

POSTER SESSION

901

Electrophysiology: Basic

Sunday, March 12, 2006, 9:00 a.m.-12:30 p.m.
 Georgia World Congress Center, Hall B1
 Presentation Hour: 11:00 a.m.-Noon

901-123 Connexin30.2 Containing Gap Junction Channels Decelerate AV-nodal Conduction

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Background: In the mammalian heart, gap junction channels between electrically coupled cardiomyocytes are necessary for impulse propagation and coordinated contraction of atria and ventricles. Recently, mouse connexin30.2 (Cx30.2) was shown to be expressed in the cardiac conduction system, predominantly in the sinoatrial and atrioventricular nodes. The corresponding gap junctional channels exhibit the lowest unitary conductance of all connexin channels. The aim of the present study was to evaluate in vivo effects of connexin30.2 depletion on murine cardiac electrophysiological properties.

Methods: 25 mice [16 male, 14 Cx30.2 deficient mice (expressing a LacZ reporter gene instead of connexin30.2 coding region: Cx30.2^{LacZ/LacZ}) and 11 wild-type littermates (Cx30.2^{+/+})] were electrophysiologically examined. Transvenous catheterization with intracardiac recording and stimulation was performed in all animals. Surface ECG and standard electrophysiological parameters were analyzed.

Results: Cx30.2^{LacZ/LacZ} exhibit, at equal P-wave durations, a PQ interval that is about 25% shorter as compared to Cx30.2^{+/+} (35 ± 3.9 ms versus 47 ± 4.9 ms, P<0.0001). Atrial (A), His (H) and ventricular (V) signals show that this acceleration of AV-nodal conduction is attributed to significantly accelerated supra-Hisian conduction (AH: 27.9 ± 5.1 ms in Cx30.2^{LacZ/LacZ} compared to 37.1 ± 4.1 ms in Cx30.2^{+/+}; P<0.0001), whereas infra-Hisian conduction is unchanged. In analogy, atrial fixed rate stimulation revealed a significantly reduced Wenckebach periodicity of 78 ± 7.5 ms in Cx30.2^{LacZ/LacZ} versus 87 ± 7.9 ms in wild type mice (P=0.018). **Conclusions:** Our results show that the newly discovered Cx30.2 accounts for a relevant slow-down of impulse propagation in the murine AV-node, which is significantly accelerated when Cx30.2 is missing. Thus, Cx30.2 and its human orthologue, Cx31.9 are likely to contribute to the protective function of the AV-node against rapid conduction of supraventricular tachyarrhythmias. Moreover, they might be pathophysiologically involved in functional and morphological disorders of the AV-node, such as dual-pathway formation in AV-nodal reentry tachycardias.

901-124 Forced Expression of Human Myocardin Increases Electrical Conduction Velocity Across Human Adult Mesenchymal Stem Cells to Levels Comparable to Cardiomyocytes.

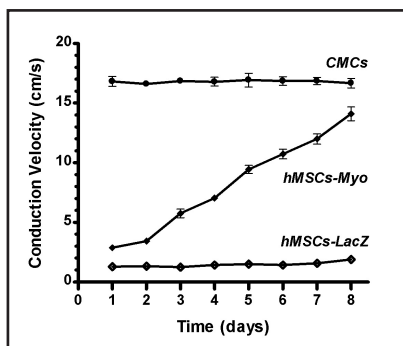
Daniël A. Pijnappels, John van Tuyn, Arnoud van der Laarse, Twan A. de Vries, Ernst E. van der Wall, Martin J. Schalij, Douwe E. Atsma, Department of Cardiology, Leiden University Medical Center, Leiden, The Netherlands

Background: Previously we showed that human adult mesenchymal stem cells (hMSCs) can repair experimental conduction block. Secondly, after forced expression of human cardiogenic transcription factor myocardin (Myo) hMSCs express cardiac muscle genes. We studied the conduction properties of Myo-hMSCs in a model of experimental conduction block.

Methods: Neonatal rat cardiomyocytes (CMCs) are cultured in Multi Electrode Arrays (Multichannel Systems, Germany). By abrasion of a central channel in a spontaneously beating monolayer, two asynchronously beating CMC fields are created. Then, either 5x10⁴ GFP labelled Myo-hMSCs are applied crossing the channel, or LacZ-hMSCs, which serve as control. After 24 h, current conduction between the two CMC fields is present for both cell types. Conduction velocity (CV) across the channel with Myo-hMSCs is measured for 8 days, and compared with CV across LacZ-hMSCs and CMCs.

Results: At day 1, CV across CMCs (n=9) is 16.9±0.8 cm/s compared to 1.1±0.1 cm/s and 2.9±0.1 cm/s across LacZ-hMSCs (n=5) and Myo-hMSCs (n=4), respectively (fig). CV across Myo-hMSCs increases steadily to 14.1±1.9 cm/s after 8 days, while CV across CMCs and LacZ-hMSCs does not change significantly. Immunostaining shows a time-dependent increase in fast-sodium ion channel (SCN5A) expression in Myo-hMSCs.

Conclusions: hMSCs expressing myocardin exhibit an increase in CV that is comparable to CMCs. Increased expression of SCN5A in hMSCs expressing myocardin may contribute to the increased CV.



901-125

Long-Term Electrical Conduction Across Human Adult Mesenchymal Stem Cells Connecting Two Fields of Cultured Cardiomyocytes and the Effect of Cx43 Knockdown by RNA Interference

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Background: Previously we showed the ability of bone-marrow derived human adult mesenchymal stem cells (hMSCs) to restore a conduction block for 48 h. To assess whether this beneficial effect is sustained we studied the long-term conduction properties of hMSCs. Furthermore we studied the role of Connexin43 (Cx43), a major component of gap junctions, in current conduction across hMSCs using RNA interference (RNAi) technique.

Methods: Neonatal rat cardiomyocytes (CMCs) are cultured in Multi Electrode Arrays (Multichannel Systems, Germany). After 2 days, a spontaneously and synchronously beating monolayer is present. By abrasion of a central channel in this monolayer, two asynchronously beating CMC fields are created. hMSCs are transfected by adeno-viral constructs knocking down Cx43 (hMSCs-Cx43[↓]) or Firefly luciferase (pLuc) (hMSCs-pLuc[↓]) as control. Then, 5x10⁴ hMSCs-Cx43[↓] or hMSCs-pLuc[↓] are applied in the channel. Conduction velocity (CV) across the channel with hMSCs is measured for up to 14 days and compared with CV across CMCs.

Results: In the control group, hMSCs-pLuc[↓] (n=4) restored conduction between two CMC fields in all monolayers after 24 h. This was sustained for at least 14 days. CV across hMSCs-pLuc[↓] was stable from 1.4 ± 0.3 cm/s (day 1) to 1.5 ± 0.6 cm/s (day 7). However, from day 7 onwards CV increased persistently to 3.5 ± 0.5 cm/s (day 14). On the other hand, hMSCs-Cx43[↓] (n=5) did not restore conduction between two CMC fields. Western blot analysis showed a >70% decrease in Cx43 expression in hMSCs-Cx43[↓] compared to hMSCs-pLuc[↓]. Across CMCs (n=9) CV was constant at 14-15 cm/s throughout 14 days. Cx43 immunostaining was observed between 1. adjacent CMCs and 2. adjacent CMCs and hMSCs-pLuc[↓]. However, no Cx43 immunostaining could be observed in hMSCs-Cx43[↓].

Conclusions: Bone-marrow derived human adult mesenchymal stem cells (hMSCs) are able to restore conduction for at least 14 days. Conduction velocity (CV) across hMSCs increases over time, however it remains lower than CV across cardiomyocytes (CMCs). hMSCs with a reduction of at least 70% in Connexin43 (Cx43) expression are not able to restore electrical conduction. Cx43 is essential for electrical coupling between CMCs and hMSCs.

901-126

Significant Low-Voltage ECG and Impaired Systolic Cardiac Function in Neonatal Mice Expressing Connexin 31 Instead of 43

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Background: Deficiency for Connexin43 (Cx43) is the cause for early postnatal death in mice due to obstruction of the right ventricular outflow tract. Aim of the study was to determine the impact of substitution of Cx43 with Cx31 in Cx43-knock-in-Cx31 mouse model (Cx43KI31).

Methods: 6-lead ECG was performed in 81 neonatal mice (23 wild type (WT), 43 heterozygous (HT), 15 homozygous (HO)) on first postnatal day (P0). ECG channels were amplified, filtered between 10 and 100 Hz and sampled with a rate of 2 kHz. All standard ECG parameters were evaluated off-line in signal-averaged ECG (ADInstruments, Milford, MA, USA). High-resolution 2-D echocardiography (HDI 5000, Philips Ultrasound, Bothell, WA, USA) was performed in 18 mice (4 WT, 9 HT, 5 HO) on P4.

Results: The offspring of heterozygous and homozygous Cx43KI31 mice resulted in Mendelian frequencies, but all homozygous Cx43KI31 mice died before P12. Neonatal homozygous Cx43KI31 hearts showed irregular hypertrophic trabeculae with abnormal pouches in the subpulmonary outlet of the right ventricle similar to general Cx43 deficient mice. Electrocardiography of P0 mice revealed significantly lower heart rates in the HO group (295 bpm ± 25) as compared to WT and HT (362 bpm ± 65, 325 bpm ± 35, p < 0.05). Moreover, voltage of the QRS complex - expressed as mean sum of Einthoven's leads I and II - was significantly lower in homozygous Cx43KI31 animals (188 μV ± 77) as compared to WT and HT (1300 μV ± 418, 1096 μV ± 390, p<0.001). Echocardiography revealed significantly lower ejection fraction in HO mice (65% ± 10) as compared to WT and HT mice (87% ± 7, 78% ± 10, p<0.01) indicating reduced systolic function in mice lacking Cx43.

Conclusion: Lack of Cx43 in homozygous Cx43KI31 mice might increase proportion of slow signal progression in the transverse direction, resulting in destruction of cardiac uniform anisotropy. Dispersion of the electrical vector might explain significant low voltage and impaired systolic left-ventricular function.

901-127

Conditional Expression of a Gain of Function Alpha-5 Integrin in Adult Mouse Heart Increases Ventricular Automaticity

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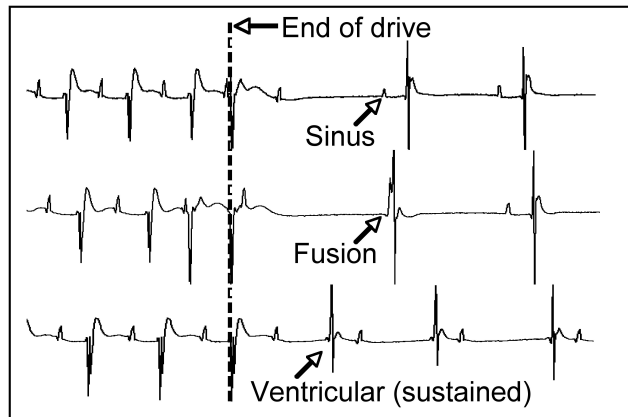
Background: Previous studies have shown contractile dysfunction, reduced ECG voltage, reduced connexin43 expression, and increased mortality in transgenic mice expressing a gain-of-function alpha-5 integrin. To determine the electrophysiological consequences of this mutation, we performed serial epicardial in vivo EP studies, before and after activation of the doxycycline (Dox) regulated transgene.

