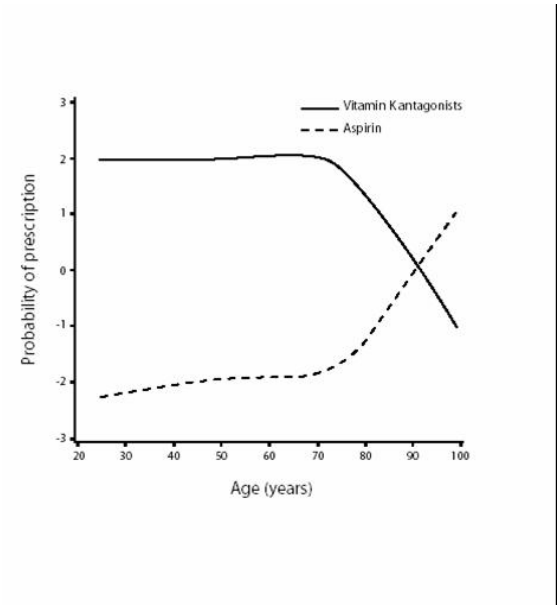
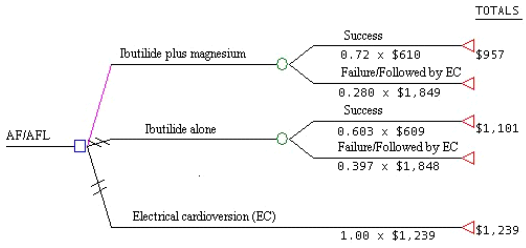
receiving antithrombotic therapy. However, the use of VKA was not optimal in elderly patients and better prophylactic strategies may be warranted for them .



1129-217 **A Decision-Tree Model Comparing First-Line Electrical Cardioversion to Ibutilide With or Without Magnesium Prophylaxis in the Treatment of Atrial Fibrillation**

Craig I. Coleman, James S. Kalus, C. Michael White, Jeffrey Kluger, University of Connecticut, Storrs, CT, Hartford Hospital, Hartford, CT

Background: Ibutilide is cost-effective when compared to first-line electrical cardioversion (EC) for atrial fibrillation (AF); however, these results are sensitive to alterations in conversion rate. Prophylactic magnesium augments the efficacy of ibutilide as demonstrated by an increased rate of successful conversion. The objective of this evaluation was to compare the costs associated with first-line EC and ibutilide in the presence and absence of magnesium prophylaxis for the conversion of AF. **Methods:** A decision-tree model was developed to estimate the cost-effectiveness of first-line EC compared to ibutilide with or without prophylactic intravenous magnesium sulfate followed by EC in those patients who do not convert. Conversion rates for patients receiving ibutilide with or without magnesium were based upon results of a multi-center, retrospective, cohort study (n=319). Healthcare utilization costs including drugs, intravenous admixture and administration, EC, electrocardiographs and physicians' fees were based upon actual costs from our institution. Cost-effectiveness was calculated by multiplying the cost of a successful and unsuccessful outcome by their probability of occurrence and then adding these two figures to determine total cost. **Results:** Ibutilide+magnesium was found to be the most cost-effective for conversion of AF (see figure). **Conclusion:** The decision-tree model suggests that ibutilide+magnesium is more cost-effective than ibutilide alone or first-line EC.



1129-218 **Ibutilide Improves Cardioversion Success Rates in Patients on Chronic Amiodarone Therapy With Persistent Atrial Fibrillation**

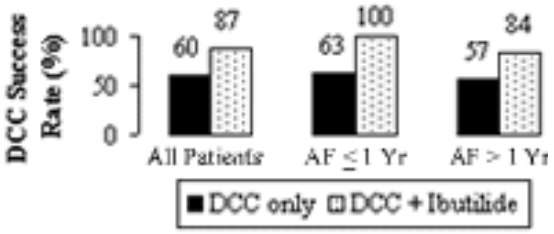
Jenny C. Hu, Kelly Machuca, Shelley DePeralta, Bramah Singh, Zenaida Feliciano, VA Greater Los Angeles Healthcare System, Los Angeles, CA

