96-77

PHENOTYPIC SPECTRUM OF HCN4 MUTATIONS: FURTHER EVIDENCE OF INVOLVEMENT IN LEFT VENTRICULAR NON-COMPACTION, SICK SINUS SYNDROME, AND MOOD- AND ANXIETY DISORDER

Helge Servatius[1], Stephan A. Pless[2], Andre Schaller[3], Timothy Lynagh[2], Hildegard Tanner[1], Claudine Rieubland[3], Laurent Roten[1], Jens Seiler[1], Fabian Noti[1], V. Nam Tran[1], Andreas Haeberlin[1], Anna Lam[1], Sabina Gallati[3], Juerg Fuhrer[1], and Argelia Medeiros Domingo[1]

[1]Department of Cardiology, Inselspital, Bern University Hospital, Switzerland; [2]University of Copenhagen, Denmark; and [3]Department of Pediatrics, Inselspital, Bern University Hospital, Switzerland

Introduction: Mutations in *HCN4* have been reported in patients with bradycardia, sick sinus syndrome, left ventricular non-compaction cardiomyopathy and mood and anxiety disorders. We present here the clinical and functional characterization of 2 novel *HCN4*-pore mutations in a 45 y old man who exhibits all of the above phenotypes and vulnerability to ventricular fibrillation.
Methods: After obtaining informed consent, DNA was extracted from peripheral blood. Clinical exome was performed using the TrueSight One Sequencing Panel (Illumina, San Diego, CA; USA) which includes 4,813 genes associated with known clinical phenotypes. Fifty genes previously associated with cardiac channelopathies were analyzed. Read alignment and local realignment of indels was performed using CLC Workbench v7.5.1. Variant prediction was done using Polyphen2, SIFT and Mutation Taster and the following databases were used for data interpretation: human gene mutation database (HGMD, Biobase), 1000 genoms and ExAC browser. The HCN4-associated mutations were incorporated by site-directed mutagenesis and injected into *Xenopus laevis* oocytes for functional chraracterization using the two-electrode voltage-clamp technique.
Results: Two novel mutations in the *HCN4*-gene were found: c.1454C > A (p.Ala485Glu) and c.1435A > G (p.Ile479Val). Both variants are present in the same reads suggesting that they are *in cis* c.[1454C > A; 1435A > G] . They both localize to the pore region of the channel and were predicted to be pathogenic by SIFT, Polyphen2, Mutation Taster and were absent in HGMD, 1000 genomes and ExAC Browser encompassing >60,000 sequenced whole exomes.
Cells expressing the *HCN4*-A485E mutation exhibit significant changes in voltage-dependent gating, while *HCN4*-I479V has little effect on channel function.
Conclusion: *HCN4* mutations confer a variable expression of diseases, characterized by the previously described bradycardia, sick sinus syndrome, left ventricular non-compaction cardiomyopathy, mood and anxiety and newly described susceptibility for ventricular arrhythmias.
Conflict of interest: none

96-78

TITLE: HEART RATE OF SUPPORTERS DURING FIFA WORLD CUPS

Fabrice Demoniere[1], and Choquet Dominique[2]

[1]fort de france, France; and [2]Noumea, New Caledonia

Introduction: 102 fans of different national football teams participate in a simple, non-binding study devoted to football supporters during the last three FIFA world cups. We studied changes occurring in heart rate during football matches, taking into account both the cardiovascular risk factors of the participants, and the relative importance of the match as first round, last sixteen to semi finale, and finale.
Methods: Data were prospectively collected in 102 patients between june 2006 and july 2014 during the last three FIFA world cup of football. Participants were 18 to 62 years old.
Heart rate and cardiac events were recorded in the 10 minutes before and during the match using a five derivations Holter ECG monitoring device (Searlight GE and Spiderview Sorin Group). Cardiovascular risk factors, medications and score of passion were also recorded.
Results: Average heart rate significantly increased during the matches (mean change 30 beats per minutes, p= 0.02). The maximum heart rate reached 95% or more of the maximal heart rate for age in 80% of the participants. Supra ventricular ectopic beats and paroxymal atrial fibrillations were observed in 10 subjects (9.8%).
In bivariate analysis, goals, faults, supported team's victory, relative importance of the event and higher scale of passion were positively associated with average heart rate during matches and with cardiac events (all p < 0.05) (all p <0.05).
Conclusions: During football competitions in World cup, supporters experience abrupt increases in heart rate, which compare to changes expected in maximal treadmill exercise tests, what should be taken into account, especially for those with overt cardiac diseases, or high global cardiovascular risk.
Table 1:Maximal heart rate of supporters during the last three World Cups of football (percentage refers to maximal theoretical heart rate).