Methods: EP studies were performed using a multi-electrode catheter placed on the

anterior epicardium via left-sided thoracotomy. Studies were performed at baseline and after 5-10 days of Dox (n=5).

Results: Baseline rhythm, RR, PR, and QRS intervals, AV conduction, and atrial / ventricular refractory periods did not change significantly. The mean QTc increased (113 vs. 140ms, p<0.05). At baseline, recovery after all pacing drives during EP study occurred mainly via sinus node (88%) or fusion beats (8%). After transgene activation, recovery was mainly via nonsustained ventricular rhythms (21%) or sustained ventricular rhythms (65%). This trend was seen equally with atrial or ventricular pacing (p=0.67). See figure for example tracings.

Conclusions: Despite stable sinus and AV nodal function, there is a dramatic shift toward earlier ventricular activation and sustained ventricular rhythms in recovery from pacing drives in mice expressing a gain-of-function integrin alpha-5 transgene. This finding suggests a possible important role of integrin dysregulation in ventricular arrhythmogenesis.



901-128

Cardiac Kir2.x Channels in Homomeric and Heteromeric Composition Are Markedly Activated by Adrenergic β -3-Receptors: Role of Protein Kinases A and C

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Background: In human cardiomyocytes the cardiac inwardly rectifying potassium current I_{K1} is essential to maintain the resting membrane potential. An increase of cardiac I_{K1} current is associated with novel Short QT Syndrome Type 3. Adrenergic β -3-receptors are increasingly recognised to contribute to cardiac physiology and pathophysiology. There is mounting evidence that heteromeric assembly of Kir2.1, Kir2.2 and Kir2.3 potassium channels underlies a main part of the I_{K1} current. Therefore, we investigated the regulation of these channel subunits by β 3 adrenergic receptors.

Methods: Human adrenergic β -3-receptors and Kir2.1, Kir2.2 and Kir2.3 potassium channels were coexpressed in *Xenopus* oocytes. Experiments were performed using two-microelectrode voltage-clamp.

Results: Activation of β -3-receptors with isoproterenol (10 μ M) resulted in markedly increased currents in Kir2.1 (+50%) and in Kir2.2 (+104%) potassium channels. In Kir2.3 channels, activation was only weak (+15%). Coapplication of specific inhibitors of protein kinase A (KT-5720) and calmodulin kinase (KN-93) had no effects on the observed regulation in Kir2.1. However, coapplication of protein kinase C inhibitors staurosporine and chelerythrine suppressed the observed effect. In Kir2.2, coapplication of KT-5720 (+39%) reduced the effect of β -3-receptor activation. No differences in current increase after application of isoproterenol (10 μ M) were observed between mutant Kir2.2 potassium channels lacking all functional PKC phosphorylation sites and Kir2.2 wild-type channels. In heteromeric Kir2.x channels, all types of heteromers were activated: In Kir2.1/Kir2.3 channels (+31%) activation was only weak. However, in Kir2.1/Kir2.2 (+72%) and in Kir2.2/Kir2.3 channels (+141%) activation was very pronounced.

Conclusions:

Homomeric and heteromeric Kir2.x channels are activated by β 3 adrenergic receptors via different protein kinase dependent pathways: Kir2.1 subunits are modulated by PKC whereas Kir2.2 is modulated by PKA. Kir2.2 channel subunits seem to play a major role in this regulation. These results elucidate further details of the molecular mechanisms of adrenergic regulation of cardiac I_{K1} current.

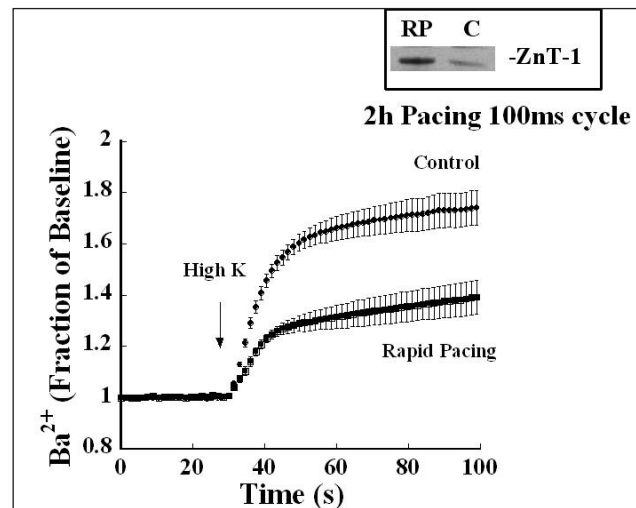
901-129

ZnT-1, A Missing Link in the Regulation of Cardiac L-Type Calcium Channels

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BACKGROUND: L-type calcium channels (LTCC) play a key role in cardiac function. ZnT-1 is a ubiquitous protein shown to inhibit cationic influx. We studied ZnT-1 effects on the LTCC activity in *Xenopus* oocytes and cardiomyocytes in culture attempting to elucidate its, yet unknown activity, in the heart. **METHODS AND RESULTS:** In *Xenopus* oocytes, two electrode voltage clamp measurements showed that ZnT-1 co expressed with the LTCC led to reduction of the LTCC current with no apparent shift in the current-voltage relationship (n=5). In isolated rat cardiomyocytes, ZnT-1 expression was increased by transfection to 464±55 % of control (n=5, p<0.05), while siRNA designed to inhibit ZnT-1 expression, decreased the expression of ZnT-1 in cardiomyocytes to 60.6±3.6 % of

control (n=4, p<0.05). In the cardiomyocytes the nifedipine sensitive Ba^{2+} influx, assessed by fura-2 and application of high K^+ (figure), was reduced in ZnT-1 transfected cells to 51.0±2.5 % of controls (p<0.01), while siRNA increased the influx to 167.0±4.25 % (p<0.01). The figure shows that rapid pacing of cardiomyocytes, at double threshold intensity, increased ZnT-1 expression to 175±18 % of controls (C) (p<0.01, n=4) and reduced Ba^{2+} influx to 48.0±1.8 % (p<0.01). This was without changes in expression of the LTCC α_1C subunit. **CONCLUSIONS:** Our findings are consistent with ZnT-1 being a major physiological inhibitor of the cardiac LTCC. Consequently, ZnT-1 seems to be a missing link in tachycardia-induced cardiac electrical remodeling.



901-130

Hydrogen Peroxide-Induced Arrhythmogenic Activity and Contractile Dysfunction of Ventricular Myocytes is Reduced by a Blocker of Late Sodium Current

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Background: Reactive oxygen species, including hydrogen peroxide (H_2O_2), cause intracellular calcium overload and ischemia-reperfusion damage. This study examined the hypothesis that H_2O_2 -induced arrhythmic activity and contractile dysfunction are the result of an effect of H_2O_2 to increase the magnitude of the late sodium current (late I_{Na}). **Methods:** Guinea pig isolated ventricular myocytes were exposed to H_2O_2 (200 μ M/L) for up to 15 min. Transmembrane voltages and currents, and twitch shortening were measured using the whole-cell patch-clamp technique and a video edge detector, respectively. **Results:** H_2O_2 markedly and time-dependently prolonged the action potential duration (APD) and induced early afterdepolarizations (EADs). H_2O_2 caused a persistent late I_{Na} that was almost completely inhibited by tetrodotoxin (10 μ M/L; n = 5). H_2O_2 slowed the relaxation rate of a contraction from 12.2±1.0 to 7.3±1.3 μ m/sec and induced EADs. Ranolazine (10 μ M/L), a novel inhibitor of late I_{Na} , attenuated H_2O_2 -induced late I_{Na} by 51±9 % (n = 10, p < 0.01). Ranolazine (10 μ M/L) attenuated H_2O_2 -induced APD prolongation by 58±8% (n = 8, p < 0.001) and inhibited the EADs (n = 3). Ranolazine delayed the development of APD prolongation caused by exposure to H_2O_2 . The increases in APD after a 9-min exposure of myocytes to H_2O_2 in the presence and absence of ranolazine (10 μ M/L) were 6±4% and 42±6%, respectively (n = 6, p < 0.001). Ranolazine (10 μ M/L) increased the twitch relaxation rate from 7.3±1.3 to 15.0±1.9 μ m/sec in the presence of H_2O_2 (n = 5, p < 0.001) and abolished H_2O_2 -induced aftercontractions. **Conclusion:** The results confirm the hypothesis that an increase of late I_{Na} during exposure of ventricular myocytes to H_2O_2 contributes to electrical and contractile dysfunction, and suggest that inhibition of late I_{Na} may offer protection against free radical-induced sodium-calcium overload and myocyte damage.

901-131

Cardiac Pacemaker Precursor Cells Can Be Obtained From Human Endometrial Mesenchymal Stem Cells for Biological Pacemaker Cell Transplantation.

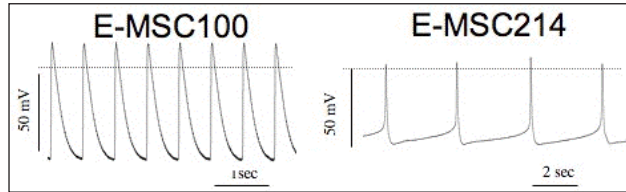
Shunichiro Miyoshi, Nobuhiro Nishiyama, Naoko Hida, Yukinori Ikegami, Yoko Hagiwara, Kazuma Okamoto, Taro Uyama, Kenji Miyado, Michie Sakamoto, Satoshi Ogawa, Akihiro Umezawa, Keio University school of Medicine, Tokyo, Japan, National Research Institute for Child Health and Development, Tokyo, Japan

Background: Mesenchymal stem cell (MSC)-derived cardiomyocyte with pacemaker potential provides us a promising cellular source for making biological pacemaker. The pacemaker activity of the MSC-derived cardiomyocyte might disappear after the maturation of the cell, thus longevity of the pacemaker activity is important. We have reported that the human endometrial MSC (E-MSC) have a higher cardiomyogenic potential than marrow derived MSC.

Methods and results: E-MSCs were obtained by the limiting dilution method. Two cell-lines were selected for the experiment. On day 5 of cardiomyogenic induction, almost all of the E-MSC (E-MSC100; 64.1%, E-MSC214; 82.7%) contracted rhythmically and synchronously. The cardiomyocyte-specific action potential (AP) was recorded. The observed ratio of pacemaker like potential was significantly higher in E-MSC214 (29/41) than in E-MSC100 (1/28, p<0.01). The incidence of pacemaker activity did not decrease as a function of time after the induction (1w; 63, 2w; 65, 3w; 100%). The duration of

AP was significantly shorter in E-MSC214 than E-MSC100 (185 ± 16 vs 326 ± 12 msec, $p < 0.01$). Surface antigen of CD-133 was weakly detected in E-MSC214 while not in E-MSC100.

