ABNORMAL QT DYNAMICS AND NOCTURNAL TEMPORAL QT DISPARITY IN BRUGADA SYNDROME

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In Brugada syndrome (BS), controversy exists about mechanism of ventricular arrhythmia and for risk stratification. In 41 patients with structurally normal hearts and BS showing BS pattern, we assessed heart rate variability (HRV), temporal QT dispersion (QTD) and QT dynamics on 24h ambulatory ECG. Type 1 BS pattern was present in 34/41 patients and type 2 in 7/41. The QT intervals were measured automatically with a Holter system. QT dynamics was related to measurement of QT/RRI slopes over 24h and during daytime and nighttime.

History of syncope was present in 16/41 patients (39%). Late ventricular potentials were present in 21/41 patients (51%). Stimulated induction of polymorphic ventricular tachycardia in 12/41 (29%). Compared to a control group matched for sex and age, HRV was slightly decreased during nighttime in BS while all QT/QRR slopes were markedly decreased (24h: -32%, daytime: -31%, nighttime: -40%, p range 0.003 to <0.0001). QT/RRI slopes were similar between symptomatic and asymptomatic patients. By contrast, nighttime QTD was higher in symptomatic BS patients compared to asymptomatic ones (14.1±6.2 ms vs 9.9±2.0 ms, p=0.003).

Conclusion: BS is associated with lower QT/RRI slopes. Moreover, high risk patients had an increased nocturnal QTSD. These unique repolarization dynamics may be related to the frequent occurrence of VF episodes at night.

BRUGADA-LIKE ECG FINDINGS DETECTED AFTER RESECTION OF ESOPHAGEAL CANCER

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We have observed 3 cases of Brugada like ECG findings after the resection of esophageal cancer. Case 1. A 63 year-old male, who had paroxysmal AF and esophageal cancer, was operated with transhiatal ablation (AF) was diagnosed as affected by esophageal cancer and underwent the resection of esophagus with subsequent reconstruction using stomach into retro-sternum. Post-operative ECG showed coved type ST elevation in lead V1. This finally gradually reverted in ten days after operation and normalized within 2 weeks. Case 2. A 69 year-old male, who had paroxysmal AF and esophageal cancer, received the same procedure as in case 1. His ECG revealed abnormal ST elevation in V3. In thoracic CT image, right ventricle (RV) was compressed by the reconstructed stomach. Case 2. A 68 year-old male underwent the same operation as described above. His post-operative ECG showed Brugada like ST elevation in V1. This ST change disappeared within 3 weeks. In none of these 3 cases, there was a family history of sudden death or syncope, and the previous ECG showed no ST segment elevation. The compression of the RV by lifted stomach was considered to induce the preordial ST elevation mimicking Brugada syndrome.

FEMALE GENDER IS A RISK FACTOR FOR DRUG-INDUCED LONG QT AND EARLY AFTERDEPOLARIZATIONS (EADs) IN ANESTHETIZED DOGS


Clinical observations and experimental data in isolated rabbit and dog Purkinje fibers and in vivo in rabbits indicate that female gender is more sensitive to drug-induced long QT and cardiac arrhythmia. However, to-date there has been no demonstration of a gender difference in vivo in dogs and therefore male dogs tend to be the chosen sex for cardiovascular safety pharmacology tests. As such, this may potentially lead to wrong conclusions on the QT-related arrhythmogenic risk of a new chemical entity.

Methods and Results: We evaluated potential gender differences in the following variables, in neuromuscular blocked, mechanically ventilated anesthetized dogs: ventricular repolarization (ECG lead II, QT and QTcV; right ventricular endocarade monoatomic action potential (MAP), duration at 90% repolarization, APD90, and APD90cV), spatial dispersion of the T wave (Tp-Te), instability of QTend (QT TI: total instability) and occurrence of EADs on the MAP signal. These parameters were derived from continuous recording of ECG and MAP signals. 20 female and 18 male dogs were treated with dofetilide (0.05 mg/kg i.v. infusion over 10 min). At baseline, there was no statistically significant gender difference observed in the values of the various parameters, while dofetilide infusion produced marked prolongation. Median maximum percentage changes of baseline in females versus males were respectively: heart rate (+3% / +6%, ns), QT (+23% / +14%, p=0.003), QTcV (+20% / +15%, p=0.03), APD90 (+26% / +17%, p=0.006), and APD90cV (+24% / +18%, p=0.009). In addition, dofetilde tended to differently increase Tp-Te (+40% / +23%, ns) and QT TI (+150% / +104%, ns), more in female than in male animals.

Furthermore, dofetilde infusion elicited more incidences of EADs on the MAP signal in female than in male dogs (73% versus 48%).

Conclusion: The present study confirms that female gender may be a risk factor for drug-induced long QT in the dog. Indeed, since significant alterations in additional markers beyond QT interval itself are more pronounced in female dogs and EADs occur more frequently in this sex, female dogs could be more sensitive to induction of polymorphic ventricular tachycardia (TdP). As such, consideration should be given to incorporation of female dogs into standard cardiovascular safety evaluations, or at least the chosen single sex for drug safety evaluation for the identification of QT/TdP related adverse effects.

ELECTROANATOMIC VOLTAGE MAPPING IN ARRHYTHMOGENIC RIGHT VENTRICULAR CARDIOMYOPATHY

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Background: Electroanatomic (EA) voltage mapping of the right ventricle (RV) by CARTO System has recently been proposed as a new diagnostic tool to identify dysplastic regions in patients affected with arrhythmogenic right ventricular cardiomyopathy (ARVC). Three-dimensional reconstruction of endocardioatrophic distribution, performed by CARTO System, would allow the identification of RV low voltage areas, reflecting fibrofatty myocardial replacement. The purpose of our study was to compare EA voltage mapping during sinus rhythm with RV non-invasive assessment in ARVC patients.

Methods: We enrolled ten consecutive patients fulfilling standardized diagnostic criteria for ARVC (age range: 28-46 years, 5 males), with indication to electrophysiological test to evaluate ventricular electrical vulnerability or to validate an empirically selected antiarrhythmic treatment. After an integrated ECHO + MRI evaluation, an invasive EA reconstruction of RV by CARTO System has recently been proposed as a new diagnostic tool to identify dysplastic regions in patients affected with arrhythmogenic right ventricular cardiomyopathy (ARVC). Three-dimensional reconstruction of endocardioatrophic distribution, performed by CARTO System, would allow the identification of RV low voltage areas, reflecting fibrofatty myocardial replacement. The purpose of our study was to compare EA voltage mapping during sinus rhythm with RV non-invasive assessment in ARVC patients.

Methods: We enrolled ten consecutive patients fulfilling standardized diagnostic criteria for ARVC (age range: 28-46 years, 5 males), with indication to electrophysiological test to evaluate ventricular electrical vulnerability or to validate an empirically selected antiarrhythmic treatment. After an integrated ECHO + MRI evaluation, an invasive EA reconstruction of RV was performed sampling multiple endocardial sites (202 +/- 61) during sinus rhythm. Voltage mapping analysis was performed with a 0.5-1.5 mV colour range setting of voltage display.

Results: in all patients voltage mapping documented very low voltage areas (<0.5 mV) consisting with transmural fibrofatty replacement. Voltage mapping demonstrated in 7 patients different degrees of involvement of RV segments and a marked dispersion of amplitude and duration values (unipolar and bipolar). Analysis of EA distribution of low voltage areas documented a