NOS1AP POLYMORPHISMS AFFECT NOS1AP RNA LEVELS IN CARDIAC TISSUE RECOVERED FROM EXTRACTED PACEMAKER AND DEFIBRILLATOR LEADS

ACC Oral Contributions
Ernest N. Morial Convention Center, Room 245
Sunday, April 03, 2011, 8:45 a.m.-9:00 a.m.

Session Title: Basic Cardiac Electrophysiology
Abstract Category: 25. Electrophysiology—Basic
Presentation Number: 901-6

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Background: There is scarcity of cardiac tissue available for research. We investigated the feasibility of obtaining myocardial tissue from extracted pacemaker (PM) and defibrillator (ICD) leads and examined the nitric oxide 1 adaptor protein (NOS1AP) RNA expression and repolarization times by patient genotype.

Methods: 17 patients were genotyped for two NOS1AP SNPs {rs10494366 (T to G) and rs10918594 (C to G)} and had RNA levels measured by RT-PCR. Ventricular tissue obtained from 3 failing hearts at transplantation served as reference.

Results: A high ratio of cardiac troponin I/collagen I RNA identified 9 of 17 patient samples (muscle rich) in which the gene expression profile (Cav1.2, Kv4.3, HERG, KvLQT1, Connexin43, NOS1AP, NCX) was similar to that of the reference ventricular samples and significantly different (p<0.003) from the expression profile of lead tissue samples with a low troponin I/collagen ratio (muscle poor). As shown in the figure, TT and CC polymorphisms were associated with significantly lower NOS1AP RNA levels and shorter JT intervals (p<0.01 compared to the GG genotype).

Conclusion: Performing gene expression analyses on RV tissue samples extracted with PM and ICD leads is feasible. Approximately half of the samples contain cardiomyocytes that express Troponin I and ion channels at levels comparable to those seen in ventricular tissue from explanted hearts. Decreased NOS1AP expression in rs10494366 TT and rs10918594 CC homozygotes may underlie shorter repolarization times.