Conclusion: The phenotype of cardiac pacemaker cell was stably observed in the monoclonal cell line of E-MSC214, but not E-MSC100. Our data suggest the presence of precursor cells in CD-133 positive E-MSC that were destined to be a pacemaker cell and may be good biomaterial for making cardiac biological pacemaker.



901-132 In-Vivo Sympathetic Nerve Stimulation Induces Ectopic Beats and Focal Atrial Tachycardia from Thoracic Veins in Dogs: Insights From Sympathetic Nerve Recording and High Density Mapping

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BACKGROUND: The effects of sympathetic tone on thoracic vein arrhythmogenicity remain unclear.

METHODS: We performed in-vivo recording of stellate ganglia nerve activity (SGNA), epicardial thoracic vein mapping with 1792-bipolar electrodes and stellate ganglia (SG) stimulation (20Hz, 10-50mA) before and after sinus node (SN) crushing in 8 normal dogs followed by Periodic Acid Schiff (PAS) and immunostaining of tissues.

RESULTS: No spontaneous arrhythmia was present at baseline. SG stimulation triggered SGNA, with significant elevations of transcardiac norepinephrine (NE) levels from -20 ± 78 to 1752 ± 339 pg/ml, $P < 0.001$, blood pressure from 77 ± 25 to 142 ± 33 mmHg ($P < 0.01$) and heart rate from 115 ± 14 to 195 ± 35 bpm ($P < 0.01$). Before SN crushing, SG stimulation induced atrial tachycardia in 2/8 dogs, arising from the anterior RA and left superior pulmonary vein (LSPV) respectively. After SN crushing but without SG stimulation, a slow junctional rhythm (51 ± 6 bpm) was observed. Subsequent SG stimulation resulted in induction of ectopic beats in 7/8 dogs ($n=20$ episodes) arising from the LA ($n=2$), RA ($n=5$), PVs ($n=11$) and vein of Marshall (VOM, $n=2$). The removal of the SN coupled with SG stimulation increased the propensity for left sided ectopic rhythms ($P < 0.001$), and increased the incidence of thoracic vein (PV or VOM) ectopy formation (1/8 dogs vs 7/8 dogs, $p < 0.05$) compared to SG stimulation with functional SN. PV tachycardia occurred during SG stimulation in 3/8 dogs (CL 273 ± 35 ms, duration 16 ± 4 sec). No difference in thoracic vein ectopy inducibility was observed between left and right SG stimulation (6 vs 7 episodes). PAS staining at the site of ectopy showed abundant pale-looking glycogen rich cells morphologically consistent with specialized conducting (Purkinje) cells. Immunostaining showed abundant sympathetic (tyrosine hydroxylase positive) nerves at those sites.

CONCLUSIONS: Sympathetic nerve stimulation results in local release of NE from cardiac nerves. In the absence of a SN, thoracic veins became dominant sites for ectopy during SG stimulation. Hyperadrenergic automaticity from PAS-positive specialized conduction cells in the PVs are likely sources of ectopic activity.

901-133 Intracellular Calcium Transient Dynamics and the Mechanism of Shock-Induced Ventricular Fibrillation and Defibrillation in Rabbit Hearts

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Background: The relation between intracellular calcium (Ca_i) dynamics and the mechanisms of shock-induced ventricular fibrillation (VF) (vulnerability) and defibrillation (DF) is unclear.

Methods: In 17 Langendorff-perfused rabbit ventricles, we simultaneously mapped membrane potential (V_m) and Ca_i during upper limit of vulnerability (ULV) testing by shock on T, and during DF threshold (DFT) testing with up-down protocol using biphasic shocks. We analyzed 89 episodes of VF induction by shocks on T and 173 episodes of attempted defibrillation. We selected for analyses 80 episodes with postshock activation that started from the center of the mapped region.

Results: The ULV and the DFT were 217 ± 81 V and 266 ± 79 V, respectively ($p = NS$). Shock-induced activation resulted in a heterogeneous postshock distribution of Ca_i with the emergence of an area characterized with low Ca_i surrounded by areas of elevated Ca_i ("Ca_i sinkhole"). These Ca_i sinkholes emerged on the Ca_i map 43 ± 16 ms after the shock. The first postshock Vm activation always originated from the sinkhole hole 73 ± 20 ms after shock, and spread in a centrifugal pattern. Sinkholes were present in type-B but not type-A successful defibrillation. For shock on T, a Ca_i sinkhole was present 46 ± 40 ms after the shock. The sinkhole was followed 30 ± 19 ms later by propagated wavefronts that arose from the sinkhole during late phase 3 of action potential, leading to a spiral wave that initiates VF. Assuming that the membrane potential varied from -75 mV to $+15$ mV in S₁-paced beats, the take off potential of the first postshock activation was -46.2 ± 0.7 mV. No sinkhole was present at shock strengths above the ULV. Thapsigargin (200 nM) and ryanodine (5 μM) increased APD₅₀ from 176 ± 40 ms to 273 ± 46 ms ($P = 0.009$), sinus cycle length from 492 ± 281 ms to 997 ± 244 ms ($p = 0.02$), decreased ULV from 393 ± 137 V to 171 ± 99 V ($p = 0.007$) and DFT from 429 ± 141 V to 271 ± 202 V ($p = 0.005$).

Conclusions: We conclude that Ca_i dynamics is important in the mechanisms of vulnerability and defibrillation. The formation of Ca_i sinkhole in the immediate postshock period appears necessary for the initiation of postshock activation perhaps mediated by a Ca_i dependent mechanism.

901-134 Genetic Analysis of Hyperpolarization-activated and Cyclic Nucleotide-gated Cation Channels 4 (HCN4) in Patients With Bradyarrhythmia

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Background: Sinus rate in heart is primarily determined by pacemaker current, I_p. Hyperpolarization-activated cyclic nucleotide gated cation channels (encoded by HCN4) play a key role in generating I_p. It remains however unknown whether HCN4 mutations correlate to bradyarrhythmias, such as sinus nodal dysfunction or AV conduction defect.

Methods and Results: Extensive mutational analyses were conducted for HCN4, in patients with bradyarrhythmia ($n=32$) and their family members ($n=8$). Written informed consent was obtained from all participants according to the guidelines of the Institutional Ethics Committee. At first, we collected genomic DNAs isolated from leukocytes, and screened by exonic PCR amplification and denaturing high-performance liquid chromatography (DHPLC). Abnormal conformers were analyzed by bidirectional sequencing. In a 72-year-old man with sinus bradycardia and AV conduction defect, we identified a single base pair substitution (C to G) of HCN4 at the position of 2900. This variation resulted in a missense mutation (S967C), and was not detected in > 80 healthy individuals. In this patient, we also identified an SCN5A mutation (4729 ins AA), suggesting that he has compound heterozygous mutations of cardiac ion channels. The location of S967C was in a C-terminus of HCN4 channel, nearby the cyclic nucleotide binding domain which contributes to the regulation of channel gating. Thus, the S967C mutation should affect the function of HCN4 channel, and thereby alter the I_p current properties. Among other patients, we also identified 2 silent mutations; F613F ($n=3$; 7.5%) and P1200P ($n=6$; 15%) in 9 probands independent of each.

Conclusions: We identified a novel missense mutation of HCN4 in a patient with bradycardia and atrioventricular conduction defect among 40 cases of bradyarrhythmia. Mutations of HCN4 appear to be rare in bradyarrhythmias.

901-135 Cardiac P2X₂ Receptors: A Physiologic Role in Mediating ATP-evoked Current and Regulation in Human Atrial Fibrillation

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Background: Extracellular ATP can regulate cardiac function by augmenting contractility. It is not clear how ATP exerts such an effect. The objective here was to determine a possible role of the P2X₂ receptor (P2X₂R) in mediating the extracellular action of ATP in cardiac myocytes. Membrane current under voltage clamp was performed in ventricular myocytes of wild type (WT) and transgenic (TG) mice with cardiac-specific overexpression of human P2X₂R. **Methods and Results:** Potassium currents and the Na/K pump current were suppressed by Cs⁺ and ouabain, respectively. The P2X₂ receptor agonist 2-meSAMP induced an inward current at -100 mV that was greater in magnitude (2-fold) in cells from TG mice. Replacing external Na⁺ led to a 2-meSAMP-stimulated current outward at all potentials positive to -124 mV indicating Na⁺ and Cs⁺ as the main charge carriers. In the presence of $10 \mu M Zn^{2+}$, or the P2X₂R-selective allosteric enhancer ivermectin ($3 \mu M$), the agonist-stimulated current increased significantly in cardiac myocytes from both TG and WT hearts. That the 2-meSAMP-induced current reversed at 0 mV and that the P2X₂R-selective allosteric enhancer ivermectin could potentiate the agonist-evoked current in not only the TG but also the WT myocytes suggest a physiologic role of this receptor in the action of extracellular ATP. The regulation of P2X₂R was examined in human atria obtained from patients with normal sinus rhythm (NSR) or chronic atrial fibrillation (AF). After matching for gender, age and cardiac function, the atria of chronic AF patients showed a significant up-regulation of the P2X₂R (AF: 1999 ± 1299 I.U. vs. NSR: 978 ± 602 I.U., $P = 0.027$, $n = 9$ pairs, Wilcoxon Signed Rank Sum test) as determined by quantitative immunoblotting (Am J Physiol 287: H1096, 2004). **Conclusion:** P2X₂R is an important part of the native P2X₂ receptor that mediates the extracellular ATP-induced current in mammalian cardiac myocytes. This receptor channel is up-regulated in atria of patients with chronic AF.

901-136 New in-vivo Canine Model of Drug-induced Long-QT₁ Syndrome: Beta-adrenergic Challenges Trigger Torsade De Pointes

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Background: the congenital long-QT1 syndrome (LQT1) is caused by genetic defects in I_{Ks}. Stress and exercise are notorious sympathetic triggers of life-threatening torsade de pointes (TdP). β-Adrenergic receptor (β-AR) stimulation plays a key proarrhythmic role. The electrophysiological mechanisms leading to TdP in LQT1 are still poorly resolved. An in-vivo experimental model is lacking.

Methods: adult beagle dogs of either sex (12.0 ± 1.6 kg) were anesthetized with fentanyl/etomidate. β-AR activity is preserved under these conditions, evident from intact chronotropic, inotropic and baroreflex responses. The I_{Ks} blocker HMR1556 (HMR) was administered i.v. to mimic LQT1. Temporal and spatial repolarization parameters were measured from ECG lead II and monophasic action potentials (MAP) from left and

right ventricular endocardium. The selectivity of HMR for I_{Kd} over I_{Kr} was studied on stably-transfected HEK293 or CHO cells expressing either KCNQ1 and KCNE1 or KCNH2.