Background: Atrial fibrillation (AF) is the most common arrhythmia, affecting approximately 2.2 million people in the United States. A combination of amiodarone and ibutilide has been used with results suggesting an additive or synergistic effect on AF conversion. **Methods:** We retrospectively studied 90 consecutive patients with persistent AF receiving oral amiodarone therapy who elected for electrical cardioversion. Patients underwent either direct current cardioversion (DCC) (Group A, n=67) or DCC with ibutilide pretreatment (Group B, n=23). To evaluate the effect of AF duration on DCC success rate, patients were further divided into AF duration ≤ 1 year (Group A_1, n=30 and Group B_1, n=4) and AF duration > 1 year (Group A_2, n=37 and Group B_2, n=19). Chi-square analysis was used to evaluate the statistical significance (set at $p<0.05$) between groups.

Results:

All patients were male, mostly hypertensive (86%) and age 64 ± 9.6 years, body mass index 34 ± 8.1 kg/m^2, left atrial size 52 ± 8.4 mm, ejection fraction 52 ± 10 %, and AF duration 2.8 years ± 3.1 years. DCC success rates were 60% in Group A and 87% in Group B (p=0.02). A trend for DCC success rate improvement with ibutilide was seen in patients with AF duration > 1 year (Group A_2=57% vs. Group B_2=84%, p=0.07). One patient in the ibutilide pretreatment group developed *torsade de pointes*.

Conclusion: Ibutilide pretreatment for DCC may be a safe and effective method of improving DCC success rates in patients with long duration persistent AF receiving amiodarone therapy.



POSTER SESSION

1130

Channelopathies and Idiopathic Ventricular Tachycardia

Tuesday, March 09, 2004, 9:00 a.m.-11:00 a.m.
Morial Convention Center, Hall G
Presentation Hour: 10:00 a.m.-11:00 a.m.

1130-207 **Prevalence and Spectrum of Mutations in the Cardiac Ryanodine Receptor in Patients Referred for Long QT Syndrome Genetic Testing**

Laura J. Kopplin, David J. Tester, Michael J. Ackerman, Mayo Clinic, Rochester, MN

Background: Pathogenic mutations in the gene, *RYR2,* encoding the cardiac ryanodine receptor cause type 1 catecholaminergic polymorphic ventricular tachycardia (CPVT1). There is phenotypic overlap between the clinical presentation of CPVT and long QT syndrome (LQTS). Because the diagnosis of CPVT can be elusive, we sought to determine the spectrum and prevalence of *RYR2* mutations in a cohort of unrelated patients referred specifically for LQTS genetic testing.

Methods: Since 1997, nearly 500 unrelated patients have been referred to Mayo Clinic's Sudden Death Genomics Laboratory for LQTS genetic testing. Putative pathogenic mutations in the known LQTS-causing genes have been identified in approximately 50% of the cases. Mutational analysis of 18 exons of *RYR2* previously implicated in CPVT was performed on genomic DNA from 240 genotype-negative subjects using polymerase chain reaction, denaturing high performance liquid chromatography, and direct DNA sequencing.

Results: Seventeen distinct *RYR2* mutations (16 missense, 1 duplication insertion, 15 novel) were found in 20 out of 240 genotype-negative subjects (8.3%). None of these mutations were present in 400 reference alleles. Two mutations localized to the FKBP12.6 binding domain. Upon review of the clinical records, the referral diagnosis for 19 out of 20 patients was "atypical" or "borderline" LQTS rather than CPVT. None of the individuals displayed diagnostic QT prolongation (QTc > 470 ms).

Conclusion: Putative pathogenic CPVT1-causing mutations in *RYR2* were detected in nearly 10% of unrelated and LQTS genotype-negative patients who were referred for LQTS genetic testing. These findings suggest that CPVT may be under-recognized among physicians referring patients with a suspected channelopathy. A diagnosis of "atypical LQTS" may warrant consideration of CPVT and analysis of *RYR2* if the primary LQTS-causing channel screen is negative.

