

**C486****HEART RATE VARIABILITY MODIFICATIONS INDUCED BY IVABRADINE THERAPY**

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**Objectives.** Ivabradine is a novel antianginal agent that reduces heart rate by directly affecting spontaneous sinus node depolarization. We developed this study in order to investigate whether ivabradine had an effect on heart rate variability (HRV), an expression of sympathovagal drive on the heart.

**Methods.** Eleven subjects, aged 71-83, affected by chronic stable angina that had contraindications to  $\beta$  blockers were recruited. Before beginning ivabradine therapy we collected 30-minute continuous ECG recordings in the supine position in a quiet room at a constant temperature, with an ECG Holter device. The same protocol was applied one month after the beginning of treatment (ivabradine 7.5 mg twice daily orally). Data were collected and analyzed according to 1996 guidelines of the task force of The European Society of Cardiology and The North American Society of Pacing and Electrophysiology. Data were analyzed both in time and frequency domain, to obtain a wide array of HRV measurements.

**Results.** Ivabradine reduced heart rate (-15.2%,  $p < 0.01$ ). The most relevant modifications of HRV we observed were an increase of variability in time domain (RMS SD +37.6%,  $p < 0.05$ ), an increase of short-term parameter of Poincaré plot (SD1 +37.5%,  $p < 0.05$ ) without a significant modification of long term variability (SD2 +28.6%) and an increase of the vagal component of sympathetic balance in the frequency domain (LF normalized units -23.2%,  $p < 0.01$ ; HF normalized units +69.9%,  $p < 0.01$ ; LF/HF 42.5%,  $p < 0.05$ ).

**Conclusions.** Previous studies demonstrated that acute administration of ivabradine on healthy human subjects induces a vagal shift on autonomic control of the heart (reduction of LF/HF ratio), and that continuous therapy induces an increase of heart rate variability on post-ischemic severe heart failure in rats. Our preliminary data, if confirmed in a wider population, could demonstrate that HR reduction by ivabradine might downregulate sympathetic activity, leading to beneficial effects on left ventricular (LV) remodeling and preventing worsening of LV dysfunction.

**C487****EFFECTS OF PHYSIOTHERAPY (PHASE I OF CARDIAC REHABILITATION) ON HEART RATE VARIABILITY OF PATIENTS WITH ACUTE MYOCARDIAL INFARCTION**

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**Background.** Heart rate variability (HRV) decreases after an acute myocardial infarction (AMI) due to changes in cardiac autonomic balance.

**Objective.** Thus, the purpose of the present study was to evaluate the effects of cardiovascular physiotherapy (CPT) on HRV of inpatients with AMI.

**Methods.** Thirty-seven patients were studied. All of them presented first non-complicated AMI, were hemodynamically stable and used conventional medications. The control group (CG,  $n=16$ , age= $54 \pm 11$  years) did not receive CPT but its HRV was evaluated every day until hospital discharge, while the treated group (TG,  $n=21$ , age= $52 \pm 12$  years) received 5 days of CPT. The progression in the CPT protocol, that included periods of rest in supine position, respiratory exercises and dynamic physical exercises performed in different positions, was done based on the daily clinical evaluations of each patient. Instantaneous heart rate (HR) and R-R interval were acquired by a HR monitor (Polar<sup>®</sup>, S810i). The HRV was analyzed by frequency domain methods. The power spectral density was expressed as normalized units (nu) at low (LF) and high (HF) frequencies, and as LF/HF.

**Results.** After 5 days of application of the CPT, only the TG showed increase of HFnu ( $35.9 \pm 19.5$  to  $65.19 \pm 25.4$ ) and decrease of LFnu and LF/HF ( $58.9 \pm 21.4$  to  $32.47 \pm 24.1$ ;  $3.12 \pm 4.0$  to  $0.96 \pm 1.5$ , respectively) ( $p < 0.05$ ) in resting conditions.

**Conclusions.** The CPT associated with clinical intervention, carried out in the phase I of the cardiac rehabilitation, increased vagal and decreased sympathetic modulation in resting condition.

**C488****THE LOSS OF HEART RATE CIRCADIAN RHYTHM AS A CLINICAL SIGN OF THE SO-CALLED "SILENT CARDIAC DYSAUTONOMIA"**

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**Aim.** To perform an early diagnosis of "silent (S) cardiac dysautonomia (CD)" by utilizing very high-sensitive and non-invasive techniques for exploring cardiac pacing via abnormalities of blood pressure (BP) and heart rate (HR) circadian rhythm (CR) investigated by mean of ambulatory (A) BP monitoring (M).

