Effects of Verapamil: Suggest that Calcium Current is Important in Maintaining Ventricular Fibrillation Lasting More Than 3 to 4 Minutes

Chi Jin, Raymond E. Ideker, Jian Huang, Shanghai Rui Jin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, People’s Republic of China, University of Alabama at Birmingham, Birmingham, AL

Background: While it is known that both the Na+ and Ca2+ currents are active during the first seconds of ventricular fibrillation (VF), it is not known if both channels remain active during the long duration VF of cardiac arrest. The increased membrane potential caused by the global ischemia of VF would be expected to inactivate Na+ channels as VF progressed, so that Ca2+ channels should become more important in long duration VF maintenance. We used verapamil, an L-type Ca2+ channel blocker, to test this hypothesis.

Methods: Six open-chest pigs received intravenous verapamil (0.136 mg/kg). Another six pigs received intravenous 0.9% sodium chloride as controls. Recordings from a 21x24 unpolar electrode plaque (2 mm spacing) saturated to the lateral posterior epicardium were analyzed throughout the first 10 min of VF to calculate wavefront propagation velocity and activation rate.

Results: After 200 s, wavefronts propagated significantly more slowly and the activation rate was significantly slower in pigs treated with verapamil than in control pigs (Figures). Conclusion: Verapamil significantly slowed activation and wavefront propagation. In the absence of VF suggesting that, while Na+ channels are active during the early stages of VF, their activity decreases after 200 s of VF, Ca2+ channels remain active after this time and are important in the maintenance of long duration VF.

The Effects of Chiral Isolates of Methadone on HERG Current

Congrong Lin, Vasant Ranade, Xiaogang Ke, Janos Molnar, John C. Somberg, Rush University Medical Center, Chicago, IL

Methadone (M) is a synthetic opioid that has been used as an analgesic and in the treatment of narcotic addiction. Drug induced QT prolongation has been noted. And Torsade de Pointes ventricular tachycardia and death have been reported with M. The proarrhythmic toxicity is related to the inhibition of cardiac IKr channel and prolongation of the action potential. M is a racemate mixture of d- and l-methadone. We hypothesized that the two isomers of M may have different effects on the cardiac IKr channel, and separation of these isomers may produce an effective drug with less QT effect. The effect of M and its two isomers on IKr were evaluated by using an oocyte system with heterogeneously expressed human-ether-a-go-go-related gene (HERG). Two electrode voltage clamp technique was employed and the experiments were performed at room temperature.

Results: After 200 s, wavefronts propagated significantly more slowly and the activation rate was significantly slower in pigs treated with verapamil than in control pigs. Conclusion: Verapamil significantly slowed activation and wavefront propagation. In the absence of VF suggesting that, while Na+ channels are active during the early stages of VF, their activity decreases after 200 s of VF, Ca2+ channels remain active after this time and are important in the maintenance of long duration VF.

Molecular basis of the inhibition of cardiac IKr1 current by protein kinase C: role of PKC beta and Kir2.6 channel subunit heterogeneity

Claudia Kieneker, Daniel Scherer, Edgar Ziltron, Eberhard P. Scholz, Martin Kulzer, Ramona Blohes, Dirk Thomas, Alexander Bauer, Christoph A. Korte, University Hospital Heidelberg, Heidelberg, Germany

Background: The cardiac IKr1 current is essential to maintain the resting membrane potential of cardiac myocytes. On the molecular level, IKr1 is mediated by three channel subunits: Kir2.1, Kir2.2 and Kir2.3. The PKC system has been shown to play a major role in the regulation of IKr1. However, the underlying molecular mechanisms have not been elucidated yet. Therefore, we studied the regulation of Kir2 currents by PKC and the role of different PKC isoforms.

Methods: Kir2 channels were expressed in Xenopus oocytes and experiments were performed using two-microelectrode voltage clamp. Native IKr currents were first characterized with the whole-cell patch clamp technique in isolated rat ventricular cardiomyocytes.

Results: Activation of PKC with PMA (1µM) which activates conventional and novel isoforms of PKC inhibited IKr1 currents in all homomeric Kir2 channels. In Kir2.1, inhibition was only weak. In Kir2.2 and Kir2.3 channels the inhibition effect was very pronounced. Heteromeric channels exhibited differing sensitivity: In Kir2.1/Kir2.2 and Kir2.1/Kir2.3 heteromers the inhibition effect was markedly attenuated, whereas it was very pronounced in Kir2.2/Kir2.3.

Mythaleotaxin (100µM), a small molecule activator of cPKC isoenzymes, induced a strong inhibition of Kir2.2, thereby reproducing the effect of PMA, pointing to a prominent role of cPKC for this regulation. The small molecule antagonist PKC-beta-inhibitor (1µM) significantly attenuated the effect of mythaleotaxin in Kir2.2. In contrast, mythaleotaxin did not reproduce the PMA effect in Kir2.3 and only induced a mild inhibition.

Conclusions: Kir2.2 channels are inhibited by Xenopus oocytes and experiments were performed using two-microelectrode voltage clamp. Native IKr currents were first characterized with the whole-cell patch clamp technique in isolated rat ventricular cardiomyocytes. Activation of PKC with PMA (1µM) which activates conventional and novel isoforms of PKC inhibited IKr1 currents in all homomeric Kir2 channels. Kir2.1, inhibition was only weak. In Kir2.2 and Kir2.3 channels the inhibition effect was very pronounced. Heteromeric channels exhibited differing sensitivity: In Kir2.1/Kir2.2 and Kir2.1/Kir2.3 heteromers the inhibition effect was markedly attenuated, whereas it was very pronounced in Kir2.2/Kir2.3.

ABSTRACTS - Cardiac Arrhythmias

Impact Energy Does Not Alter Narrow Time Window of Vulnerability in Ventricular Fibrillation (Commotio Cordis)

ALAWI A. ALSHEIKH-ALI, CHRISTOPHER MADIAS, BARRY J. MARON, JONATHAN WEINSTOCK, N. A. MARK ESTES, II, MARK S. LINK, TUFFTS-NEW ENGLAND MEDICAL CENTER, BOSTON, MA

BACKGROUND: In an experimental model of sudden death with chest wall impact (commotio cordis), both energy and timing of the impact to a narrow window on the upslope of the T-wave are critical determinants of ventricular fibrillation (VF) induction. Whether changes in the energy of the impact alter the critical window of vulnerability to VF is unknown. The present study sought to determine the effect of impact energy on the timing limits of vulnerability to VF in an animal model of commotio cordis.

The P-selectin Gene Polymorphism val166met: A Novel Risk Marker for the Occurrence of Primary Ventricular Fibrillation During Acute Myocardial Infarction

Elif Elmas, Peter Bugert, Talatna Popp, Siegfried Lang, Christel Weiss, Christian Woltpert, Marina Brueckmann, Martin Borggreve, Thorsten Kaeslin, University Hospital Mannheim, Medical Faculty Mannheim, University of Heidelberg, Germany, Mannheim, Germany, Institute of Transfusion Medicine and Immunology, Mannheim, Germany

Background: Ventricular fibrillation (VF) in the context of myocardial infarction (MI) is the leading cause of sudden cardiac death (SCD). Family history of SCD is described as risk factor for primary VF during acute MI. Genetic factors may be associated with primary VF. Therefore, the aim was to examine polymorphisms in various candidate genes of patients with and without VF in the setting of MI and among healthy controls.

Methods: 240 patients with a history of MI and 475 healthy controls were studied. 73 patients (30%) had primary VF during acute MI. By using PCR techniques with sequence-specific primers (PCR-SSP) we genotyped 5 single nucleotide polymorphisms (SNPs) in P-Selectin (PSE1) (V168M, S296N, N952D, S596L, T715P), 2 SNPs in P-selectin glycoprotein ligand-1 (PSGL-1) (G214R, S273F), 1 SNP in CD40L (A-3459G, A122C, A123C, T148C, intrA_T13C). In addition, length polymorphisms in PSGL-1 (36bptandem repeat) and CD40L (CA-repeat) were genotyped by PCR methods. Results were evaluated by two-sided t-tests, chi square tests and logistic regression analyses.

Results: Overall, the PSEL variant 168M was found in 27 of 240 patients (11.25%) which was very similar to the frequency among healthy controls (approx. 12%). Among patients with a history of VF however, the PSEL 168M allele showed a significantly higher prevalence (14/73 patients; 19%) as compared to patients without VF (13/167 patients; 8%) (p<0.01). This association remained significant in a logistic regression analysis after adjustment for age and gender (p<0.01; Odds ratio 2.8; confidence interval 1.2-6.3). There was no significant associations found between the remaining polymorphisms and the occurrence of VF or MI.

Conclusions: This is the first description of an association of the PSEL gene variant 168M with primary VF during acute MI. This variant may be a candidate polymorphism for evaluating the susceptibility for VF in the setting of acute MI.
METHODS: Anesthetized juvenile swine (8 to 25 kg) were placed prone in a sling to receive chest wall strikes with varying impact velocities and at different time intervals during ventricular repolarization. Vulnerability to VF (defined as % impacts resulting in VF) was assessed across the following impact velocities (<30, 30, 40, and >40 MPH). RESULTS: In 260 animals with 1062 impacts, VF was induced in 221 times. Across all categories of impact velocity, VF induction was critically dependent on timing of the impact to the same narrow 30 ms window on the upslope of the T-wave (FIGURE). CONCLUSION: In an animal model of commotio cordis, the narrow time window of vulnerability to VF during ventricular repolarization is constant across varying impact velocities and is independent of impact energy. These data may in part explain the relatively uncommon occurrence of sudden death due to chest blow on the athletic field.

ABSTRACTS - Cardiac Arrhythmias

Placebo-Controlled Double-Blind Dose-Ranging Study of the Efficacy and Safety of Celivarone for the Prevention of Ventricular Arrhythmia-Triggered ICD Interventions

Peter R. Kowey, Etienne M. Eliot, Alessandro Capucci, Stuart J. Connolly, Harry Crijns, Stefan H. Hohnloser, Piotr Kulakowski, Denis Roy, David Radzick, Main Line Health Heart Center Lankenau, Wynnewood, PA, Sanofi-Aventis R&D, Paris, France

Background: Celivarone (C) is a new long-acting benzofuran derivative without iodine with an electrophysiological profile similar to amiodarone. Methods: In this study patients (pts) with an implantable cardioverter defibrillator (ICD) for life-threatening ventricular arrhythmia and left ventricular ejection fraction of 40% or less were randomized at centers in Europe and the US to receive C orally: 100mg (P), 100mg + 100mg (C100), 300mg (C300) or placebo (P, n=53) once daily for 6 months. The primary endpoint was the occurrence of all ventricular tachycardia (VT) or fibrillation (VF) episodes documented by ICD interrogation requiring therapy. Results: Mean age was 64.2 yrs, 91% were males with coronary artery disease. A 46% reduction in the number of sustained VT or VF episodes was observed in the C300 group compared to P over 180 days (p = 0.001). Addition of 100mg to the dose regimen did not result in a further decrease in arrhythmic events (p = 0.149). In all treatment groups, the proportion of treated pts with adverse events requiring treatment discontinuation was similar: 13.2%, 11.8% and 10.6% in the P, C100 and C300 groups respectively. Conclusions: These results suggest that C could be effective for the prevention of ventricular arrhythmia triggered interventions in ICD pts and warrant investigation in a larger cohort. Tolerability was good across doses with no evidence of proarrhythmia or organ toxicity.

The Effects of Chronic Nicotine Administration on Atrial Fibrillation and Atrial Vulnerability to Fibrillation in Normal and Hypertensive Rats: Implication for Atrial Fibrillation in Smokers

Miyako Miyasaka, Yasuhiro Miyasaka, Reiko Okazaki, Yu-ki Waseda, Yoshinobu Kobayashi, Tako Kosh, Kiyoshi Mizuno, Nippon Medical School, Tokyo, Japan

Background: Smoking is associated with an increased risk of atrial tachyarrhythmias. We hypothesized nicotine develops proarrhythmic effects through inducing increase of fibrosis in atria. Methods: Twenty-six normal rats (WKY) and 15 hypertensive rats (SHR, 12-16W) were anesthetized and implanted an osmotic pump filled with nicotine at several concentrations (0, 1, 5, 10, 20 and 40mg/kg/day) subcutaneously. After four weeks of continuous administration of nicotine, the heart and lung were removed and vulnerability to atrial fibrillation was tested under Langendorff perfusion. The tissue was stained with Masson-Trichrome to quantify the amount of atrial fibrosis. Results: Plasma levels of nicotine were 0.065±0.045ng/ml that were equivalent to those in habitual smokers in rats with 5mg/kg/day dose nicotine. In normal rats, %fibrosis in atria was 5.9±0.6% in 0 mg (control) group, and modestly increased in 5mg group (11.1±3.8%, p=0.08), while it was significantly increased in 10mg group (19.3±3.0% in 10mg group, p<0.01). In 20mg and 40mg groups, atrial fibrosis was markedly increased to 25.59±7.8% in 20mg group, and markedly increased to 25.59±7.8% in 10mg group. In normal rats, repetitive atrial response with short duration (<1sec) or atrial tachycardia could be induced in rats treated with very high dose (>10mg/ kg/day) nicotine. On the other hand, in SHR treated with nicotine at levels of habitual smokers (5mg/kg/day), sustained AF could be induced and continued for more than 30 sec, while AF of short duration or atrial fibrillation were induced in control rats. Conclusions: Chronic nicotine exposure at level of habitual smokers induced significant atrial fibrosis and vulnerability to atrial fibrillation in SHR, whereas the effects were modest in normal rats. That may explain the increased incidence of atrial fibrillation in habitual smokers with hypertension.

Deficiency of Inositol 1,4,5-Triphosphate Receptor Type 1 in the Murine Heart Causes HV Prolongation Without Alteration in Cardiac Structure or Function

Amaredeh Saluja, Andrew M. Bellinger, Shinchi Okuda, Daniel O. Cervantes, James Coromillas, Andrew R. Marks, Columbia University, New York, NY

Background: The type 1 inositol 1,4,5-triphosphate receptor (IP3R1) is a sarcoplasmic reticulum calcium release channel. In the heart, it has been localized primarily to His-Purkinje tissue, however its function is unclear. We studied the functional and electrophysiological (EP) phenotype of two different mouse models: a cardiac-specific knockout (KO) with absence of IP3R1 expression and a hypomorph (HM) with attenuated expression. Methods: HM mice with ~75% globally attenuated IP3R1 expression were induced by partially disrupting the IP3R1 promoter with loxP motifs. Crossbreeding with tissue-specific Cre-expressing mice produced cardiac-specific KOs. Cardiac structure and function was assessed by histology, echocardiography, surface EKG, and Holter monitoring. EP studies were performed on 11 WT, 20 HM, and 15 KO mice by two blinded operators. Mice were intubated after injection with 0.5 mg/kg

A2 ABSTRACTS - Cardiac Arrhythmias

1001-94A Left Ventricular Structural Remodeling Increases Cardiac Electrical Stability in Exercised Rat

Horeash Dor-Haim, Shimon Rosenheck, Chaim Lotan, Moshe Swissa, Hadasah Hebrew University, Jerusalem, Israel, Kaplan Medical Center, Rehovot, Israel

Background: Aerobic training reduces the occurrence of sudden cardiac death, despite the induction of LVH. We looked into the electrophysiological changes following aerobic training that might explain reduction in ventricular arrhythmias. Methods: Thirty adult rats were studied for 8 weeks. Seven of them were trained for 4 weeks in a moderate treadmill exercise program (MTX), seven trained for 8 weeks in an intensive treadmill exercise program (ITP) and sixteen served as sedentary control (SCN). EPS study was performed on the isolated Langendorff perfusion system. Results: Isolated trained hearts showed up to 3-fold improvement in their tolerance to the induction of ventricular fibrillation (VF) in a dose response manner. More intense training protocol caused a higher ventricular fibrillation threshold (VF), shorter VF duration and lower VF probability. Training also significantly decreased VF vulnerability. Significant concordant LVH was found in ITP and MTX animals. VF strongly correlated to heart weight in ITP (r = 0.94, P<0.01). Addition of heart rate and high training intensity (r = 0.8, p<0.001), rats fitness level (r = 0.51, p<0.05) and low body weight (r = 0.49, p<0.05). Exercise did not decrease ventricular tachycardia (VT) probability. Conclusion: This study is the first to show a positive relationship between LVH and electrical stability. A multiple regression analysis has shown an independent effect of training on VF. This effect was mediated through decreased body weight, increased aerobic fitness and increased hypertrophy. Therefore, exercise-induced cardiac structural remodeling, may positively effect the enhancement of electrophysiological remodeling. The specific mechanism may be related to an enhanced cardiac conductance and action potential spatiotemporal organization.
The Natural Compound Acacetin Prolongs Atrial Refractory Period and Prevents Experimental Atrial Fibrillation in Anesthetized Dogs

Guo-Feng Li, Man-Wen Jin, Qiang Tang, Guo-Wei Qin, Hong-Bing Wang, Xiao-Hua Zhang, Hung-Fat Tse, Chu-Pak Lau, The University of Hong Kong, Pokfulam, Hong Kong

Background: We have recently demonstrated that the natural compound acacetin from the traditional Chinese medicine Xuelianhuo preferentially blocks the ultra-rapid delayed rectifier potassium channel current (I_{Kr}) prolongs atrial action potential duration in human atrial myocytes, and also inhibits acetylcholine-activated potassium channel current (I_{KAC}) in guinea pig atrial myocytes. The agent has no long QT risk potential. The present study was designed to investigate whether this compound would have anti-atrial fibrillation (AF) effect. Methods: Atrial effective refractory period (ERP) was measured by inducing pacing and mono-phasic action potential recording electrodes to right and left atria, respectively, and AF was generated by extra stimulus at right atrium with stimulation of two sides of vagal nerves in anesthetized dogs. Results: Acacetin at 5 mg/kg significantly prolonged ERP at baseline, right and left atria at post 1-4 h duodenal administration without QTc prolongation. However, sotalol at 5 mg/kg prolonged both atrial ERP and QTc interval at 1-4 h post duodenal administration. Interestingly, acacetin significantly prevented AF at 2.5 mg/kg (50%, n = 6, P < 0.01 vs vehicle, 0%, n = 4), 5 mg/kg (71.4%, n = 7, P < 0.01 vs vehicle) and 10 mg/kg (71.4%, n = 7, P < 0.01 vs vehicle) at 1:5-2:5 h post administration. Sotalol at 5 mg/kg also significantly prevented AF at 1:5-2:5 h post administration (60%, n = 5, P < 0.01 vs vehicle). Conclusions: Acacetin prolongs atrial ERP without prolonging QTc interval, and effectively prevents AF in anesthetized dogs after duodenal administration. These results suggest that the natural compound acacetin from traditional Chinese medicine is likely an orally effective promising atrial-selective anti-atrial fibrillation agent.

10:00 a.m.
Cardiac Arrhythmias

A4 - Abstracts - Cardiac Arrhythmias

1001-104
Induction of Remodeling Gene Expression During Ectopic Activity in Isolated Rat Left Atrial Appendages
Paul E. Wolkowicz, Hernan E. Grenett, Jian Huang, Edlue Tabengwa, Ferdinand Urtzahr, David D. Ku, University of Alabama at Birmingham, Birmingham, AL

Background: Clinical atrial tachyarrhythmias alter atrial gene expression to transform atrial electrical properties and induce fibrosis, both of which increase risk for fibrillation. Identifying models of atrial arrhythmias that provokes such molecular changes can help in elucidating molecular mechanisms affecting atrial remodeling. We have reported that a novel calcium leak provokes spontaneous ectopic events in isolated, untreated rat left atrial appendages (LAA) ( doi:10.1016/j.epac.2007.08.004 ). Here we determine whether remodeling gene expression is induced during this ectopic activity.

Methods: Isolated rat LAA (n ≥ 4 per group) were paced at 3Hz, superfused in Krebs-Henseleit (KH) buffer at 37°C and then were exposed to the calcium leak inducer 2-aminoethoxydiphenylborate (20M; 2APB) for 40min to provoke sporadic ectopic activity or were maintained in normal KH for 40min. LAA mechanical and electrical activity was recorded with force transducers and glass microelectrodes, respectively. Total LAA mRNA was extracted with TriZol and analyzed using reverse transcriptase-polymerase chain amplification with appropriate primers.

Results: LAA superfused with KH and 2APB exhibit ectopic electrical and mechanical events at a rate of 46±6 events/min in the absence of pacing while untreated LAA are quiescent. 3Hz-Paced LAA experiencing this calcium-leak induced ectopy show significant increases in (i) their c-fos/GAPDH mRNA ratio (0.9 vs. 0.25), (ii) their connective tissue growth factor/GAPDH mRNA ratio (1.6 vs. 0.3) and (iii) their transforming growth factor β1/GAPDH mRNA ratio (0.55 vs. 0.15) compared to untreated LAA. In contrast the Kv4.2/GAPDH mRNA ratio increases only slightly (0.8 vs. 0.50; 2APB vs. untreated).

Conclusions: The expression of key remodeling genes increases in isolated, normal rat LAA during acute, calcium leak-induced sporadic ectopic activity. This suggests that atrial calcium leaks which provoke ectopy may also alter LAA gene expression to enhance fibrosis. Such novel leak may act both to trigger arrhythmias and create an electrical substrate that favors more severe rhythm disturbances.

1001-105
Ranolazine Suppresses Ectopic Activity in Isolated Rat Left Atrial Appendage
Paul E. Wolkowicz, Jian Huang, Hernan E. Grenett, Edlue Tabengwa, Ferdinand Urtzahr, David D. Ku, University of Alabama at Birmingham, Birmingham, AL

Background: Myocardial sodium (Na) and calcium (Ca) overload predispose to triggered cardiac rhythm disturbances. Ranolazine inhibits the late sodium current (IC50~100μM), thereby decreasing myocardial Na & Ca overload, and clinical data suggest it as a promising pharmaceutical intervention against arrhythmias. We have reported that a novel sarcoplasmic reticulum calcium leak inducer, 2-aminoethoxydiphenylborate (20M; 2APB) for 40min to provoke sporadic ectopic activity or were maintained in normal KH for 40min. LAA mechanical and electrical activity was recorded with force transducers and glass microelectrodes, respectively. Total LAA mRNA was extracted with TriZol and analyzed using reverse transcriptase-polymerase chain amplification with appropriate primers.

Results: LAA superfused with KH and 2APB exhibit ectopic electrical and mechanical events at a rate of 46±6 events/min in the absence of pacing while untreated LAA are quiescent. 3Hz-Paced LAA experiencing this calcium-leak induced ectopy show significant increases in (i) their c-fos/GAPDH mRNA ratio (0.9 vs. 0.25), (ii) their connective tissue growth factor/GAPDH mRNA ratio (1.6 vs. 0.3) and (iii) their transforming growth factor β1/GAPDH mRNA ratio (0.55 vs. 0.15) compared to untreated LAA. In contrast the Kv4.2/GAPDH mRNA ratio increases only slightly (0.8 vs. 0.50; 2APB vs. untreated).

Conclusions: The expression of key remodeling genes increases in isolated, normal rat LAA during acute, calcium leak-induced sporadic ectopic activity. This suggests that atrial calcium leaks which provoke ectopy may also alter LAA gene expression to enhance fibrosis. Such novel leak may act both to trigger arrhythmias and create an electrical substrate that favors more severe rhythm disturbances.

1001-106
Cryoblation of Extrinsic Cardiac Sympathovagal Nerves Prevents Paroxysmal Atrial Tachyarrhythmias in Remodeled Canine Atria
Alex Y. Tan, Shengmei Zhou, Masahito Ogawa, Juan Song, Matthew Chiu, Hongmei Li, Michael C. Fishbein, Shien-Fong Lin, Lan S. Chen, Peng-Sheng Chen, Cedars-Sinai Medical Center, Los Angeles, CA, Kranert Institute of Cardiology, Indianapolis, IN

Background:Simultaneous sympathetic disconnection is associated with spontaneous onset of atrial tachyarrhythmias in ambulatory dogs. We sought to determine if sympathovagal disconnection can effectively prevent the atrial tachyarrhythmia.

Methods: We used implanted radiofrequency electrodes to continuously record stellate ganglia (SG) and vagal nerve activity (VNA) in 13 ambulatory dogs. Group 1 dogs (n=7) had cryoblation of both SG and cardiac branch of vagal nerve. Group 2 dogs (n=6) were treated with cryoblation by SG alone.

Results: On post-operative day 1 (POD1), but not POD10, group 1 dogs had decreased levels of SGNA, VNA and mean RR. The standard deviation (SD) of RR (SDRR) was significantly lower in Group 1 than Group 2 (p<0.05). Group 1 and 2 dogs developed sustained AF after 7±4 and 3±1 weeks respectively (p<0.01). Compared to group 2 dogs, group 1 dogs had less episodes of premature atrial contractions (2±1 vs 4±1 episodes/d, p<0.01), no episodes of paroxysmal atrial fibrillation (vs. 4±2 episodes/d in 3/7 group 2 dogs, p<0.01) and no episodes of paroxysmal atrial tachycardia (vs. 10±3 episodes/d, p<0.01). Both groups had significant reductions in HR and in cycle length of atrial tachyarrhythmias (p<0.05).

Conclusions: Sympathovagal activation is a trigger for paroxysmal atrial arrhythmias in ambulatory dogs. Cryoblation of extracardiac autonomic nerves, without left atrial ablation, can effectively prevent paroxysmal atrial tachyarrhythmias even in the presence of a remodeling atrial substrate.