1130-208 **Diagnostic Value of the Ajmaline Test Based on the Gene Analysis in Concealed Brugada Syndrome**

Kui Hong, Kiyotaka Matsuo, Antonio Berruezo Sanchez, Matteo Vatta, Jeff Towbin, Josep Brugada, Pedro Brugada, Carlos Piñero Galvez, Charles Antzelevitch, Ramon Brugada, Masonic Medical Research Laboratory, Utica, NY

Background Brugada syndrome is an arrhythmogenic disease caused in part by mutations in the cardiac sodium channel gene, *SCN5A*. The electrocardiogram in Brugada syndrome is variable over time up to the point of normalization in some individuals. Diagnosis of possible affected individuals is performed with the use of sodium channel-blocking agents which unmask the EKG abnormality. However, validation of the testing has not been performed. The use of genetic data as a gold standard in large families allows to examine the effectiveness of ajmaline for diagnosis.

Methods We collected 4 large families with a total of 128 members. Ninety members were relatives at possible risk of Brugada syndrome. Sixteen had a positive EKG at base-

line. The remaining 74 subject (31 males and 43 females), who had negative ECG at baseline, received intravenous class 1 blocker (ajmaline 1mg/kg). The ECG was considered positive if the ST-segment in leads V1 and V2 (V3) was elevated ≥0.2 mV and showed "coved"-type morphology before or after the infusion of ajmaline. The exons of SCN5A were screened in the families using direct sequencing.
Results All 4 families had a mutation in SCN5A. The 16 subjects with positive ECG at baseline had *SCN5A* Mutation. Of the 74 individuals who received ajmaline test there were 29 positives and 45 negatives. Two positives did not have the mutation, and 7 negatives had the mutation. All results on the ajmaline test are shown in the table. The Sensitivity, specificity, and positive or negative predictive value of the test is 79.4%, 95.0%, and 93.1% or 84.4%, respectively.
(male/female).
Conclusion A specificity of 95% and a sensitivity of close to 80% indicate that the ajmaline test is very valuable in the diagnosis of SCN5A carriers in families with Brugada syndrome. There are two false positives that raises an issue of a second gene in the family or an iatrogenic false positive.

1130-219 Conus Branch Ischemia Provokes Brugada-Type ST-Segment Changes in Patients With Coronary Artery Disease

Masaru Yamaki, Takeshi Nishiura, Toru Kaji, Mitsuru Gima, Naoki Funayama, Katsumi Ohbori, Nobuyuki Sato, Yuichiro Kawamura, Naoyuki Hasebe, Kenjiro Kikuchi, Hokkaido Cardiovascular Hospital, Sapporo, Japan, Asahikawa Medical College, Asahikawa, Japan

Recently, the intriguing coexistence of vasospastic angina and Brugada syndrome have been reported in some cases. However, the mechanistic relationship between Brugada type ECG abnormalities and ischemia of the right ventricular outflow tract has not been fully elucidated. Here we present four cases with coronary artery disease who presented with ECG abnormalities induced by ischemia of the conus branch (CB) of the right coronary artery. The twelve-lead ECGs at rest showed normal sinus rhythm in all cases. Surprisingly, the saddle back-type ST segment elevation in leads V1-V3 was observed either during the percutaneous transluminal angioplasty procedure of the proximal right coronary artery or with an intracoronary ergonovine injection into the right coronary artery. The coronary angiogram exhibited a total occlusion or 99% stenosis with a delay in the CB and significant stenosis of the proximal right coronary artery in three cases and coronary vasospasms of the CB and right coronary artery in the remaining case. These Brugada-type ECG changes reversibly disappeared after cessation of the ischemia from the CB lesion. In the fourth patient which had vasospasms of the right coronary artery, remarkable coved-type ST segment elevation was also induced by the class IC antiarrhythmic agent, pilsicainide, suggesting a concealed form of Brugada syndrome. These results suggest that the free wall of the right ventricular outflow tract supplied by the CB plays a pivotal role in the genesis of the Brugada-type ECG changes, and the ischemia from CB lesions, at least in part, contributes to the Brugada-type ST segment changes.

