Noon

1116-39 **QRS Duration Does Not Predict Occurrence of Ventricular Tachyarrhythmias in Primary Prevention Patients With Implantable Cardioverter-Defibrillators**

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Background: QRS duration (QRSd), measured on a standard ECG, correlates with total mortality risk in coronary artery disease (CAD) patients (pts) at high risk for sudden death. However, the relationship between QRSd and risk of ventricular tachyarrhythmias (VT/VF) is unclear.
Methods: PainFREE RX II (N=636) was a randomized trial comparing efficacy of anti-tachycardia pacing vs. shock therapy for fast VT (cycle length (CL) <=320msec) in pts receiving implanted cardioverter-defibrillators (ICD). Detection criteria were programmed uniformly, and available stored electrograms of VT/VF episodes were analyzed by an expert panel to verify ventricular origin of tachycardias. We correlated the QRSd on the 12 Lead ECG at study entry with occurrence of VT/VF during the trial.
Results: Of 168 CAD pts enrolled for primary prevention, 91 had QRSd <=120 msec, 77 had QRSd >120 msec. Over a mean follow-up of 11±3 months, VT/VF episodes occurred in 19/91 (21%) pts with QRSd <=120 msec vs. 17/77 (22%) pts with QRSd >120 msec. The odds of episodes in pts with QRS >120msec is 1.07 times that of patients with QRSd <=120 (95% C.I. =0.51-2.25; p=0.85). We evaluated the sensitivity and specificity of QRSd in intervals of 0 msec ranging from 70 to 200. Sensitivity is the proportion of pts experiencing VT/VF episodes above each QRSd, reported in msec. Specificity is the proportion of true negatives below each reported QRSd. The optimal combination of sensitivity (75%)and specificity (42%) was obtained at QRSd 110 msec. Among patients who had VT/VF episodes, patients with QRSd >120 msec (median 2/pt) did not have significantly more episodes than those with QRSd <=120 msec (median 1/pt) (p=0.34).
Summary: 1. There is no evidence of a difference in the proportion of patients experiencing VT/VF having QRSd >120 vs <=120 msec. 2. We found no QRSd that resulted in acceptable sensitivity and specificity in this study population.
Conclusions: 1. QRSd is not useful clinically to predict primary prevention pts who will benefit from ICDs. 2. The utility of QRSd to predict VT/VF events in patients with CAD requires further prospective evaluation.

Noon

1116-40 **Regional Distribution of Depolarization Alternans Preceding Ventricular Fibrillation Onset in a Canine Ischemic Model**

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Repolarization alternans is associated with spontaneous arrhythmias. We devised an algorithm to quantify the degree of alternans in a 4 second window and tested it on epicardial electrograms from normal and ischemic dogs during sinus rhythm. Methods: Unipolar electrograms were recorded from a 112 electrode plaque placed on the left ventricle from 21 dogs before and 3-5 minutes after ligation of the left anterior descending artery (LAD). Sites were graded into R1(no ischemia),R2 and R3 (severe ischemia). The algorithm was used to detect alternans in the QRS and ST-T segment by fitting a saw-tooth against sequential peak-to-peak QRS and T wave amplitudes. The amplitude of the best fit saw-tooth was the alternans amplitude (AA). The alternans index (AI) was computed as the ratio of the AA divided by an error term. Results: The baseline QRS and ST/T AI was 1.06 ±1.2 and 1.48±2.06 and it increased to 2.99±6.31 and 5.73 ±11.0 respectively (P<0.0001 for each) after LAD occlusion. Six dogs developed spontaneous VF during ischemia and had a higher mean QRS and ST/T AI at sites with maximal ischemia before VF onset as opposed to dogs with no spontaneous VF who had the highest AI at sites with no ischemia (Table).Conclusions: This algorithm showed that depolarization and repolarization alternans increase during ischemia. In dogs with VF depolarization alternans preceding VF originates in the ischemic zone whereas dogs without VF have more alternans in regions without ischemia. This may simplify clinical alternans measurements.

Regional variability in QRS and ST/T AI in dogs with and without spontaneous VF

	No VF			Spontaneous VF		
	R1	R2	R3	R1	R2	R3
QRS AI	3.41±9.19*	2.26±4.74	2.02±3.01	1.68±1.56	1.93±2.91	5.86±7.57†
ST/T AI	4.97±9.51*	3.68±7.61	2.88±6.01	4.27±5.75	7.23±8.26§	13.73±18.78‡

* p < 0.005 vs R2 and R3, † p < 0.05 vs. R1 and R2, ‡ p < 0.001 vs R1, § p < 0.0.001 vs R1

Noon

1116-40A **Spectrum and Frequency of Channelopathies in Near-Drownings**

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Background: Among families with clinical evidence of long QT syndrome (LQTS), a personal/family history of a swimming-triggered cardiac event is virtually synonymous for type 1 LQTS (LQT1). However, the spectrum and frequency of cardiac channel mutations is unknown when the principal presentation involves a near-drowning or drowning.
Methods: Nearly 500 unrelated patients have been referred to Mayo Clinic's Sudden Death Genomics Laboratory for LQTS genetic testing since 1997. The results of the cardiac channel gene screen that included KCNQ1 (LQT1), KCNH2 (LQT2), SCN5A (LQT3), KCNE1 (LQT5), KCNE2 (LQT6), KCNJ2 (Andersen syndrome 1), and RYR2 (catecholaminergic polymorphic ventricular tachycardia, CPVT1) were reviewed retrospectively in those patients with a personal and/or family history of an unexplained near-drowning or drowning.
Results: Approximately 7% (N=35) of the entire cohort was referred on the basis of either a personal (N=23) and/or family history (N=14) of near-drowning or drowning. Among the LQTS-causing genes, LQT1-causing mutations were identified in 21 (60%) and LQT2-causing mutations in 2 (5.7%). No mutations were identified in SCN5A, KCNE1, KCNE2, or KCNJ2. However, 8 patients (22.8%) had putative CPVT1-causing mutations involving the cardiac ryanodine receptor encoded by RYR2.
Conclusion: In contrast to previous studies that involved patients with a clinical diagnosis of LQTS, there is genetic heterogeneity associated with swimming-triggered cardiac events when a channelopathy is suspected chiefly because of a near-drowning or drowning. In this setting, LQT1 accounts for 60% of the entire cohort and comprised the vast majority of LQTS-causing genotypes (91%). To our surprise, nearly 1 out of 4 cases involving a near-drowning or drowning had a putative CPVT1-causing RYR2 mutation. CPVT and strategic genotyping of RYR2 should be considered when LQT1 is excluded in the pathogenesis of an unexplained near-drowning.