1001-107
Role of Sterol Regulatory Element Binding Protein (SREBP) in the Regulation of the Parasympathetic Response and Inducible Ventricular Arrhythmia
Christopher Madhas, Ho-Jin Park, Yali Zhang, Serban P. Georgescu, Richard D. Patten, Mark J. Aronovitz, Hitoshi Shimano, Richard H. Karas, Mark S. Link, Jonas B. Galper, Tufts-New England Medical Center, Boston, MA, University of Tsukuba, Tsukuba, Japan

Background: Preserved parasympathetic tone is protective against sudden death after myocardial infarction (MI). In cultured atrial myocytes, sterol regulatory element binding protein 1 (SREBP1), regulates expression of the G-protein coupled inward rectifying K+ channel (GIRK1), which mediates the parasympathetic response of the heart. Here, we determined whether expression of GIRK1 was decreased in a model of atrial remodeling and whether SREBP1 KO mice have an increased susceptibility to post-MI ventricular tachycardia (VT).

Methods: GIRK1 expression was determined by Western blot analysis. In vivo programmed ventricular stimulation with single, double, and triple extrastimuli was performed 2 weeks post-ligation of the left anterior descending artery in SREBP1 KO and WT mice. Induction of six or more repetitive ventricular beats was considered a positive test. MI size was determined by echocardiography or by planimetry of scar.

Results: In atrial extracts of SREBP1 KO mice GIRK1 was decreased by 48 ± 7% (p<0.001) as compared to WT mice. SREBP1 KO mice showed no difference in infarct size or fractional shortening as compared to WT (see Table). With programmed stimulation, SREBP1 KO mice were more likely to be induced to VT than WT mice (89% SREBP1 KO vs. 43% WT, p< 0.05).

Conclusions: As compared to WT mice, SREBP1 KO mice demonstrate decreased expression of GIRK1 and an increased incidence of inducible arrhythmias post-MI. These data support a novel role of SREBP1 in the development of arrhythmia.

1001-108
Chemical Ablation of Subendocardium and Purkinje Fibers in Dogs Causes Early Termination and Activation Rate Slowing of Long Duration Ventricular Fibrillation
Derek J. Dosdall, Paul B. Tabereaux, Jong J. Kim, Gregory P. Walcott, Jack M. Rogers, Sam M. Sapp, Kevin J. Prunty, William A. Schillinger, William M. Smith, Raymond E. Iskander, University of Alabama at Birmingham, Birmingham, AL

Background: Endocardial mapping has suggested that Purkinje fibers may play a role in the maintenance of long duration ventricular fibrillation (LDVF). To determine the influence of Purkinje fibers on LDVF, we chemically ablated the Purkinje fiber system and mapped
Concordance of Sites With Latest Activation and Epidural Left Ventricular Lead Fixation is a Strong Predictor of Response to Robotically Implanted Cardiac Resynchronization Therapy


Background and Objective
Robotically implanted CRT is a rescue therapy for pts with failed endovascular implants with advantage to place left ventricular (LV) lead over the latest dysynchronous myocardial region. The value of concordance of dysynchrony and LV lead fixation site in improving response to CRT in these pts is not defined.

Methods: 30 pts (67±12yrs; 53% male; LVEF 18±6%) with end-stage heart failure, LVEF ≤35%, QRS >120ms and LBBB were included. LV dysynchrony (DYS) was defined as > 65ms opposing LV wall delay in peak systolic contraction by Tissue Synchronization Imaging. CON was defined as site of most delayed contraction and robotic LV lead fixation were same. Responders were defined by improvement in LVEF of ≥15% from baseline during follow-up of 8 ± 3 mos.

Results: 25 pts (73%) had dyssynchrony. 17 pts (56%) had CON, of whom 15 (88%) were responders, compared to discordance in 13 (44%), of whom 6 (46%; p = 0.001) were responders. Uni and multivariate analysis showed that concordance is a strong predictor of response to CRT (OR=36; p=0.003). In pts with no concordance the LVEF changed from 16±4 to 22±16 (p = 0.2) compared to pts with concordance in whom the LVEF changed from 19±6 vs. 31±12 (p < 0.0001).

Conclusion: Concordance results in improved outcome after robotically-assisted CRT. Direct epidural LV lead placement is an effective alternative to transvenous placement, and may offer superior opportunity to achieve concordance, a hypothesis that should be tested in clinical trials.

ABSTRACTS - Cardiac Arrhythmias

1001-110 Chronotropic incompetence (CI) in chronic heart failure - Time to pace?

Emma Amezi, Ulrich J. Jorde, Columbia University, New York, NY

CI, defined as the inability to reach 80% of maximally predicted age-adjusted heart rate (HR) occurs in approximately 70% of CHF patients with peak VO2 (pVO2) < 14 and contributes to exercise intolerance. Safety concerns prohibit restoring maximal exercise heart rate in CHF, but the possible benefits of rate responsive pacing (RRP) at low levels of exercise are less well studied. We propose that maintenance of stroke volume (SV) during heart rate increases might be an appropriate early safety measure.

Methods and Results: 99 male and 36 female subjects underwent the Modified Naughton protocol and were stratified according to pVO2 (ml/kg/min) (< 14.00 = Group A (n=54), 14.01 -17.99 = Group B (n=50), > 18.00 = Group C (n=31)). Beta blocker use was 74, 72, and 68% respectively (p=NS). HR and oxygen pulse (O2 pulse = VO2/HR, an indirect measure of SV) were recorded throughout exercise at 1 minute intervals. O2 pulse increased throughout the first 5 min in all subjects. HR=100 was reached within 2.5 min in group B and C, but not until 4 min in group A (≈ VO2 < 14).

Discussion: In the early phase of exercise at least to HR of 100 bpm, O2 pulse increases in subjects with CHF including those with most advanced disease. However, and despite a strictly standardized work load, time to reach HR 100 is significantly prolonged in subjects with most advanced disease. RRP to reach HR 100 early (if necessary in conjunction with CRT to avoid dyssynchrony) may improve functional capacity of subjects with CHF through early cardiac output (HR xSV) increase.

1001-111 Three Dimensional and Biatrial Mapping of Atrial Tachyarrhythmias in Coronary and Hypertensive Heart Disease: Identifying Mechanisms that Initiate and Maintain Persistent Atrial Fibrillation

Sanjeev Rakesh, Nicholas Skadsberg, Electrophysiology Research Foundation, Warren, NJ

Background: Atrial tachyarrhythmias (ATs) are being identified in pts with persistent atrial fibrillation (AF) but their role and relationship to structural heart disease (SHD) remains unclear. Methods: Spontaneous atrial premature beats (APBs) & ATs were mapped with simultaneous biatrial catheter & 3-D non-contact mapping (NCM) in pts with refractory AF at AF onset and maintenance in pts without structural heart disease (AF-NSHD, Group 1) and compared to with AF pts with coronary artery disease (AF-CAD, Group 2), systemic hypertension (AF-HTN, Group 3) and when both CAD & HTN were present (AF-CAD-HTN, Group 4). Results: 53 pts (Gp. 1 = 19 pts; Gp. 2 = 8 pts; Gp. 3 = 15 pts and Gp. 4 = 11 pts) were studied. Mean LA diameter, mean LV ejection fraction and mean P-wave duration in the 4 groups were comparable (p=ns). The origin of APBs was biatrial and also not significantly different (Gp. 1 = 35% in LA, Gp. 2 = 30% in LA, Gp. 3 = 30% in LA, and Gp. 4 = 28% in LA). However, the distribution of spontaneous ATs at AF onset was biatrial in Gps 1, 2 & 3 but predominated in the right atrium (RA) & septum in Gp 4. Persistent AF was associated with a wider distribution of ATs, particularly in the RA & septum. (Figure, p<.05) Conclusions: Atrial distribution of triggers and ATs suggests either biatrial structural changes and/or autonomic mechanisms are present particularly in persistent AF and can be identified both at the AF onset & maintenance. 2. A shift to RA & septal ATs with the coexistence of CAD & HTN suggests an expanding RA substrate.
Improvement of Left Atrial Function is Associated with Lower Incidence of Atrial Fibrillation and Mortality after Cardiac Resynchronization Therapy

Jeffrey WH Fung, Gabriel WK Yip, Fang Fang, Qiong Zhang, Joseph YS Chan, Chun-mei Li, Li-wen Wu, Gary CP Chan, Hamish CK Chan, Cheuk-man Yu, The Chinese University of Hong Kong, Shatin, Hong Kong

Background: Left atrial (LA) volume is a predictor of cardiovascular events in patients with heart failure (HF). Improvement of LA function and reverse remodeling was observed after cardiac resynchronization therapy (CRT). The current study aims to explore the clinical significance of improvement in LA function after CRT.

Methods: Echocardiographic studies were performed before and 3 months after CRT in 97 patients (age: 63.8 ± 13.3, male = 72) with standard CRT indication but without history of atrial fibrillation (AF). LA active emptying fraction based on the change in volumes (LAV-EF) was calculated and significant improvement in LA function (LA responder) was defined as a relative increase of > 50% from baseline LAV-EF. The primary endpoints were newly developed AF detected by ECG or device and all-cause mortality.

Results: After 1200 ± 705 days of follow-up, LA responders (n = 47, 48.5%) had significantly lower incidence of AF (12.8% Vs 40%; p = 0.002) and mortality (17% Vs 44%; p = 0.004) than LA non-responders. In the Cox proportional hazard analysis, LA responders was the only independent predictor of lower risk of new-onset AF (HR 0.22; 95% CI: 0.08-0.61; p = 0.003) while both LA responders (HR 0.22; 95% CI: 0.09-0.63; p = 0.001) and LV reverse remodeling (>10% reduction in LV end-systolic volume at 3 months) (HR 0.96, 95% CI: 0.93-0.99; p = 0.03) were independent predictors of lower risk of death after CRT.

Conclusion: Improvement of LA function after CRT was associated with lower incidence of AF and mortality in AF naïve patients with severe HF.

Under-Retention of Women for Atrial Fibrillation Ablation: Can This Be Explained by Gender Differences in Outcome?

Andrea M. Russo, Eric Zado, Edward P Gestenfeld, Rupa Bala, Ralph J. Verdio, Fermín García, David Lin, Sanjay Dixit, Joshua Cooper, David J. Callans, Mathew Hutchinson, Michael Riley, Francis E. Marchlinski, University of Pennsylvania, Philadelphia, PA

Background: Although women represent over one half of patients with atrial fibrillation (AF) in the United States, they are less often referred for AF ablation than men. It is currently unclear whether or not gender differences in outcome may contribute to this under-referral.

Methods: We compared baseline characteristics and outcome of 975 consecutive men and women who underwent AF ablation at our center.

Results: Women represented 23% of the cohort who underwent AF ablation. Mean follow-up was 17.8 ± 14.1 months for women and 18.6 ± 15.3 months for men (p = NS). Compared with men, women were older, had a smaller left atrial size, higher LVEF, and were less likely to have persistent AF. Women were less likely to undergo repeat ablation (17% versus 28%, p = 0.01). At last follow-up, 88% of women and 92% of men had arrhythmia control on or off antiarrhythmic agents (p = 0.07). This trend toward a difference in outcome could be related to fewer repeat ablations performed in women.

Following ablation, 19 women (9%) and 57 men (8%) were restarted on antiarrhythmic agents to obtain arrhythmia control after AF recurrence (p = NS).

Conclusions: Baseline characteristics differ between men and women undergoing AF ablation. In spite of these differences, good arrhythmia control was apparent in both genders. The results suggest that the tendency to limit ablative therapy in women, reflected by a comparison of overall AF incidence and percentage of women referred for ablation, is not justified based on clinical outcome.

Association of Paroxysmal Atrial Tachyarrhythmias with Heart Failure Exacerbations: Assessment Using Implanted Pacemakers With Trans-Pulmonary Impedance Capability (OptiVol®)

Rajat Jhajhli, Grant Templeton, John Nguyen, Cengiz Ermiş, Laura Van Heel, Keith Lure, Simon Mistleton, David Benfield, University of Minnesota, Minneapolis, MN, Central Minnesota Heart Center, St. Cloud, MN.

Background: Clinical experience suggests that susceptibility to atrial tachyarrhythmias (AT), particularly atrial fibrillation, is increased during worsening heart failure (HF). However, quantifying this association is challenging. Recently, certain pacemakers can assess HF status by estimating pulmonary fluid volume over time using a measure of trans-pulmonary electrical impedance change (OptiVol index® (OII), Medtronic, Inc, Minneapolis MN). This study utilized OII value to evaluate AT versus HF relationship in patients implanted with an OI-capable cardiac pacemaker, left ventricular dysfunction and HF. Specifically, we assessed the frequency with which AT accompanies HF, and determined whether OII value predicts increased HF susceptibility.

Methods: AT frequency was assessed for 3 subsets of OII values: <40 (Group 1), 40-70 (Group 2) and >70 (Group 3). Chi-squared test was used to measure association between OI and AT frequency. AT duration was compared between groups using ANOVA.

Results: OI and AT events were examined in 45 patients (mean age ± SD = 66 ± 10.5 years; 76% male, ischemic cardiomyopathy 46%). Three patients with p-hydroxybutyrate AT, and 2 with incomplete data, and one without HF history were excluded. Average left ventricular ejection fraction was 27 ±10%. OI and AT were evaluated at a total of 116 patient follow-up visits, with a mean follow-up of 2.7 ± 1.7 months. There were 65 visits in Group 1, 29 in Group 2, and 22 in Group 3. The corresponding frequencies of paroxysmal AT episodes in each of the 3 groups were: 21(32%), 13(45%), and 19(86%), X2=19.4, p<0.0001. Mean hours of AT duration (AT burden) was 17.9, 1.7, and 287 for Groups 1, 2, and 3 respectively. AT burden differed significantly between Groups 1 and 3 (p<0.0001), and Groups 2 and 3 (p=0.0002). Groups 1 and 2 were statistically indistinguishable (p=0.78).

Conclusion: In HF patients with cardiac pacemakers, increased OII value was associated with increased AF frequency. In particular, an OptiVol Index® >70 was accompanied by both significantly greater AT frequency and AT burden.

High Density Mapping of Atrial Fibrillation in Humans: Relationship Between High Frequency Activation and Electrogram Fractionation

Martin K. Sites, Anthony G. Brooks, Pawel Kulik, Bobby John, Glenn D. Young, Prashanthan Sanders, Cardiovascular Research Centre, Royal Adelaide Hospital and University of Adelaide, Adelaide, Australia

Background: Sites of complex fractionated atrial electrograms (CFAEs) and dominant frequency (DF) have been implicated in maintaining atrial fibrillation (AF), however their relationship is poorly understood.

Methods: Twenty patients (68 ± 16 y, 16 male) with AF were studied. High-density mapping (507±150 point/patient) was performed of both atria during AF prior to catheter ablation.

CFAE characterization using NavX software provided a representation of electrogram complexity (CFAE-mean). Offline spectral analysis defined DF as the frequency with greatest power.

Results: Median CFAE-mean was 103ms (IQR 76-143ms) for the right and 98ms (72-139ms) for left atria (p<0.001); 117ms (85-161ms) in paroxysmal and 92ms (70-127ms) in persistent AF (p<0.001). Median DF was 5.4Hz (4.9-6.1Hz for the right and 5.57Hz (4.9-6.3Hz) for the left atria (p=0.02); 5.27Hz (4.6-5.7Hz) in paroxysmal and 5.93Hz (5.35-6.67Hz) in persistent AF (p<0.001). Regional analysis revealed pulmonary veins, appendages and the left atrial roof as preferential areas with high DF in paroxysmal (p<0.05) but not persistent AF where regional differences were less apparent. Highest DF points were clustered together, such that the mean number of high DF clusters was 5.2±1.7 per patient. The correlation between CFAE-mean and DF was poor on a point-by-point basis (r=0.17), but was moderate at the atrial level (r=0.50). Evaluation of the spatial relationship demonstrated CFAEs to be in close proximity to high DF sites; superimposed in 17%, within 10 mm in 63% and 10-20mm in 10%.

Conclusions: Greater fractionation (low CFAE-mean) and higher DF are seen in persistent AF and in left atria. Preferential areas of high DF are observed in paroxysmal but not persistent AF. While there is little correlation between CFAEs and DF on a point-by-point basis these factors demonstrate a relationship at the atrial level. With high-density mapping, 80% of clusters of high DF were observed to be at or adjacent to areas of CFAEs.

ACC.Poster Contributions

Clinical Electrophysiology—Supraventricular Arrhythmias

Sunday, March 30, 2008, 1:00 p.m.-4:30 p.m.
McCormick Place, South Hall

Atrial Fibrillation Progression in Patients With and Without Lone Atrial Fibrillation: A Five-Year Prospective Follow-Up Study

Vincenzo Santinelli, Andrea Radinovic, Francesca Manguso, Simone Sala, Gabriele Vicedomini, Patrizio Mazzone, Giuseppe Ciconte, Enrico Frigoli, Giuseppe Angelillo, Emma Geleria, Simone Galletta, Massimo Saviano, Alessia Pappone, Gabriele Pagnini, Carlo Pappone, San Raffaele Hospital, Milan, Italy

Background: There are no prospective data on progression of AF in patients with and without lone AF.

Methods: All consecutive patients with first-detected paroxysmal AF were analyzed. Primary end-point was the cumulative probability of progression to permanent AF within 5 years, adjusted for related risk factors.

Results: Among 402 screened patients, 106 (mean age, 57.5 years) were enrolled. Of them, 54 (mean age, 53.3 years) had lone AF and 52 (mean age, 62.0 years) had comorbidities. At the end of the 5-year follow-up, 50 patients (47%) had no episodes, 31 (29%) had recurrent paroxysmal AF episodes, 9 (9%) had persistent episodes, and 16 (15%) definitely progressed to the permanent AF. Patients with lone AF were less likely to progress to recurrent paroxysmal/persistent and permanent arrhythmia (<0.001). Age was the common predictor for all clinical forms regardless of comorbidities presence. Comorbidities predicted progression to persistent (p=0.003) and permanent AF (p=0.028) but not to paroxysmal AF. Persistent AF (p=0.005), heart failure (p=0.006) and diabetes mellitus (p=0.007) predicted progression to permanent AF.
Background: Cryoenergy (CE) is assumed to be safer than RF energy due to its rapid reversibility. While this assumption is based on limited data, it has led to use of CE for ablations around the AV node and in pediatric patients. To address the issue of safety, this study was designed to test the reversibility of cryo-induced complete heart block (CHB).

Methods: In five patients (51.8 years) with a clinical indication for AV node ablation, CE was delivered to the AV node region using a 6mm tip cryocatheter (Cryocath) at a temperature of -80°C. If CHB was observed, cryoenergy was continued for an additional 10s. The heart rhythm was monitored for 30 min to assess recovery of conduction. If the effect was temporary an additional 20s of CE was delivered after development of CHB. The primary endpoint was the creation of CHB persisting for >30min after only 10s of additional CE. The secondary endpoint was any documented damage to the native conduction system.

Results: Primary endpoint of CHB>30min was observed in two of five patients (40%). Time interval from CE-onset to CHB was 10.5±7s (range 10-11s). Time of cryoaplication after CHB was 11.0±2.7s. The secondary endpoint of any effect on the conduction system (CHB or RBBB) was observed in all five patients (100%). Persisting CHB and RBBB of >30min was observed after additional 20s of CE in patient four and five, respectively. Conclusions: CHB persisting >30min was observed in 40% of the patients with only 10s of additional cryoenergy after onset of CHB. There are significant effects of CE on the native conduction system, which last >30min in 80% of patients. These findings raise considerable concerns about the rapid reversibility of cryo-induced effects on the human conduction system.

http://dx.doi.org/10.1016/j.jacc.2008.06.081

A Prognosis and Risk Factor Analysis in Paroxysmal, Persistent and Permanent Atrial Fibrillation

Laurent Fauchier, Bruno Raouzy, Emile Nonin, Laurent Gorin, Bertrand Pierre, Caroline Grimard, Axel de Labriolle, Dominique Babuty, Bernard Charbonnier, Centre Hospitalier Universitaire Trousseau, Tours, France, Faculté de Médecine, Tours, France

Background: The presentation of atrial fibrillation (AF) has been categorized into 3 general patterns: paroxysmal, persistent, and permanent AF. Whether AF pattern affects survival is poorly recognized.

Methods: Patients seen in the cardiology department in our institution (academic hospital, tertiary referral center) with AF between January 2000 and July 2007 were retrospectively identified and prospectively followed. The patients were identified by a search in the hospital discharge records which include information on type of AF, primary diagnoses and co-existing conditions, performed procedures, date of admission, discharge, and in-hospital death.

Results: Among 6517 patients, those who died or were lost to follow-up within 30 days of their index event were excluded. In the remaining 4058 patients, (age 71±14 years; 2523 men [62%]), 2167 had paroxysmal AF, 220 had persistent AF, and 1671 had permanent AF. During a follow-up of 945±767 days, 553 of them died. The mean annual mortality rate was 5.3%.

CHADS2 score was 1.53±1.08 in paroxysmal AF, 1.51±1.16 in persistent AF (p<0.05 vs paroxysmal AF) and 1.68±1.14 in permanent AF (p=0.001 vs paroxysmal AF, p=0.03 vs persistent AF). Permanent AF was associated with higher mortality than paroxysmal AF (relative risk=1.45, 95% CI 1.30-1.62) and persistent AF (relative risk=2.8, 95% CI 2.16-3.81). Persistent AF was associated with a better survival than paroxysmal AF (relative risk=1.98, 95% CI 1.49-2.62) (all p<0.001). The factors independently associated with increased mortality (Cox proportional hazards model) were concomitant heart failure (p<0.001), older age (p<0.001), history of stroke (p<0.002), male sex (p<0.007), diabetes (p<0.009) and AF pattern with paroxysmal or permanent AF (compared to persistent AF, p=0.003). Conclusion: Survival among patients with persistent AF was significantly better than that among patients with paroxysmal AF or permanent AF. The fact that paroxysmal and permanent AF were independently associated with increased mortality does not appear to be only related to concomitant cardiovascular risk factors. The decision and ability to maintain sinus rhythm may be associated with a better survival.

http://dx.doi.org/10.1016/j.jacc.2008.06.082

Clinical Characteristics of Patients With Very Late Recurrence of Atrial Fibrillation Post Ablation

Chii Ivena Ching, Claude S. Elayi, Luigi Di Biase, Barrett Connor, Meulet John, Thomas Callahan, John Zakalka, Robert Schuessler, Waldid Sellsa, Oussama Wazni, Mauricio Amuda, Jennifer Cummings, Mohamed Kanji, Andrea Natale, Cleveland Clinic, Cleveland, Ohio

Background: Recurrence of atrial fibrillation (AF) usually occurred within 6 months post ablation. Very late recurrence (>12 months) is uncommon and these patients may have unique clinical characteristics. We aim to describe the clinical characteristics of patients with very late AF recurrence post ablation.

Methods: Consecutive patients who underwent AF ablation over a period of 2 years were included. We identified 13 of 1971 patients (0.7%) with very late recurrence; defined as 12 months post ablation. Demographic, clinical and electrophysiologic data were collected at time of procedure and on subsequent follow-up visits. All patients underwent circular mapping catheter pulmonary vein isolation (PVI) to achieve electrical isolation of all pulmonary veins (PV) arra, verified by entry block to the respective PV. In addition, superior vena cava was also electrically isolated.

Results: The mean age of patients was 56 ± 10 years old with a preponderance of male (69%). The mean time to AF recurrence post ablation was 16 ± 4 months (range 12 to 23 months). The left atrial size was 42 ± 5 mm with a left atrial cavity area of 23 ± 5 cm2. Of note, most of these patients (60%) were not on anti-arrhythmic drugs at time of AF recurrence. There was no difference between incidence of paroxysmal vs non-paroxysmal AF. Ablation catheters used for the index ablation was non irrigated tip (77%) vs open irrigated tip (23%). PVI reconnection was found in almost all patients (92%) in the following frequency: RIPv (92%), LSPV (61.5%), RSPV (54%), LIPv (39%). Non-PV triggers were identified in 39%, either localized to the right interstitial septum or within the coronary sinus.

Conclusions: Majority of patients with very late AF recurrence post ablation demonstrated PV reconnection in addition to a high prevalence of non-PV triggers which were not seen at the time of the initial ablation.
Background: Widespread adaptation of radiofrequency catheter ablation (RFCA) of chronic atrial fibrillation (CAF) has been limited by long procedure times and low efficacy. This study was designed to evaluate the safety and efficacy of multi-array catheters combined with phased radiofrequency energy for RFCA of CAF.

Methods: Fifty-three patients with CAF underwent RFCA using a combination of three multi-array mapping and ablation catheters: a circumlinear 10-electrode catheter for antral pulmonary vein (PV) isolation, a 3-arm, 12 electrode catheter for septal ablation of complex fractionated atrial electrograms (CFAEs), and a 4-arm, 8 electrode catheter for CFAE ablation of the roof and other areas of the left atrium. Bipolar/unipolar phased radiofrequency was selectively delivered through all chosen electrodes at ratios of 1:1, 2:1, and 4:1, depending on the desired lesion depth. Non-fluoroscopic navigation systems were not utilized during the procedures. Power was limited to 10 watts/endpoint. Acute success was defined as complete isolation of all PVs and stable sinus rhythm at the end of the procedure. Chronic efficacy was assessed with a continuous 7-day Holter monitor at six months post procedure.