Results: HMR (1 mg/kg) prolonged the QT_c interval from 246±6.7 to 305±12.7 ms (+24%), prolonged T_{peak}-T_{end} from 25±2.7 to 70±9.2 ms (+180%), increased beat-to-beat QT instability from 2.7±1.0 to 6.0±1.5 ms (+122%) and exaggerated interventricular dispersion duration from 29±3.7 to 73±15.5 ms (+152%). All changes: $p < 0.05$ vs baseline and vs solvent. β -AR challenges with isoproterenol (2.5 μ g/kg i.v. bolus; n=6) on top of HMR exaggerated repolarization abnormalities further, elicited ectopic R on T waves and then acceleration-induced TdP in 6/6 dogs vs 0/6 dogs, with either HMR or isoproterenol alone. The β -AR blocker esmolol (5 mg/kg i.v.; n=4) largely prevented HMR- and isoproterenol-induced changes. Free plasma level of HMR after 1 mg/kg i.v. was 392 ng/mL (0.94 μ mol/L) indicating selective I_{Kd} inhibition (IC₅₀ = 0.07 μ mol/L for I_{Kd} vs >10 μ mol/L for I_{Kr}), concurrent with data in canine ventricular myocytes.

Conclusions: We have developed a new canine model of drug-induced LQT1 with pronounced repolarization instability. Sudden β -adrenergic challenges trigger TdP in 100% of cases. This model could be used to further elucidate the electrophysiological mechanisms of LQT1-related TdP *in vivo* and find an adequate therapy.

901-137 Circadian, Daily, and Seasonal Distributions of Ventricular Tachyarrhythmias in Patients With Implantable Cardioverter-Defibrillator

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Background: The aim of this study was to investigate the circadian, daily, and seasonal distributions of ventricular tachycardias (VT) and ventricular tachycardias/fibrillation requiring antitachycardia pacing/shock therapy (VT/VF), in patients with implantable cardioverter-defibrillators (ICD) with ischemic (IHD) and non-ischemic heart disease (NIHD).

Methods: We performed retrospective chart reviews of ICD patients at Creighton University Medical Center between January 2000 and December 2004.

Results: We analyzed data from 154 consecutive patients (mean age of 67 years, 78% male, 71% with IHD, and a mean left ventricular ejection fraction of 34%) during a mean follow-up of 34 months. A total of 1,055 episodes of VT and 612 episodes of VT/VF occurred. We observed similar distributions in incidence of VT and VT/VF in patients with IHD and NIHD. The largest percentage of episodes occurred in January (18% of VT, 17% of VT/VF), February (16% of VT, 18% of VT/VF), and December (13% of VT, 15% of VT/VF). The percentage of episodes was highest in winter (47% of VT, 51% of VT/VF), lowest in summer (14% of VT, 13% of VT/VF), and intermediate in spring (24% of VT, 19% of VT/VF) and fall (15% of VT, 17% of VT/VF). A linear regression between number of episodes and average daily temperature was statistically significant for patients with IHD (R²=0.65, p=0.0016) and NIHD (R²=0.71, p=0.0006), and for episodes of VT (R²=0.66, p=0.0013) and VT/VF (R²=0.82, p<0.0001), suggesting a greater likelihood of both events on colder days irrespective of cardiac disease etiology. A daily variation (p<0.0001) with the greatest number of episodes occurring on Fridays (16.5%) and the least occurring on Sundays (8.2%) was also present. In addition, a bimodal circadian distribution of episodes (p<0.0001) with the largest peak between 8 AM and 1 PM and a smaller peak between 5 PM and 10 PM was noted.

Conclusions: Occurrence of ventricular tachyarrhythmias appears to follow a circadian, daily, and seasonal distribution that is similar in patients with IHD and NIHD. The incidence inversely correlates with average daily temperatures implicating a possible role for environmental triggers. These findings may have therapeutic implications.

901-138 Reentry during Ventricular Fibrillation Is Less Common Intramurally than Epicardially in Swine

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Background: Reentry is relatively uncommon on the epicardium during ventricular fibrillation (VF) in the pig. A simulation study by others demonstrated that the filament about which reentry rotates occurs much more commonly along than across the long axis of myocardial fibers. Since the long axis of fibers is almost parallel to the epicardium and endocardium, this simulation suggests that most reentry is intramural during VF. We tested this hypothesis.

Methods: Using two 528 channel mapping systems in tandem, we mapped VF from three unipolar electrode arrays in 6 open-chest pigs. Two of these arrays consisted of two rows of crisscross plunge needles (horizontal and vertical) punched through the midlines of the third array, an epicardial mapping plaque (21x24, 2 mm apart). This plaque was sutured on the anterior-lateral left ventricular epicardium. The horizontal row consisted of 21 needles and the vertical row 24 needles. Each plunge needle held 12 electrodes placed 2 mm apart. Thus these three arrays formed three orthogonal mapping planes. The vertical row of plunge needles was directed from base to apex of the heart. Four electrically-induced VF episodes were mapped simultaneously with these three arrays for 20 sec. We quantified the percentage of time reentry was present within each array.

Results: Reentry was present significantly more often in the epicardial array (mean ±sd of 0.8%±0.2% of VF wavefronts) than in the horizontal array (0.2%±0.4%) or the vertical array (0.6%±0.2%).

Conclusions: Contrary to the hypothesis, reentry was identified on the epicardial surface more often than on the horizontal or vertical intramural surfaces, indicating that the filament of reentry was more commonly oriented perpendicular to the epicardium than parallel to it. Reentry was sparse in all three planes, suggesting that the number of simultaneous reentrant circuits present during VF is small.

901-139

Does the Point of Closest Approach Between the Esophagus and the Posterior Left Atrium Move with the Cardiac Cycle?

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Background: Recent approaches to left atrial (LA) ablation for patients with atrial fibrillation (AF) have included linear ablations in the posterior LA. This approach has raised questions about potentially serious complications - the creation of a fistula in the esophagus leading to exsanguination or esophageal perforation leading to mediastinitis. We used computed tomography (CT) to determine the areas of the LA and esophagus most vulnerable to perforation and to assess the relative movement of these structures throughout the cardiac cycle.

Methods: 10 consecutive patients (52.8 ± 9.0 y/o, 4 females, 6 males) undergoing LA ablation underwent CT scanning with ECG gated acquisition. Axial image sets were generated from data acquired throughout the cardiac cycle in 10 phases, and left atrial and esophageal segmentation was performed on a workstation (Advantage Windows, GE Health Care, Waukesha, WI). Three dimensional volumes, as well as axial and oblique views of the LA and esophagus were analyzed in ten steps (5%, 15%, 25% . . . 95% of the R-R interval) to determine if relative movement between the left atrium and the esophagus occurred throughout the cardiac cycle. The point of closest approach between the posterior LA and the esophagus was tracked to determine if the most vulnerable area moved during systole.

Results: The mean distance from the LA endocardium to the esophageal lumen at the point of closest approach varied from 5.1 to 5.7 mm throughout the cardiac cycle. The location of this point moved laterally 1.2 mm throughout the cardiac cycle, superior-inferiorly (S-I) 5.2 mm, and anterior-posteriorly (A-P) 2.0 mm. For comparison, the center of mass of the LA moved laterally 1.9 mm throughout the cardiac cycle, S-I 3.9 mm, and A-P 2.8 mm.

Conclusions: Creation of RF lesions in the posterior LA that extend through to the lumen of the esophagus is a possibility. Linear lesions connecting the left PVs to the right PVs actually bisect the area of greatest vulnerability. There is some movement of the most vulnerable area with the cardiac cycle, so keeping approximately 6 mm from this location, perhaps by locating this line more superiorly across the dome of the left atrium, may minimize the risk of complications.

901-140

Atrial Arrhythmias Post Atricle Radiofrequency Ablation for Atrial Fibrillation: Findings During Catheter Ablation

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Background: The Atricle bipolar radiofrequency (RF) system is being used for intraoperative ablation of atrial fibrillation (AF).

We describe our findings in patients undergoing ablation of recurrent atrial arrhythmias after Atricle RF ablation for atrial fibrillation.

Methods and results: The management and clinical course of consecutive patients with post Atricle arrhythmias refractory to antiarrhythmic drugs between Jan 2003- Dec 2004 are presented. Fifteen patients presented after 12± 8 months after RF ablation with the Atricle for treatment of AF. Three patients underwent the procedure for lone AF with no other surgical indication. Twelve patients underwent another surgical procedure: mitral valve surgery (6 patients) and CABG (6 patients). Seven patients (47%) had recurrent AF secondary to recovered pulmonary vein ostial conduction. Two patients were documented to have focal atrial tachycardia which was mapped to the coronary sinus in one patient, and to the left atrial (LA) septum in another. Two patients had typical cavotricuspid isthmus dependent RA atrial flutter (AFL), one patient had RA incisional AFL and 3 had LA incisional AFL which was mapped around the right pulmonary veins in one patient and around the mitral valve annulus in 2 patients. All patients were treated successfully with radiofrequency ablation . At one-year followup all patients were arrhythmia free on no antiarrhythmic medications.

Conclusion: After Atricle radiofrequency ablation approximately 40% of patients experiencing atrial arrhythmias have AF secondary to PV-LA conduction recovery. Moreover, incisional AFL seems to be a common finding in this group of patients. Catheter based mapping and ablation of these arrhythmias seems to be feasible and effective.

901-141

Safety and Efficacy of Remote Ablation by Magnetic Catheter in Patients With WPW Syndrome

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Background: Accessory pathway (AP) itself rather than its insertion is the best target for successful ablation but AP electrograms are rarely recorded. We report our experience on safety, feasibility and efficacy of remote magnetic catheter (MC) guidance in patients with WPW syndrome undergoing transcatheter APs ablation.

Methods and Results: 118 consecutive symptomatic patients (76 males; median age, 23 years) with manifest APs and reproducibly induced atrioventricular reentrant tachycardia (AVRT) underwent ablation of 128 APs using MC by remote navigation system NIOBE (Stereotaxis, Inc). Transeptal approach was used in 60 patients for mapping and ablation of left APs. After catheter positioning, ablation was performed from the control room with MC in a temperature-controlled mode (55°C, max 50 W, 60 sec). Ablation end point was d wave disappearance, absence of anterograde and retrograde conduction over AP, and failure to induce AVRT. MC ablation was successful in all patients in a single session without switch to standard catheters (SC). The overall median mapping and ablation time was 10 min (range 2 - 30 min), much longer in the first 10 patients (24 min; P<0.001). MC

recorded electrical activation of Kent bundle in 115/118 patients, that disappeared within a few seconds after RF application onset simultaneously with passage of a preexcited to a normal QRS complex. Two RF applications of 60 seconds each were delivered in all patients. The sites of Kent APs were left-sided in 65, right-sided in 17, para-septal in 27 and septal in 19 patients. Multiple APs were found in 5 patients. No adverse effects occurred during the procedure. At a mean follow-up of 6.2 months neither ventricular preexcitation on the ECG nor arrhythmia recurrence occurred.

Conclusions: Electrical recording of Kent bundle and successful ablation of the accessory pathway can be commonly obtained by magnetic catheters even in challenging sites without complications.