1130-220 Brugada-Type Electrocardiographic Pattern and ST-Segment Alternans in Right Precordial Leads During Percutaneous Coronary Intervention of the Proximal Right Coronary Artery

Naoki Fujimoto, Chikaya Omichi, Takafumi Koji, Atsushi Kawasaki, Shigeki Kato, Atsunobu Kasai, National Mie Central Hospital, Hisai, Japan

Background: Brugada syndrome is characterized by a right bundle branch block pattern and ST segment elevation in the right precordial leads. The Brugada-type electrocardiographic (ECG) pattern can be observed in asymptmatic healthy patients (pts) or conditions other than true Brugada syndrome. The mechanisms of Brugada-type ECG pattern are not fully understood.
Methods: We performed percutaneous coronary intervention (PCI) of proximal right coronary artery (RCA) for ischemic heart diseases in 12 pts. No significant stenosis was observed in left coronary arteries in all pts. The ST changes were evaluated during PCI. Angiographical changes were carefully observed from major branches of RCA to small branches during PCI. We measured ST elevation in right precordial leads with class I antiarrhythmic drug administration: pilsicainide 50 mg (pure sodium channel blocker) after PCI. ST changes were compared with true Brugada syndrome (n=5).
Results: Brugada-type ECG was observed in 5 pts (42%) but not in 7 pts (58%) during PCI of proximal RCA. All 5 pts who had Brugada-type ECG demonstrated ST segment alternans from coved shape to saddle back shape during PCI. These ECG changes returned to normal after PCI. These pts who had Brugada-type ECG with ST alternans demonstrated selective small RV branch occlusion or vasospasm during PCI, which perfused RV anterior wall or RV outflow. However pts without Brugada-type ECG did not show RV branch occlusion. The class I antiarrhythmic drug administration showed no significant ST elevation both in pts with Brugada-type ECG and in pts without Brugada-type ECG (0.70±0.54mv, vs 0.46±0.21mv, p=NS). There was a significant difference in ST elevation between pts with Brugada-type ECG during PCI and pts with true Brugada syndrome. (0.70±0.54mv, vs 2.86±0.61mv, p<0.05)
Conclusions: The pts who had RV branch occlusion during PCI showed Brugada-type ECG and ST alternans. Sodium channel impairment was not associated with these ECG changes. ST alternans might be considered as prerequisites before developing ventricular arrhythmia. These data suggest that merely ischemia of small RV branch could be one of the different entities showing Brugada-type ECG from true Brugada syndrome.

1130-221 Prior Ischemia Enhances Arrhythmogenicity in Isolated Canine Ventricular Wedge Model of Long QT 3

Norihiro Ueda, Douglas P. Zipes, Jiashin Wu, Krannert Institute of Cardiology, Indianapolis, IN

Background: Ventricular tachyarrhythmias (VTs) occur frequently in patients having long QT syndrome (LQTS) or after acute myocardial ischemia. However, the synergistic effects of ischemia and LQTS on arrhythmia development are unclear. We evaluated the contribution of a prior episode of ischemia on the arrhythmogenicity of the LQTS. ***Methods :*** Using a 256-channel optical mapping system, we mapped action potentials on the cut-exposed transmural surfaces of arterially perfused muscle wedges isolated from canine left ventricular free walls and recorded their transmural electrocardiogram (ECG). ***Results:*** We observed that 40 minutes of global ischemia (no perfusion) followed by 60 minutes of reperfusion, at which time action potential duration (APD) and conduction velocity had recovered, significantly enhanced the APD prolongation produced by anemone toxin II (ATX-II, 20 nmol/L), which delays the inactivation of sodium current and produces type 3 LQTS. The combination of ischemia, reperfusion, and ATX-II caused early afterdepolarization (EAD) development in 8/8 wedges (100%) and spontaneous VTs in 7/8 wedges (87.5%) at a time when perfusion was normal. We observed epicardial, midmyocardial, and endocardial occurrences of EADs in 1, 7, and 4 wedges, respectively. Focal EAD and reentry were responsible for 73% and 18% of the repetitive activations in the VTs. Reentry, transmural APD heterogeneity, and EADs originating from multiple focal sites generated polymorphic VT in the transmural ECG. In contrast, neither EADs (0%) nor VTs (0%) occurred in 8 control wedges having the same protocol except without ischemia (ATX-II only), and VT occurred in 2/10 wedges (20%) after ischemia but before ATX-II (ischemia only). ***Conclusions:*** A prior episode of acute ischemia, even after apparent electrophysiologic recovery, enhances the arrhythmogenicity of LQTS induced by ATX-II through the development of EADs and reentry. The results imply that patients with both LQTS and ischemic heart disease or those with myocardial ischemia or infarction who take medications that prolong APD could be at increased risk for developing VT.