Results: Acute efficacy was documented in 50/53 patients (94.3%). Procedure times once a trans septal puncture was completed was 2 hours and 8 minutes. 21/53 (40%) of patients required two ablation procedures. 27 patients had a 7-day Holter monitoring recording six months post ablation. 7 days of continuous sinus rhythm have been documented in 23/27 patients (79.4%). 2 patients demonstrated intermittent episodes of self terminating PAF totaling 3.3 and 11% of the total recording. Of the 23/27 (79.4%) chronic success patients 2 remained on an AAD. The only serious complication was a transient neurologic event in one patient.

Conclusions: Multi-array catheters in conjunction with phased radiofrequency energy may allow good safety and long term efficacy when ablating CAF.

Safety, Efficacy, and Follow-up of Circumferential Pulmonary Vein Ablation in Octogenarians

Vincenzo Santinelli, Andrea Rardinovic, Simone Sala, Gabriele Vicedomini, Patrizio Mazzone, Simone Gulletta, Cristianio Cicco, Giuseppe Cincro, Gabriele Paglino, Giuseppe Augello, Emma Geler, Enrico Frigoli, Andreina Santagostino, Carlo Pappone, San Raffaele Hospital, Milan, Italy

Background. CPVA is an effective strategy for patients with atrial fibrillation (AF), but its safety and efficacy in the elderly have never been reported.

Methods. Between January 2005 and December 2006, all consecutive patients over the age of 80 referred for CPVA were enrolled. Complications and long-term outcomes were prospectively assessed by daily transtelephonic monitoring (TTM) and echocardiography. Results. The study population consisted of 172 patients (mean age, 83±2, male 55%) with paroxysmal AF (60 patients), persistent AF (60 patients), and permanent AF (52 patients). The average duration of AF prior to ablation was 7.4±5.5 years. Multiple comorbidities were present in 73% of patients (CAD in 38%, valvular heart disease in 46%, hypertension in 77%, diabetes in 20%, heart failure 15%, respiratory disease 10%). Respiratory arrest during anesthesia occurred in 5 patients. Complications during the procedure occurred in 4 patients including femoral pseudoaneurysm, anterovernous fistula, or tamponade not requiring surgical intervention. Over a mean follow-up of 18±5 months, 147/172 patients with comorbidities (heart failure, diabetes and hypertension) had AF recurrences with an overall success rate of 79%. In particular, 54 patients (90%) with paroxysmal AF, 38 (76%) with persistent AF and 37 patients (60%) with permanent AF were in sinus rhythm. AF recurrences, as documented by TTM, were silent in 23/43 patients (53%). A repeat procedure was done in 6/36 patients and the remaining patients were cured medically. Embolic events occurred in 6 patients (3.5%) despite optimal anticoagulation. In patients with permanent AF and sinus rhythm after ablation an inadequate atrial function persisted up to 1 year after procedure.

Conclusions. In octogenarians, CPVA is a safe and effective treatment particularly for paroxysmal and persistent AF. Greater attention is required during the procedure considering a higher number of procedure-related complications. Asymptomatic recurrences after ablation are frequent underestimating the true recurrence rate in such population supporting the need to continue anticoagulation even in the presence of sinus rhythm.

Visualizing Ablation Gaps in Vitro Using a Deflectable Fiber Optic Endocardial Visualization Catheter

Alnara M. Irani, Bryant Lin, Christian Eversull, Paul J. Wang, Amin Al-Ahmad, Stanford University Medical School, Stanford, CA, Acumen Medical, Sunnyvale, CA

Background: The efficacy of pulmonary vein isolation for the treatment of atrial fibrillation (AF) may be limited by a clinician’s ability to make a continuous lesion with a catheter based system. Gaps often persist between ablation lesions leading to failed electrical isolation, leading to recurrence of AF or the genesis of atrial flutter. Methods: Ninety-four radiofrequency lesions (RF) were delivered to ex vivo porcine endocardium. Gaps between the lesions ranged between 0.1mm and 9.8mm. We utilize a deflectable fiberoptic endocardial visualization catheter using light in the visible spectrum to visualize the endocardial surface and lesions. Videos were taken of the lesions and shown to two blinded readers who were asked to identify the gaps ranging from less than 0.1mm to 9.8mm. Results: Ninety-four lesions were reviewed. The readers demonstrated a combined accuracy of 98.4% at identifying lesion gaps. Figure 1 shows a 0.4 mm gap between two ablation lesions. The left panel shows the video capture from the direct visualization catheter, and the right panel shows the gross specimen of the same sample.

Conclusion: Gaps between ablation lesions can be accurately identified down to less than 1 mm distances in vitro using a direct visualization catheter. Further studies are warranted to confirm these finding in vivo.
Conclusions: In 2 randomized, controlled trials and 1 open-label study in patients with recent-onset AF (in the RCTs, 1 patient given PBO had torsade de pointes), the incidence with PBO was 12.6%. There were no cases of torsade de pointes with VNK in PBO, n=159), in which 51.1% of those given VNK were responders (vs 3.8% with PBO, n=159) in both trials. Efficacy assessments included vital signs, Holter monitoring, heart rhythm monitoring (telemetry), 12-lead ECG, clinical laboratory testing, physical examination, and adverse events. Registration of CT images to ECG-gated fluoroscopic images during AF ablation is feasible. The retrospective gating technique works better than the prospective technique, especially in patients with AF at the time of registration.

Methods: We enrolled 32 consecutive patients (mean age 62±9 years) who underwent an open-chest operation with cardiac arrest and were then successfully resuscitated. Efficacy assessments included vital signs, Holter monitoring, heart rhythm monitoring (telemetry), 12-lead ECG, clinical laboratory testing, physical examination, and adverse events. Results: In the OLS (n=167), 50.9% of patients were responders with a median time to conversion of 14 min. Three results were similar to those in the 2 RCTs (VNK, n=336; PBO, n=195), in which 51.1% of those given VNK were responders (vs 3.8% with PBO, P<0.001), with a 10-min median time to conversion. The incidence of serious adverse events with VNK was similar in the OLS and RCTs, 12.0% and 13.0%, respectively; the incidence with PBO was 12.6%. There were no cases of torsade de pointes with VNK in these patients. In patients treated with onset AF in the RCT (n=159) given PBO (or torsade de pointes). Adverse events with VNK were similar in the OLS and RCTs. The most common adverse events with VNK in the OLS were dysgeusia (altered sense of taste), sneezing, paresthesia, and hypertension. The most common adverse events with VNK in the RCTs were dysgeusia, paresthesia, dizziness, nausea, and headache.

Conclusions: In 2 randomized, controlled trials and 1 open-label study in patients with recent-onset AF, VNK rapidly and effectively converted AF to sinus rhythm and was well tolerated.
The present study was undertaken to assess the impact of the ACE I/D polymorphisms on circulating markers of collagen type I synthesis and degradation and the effect of therapy with ACE inhibitors on these markers in hypertensive patients with AF.

Methods: ACE I/D genotypes were assessed in 158 hypertensive patients (71±9 years, 72 male) with AF and 174 patients with arterial hypertension in sinus rhythm (SHR) (71±9 years, 88 male). Serum concentrations of amino-terminal propeptide of type I collagen (PINP) and of carboxy-terminal telopeptide of collagen type I (ICTP), indexes of collagen type I synthesis and degradation respectively, were measured.

Results: Of the 332 study participants 74 (22.3%) were I/I, 158 (47.6%) I/D and 100 (30.1%) D/D carriers. Genetic variation in ACE significantly influenced serum CTIP levels in AF patients (p=0.011). CTIP levels were lower in D allele carriers (D/D and ID) compared to I/I. There was no difference in PINP levels between the different ACE genotype groups (p=0.302). Patients treated with ACE inhibitors had higher CTIP levels compared to those not treated (p=0.036).

Conclusions: This study suggests that the presence of the D allele in hypertensive patients with AF is associated with attenuation of type I collagen degradation and that therapy with ACE inhibitors increases degradation of collagen type I. The data indicate a subgroup of patients with AF arterial and hypertension who may benefit more from therapy with ACE inhibitors, thus, providing a basis for pharmacogenetics.
Extracellular Matrix Alterations in Patients With Paroxysmal and Persistent Atrial Fibrillation.

Biochemical Assessment of Collagen Type I Turnover

Eleftherios M. Kallergis, Emmanuel G. Manios, Emmanuel M. Kanoupakis, Hercules E. Mavrikas, Dimitris A. Arafaki, Niki E. Malliaraki, Chrisovalantis E. Lathourakis, Panos E. Varas, Heraklion University Hospital, Heraklion, Crete, Greece

Background: Structural alterations and fibrosis have been implicated in the generation and perpetuation of AF.

Methods: We investigated whether the serum markers of collagen turnover differed in various forms of atrial fibrillation (AF) and in sinus rhythm (SR) in humans. Serum C-terminal propeptide of collagen type I (CICP), C-terminal telopeptide of collagen type I (CTIP), matrix metalloproteinase-1 (MMP-1), and tissue inhibitor of matrix metalloproteinases-1 (TIMP-1) were measured as markers of collagen synthesis and degradation in 70 patients with AF and 20 healthy controls in SR.

Results: CICP and CTIP were significantly higher in AF patients than in controls (91.37±27.26 ng/ml vs. 67.30±11.05 ng/ml, p<0.001 and 3.88±0.20 ng/ml vs. 2.55±0.08 ng/ml, p<0.001, respectively). Persistent AF patients had higher levels of CICP but not CTIP, compared to those with paroxysmal AF (105.06±27.57 ng/ml vs. 79.84±2.23 ng/ml, p<0.001). Patients with persistent AF had lower levels of MMP-1 but increased levels of TIMP-1 compared to patients with paroxysmal AF (11.55±4.97 ng/ml vs. 14.98±2.86 ng/ml, p=0.01 and 1.59±0.81 ng/ml vs. 0.91±0.10 ng/ml, p<0.001, respectively). TIMP-1 levels were significantly lower in control subjects compared with both paroxysmal and persistent AF patients (102.10±15.13 ng/ml vs. 129.75±37.92 ng/ml vs. 154.90±44.91 ng/ml, respectively, p<0.001).

Conclusions: Serum markers of collagen type I turnover differed significantly between patients with AF and SR. Furthermore, these markers also differed significantly between paroxysmal and persistent AF patients, suggesting that the intensity of the extracellular synthesis and degradation of collagen type-I may be related to the burden or type of AF.

Hospitalization after First Atrial Fibrillation Diagnosis: Changing Trends and Relation to Practice Pattern

Yoko Miyasaka, Marion E. Barnes, Stephen S. Cha, Kent R. Bailey, Teresa S.M Tsang, Mayo Clinic, Rochester, MN

Background: Data suggest that there has been an increase in hospital admissions for cardiovascular reasons after first atrial fibrillation (AF). Whether this was related to a change in practice pattern remains uncertain.

Methods: Olmsted County, Minnesota residents diagnosed with first AF during 1980-2000 were identified and hospital admissions for any cardiovascular causes following the first AF diagnosis were reviewed and classified. For admissions specifically for heart rate or rhythm control, we determined the specific mode of therapy that the patient received: initiation of antiarrhythmic or anticoagulation therapy, electrical cardioversion, device therapy (pacemaker or cardioverter-defibrillator implant), or catheter/surgical ablation.

Results: Of a total of 4,678 subjects diagnosed with first AF (mean age 73±14 years; 51% men), 2,503 (56%) were admitted at least once to the hospital for any cardiovascular causes following the first AF diagnosis (total number of admissions, 6,990) during a mean follow-up time of 5.5±5.0 years. The age-sex-adjusted rate of first hospitalization over time to the trend of increased hospitalization over the last two decades was examined.

Results: A total of 4,618 subjects diagnosed with first AF (mean age 73±14 years; 51% men), 2,503 (56%) were admitted at least once to the hospital for any cardiovascular causes following the first AF diagnosis (total number of admissions, 6,990) during a mean follow-up time of 5.5±5.0 years. The age-sex adjusted rate of first hospitalization for any cardiovascular cause after first AF diagnosis increased, on average, by 2.5% a year, even after multivariable adjustment for comorbidities (P<0.001). The age-sex adjusted rate of first hospitalization with a primary reason of rhythm or rate control also increased significantly, on average, by 7.6% a year, even after multivariable adjustment (P<0.001). When we excluded the hospital admissions for the purpose of rhythm or rate control, the increase in hospital admission was only 0.8% per year, which was not significant after multivariable adjustment (P=0.25).

Conclusions: The trend of increase in hospital admission after first AF diagnosis was largely related to changing practice pattern with AF management, independent of the changes over time in the distribution of age, sex, and comorbidities. With the anticipated increase in AF over the next few decades, these findings represent major socioeconomic burden to our healthcare system.

Long-Term Experience in Cryoablation of Pulmonary Veins with Balloon Technique in Paroxysmal Atrial Fibrillation

Jürgen Vogt, Anja Dorszewski, Johannes Heinrich, Ursula Scholtz, Ulrike Wetzl, Sven Oettermoller, Lam Luong Thanh, Dieter Horstkotte, Department of Cardiology, Heart and Diabetes Center North Rhine-Westphalia, Ruhr University Bochum, Bad Oeynhausen, Germany

Background: In the treatment of paroxysmal atrial fibrillation (AF) circumferential substrate ablation of the pulmonary veins (PV) seems superior in comparison to segmental methods. However, with radiofrequency energy, a risk of PV stenoses and esophago-left atrial fistula exists. This study reports on the long-term experience in isolating PV ostia and parts of the atrium with the cryoballoon technique.

Methods: After PV angiography the PV ostium was isolated with best fitting 28/23mm balloon (Arctic Front, Cryocath, Canada). The inflated over the wire balloon occluded the venous ostium and parts of venous antrum freezing down to 75°C with 6 minutes twice per vein with nitrous oxide. Lasso mapped rest potentials were eliminated with additional balloon freezes or 8/f 330µm Freezer Max catheter. Patients (p) were followed three monthly with 7-day Holter.

Results: We treated 147 p (45 women, mean age 59±10 years,136 with paroxysmal,1 persistent af, all atrium 42±5 mm, 65 with lobe af, 59 hypertension, 23 mild structural heart disease (enlarged vein diameter) with 23/28 mm balloon catheter. Mean follow-up time was 5.5±4 years. With balloon catheter in 68% of the patients 18/58 mm with an additional freeze of 35±15 mm balloon. With a mean number of 2.4±0.7 impulses we isolated up to 87% of the left pv and the right upper pv and 82% of the right lower pv with balloon only; in the last 40 p all 4 pv with balloon only could be isolated! In 30% we combined 23/28 mm balloon. We isolated 100% of the pv during a procedure with a median time of 18±5 min and a median number of 68±19 impulses. Phrenic neural palsy in 6 p recovered within 3 to 9 months. During a mean follow-up of 8.5 months and 1.1 procedures per p (12 redos) of 96 p controlled with serial 7-day holter and symptoms 78% (75 p) were free of af. 16 showed marked reduction of atrial fibrillation. In the 12 redos 68% of the 37 reconducting veins were initially isolated with the 28 mm balloon.

Conclusions: Cryoablation of ostia and antrum of the PV with balloon technique is safe and shows a convincing outcome in long term experience. The superiority in comparison to substrate modification with RF will be an early and first line therapy of left atrial atrial fibrillation. Avoidance of phrenic nerve lesion and focus on improvement of balloon design may be essential.

Up-regulation of Toll-like Receptor 2 Expression Levels in non-Valvular Atrial Fibrillation: Comparison between blood samples from peripheral vein and left atrium

Yasunasa Iriki, Koji Ohirana, Sanemasa Ishida, Shuichi Hamasaki, Masayuki Ogawa, Tetsuro Kataoka, Toshikiri Matsumoto, Ryuto Oba, Hirokyi Hirai, Kinya Nagata, Choua Tei, Graduate School of Medicine, Kagoshima University, Kagoshima, Japan

Background: Many studies have suggested that an inflammation may participate in the pathogenesis of non-valvular atrial fibrillation (AF). Most recently we reported that Toll-like receptor 2 (TLR2) levels on monocytes derived from peripheral venous blood in patients (n = 18) with paroxysmal/persistent non-valvular AF were significantly higher than those in patients n = 24 with sinus rhythm (controls), simultaneously showing that non- valve AF patients had significantly higher CRP levels than controls. Furthermore, we have observed that T-helper type 1 (Th1) -cytokine, such as interferon-γ and tumor necrosis factor α, have a potency to up-regulate TLR2 levels, and that interleukin-4 down-regulates them.

Purpose: Our purpose is to test the hypothesis that there is a difference in TLR2 levels on monocytes between blood samples from peripheral vein and left atrium.

Methods: The consecutive 14 patients with non-valvular AF who were hospitalized for catheter ablation were enrolled in this study. Blood samples control from peripheral vein and left atrium were taken at the same time just before catheter ablation. TLR2 levels on monocytes were assayed by using our developed flow-cytometric analysis system, and they were represented by the number of anti-TLR2 monoclonal antibody binding sites on a monocyte.

Results: TLR2 levels between blood samples from peripheral vein and from left atrium were compared in 14 patients with non-valvular AF by using Wilcoxon signed-rank test. TLR2 levels on monocytes from left atrium were significantly higher than those from peripheral venous blood (median, 4866 [95% CI, 4342 to 6690] vs. 5493 [95% CI, 4342 to 6690] sites/cell; p = 0.02).

Conclusions: Our results suggest that high level of TLR2 in non- valvular AF patients may be due to not systemic inflammation but to dominant inflammation in left atrium.
ABSTRACTS - Cardiac Arrhythmias

2:00 p.m.

**1008-113** Older Age and Sick Sinus Syndrome Predict Newly Diagnosed Atrial Fibrillation After Dual Chamber Pacemaker Implantation

Sunee Mittal, Kenneth Stein, F. Roosevelt Gilliam, Stacia Merkel, Shelly Christman, Boston Scientific CRM, St. Paul, MN

**Background:** Following dual chamber pacemaker (PPM) implant, atrial fibrillation (AF) is often diagnosed for the first time based on detection of stored atrial high rate episodes (AHRE). Predictors of newly diagnosed AF after PPM implant in patients with no history of AF remain obscure.

**Methods:** We evaluated data from the Silent Atrial Fibrillation Detection with Stored EGMs (SAFE) registry, which was a multi-center, prospective registry of patients undergoing dual chamber PPM implantation. No patient had prior history of AF. Device interrogations were performed at 2-week, 3-, 6-, and 12-months post-implant. An AHRE was defined as ≥180 bpm lasting ≥5 minutes.

**Results:** 1482 patients (56% male, 74 ± 12 years) underwent dual chamber PPM implantation. 1050 (71%) patients were followed for ≥6 months, with a median follow-up time of 349 ± 147 days (mean=267 days). During 6 months of follow-up, 150 patients (10.1%) were diagnosed with AF. The majority of AHREs lasted between 5 minutes and 1 hour (19%), while only 4% lasted greater than 24 hours. Patients ≥80 years of age were at greater risk of developing AF than patients ≥65 years of age (p=0.019). Patients with sick sinus syndrome were at a greater risk of developing AF than patients without sick sinus syndrome (HR=1.512, p=0.034).

**Conclusions:** In the SAFE registry, 10.1% of patients followed for six months were diagnosed with AF for the first time. Age ≥80 years and presence of sick sinus syndrome were risk factors for development of AF in patients with no history of AF.

<table>
<thead>
<tr>
<th>Baseline Characteristics</th>
<th>AF-Yes (n=159)</th>
<th>AF-No (n=1322)</th>
<th>Hazard Ratio</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>730 (55%)</td>
<td>707 (46%)</td>
<td>0.756</td>
<td>0.097</td>
</tr>
<tr>
<td>Male</td>
<td>730 (55%)</td>
<td>707 (46%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Age (years)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 65</td>
<td>40 (4%)</td>
<td>522 (40%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>65 and &lt; 80</td>
<td>256 (19%)</td>
<td>618 (47%)</td>
<td>0.539</td>
<td>0.019</td>
</tr>
<tr>
<td>≥ 80</td>
<td>618 (47%)</td>
<td>40 (4%)</td>
<td>0.821</td>
<td>0.261</td>
</tr>
<tr>
<td><strong>Structural Heart Disease</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>78 (52%)</td>
<td>735 (54%)</td>
<td>1.281</td>
<td>0.1305</td>
</tr>
<tr>
<td>No</td>
<td>616 (88%)</td>
<td>622 (72%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Sick Sinus Syndrome</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>116 (77%)</td>
<td>922 (69%)</td>
<td>1.512</td>
<td>0.034</td>
</tr>
<tr>
<td>No</td>
<td>76 (50%)</td>
<td>410 (31%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Left Block</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>82 (41%)</td>
<td>635 (48%)</td>
<td>0.758</td>
<td>0.095</td>
</tr>
<tr>
<td>No</td>
<td>98 (59%)</td>
<td>697 (52%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>EF%</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 40</td>
<td>20 (19%)</td>
<td>143 (16%)</td>
<td>1.356</td>
<td>0.219</td>
</tr>
<tr>
<td>≥ 40</td>
<td>83 (81%)</td>
<td>746 (84%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**2:00 p.m.**

**1008-114** Magnetic Catheter Ablation of Right Atrial Flutter - The Importance of an 8mm Tip Electrode to Achieve Bidirectional Block

Sabine Ernst, Bueulent Koektuerk, Julian KR Chun, Feiyan Ouyang, Karl-Heinz Kuck, St. Georg General Hospital, Hamburg, Germany

**Background:** The novel magnetic navigation system (MNS) (Niobe, Stereotaxis) controls the distal magnetic tip of an ablation catheter in conjunction with a catheter advancement system. The aim of this study was to deploy a complete linear lesion to treat typical atrial flutter in a remote-controlled fashion.

**Methods & Results:** In a total of 36 pts (32 males, 62 ± 11 years) complete bidirectional right atrial isthmus block was attempted using a variety of magnetic ablation catheters. Three 4 mm tip and one 8mm tip catheter became successively available: First generation bipolar single magnet catheter (1M, n = 9 pts), second generation bipolar catheter with 3 magnets (3M, n = 9), third generation quadrupolar 3-magnet tip catheter (3M quad, n = 5) and finally a 3-magnet catheter with a large tip (3M 8mm, n = 13 pts) were used. Successful remote-controlled isthmus block was achieved in 33%, 66%, 0% and 92%, respectively. Besides the favourable ablation result, the use of the 3M 8mm catheter resulted in a marked decrease of total fluoroscopy duration (median 2.4, interquartile range 2.2 - 7.1) as well as exposure time for the investigator (median 2.2 min, 1.5 - 5.4). No complications occurred.

**Conclusions:** This is the first report of remote-controlled linear lesion deployment in the right-atrial isthmus using magnetic navigation. In comparison to several 4mm tip magnetic catheters, superiority of the 8mm tip electrode to achieve bidirectional block with regards to effectiveness and fluoroscopy exposure was demonstrated.

**2:00 p.m.**

**1008-115** Paracardioscopic Creation of a Comprehensive BltrialLesion Pattern During Minimally Invasive Atrial Fibrillation Treatment

Andy C. Kiese, Jerzy Sadowski, Boguslaw Kapelak, Krzysztof Bartus, Gerhard Wimmer-Greinecker, Pinashurlt Surgical, Pinashurlt, NC

**Background:** Current minimally invasive (MI) treatments for atrial fibrillation (AF) focus on pulmonary vein isolation (PVI). Patients with structural heart disease and wavelet AF require a comprehensive, bi-atrial lesion pattern. Paracardioscopic access through the diaphragm in combination with a small right mid-axillary incision provides MI access and direct visualization to create a comprehensive bi-atrial lesion pattern.

**Methods:** Ten patients with isolated AF (persistent=4, permanent=6) underwent a paracardioscopic Ex-Maze procedure (Figure). Epicardial lesions were created with radio frequency energy delivered through a novel, vacuum-assisted device. All patients had lesions along the pericardial reflections (1,2,4,5,6) to isolate the pulmonary veins (PVs), and additional right and left atrial lesions (2,3,7,8) to complete the Ex-Maze pattern.

**Results:** A complete Ex-Maze lesion pattern was created in all patients. PVI was confirmed in all patients tested for exit block at 15 mA. The transdiaphragmatic access healed without event in all patients. Four patients have reached 1 month follow-up and are in sinus rhythm without cardioversion or class I or III antiarrhythmic drugs.

**Conclusions:** Paracardioscopy enables direct MI access and visualization of the posterior heart for creation of a comprehensive, bi-atrial lesion pattern. Early results with the Paracardioscopic approach are encouraging, and studies are ongoing to confirm the efficacy of the MI Ex-Maze lesion pattern.
802-4
A Novel Pacing Paradigm for Cardiac Resynchronization Therapy in Desynchronized Acute LV Dysfunction during Atrial Fibrillation
Pascal Lim, Georges E. Yanovsky, Youhua Yang, Richard A. Grimm, Don W. Wallack, Cleveland Clinic, Cleveland, OH, APH-HP Henri Mondor Hospital, Creteil-Paris, France

Background: Heart failure (HF) patients with drugs refractory atrial fibrillation (AF) may require ablation therapy to benefit from Cardiac Resynchronization Therapy (CRT). One alternative is CRT with coupled pacing (CRT-CP) which consists of delivering an additional stimulus after the refractory period.