901-142 Remote Radiofrequency Ablation of Left Sided Accessory Pathways Using the Retrograde Transaortic Approach: A Comparison of Catheters With Different Magnetic Mass

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Background: A novel magnetic navigation system (Stereotaxis, St. Louis, MO, USA) has been designed with the purpose of allowing remote guidance of radiofrequency (RF) ablation catheters and guide-wires. The different magnetic masses (Mm) of these catheters probably determine their ability to be remotely steered and consequently their performance during RF ablation. Our objectives were to evaluate the feasibility of performing RF ablations of left sided accessory pathways (AP) using the retrograde trans-aortic approach and to compare the performance of 2 catheters with different magnetic mass.

Methods: 18 consecutive pts with left sided AP were included. In all cases RF ablation was performed using a retrograde trans-aortic approach. In 6 pts a Helios II (Stereotaxis) RF catheter with lower Mm was used (**Low Mm**). In 12 pts a Celsius RMT (Biosense Webster) with higher Mm was used (**High Mm**).

Results:

	Low Mm	High Mm	P value
N	6	12	
Success (y/n)	3/3	10/2	
Proc. Time (min)	232±51	175±48	0.0001
Physician fluoro time (min)	5.7±2.7	3±1.95	0.001
Pt. Fluoro time	35±23	27±21	0.015
RF time (min)	8.2±5.7	4±3.15	0.005
# RF applications	14.5±12	9.6±9	0.012

No complications were observed in any group. The failed ablations were all successfully treated with a conventional RF catheter, in the Low Mn group all retrogradely, and in the High Mm group 1 retrogradely, while 1 required a transseptal approach.

Conclusions: Remote ablation of left sided APs is safe and feasible using the retrograde trans-aortic approach. It also reduces physician's exposure to fluoroscopy. Using a catheter with higher magnetic mass significantly improves success rate, and reduces procedure and fluoroscopy times in this patient group.

901-143 Clopidogrel is Associated With a Reduced Thrombogenic Response in Radiofrequency Ablation Procedures Compared to Aspirin

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Background: We aimed to investigate the hemostatic system activation after aspirin or clopidogrel pretreatment, during RFA procedures.

Methods: We studied 45 patients (19 men) who underwent RFA for supraventricular tachyarrhythmias in the right heart (atrioventricular nodal re-entry tachycardia n=32, atrioventricular re-entry tachycardia due to right-sided accessory pathways n=11, and typical atrial flutter n=2). Twenty-two patients received aspirin (325 mg the day before RFA, followed by 325 mg for one month) and twenty-three received clopidogrel (300 mg the day before RFA, followed by 75 mg for one month). Adenosine diphosphate (ADP, 10 µmol/L) and collagen (2 µg/ml) induced platelet aggregation (PA) was assessed, and D-dimer (D-d) and thrombin-antithrombin complex (TAT) levels were determined. Blood samples were collected at baseline, before sheath insertion (T1), after completion of the procedure (T2), 24 hours later (T3) and after 1 month (T4).

Results: A significant inhibition of PA and significantly lower D-d values were observed in the clopidogrel arm, while TAT levels were similar in both groups. (Table)

Conclusions:

n patients undergoing RFA procedures, clopidogrel significantly inhibited platelet aggregation and attenuated fibrinolysis, compared to aspirin. Thrombin generation was not affected. Clopidogrel treatment requires further evaluation for establishing its beneficial effect in preventing thromboembolism during RFA.

	Values of PA (%), D-d (µg/L), and TAT (µg/L)		
	Aspirin	Clopidogrel	p value
T1 ADP	69±9	39±13	p<0.001
T2 ADP	72±7	46±9	p<0.001
T3 ADP	75±8	48±10	p<0.001
T4 ADP	70±9	47±8	p<0.001
T1 collagen	73±10	66±12	p=0.04
T2 collagen	74±6	44±11	p<0.001
T3 collagen	76±8	47±10	p<0.001
T4 collagen	73±8	49±9	p<0.001
T1 D-d	26±20	19±9	NS
T2 D-d	111±15	72±16	p<0.001
T3 D-d	160±91	92±31	p<0.001
T4 D-d	23±12	21±9	NS
T1 TAT	2.1±0.6	1.8±0.4	NS
T2 TAT	18.1±8.5	17.2±8.3	NS
T3 TAT	9.7±4.7	7.8±4.2	NS
T4 TAT	1.8±0.8	1.6±0.4	NS

POSTER SESSION

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Clinical Electrophysiology: Ventricular Arrhythmias

Sunday, March 12, 2006, 1:30 p.m.-5:00 p.m.
Georgia World Congress Center, Hall B1
Presentation Hour: 3:30 p.m.-4:30 p.m.

924-123 QRS Duration and Microvolt T Wave Alternans Testing in Patients With Ischemic Cardiomyopathy

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Background: Prior studies assessing the relative prognostic utility of microvolt T-wave alternans (MTWA) and QRS>120ms have been limited by small sample sizes and study design limitations. These studies also suggested that MTWA was not predictive in patients with QRS>120msec.

Objective: To determine the relative predictive value of MTWA and QRS>120ms for mortality in patients with ischemic cardiomyopathy, and assess whether QRS duration interacts with the prognostic accuracy of MTWA.

Methods: We developed a prospective database of 768 patients with ischemic cardiomyopathy (LVEF≤35%) and no prior history of sustained ventricular arrhythmia, of which 392 (52%) received ICDs. Mean follow up was 18±10 months. We assessed the degree to which a non-negative (positive and indeterminate) MTWA test and a QRS>120ms predicted mortality risk using stratified (by ICD status) Cox proportional hazards analyses that controlled for demographic, clinical, and medication treatment variables.

Results: In our cohort, 67% of patients had a non-negative MTWA test and 32% had a QRS>120ms on ECG. Unadjusted Kaplan-Meier survival estimates showed that both a non-negative MTWA [stratified log-rank test=13.5; p=0.0002] and a QRS>120ms [stratified log-rank test= 9.7; p=0.0018] were associated with lower survival probability. After multivariable adjustment, MTWA remained an independent predictor of mortality [stratified hazard ratio=2.24 (1.33, 3.76); p=0.0023], whereas QRS>120ms was no longer predictive [stratified hazard ratio=1.51 (0.90, 2.51); p=0.12]. No significant interaction existed between ICD and MTWA status (p=0.47) or between MTWA and QRS>120ms (p=0.25).

Conclusion: MTWA, but not QRS>120ms, is predictive of mortality in patients with ischemic cardiomyopathy. QRS duration does not affect the prognostic ability of MTWA.

924-124 Do All Phenotypic Forms of Outflow Tract Arrhythmias Have a Similar Mechanism?

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Background: Pts with exercise-induced sustained ventricular outflow tract (OT) tachycardia have an electropharmacologic profile that is consistent with cAMP-mediated triggered activity. These pts generally have inducible VT which terminates with adenosine and verapamil. The purpose of this study was to examine pts with OT arrhythmias who present with either non-sustained ventricular tachycardia (NSVT) or repetitive monomorphic PVCs, and to determine whether they share a similar electropharmacologic profile to those with sustained VT. **Methods:** All pts underwent electrophysiologic testing.

Results: Of 126 consecutive pts presenting with OT arrhythmias, 44 presented with sustained VT, 37 with NSVT, and 45 with PVCs. There was no difference among the three groups of pts with respect to age, gender, presence of structural heart disease or CAD. Sustained VT was inducible in 46% with NSVT vs. 9% with PVCs. Induction of sustained VT was catecholamine-dependent in a similar proportion of pts from both groups (Table). Adenosine terminated induced VT in a similar proportion of pts in both groups. **Conclusions:** Despite differences in clinical presentation, a significant subset of pts with non-sustained OT arrhythmias show mechanistic evidence for cAMP-mediated triggered activity. Whether pts who are non-inducible have a different underlying cellular mechanism or a different threshold for inducibility remains unclear.

Parameter	NSVT (n=37)	PVCs (n=45)	p value
Sustained VT at EPS	46% (17)	9% (4)	p<0.001
Required catecholamine infusion for induction	82% (14)	75% (3)	p=NS
Adenosine terminated induced VT	87% (13/15)	75% (3/4)	p=NS

924-125 Three Dimensional Activation Patterns During Ventricular Fibrillation in Swine Heart

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Background: Most studies of ventricular fibrillation (VF) are based on epicardial or endocardial recordings. We applied plunge needles with a sufficient density of electrodes to observe the transmural activity of VF.

Methods: We mapped VF from three planes of bipolar electrode arrays in 6 pigs with electrodes spaced 2 mm apart. The vertical array was a row of 24 plunge needles and the horizontal was 21 plunge needles. Each plunge needle held 12 electrodes. The epicardial array was placed to surround the two lines of plunge needles to form a 22x25 array. Four VF episodes were mapped for 20 sec each. We quantified within each array (1) the number of wavefronts per cm² (WFs); (2) percent of WFs that arose within the mapped region by breakthrough/focal activity (F); (3) multiplicity, the number of distinct activation pathways (M); (4) mean area activated by WFs (A); (5) percentage of all VF wavefronts that completed at least one cycle of reentry (Re).

Results: The number of WFs, M, A, and Re were significantly greater epicardially than intramurally. The F and M were significantly greater in the vertical plane than horizontal plane. However, the A and the Re were significantly greater in the horizontal than the vertical plane.

Conclusions: VF activation sequences differ in different planes. The increased F, increased M, decreased Re and decreased A in the vertical plane compared to horizontal plane with a similar number of WFs in both planes indicate that more VF wavefronts propagate around versus along the long axis of the LV.

*=p<0.01 compared with both transmural arrays **=p<0.01 between horizontal and vertical data

	Epicardial	Horizontal	Vertical
WFs/cm ²	3.2±0.67*	2.02±0.13	2.07±0.16
F%	36±12*	45±18**	66±15
M	9.8±2.2*	3.7±1.3**	4.5±1.4
A mm ²	202±33*	182±46**	161±32

924-126 Patients With Coronary Artery Disease that Suffer Sudden Cardiac Death Have Exaggerated Prolongation of Ventricular Repolarization: A Three-Year Community-Wide Study

Tejwant Singh, Erin Wallace, Carmen Socoteanu, Kyndaron Reinier, Celia Dervan, Eric C. Stecker, Catherine Vickers, Wendy Post, Peter Spooner, Karen Gunson, Jonathan Jui, Sumeet Chugh, Oregon Health and Science University, Portland, OR, The Johns Hopkins Reynolds Cardiovascular Center, Baltimore, MD

Background: The potential role of the corrected QT interval (QTc) as a predictor of sudden cardiac death (SCD) among patients with significant coronary artery disease (CAD) has been assessed in cohort studies, but not in the general population.

