Post Pacing Abnormal Repolarization in a Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT) Family Associated with a RyR2 Mutation

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Introduction: CPVT is characterized by exercise induced ventricular arrhythmias. EPS is not known to be of value. We present a CPVT family in which post pacing abnormal repolarization during EPS was the only consistent phenotypic manifestation of RyR2 mutation carriers

Methods: A family presenting with 5 cases of SCD was evaluated using exercise, flecainide, epinephrine and adenosine provocative testing. EPS included ventricular pacing at various cycle lengths and extrastimulation using a short-long sequence. Genetic screening involved direct sequencing of *KCNQ1, KCNH2, SCN5A, KCNE1, KCNE2, CACANA1C* and *RyR2* genes.

Results: Basic QTc was in normal range (410± 33 ms). Non-invasive clinical tests were normal in the 9 patients evaluated except for exercise induced ventricular arrhythmias in 1. Six patients demonstrated a marked increase in QT and QT $_{peak\text{-}end}$ only in the first beat after cessation of ventricular pacing and/or extrastimulation (Table). All 6 were found to have a heterozygous missense mutation (M4109R) in RyR2. Two of them, presenting with aborted SCD, also had a 2nd missense mutation (I406T- RyR2). Two family members without RyR2 mutations did not display prominent post-pacing QT changes.

Conclusions: M4109R- RyR2 is associated with a high incidence of SCD. The contribution of I406T to the clinical phenotype is unclear. Arrhythmias during exercise testing, considered as the hallmark of CPVT were not present in most affected family members. Marked post pacing repolarization changes in a single beat accurately predicted carriers of M4109R- RyR2 in this family.

RyR2	Post pacing QT interval (ms)		Average increase between 1st and 2nd beat (%)	Post pacing T $_{peak\text{-}end}$ interval (ms)		Average increase between 1st and 2nd beat (%)
	1st beat	2nd beat		1st beat	2nd beat	
M4109R	**516± 31**	**355± 41**	**47± 2.1***	**195± 17**	**105± 10**	**88± 3.1***
WT	**380± 0**	**360± 14**	**5± 0.4**	**95± 7**	**85± 7**	**11± 0.1**

*$p<0.05$