.

**Design and method:** This work consists of performing in a series of 128 hypertensive patients divided into two subgroups: 58 obese patients and 70 patients with normal BMI. A complete cardiographic echo study was performed in both subgroups, including LVEF by Simpson biplane method, calculation of indexed left ventricular mass and parietal relative thickness, analysis of diastolic function and finally study of longitudinal LV deformation by speckle tracking technique.

**Results:** We note in this work that dyslipidemia and diabetes were significantly more prevalent in the HTA+obesity arm. The average blood pressure figures were slightly higher in the HTA+obesity arm.

LVH was clearly predominant in the HTA+obesity arm with a more consequent decrease in the longitudinal contraction index. In obese hypertensive patients, LVH was most often concentric (53.4%). An increase in filling pressures was found in 11 obese hypertensive patients compared to only 4 non-obese hypertensive patients ( $p = 0.0001$ ), with a good correlation with the decrease in GLS.

These results suggest that increased BMI is closely associated with atrioventricular interaction in patients with hypertension, with a perfect correlation with impairment of longitudinal systolic function and diastolic function compared to the control group.

**Conclusions:** Although the pathophysiological mechanism behind obesity is disputed, several possible explanations have been proposed: obesity has been considered a state of chronic volume overload, increased blood volume, neurohormonal activation, thus increasing oxidative stress. Therefore, obesity is associated with mild ventricular dilation (eccentric remodeling). However, this finding is in contrast to other studies that associate obesity with a concentric rather than eccentric remodeling of the LV.

#### DYSLIPIDEMIA AND HYPERGLYCEMIA IN HYPERTENSIVE PATIENTS ASSOCIATE WITH GNB3 (RS5443) AND NOS3 (RS2070744) GENES' ALLELIC STATE

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**Objective:** More than 700 million people worldwide live with untreated essential arterial hypertension (EAH). The objective of the study was to evaluate the risks

of metabolic disorders in EAH patients depending on guanine nucleotide-binding protein-β3 subunit (GNB3, rs5443) and endothelial nitric oxide synthase (NOS3, rs2070744) genes' allelic state.

**Design and method:** The cohort case-control study involved 100 EAH patients (moderate-very high cardiovascular risks, aged 45-65 years) and 48 practically healthy (control). Metabolic disorders were evaluated by glucose blood value and lipids panel: total cholesterol (TC), triglycerides (TG), Low-, and High- density lipoprotein cholesterol (LDL-C, HDL-C) levels. The atherogenic index (AI) was calculated by the equation: (TC-HDL-C)/HDL-C. GNB3 (rs5443) and NOS3 (rs2070744) genotyping performed by TaqMan probes in CFX96 Real-Time PCR Detection System.

**Results:** Hyperglycemia (>6.1 mmol/l), hypertriglyceridemia (TG>1.7 mmol/l) and decreased HDL-C (<1.2 mmol/l) were relatively more common in EAH patients than in the control group by 36.11% ( $\chi^2 = 17.88$ ;  $p < 0.001$ ), 23.61% ( $\chi^2 = 6.43$ ;  $p = 0.011$ ) and 25.0% ( $\chi^2 = 8.32$ ;  $p = 0.004$ ) respectively. Therefore, the fasting hyperglycemia increases the EAH risk in the examined population ninefold [OR95%CI:2.86-27.08;  $p < 0.001$ ], hypertriglyceridemia and decreased HDL-C elevates the risk almost 3 and 3.5 times as well [OR95%CI:1.23-5.56;  $p = 0.009$  and OR95%CI:1.46-8.71;  $p = 0.003$ ], respectively. The risk of metabolic disorders (dyslipidemia and hyperglycemia) in EAH patients does not depend on NOS3 gene polymorphism (rs2070744).

Contrary, in T-allele patients of the GNB3 gene (rs5443) prevailed subjects with elevated LDL-C (>3.0 mmol/l) over those with CC-genotype by 13.89% ( $p = 0.05$ ). Other parameters of lipid metabolism and hyperglycemia did not differ significantly between GNB3 (rs5443) genes allelic state. However, the mutational T-allele of the GNB3 gene (825C>T) increases the risk of hyperlipidemia 8.5 times [OR 95%CI:1.99-72.70;  $p = 0.05$ ] due to atherogenic LDL-C, with the protective role of CC-genotype [OR = 0.12; OR 95%CI:0.01-1.0;  $p = 0.048$ ].

**Conclusions:** Fasting hyperglycemia, hypertriglyceridemia and lowered HDL-C, enhance the arterial hypertension risk 3-9 times ( $p < 0.01$ ). The polymorphic site of GNB3 (rs5443) gene, but not NOS3 (rs2070744) gene associate with hyperlipidemia in hypertensive patients.

**METABOLIC PROFILE OF SUBJECTS WITH NAIVE ISOLATED SYSTOLIC HYPERTENSION**

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**Objective:** Even though hypertension is an important contributor to cardiovascular disease (CVD), and its treatment has established mortality benefits, uncertainty lies in the management of isolated systolic hypertension (ISH). Although the association of ISH with CVD and mortality has been established, the metabolic characteristics of this population have not been adequately described. The aim of this study was to describe the metabolic profiles of patients with isolated systolic hypertension.

**Design and method:** An observational study of patients attending the Hypertension Unit of the University Hospital of Heraklion, Heraklion, Greece, was performed.