Methods: In the ongoing Oregon Sudden Unexpected Death Study (Ore-SUDS) all adult residents of Multnomah County, OR (population 700,000) who suffered SCD were identified prospectively (2002-2005). Of these, we identified the subgroup of SCDs that underwent 12-lead ECG prior to death and also had known associated CAD. Comparisons were conducted with a geographically matched control group of subjects with known CAD, but no history of SCD, ventricular arrhythmia or syncope. QTc and JTc were measured from the 12-lead ECG (Bazett's correction). Patients with atrial fibrillation/flutter or ventricular pacing on ECG were excluded for JTc and QTc comparisons and those with wide QRS (≥120 ms) were excluded for QTc comparisons.

Results: A total of 286 SCD cases had ECGs performed prior to death and 136 (48% of total, 31% female) had CAD based on medical records or autopsy findings. Among controls, 313 (94% of total, 34% female) had an ECG available. For SCD cases, ECGs analyzed were performed a mean of one year prior to SCD. Male SCD cases had significantly longer QTc (mean 470±56 vs. 430±39 ms, p<0.0001) and JTc (mean 368±46 vs. 341±39 ms, p<0.0001) vs. male controls. Differences were similar but smaller in females: (mean QTc 464±46 vs. 446±31 ms, p=0.04) and JTc (mean 376±52 vs. 359±35 ms, p=0.07). In an analysis of covariance model controlling for age, sex, and heart rate, cases had significantly longer adjusted mean QTc (466 vs. 437 ms, p<0.0001) and JTc (372 vs. 350 ms, p<0.0001).

Conclusion: CAD patients that had SCD were distinguishable by significantly longer QTc and JTc on the 12-lead ECG, after controlling for age, sex and heart rate. These data have implications for SCD risk stratification in subjects with coronary artery disease.

924-127 Predictors of Successful Catheter Ablation of Ventricular Tachycardia in Ischemic and Nonischemic Cardiomyopathy

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Background: Radiofrequency ablation (RFA) is the only curative therapy for refractory ventricular tachycardia in patients with ischemic and nonischemic cardiomyopathy. However, the success rate of RFA in ischemic than non-ischemic cardiomyopathy differs.

In this study, we examined the differences in electrophysiologic properties and predictive factors for acute success between ischemic (I) and non-ischemic (NI) ventricular tachycardia (VT).

Methods: We studied the demographics and electrophysiological findings of patients undergoing RF ablation for inducible sustained VT in patients with ischemic and nonischemic cardiomyopathy. Ablation success was defined as non-inducibility of the targeted VT at study conclusion.

Results: 118 VT (I VT: 77, and NI VT: 41) were observed in 42 patients (I: 26; NI: 16). Patients with NI VT were younger (NI, 57.7 ± 16.4; I, 64.4 ± 10.5 years, p<0.01), more often women (NI: 33%; I: 4%, p<0.001), and less likely to have hypertension (NI: 26; I: 44 percent, p<0.001). They had smaller ventricles (LVDD NI, 5.22 ± 0.98; LVDD I, 5.90 ± 0.63cm, p=0.001) but the ejection fraction was not different (NI, 31.4 ± 14.9; I, 26.7 ± 8.3, p=0.08). At EP study, patients with NI VTs had a shorter H-V (NI: 57.5 ± 9.0; I: 67.7 ± 14.3ms, p<0.001). The VT cycle length (NI VT: 384 ± 16 ms and I VT: 411 ± 12 ms, p = 0.19) and number of RFA (NI VT: 10.4 ± 2.1, I VT: 9.1 ± 1.6, P=NS) were not different in these two groups. The incidence of posterobasal VT was significantly higher in NI VT (n=31/41, 76%) than in I VT (29/77, 38%). However, better pacemap (I VT: 11.1 ± 0.3 leads, NI VT: 7.5 ± 1.0 leads, p<0.01) and entrainment (I VT: 46; NI VT: 10; p<0.01) was achieved in I VT than NI VT. The mid-diastolic potential to QRS signal (NI VT: 83.7 ± 99.4; I VT: 118.9 ± 61.1ms, p=0.047) during VT and RFA success was higher in I VT (69/77) compared to NI VT (26/41, p<0.001).

Conclusion: I VT is associated with significantly better pacemap, higher rate for entrainment and longer diastolic potential to QRS (during VT) as compared to NI VT, which may explain a higher success rate in I VT.

924-128 Sustained Polymorphic Arrhythmias Induced by Programmed Ventricular Stimulation Have Prognostic Value in Patients Receiving Defibrillators for Primary Prevention of Sudden Cardiac Death

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Background: Patients with ischemic cardiomyopathy (ICM) who have monomorphic ventricular tachycardia (VT) induced by programmed ventricular stimulation (PVS) are at increased risk of sudden cardiac death (SCD). Whether patients with induced, sustained polymorphic arrhythmias have similar rates of spontaneous arrhythmia occurrences is unknown. Our objective was to determine whether the induction of sustained, polymorphic ventricular arrhythmias predicts clinical arrhythmias in patients receiving an implantable cardioverter defibrillator (ICD) for primary prevention of SCD.

Methods: We retrospectively evaluated 105 consecutive patients who received an ICD for primary prevention of SCD in the setting of ICM and non-sustained VT. At baseline, 75 patients had induction of monomorphic VT (Group I) and 30 patients had a ventricular arrhythmia other than monomorphic VT (including ventricular flutter, ventricular fibrillation, and polymorphic VT) induced during PVS (Group II). Mean follow-up was 27.8 ± 14.1 months.

Results: Baseline characteristics were similar between Group I and Group II except for EF (25% vs 31%, p=0.0001) and QRS width (123ms vs 109ms, p=0.04). 16 of 75 (21.3%) patients in Group I and 6 of 30 (20%) patients in Group II had an appropriate ICD therapy (p=0.88). Survival free from ICD therapy was similar between groups (p=0.54). There was no difference in mean number of appropriate ICD therapies administered (p=0.8). There was a trend toward increased all-cause mortality among patients in Group I by Kaplan Meier (p=0.08). However, when adjusted for age, EF and QRS duration, there was no difference in mortality between groups (p=0.45). Among patients for whom data was available, induced tachycardia cycle length demonstrated a trend toward predicting subsequent clinical ventricular tachyarrhythmia cycle length (R² =0.22; p=0.058).

Conclusions: There is no difference in rates of appropriate ICD discharge or mortality between patients dichotomized by type of rhythm induced during PVS. This study provides evidence that the induction of VF and polymorphic VT are clinically meaningful and supports the current guidelines recommending ICD implantation in this population.

924-129 Effect of Bundle Branch Block on Microvolt T-Wave Alternans

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Background: Microvolt T wave alternans (TWA) has been proposed as a means of risk stratification for sudden cardiac death (SCD). It is unknown whether bundle branch block influences TWA.

Methods: We evaluated 317 consecutive pts with CAD, NSVT, and LVEF ≤ 40% (254 [80.1%] men, age 66.5±10.7 years). Pts underwent TWA testing and EPS with up to three ventricular extrastimuli (VES) from two right ventricular sites. Positive EPS was defined as inducibility of sustained monomorphic VT with up to triple VES, or VF or polymorphic VT with up to double VES. A physician blinded to the results of TWA and EPS examined each pt's ECG for evidence of conduction delay.

Results: There was no difference in the TWA indeterminacy rate between normals and pts with left hemiblock (HB), LBBB, RBBB, or IVCD (all p>0.05). Excluding indeterminates, more pts with LBBB than normals had positive TWA (80% vs. 54%, p=0.02). There was a nonsignificant increase in the EPS positivity rate in the LBBB group (p=0.07). There was no significant difference in the TWA positivity rate between normals and pts with left hemiblock, IVCD, or RBBB (p=0.56, 0.39, and 0.79 respectively), nor in EPS results between normals and pts with left hemiblock, IVCD, or RBBB (p=0.86, 0.33, and 0.42).

Conclusions: Compared with normals, TWA is more often positive in pts with LBBB, but not in pts with left hemiblock, IVCD, or RBBB. This may reflect either increased sensitivity or diminished specificity of TWA testing in the setting of LBBB.

	QRS width, ms (mean, SD)	EF, % (mean, SD)	TWA Pos (n, %)	TWA Neg (n, %)	TWA Ind (n, %)	TWA Pos/(Pos+Neg)	EPS Pos (n, %)	EPS Neg (n, %)
Normal (n=179, 56.5%)	97.1 (11.5)	29.7 (7.8)	69 (38.5)	59 (33.0)	51 (28.5)	0.539	85 (47.5)	94 (52.5)
HB (n=42, 13.2%)	100.5 (10.5)	31.8 (7.0)	16 (38.1)	18 (42.9)	8 (19.0)	0.471	21 (50.0)	21 (50.0)
LBBB (n=37, 11.7%)	148.3 (17.7)	25.2 (7.5)	20 (54.1)	5 (13.5)	12 (32.4)	0.800	24 (64.9)	13 (35.1)
IVCD (n=31, 9.8%)	126.7 (14.1)	26.7 (8.9)	17 (54.8)	9 (29.0)	5 (16.1)	0.654	18 (58.1)	13 (41.9)
RBBB (n=28, 8.8%)	145.2 (19.0)	28.7 (8.4)	9 (32.1)	6 (21.4)	13 (46.4)	0.600	16 (57.1)	12 (42.8)

924-130 Sudden Cardiac Arrest with Normal Ejection Fraction: How Often Is Coronary Ischemia the Trigger?

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Background: A significant proportion of sudden cardiac arrests (SCAs) may occur in patients with normal LV systolic function. Coronary ischemia is likely to be a precipitating factor, but the frequency of occurrence has not been evaluated in the general population. **Methods:** All residents of Multnomah County, OR (Pop. 660,486; 2002-2005) who suffered SCA (sudden unexpected arrest within 1 hour of symptom onset) were identified via first responders, medical examiner and local hospitals. The subgroup of patients that survived to hospital admission and had an assessment of LV ejection fraction (EF) by echocardiography or ventriculography within 48 hours were analyzed. EF was defined as normal when ≥ 0.55 , mild to moderately reduced when 0.36-0.54 and severely reduced when ≤ 0.35 . Acute myocardial infarction (AMI) was defined as ST elevation on EKG or a clinical diagnosis of NSTEMI by symptoms, EKG and serum markers. Ischemic symptoms were defined as any pain above the waist or shortness of breath prior to SCA. Significant obstructive CAD was defined as any coronary stenosis $\geq 70\%$ on coronary angiography performed within 48 hours of SCA.

Results: From a total of 202 SCA patients who survived to hospital admission, 55 (27%) had EF assessed after SCA (mean age 63 \pm 16 yrs, 47% female). LV EF was normal in 23 (42%), mild to moderately reduced in 11 (20%) and severely reduced in 21 (38%). Overall, 46 (84%) had either serum markers drawn or cardiac catheterization performed following SCA, leading to diagnosis of AMI or obstructive CAD in 32 (58%). Of the patients with normal EF, AMI was diagnosed in 11 (48%). AMI, ischemic symptoms or obstructive CAD on angiography were observed in 14 patients (61%). Five patients (22%) had no evidence of coronary ischemia despite detailed evaluation.