	World Cup 2006 N = 22	World Cup 2010 N = 30	World Cup 2014 N = 50
Final	190 /min (94%)	180/ min (90%)	182 / min (92%)
Semi-final	170/ min (85%)	162/min (84%)	169/min (86 %)
Last sixteen to quarter	158/ min (83%)	152/min (78%)	168/min (88%)
First round	130/min (70%)	140/ min (82%)	146/min (78%)

Conflict of interest: none

96-79

EVALUATION OF VENTRICULAR ARRHYTHMOGENESIS IN CHILDREN WITH AORTIC STENOSIS

Cem Karadeniz, Demirol Mustafa, Rahmi Ozdemir, Senay Coban, Timur Mese, and Nurettin Unal

Izmir, Turkey

Objective: As Tp-e interval, Tp-e/QT ratio is also used as an index of ventricular repolarization. Prolongation of Tp-e interval and increased Tp-e/QT ratio have been found associated with malignant ventricular arrhythmias. Although, these parameters have been studied in adult patients. The novel repolarization indexes Tp-e and Tp-e/QT have not been studied among children with aortic stenosis (AS) previously. The aim of this study was to evaluate Tp-e interval and Tp-e/QT ratio in children with AS.
Methods: The standard 12-lead electrocardiograms of 66 children with aortic stenosis and 58 age-and-sex matched healthy children were assessed by a blinded specialist.
Results: Tp-e interval, Tp-e/QT and Tp-e/QTc ratios, QTc and QT dispersions were found significantly higher in AS group compared to healthy subjects. When AS patients were compared according to degree of aortic stenosis (mild, moderate and severe). Tp-e interval, Tp-e dispersion, QT dispersion, Tp-e/QT and Tp-e/QTc ratios were found higher in severe AS group (Table 2).
Conclusions: Our study showed that Tp-e interval, Tp-e/QT and Tp-e/QTc ratios, QTc and QT dispersions were increased in children with AS and these parameters are related to the severity of Aortic stenosis. These ventricular repolarization parameters may be used as a prognostic factor in these group of patients Further prospective studies are needed for demonstrating the clinical importance of these parameters.
Table. Electrocardiographic characteristics of the AS patients

	Mild AS (n = 14)	Moderate AS (n = 42)	Severe AS (n = 10)	P
Age*	7.5 (13.7)	6 (10)	6.5 (10.8)	0.83
Gender (M/F)	9/5	33/9	7/3	0.54
Tp-e interval (ms)	71.4 ± 18.7	97.3 ± 13.6	111 ± 11.9	<0.001
Tp-e interval dispersion* (ms)	10 (16.2)	34 (10)	60 (12)	<0.001
QT dispersion (ms)*	10 (5.2)	35 (12)	48 (11)	<0.001
QTc dispersion (ms)*	8 (7)	30 (13.5)	49.5 (12.5)	<0.001
Tp-e /QT	0.22 ± 0.05	0.29 ± 0.03	0.36 ± 0.03	<0.001
Tp-e/QTc, mean ± SD	0.17 ± 0.05	0.25 ± 0.03	0.29 ± 0.01	<0.001

Conflict of interest: none

96-80

INCIDENCE OF ADVERSE EVENTS AT 7, 30 Y 90 DAYS IN COLOMBIAN PATIENTS WITH SYNCOPE ACCORDING TO RISK SCORE EGSYS

Guillermo Mora, and Alejandro Olaya

Bogotá, Colombia

Objective: To describe the incidence of adverse events at 7, 30, 90 days in patients with syncope who have applied the risk scale EGSYS.
Materials and method: A cohort study was conducted; the two comparison groups were patients at high and low risk according to EGSYS scale who consulted the emergency department of five hospitals in Colombia with diagnosis of syncope. At the time of the consultation a complete history of which data were obtained for a score and classification according to EGSYS scale; then were followed up at 7, 30, and 90 days for assessment of adverse events.
Statistical analysis: qualitative variables were described by absolute and relative frequencies and quantitative variables by means and standard deviations. Once patients at high and low risk were classified, the cumulative incidence of adverse events (death, re-hospitalization, recurrence, invasive cardiac procedures and neurological events) was calculated and compared between groups using relative risks and Multiple Correspondence Analysis (MCA). Additionally, the frequency of adverse events according to the score obtained on the scale was described.
Results: We included 173 patients with a median age of 69 years (IQR 50-80 years old); 57.8% were women. The clinical variable considered in the most common were the absence scale EGSYS prodrome and abnormal ECG. The most frequent scores were above 2; 60% of patients were classified at high risk. The incidence at 90 days of follow-averse events was 42 % for high-risk group and 21 % in the low risk group (RR 1.94, 95% CI 1.17 to 3.21); The main events were cardiologic interventions (26.9 % versus 10.1%) being higher in the high risk group (RR 2.6 IC 95% 1.22 to 5.73) This association was also observed in the MCA. The non-parametric analysis showed significant differences between the high and low risk curves at 90 days (p = 0.013); Cox regression showed increased risk for any adverse events in the group of patients with greater than or equal to 3 score (HR = 2.05, 95% CI 1.14 to 3.70). This association was also observed in the ACM.
Conclusions: The classification of risk score EGSYS applied to patients with syncope is related to the incidence of adverse events at 90 days follow-up. The Egsys score can assist decision-making on inpatient or outpatient management and the rational use of diagnostic aids.
Conflict of interest: none