Methods: CRT and CRT-CP were compared in 6 dogs with AF induced by atrial pacing and desynchronized HF by right ventricular (RV) pacing. For CRT-CP, an RV premature beat was systematically applied after CRT (170±19ms). AV node conduction was depressed by selective parasympathetic nerve stimulation to allow CRT rate to be similar to CRT-CP. LV ejection fraction (LVEF), stroke volume (SV) and global peak strain (ε) were used to assess contractility. Diastolic period and LV dysynchrony were expressed as % of RR interval.

Results: Compared to sinus rhythm, RV pacing during AF increased LV dysynchrony (72±4% vs. 19±3%, p=0.001) and reduced diastolic period (40±6% vs. 30±7%, p=0.01), LVEF (25±4% vs. 18±6%, p=0.01), SV (25±5ml vs. 12±3ml, p=0.006) and ε (4±2% vs. 12±2%, p=0.003). Importantly, CRT-CP slowed the ventricular rate by half (116±17bpm vs. 25±14bpm) and compared to CRT at similar rate, dramatically increased diastolic period (25±3% vs. 48±6%, p=0.002) and trended to improve SV and ε.

Conclusions: CRT-CP slows the ventricular rate during AF and increases contractility and diastolic function compared to CRT at a similar rate.

802-5
Cardiac Rhythm Device Therapy
Monday, March 31, 2008, 8:00 a.m.-9:30 a.m.
McCormick Place, Room S403

802-6
Acute versus Late Reduction in Mitral Regurgitation after Cardiac Resynchronization Therapy
Claudia Yoenburg, Patrizio Lancelotti, Lauren F. Tops, Eric Boersma, Gabe B. Bleeker, Eduard R. Holman, James D. Thomas, Martin J. Schalij, Luc A. Pierard, Jeroen J. Bax, Leiden University Medical Center, Leiden, The Netherlands, University Hospital Sart Tilman, Liege, Belgium

Background: The aim of the current study was to evaluate the relationship between presence of LV dysynchrony at baseline and reduction in mitral regurgitation (MR) acute and late after cardiac resynchronization therapy (CRT).

Methods: Sixty-eight consecutive patients (ejection fraction 23±8%, 57% ischemic cardiomyopathy) with at least moderate MR were included. Echocardiography was performed at baseline, one day after CRT initiation and at 6 months follow-up. MR severity was graded semi-quantitatively (mild = jet area/LA area <10%, moderate = jet area/LA area 10-20%, severe = jet area/LA area 20-40%, moderate/severe = jet area/LA area >45%) and improvement in MR was defined as improvement of at least 1 grade. LV dysynchrony was assessed using speckle tracking radial strain analysis and defined as the maximum delay between the 6 LV segments. The segment of latest activation was also noted.

Results: Twenty-nine patients showed an acute reduction in MR (‘early responders’) and 12 patients showed a reduction in MR after 6 months follow-up. MR severity was graded semi-quantitatively (mild = jet area/LA area <10%, moderate = jet area/LA area 10-20%, severe = jet area/LA area 20-40%, moderate/severe = jet area/LA area >45%) and improvement in MR was defined as improvement of at least 1 grade. LV dysynchrony was assessed using speckle tracking radial strain analysis and defined as the maximum delay between the 6 LV segments. The segment of latest activation was also noted.

Conclusion: Presence of baseline LV dysynchrony is related to improvement in MR after CRT. LV dysynchrony involves the posterior papillary muscle an immediate reduction in MR can be expected, whereas in patients with LV dysynchrony not involving the posterior papillary muscle late improvement in MR can be expected.
Heart Failure Deterioration and All-Cause Mortality in Relation to Percent Biventricular Pacing: Is a Goal of 100% Biventricular Pacing Necessary?

Bruce A. Kaplan, Stan Weiner, Andrew J. Kaplan, Paul W. Jones, Mylan Seth, Shelly A. Christman, Brigham and Women’s Hospital, Boston, MA

Background: Cardiac resynchronization (CRT) decreases the combined risk of death and heart failure (HF) hospitalization. However, the appropriate target for biventricular (BiV) pacing percentage is ill-defined.

Methods: Mortality and HF hospitalization from CRT patients (pts) in two trials (CRT RENEWAL & REFLEX; n=1,815) were analyzed in a post hoc fashion. Pts were grouped based on % BiV pacing using Kaplan-Meier survival analysis with a combined endpoint of HF hospitalization and all-cause mortality. A cut-off dividing the pts into two pacing groups with a maximally different survival pattern was found by an iterative search, maximizing the log rank statistic.

Results: Pts characteristics were: age 72 ± 11 years, 72% male, 67% CAD. Pts paced 80-90% (n = 202) and 0-80% (n = 168) had similar outcomes (HR 0.87, p = 0.53). Pts paced 91-95% (n = 321) had a 37% reduction in risk of an event compared to ≤90% after adjusting for covariates (HR 0.63, p < 0.01). Pts paced >95% (n = 1121) received no benefit over those paced 91-95%. (HR 0.92, p = 0.59). The greatest magnitude of difference in survival free from an event was found with a cutoff of 92% BiV. Pts paced >92% had a 43% reduction in odds of an event compared to ≤92% after adjusting for covariates (HR 0.57, p < 0.00001). Pts with a history of atrial arrhythmia were more likely to be paced ≤92% (p = 0.001).

Conclusions: For the CRT pts, the greatest magnitude of benefit was observed with a cutoff of >92% vs. ≤92% BiV pacing. No incremental benefit was observed in pts paced >95% vs. 90-95%.

Dynamic Time Warping: A Novel Algorithm for Rhythm Discrimination in ICDs

Baharan Kamrouzi, Bryant Lin, Gregory Lee, Amin Al-Ahmad, Henry H. Hsie, Paul C. Zei, Paul J. Wang, Stanford University School of Medicine, Stanford, CA

Background: Inappropriate shocks for supraventricular arrhythmias remain a major problem in the care of patients with ICDS. Pattern recognition algorithms have been successful for many non-medical applications. Dynamic Time Warping (DTW), originally used in automatic speech recognition, is a method to measure the overall similarity in pattern regardless of differences in time or speed by non-linearly warping them in the time dimension. In this study, we use DTW to distinguish Ventricular Tachycardia (VT) from other rhythms such as Supraventricular Tachycardia (SVT).

Methods: We examined 69 ICD episodes due to SVT or VT detection. The digital ICD electrograms were imported into a MATLAB program used to perform DTW on the individual ICD episodes. For each beat of the ICD episode, the DTW cost value was calculated. After the DTW algorithm was applied to each beat, the mean DTW value was calculated for the episode. Results: The DTW algorithm was able to correctly classify 67 episodes, giving the accuracy of 97%. One SVT episode was classified as VT and one VT episode was classified as SVT. (See Figure)

Conclusions: The present data suggest that DTW may be a promising method for ICD rhythm classification and may decrease inappropriate shocks. Further modifications of DTW may increase the sensitivity while maintaining the excellent specificity.
Angiotensin Inhibitors Prevent Atrial Fibrillation after Cardiac Surgery

James S. Kalus, Henry Ford Hospital, Detroit, MI, Wayne State University, Detroit, MI

Background: Approximately 30% of patients undergoing cardiac surgery (CTS) develop postoperative atrial fibrillation (Af). Cardiac remodeling likely plays a role in the pathophysiology of non-CTS Af and angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin-receptor blockers (ARBs) prevent recurrence of non-CTS Af, possibly by reducing atrial remodeling. The importance of cardiac remodeling in the pathophysiology of postoperative Af is unclear; however, the presence of disease states associated with cardiac structural changes, such as systolic heart failure or valvular disease increases the risk for postoperative Af. We assessed the hypothesis that ACEI or ARB treatment for > 3 months prior to CTS reduces the rate of postoperative Af.

Methods: Medical records of patients undergoing CTS were reviewed. Patients with a history of Af or who took an ACEI or ARB for < 3 months prior to CTS were excluded. Those taking ACEI or ARB for at least 3 months prior to CTS were included in the treatment group and those not exposed to ACEI or ARB during the year before CTS made up the control group. Data were collected for 125 treatment and 250 control patients. Propensity scores were used to match the treatment and control groups (1:1) for age, gender, type of surgery, use of antiarrhythmic drugs after surgery and presence of hypertension, diabetes, or heart failure. Rate of postoperative Af was compared between the treatment and control groups in 250 matched patients (67.7 ± 11.0 years, 68% male, 31.6% valve surgery).

Results: The treatment group was more likely to have diabetes, coronary artery disease and heart failure. Other demographics were similar between groups. Patients in the treatment group used ACEIs or ARBs for 58.7 ± 45.8 mos. Rate of postoperative Af was lower in the treatment group than in the control group (19.2% vs 33.6%, p < 0.01). Use of antiarrhythmic drugs at discharge was less common in the treatment group as well (39% vs. 61%, p = 0.053). Length of stay was similar between groups (p = 0.760).

Conclusion: Use of ACEI/ARB for at least 3 months prior to cardiac surgery is associated with a reduction in postoperative Af.

First Human Experience with Real Time Integration of Intracardiac Echocardiography and 3D Electroanatomical Imaging to Guide Pulmonary Vein Antrum Isolation

Vaer Khaykin, Oler Klemm, Bonnie Whaley, Catherine Seabrook, Marianne Beardsall, Zaez A. Wulfhart, Ata Verma, Southlake Regional Health Center, Newmarket, ON, Canada

Background: Catheter ablation of atrial fibrillation (Af) is typically guided by 3D mapping. This involves point-by-point reconstruction of the 3D virtual anatomy and may be time consuming and require substantial fluoroscopy exposure. Intracardiac echocardiography (ICE) affords real time imaging of the cardiac structures during mapping and ablation.

Methods: Between February and September 2007, 15 patients presenting for Af ablation were offered mapping using a novel system integrating 3D mapping and ICE. A modified ICE probe with location sensor tracked by the mapping system was positioned in the right atrium (RA). This allowed acquisition of ECG gated images of the left atrium (LA). Endocardial contours were traced on each image and were used to generate a registered 3D map.

Results: 3D maps took a mean of 45 min (13-110) to create, PRIOR to entering the LA and without fluoroscopy. Pulmonary veins and the esophagus were rendered in 3D. A complete map was built from a mean of 42 contours (20-93). Figure depicts a 3D map of the LA. Green lines represent individual registered contours traced on ICE.

Conclusion: A mapping system combining ICE and 3D electroanatomical mapping can feasibly reconstruct a 3D shell of the LA and the pulmonary veins without the need to enter the left heart.

Ranolazine Shortens Repolarization and Improves Myocardial Relaxation in Patients With Type-3 Long QT Syndrome

Arthur J. Moss, Wojciech Zareba, Karl O. Schwartz, Spencer Roseno, Scott McNitt, Jennifer L. Robinson, University of Rochester Medical Center, Rochester, NY

Background: One form of the hereditary long QT-syndrome, LQT3-deltaKbPQ, is associated with sustained inward sodium current during membrane depolarization, and we hypothesized that therapy with ranolazine would have favorable electro-mechanical effects in patients with this genetic disorder.

Methods: Five patients with this LQT3 mutation were prospectively investigated during 8-hour intravenous infusions of ranolazine, with ECG and ECHO evaluation before, during, and after ranolazine.

Results: Over the entire 8-hour ranolazine infusion, the mean reduction in QTc from baseline was 26.4±3.3ms (p=0.0001), i.e., from 558±55ms at baseline to 532±46ms during ranolazine. As shown in the figure, QTc shortened in a concentration-dependent manner with an average slope of QTc vs. ranolazine plasma concentration of -24 ms per 1000 ng/ml (p=0.008). At peak ranolazine infusion, there was significant 13% shortening in left ventricular isovolumic relaxation time and a significant 25% increase in molar E-wave velocity. No adverse effects of ranolazine were observed.

Conclusions: Ranolazine shortens the QT interval and improves myocardial relaxation in LQT3 patients with the SCN5A-deltaKbPQ mutation.

Long QT Syndrome in Patients Over 40 Years of Age: Increased Risk for LQTS-Related Cardiac Events in Patients With Coronary Disease


Background: Previous studies of Long QT Syndrome (LQTS) have focused primarily on the clinical course of affected patients within the first four decades of life.

Methods: The study population involved 641 patients older than age 40 who had QTc>449ms. Patients were identified as having coronary disease if they had a history of hospitalization for myocardial infarction, coronary angioplasty, coronary artery bypass graft surgery, or were treated with medication for angina. LQTS-related cardiac events included the first occurrence of syncope, aborted cardiac arrest, or sudden cardiac death without evidence suggestive of an acute coronary event. Cox proportional hazards regression modeling was used to analyze the independent contribution of coronary disease to LQTS-related cardiac events.

Results: Time-dependent coronary disease was associated with an increased risk of LQTS-related cardiac events as shown in the Mantel-byar graph and by Cox analysis (hazard ratio 2.2, 95% confidence interval 1.24-4.04, p=0.008) after adjustment for syncopal history before age 40, QTc, and gender. Factors such as diabetes and hypertension that increase the risk for coronary disease were not associated with an increased risk for LQTS-related cardiac events.

Conclusions: This is the first study to demonstrate that coronary disease augments the risk for LQTS-related cardiac events in LQTS. The findings highlight the need for more focused preventive therapy in LQTS patients above the age of 40.
Conversely, blockade of cardiac K<sub>ATP</sub> channels may predispose to ischemic injury and thus may increase the propensity for ischemic VF.

These findings may provide an explanation why clinical outcomes with TZDs have been mixed when used in asthmatic patients with LQTS, and this risk was diminished in patients receiving beta-blocker therapy. Still, 57% did not experience appropriate ICD therapy during long-term follow-up. Therapy-free survival at 1-year was 72% (figure). Furthermore, 64 patients (13%) experienced inappropriate shocks.

Conclusions: Ischemic secondary prevention patients exhibit a high risk of VF recurrence. The aim of the current study was to determine the actual rate of recurrent events. The aim of the current study was to determine the actual rate of recurrent events. The aim of the current study was to determine the actual rate of recurrent events. The aim of the current study was to determine the actual rate of recurrent events. The aim of the current study was to determine the actual rate of recurrent events.
Doppler imaging (TDI) provides accurate quantification of regional myocardial velocities and time intervals. Since LQTS is associated with heterogeneous prolongation of action potentials, we investigated if prolonged myocardial contraction heterogeneity in duration of contraction assessed by TDI may serve as markers of risk in LQTS patients. Methods: Sixty patients with molecularly defined LQTS were studied. Of these, 31 patients had syncope or cardiac arrest and 29 were asymptomatic. We used 20 healthy individuals as a control group. Regional myocardial contraction time was assessed by TDI. Results: Significant differences in contraction time were observed in all patients with a history of syncope or cardiac arrest compared to healthy controls. Conclusions: This study shows that dispersion of myocardial contraction is increased in LQTS patients. TDI can be of incremental value in risk stratification in these patients.

Is J-Point Elevation a Specific Electrocardiographic Marker of Idiopathic Ventricular Fibrillation?

Raphael Rosso, On Rogowski, Bernard Behlansen, Melvin M. Scheinman, Sami Velleri, Tel Aviv Medical Center, Tel Aviv, Israel, University of California San Francisco, San Francisco, CA

Background: Marked J-point elevation in the inferior leads during sinus rhythm has been proposed as a marker of idiopathic ventricular fibrillation (VF). However, data on the presence of J-point elevation in idiopathic VF comes exclusively from case reports and there are no series determining the frequency of J-point elevation in consecutive patients with idiopathic VF in a controlled fashion. This limitation is important because J-point elevation (usually termed “early repolarization”) may also be present in healthy individuals.

Methods: The study group consisted of 33 consecutive patients with idiopathic VF. Patients with ST elevation in the precordial leads were considered to have Brugada syndrome and were excluded from this series. All patients (age 31 ± 17 years) have documented spontaneous VF. The control group consisted of 162 age- and gender-matched healthy controls (5 controls per patient). Electrocardiograms were compared by readers blinded to patient assignment. Specifically, the presence and amplitude (“high-take off” type) and terminal slurring of the R-wave were recorded. “Large J waves” were considered to be present when the J-point elevation exceeded 0.1 mV.

Results: J-point elevation was observed with similar frequency among patients with idiopathic VF and controls. This was true for J-point elevation in the inferior leads (26% of idiopathic VF vs. 22% of controls, p=NS) and for J-point elevation in lateral leads (15% vs. 11%, p=NS). However, “large J waves” in the inferior leads were more commonly seen in the idiopathic VF group (14% vs. 5%, p=0.043). Similarly, large J waves in lateral leads were rarely observed in the idiopathic VF group (5%) but were never seen in controls (8% vs. p=0.0032). High take-off ST-elevation and R-wave slurring did not identify patients with idiopathic VF.

Conclusions: Large J-waves (marked J-point elevation) are more commonly seen among patients with idiopathic VF than among controls. Although the difference is statistically significant, the clinical relevance of this finding is limited by poor sensitivity and/or specificity.

Prognostic Value of Microvolt T-wave Alternans in Patients With Moderate Ischemic Left Ventricular Dysfunction: Results From The MASTER II Trial

Theodore Chow, Dean J. Kereiakes, John Onuffer, Alan Woolf, Sanir Gunsoy, Brett J. Peterson, Mark L. Brown, Wens Pui, David G. Benditt, on behalf of the MASTER Investigators, Lindner Center at The Christ Hospital, Cincinnati, OH

Background: Microvolt T-wave alternans (MTWA) has been proposed as a risk stratifier for the lifesaving ventricular tachyarrhythmic events (VT/ VF), particularly in patients with left ventricular ejection fraction (LVEF) ≤ 40%. However, relatively little data exist on the prognostic ability of MTWA in patients with moderate ischemic left ventricular dysfunction (ILVD) (i.e. LVEF 31-40%).

Methods: MASTER II is a prospective registry conducted at 50 US centers studying primarily community-based post-infarction patients with LVEF 31-40%. Baseline MTWA testing was classified according to standard criteria by a blinded expert reader, with repeat testing of indeterminate tests. According to the study protocol, only patients with a positive or negative MTWA test were included in analysis. Patient treatment, including ICD implantation and programming, was left to physician discretion. Clinical and ICD events were classified by a physician committee blinded to patient characteristics. The primary outcome was LVTTE, defined as sustained spontaneous VT/VF, sudden cardiac death, or appropriate ICD discharge. Cox proportional hazards analyses were stratified according to whether or not an ICD was implanted.

Results: After exclusion of 45 patients testing indeterminate for MTWA, analyses were conducted on 303 patients (85% males, mean age 64 ± 10, mean LVEF 36 ± 3% who were followed for 2.2 ± 0.7 years. The final distribution of MTWA test results was “positive” in 132 (44%), and “negative” in 171 (56%). ICDs were implanted in 48% of patients. During follow-up LVTTE occurred in 7 MTWA positive and 4 MTWA negative patients with actuarial event rates being 2.3%/yr and 1.0%/yr, respectively (p=0.25). A positive MTWA test was not associated with increased LVTTE (stratified HR=1.22; 95% CI: 0.34-4.39, p=0.76), including after multivariate adjustment (stratified HR=1.20; 95% CI: 0.33-4.31, p<0.001). However, the ability to detect a significant difference may have been affected by the low event rate.

Conclusions: MTWA test result does not significantly discriminate risk of LVTTE in patients with LVED and ICD 31-40%. However the incidence of LVTTE among these patients in contemporary community practice is low.

Evaluation of Microvolt T-Wave Alternans Test Result Concordance Over Time in the MASTER Trial

Theodore Chow, Dean J. Kereiakes, John Onuffer, Sanir Gunsoy, Anastasios Manaris, Fei Lu, Brett J. Peterson, Mark L. Brown, Wens Pui, David G. Benditt, on behalf of the MASTER Investigators, The Lindner Center at The Christ Hospital, Cincinnati, OH

Background: Microvolt T-wave alternans (MTWA) results may change over time in individual patients. However, while the frequency of MTWA change in specific patient populations is not well characterized, such changes impact clinical utility and strategies for testing, including periodic re-testing.

Methods: MASTER I and II are prospective trials conducted at 50 US centers in patients with ischemic left ventricular (LV) dysfunction (LIVD) and LV ejection fraction ≤ 40% underwent annual MTWA testing. The protocol requested the same method of testing of indeterminate tests. According to the study protocol, only patients with a positive or negative MTWA test were included in analysis. Patient treatment, including ICD implantation and programming, was left to physician discretion. Clinical and ICD events were classified by a physician committee blinded to patient characteristics. The primary outcome was LVTTE, defined as sustained spontaneous VT/VF, sudden cardiac death, or appropriate ICD discharge. Cox proportional hazards analyses were stratified according to whether or not an ICD was implanted.

Results: After exclusion of 45 patients testing indeterminate for MTWA, analyses were conducted on 303 patients (85% males, mean age 64 ± 10, mean LVEF 36 ± 3% who were followed for 2.2 ± 0.7 years. The final distribution of MTWA test results was “positive” in 132 (44%), and “negative” in 171 (56%). ICDs were implanted in 48% of patients. During follow-up LVTTE occurred in 7 MTWA positive and 4 MTWA negative patients with actuarial event rates being 2.3%/yr and 1.0%/yr, respectively (p=0.25). A positive MTWA test was not associated with increased LVTTE (stratified HR=1.22; 95% CI: 0.34-4.39, p=0.76), including after multivariate adjustment (stratified HR=1.20; 95% CI: 0.33-4.31, p<0.001). However, the ability to detect a significant difference may have been affected by the low event rate.

Conclusions: MTWA test result does not significantly discriminate risk of LVTTE in patients with LIVD and ICD 31-40%. However the incidence of LVTTE among these patients in contemporary community practice is low.
Cardiac Arrhythmias

heart rate (HR) elevation be utilized for baseline and follow-up tests (treadmill exercise in 80%). All tests were interpreted by a Core Lab blinded to patient characteristics. MTWA indeterminates were excluded from analysis.

Results: 628 patients had at least one follow-up MTWA test. Baseline testing was "+" in 346 (55%) and "-" in 282 (45%). For patients testing "-" at baseline, an estimated 30% tested "+" at their 1st annual test and after their 2nd annual test, 60% had tested "+" at least once. Annual change in MTWA was more common if beta-blocker treatment status also changed (41% vs. 32%, p=0.04). Maximum negative HR during testing did not predict MTWA "-" to "+" conversion. However, MTWA "+" to "-" conversion was associated with a slightly higher onset HR for arrhythmias (103.5 bpm vs. 101.1 bpm, p=0.01).

Conclusions: Year-to-year change in MTWA is common in patients with ILVD. The time course and clinical significance of MTWA changes has important implications for patient testing, and requires further study.

10:00 a.m.

T015-107 Cardiac Arrest Survivors With Concomitant Myocardial Infarction Continue to Have a High Recurrence of Ventricular Arrhythmia

Kevin J. Makaji, Benjamin Kalsmith, Sara Baig, Emily Mackey, John Kilan, Munther Homoud, Jonathan Weinstock, N.A. Mark Estes, III, Mark S. Link, Tufts University-New England Medical Center, Boston, MA

Background: Patients presenting with cardiac arrest (CA) or sustained ventricular arrhythmia in the setting of STEMI are considered reasonably low risk for future SCD. Whether this low risk is conferred to patients with NSTEMI in the era of sensitive biomarkers is unclear.

Methods: Using a prospectively maintained ICD registry, 348 ICD recipients of 1800 from 1996 to 2006 were identified who presented with CA or sustained ventricular arrhythmia in the absence of STEMI. Patients were divided by enzyme status into 3 categories: 1. TnI <0.1mg/dL, 2. TnI 1-4.9 mg/dL, and 3. TnI ≥ 5mg/dL. Time to first appropriate device therapy for lethal arrhythmia defined as VF/ventricular flutter with cycle lengths >260ms were estimated by the Kaplan Meier method and compared by the Log-rank test.

Results: Of 348 patients, 176 (45%) had TnI <0.1mg/dL, 69 (18%) had TnI 0.1 - 4.9 mg/dL, and 82 (22%) had TnI ≥ 5mg/dL. Appropriate device therapy was delivered in 13.8% of patients for potentially lethal arrhythmias over follow up of 30.2 ± 32.1 months. Lethal arrhythmia were equivalent between groups regardless of TnI threshold values.

Conclusions: Patients with CA or sustained ventricular arrhythmias and NSTEMI should be considered for ICDs to prevent subsequent SCD. Prospective studies are needed to identify high-risk features in this subset of patients.

10:00 a.m.

T015-108 Mapping and Ablation of Frequent Post-Infarction Premature Ventricular Complexes

Jean-Francois Sarrazin, Eric Good, Michael Kuhne, Darryl Wells, Nagib Chafloun, Thomas Crawford, Sujaya Dey, Warangkina Bocynapist, Hakam Oral, Frank Pelosi, Aman Chugh, Krit Jongnarangsin, Fred Morady, Frank Bogun, University of Michigan, Ann Arbor, MI

Background: Premature ventricular complexes (PVCs) occur frequently in patients with heart disease. Neither site of origin nor feasibility of mapping and ablation of post myocardial infarction (MI) PVCs has been systematically assessed.

Methods: In 24 consecutive patients (22 men, age 60 ± 9, EF 36 ± 14) with prior MI, mapping and ablation of frequent PVCs was attempted using a 3.5 mm irrigated tip catheter in conjunction with an electroanatomic mapping system (CARTO, Biosense). PVCs occurring frequently (bigeretal or quadrigeminal patterns) were mapped with activation mapping; and PVCs occurring less frequently were mapped with pace-mapping. The site of origin (OOI) was determined to be within low voltage (scar) tissue (amplitude < 1.0 mV) or tissue with preserved voltage (> 1.0 mV).