1130-222 High Incidence of Prolonged QTc in Asthmatics

Craig D. Williams, Richard J. Kovacs, Sandip Sheth, Cindy Calley, Purdue University School of Pharmacy, Indianapolis, IN, Indiana University School of Medicine, Indianapolis, IN

Background: A high incidence of asthma has been reported amoung registrants of the International Long QT Syndrome (LQTS) Registry. Asthma is associated with a risk of sudden death that is not always explained by pulmonary findings at autopsy.
Objective: To determine if a higher than expected rate of LQTS occurs in an identified cohort of patients with asthma.
Methods: Patients over 18 years of age admitted to a city-county hospital with a primary diagnosis of asthma between February 1, 2001 and September 30, 2002 were identified. Patients with a documented ECG performed since December 2000 were enrolled. A single cardiologist read all ECGs to determine the QT interval which was then corrected with a Bazetts calculation to determine QTc. Lead II was used for QT interval measurement. If lead II was unreadable, lead V_5 or aVF was used. The reported, uncorrected QT interval was an average of the measurement of three different complexes in the same lead. QTc results were compared to a published cohort of 420 non-asthamtic adults. Prolonged QTc was defined as > 455 msec in men and > 475 msec in women which defined the upper 1% of QTc in the non-asthmatic cohort. No patients were on anti-psychotic or anti-arrhythmic medications. Patients were excluded from analysis if they had a previous documented myocardial infarction (1 patient), or documented hypokalemia (2 patients), hypocalcemia (1 patient), or hypomagnesemia (1 patient) within 1 week of their recorded ECG.
Results: 193 patients were identified, 130 of whom had a readable ECG. The incidence of prolonged QTc was 19.8% (17/86) in females, 28.2% (11/39) in males and 22.4% (28/125) overall. Compared to the 1% incidence of prolonged QTc in the published non-asthmatic cohort, a one sample test of proportions was statistically significant for all 3 data sets (p< 0.001 for male, female and overall).
Conclusion: Asthmatics appear to have an unusually high incidence of prolonged QTc intervals.

1130-223 Utility of Adenosine in Differentiation of Patients With Right Ventricular Outflow Tract Tachycardia and Arrhythmogenic Right Ventricular Dysplasia

Sei Iwai, Kenneth M. Stein, Steven M. Markowitz, Suneet Mittal, Amit B. Guttigoli, Bindi K. Shah, Ravi K. Yarlagadda, Bruce B. Lerman, Cornell University Medical Center, New York, NY

Background: Patients with right ventricular outflow tract (RVOT) tachycardia and arrhythmogenic right ventricular dysplasia (ARVD) can both present with left bundle branch block inferior axis ventricular tachycardia (VT). However, the management and prognosis of the two entities is very different, and clear differentiation of these etiologies of VT would be clinically useful. Termination with adenosine is thought to be specific for arrhythmias due to cyclic AMP-mediated triggered activity; adenosine, with rare exceptions, has no effect on arrhythmias due to reentry. **Methods and Results**: We compared the sensitivity of VT to adenosine in patients with RVOT tachycardia and those with ARVD. VT was sensitive to adenosine in 35 of 40 patients with RVOT tachycardia. Of note, 2 of the 5 pts with adenosine-insensitive VT were subsequently found to have a somatic mutation in the inhibitory G-protein, G_i, impairing intracellular cyclic AMP regulation. In contrast, 10 of 10 patients with ARVD had VT which was adenosine-insensitive. Therefore, the sensitivity of adenosine termination of VT in identifying pts with RVOT tachycardia was 88% while the specificity was 100%. **Conclusions**: These findings suggest that response of VT to adenosine may be a simple and effective clinical tool for differentiating patients with RVOT tachycardia from those with VT due to ARVD.