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### Gene-based $\beta$ -blocker therapy for long-QT syndrome type 2: comparison between Nadolol and Propranolol

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**Background:** Nadolol is recently preferred as a specific  $\beta$ -blocker for patients with long-QT syndrome type-2 (LQT2). However, it is still unclear why nadolol is superior than other  $\beta$ -blockers in suppression of QT interval prolongation and subsequent arrhythmias during acute sympathetic stress.

**Methods:** This study enrolled 13 consecutive LQT2 patients (10 female) who had been administered nadolol (30–60mg/day) as a de-novo treatment (n=6) or replaced by other  $\beta$ -blockers such as propranolol (n=5), bisoprolol (n=1) and atenolol (n=1) due to syncope events. Seven patients underwent epinephrine test (bolus:0.1 $\mu$ g/kg follow by continuous injection:0.1 $\mu$ g/kg/min) before (no- $\beta$ -blocker) and after propranolol and switched to nadolol.

**Results:** Epinephrine-test significantly prolonged the QTc interval ( $\Delta$ QTc= +62+/-63ms) at no- $\beta$ -blocker, in contrast, either nadolol (n=7) or propranolol (n=2) completely suppressed, or rather shortened the QTc interval ( $\Delta$ QTc: -64+/-39ms and -92+/-11ms, respectively). Moreover, no significant difference was observed in the  $\Delta$ QTc between propranolol and nadolol. On the other hand, 7 of 13 (54%) had syncope attack in spite of taking  $\beta$ -blockers except nadolol. However, although a short-term follow-up periods (203 (79–352) days), no events occurred and the baseline QTc interval was significantly shortened after nadolol (491+/-39 to 447+/-23ms, p<0.01).

**Conclusions:** Nadolol and propranolol have a similar protective effect against the acute sympathetic stimulation, however, nadolol may have a potent superiority in abbreviation of QTc interval and suppression of arrhythmic events in LQT2.

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### Nonlinear parameters of heart rate variability and detection of high risk patients after myocardial infarction based on artificial intelligence analysis

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**Background:** Data mining using data driven learning model is widely used in almost all fields of scientific research, including medicine.

**Goal:** The main aim is to assess predictive value of nonlinear parameters of heart rate variability using using classical statistical analysis and artificial intelligence in order to reveal the best approach of analysis.

**Methods:** In our study 1705 patients were included, 286 (16.77%) died from all cardiac causes. We analyzed next nonlinear parameters: Hurst exponent (H), Approximate entropy (ApEn), SD1 index of Poincare plot (SD1), SD2 index of Poincare plot (SD2), Sd1/Sd2 ratio, Alpha 1 index (Alpha 1), Alpha 2 index (Alpha 2), age and gender. All parameters were extracted from Task force system with real beat to beat analysis (Graz, Austria). Multilayer Perceptions (MLP), performing supervised learning technique (backpropagation). The training is performed at 50% of the examples (911) and the model is tested for 910 of the remaining examples.

**Results:** The separately impact of each variable was in values: Hurst exponent (H) (6.9349) Approximate entropy (ApEn) (6,1641), SD1 index of Poincare plot (SD1) (2,5351), SD2 index of Poincare plot (SD2) (16,3996), Sd1/Sd2 ratio (17,5156), 1Alpha 1 index (Alpha 1) (1,9395), Alpha 2 index (Alpha 2) (3,7857), age and gender. Final conclusion was that strongest predictors were Sd1/Sd2 ratio and Sd2 index, practically the same results using survival analysis (Cox regression and Kaplan Meier analysis). Classification on the test sample was unexpectedly accurate with highly reliable discrimination of high risk patients after myocardial infarction and patients without risk.

**Conclusion:** The model-based MLP structure of artificial intelligence is very strong mathematical approach in risk stratification in combination with standard statistical procedures with advantage to create system of analysis without errors.

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### Comparison of the Influences for Autonomic Tone between Cryo-balloon and Hot-balloon Ablation for Paroxysmal Atrial Fibrillation

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**Background:** Previous studies suggested that cryo-balloon ablation (CBA) for paroxysmal atrial fibrillation (PAF) influences ganglionated plexi (GP) in epicardial fat pad. Therefore, heart rate variability (HRV) changes after procedure. However, the effect for HRV by hot-balloon ablation (HBA) has not been investigated.

**Objective:** The aim of this study is to compare the influences for autonomic tone after CBA and HBA procedure.

**Methods:** Twenty seven patients (68.0 $\pm$ 9.7 year old, 20 male) who performed pulmonary vein isolation (PVI) for PAF and underwent

24-hour Holter recording before and after procedure were enrolled. PVI was performed by CBA (CBA group: n=15) and by HBA (HBA group: n=12). Touch up radio frequency application was performed in case pulmonary vein potential remain after balloon ablation. Frequency-domain HRV parameters were analyzed based on maximum entropy method and compared in each groups.

**Results:** The PVI was achieved at the end of session in all patients. In CBA group, LF components, LF/HF ratio and heart rate (HR) were significantly changed before and after procedure ( $-226.0 \pm 244.4$ ;  $p = 0.03$ ,  $-1.67 \pm 1.41$ ;  $p < 0.01$ ,  $4.19 \pm 7.23$ ;  $p = 0.04$ ). However, HF components were reduced after procedure, though the difference was not statistically significant ( $-37.0 \pm 152.0$ ;  $p = 0.36$ ). In HBA group, LF and HF components were significantly changed before and after procedure ( $-122.8 \pm 183.7$ ;  $p = 0.04$ ,  $-39.4 \pm 54.2$ ;  $p = 0.02$ ). Meanwhile, LF/HF ratio and HR were less affected ( $-0.62 \pm 1.40$ ;  $p = 0.15$ ,  $2.39 \pm 7.00$ ;  $p = 0.26$ ).