Results: The SOO in 20/24 (83%) patients was confined to scar tissue. At the SOO, the local endocardial activation preceded the PVC by 60 ± 16 msec, and the electrogram amplitude during sinus rhythm was 0.44 ± 0.33 mV. The SOO was in preserved tissue in 3/24 patients. The SOO could not be identified in one patient. PVCs could be effectively ablated in 20/24 patients resulting in a decrease of PVC burden from 13.4 ± 12.1 to 2.8 ± 4% (p<0.006). The most frequent SOO was from the septum (7 patients), followed by the papillary muscle (6 patients), the left ventricular outflow tract (3 patients), the inferior or posterior wall (2 patients), and the antero-lateral wall (2 patients). Other less common sites were the aorto-mitral continuity, the coronary sinus, and the epicardium. The only complication was 2:1 AV block with new LBBB during ablation around the left posterior fascicle in a patient with known RBBB and prolonged HV interval. This patient already had an implantable cardioverter defibrillator (ICD).

Conclusions: Similar to post-MI ventricular tachycardia, PVCs after prior MI most often originate from scar tissue. Mapping and ablation can be performed with a high success rate.

10:00 a.m.

T015-109 Search for Cardiac Calcium Cycling Gene Mutations in Familial Ventricular Arrhythmias Resembling Catecholaminergic Polymorphic Ventricular Tachycardia

Annukka Marjamaki, Päivi Laitinen-Forsblom, Kimmo Kontula, Lauri Toivonen, Heikki Swan, University of Helsinki, Helsinki, Finland

Background: Catecholaminergic polymorphic ventricular tachycardia (CPVT) caused by mutations in the ryanodine receptor type 2 (RYR2) gene is a severe inherited cardiac disorder presenting with stress-induced syncope and sudden death. We examined whether mutations in genes affecting cardiac calcium cycling were detectable in CPVT and in less typical familial exercise-related ventricular arrhythmias.

Methods: We recruited 33 consecutive patients who had frequent ventricular premature complexes (VPBs) occurring during exercise and often history of syncope or sudden death in family. None had structural heart disease or prolonged QT interval. Exercise stress test, echocardiography and 24-hour ECG recording were performed to each proband and family member (n=230). We sequenced all the coding exons of the RYR2, FKBP12.6, ATP2A2 and NCX1 genes from the index patients. A total of 300 healthy blood donors served as controls. Single channel recordings of the mutant RYR2s were conducted in planar lipid bilayers.

Results: Sixteen of the probands presented features typical of CPVT (Group A). The remaining 17 subjects had frequent VPBs and often salvos of VPBs also at rest, thus differing from CPVT phenotype (Group B). Familial background was evident in 42% of cases (n=14). The probands in group B had statistically significantly more VPBs/c24 h (13860 ± 11 000 vs. 560 ± 800, p<0.001) and QT prolongation (CARTO VA H 8 ± 1 vs. 1 ± 1) than those in group A. No statistically significant difference was evident between the groups in the occurrence of syncope or sudden juvenile deaths in family. CPVT patients exhibited two novel RYR2 missense mutations R1051P and S616L explaining 13% of the phenotypes. A rare variant RYR2 N3308S with open probabilities similar to the wild type channels in vitro, was detectable in group B. No disease-causing variants were evident in the FKBP12.6, ATP2A2 or NCX1 genes.

Conclusions: We report two novel CPVT-causing RYR2 mutations in 13% of the CPVT probands and a novel RYR2 variation with improbable phenotypic effects in a patient with abundant resting VPBs. FKBP12.6, ATP2A2 and NCX1 genes mutations are rarely involved in familiar malignant arrhythmia syndromes of unknown etiology.

10:00 a.m.

T015-110 Microvolt T-wave Alternans and Electrophysiological Testing Predict Different Arrhythmia Outcomes: Lessons from the Alternans Before Cardioverter Defibrillator (ABCD) Trial

Guy Amit, Otto Costantini, Dennis M. Super, David S. Rosenberg, MetroHealth Campus of Case Western Reserve University, Cleveland, OH

Background: Although microvolt T-wave Alternans (MTWA) and electrophysiological study (EPS) are both markers for sudden cardiac death (SCD), the ABCD trial, found the combination to be more predictive than each alone. Therefore, we hypothesized that the two tests measure elements of the arrhythmogenic substrate, which lead to different arrhythmia outcomes.

Methods: The ABCD Trial included 566 patients with ischemic cardiomyopathy, left ventricular ejection fraction (LVEF) ≤ 30%, and documented non-sustained ventricular tachycardia. All patients underwent both MTWA test and EPS at enrollment. Implantable cardioverter defibrillators (ICD) were implanted in 87% of patients. The primary end-point was first appropriate ICD therapy or SCD. MTWA and EPS Core Laboratories blinded to outcomes adjudicated the tests, and an Events Committee blinded to the results of the tests.

Results: MTWA was normal in 29% and abnormal in 71%, and EPS was negative in 61% and positive in 39% of patients. The primary end-point was 42 MVT events and 24 PVT/VF/SCD events, (8.8% and 5.6% 2-year event rate, respectively). At 1-year, MTWA predicted PVT/VF/SCD (event rate: 2.7% vs. 0% for MTWA abnormal vs. normal; p=0.04), but not MVT. In contrast, EPS predicted MVT (event rate 9.7% vs. 2.2% for EPS + vs. EPS - p<0.01), but not PVT/ VF/SCD. At 2 years MTWA was not a significant predictor of either arrhythmia outcome, but a positive EPS remained predictive of MVT (14.7% vs. 4.7%; p<0.01). Finally, LVEF dichotomized by LVEF ≤ 30% was not predictive of either arrhythmia outcome. MTWA and EPS differ in the arrhythmia outcome they predict, and the time frame of prediction, suggesting that they identify different arrhythmogenic substrates. These data further suggest that multiple risk markers used in combination may better define and predict the complex electro-anatomical substrates which underlie the risk of SCD.

A18 ABSTRACTS - Cardiac Arrhythmias

JACC March 11, 2008
Follow-Up Left Ventricular Ejection Fraction in the DEFINITE Trial Population Predicts Outcome Regardless of Cardioverter-Defibrillator Status

Jorge E. Schlakman, Alan Kadish, Haris Subacius, Alaa Shalaby, Ardi Schaechter, Joseph H. Levine, Jeffrey J. Goldberg, Northwestern Memorial Hospital, Feinberg School of Medicine, Northwestern University, Chicago, IL

Background: The DEFINITE Trial demonstrated that in nonischemic dilated cardiomyopathy (NICDM), implantation of a cardioverter-defibrillator (ICD) reduced sudden death and was associated with a non-significant reduction in all-cause mortality.

Methods: This study examines the outcomes in DEFINITE based on follow-up (FU) of left ventricular ejection fraction (LVEF) measurements obtained 90-730 days after trial enrollment. Of 458 patients enrolled, 176 (38%) had FU LVEF (85 randomized to the ICD arm). Mean age was 56.6±12.2 years and 132 were male. Patients were divided into 3 groups based on the change in LVEF: Group I-LVEF increase by >5%, Group II-LVEF change ≤5%, Group III-LVEF decrease by ≤5%.

Results: There was no difference in survival between group I and II: these groups were then combined for further analysis. Group III had increased mortality versus groups I/II (Figure). There was no difference in time to first appropriate shock in the 3 groups. There was no difference in ICD benefit in each group.

Conclusions: NICDM patients with LVEF decline is associated with worse outcome, but not increased shocks or a change in ICD benefit. In these patients, LVEF may serve less as a predictor of arrhythmic events and more as a predictor of death from competing causes.

Mortality Risk Increases for Each Subsequent Ventricular Arrhythmia Treated with an ICD Shock: Results from the Sudden Cardiac Death in Heart Failure Trial

Wai Shun Wong, Jeanne E. Poole, Anne S. Hellkamp, George W. Johnson, Jill Anderson, Daniel B. Mark, Kerry L. Lee, Gust H. Bardy, University of Washington Medical Center, Seattle, WA

Background: We have previously demonstrated an increased mortality in the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT) patients who received at least one ICD shock intervention for high rate rhythm triggers. This was true both for appropriate (ventricular tachycardia, ventricular fibrillation) and inappropriate (supraventricular rhythms or over-sensing) rhythm triggers. To evaluate whether multiple rhythm events or cumulative ICD shock energy further worsens risk, we evaluated the association between cumulative shock energy, cumulative ventricular arrhythmia (VA) episodes, and mortality in patients who received an ICD in the SCD-HeFT.

Methods: Date, time, number, and energy of shocks delivered were recorded from all rhythm events triggering ICD shock therapy. Cox proportional hazards modeling adjusting for baseline prognostic factors evaluated the relationship between mortality and 2 time-dependent variables, cumulative shock energy and cumulative episodes of VA. Patients who had their ICD removed during follow-up were censored at the time of device removal. Results: Of the 2,521 patients in SCD-HeFT, 811 patients received an ICD. A total of 173 deaths occurred including 10 deaths in patients whose devices were removed for transplant or other reasons. Of the 811 patients, 33.8% had one or more cumulative ICD shocks for any cause, with a median of 2 rhythm episodes requiring ICD shock therapy/patient (inter-quartile range 1, 4), 1 shock/episode (1, 1), 20 J of shock energy/episode (20, 30), and 3 shocks/patient (1, 6). The relative risk of death was 20% higher with each additional episode of VA [HR 1.20 (95% CI 1.10-1.30), p < 0.0001]. Cumulative shock energy was not found to be associated with mortality [HR 1.02 for each 50 J increase (95% CI 0.92-1.14), p = 0.70] after adjusting for the number of VA episodes.

Conclusions: Mortality in SCD-HeFT patients increased significantly for each recurrent episode of ventricular tachycardia or ventricular fibrillation triggering ICD shock interventions. Cumulative joules of ICD shock energy did not increase the risk independent of the risk associated with cumulative episodes of ventricular arrhythmia.

Impact of Transvenous Ventricular Pacing Leads on Tricuspid Regurgitation in Pediatric and Congenital Heart Disease Patients

Gregory Webster, Renee Margossian, Mark E. Alexander, Frank Cecchin, John K. Triedman, Edward P. Walsh, Charles I. Berul, Children's Hospital, Boston, Boston, MA

Introduction: Transvenous ventricular pacing leads across the tricuspid valve may cause or exacerbate tricuspid regurgitation (TR). The literature in adults is inconclusive and no studies have investigated the association between pacing leads and TR in children.

We hypothesize that TR may be more clinically significant in children due to growth and the higher incidences of congenital heart disease (CHD). Methods: A retrospective chart review was conducted at a large children's hospital, yielding 1106 patients implanted between 2000 - 2006. 123 underwent initial placement of a transvenous lead across their tricuspid valve and had both pre- and post-procedure echos available for review. The pre-procedure echo was compared both to the first echo after lead placement and the most recent echo. TR was recorded on an ordinal scale (0 = absent, 1 = trivial, 2 = mild, 3 = moderate, 4 = severe). Results: The median age was 16 years (range 2-52) at time of lead placement. The change in TR was not significant by age, either >18 or ≤18 yrs (p=0.09). Median time was 242 days from implant to first echo, and 827 days to most recent echo. There was no difference in TR between the pre-procedure echo and first follow-up echo (p=0.97). However, TR was more likely to progress mildly between the pre-procedure echo and most recent echo (p < 0.0001). Mortality risk increases for each recurrent ventricular arrhythmia treated with a ICD shock: Results from the Sudden Cardiac Death in Heart Failure Trial: 

Mortality Risk Increases for Each Subsequent Ventricular Arrhythmia Treated with an ICD Shock: Results from the Sudden Cardiac Death in Heart Failure Trial

Impact of Scar Burden and Dyssynchrony on Response to Cardiac Resynchronization Therapy In Ischemic Cardiomyopathy

Glen Miske, Hidekazu Tanaka, Evan Ateleidian, Masaki Tanabe, Prem Soman, Samir Saba, John Gonsan, III, University of Pittsburgh, Pittsburgh, PA

Background: Although mechanical dyssynchrony is associated with response to resynchronization therapy (CRT), there is little data on how much scatter is present for scar burden. Our objective was to test the hypothesis that a high scar burden may impact response to CRT in patients with ICM, regardless of dyssynchrony.

Methods: Forty-five ICM patients aged 67±9 yrs, ejection fraction (EF) 27±8%, QRS duration 166±31 ms were studied who had resting (HR 0.02) with a mean increase from 1.54 to 1.69 on the 0 to 1 ordinal scale. There were 76 pts (62%) with CHD. Mean pre-procedure TR was 1.82 in right-sided CHD (e.g., tetralogy of Fallot, repaired AV canal) vs. 1.43 without right-sided CHD (P=0.01). TR did not increase in pts with right-sided CHD, but did increase in pts without right-sided CHD (p=0.05). No patients progressed from 0 or 1 on the ordinal scale to moderate or severe TR. Conclusions: In patients with transvenous ventricular leads across the tricuspid valve, echocardiography demonstrates unchanged TR after lead placement; however, after extended follow-up, the increase in TR is statistically significant, albeit likely of no significant clinical consequence. The detected change is minimal, suggesting that there is little impact of transvenous leads on TR, even in growing children or patients with right-sided structural heart disease.
**10T5-115**

**Female gender is Associated with a more Favourable Response to Cardiac Resynchronization Therapy**

Paul William Foley, Kayvan Khadjooi, Shajil Chalil, Nick Irwin, Russell EA Smith, Michael P Frenneaux, Francesco Leyva, Good Hope Hospital, University of Birmingham, Sutton Coldfield, United Kingdom

Background: Limited data suggests that female gender is associated with a better response to cardiac resynchronization therapy (CRT). We explored the relationships between gender and both mortality and morbidity in consecutive patients undergoing CRT.

Methods: 311 patients (age 67.1 ± 10.6 years (mean ± SD), 62 female (F), QRS duration ≥ 120 ms, LVF-EFS<35%) with heart failure (HF) due to ischemic (n=221) or non-ischemic (n=90) cardiomyopathy in NYHA class III (n = 210) or IV (n=101) underwent CRT. Clinical events were collected over a follow-up period of 6.5 years following implantation.

Results: In Kaplan-Meier survival analyses, males (M) were more likely to reach the composite endpoints of death from any cause or HF hospitalizations (F: 13/62 vs M: 92/249, log-rank p=0.007, see Figure) as well as death from any cause (F: 11/62, M: 78/249; p=0.016) and cardiovascular death (F: 9/62 vs M: 68/249, p=0.0145). Changes from baseline in NYHA class (F: -1.3 ± 0.9, M: -1.2 ± 0.8), 6-min walking distance (F: 87.7 ± 15.0, M: 88.5 ± 11.6 cm) and quality of life scores (Minnesota Living with Heart Failure questionnaire, F: -27.0 ± 28.8, M: -18.7 ± 26.0) left ventricular end-systolic (F: -35.1 ± 55.3, M: -26.3 ± 61.3 mL) and end-diastolic (F: -29.6 ± 62.0, M: -19.7 ± 61.2 mL) volumes, and LVEF (F: 6.3 ± 14.5, M: 4.8 ± 13.1 %) were comparable.

Conclusions: Female gender is associated with a more favourable response to CRT, in terms of heart failure hospitalizations and mortality. Symptomatic improvement is similar to that observed in males.

**4076**

**Effects of Electrocautery on Transvenous Lead Insulations**

Kiam-Khiang Lim, Shantaru Reddy, Shrijay Desai, Eric Kessler, Chotikom Khuranawat, Matthew Smelley, Susan S. Kim, John Beshai, Albert C. Lin, Martin C. Burke, Bradley P. Knight, University of Chicago Hospitals, Chicago, IL, Boston Scientific, St Paul, MN

Background. Electrocautery is commonly used during cardiac device implantation and pulse generator changes. The purpose of this study was to examine the effects of cautery on a variety of insulation materials.

Results. Commercially available cardiac transvenous leads were selected to include Polyurethane 55D (PU55D), silicone rubber, or a silicone/polyurethane co-polymer outer insulating materials. Each lead was tunnelled through grounded chicken breast tissue leaving a thin layer of tissue covering the lead. An electrocautery pen blade and a monopolar cautery unit (Surgistat II; Valleylab, Boulder, Colorado) were used to dissect a segment of the lead from the tissue with the cutting mode and outputs of 10, 20, and 30 Watts. Cautery durations were 1 and 3 seconds with both a parallel and perpendicular blade tip orientation. The insulation was inspected microscopically.

Conclusions. Polyurethane outer insulation has low thermal stability and is highly susceptible to thermal damage during electrocautery, even at low cutting power. Silicone is resistant to damage by cautery, but can be mechanically damaged when the blade is used perpendicularly. These findings should be considered when implanting transvenous leads and during pulse generator replacements.

**ACC.Poster Contributions**

**1022**

**Cardiac Pacing; Implantable Devices**

Monday, March 31, 2008, 1:00 p.m.-4:30 p.m.
McCormick Place, South Hall

**2:00 p.m.**

**1022-89**

**Novel Method for Assessing Intraventricular Dyssynchrony Using Quantitative Analysis of Regional Wall Thickness by Multi-Detector Computed Tomography**

Guyen A. Truong, Ammar Sanwar, Christopher P Cannon, Khurram Nasir, Mark Handschuhamer, Mannudeep Kalra, Antonio Sorgente, Cristina Conca, Francesco Faltera, Angelo Auricchio, Tiziano Mocciotti, Jagmeet Singh, Udo Hoffmann, Massachusetts General Hospital, Boston, MA, Cardiocentro Ticino, Lugano, Switzerland

Background: The degree of intraventricular dyssynchrony has been suggested as a predictor of response to cardiac resynchronization therapy (CRT), but no imaging modality has proved reliable enough to become the gold standard. We aimed to use a novel CT-based method to quantify dyssynchrony.

Methods: In this case-control study, we measured the extent of LV dyssynchrony in 16 subjects with heart failure (HF) meeting Echo and ECG criteria for CRT (EF <35%, QRS >120 ms) and 11 age-matched controls (EF >55%, QRS <120 ms). All subjects underwent ECG gated contrast enhanced 64-slice MDCT and 8mm thick short axis images were reconstructed in 10% increments over the entire RR-cycle. After delineation of endo- and epicardial boundaries, the time from R-wave to maximal LV wall thickness was measured in six standardized segments per slice using dedicated software. The standard deviation of these measurements per slice was averaged across the entire heart and was defined as the CT dyssynchrony index (DI) per patient. On average, 500 datapoints (9 ± 3 slices, 6 segments, 10 phases) were analyzed per patient. Two readers performed both reconstructions and measurements independently.

Results: The DI inter- and intraobserver reproducibility was excellent (r=0.89 and r=0.93, respectively). The extent of LV dyssynchrony was significantly higher in the HF group (150 ± 50 ms vs 120 ± 20 ms; p=0.004 and 0.004, respectively) but did not differ when subgrouped by median EF of 19.5%, presence of CAD, LBBB, or NYHA class. In adjusted multivariate analysis, median QRS duration was no longer significant and only pacemaker remained an independent predictor of higher DI (p=0.03).

Conclusions: We demonstrate that quantitative CT analysis of LV dyssynchrony using regional changes in LV wall thickness is feasible and reproducible. Our initial results suggest that CT may detect differences in dyssynchrony independent of EF and QRS duration. Further studies are needed to correlate this method to CRT response.

**1022-91**

**Greater Anatomic and Electrical Interelectrode Distance Predicts Clinical Response to Chronic Resynchronization Therapy**

Ian L. Weisberg, Binu Jacob, M. Kamran Aslam, Lori McMullan, Alan B. Miller, Robert Percy, Steve S. Hsu, University of Florida, Jacksonville, FL

Background: Cardiac resynchronization therapy (CRT) in heart failure leads to a significant improvement in quality of life; however, 20-30% of patients are non-responders. Although there are echocardiographic parameters of dyssynchrony that suggest which patients will improve in quality of life; however, 20-30% of patients are non-responders. Although there are echocardiographic parameters of dyssynchrony that suggest which patients will respond to CRT, anatomy may preclude placing the left ventricular lead in the desired region. There is minimal prospective data on intraprocedural parameters that can predict clinical response to CRT. We assessed the hypothesis that greater left ventricular (LV) to right ventricular (RV) anatomic and electrical interelectrode distances would predict an improved clinical response to CRT.

Methods: We prospectively studied 36 patients who met criteria for CRT and received endovascular leads. At implant, simultaneous orthogonal images of the LV to RV interelectrode tip distances, with a tape ruler at cardiac level to standardize the anatomic distance, as well as the electrical distance between the LV and RV leads at baseline and during RV and LV pacing were obtained. A blinded heart failure physician determined responders (n=23) and non-responders (n=13) based on improvement in New York Heart Association (NYHA) functional class. There was no baseline difference between the two
ABSTRACTS - Cardiac Arrhythmias

T022-92
Independent AV/VV Pacing Optimization Requires Operation Along Mechanical AV Delay Isochrones

Robert G. Turcott, Ronald Witteles, Paul J. Wang, Euan A. Ashley, Stanford School of Medicine, Stanford, CA

Background: Pacing interval optimization improves hemodynamics in patients with biventricular devices. Optimization of atrio-ventricular delay (AVD) and interventricular interval (VVI) are frequently performed independently under the assumption that these parameters independently determine preload and dysynchrony. We hypothesize that the timing from atrial event to onset of left ventricular systole, ie, the mechanical AVD, determines loading conditions and is distinct from the nominal programmed AVD.

Methods: The dependence of mechanical AVD on A-LV and A-RV pacing intervals was modeled using 5 different assumptions: mechanical systole depends on time to 1) LV pace only, 2) RV pace only, 3) first ventricular pace, 4) both LV, RV pace with linear or 5) radial propagation. The relationship among A-LV, A-RV and mechanical AVD was determined.

Results: Families of curves of A-LV and A-RV combinations that yield the same mechanical AVD were derived. These vary markedly among the models. One sample curve from each model is shown below. Conclusion: The relationship of mechanical AVD and A-R/A-VV intervals depends sensitively on the model and is distinct from the nominal AVD and VVI. This result has critical implications for optimization methods. In particular, maintaining fixed preload while optimizing VVI requires changes in A-RV and A-LV that maintain a fixed mechanical AVD. Empirically identifying the appropriate model will yield important insights into the relative contribution of AV and VV timing.

T022-93
Registration of Three-Dimensional Coronary Venous System Computed Tomographic Images With Projection Images Obtained Using Fluoroscopy

Antonio Conpente, Francesco F. Galetra, Cristina Conca, Elisabeth Soubelet, Regis Vaillant, Eliana Pascotto, Giovanni B. Pedrazzini, Tiziano Moccetti, Angelo Auricchio, Cardiocentro Ticino, Lugano, Switzerland, GE Healthcare, Buc, France

Background: Coronary sinus (CS) and coronary veins (CV) are not usually delineated by fluoroscopy. Their representation obtained from computed tomography (CT) and subsequent projection of these images over the fluoroscopy system may help in cannulation of CS and its branches during cardiac resynchronization therapy (CRT) procedures.

Methods: In this feasibility study, in vitro experiments were performed with a plastic heart model (phantom). Subsequently, 18 consecutive patients underwent contrast-enhanced, ECG-gated CT scanning, CS and CV together with the superior vena cava, the distal portion of the trachea and of the two bronchi generated from the reconstructed data at 75% of the R-R interval of the cardiac cycle were registered and superimposed over the coronary sinus angiogram obtained from fluoroscopy. Registration accuracy was verified by assessing the overlap of CS borders seen both in the CT and the fluoroscopy images after contrast medium injection.

Results: The mean registration error was 0.73 mm (range 0.01 to 2.22 mm) for the body of CS while it was 0.8 mm (range 0.06 to 2.64 mm) for first order branches of CS. No differences were found in the measurements of the diameter of CS (p = 0.463) and first order coronary veins (p = 0.479) obtained respectively with CT and fluoroscopy.

T022-BM
The Comparison of the Efficacy of Over-the-Wire and Monorail Balloon System for Intracoronary Pacing

Wei Cui, Fan Liu, Puqiun Xie, Jingchao Lu, Guoqiang Gu, Hongmei Zheng, Baoxua Li, Jinfeng Wu, Jun Du, The Second Hospital of Hebei Medical University, Shijiazhuang, People’s Republic of China

Background: Temporary transcoronary pacing has recently been proposed as a safe and reliable alternative method to treat severe bradycardia during percutaneous coronary intervention (PCI). The previous study usually used a over-the-wire system for intracoronary pacing, which is less used in the current clinical practice, and therefore limits its use in emergency situations. The aim of this study is to test the validity of the commonly used monorail balloon system for intracoronary pacing, and to compare the efficacy of these two balloon systems in transcoronary pacing during different conditions.

Methods: Eleven York pigs were randomly assigned to the monorail balloon group or the over-the-wire balloon group. A 0.014 inch BMW (Cordis) guidewire together with the delivery catheter were used. The previous study usually used an over-the-wire system for intracoronary pacing, which is less used in the current clinical practice, and therefore limits its use in emergency situations. The aim of this study is to test the validity of the commonly used monorail balloon system for intracoronary pacing, and to compare the efficacy of these two balloon systems in transcoronary pacing during different conditions.