**Results:** In total, 809 hypertensive patients not on any anti-hypertensive treatment were identified. Among them, 44.7% were men; age was 55.6±12.5years, while 29.7% were smokers. Systolic blood pressure was 161.3±15.8mmHg and diastolic blood pressure was 96.1±11.3mmHg. Body mass index (BMI) was 31±5.3kg/m2, while 9.6% had type 2 diabetes mellitus (DM).

A comparison of subjects with ISH with the rest hypertensives, revealed that persons with ISH were older, had lower SBP and higher pulse pressure, while they also had lower total cholesterol and LDL, and were more likely to have DM even though they had a slightly lower BMI. On the other hand, they did not have any difference in terms of gender, smoking status, HDL, triglycerides, liver biochemistry, uric acid or prevalence of impaired fasting glucose.

**Conclusions:** Subjects with ISH were older, with lower SBP, total cholesterol and LDL and higher pulse pressure and higher prevalence of DM.

**ARTERIAL HYPERTENSION DOES NOT SLEEP**

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**Objective:** Sleep apnea is a secondary cause of hypertension and is suggested by non-dipper profile at ambulatory blood pressure monitoring (ABPM). The prevalence is estimated between 30-50% in hypertensive patients.

Respiratory polygraphy pre-CPAP		Respiratory polygraphy post-CPAP	
Respiratory evaluation	Findings	Respiratory evaluation	Findings
AHI (Desat-Cor.) [Per hour]	13.8 (0.8)	AHI (Desat-Cor.) [Per hour]	0.4 (0.4)
Apnea Index AI (Desat-Cor.) [Per hour]	9.3 (0.5)	Apnea Index AI (Desat-Cor.) [Per hour]	0.0 (0)
Hypopnea Index HI (Desat-Cor.) [Per hour]	4.5 (0.3)	Hypopnea Index HI (Desat-Cor.) [Per hour]	0.4 (0.4)
CSBI (Desat-Cor.) [Per hour]	0 (0)	CSBI (Desat-Cor.) [Per hour]	0 (0)
Lowest Desaturation [%] (01:42:27)	74	Lowest Desaturation [%] (05:24:07)	88
Longest Desaturation [Min] (01:53:41)	3:28	Longest Desaturation [Min] (23:32:05)	1:28
Mean Duration [Sec]	27	Mean Duration [Sec]	27
Mean Desaturation [%]	85	Mean Desaturation [%]	88
Mean Saturation [%]	88	Mean Saturation [%]	91
Max. Saturation [%] (03:20:09)	96	Max. Saturation [%] (05:31:21)	96
Min. Saturation [%] (20:24:38)	95	Min. Saturation [%] (05:24:06)	98
SO <sub>2</sub> [%]	57	SO <sub>2</sub> [%]	41
Min. Pulse (20:31:31) [1/min]	23	Min. Pulse (05:15:15) [1/min]	54
Max. Pulse (20:24:41) [1/min]	100	Max. Pulse (22:02:34) [1/min]	80
Mean Pulse [1/min]	70	Mean Pulse [1/min]	66
Pulse variances [n]	605	Pulse variances [n]	85
Pulse variance index [Per hour]	13.8	Pulse variance index [Per hour]	5.1

Figure 1



Figure 2

**Design and method:** A 60-year-old man with cardiovascular risk factors (hypertension, diabetes, dyslipidemia, obesity, transient ischemic attack) presented to the outpatient clinic with high values of self-monitoring blood pressure despite multiple lowering blood pressure therapy. On physical examination his body mass index was 39.6 kg/m2, neck circumference 50 cm. The ECG was in sinus rhythm with hypertrophic phenotype confirmed by echocardiogram, which also showed left ventricle preserved ejection fraction, grade III diastolic dysfunction, mildly enlarged left atrium. Laboratory tests excluded endocrinologic and renal causes. Despite lifestyle changes and a good adherence to multiple associated antihypertensive treatment, ABPM revealed a non-dipper profile (dipping index 4.86%) (figure 1). The patient underwent the polygraphy test which showed the apnea-hypopnea index (AHI) of 10.6, which led to a diagnosis of mild sleep apnea, the t90% of 57 pointed out severe hypoxia and high pulse variances 104 (figure 1). The further Holter monitoring revealed episodes of atrial flutter and atrial fibrillation.

**Results:** After 3 months of continuous positive airways pressure (CPAP) therapy, on top of the same antihypertensive drugs and anticoagulation, led to optimal blood pressure values and normal ABPM profile (figure 2). The polygraphy parameters AHI, t90% and pulse variances normalised too. (figure 1)

**Conclusions:** Obstructive sleep apnea is a prevalent secondary cause of hypertension and atrial arrhythmias, still greatly underdiagnosed. It is associated with abdominal obesity, large neck, snoring, daytime fatigue and a decrease in the quality of life. Polygraphy is a feasible method for diagnose sleep apnea and monitoring the treatment. CPAP treatment abolishes apnea, normalises blood oxygenation thereby prevents arterial pressure surges, restoring the nocturnal 'dipping' pattern and normal sinus rhythm.

**ASSESSMENT OF MACROPHAGE INFLAMMATORY ACTIVITY ON VISCERAL ADIPOSE TISSUE IN HIGH-FAT DIET-INDUCED OBESE MICE BY 18F- FDG PET/CT**

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**Objective:** Obesity induced inflamed visceral adipose tissue (VAT) secretes pro-inflammatory cytokines thereby promoting systemic inflammation and insulin resistance which further exacerbate obesity-related cardiovascular disease (CVD).