**Conclusion:** HBA may not affect sympathetic nerve activity after procedure.

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### Evaluation of the mortality in patients with atrial fibrillation in a large electronic cohort: Clinical Outcomes in Digital Electrocardiography (CODE) study

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**Introduction/Background:** Atrial fibrillation (AF), a major abnormality of ECG, is a public health problem with increasing prevalence as the population ages, associated with cardiovascular mortality and morbidity. We evaluated the prognostic value of the presence of AF in 12-lead ECG in a large electronic cohort.

**Methods:** This is an observational retrospective study, developed using the database of digital ECGs from the Telehealth Network of Minas Gerais (TNMG). The TNMG is a large public Brazilian telehealth system that provides tele-ECG services for more than 780 municipalities, mostly to Primary Health Centers. For this study, all ECGs from patients of at least 10 years-old from 2010 to 2016 were assessed. The electronic cohort was obtained linking data from the ECG exams and those from the national mortality information system, using standard probabilistic linkage methods. From a dataset of 1,976,709 available ECGs, 1,600,948 patients with ECGs were obtained, after exclusion of invalid and repeated exams. Clinical data were self-reported, and ECGs were interpreted by a team of trained cardiologists using standardized criteria.

**Results:** The mean (SD) age of the sample was 52.76 (19.48) years, 41% male. The mean follow-up was 3.5 years with 44,523 (2.78%) deaths for all causes. The prevalence of AF was 1.26% overall with mortality rate of 11.48%. In univariate analysis, patients with AF had increased risk of death for all causes (HR 4.07; CI 95% 3.91 – 4.25). After adjusting for sex and age, AF remains related to increased risk of death (HR 2.31; CI 95% 2.22 – 2.41). Male sex was a predictor of death risk in AF patients (HR 1.7; CI 95% 1.66 – 1.72).

**Conclusions:** Electronic cohort are useful in the determination of the prognostic value of electrocardiographic abnormalities. In our study, AF was a strong predictor of mortality for all causes in primary care population.

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### Modulation of Autonomic Response and Atrial Conduction after Cryoablation versus Radiofrequency Ablation for Paroxysmal Atrial Fibrillation

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**Background:** Cryoablation (CRYO) has emerged as an alternative to radiofrequency catheter ablation (RFCA) for the treatment of paroxysmal atrial fibrillation (PAF). The purpose of this study was to investigate the influence of cardiac autonomic system and atrial late potential (ALP) modulated by CRYO or RFCA during 6 months follow-up.

**Methods:** Thirty consecutive patients with PAF of non-structural heart disease underwent CRYO (n=15) or RFCA (n=15) for PV isolation. Heart rate variability (HRV) and deceleration capacity (DC), and ALPs were examined by high resolution ambulatory ECG (HR-ambulatory ECG) before ablation and after, 1 month and 6 months following ablation.

**Results:** Eleven (73%) in CRYO group and 12 patients (80%) in RFCA group were free from PAF during 6 months after procedure ( $p = n.s.$ ). SDANN of HRV and DC significantly decreased after 1 month in both groups. These changes reversed toward values as baseline at 6 months in CRYO group, however maintained inhibiting as an adornment in RFCA group. P-wave duration of ALP increased after CRYO at 1 month, while changed toward values of baseline at 6 months. The changes of ALP were not observed in RFCA group.

**Conclusions:** PV isolation for PAF by CRYO is as effective as RFCA until 6 months. The analysis by using the HR-ambulatory ECG indicated the difference of time-course modulations in parasympathetic autonomic response and atrial conduction delay between CRYO and RFCA procedure. Longer follow-up more than 6 months should be needed to evaluate whether these differences are associated with a recurrence rate of PAF after ablation.

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### Signal-averaged Electrocardiograph Can Evaluate Citrate Response and Vasovagal Reflex During Apheresis Donation

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**Background:** Adverse event of apheresis donation include citrate response and vasovagal reflex (VVR). Hypocalcemia may relate in the citric acid reaction, and there is a possibility of arrhythmia induction. We verified a risk for citric acid reaction and VVR. Our hypothesis is that QTc interval may reflect citrate response, and signal-averaged electrocardiograph (ECG) may be valuable for verifying a pathophysiology of VVR.

**Methods:** The subjects were 69 consecutive subjects who received platelets apheresis donation using bowl type blood collection equipment. All ECG data were recorded during apheresis donation all steps (4 to 5 cycles) from before puncture until after needle-drawn. This examination was approved by ethics committee (No.2016-027). We analyzed heart rate (HR), sympathetic nerve activity (LF/HF), QTc interval using signal-averaged ECG, and processed blood volume and amount of ACD-A solution.

**Results:** HR was  $70 \pm 10$  bpm at control, and  $78 \pm 10$  bpm at 4 cycles ( $p < 0.001$ ). LF / HF was  $1.0 \pm 0.2$  at control, and  $1.3 \pm 0.3$  at 4 cycles ( $p < 0.01$ ). QTc time was  $398 \pm 15$  ms at control,  $417 \pm 14$  ms at 4 cycles ( $p < 0.001$ ). There was a positive correlation trend between ACD-A amount and QTc difference ( $p = 0.016$ ). In 4 donors,