Results: Both the monorail and over-the-wire systems were used to stabilize the lead in all cases. There were no significant differences with respect to pacing threshold between the monorail balloon group and the over-the-wire balloon group (0.040 ± 0.024 V vs. 0.041 ± 0.023 V at baseline, 1.050 ± 0.44 V vs. 0.880 ± 0.27 V during ischemia, and 1.360 ± 0.26 V vs. 1.670 ± 0.31 V all p > 0.05).

Conclusions: Both the monorail and over-the-wire balloon systems can be effectively used for transcoronary pacing during PCI with equal efficacy.
Left Ventricle Diastolic Function Deteriorated More in Patients with Pre-existing Diastolic Dysfunction by Right Ventricle Apical Pacing

Fang Fang, Qiang Zhang, Joseph YS Chan, Jeffrey WH Fung, Gabriel WK Yip, Anna KY Chan, Yat-yin Lam, Eugene B. Wu, Gary CP Chan, Cheuk-man Yu, The Chinese University of Hong Kong, Hong Kong, Hong Kong

Background: Little is known if right ventricle apical (RVA) pacing will exert harmful effect on left ventricle (LV) diastolic function (LVDF). This study compared the effect of RVA pacing with that of bi-ventricular pacing in patients with pre-existing LV diastolic dysfunction (DD).

Methods: Sixty patients with pre-existing DD showed that E at septal and lateral mitral annulus was reduced and E' at septal and lateral mitral annulus was increased. The correlation between septal E' and LVESV was $r=0.46$ ($p<0.05$)

Results: RVA pacing caused LVDF deterioration as indicated by $E/E'<2$ (as observed in bi-ventricular pacing). The deterioration was more severe in patients with more pronounced RVA pacing effect (DD Severity $>$ 3).

Conclusions: RVA pacing can worsen LVDF as compared to bi-ventricular pacing. The extent of deterioration depends on the severity of RVA pacing effect in patients with pre-existing LVDD.
Conventional time-to-peak analysis showed no differences between the groups (p = 0.43). See Figure.

**Conclusions:** Cross-correlation analysis revealed an increased prevalence of mechanical dyssynchrony in cardiac patients with systolic dysfunction and an even higher prevalence in patients with indication for CRT, which is in line with theoretical predictions. Conventional time-to-peak measures failed to differentiate between the groups. The data suggest improved specificity of the new method, a finding that has potential implications for the selection of patients for CRT.

**Background:** The value of echocardiography in cardiac resynchronization therapy (CRT) has not been conclusively determined. Importantly, current methods for detecting dyssynchrony are influenced by regional differences in myocardial performance. We introduce a new and potentially more reliable method based on analyzing myocardial acceleration during the entire systole.

**Methods:** We studied a group of 107 unselected cardiac patients (divided into 2 groups, LVEF >35%, n = 80 and LVEF ≤35%, n = 27), and 25 patients referred for CRT. All patients were examined with tissue Doppler echocardiography. Results: Cross-correlation analysis of myocardial acceleration showed marked differences between the 3 groups: the maximal activation delay was very low in the mixed group with LVEF >35% (median 6.5 ms), higher in the group with LVEF ≤35% (18.7 ms, p = 0.001) and markedly increased in the CRT group (56.3 ms, p = 0.02 vs. group with LVEF ≤35%).

**Background:** The value of echocardiography in cardiac resynchronization therapy (CRT) has not been conclusively determined. Importantly, current methods for detecting dyssynchrony are influenced by regional differences in myocardial performance. We introduce a new and potentially more reliable method based on analyzing myocardial acceleration during the entire systole.

**Methods:** We studied a group of 107 unselected cardiac patients (divided into 2 groups, LVEF >35%, n = 80 and LVEF ≤35%, n = 27), and 25 patients referred for CRT. All patients were examined with tissue Doppler echocardiography. Results: Cross-correlation analysis of myocardial acceleration showed marked differences between the 3 groups: the maximal activation delay was very low in the mixed group with LVEF >35% (median 6.5 ms), higher in the group with LVEF ≤35% (18.7 ms, p = 0.001) and markedly increased in the CRT group (56.3 ms, p = 0.02 vs. group with LVEF ≤35%).

**Conclusion:** The strain delay index has a strong predictive value for predicting response to CRT in both ischemic and non-ischemic patients.
terminated and chronic AF was induced by rapid atrial pacing. After 2-4 weeks of AF, sustained ventricular CP was delivered for 2-4 weeks with a time interval between the CP beat and the intrinsic ventricular activation set as to minimize a subsequent mechanical contraction. Changes in LV end diastolic volume (EDV), atrial size and LVEF were quantified by echocardiography.

Results: Compared to sinus rhythm, RV pacing followed by chronic AF was associated with a reduced EF (42±16% vs. 28±11%, p<0.04), increased EDV (75±12ml vs. 96±10ml, p<0.05) and LA size (21±10 vs. 37±7ml, p=0.01). When CP was applied, a sustained decrease of heart rate was observed (159±39bpm vs. 104±21bpm, p<0.05). Under CP no sudden death and ventricular arrhythmia were observed and importantly EDV (-19±11%, p<0.04) and LA size (-6±5%, p=0.02) were reduced and EF tended to increase (28±15% vs. 47±12%, p=0.08).

Conclusion: Chronic CP was safely delivered in HF animals with chronic AF to slow the ventricular contractile rate and improve contractility which resulted in reverse remodeling.

2:00 p.m.

The Impact of Improvement of Mitral Regurgitation on 1-Year Clinical Outcomes in Patients Undergoing Cardiac Resynchronization Therapy
Ani Kejji, Yoshimatsu Soga, Shinichi Shirai, Takeshi Arita, Masahiko Goya, Masashi Iwabuchi, Hiroaki Yokoi, Hideto Yasumoto, Hideyuki Nosaka, Masakiyo Nobuyoshi, Department of Cardiology, Kokura Memorial Hospital, Kitakyushu, Japan

Background: It is not well known whether improvement of mitral regurgitation (MR) after cardiac resynchronization therapy (CRT) affects long-term clinical outcomes.

Methods: We investigated 110 pts received CRT (age 71±10 years, NYHA class 3.1±0.5, LVEF 26±7%, LVEDD 61±7mm, pre QRS duration 178±28ms) and divided into two groups, 48 pts with improvement of MR after CRT (CRT+ group) and 62 pts without improvement of MR (CRT- group). Improvement of MR was defined as echocardiographic MR decreased at least 1 grade after 3-6 months CRT. 1-year clinical data were obtained.

Results: Baseline MR grade was significantly greater in MR improve group than MR no-improve group (2.0±0.6 in MR improve group vs. 1.5±0.8 in MR no-improve group, p<0.005), but after 3-6 month, MR grade was significantly smaller in MR improve group (0.7±0.6 in MR improve group vs. 1.6±0.9 in MR no-improve group, p<0.0001).

At 1-year follow up, NYHA functional class was similar between two groups (2.3±0.7 in MR improve group vs. 2.2±0.6 in MR no-improve group, p=ns). However, event free survival rate from combined death and heart failure hospitalization was significantly higher in MR improve group (85% vs. 67% at 1 year, Log-rank p=0.025).

Conclusion: Pts with improvement of MR after 3-6month CRT had better 1-year clinical outcomes than pts without improvement of MR.

2:00 p.m.

Impact of Anterior Versus Posterior Left Ventricular Lead Position on Clinical Outcome in Cardiac Resynchronization Therapy
Thomas Klemm, Timo Becker, Margit Struass, Steffen Schneider, Ralf Zahn, Jochen Senges, Kartheinz Seidl, Herzcentrum Ludwigsheiden, Ludwigsheiden, Germany

Background: A posterolateral position of the left ventricular pacing lead is recommended for cardiac resynchronization therapy (CRT). However, the clinical outcome of patients with anterior position of the left ventricular lead compared to those with posterolateral lead position is not known. Aim of the study was to evaluate the clinical outcome of patients receiving CRT depending on the left ventricular (LV) lead position.

Methods: 169 consecutive patients with advanced heart failure who received CRT were analyzed. The position of the left ventricular lead was determined by biplane chest x-ray after implantation. After 3 months of follow-up patients were classified as responders or nonresponders, based on the presence or absence of NYHA class improvement by postero-lateral 19.6% and antero-lateral wall 11.8%. In 82.4% cases, the LV lead position on CXR and RCVA were analyzed separately by two different blinded physicians.

Results: 24% of the LV leads (73%) were positioned in the posterior region and 45 LV leads (23%) in the anterior region. The total median follow-up time was 704 (479/1063) days.

Conclusions: 1/3 of the patients receiving CRT had a clinical improvement in NYHA class after 3 months. 2. This improvement was observed independently of the LV lead position. 3. The total mortality rate after nearly 2 years was more than two-fold increased in patients with anterior LV leads compared to those with posterior LV leads.

2:00 p.m.

Classification of the Post-implant Final Left Ventricular Lead Position: A Comparative Study between Radiographic and Angiographic Modalities
K Yves Nandrag, E Kevin Heist, Dan Blendea, Andre D’Avila, Vivek Y. Reddy, Theofanie Mela, Jeremy Ruskin, Jagmeet P. Singh, Massachusetts General Hospital, Boston, MA

Background: Post-implant lateral and posterocorridor chest X-rays (CXR) are often utilized to determine the final LV lead tip position after cardiac resynchronization therapy (CRT). Although it is apparent that cardiac dilation and rotation in patients with heart failure is unpredictable, there is limited data examining the accuracy of CXR to interpret LV lead localization.

Objective: This study compared the ability of post-implant CXRs with intra-procedural rotational coronary angiography (RCVA) to localize the final LV lead position.

Methods: We analyzed CXR and RCVs from 51 patients undergoing CRT. CXR involves recording a rapid 4-sect isocentric cine-loop from RAO 550 to LAO 550 (120 frames), thereby enabling a three-dimensional, multi-angle view of the CS and its branches. This served as the gold standard for LV lead location. CRT criteria for LV lead localization involved using the lateral view to ascribe the ventricular wall (e.g., anterior, anterolateral, lateral, posterolateral, or posterior) while the posteroanterior view was used to characterize the location as basal, mid, or apical. The LV lead position on CRT and RCVA were analyzed separately by two different blinded physicians.

Results: 51 patients (69.3 ± 10.6 years; males 70.6%; ischemic 64.6%; NYHA class 3±0.4 and LV ejection fraction 23.3±8.5%) were analyzed for their LV lead pacing site position. Among the study group lateral wall was the most common pacing site 66.7% followed by posterolateralateral 19.6% and antero-lateral wall 11.8%. In 82.4% cases, the LV lead position was misclassified based on CRT as compared to RCVA. Among the 42 cases misclassified with the CRT approach, 32 were lateral wall positions misclassified as posterolateral (59%) and posterior (41%); 7 cases of posterolateral wall position were misclassified as either lateral (3) or posterior (4) and 3 antero-lateral positions were erroneously classified as lateral (3) and posterolateral (1).

Conclusion: CRT is not an accurate method for determining the LV lead tip position and intra-procedural angiography should remain the gold standard for classifying the LV lead location.

2:00 p.m.

Forward Flow Fraction: A Novel Parameter of Cardiac Remodeling that Accurately Predicts Functional Response in Patients with Cardiac Resynchronization Therapy
Sanjay Kumar, Richard A. Grimm, Cleveland Clinic Foundation, Cleveland, OH

Background: Cardiac Resynchronization Therapy (CRT) is performed in patients with heart failure however an accurate parameter to evaluate the physiologic response is lacking. The discrepancy between clinical response and echocardiographic parameters like Ejection Fraction (EF), Left Ventricular End Systolic Volume (LVESV) and Tei Index (TI) is common. Forward Flow Fraction (FFFF) measures the efficiency in contractility of myocardium in ejecting blood towards the aorta at the instant of end systole. Forward Flow Fraction was calculated with a formula consisting of Stroke Volume (SV), Ejection Time (ET), Systolic Time Interval (STI) and Left Ventricular End Systolic Diameter (LVESD).

FFFF = (SV*ET x STI) / 100 / (STI x LVESDcm²)

Methods: Sixty-one patients (Age 68 ± 10, M: F 46:15) who underwent CRT and comprehensive follow up were studied. Echocardiographic and NYHA functional assessment was performed before and 6 months after CRT. 34 patients (55%) had improvement in NYHA class after implant. A significant improvement (>15% change) in EF, LVESV and TI was noted in 34 (55%), 22 (36%) and 22 (36%) patients respectively.

Results: Improvement in FFF was noted in 36 (60%) patients and was significantly associated with NYHA class improvement (p<0.001), but after 3-6 month, MR grade was significantly smaller in MR improve group (2.0±0.6 in MR improve group vs. 1.5±0.8 in MR no-improve group, p<0.0001). Increase in TI correlated significantly with a decrease in LVESV and LVESD (r =-0.38, p<0.01 and -0.51, p<0.001). Increase in FFF correlated significantly with NYHA class improvement (p< 0.001) and dimensional remodeling. Change in LV end diastolic volume (EDV), atrial size and LVEF were only marginally associated with clinical response (p 0.03, p 0.08, p=0.01 respectively). Only FFF, but not EF nor LVESV, improved significantly in groups with...
improvement in wall motion and reduction in grade of mitral regurgitation (p < 0.05). Conclusions: FFF is a physiologic parameter sensitive to changes in global function and processes involved in ventricular remodeling. FFF is superior to EF, LVEVF and TDI in predicting and monitoring functional response in CRT patients.

To 2:00 p.m.

To 2:00 p.m.

Increased Risk of Stroke in Patients with Permanent Pacemaker Leads and Patent Foramen Ovale

Orlando Gurdjie, David Paniagua, Jose Antonio Condado, J De Fretas, Amit H. Manhas, B. Amzezega, Baylor College of Medicine, Houston, TX

Background: The prevalence of Patent Foramen Ovale (PFO) in adults is around 25% and more than 100,000 pacers are implanted annually. An association between PFO, stroke and migraines is known. An increased incidence of thromboembolism in patients with transvenous pacer leads (TVPL) and intracardiac shunts (ASD, VSD) has been published. The association of PFO and TVPL and stroke is unknown.

Objectives: To determine the risk of stroke in patients with TVPL and PFO.

Methods: Sixty consecutive patients from the Pacemaker Clinic at our institution were studied for the presence of stroke and PFO. Electrocardiogram, transthoracic Eco-Doppler with bubble studies, complete neurological assessment and brain imaging were performed on each patient to determine the prevalence of PFO, atrial fibrillation (AF) and stroke. The population was divided into two groups: PFO and no PFO. Statistical comparison was made using chi square, t test, and odds ratio.

Results: Forty three percent of patients were male, mean age was 77 years ± 9, 15% of patients had diabetes, and 40% had hypertension. PFO was present in 10 patients with TVPL (16.6%). Four patients with PFO had a stroke (36%) compared to 7 out of 42 without PFO (16%). Odds ratio for stroke in PFO was 3.47. Both groups had similar demographics including the same prevalence of atrial fibrillation.

Conclusions: PFO is associated with an increased risk of stroke in patients with TVPL. LARGER controlled clinical studies to test these preliminary findings are required. If these findings are verified, a recommendation for screening and closing PFOs in this group may be justified.

To 2:00 p.m.

Cardiac Resynchronization and Defibrillator Therapy (CRT-D) Improves Survival Compared to CRT Alone (CRT-P) in Heart Failure Patients

William T. Abraham, James B. Young, Kevin Wheelan, W Ben Johnson, Andrew Smith, Yanping Chang, Malathi Jakkula, For the InSync Registry and InSync ICD Registry Investigators, Medtronic, Inc, Fridley, MN

Background: Multiple large, randomized controlled trials have demonstrated the benefit of cardiac resynchronization therapy on functional status and mortality/fatality in heart failure patients. The survival rates of patients receiving CRT-D versus CRT-P in the general population have not been adequately evaluated.

Methods: Analyses were based on 1,471 patients enrolled in the InSync ICD Registry of CRT-D (N=373) and InSync Registry of CRT-P (N=1,098). Six-month cumulative survival curves were constructed using the Kaplan-Meier method and the difference between the curves was tested for significance by the adjusted p-value from the stratified Proportional Hazards Model to adjust for differences in baseline demographics.

Results: Compared to CRT-P, CRT-D patients were younger (67.7 vs. 70.7; p<0.0001), had a lower mean NYHA class ranking (3.0 vs. 3.1; p=0.0012), and a lower mean LVEF (22.8 vs. 25.4; p<0.0001). CRT-D patients were more likely to have ischemic heart condition (p<0.0001), myocardial infarction (p<0.0001), coronary artery disease (p<0.0001), and receive beta blockers (p<0.0001).

Six month survival rates were 94.9% for CRT-D and 89.9% for CRT-P (adjusted p=0.014; Figure 1). When sudden cardiac death (SCD) mortality was excluded from the analysis, there was no difference observed between groups (p=0.10).

Conclusions: These observations suggest that more lives may be saved by CRT-D compared to CRT-P, primarily through the added reduction in SCD with defibrillator therapy.

To 2:00 p.m.

ICD Patients With Electrical Storm: Clinical Characteristics, Concomitants and Outcome in a Single Center

Torsten Becker, Thomas Kleemann, Margit Strauss, Klaus Doenges, Karthein Seidl, Heartcenter Ludwigshafen, Ludwigshafen, Germany

Background: In 10 to 30% of all ICD patients (Pts) the phenomenon of electrical storm (ES) occurs. This term denotes a temporal clustering of ventricular tachyarrhythmia with consecutive therapy by the ICD. Patients suffering ES are only poorly described.

Methods: Out of our prospective single center ICD registry, pts suffering ES were identified and analyzed for clinical characteristics, concomitants, treatment and outcome as well as for differences in mortality in different patient subsets. Definition of ES: 3 > 2 episodes of ventricular tachycardial fibrillation (VT/VF) within 24 hours, end of ES: freedom from arrhythmia for 14 consecutive days.

Results: Out of 1362 pts, 171 pts (13%) suffered 253 episodes of ES. Clinical characteristics, concomitants and treatment are outlined in Table 1.

<table>
<thead>
<tr>
<th>Age at ICD implantation (y)</th>
<th>62 ± 11</th>
<th>ES episodes with secondary causes</th>
<th>43/253 (17%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male gender</td>
<td>133 (78%)</td>
<td>Pts with VT ES only</td>
<td>115 (67%)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>114 (67%)</td>
<td>Pts with VT and/or VF ES</td>
<td>96 (33%)</td>
</tr>
<tr>
<td>Dilated cardiomyopathy</td>
<td>89 (23%)</td>
<td>ES episodes with ATP only</td>
<td>70/253 (28%)</td>
</tr>
<tr>
<td>Pure electrical disease</td>
<td>6 (5%)</td>
<td>ES episodes with shock</td>
<td>6/3 (2%)</td>
</tr>
<tr>
<td>EF &lt; 40 %</td>
<td>73 (48%)</td>
<td>Pts treated with betablocker</td>
<td>135 (79%)</td>
</tr>
<tr>
<td>ICD for secondary prevention</td>
<td>197 (92%)</td>
<td>Pts treated with amiodarone</td>
<td>65 (38%)</td>
</tr>
<tr>
<td>Time ICD implantation to first ES (d)</td>
<td>64 ± 1067</td>
<td>Pts treated with Class-I drug</td>
<td>43 (25%)</td>
</tr>
<tr>
<td>Time first ES to end of follow-up (d)</td>
<td>933 ± 859</td>
<td>Pts treated with catheter ablation</td>
<td>24 (14%)</td>
</tr>
</tbody>
</table>

Of pts with ES, 66 (39%) died during follow-up. According to the presence or absence of a secondary cause for ES, or to the arrhythmia causative for ES (VT versus VF), cumulative survival did not differ significantly (p = 0.22 and 0.3 respectively).

Conclusions: 1. Mortality rate over a period of 2.6 years was 40% in ICD pts suffering ES 2. Secondary causes were present in every sixth episode of ES 3. VT was the causative arrhythmia in most of the pts. However, the majority of ES therapies included ICD shocks 4. According to the presence of a secondary cause, or the arrhythmia causative for ES there was no significant difference in survival

To 2:00 p.m.

Contemporary implantable Cardioverter defibrillator complications at a University Center

Andrea M. Stuess, Ralph J. Verdin, Edward Gensler, Ferrin Garcia, Rupa Bala, David Lin, Sanjay Doshi, Joshua Cooper, Matthew Hutchinson, David J. Callans, Michael Riley, Francis E. Marchlinski, University of Pennsylvania, Philadelphia, PA

Background: Previously published reports regarding implantable cardioverter defibrillator (ICD) complications demonstrate a variety of complications and limited mortality. Patients (pts) enrolled in clinical trials may represent select cohorts, and not necessarily a "real life" population.

Methods: Our center has a formalized EP Quality Assurance program where all pts are followed prospectively from implant to hospital discharge, and at least one outpatient follow-up visit. We summarize data from January 2000 to July 2006, which includes 1397 consecutive pts undergoing ICD implantation. Procedures were performed by 11 full-time electrophysiologists at our teaching hospital where fellows are trained.

Results: A total of 67 acute or subacute complications were noted in 1397 consecutive ICD implants (4.8%), which include initial implants, generator replacements, and upgrades. Specific complications include infection, requiring device and lead explant (5 pts) or antibiotics alone (4 pts); pneumothorax (5 pts); hematoma >10 cm, requiring drainage (2 pts) or observation (21 pts), 65% on anticoagulation; pericardial effusion with tamponade (3 pts); lead perforation (1 pt) without tamponade; lead (RA, RV, CS) dislodgement requiring revision (15 pts); early infection breaks requiring revision (2 pts); poor lead connection requiring revision (2 pts); pulmonary contusion (1 pt); SVC Syndrome (1 pt); and embolic CVA (2 pts), leading to death in 1 pt. There were additional 3 deaths (0.21%) related to the implantation procedure with pulseless electrical activity or incessant VT/VF, and 2 of these deaths occurred in pts who did not undergo defibrillation testing. Conclusions: (1) Overall acute and subacute ICD implantation complications occur in <5% of implants at a teaching hospital. (2) Complications are due to hematomas in 34% of cases, most of which did not require drainage, typically occurring in pts on anticoagulation. (3) The majority (61%) of complications are lead-related. Investigation is warranted to determine if complications can be reduced by modifying lead implantation techniques or technology and also optimizing strategies to minimize hematoma formation.

Figure 1: Kaplan-Meier Estimates of the Time of Death in CRT-D and CRT-P Patients

ABSTRACTS - Cardiac Arrhythmias

A25

To 2:00 p.m.

ABSTRACTS - Cardiac Arrhythmias

A25

To 2:00 p.m.
Limited Relevance of Invasive Electrophysiologic Testing in Patients Meeting Current Primary Prevention Indications for an Implantable Cardioverter-Defibrillator

Alawi A. Alsheikh-Ali, Benjamin Kalsmith, N. A. Mark Estes, III, Mark S. Link, Tufts-New England Medical Center, Boston, MA

Background: The clinical relevance of invasive electrophysiologic study (EPS) in patients meeting current primary prevention indications for an ICD is uncertain. Using a prospectively maintained single center ICD registry, we examined the utility of EPS in predicting future ventricular tachyarrhythmias (VA) in a primary prevention population with CAD and low ejection fraction (EF).

Methods: ICD recipients with CAD and EF ≤35% at our institution (1995-2005, excluding those with cardiac arrest, sustained VA, or syncope) were categorized as: EPS not done, EPS inducible, EPS non-inducible. Inducibility was defined as sustained monomorphic ventricular tachycardia (MVT) with ≤3 extrastimuli, or sustained polymorphic ventricular tachycardia or ventricular fibrillation with ≤2 extrastimuli. Future risk of VA for each group was estimated using the Kaplan-Meier method, and compared by the log-rank test. Results: We identified 525 ICD recipients (age 67±11, male 81%, EF 23±7, EPS not done 55%, EPS inducible 22%, EPS non-inducible 23%). Risk of VA requiring ICD therapy did not differ by EPS category (Figure). Likewise, EPS category did not predict risk of ICD therapy for potentially life-threatening VA (cycle length ≤260 ms). Similar findings were obtained when inducibility was defined as only MVT with ≤3 extrastimuli.

Conclusion: EPS is of limited relevance to predicting VA in ICD recipients with CAD and EF ≤35% meeting current primary prevention indications. Non-inducible patients remain at high risk of VA.
open irrigation tip electrode incorporating optical sensors, 2) a workstation for continuous display of electrode tip-tissue interface force (axial and lateral) and tip orientation (variable degrees between perpendicular and parallel). A 3-D map display (Navigator, St. Jude Medical) was used for atrial and ventricular geometry reconstruction. Continuous force feedback allows the operator to optimize force maintain adequate catheter tip-tissue interface contact. When blinded to the force display, the operator consistently applies higher forces in the ventricles (>30 g) compared to the atria (<20 g). A significant difference of 30 g was observed between forces in atrial tricuspid annuli. At the tricuspid annulus, correlation was 1.0. The operator consistently applies higher forces in the atria than in the ventricles. The display of electrode tip-tissue interface force (axial and lateral) and tip orientation enabled the operator to optimize force during RFCA. When blinded to the force display, the operator consistently applies higher forces in the atria than in the ventricles. The display of electrode tip-tissue interface force (axial and lateral) and tip orientation enabled the operator to optimize force during RFCA.