Conclusions: A substantial proportion (42%) of evaluated SCAs had normal LV EF and acute coronary syndromes/AMI were likely precipitants for the majority. However, in a small but distinct minority (22%), there was no evidence of coronary ischemia and alternative trigger factors merit further consideration.

924-131 Eplerenone Attenuates Ventricular Electrical Remodeling in Experimental Heart Failure: Mechanism of Reduced Risk of Sudden Cardiac Death with Aldosterone Blockade?

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Background Aldosterone blockade decreases sudden death in heart failure; however mechanisms underlying this beneficial effect are unclear. We hypothesized that aldosterone blockade attenuates ventricular electrical remodeling in heart failure, which reduces ventricular tachyarrhythmia (VTA) vulnerability. This study evaluated efficacy of eplerenone (EPL) to reduce remodeling of ventricular effective refractory periods (VERPs) and inducibility of VTAs in rapid ventricular pacing (RVP)-induced heart failure.

Methods 13 dogs underwent RVP at 230 bpm and received oral EPL (50 mg/day, n=8) or placebo (PLB, n=5). After 5 weeks, VERPs and VTA inducibility were determined with programmed stimulation from 4 epicardial sites (left, right ventricular [LV, RV] apex and base) and mid-myocardial RV apex with up to 4 extrastimuli at 2 cycle lengths (400, 300 ms). **Results** VERPs at epicardial LV apex and RV base and mid-myocardial RV apex were shorter and VERP dispersion was reduced in EPL vs. PLB RVP dogs. Among EPL RVP dogs, sustained VTAs were induced with 3.3 \pm 0.6 extrastimuli in 4 (50%) and could not be induced in 4 dogs. Among PLB RVP dogs, sustained VTAs were induced with 2.2 \pm 1.3 extrastimuli in 5 of 5 dogs. All VTAs were ventricular fibrillation. LV volumes and ejection fraction did not differ in EPL vs PLB RVP dogs. **Conclusions** Selective aldosterone blockade with EPL attenuates electrical remodeling in heart failure reducing VERP prolongation and dispersion, which contributes to suppression of VTA inducibility.

	EPL + RVP (n=8)	PLB + RVP (n=5)	p-value
Sustained VTAs (n)	4	5	0.10
VERP at 300 ms (ms)			
Epicardial LV Base	194 \pm 8	210 \pm 10	>0.05
Epicardial LV Apex	181 \pm 7	211 \pm 29	<0.05
Epicardial RV Base	197 \pm 9	222 \pm 20	<0.01
Epicardial RV Apex	193 \pm 12	205 \pm 15	>0.05
Mid-Myocardial RV Apex	203 \pm 8	236 \pm 12	<0.05
VERP dispersion (ms)			
Epicardial	22 \pm 10	38 \pm 16	<0.05
Transmural	7 \pm 6	30 \pm 8	<0.05

924-132 Myocardial Fibrosis assessed by Contrast-Enhanced Cardiovascular Magnetic Resonance and Prevalence of Malignant Ventricular Arrhythmias in Arrhythmogenic Right Ventricular Cardiomyopathy

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Background: Arrhythmogenic right ventricular cardiomyopathy (ARVC) is a disease characterized by the replacement of the right ventricle (RV) myocardium by fatty and fibrous tissue, leading to malignant ventricular arrhythmias (MVA). Contrast-enhanced cardiovascular magnetic resonance (CE-CMR) can well characterize areas of myocardial fibrosis. We therefore investigated the association of myocardial fibrosis documented by CE-CMR with the presence of MVA in ARVC patients (pts).

Methods: We studied 60 consecutive pts (26 males; mean age 37 \pm 11 years) under investigation of ARVC based on the task force diagnosis criteria (Br Heart J. 1994; 71(3): 215-8). MVA was defined as sustained ventricular tachycardia (SVT) or ventricular fibrillation that leads to aborted sudden death or SVT induced during electrophysiological study. CE-CMR was performed using a 1.5T magnet and the pulse sequence was a contrast-enhanced (gadolinium-based) fast gradient-echo with an inversion-recovery preparation pulse.

Results: Myocardial fibrosis was detected in the RV in 5 pts (8.3%) and in all of these (100%) it was documented MVA. We did not find out myocardial fibrosis in 55 pts (91.7%) and MVA were not documented in these pts (p<0.01).

Conclusions: In this sample of pts under investigation of ARVC, the finding of myocardial fibrosis assessed by CE-CMR was associated with MVA. These data suggest the potential usefulness of CE-CMR for early risk stratification of ARVC.



CE-MRI: Fibrosis (high intensity signal) in RV free wall

924-133 Radiofrequency Catheter Ablation of Frequent, Idiopathic Premature Ventricular Complexes: Effects on Left Ventricular Function

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Background: Idiopathic premature ventricular complexes (PVCs) are considered to be associated with a benign long-term prognosis, even when frequent. However, some case reports have demonstrated a possible link between frequent PVCs and left ventricular (LV) dysfunction. In addition, frequent PVCs recently were demonstrated to be associated with increased LV dimensions and cardiomyopathy.

Methods and Results: Among 46 patients with idiopathic, frequent PVCs (>10/hour), a reduced LV ejection fraction (mean 37 \pm 10%) was present in 16 (35%). Patients with decreased LV function had a greater PVC burden on a 24-hour Holter monitor than patients with normal LV function (37 \pm 14% versus 11 \pm 10% of all QRS complexes; P<0.0001). There was a significant inverse correlation between the PVC burden and the ejection fraction before ablation (R=0.72, p<0.0001). The PVCs originated in the right ventricular outflow tract in 24/46 patients (52%), the left ventricular outflow tract in 8/46 patients (17%), and in other sites in 9/46 patients (20%). The PVC origin could not be determined in 5 patients. Ablation was completely successful in 37 patients (80%), partially successful in 4 patients (9%), and ineffective in 5 patients (11%). In patients with a decreased LV ejection fraction

before ablation, LV function became normal or improved in 13/16 patients, remained the same in 2/16 patients, and declined in 1/16 patients. None of the latter 3 patients had a completely successful outcome from catheter ablation.

Conclusion: Left ventricular dysfunction is common in the setting of frequent, idiopathic PVCs and may represent a form of cardiomyopathy that can be corrected by catheter ablation of the PVCs.

924-134 Increased Sudden Death Risk Conferred by LVH is Independent of Age and Left Ventricular Dysfunction: A Three-Year Community-Wide Study in Patients with Established Significant Coronary Artery Disease

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Background: The Framingham Heart Study reported an association between increased LV mass/hypertrophy and sudden death that was independent of coronary risk factors. However, this relationship has not been evaluated in patients who suffer sudden cardiac death (SCD) in the presence of established significant coronary artery disease (CAD).

Methods: In the ongoing Oregon Sudden Unexpected Death Study (Ore-SUDS), adult residents of the Portland, Oregon metro area (population 1,000,000) who suffered SCD were identified prospectively (2002-2005). The subgroup of consecutive SCDs that had a cardiac echo performed prior to, and remote from cardiac arrest was identified. For those that had CAD from medical records or autopsy, LV mass was calculated (American Society of Echocardiography modified equation, LV mass/body surface area). Comparisons were conducted with a geographically matched control group of subjects with known CAD, but no history of SCD, ventricular arrhythmia or syncope. A logistic regression model was employed to evaluate the relationship between SCD, LVH by increased LV mass, severe LV dysfunction (LV EF \leq 35%) and age in patients with established CAD.

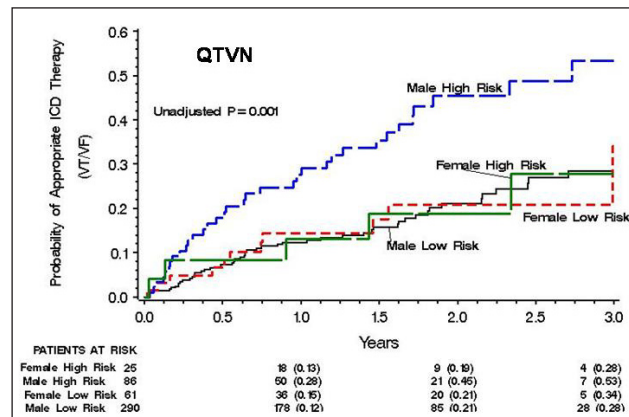
Results: LV mass was calculated for 163 SCDs of which 91 had definitive CAD (mean age 71, 29% female) as well as 100 controls (mean age 68, 32% female). Patients with severe aortic stenosis or hypertrophic cardiomyopathy were excluded from analysis (n=8; 6 SCDs, 2 controls). Among SCD cases, 38% had LVH vs. 22% in controls (p=0.03). In the logistic regression model, LVH was independently associated with SCD (OR 2.0, 95% CI 1.0 - 3.9, p=0.04).

Conclusions: Increased LV mass/hypertrophy, in the absence of hypertrophic cardiomyopathy or aortic stenosis, doubles the risk of sudden cardiac death among residents of the general population that have known significant coronary artery disease.

924-135 Gender Difference in the QT Interval and Ventricular Tachycardia or Fibrillation in MADIT II

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Background: Healthy women have longer QT intervals and more drug induced proarrhythmia, yet those with ICDs have fewer episodes of VT/VF than men. We hypothesized that women with structural heart disease would have longer QT intervals but less QT variability and VT/VF compared to men. **Methods:** All MADIT II study patients not in atrial fibrillation or paced had QT interval variability (QTV) assessed in 10 minute, resting digitized recordings at study entry. QT and heart rate were measured for each beat with a semi-automated method. "U" waves were included in the measure of the QT interval. QTV was normalized for mean QT (QTVN) or for HR variability (QTVI). Incidence of VT/VF was determined by ICD interrogation. **Results:** There were 805 usable recordings (142 females); 462 received ICDs (86 females). Contrary to our hypothesis, there was no difference in mean or median QT (471 ms men; 469 ms women, p=0.11), QTc, or heart rate. QTVN was slightly lower in females than males (p<0.05) whereas QTVI (adjusted for heart rate variance) was slightly higher. The time until VT/VF was significantly shorter in males in the top quartile ("high risk") for both QTVI and QTVN (figure) than in women (VT/VF at 2 years 45% in men vs. 19% in women). **Conclusions:** In patients with a depressed ejection fraction, increased QT variability is more predictive for VT/VF in males than females despite similar QT duration and QT variability. QT variability might be of particular importance in triggering arrhythmias in MADIT II type males, but not in females.



924-136

Isolated Potentials During Sinus Rhythm and Pace-Mapping Within Scars as Guides for Ablation of Post-Infarction Ventricular Tachycardia

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Background: Pace-mapping has been used in the scar border zone to identify the exit site of post-infarction ventricular tachycardia (VT). The purpose of this study was to identify VT isthmus sites by pace-mapping within scar tissue and to identify electrogram (EGM) characteristics that are helpful in identifying VT isthmus sites during sinus rhythm.

