Implant Defibrillator Threshold Characteristics in an Ischemia/Reperfusion Induced Intracellular Calcium Delineation of the Pericardiophrenic Vein for Optimal pericardiophrenic vein was not identified developed phrenic nerve stimulation. Whether placed in patients the pericardiophrenic vein was identified either during occlusion venography of 80% reduction in appropriate ICD therapy in these patients (18% vs 33%, log rank p<0.05).

Conclusion: ICD therapy may substantially reduce the incidence of appropriate ICD therapy in patients with CHF secondary to idiopathic DCM. These observations suggest that ACE inhibitors may have important direct and/or indirect antiarrhythmic actions.

Biventricular pacing has established benefits for the management of drug refractory heart failure. However, optimal placement of the left ventricular (LV) lead can considerably affect LV lead stability and LV lead function. Methods: LV leads with left phrenic nerve stimulation were implanted consecutively in four patients who underwent biventricular device implantation between July 2002 and September 2003. Eighty transvenous implants, one LV endocardial implant, and three surgical LV leads placed with prior delineation of the pericardiophrenic vein had any evidence of phrenic nerve stimulation. Results: In three patients the pericardiophrenic vein was not identified developed phrenic nerve stimulation. Conclusions: Identification of the pericardiophrenic vein is feasible in all patients undergoing surgical LV lead placement, and with the aide of angiography, in selected patients undergoing transcatheter LV lead implantation. Pericardiac vein stimulation by the LV leads can be avoided by placement of the leads away from the previously identified pericardiophrenic vein, reducing the incidence of phrenic nerve stimulation.

Poster Session

Monday, March 08, 2004, 3:00 p.m.-5:00 p.m.
Morial Convention Center, Hall G
Presentation Hour: 4:00 p.m.-5:00 p.m.

1110-213 Ranolazine Attenuates Increased Variability of Action Potential Duration and After Depolarizations CAUSED by Augmentation of Late Sodium Current

Yeja Song, Lin Wu, John C. Shryock, Luiz Belardinelli, University of Florida, Gainesville, FL, CV Therapeutics, Palo Alto, CA

Background: This study assessed the hypothesis that an increase of late sodium current (I NaL) exaggerates beat-to-beat variability of action potential duration (APD) and facilitates the actions of potassium-channel blockers to induce early afterdepolarizations (EADs).

Methods: I NaL and action potentials (APs) of guinea pig isolated ventricular myocytes were measured using whole-cell patch-clamp techniques. Results: The I NaL enhancer ATX-II (5 nM) increased the amplitude of I NaL by 217±39 pA (n=9, p<0.001). ATX-II (15 nM) prolonged the APD measured at 50% repolarization (APD50) by 244±24% from 281±11 to 693±61 ms (n=7, p<0.001) and induced EADs. Moreover, ATX-II increased the variability of APD50 (SD/mean of 10 consecutive APs, x10) from 1.1±0.3 to 16.2±0.7% (n=7, p<0.001). Ranolazine (10 µM), an anti- ischemic agent and a putative inhibitor of I NaL, attenuated the ATX-II-induced I NaL (by 37±3% (p<0.05)). The inhibition by ranolazine of I NaL was mimicked by tetrodotoxin (10 µM, n=5). In the presence of ATX-II, Ranolazine (10 µM) shortened the APD50 to 37±8±34 ms (p<0.001) and the EADs, and reduced the variability of APD50 to 2.8±0.4% (p<0.001). Although ATX-II at a low concentration (3 nM) increased the APD50 by only 6±2% (p=11), it facilitated the actions of E-4031 (1 µM) and chromanol 293B (30 µM), blockers of the rapid and slow components of the delayed rectifier potassium current, respectively, to prolong the APD50 (median 21 months), these patients received frequent appropriate (34%) and inappropriate (36%) ICD therapies. The first appropriate ICD therapy occurred at 7 months (median). Approximately 2/3 of these ICD therapies occurred within one year after implantation. There was no significant difference between patients on (n=81) and off ACE inhibition, in any (p=0.05). LVEF (25±6.8% vs 23±2.5%, p=0.05), or incidence of documented spontaneous or inducible sustained ventricular tachycardia / fibrillation before implantation (36% vs 48%, p<0.05). Fewer patients on ACE inhibitors were treated with amiodarone (21% vs 48%, p<0.05). After adjustment of age, gender, LVEF, use of antiarrhythmic drugs and incidence of pre-implant documented spontaneous or inducible sustained ventricular arrhythmias, the incidence of appropriate ICD therapy was significantly lower in patients on ACE inhibitors than those off ACE inhibitors (log rank p<0.05). At one year after implantation, ACE inhibitor therapy was associated with an 80% reduction in appropriate ICD therapy in these patients (18% vs 33%, log rank p<0.05).

Conclusion: ACE inhibitor therapy may substantially reduce the incidence of appropriate ICD therapy in patients with CHF secondary to idiopathic DCM. These observations suggest that ACE inhibitors may have important direct and/or indirect antiarrhythmic actions.

1110-214 Ischemia/Reperfusion Induced Intracellular Calcium Oscillations in the Intact Heart: Relation to Arrhythmogenesis

Vikram Lakireddy, Paramdeep Baweja, Gil Bub, Tamarra Baynham, Nabil El-Sherif, Downstate Medical Center, Brooklyn, NY, New York Harbor Healthcare System, Brooklyn, NY

Background: Intracellular calcium ([Ca 2+] i) loading by various mechanisms, including ischemia/reperfusion (IR), has been postulated to cause spontaneous oscillatory Ca 2+ release from the sarcoplasmic reticulum that may play a role in generation of arrhythmia. Thus far, this mechanism has been demonstrated in isolated cardiomyocytes or 2-dimentional myocyte networks. We investigate the development of Ca oscillations (O) during IR in the intact heart.

Methods: Perfusion Langendorff guinea pig hearts were subjected to global IR (20 min./ 20 min.). The heart was stained with 100 microliters of Rhod-2 AM and 25 microliters of 20 min.). The heart was stained with 100 microliters of Rhod-2 AM and 25 microliters of 200 µM) and 200µM (n=9) by 293B (p<0.001), respectively. EADs were induced by E-4031 and 293B only in the presence of ATX-II. Ranolazine (10 µM) abolished the EADs and reversed the prolongation of APD50 by 76±5% (n=5, p<0.05) and 71±4% (n=9, p<0.001), respectively. APD50 was increased by 11±2% (n=6) and 104±41% (n=8) by E-4031 (p<0.01), and 40±7% (n=6) and 202±59% (n=9) by 293B (p<0.001), respectively.

Conclusion: An augmentation of I NaL greatly increased the variability of APD and facilitated the proarrhythmic effects of potassium-channel blockers. Inhibition of I NaL, such as by ranolazine, may reverse dispersion of repolarization, drug-induced QT prolongation, and arrhythmias.

Poster Session