**8:15 a.m.**

**Impedance Phase Angle Optimizes Electrode-Tissue Contact and is Superior to Contact Force to Predict RF Lesion Formation and Tissue Popping: Improving Safety and Efficacy of Ablation Using Open Irrigation Catheters**

Mauricio Arroyo, Joe Marak, Hong Cao, Jeffrey M. Fish, Steven Miller, Saurav Paul, Luciana Armaganian, Harry Pyurey, Andrea Natale, Newark Beth Israel Medical Ctr, Newark, NJ. Cleveland Clinic, Cleveland, OH.

Background: Irrigated RF catheter ablation (RFCA) is widely used clinically, but lack of temperature and contact force (CF) feedback may compromise safety. We evaluated a new impedance phase angle (IP) method to assess contact force and energy coupling (EC) to tissue during RFCA. We compared IP to CF to predict lesion size and tissue popping during open irrigated RFCA.

Methods: 62 RFCA lesions were created on a swine thigh muscle preparation with 7 Fr 4 mm irrigated catheters (ipurred @ 13 ml/min). Ablation settings were 20 or 30W; 30s: 0, 10 or 20 gCF; and parallel or perpendicular orientation. Pseudo trabeculations (PT) were created on the thigh muscle to fit the electrode. In addition, 63 lesions, on either smooth or trabeculated myocardium (TM), were created in canine arteries perfused ventricular wedge preparations to study tissue popping.

Results: In the thigh model, IP correlated well with the lesion depth in smooth tissue (r = 0.85) compared to CF (r = 0.61). IP performed significantly better prediction for lesion depth than CF (AUC = 0.82 vs. 0.32). In the ventricular wedge preparation, lesions associated with an audible pop had a significantly greater IP value compared to those without pop (14.2 ± 4.0° vs. 9.6 ± 4.0°, n = 33 pops, p < 0.001). Conversely, the mean CF values for lesions with pops vs. those without were 10.2 ± 9.4 g vs. 7.6 ± 9.0 g (p < NS). Comparisons were made between 3 groups: cases with no pop (14.2 ± 4.0° vs. 9.6 ± 4.0°, n = 33 pops, p < 0.001). Conversely, the mean CF values for lesions with pops vs. those without were 10.2 ± 9.4 g vs. 7.6 ± 9.0 g (p < NS).

Conclusions: IP is superior to CF to predict RF lesion size and tissue popping, particularly in TM where EC is high and CF may be low. IP may improve safety and efficacy of RFCA procedures.

**8:30 a.m.**

**Prospective Comparison of the Septal Imaging Capabilities of Intracardiac Echocardiography with Transesophageal Echocardiography: The ICE-CHIP study**

Sarang Saksena, Jasbir Sra, Luc Jordans, Bradly Knight, Fred Kusumoto, Andrea Natale, Abba Keren, Navin Nanda, Mary A. Viggiano, Mary Chandler, ICE-Chip Investigator Study Group, Electrophysiology Research Foundation, Warren, NJ.

Background: Patients with atrial fibrillation (AF) have a propensity for thromboembolic events & atrial fibrillation (30-40% compared to the atria (<20 g). We showed no significant difference in atrial electrograms amplitudes changes while applying 5-20 g and no perforation occurred up to 50 g in the atrium and 80 g in the ventricle. When a correlation was shown between atrial contact force and RF lesion size at smooth myocardium has been shown, this relationship was not confirmed at trabeculated ventricular sites where large lesions, associated with "pops" (80%) were created despite low force (5g) at 45W (15 ml/min irrigation). A non-audible pop was detected by the force sensor and confirmed on gross and microscopic examination. Esophageal thermal injury occurred with 20g pressure delivered at 35W for 30 secs to the LA directly opposite to an esophageal probe.

Conclusions: This novel technology allows real time force and tip orientation monitoring. The sensor feedback optimizes electrode tip contact and may favorably impact the accuracy and safety of mapping and ablation procedures using conventional catheter manipulation and more importantly for remote navigation systems.

Included detection of patient foramen ovale (PFO), IAS defects or aneurysms. Results: 95 AF patients, mean age was 58 ± 12 yrs completed the study. ICE images were post processed by 91% of patients at each center for temperature and contact force. (p<0.02) The concordance for the image quality between ICE and TEE was 90%. In paired comparisons, ICE & TEE were concordant in PFO detection but a PFO was detected in 5 additional pts by TEE in whom a completed ICE evaluation was unavailable. IAS aneurysms were more frequently detected by ICE (11 pts) compared to TEE (2 pts). There were 5 additional pts by ICE for the detection of IAS aneurysms between ICE and TEE was 96%. No IAS defects were detected by either method in this population.

Conclusions: There is a high degree of equivalence between TEE and ICE when employed for IAS imaging. This study supports the use of ICE in interventional procedures involving the IAS and could obviate the need for esophageal cannulation & TEE.

**Who Suffers Sudden Cardiac Arrest as the First Manifestation of Heart Disease? A Population-based Comparison of Cardiac Arrest With and Without Prior Coronary Events**

Tejwant Singh, Wydarton Reiner, Audrey Uy-Evano, Ronald Mariani, Karen Gunson, Jonathan Just, Sumeet S. Chugh, Oregon Health and Science University, Portland, OR.

Background: The vast majority of sudden cardiac arrests (SCA) are related to coronary disease. Identification of risk predictors is likely to be most challenging in those who present without prior warning. We sought to identify distinguishing characteristics of SCA patients with no history of prior coronary events. Methods: In the ongoing Oregon Sudden Unexpected Death Study, all cases of SCA in Multnomah County, Oregon (population 677,813; 2002 to 2006) were prospectively ascertained. All preceding coronary events were retrospectively assessed. Of a total of 1615 SCD cases aged ≥18 years, detailed medical records were available on 1119 cases. Comparisons were made between 3 groups: cases with no prior history of coronary events, cases with remote (>2 years) and recent (<2 years) prior coronary events. Results: The majority of SCA patients had no prior coronary event (76%/1119; 71%), with SCA as the first clinical manifestation of heart disease. Subjects with a prior coronary event (324/1119; 29%) had their event a mean 5.6 years prior to SCA. Cases with no prior coronary event were less likely than patients with a remote or recent event to have diabetes (30% vs. 41% vs. 46%; p<0.0001), and were younger (65 vs. 71 vs. 73 yrs, p<0.0001). Cases with no prior event also had a higher percentage of normal ejection fraction (55% vs. 32% vs. 23%; p<0.05). There were no significant differences in the remote vs. recent coronary event groups.

Conclusions: SCA without prior coronary event may be more common than previously recognized and were distinguishable by younger age, less diabetes and significantly higher likelihood of normal left ventricular systolic function. Risk stratification for this subgroup may involve the identification of novel risk predictors.
Variability in Risk with Different Hot-spot Mutations Involving the LQT1-KCNQ1 Gene

Christian Jones, Arthur J. Moss, Scott McNitt, Wojciech Zareba, Jennifer L. Robinson, Ming Qi, International Long QT Syndrome Investigative Group, The Heart Research Follow-up Program, University of Rochester Medical Center, Rochester, NY

Background: This study focuses on the risk associated with the individual missense mutations located in hotspot areas of the LQT1-KCNQ1 gene.

Methods: Using the International LQTS registry we identified 528 subjects with known missense mutations in the KCNQ1 gene. We defined a KCNQ1 hotspot polymorphism when a specific missense mutation involved ten or more individuals in the database. Cox proportional regression analysis was used to evaluate time dependent hazard ratios.

Results: We identified 15 hotspot mutations: 2 mutations (V254M, A341V) were associated with a similar high risk for cardiac events (hazard ratio = 3.47, p = 0.001) and cardiac death (hazard ratio = 4.44, p = 0.0026); 2 mutations (G345R, S349W) were associated with a more moderate increased risk of cardiac events (hazard ratio = 2.01, p = 0.027) but not an increased risk of cardiac death (hazard ratio = 1.20, p = 0.15) when compared to the 11 low risk hotspots (figure).

Conclusions: This genotype was independent of QTc, gender and beta-blocker therapy. The risk of the genotype was independent of the location in the channel, with several low-risk missense mutations located only few base-pairs away from the high-risk mutations. Beta-blockers significantly reduced the risk in all three groups.

ACC.Poster Contributions
1029
Defibrillation/Implantable Devices; ECG/Ambulatory Monitoring—Signal Averaging
Tuesday, April 01, 2008, 9:00 a.m.-12:30 p.m.
McCormick Place, South Hall

1029-95 Implanted Cardioverter-Defibrillator Outcomes in Cocaine Abusers

Background: The ACC/AHA guidelines for sudden cardiac death (SCD) prevention in cocaine abusers using implantable cardioverter-defibrillator (ICD) are not clear. We tested the hypothesis that the increased complications in cocaine abusers associated with ICD placement outweigh the benefit.

Methods: A retrospective analysis was performed on 36 patients who received ICD for prevention of SCD. They were divided into 2 matched groups: Group A with a history of cocaine abuse (n=18; mean age 48.8±7.1 years) and Group B with no known history of cocaine abuse (n=18; same mean age). We compared defibrillator threshold (DFT), ICD pocket-related complications (infection or bleed), ICD shocks, use of antiarrhythmic medication, compliance, hospital readmissions and associated costs, cardiac and all-cause mortality.

Results: Per ACC/AHA guidelines, in Group B, ICDS were implanted after maximizing medical therapy for 3 to 9 months (0.9±1.2 years). In Group A, ICD implant was delayed in order to substantiate freedom from cocaine abuse over a period of 2±1.6 years (p=0.03). There were no statistical differences in baseline characteristics between the two groups with the exception of a higher number of alcoholics (88.9% vs. 22%, p=0.001) and the presence of more non-ischemic cardiomyopathy (88.9% vs. 50%, p=0.033) in Group A. In line with earlier findings, the DFT at the time of implantation was higher in Group A than Group B (24.3±5.9 joules vs. 19.3±4 joules, p=0.01). At a mean follow-up of 1.6±1.2 years in Group A and 2.3±1.6 years in Group B, the following were found to be worse in Group A: ICD shocks (50% vs. 8.6%, p=0.01), poor compliance (66.7% vs. 5.6%, p=0.001) and total healthcare readmission costs (Group A, $768,247 for 19 readmissions; Group B, $35,259 for 2 readmissions). There was one cardiac-related mortality (SCD) in Group A and none in Group B.

Conclusions: 1) ICD implantation in cocaine abusers is associated with a higher number of dysrhythmic episodes and ICD shocks. 2) Cocaine abusers have a higher rate of complications and related hospital readmissions resulting in substantially higher healthcare costs.

1029-96 Implantable Cardiac Defibrillator for Sudden Cardiac Death Prophylaxis Therapy Rates After Primary Percutaneous Coronary Intervention
Brian Lindsay, Timothy D. Henry, William T. Katsiyiannis, Chuen Y. Tang, Charles C. Gornick, Adrian K. Almquist, Daniel P. Melby, Minneapolis Heart Institute Foundation at Abbott Northwestern Hospital, Minneapolis, MN

Background: Currently there is no data on the percentage of patients who have an indication for Implantable Cardiac Defibrillator (ICD) therapy following ST-segment myocardial infarction (STEMI). Primary percutaneous coronary intervention (PCI) is the preferred method of treatment for STEMI with reduced rates of death and recurrent ischemia compared to other treatment modalities. The purpose of this study is to determine the prevalence of class I indications for prophylactic ICD therapy in a large cohort of STEMI patients treated with primary PCI at a tertiary cardiac catheterization center.

Methods: The Minneapolis Heart Institute Level I MI Program represents a dedicated STEMI recognition and transfer system for primary PCI treatment at a tertiary hospital. Primary PCI was available to patients presenting up to 210 miles away. All patients underwent LVEF assessment during the index hospitalization, and again within 6 months after the initial LVEF was <50%. Patient data from this program were analyzed including baseline characteristics, infarct location, revascularization, post infarct LVEF and indication for ICD therapy.

Results: A total of 1132 patients underwent primary PCI for acute STEMI. During the index hospitalization, 235 (20.8%) patients were identified as having an LVEF less than or equal to 35%. At mean 2.5 year follow-up, only 53 (4.7%) patients had persistent LV dysfunction as an indication for primary ICD therapy. Of those with a primary prevention indication, 23 (2.0%) underwent implantation, 30 (2.7%) did not due to patient therapy refusal, contraindications, loss of follow-up, and other reasons. A total of 21 patients (1.9%) underwent ICD implantation for secondary prevention indications.

Conclusions: This data represents the only modern study on the rate of ICD indication in patients post-STEMI. In this large cohort we found a low rate of persistent LV dysfunction and need for prophylactic ICD therapy following primary PCI for STEMI. The majority of patients with a low initial EF during index hospitalization for primary PCI treatment recover significant LV function with only 6.5% of patients ultimately demonstrating a primary or secondary indication for ICD post-primary PCI.

1029-97 Prediction of Recurrent Implantable-Cardioverter Discharges
John N. Catanazzo, Amsgd N. Makaryus, Christina Sison, Ram L. Jadonath, North Shore University Hospital, Manhasset, NY

Background: Predictors of appropriate implantable cardioverter-defibrillator (ICD) discharge have been described in the literature. Changes in cardiac structure and electrophysiology after ICD implantation can lead to recurrent discharge. In the era of more aggressive follow up and pharmacotherapy, we sought to examine predictors of recurrent ICD discharge.

Methods: Recurrent discharge was defined as any occurrence of a discharge (appropriate or inappropriate) after the first discharge. There were 53 patients experiencing a recurrent discharge identified from a group of 591 patients (474 males; mean age 67.9±13 years; mean follow-up 10.9±14.9 months [0-120 mo]) who were receiving medical therapy including beta blockers, ace-inhibitors, and antiarrhythmics. Clinical predictors (age, gender, hypertension, diabetes, syncope, atrial fibrillation (AF)), and medications were analyzed to determine association with recurrent ICD discharge.

Results: Risk factors individually associated with any recurrent discharge included: atrial fibrillation (p<0.001), age >65 (p=0.049), and any valve repair (p=0.015) Subjects who had a history of AF were 1.8 times more likely to have a recurrent discharge. A logistic regression utilizing a backward elimination algorithm yielded age>65 (p=0.015) and any valve repair (p=0.003) as being associated with recurrent discharge. Subjects who had any valve repair were 3.5 times more likely to have a recurrent discharge. Subjects who are less than 65 years of age were 2.5 times more likely to have a recurrent discharge.

Conclusion: The main factors associated with recurrent ICD discharge are: age >65 and any valve repair. These patient subgroups may require more aggressive therapy with anti-arrhythmic drugs and ICD programming to prevent recurrent discharge and to maximize necessary therapy for the avoidance of sudden cardiac death.

1029-98 Intraventricular Conduction Delays on a 12-Lead ECG Is Associated With Significantly Higher Arrhythmic Events Than Bundle Branch Block in Patients With an Implanted Cardioverter-Defibrillator
Wardath Maskouk, Hussam Suraide, Jo Mahenthiran, Mithilesh K. Das, Indiana University, Indianapolis, IN

Background: Wide QRS (qQRS, qQRS >120ms) on a 12-lead ECG with or without typical bundle branch block (BBB) is associated with increased arrhythmic events (AE) in patients (pts) with an ICD. qQRS occurs due to BBB or intraventricular conduction delays (IVCD). We postulate that IVCD, which most likely represents myocardial disease, is associated with a significantly higher risk for AE than BBB, which is primarily due to conduction...
system disease and may or may not be associated with significant myocardial scar.
Methods: ECGs and AE (appropriate ICD shock & antitachycardia therapy) in 352 ICD pts were studied. BBB group included right and left BBB. IVC group included pts with QRS > 120 ms who did not meet the standard criteria for a BBB.
Results: 158 pts had wQRS (age: 66 + 11 years, male: 91%, ischemic cardiomyopathy: 72%, primary prevention indications: 57%, mean follow-up: 12 + 9 months) and 36% of the pts (n = 57) had BBB (LABB: 72%). Age and EF did not differ between the IVC and BBB groups. 41 (23%) pts had AE. The IVC group had significantly higher AE than the BBB group (35% vs. 8.7%, p<0.001). CoxRegression analysis revealed that IVC was the only univariate predictor of AE (p = 0.003, RR: 1.9, 95% CI [1.3-2.7]); age, EF, CHF class, or secondary prophylaxis indication did not predict AE. Kaplan-Meier survival analysis revealed a significantly decreased AE-free survival in the IVC group vs. BBB group (p = 0.012).
Conclusion: IVC on a 12-lead ECG is a significant independent predictor of AE as compared to BBB in ICD pts with a wQRS.

10:00 a.m.

T029-93
Clinical Predictors of Increased Mortality in Patients With Infected Cardiac Devices
Timir S. Damani, Sanjaya K. Gupta, Javier A. Valle, Elina Yamada, University of Michigan, Ann Arbor, MI
Background: The utility of clinical parameters as a predictive tool for mortality in patients with infected cardiac devices is unknown.
Methods: We conducted a retrospective chart review of patients at the University of Michigan admitted with infected pacemakers and defibrillators between January 1997 and April 2007. Key clinical parameters at baseline were collected along with demographic, clinical, and outcomes data.
Results: 210 patients met inclusion criteria for the study. During a six-month follow-up period, death due to all-cause mortality occurred in 17% (n=36). Adjusting for age, gender, and treatment we identified the following clinical parameters to be associated with increased mortality: acute renal failure (HR 2.0, p<0.01), pulmonary abscess (HR 7.7, p<0.01), systemic embolization (HR 7.2, p<0.01), bacteremia (HR 7.1, p<0.01), end stage renal disease (HR 6.5, p<0.01), evidence of lead infection (p=0.01), ischemic heart disease (HR 2.4, p<0.03), recent or present line (HR 5.3, p<0.01), and peak serum creatinine (HR 1.5, p<0.01). A final Cox proportional hazards model that simultaneously included all clinical parameters found bacteremia (HR 6.7, p<0.01), age (HR 1.8, p<0.01), and peak serum creatinine (HR 1.4, p<0.01) to be independent predictors of mortality.
Conclusion: Bacteremia, age, and creatinine were found to be more strongly correlated with mortality when compared to all other clinical parameters in patients with infected cardiac devices.
Cardiac Arrhythmias

The Prognostic Significance of QT Interval Prolongation in a Clinical Population of Male Veterans

Amir Kaykha, Kenneth B. Desser, Nathan Laufer, Robert Halligan, Ashish Pershad, Sina Nafisi, Jonathan Myers, Victor F. Froelicher, Banner Good Samaritan Medical Center, Phoenix, AZ, VA Palo Alto Health Care System, Stanford University, Palo Alto, CA

Background: Although QT prolongation has been associated with sudden death and increased mortality in selected populations of patients, its prognostic power in a large clinical population is unclear.

Methods: Computerized ECGs obtained on 42,301 male veterans were evaluated. Subjects with pacing, WPW, QRSD > 120 milliseconds (ms) and atrial fibrillation were excluded, leaving 37,279 patients for analysis. Using computerized algorithms, QT duration was analyzed and correlated QT interval (QTc) was measured according to Bazett’s formula. QTc was over-read by cardiologists. All-cause (AC) and cardiovascular (CV) deaths were used as outcomes.

Results: During a mean follow-up of 6 years, there were 2,957 CV and 8,511 AC deaths. A QTc prolongation (for age and sex without adjustment for heart rate) in a Cox model, QTc was a strong predictor of both endpoints [CV death: HR 1.5, p<0.001; AC death: HR 1.4, p<0.001; for a QTc > 450 ms], outperforming many established ECG predictors of death. For every 10 ms increase in QTc (above 400 ms), there was a 10% increase in CV death and a 7% increase in AC death. Survival curves showed significant separation according to a QTc score (defined as QTc400-1 = 401-450 <2, 451-500 >=3, >500 ms). Subgroup analyses examining in-patients and out-patients as well as patients with normal and abnormal ECG groups showed similar results.

Conclusions: QTc prolongation is a strong predictor of CV and AC mortality in a male clinical population and should be considered as part of clinical risk stratification.

Acute Sleep Deprivation Is Associated With Prolonged Electrocardiographic P-wave and QT Dispersion in Healthy Young Adults

İbrahim SARI, Vedat DAVUTOĞLU, Burcu ÖZBEL, Umut ÖZER, Muralı SUCHI, Sentar SOYDING, Yaxemin BALTAÇI, Sema YAVUZ, Mehmet AKSOY, Gaziantep University School of Medicine Cardiology Department, Gaziantep, Turkey, Gaziantep University School of Medicine Physiology Department, Gaziantep, Turkey

Background: Sleep deprivation (SD) is associated with increased incidence of adverse cardiovascular and metabolic disorders in humans, including mortality. We hypothesized that there might be an association between acute SD and electrocardiographic maximum P-wave duration (Pmax), QT duration (QTmax), QT corrected and QTc dispersion (QTd/cQTd) in otherwise healthy young adults which are known as predictors of atrial fibrillation, ventricular arrhythmias and sudden death.

Methods: 37 mentally and physically healthy volunteers were included into the study (age: 28.45±7.97; 11 women). First, we obtained electrocardiographies of the participants after a night in which they reported having regular sleep and repeated electrocardiographies to a QTc score (defined as QTc=102.16±9.46 vs 95.13±11.21; p<0.001 and 37.02±8.11 vs 20.27±10.42; p<0.001 respectively). Subgroup analyses examining in-patients and out-patients as well as patients with normal and abnormal ECG groups showed similar results.

Conclusions: QTc prolongation is a strong predictor of CV and AC mortality in a male clinical population and should be considered as part of clinical risk stratification.

The Prognostic Significance of QT Interval Prolongation in Small Animals by Micro-Magnetocardiography System With Superconducting Quantum Interference Device: Comparison With Electrocardiography

Kazuo Komamura, Yoshiaki Adachi, Jun Kawai, Masakazu Miyamoto, Masashi Inagaki, Masaru Sugimachi, Gen Uehara, National Cardiovascular Center, Suita, Japan, Kanazawa Institute of Technology, Kanazawa, Japan

Background: Drug-induced QT prolongation is a critical problem for drug development process. The guideline of International Conference on Harmonization requires evaluating pre-clinical potential hazards of drug-induced QT prolongation. We have developed a micro-magnetocardiography (MCG) system for small animals comprised of ultrafine magnetometer array of superconducting quantum interference device (SQUID) on a single silicon chip of 10mm square. MCG does not need electrodes for measurement of electric currents in the heart. We compared QT intervals in MCG with those in ECG.

Methods: Ten male Hartley guinea pigs (250g) were anesthetized with pentobarbital. Platinum needle electrodes were attached to animals. Exceptional quinidine (60mg/kg) was administered intraperitoneally. MCG and ECG were recorded simultaneously at baseline, 3, 5, 7, 10, 15 min after injection. QT interval was automatically analyzed by PowerLab and QTc was calculated by Bazett formula.

Results: QTc was prolonged from 284±10 to 299±11 msec in ECG (QTc-ECG)(p<0.01). QTc was prolongation from 280±16msec to 295±10msec in MCG (QTc-MCG)(p<0.01). QTc-MCG correlated well with QTc-ECG at baseline (r=0.944, p<0.0001) and at 15 min after injection (r=0.780, p=0.0007).

Conclusions: Micro-MCG successfully measured drug-induced QT prolongation with a close correlation with ECG in guinea pig. Non-contact characteristics of MCG may enable high throughput screening test of drug-induced QT prolongation.

The Prognostic Significance of Left Axis Deviation in Heart Failure and Coronary Artery Disease

Francesco Trivellato, Federico Moleiro, Ivan Mendoza-Britto, Central University of Venezuela, Caracas, Venezuela, Albert Einstein Hospital, Philadelphia, PA

Background: Although QRS prolongation has been reported to be a significant predictor of mortality in patients with left bundle branch block (LBBB), the prognostic value of QRS axis deviation in patients with LBBB in a large general medical population has not been reported.

Methods: Analysis were performed on the first ECG digitally recorded among 42,301 male veterans since 1987. Subset analysis were performed on those with LBBB, and patients were stratified according to QRS axis (normal axis and left axis deviation, LAD) and QRS duration (above and below 150 milliseconds ms). Cardiac (CV) mortality was the main outcome with a mean follow-up of 6 years.

Results: LBBB was present in 556 (1.3%) patients with a mean age of 57 years. Further adjusting for age and heart rate in a Cox model, QRS duration (HR 1.8, p<0.0001, for a QRS > 150 ms) and LAD (HR 1.5, p<0.0001) were strong independent predictors of CV death in patients with LBBB. When further subdivided using a QRS duration of 150 ms as the cut-off, LAD with a QRS duration >150 ms (HR 2.0, p<0.0001) was the strongest predictor of CV death, outperforming all other established ECG predictors of death. Survival curves demonstrated significant separation according to the presence or absence of LAD and QRS durations above or below 150 ms.

The Prognostic Significance of QT Interval Prolongation in Small Animals by Micro-Magnetocardiography System With Superconducting Quantum Interference Device: Comparison With Electrocardiography

Kazuo Komamura, Yoshiaki Adachi, Jun Kawai, Masakazu Miyamoto, Masashi Inagaki, Masaru Sugimachi, Gen Uehara, National Cardiovascular Center, Suita, Japan, Kanazawa Institute of Technology, Kanazawa, Japan

Background: Drug-induced QT prolongation is a critical problem for drug development process. The guideline of International Conference on Harmonization requires evaluating pre-clinical potential hazards of drug-induced QT prolongation. We have developed a micro-magnetocardiography (MCG) system for small animals comprised of ultrafine magnetometer array of superconducting quantum interference device (SQUID) on a single silicon chip of 10mm square. MCG does not need electrodes for measurement of electric currents in the heart. We compared QT intervals in MCG with those in ECG.