**Materials and methods.** The study was performed on 10 cases (mean age  $41 \pm 9$ ; 7M, 3F) and 29 cases (mean age  $73 \pm 6$ ; 17M, 13F), of, respectively, type 1 and type 2 diabetes mellitus (DM), patients who are notoriously prone to dysfunctions of the neurovegetative system (NVS). Thirty clinically healthy subjects (mean age  $50 \pm 10.8$ ; 20M, 10F) were studied as control group. None of the diabetic patients (DP) was symptomatic for a clinically manifest CD. The ABPM was performed in a working day according to the following common rules: awaking (06:00; 07:30), breakfast (06:30; 08:00), lunch (12:30; 14:00), dinner (19:30; 21:30), sleeping (22:00; 23:00). Single-cosinor, followed by population mean-cosinor, were the chronobiometric method for documenting the systolic (S) BP, diastolic (D) BP and HR CR.

**Results.** Table 1 displays the chronobiological results from which it is clearly visible that only in type 1 diabetic patients there is a documentable loss of HR CR associated with a "wandering amplitude".

**Conclusion.** Considering that HR, contrarily to BP, is regulated by the influence of the NVS on sinus node, it can be driven that the lack of HR CR in type 1 DP, the more prone to neurovegetative disorders, can be referred as an indisputable sign of SCD.

**Table 1.** Rhythmic analysis by means of population mean-cosinor of systolic (S), diastolic (D) blood pressure (BP) and Heart Rate (HR) as measured via ABPM in clinically healthy subjects and type 1 and type 2 diabetic patients.

| Rhythmic parameters                    | Clinically healthy subjects |                      |                      | Type 1 diabetic patients |                      |                     | Type 2 diabetic patients |                      |                      |
|--|-----------------------------|----------------------|----------------------|--------------------------|----------------------|---------------------|--------------------------|----------------------|----------------------|
|  | SBP (mmHg)                  | DBP (mmHg)           | HR (bpm)             | SBP (mmHg)               | DBP (mmHg)           | HR (bpm)            | SBP (mmHg)               | DBP (mmHg)           | HR (bpm)             |
| Statistical significance of rhythm (p) | <0.001                      | <0.001               | <0.001               | 0.043                    | 0.005                | 0.124               | <0.001                   | <0.001               | <0.001               |
| Mean oscillatory level (MESOR)         | 106±1                       | 64±1                 | 73±2                 | 130±4                    | 86±4                 | 82±3                | 136±3                    | 92±2                 | 74±2                 |
| Mean oscillatory amplitude             | 9 (7; 11)                   | 9 (8; 10)            | 11 (8; 13)           | 7 (1; 19)                | 8 (2; 20)            | 8 (2; 21)           | 8 (5; 11)                | 7 (5; 9)             | 7 (5; 9)             |
| Mean oscillatory acrophase (hh:mm)     | 14:52 (14:04; 15:36)        | 14:20 (13:36; 14:56) | 14:44 (14:00; 15:20) | 14:20 (10:16; 21:08)     | 12:52 (11:56; 21:08) | 14:08 (0:00; 21:08) | 13:20 (11:36; 14:44)     | 13:48 (12:28; 14:48) | 14:48 (13:52; 15:52) |

MESOR = mean  $\pm$  SEM; Amplitude and Acrophase = mean (95% CL).

**Imaging cardiovascolare****C489****LEFT ATRIAL VOLUME ENLARGEMENT IN 515 EITHER ENDURANCE OR STRENGTH COMPETITIVE ATHLETES**

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**Background.** Increase of left atrial (LA) diameter in trained athletes has been regarded as another component of the "athlete's heart". However, the prevalence of LA volume enlargement in competitive athletes is still unresolved.

**Aim of the study.** To evaluate the possible impact of competitive training on LA volume and to define reference values of LA volume index in athletes.

**Methods.** The study population included 515 subjects: 320 endurance-trained athletes (ATE) and 195 strength-trained athletes (ATS) (380 males; mean age  $24.3 \pm 15.6$  years; range: 18-40). LA maximal volume was measured at the point of mitral valve opening using the biplane area-length method, and corrected for body surface area. LA mild dilatation was defined as a LA volume index  $\geq 29$  ml/m<sup>2</sup>, while a moderate dilatation was identified by a LA volume index  $\geq 34$  ml/m<sup>2</sup>.

**Results.** Left ventricular (LV) mass index and ejection fraction did not significantly differ between the 2 groups. However, ATS showed increased sum of wall thickness (septum + LV posterior wall), LV circumferential end-systolic stress (ESSc) and relative wall thickness, while LV stroke volume and LV end-diastolic diameter were greater in ATE. The range of LA volume index was 25 to 36 ml/m<sup>2</sup> (mean  $27.5 \pm 9.2$ ) in men and 23 to 33 ml/m<sup>2</sup> (mean  $26.5 \pm 7.2$ ) in women. LA volume index was mildly enlarged in 101 athletes (19.5%), and moderately enlarged only in 14 (2.6%). Mild mitral regurgitation was observed in 47 athletes (9.5%). LA volume index was significantly greater in ATE. By multiple