Methods: Ten male Hartley guinea pigs (250g) were anesthetized with pentobarbital. Platinum needle electrodes were attached to animals. Exceptional quinidine (60mg/kg) was administered intraperitoneally. MCG and ECG were recorded simultaneously at baseline, 3, 5, 7, 10, 15 min after injection. QT interval was automatically analyzed by PowerLab and QTc was calculated by Bazett formula.

Results: QTc was prolonged from 284±10 to 299±11 msec in ECG (QTc-ECG)(p<0.01). QTc was prolongation from 280±16msec to 295±10msec in MCG (QTc-MCG)(p<0.01). QTc-MCG correlated well with QTc-ECG at baseline (r=0.944, p<0.0001) and at 15 min after injection (r=0.780, p=0.0007).

Conclusions: Micro-MCG successfully measured drug-induced QT prolongation with a close correlation with ECG in guinea pig. Non-contact characteristics of MCG may enable high throughput screening test of drug-induced QT prolongation.
Conclusions: LAD in patients with LBBB is associated with increased CV mortality despite QRS prolongation. This axis shift can be easily determined on the ECG and should be considered as part of clinical risk stratification.

The "PhysioGlove®", a New Diagnostic 12-Lead ECG Acquisition Device: Assessment of Reproducibility and Diagnostic Accuracy Compared to ECGs Acquired Using the Conventional ECG Cable

Michael Lu, Roberto M. Lang, Dan Tizvoni, Roderick Childers, Morton Arnsdorf, Irving Levi, Daniel David, University of Chicago, Chicago, IL; Tel Aviv University, Tel Aviv, Israel

Background: Presently 12 lead ECG still lacks in reproducibility (R) and diagnostic accuracy (DA). The PhysioGloved® (PG), a new ECG acquisition device incorporates all 10 electrodes in a glove placed on the left hand (Fig), for rapid (no lead wires, no skin prepping), accurate & reproducible ECG recording with minimal profiling. Methods: To compare R and DA of PG-ECGs with regular ECG cable (RC) ECGs, 207 consecutive, consenting adult cardiology outpatients (pts) were studied. Height, weight, chest circumference (CC) and diagnoses were noted. The PG was carefully designed (using modeling and extensive anthropomorphic population studies) to fit >80% of a random adult US population. All pts had three ECGs. ECG-I using the PG, ECG-II using a RC with chest electrodes (CE's) positioned in the exact location of the PG CE's, ECG-III placing the RC-CE's in the conventional anatomic locations. The CC-I & II were compared to assess R. Automatic ECG analysis was used for comparisons. Results: M/F ratio: 123/84, ages: 21-84y; >50% of African American origin, height range 57-76", weight 102-320lb. CC range 31"-55". Overall R was 95% (regardless of anthropomorphism). In pts with CC range 34"-46" (n=184/207 = 89%) DA was 96.8%. In pts with CC>46" DA was 91.8%. Conclusions: The PG showed excellent R regardless of anthropomorphism. The PG DA was 96.8% in almost 90% of a representative US cardiology outpatient clinic population, significantly exceeding the published conventional ECG R and DA.

Holter-Based T-wave Alternans Predicts Sudden Cardiac Death in High-Risk Post-MI Patients

Phyllis K. Stein, Peter P. Dimitriovich, Devang Sanghavi, Pinkash Deebanjani, Washington University School of Medicine, St. Louis, MO

Background: Microvolt T-wave alternans (TWA) measured from treadmill testing and using spectral analysis techniques identifies patients at increased risk of sudden death (SCD). TWA can be measured from 24-hour Holter recordings using a time domain method called modified moving average (MMA). The relationship of Holter TWA to SCD is unknown. Methods: The design and results of the EPHESUS study have been published previously. EPHESUS enrolled hospitalized post-MI patients with heart failure and/or diabetes with left ventricular dysfunction. Prior to randomization to drug treatment, Holter recordings were obtained from 493 patients. Of these patients, 48 died, 18 suddenly and the rest survived. The results of this study were compared to the published reports of the exact lead and position of the PG-ECGs. We also report diagnostic utility of various ECG markers in patients with SCD.

Comparison of Microvolt T-Wave Alternans with Invasive and Noninvasive Risk Stratifiers for Sudden Cardiac Death in Hypertrophic Cardiomyopathy

Frank Cuoco, Valerian Fernandes, Christopher D. Nielsen, J. Lacy Sturdivant, Robert B. Leman, J. Marcus Wharton, William H. Spencer, Michael R. Gold, Medical University of South Carolina, Charleston, SC

Introduction: Microvolt T-wave alternans (TWA) and electrophysiology studies (EPS) are commonly used to assess arrhythmia vulnerability in diverse patient populations. However, nonarrhythmic clinical parameters are typically used to risk stratify for sudden death (SCD) among patients with hypertrophic cardiomyopathy (HCM). The relationship between arrhythmia measures and these risk factors (RFs) is not well studied. Methods: We evaluated 30 patients with HCM who underwent alcohol septal ablation and were referred for EPS. The traditional RFs for SCD were assessed, including a family history of SCD, syncope, marked septal thickness, and abnormal blood pressure response during exercise. TWA was performed in all pts prior to EPS. Results: The mean age of the cohort was 50±13 years, 60% were male, and they had 1.3±1.1 RFs for SCD. Positive (pos), negative (neg), and indeterminate (ind) TWA results were 27%, 57%, and 17%, respectively. Six patients (20%) had neg EPS, while 24 patients (80%) had pos EPS. In the TWA neg group, 88% had pos EPS, whereas in the TWA non-neg (pos + ind) group, 69% had a pos EPS (p=0.36, Fisher's exact test). The table shows the relationship between TWA and EPS with the traditional RFs for SCD in HCM. Conclusions: TWA does not predict the results of EPS, and neither TWA nor EPS are associated with traditional RFs for SCD in patients with HCM. EPS was frequently positive and likely a nonspecific finding. Long term follow-up is needed to assess if TWA predicts arrhythmic events.
Conclusion: Presence of fragmented QRS complexes (fQRS) on a 12-lead ECG is a highly sensitive marker of the presence of a sub-endothelial myocardial scar related to underlying CAD, and provides greater accuracy compared to Q-waves alone for detecting occult CAD scarring of all regions by a 12-lead ECG.

Fragmentation of Wide QRS on 12-Lead ECG Predicts Myocardial Scar

Hussam Suradi, Wodlah Maskoun, Mark Michael, Hicham El Masry, Mithilesh K. Das, Kraknert Institute of Cardiology, Indiana University School of Medicine, Indianapolis, IN

Background: Fragmented QRS complexes (fQRS) on a 12-lead ECG >120 ms represents myocardial conduction delay due to myocardial infarction scar in patients with coronary artery disease (CAD). However, fQRS is not defined in presence of a wide QRS (>120 ms). We postulate that a wide fQRS (wfQRS) due to bundle branch block (fBBB), premature ventricular complexes (FVC) or a paced rhythm (fpQRS) on a 12-lead ECG signifies myocardial scar.

Methods: ECGs of pts who underwent cardiac evaluation of CAD with nuclear stress imaging or cardiac catheterization for presence of myocardial scar were studied. WfQRS was defined by the presence of ≥ 2 notches on R or S wave, in at least two or more contiguous leads representing a major coronary artery territory.

Results: 879 patients (age 67.3±11, Male 97%, mean follow-up: 29±19 months) were included in the study. 310 had BBB, 301 PVC and 266 paced rhythm. WQRS was present in 415 (47.2%) pts. Myocardial scar was present in 442 (50.3%) pts. 170 had BBB, 124 had FVCs and 121 had fpQRS. The wfQRS was an independent predictor for myocardial scar (p<0.001).

The Sensitivity, Specificity, positive and negative predictive values of wfQRS for detecting myocardial scar were 85.8%, 92.6%, 92.5% and 87.3%, respectively. The wfQRS was also associated with significantly increased mortality (35.1% vs. 18%, P<0.001) as compared to its absence.

Conclusions: The wfQRS is a highly specific novel ECG sign for myocardial scar in pts with known or suspected CAD. The wfQRS is also associated with significantly higher mortality.

A32 ABSTRACTS - Cardiac Arrhythmias

10:00 a.m.

1029-107

Fragmented QRS Complexes on a 12-lead ECG is a Marker of Greater Myocardial Scarring Related to Coronary Artery Disease by Magnetic Resonance Imaging

Mohamed Homsi, Lamaan Alsayed, Mithilesh K. Das, Jo Mahenthiran, Kranert Institute of Cardiology, Indiana University School of Medicine, Indianapolis, IN

Background: Fragmented QRS complexes (fQRS) on a 12-lead ECG is a marker of greater myocardial scarring. The possibility of coronary artery disease (CAD) as the etiology of this is not known. Hence, we evaluated this by Gadolinium-delayed enhancement (GDE) Cardiac magnetic resonance (CMR) imaging.

Method: CMR was performed on 1.5-T Siemens system. GDE was obtained 10 minutes post contrast injection (0.1 mmol/kg dose). Sub-endothelial GDE corresponding to coronary territory was considered a marker of CAD scar. The fQRS was defined by the presence of fragmented QRS, notched R or S wave, or RSR pattern in at least 2 contiguous leads in one of the major coronary artery territories (LAD: lead V1 to V6, LCx: lead l, aVL and V6, and RCA: lead II, III and aVF).

Results: We studied 33 pts (mean age 48 ± 15 years, 42% male, 33% known CAD). 12 (36%) pts had IQRS and 4 (12%) pts had Q waves on their 12-lead ECG. 82 (24%) pts had GDE. Sensitivity, specificity, positive predictive value and negative predictive value of detecting myocardial scar by fQRS were 100%, 86%, 67% and 100%; respectively with an accuracy of 97% CI (0.91-1.00); p<0.001. Results with analysis of anterior, lateral and inferior fQRS and Q wave are summarized in the table.

<table>
<thead>
<tr>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Accuracy</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>fQRS</td>
<td>88%</td>
<td>97%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Q wave</td>
<td>85%</td>
<td>100%</td>
<td>0.03</td>
</tr>
<tr>
<td>IQRS and/or Q wave</td>
<td>100%</td>
<td>84%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Anterior IQRS</td>
<td>100%</td>
<td>93%</td>
<td>0.09</td>
</tr>
<tr>
<td>Anterior Q wave</td>
<td>97%</td>
<td>100%</td>
<td>0.06</td>
</tr>
<tr>
<td>Anterior IQRS and/or Q wave</td>
<td>100%</td>
<td>93%</td>
<td>0.006</td>
</tr>
<tr>
<td>Lateral IQRS</td>
<td>83%</td>
<td>96%</td>
<td>0.003</td>
</tr>
<tr>
<td>Lateral Q wave</td>
<td>no cases</td>
<td>no cases</td>
<td></td>
</tr>
<tr>
<td>Lateral IQRS and/or Q wave</td>
<td>82%</td>
<td>96%</td>
<td>0.003</td>
</tr>
<tr>
<td>Inferior IQRS</td>
<td>100%</td>
<td>82%</td>
<td>0.004</td>
</tr>
<tr>
<td>Inferior Q wave</td>
<td>82%</td>
<td>96%</td>
<td>0.04</td>
</tr>
<tr>
<td>Inferior IQRS and/or Q wave</td>
<td>100%</td>
<td>82%</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Conclusion: Presence of fragmented QRS complexes (fQRS) on a 12-lead ECG is a highly specific novel ECG sign for myocardial scar in pts with suspected CAD, 51% known CAD, 12 (36%) pts had IQRS and 4 (12%) pts had Q waves on their 12-lead ECG. 82 (24%) pts had GDE. Sensitivity, specificity, positive predictive value and negative predictive value of detecting myocardial scar by fQRS were 82%, 84%, 0.003 and 83% respectively with an accuracy of 97% CI (0.91-1.00); p<0.001. Results. With analysis of anterior, lateral and inferior fQRS and Q wave are summarized in the table.

1029-108

Electrocardiographic Abnormalities Are Common Among Pre-participation ECGs in a Population of Elite US College Athletes

J. Jason Wieg, John M. MacKnight, Ethan N. Saliba, Benjamin S. Rose, John D. Ferguson, John P. Dimarco, John P. Dimarco, Sriraj Mahapatra, J. Paul Mounsey, Dilawar J. Mistry, University of Virginia, Charlottesville, VA

Background: Screening of elite athletes with a history and physical is recommended for the identification of those at risk of sudden cardiac death. The value of routine pre-participation ECG screening is debated, but it is not recommended by the ACC. Currently, 350-450,000 athletes compete at the U.S. collegiate level, yet the incidence of abnormal ECGs in contemporary athletes is unknown.

Methods: We obtained ECGs in 643 athletes at a Division IA university. Each ECG was screened to identify abnormalities delineated in the ESC Criteria. Sports were graded by aerobic intensity or R wave in lead V5 or V6 >=3mv. Non-LVH Abnormal ECGs encompassed all athletes with an R wave or negative Sokolow-Lyon voltage in the top quartile were more likely to suffer an ICD-terminated VT/VF (p<0.05). Kaplan-Meier analysis confirmed that those in the top quartile were more likely to experience VT/VF by one year than those in the lower quartile, 25% vs 5% (p<0.05), and during extended follow-up, 33% vs 9% (p<0.005). After adjusting for heart rate during anger and length of follow-up, the likelihood of VT/VF during follow-up for those in the top quartile was 5.4 times that of the lower quartiles (95% CI 1.7-9.0, p<0.03). In multivariable regression further controlling for ejection fraction, history of prior clinical arrhythmia, and wide QRS, anger-induced TWA was the only significant predictor of VT/VF, with likelihood in the top quartile 7.8 times that of the lower (CI 1.2-81, p<0.05.) Kaplan-Meier analysis confirmed that those in the top quartile were more likely to suffer an ICD-terminated VT/VF (p<0.05).

Conclusion: Anger-induced TWA predicts future VT/VF in patients with ICDS, suggesting that emotion-induced repolarization instability may be one mechanism linking stress and sudden death. Whether there is a clinical role for anger-induced TWA testing requires further study.

1029-109

Anger, Alternans, and Arrhythmia: Anger-Induced TWA Predicts Future Ventricular Arrhythmias in Patients With ICDS

Rachel J. Lampert, Vladimir Shusterman, Matthew Burg, William Batsford, Craig McPherson, Robert Soufer, Yale University School of Medicine, New Haven, CT, University of Pittsburgh, Pittsburgh, PA

Background: Anger can precipitate ventricular arrhythmias, and induce T-wave alternans (TWA). However, whether anger-induced TWA predicts future ventricular arrhythmias (VT/VF) is unknown.

Methods: Fifty-seven patients with ICDS (50 male, 63 ±12 years, 51 with CAD, 21 with history of prior clinical arrhythmia) underwent ambulatory ECG monitoring during a laboratory mental stress protocol including sequential resting-baseline and anger conditions, three months after implant. Pacing was programmed 720 bpm, resulting in sinus rhythm with native AV conduction in all. TWA was analyzed continuously using time-domain methods. Patients were followed for ≥ 1 year (median 36 months) and ICDS stored electrograms and event details reviewed to determine incidence of VT/VF terminated by the ICD.

Results: Patients with ICD-terminated VT/VF during follow-up (N=9) had higher mean TWA induced by anger in the laboratory, 12.8±1.0μV, compared to those without subsequent VT/VF, 9.4±0.8μV (p<0.008). To evaluate the predictive value of anger-induced TWA, the 15 subjects in the highest quartile of anger-induced TWA were compared with the 41 in the bottom quartiles. Patients in the top quartile were more likely to experience VT/VF by one year than those in the lower quartile, 25% vs 5% (p<0.05) and during extended follow-up, 33% vs 9% (p<0.005). After adjusting for heart rate during anger and length of follow-up, the likelihood of VT/VF during follow-up for those in the top quartile was 5.4 times that of the lower quartiles (95% CI 1.7-9.0, p<0.03). In multivariable regression further controlling for ejection fraction, history of prior clinical arrhythmia, and wide QRS, anger-induced TWA was the only significant predictor of VT/VF, with likelihood in the top quartile 7.8 times that of the lower (CI 1.2-81, p<0.05.) Kaplan-Meier analysis confirmed that those in the top quartile were more likely to suffer an ICD-terminated VT/VF (p<0.05).

Conclusions: Presence of fragmented QRS complexes (fQRS) on a 12-lead ECG is a highly sensitive marker of the presence of a sub-endothelial myocardial scar related to underlying CAD, and provides greater accuracy compared to Q-waves alone for detecting occult CAD scarring of all regions by a 12-lead ECG.
Conclusions: In this population of collegiate athletes, ECG abnormalities were common. LVH was the most common abnormality. Women athletes rarely demonstrated LVH on ECG, but African-American athletes commonly did. Based on ECG, further evaluation would be indicated in approximately 20% of athletes. Thus, any proposed collegiate ECG screening program should expect significant follow-up testing.

10:00 a.m.

TO29-111 Non-Sustained Ventricular Tachycardia as a Predictor of Sudden Death in Heart Failure: A Meta-Analysis

Marcos R. Sousa, Carlos A. Morillo, Fábio T. Rabelo, Antonio M. Nogueira Filho, Antonio L. Ribeiro, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil, McMaster University, Hamilton, Canada

Background: There is a clear need for improving the risk stratification of sudden death in heart failure (HF); the role of non-sustained ventricular tachycardia (NSVT) remains controversial. Our aim was to evaluate the value of NSVT on Holter monitoring as a predictor of major arrhythmic events (sustained ventricular tachycardia, resuscitated ventricular fibrillation or sudden death) in patients with HF or left ventricular dysfunction (LVD). Methods: The literature review and study selection were systematically done by 2 researchers using PubMed/LILACS databases. Studies included fulfilled the following criteria were: a) > 100 patients with HF/LVD; b) multivariate analysis; c) good quality data on the relation between NSVT type of death. We chose the Moses model to build a summary ROC curve and DerSimonian Laird method with random effects model to obtain summary Likelihood Ratios (LR) and the diagnostic Odds Ratio (OR). Results: Eleven studies were included in the meta-analysis (ischemic and non-ischemic etiology). Summary negative LR was 0.62 (95%CI 0.55-0.69) without significant heterogeneity. Summary Positive LR was 1.86 (95%CI 1.56-2.19) with significant heterogeneity (p<0.001). Summary Diagnostic OR was 3.03 (95%CI 2.44-3.76) without significant heterogeneity. The AUC of the sROC curve was 0.68 (SE=0.02), showing significant contribution of NSVT to risk stratification. Conclusion: NSVT significantly improves the prediction of sudden death in HF/LVD patients, independently of LVD.

10:00 a.m.

TO29-112 Fragmented QRS Complexes on 12-Lead ECG Predict Significant Mortality in Patients With Congestive Heart Failure

Waddah Maskoun, Bilal Saladi, Mithilesh K. Das, Indiana University, Indianapolis, IN

Background: We have previously shown that fragmented QRS (fQRS) on a 12-lead ECG without typical bundle branch block (BBB) is associated with myocardial scar and higher mortality in patients undergoing stress testing. We postulate that fQRS in patients without BBB would be indicated in approximately 20% of athletes. Thus, any proposed collegiate ECG screening program should expect significant follow-up testing.

Methods: We reviewed the ECGs of 163 CHF patients; these ECGs were performed at the time of HF/LVD. We postulate that fQRS in patients with congestive heart failure (CHF) is associated with significantly higher mortality than patients without fQRS.

Results: 39 patients with typical BBB were excluded. Of 124 patients (mean age: 60.8 ± 11.7 years, male: 97.6%, ejection fraction: 32% ± 18, mean follow-up: 5.9 ± 2.9 years), 81 patients (65%) had fQRS. Clinical and medical therapy variables, QRS duration, and ejection fraction did not differ significantly between the fQRS and non-fQRS patients. The fQRS patients had significantly higher mortality in patients undergoing stress testing. We postulate that fQRS in patients with CHF would be indicated in approximately 20% of athletes. Thus, any proposed collegiate ECG screening program should expect significant follow-up testing.

Conclusions: fQRS on a 12-lead ECG is associated with significantly increased mortality in CHF patients.

10:00 a.m.

ABSTRACTS - Cardiac Arrhythmias

Risk Prediction in Post-Infarction Patients Presenting with Atrial Fibrillation

Petra Barthe, Axel Bauer, Raphael Schneider, Alexander Müller, Anke Joening, Kurt Ulm, Georg Schmidt, 1. Medizinische Klinik, University of Technology, Munich, Germany

Background: In most studies dealing with risk stratification after acute myocardial infarction, patients presenting with atrial fibrillation (Afib) and patients with pacemakers (PM) were excluded from further analyses because all heart rate variability parameters could not be calculated in this patients. Goal of this prospective cohort study in post-infarction patients of the reperfusion era was (1) to explore the incidence and outcome of patients presenting with sinus rhythm, and (2) detect risk predictors in this patient population.

Methods: 2952 survivors of an acute myocardial infarction were prospectively enrolled. Left ventricular ejection fraction, mean heart rate, QRS duration, incidence of ventricular premature complexes and non-sustained ventricular tachycardia were assessed during the second week after the index infarction and dichotomized at pre-defined cut-off points. Primary endpoint was five year all-cause mortality. Results: 187 patients out of 2952 patients did not show sinus rhythm during the 24h-Holter recording. 110 patients presented with permanent Afib, 46 patients presented with intermittent Afib and 31 patients presented permanent or intermittent PM rhythm. On univariate Cox analysis there was no difference in the hazard rate of patients with permanent or intermittent Afib (4.2 and 4.1, p=0.001; 2.7, p=0.01 for PM rhythm). During a follow-up of 4.5 years, 64 of the 187 patients died. The probability of death of any cause at five years was comparable to patients presenting with sinus rhythm and a LVEF <30% (41% and 45%, respectively (p=0.001). On multivariate analysis, LVEF, age and QRS duration were the only significant variables (hazard ratios of 3.1, 2.8 and 1.9; p<0.001).

Conclusions: In post-infarction patients presenting with atrial fibrillation or pacemaker rhythm the survival probability at five years is almost identical with the survival probability of patients with a LVEF <30%. In these patients an impaired LVEF, advanced age and prolonged QRS duration are independent risk predictors of late mortality.

TO29-114 A highly purified omega-3 fatty acid derivative does not alter QTc interval but does reduce QT dispersion in patients with stable coronary artery disease

Sheba K. Maymandi, Mahmoud I. Traina, Mark McDonnell, Atef H. El Gassier, Mohamed R. Labedi, Tarik A. Ngab, Robin Y. Wachsner, Olive View-UCLA Medical Center, Sylmar, CA

Background: Fish oil supplementation in patients with CAD did not result in any significant effect on QTc interval. However, a significant reduction in QT dispersion was noted in a randomized, double-blind, placebo-controlled trial, 71 patients with established CAD and normal or near-normal ejection fraction received either 1 gram twice a day of a highly purified omega-3 fatty acid derivative, Lovaza, (n=37) or placebo (n=34). During the reperfusion era was (1) to explore the incidence and outcome of patients presenting with sinus rhythm, and (2) detect risk predictors in this patient population. At day 0 and day 60, electrocardiograms were obtained. Measurements of QTc were performed manually. Results: Fish oil supplementation did not result in any significant change in QTc (2.1ms in fish oil, 2.0ms in placebo, P=0.34). However, a significant reduction in QT dispersion was noted (-6.4±13.2ms in fish oil, -0.7±7.8ms in placebo, P=0.047).

Conclusions: Fish oil supplementation in patients with CAD did not result in any significant effect on QTc interval. However, there was a significant reduction in QTd. This effect may partly explain the mechanism of reduction of sudden death with fish oil supplementation.
Tonic and reflex vagal activity for prediction of mortality in diabetic post-infarction patients

Axel Bauer, Petra Barthel, Raphael Schneider, Anke Joeinig, Georg Schmidt. 1. Med. Klinik und Deutsches Herzzentrum, TU München, Munich, Germany

Introduction: Diabetic post-infarction patients are at increased risk for death. As cardiac autonomic neuropathy is a common finding in these patients, this study was performed to investigate the power of decreased tonic and reflex vagal activity for prediction of death.

Methods: The study included 2,343 survivors of acute MI in sinus rhythm. 412 suffered from diabetes mellitus. During follow-up of 5 years 61 diabetic and 120 non-diabetic patients died. Holter recordings were performed within the second week after infarction. Tonic vagal activity was assessed by means of heart rate deceleration capacity (DC). Reflex vagal activity was assessed by means of Heart-Rate Turbulence slope (TS). According to previously published cut-off values, DC and TS were considered abnormal if <= 4.5ms and <= 2.5 ms/RRI, respectively.

Results: DC and TS were significantly lower in diabetic patients compared to non-diabetic patients (4.4±3.5 vs. 5.8±3.7 and 6.1±7.3ms/RRI vs. 9.4±9.1ms/RRI; p<0.0001 respectively). Both, DC and TS were independent predictors of mortality and added to risk prediction: If both factors were abnormal, 5-year mortality rate was 43.2%. If only one factor was abnormal, this figure was 9.0%; if neither factor was abnormal, this figure was 4.1%.

Conclusions: Tonic and reflex vagal activity assessed by DC and TS are impaired in diabetic post-infarction patients. Combination of abnormal DC and TS identifies a subgroup of diabetic post-MI patients at very high risk for subsequent death.