Methods: In 19 consecutive patients (18 men, mean age 66±9 yrs, mean EF 0.25±0.13) with recurrent post-infarction VT, a left ventricular voltage map was generated during sinus rhythm. Pace-mapping was performed at sites with abnormal EGMs or isolated potentials (IPs). Radiofrequency ablation was performed at isthmus sites as defined by pace-mapping (perfect pace-map=12/12 matching ECG leads; good pace-map=10-11/12 matching ECG leads) and/or entrainment mapping.

Results: A total of 81 VTs (mean cycle length 396±124 ms) were inducible. In 16 of the 19 patients, a total of 41 distinct isthmus areas of 41 distinct VTs were identified and successfully ablated. Pace-mapping was performed at 681 distinct sites (mean EGM amplitude 0.48±0.67 mV, mean EGM width 91±52 ms). IPs were found more frequently at sites with good or perfect pace-maps than at sites with abnormal EGMs (p<0.0001). Pace-maps at 65% of sites displaying an IP were either perfect or good, compared to 5% of sites with abnormal/fragmented EGMs (p<0.0001). Twenty-one isthmus sites were identified by perfect pace-maps, 14 by good pace-maps, and 6 by entrainment mapping. All but one displayed IPs during sinus rhythm. Furthermore, 22 of the 81 VTs (27%) for which no isthmus was identified became noninducible after ablation of a targeted VT. Of the remaining 18 VTs, 16 were induced in 3 patients in whom no isthmus could be identified. The 16 patients in whom \geq 1 isthmus was identified and ablated were free of arrhythmic events during a mean follow-up of 10 months. **Conclusions:** During sinus rhythm, excellent or good pace-maps at sites of IPs within areas of scar identify areas of fixed block that are protected and part of the critical isthmus of post-infarction VT. Shared common pathways may explain why non-targeted VTs may become noninducible after ablation of other VTs.

924-137

Effects of Verapamil on the Short-Term Electrophysiological Remodeling of Superior Vena Cava in Human

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Background: Electrophysiological remodeling (ER) of the atrium has been well described. Acute ER can be demonstrated by short term rapid atrial pacing. Whether this acute ER also occurred in the superior vena cava (SVC) and the pharmacological effects remained unknown.

Methods: Fifteen pts (8 F, mean 49±12 yrs) with supraventricular tachycardia were enrolled. After catheter ablation procedures, the effective refractory periods (ERP) of the high right atrium (HRA) and SVC were determined at pacing cycle length (CL) of 600 (ERP₆₀₀) and 400 (ERP₄₀₀) msec, respectively, under intravenous (IV) esmolol infusion (150 ug/kg/min). The ERPs of the HRA and SVC were determined again each time right after 5 minutes (min) of rapid HRA and SVC pacing, respectively, at CL of 400 ms. Degrees of shortening of the ERPs right after pacing were represented as the acute ER of the atrium and SVC, respectively. The same protocols for determining the ER of HRA and SVC were repeated after IV verapamil (0.15 mg/kg).

Results: Under IV esmolol, the ERP₆₀₀ of SVC was significantly longer than that of HRA (265±20 vs 236±19 ms, P<0.05). Right after 5 min of HRA pacing at CL of 400 ms, both the ERP₆₀₀ of HRA (236±19 vs 212±18 ms) and SVC (265±20 vs 239±19 ms) were significantly shortened (P<0.05). In addition, right after 5 min of SVC pacing at CL of 400ms, both the ERP₆₀₀ of HRA (236±19 vs 215±22 ms) and SVC (265±20 vs 239±20 ms) were also significantly shortened (P<0.05). The identical acute ER of the HRA and SVC were also demonstrated at ERP₄₀₀. After IV verapamil, the ERP₆₀₀ of SVC was still longer than that of HRA (264±17 vs 241±24 ms, P<0.05). Right after 5 min of HRA pacing at CL of 400 ms, both the ERP₆₀₀ of HRA (241±24 vs 220±27 ms) and SVC (264±17 vs 240±17 ms) were also significantly shortened. Furthermore, right after 5 min of SVC pacing at CL of 400 ms, both the ERP₆₀₀ of HRA (241±24 vs 222±23 ms) and SVC (264±17 vs 243±18 ms) were also significantly shortened. These acute ER of HRA and SVC were also demonstrated at ERP₄₀₀ of HRA and SVC.

Conclusions: The acute electrophysiological remodeling of SVC can be demonstrated right after either HRA or SVC rapid pacing. Intravenous verapamil can not abolish this form of acute electrophysiological remodeling of SVC and HRA.

924-138

Neither Ramipril Nor Vitamin E Reduce the Incidence of Atrial Fibrillation. Results of the HOPE Study

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Background: Atrial fibrillation (AF) is associated with significant morbidity and mortality. Although a number of important risk factors for the development of AF have been identified, its pathophysiology is still not clear. Recently, the role of angiotensin receptor in the development of AF has been suggested with a number of clinical studies showing potential benefit of angiotensin blockade either at the receptor level or inhibiting the converting enzyme. We set out to test this hypothesis using data from the HOPE study.

Methods: ECGs (at baseline, 2 years, and end of study) from 8334 pts enrolled in the HOPE study who were in sinus rhythm at enrollment were analyzed. The HOPE study enrolled patients aged \geq 55 years with previous cardiovascular disease, or diabetes plus

one risk factor, no clinical evidence of heart failure and preserved left ventricular systolic function, randomized to one of the following: Ramipril, Vitamin E, their combination or matching placebos.

Results: Of the 8334 patients who were in sinus rhythm at enrollment, 177 (2.1%) developed AF over the follow-up period of 4.5 years. There was no statistically significant difference in the proportion of patients who developed AF in the Ramipril and the placebo groups (2% vs 2.25%, p=NS). Univariate predictors of AF development were age, systolic blood pressure, history of hypertension, body mass index (BMI) and microalbuminuria. On multivariate logistic regression analysis only age (Odds ratio [OR] 1.55, 95% CI 1.33-1.80, p<0.01), BMI (OR 1.21, 95% CI 1.05-1.42, p=0.01), and microalbuminuria (OR 1.50, 95% CI 1.07-2.11, p = 0.02) were independent predictors of development of new onset AF. Ramipril had no protective effect on development of AF (OR 0.92, 95% CI 0.68-1.24, p=0.57). Vitamin E also showed no protective effect on development of AF (OR 0.86, 95% CI 0.64-1.16, p=0.33).

Conclusions: In high risk population use of the ACE inhibitor Ramipril or Vitamin E does not reduce the incidence of new onset atrial fibrillation.

924-139 Does Reduction in Left Atrial Diameter During Antihypertensive Treatment Reduce New-Onset Atrial Fibrillation in Hypertensive Patients with Left Ventricular Hypertrophy: The LIFE Study

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Background: It is unclear whether improvement of left atrial (LA) and ventricular (LV) structure results in reduction in new-onset atrial fibrillation (AF). The aim of the present study was to examine whether LA diameter and LV mass at baseline and during 4.8 years of antihypertensive treatment were related to changes in risk of new-onset AF in hypertensive patients with electrocardiographic LV hypertrophy.

Methods: We followed 939 hypertensive patients with electrocardiographic LV hypertrophy randomized to atenolol or losartan-based regimens in the LIFE Study for 4,450 patient-years of follow-up with echocardiograms at enrolment and annually during treatment.

Results: New-onset AF occurred in 58 patients (13.1/1000 patient-years of follow-up). At baseline, patients with new-onset AF were older, had higher systolic blood pressure and heart rate as well as higher prevalence of LA dilatation, but had similar prevalences of LV hypertrophy and mitral or aortic valve disease. In univariate Cox analysis baseline LA diameter (HR=4.68 per cm increase [95%CI: 2.86-7.65], p<0.001) and LV mass (HR=1.11 per 10 g/m² increase [95%CI: 1.01-1.22], p<0.05) both predicted new-onset AF. In Cox analysis, LA diameter at baseline increased the risk of new-onset AF (HR=1.93 per cm higher [95%CI: 1.01-3.71], p<0.05) whereas reduction of in-treatment LA diameter reduced the risk (HR=0.23 per cm lower [95%CI: 0.14-0.38], p<0.001) with adjustment for baseline and in-treatment LV mass and systolic blood pressure.

Conclusion: LA diameter at baseline and especially during antihypertensive treatment was a strong predictor of new-onset AF independent of the level of arterial pressure and other covariates. We propose that monitoring LA diameter may contribute to prevention of AF during antihypertensive treatment by prompting further intervention directed towards blood pressure control and LA size reduction if LA dilatation is not reversed by initial treatment.

924-140 Prevention of Atrial Fibrillation Via Abrogation of the Renin-Angiotensin System: A Pooled Meta-Analysis of Randomized Controlled Clinical Trials

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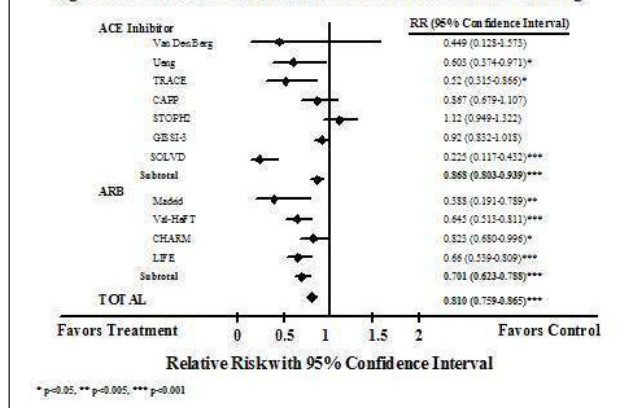
Background: The renin-angiotensin-aldosterone system (RAAS) has emerged as an important hormonal system in the initiation and pathogenesis of atrial fibrillation. Therefore, angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs) may be novel drugs for the prevention of atrial fibrillation (AF).

Methods: Eleven randomized controlled clinical trials were identified that meet the criteria for a meta-analysis and were used to estimate the efficacy of ACEIs and ARBs in the prevention of AF, in different cardio-vascular subsets.

Results: Treatment with ACEIs or ARBs reduced the relative risk of AF in patients with hypertension by 23% (RR: 0.769, p<0.001, 95 CI 0.686 - 0.862) and by 11% in patients following myocardial infarction (RR: 0.898, p<0.05, 95 CI 0.814 - 0.992). Reduction in AF was greatest in patients following electrical cardio version (RR: 0.491, p<0.001, 95 CI 0.334 - 0.720) and in patients with heart failure, (RR: 0.684, p<0.001, 95 CI 0.594 - 0.787). Overall, inhibition of the RAAS reduced the relative risk of AF by 19% (RR: 0.810, p<0.001, 95 CI 0.759 - 0.865).

Conclusions: Our meta-analysis revealed that both ACEIs and ARBs significantly reduce the risk of AF in subsets of patients with hypertension and post myocardial infarction patients. The benefit in risk reduction was greatest in patients with heart failure and post electrical cardioversion. Further prospective randomized studies are necessary to evaluate this observation.

Figure 1. Effect of treatment on atrial fibrillation based on class of drug



924-141 Irbesartan Reduces Left Atrial Stunning After Electrical Cardioversion of Atrial Fibrillation

Nikolaos Dargēs, George Karatasakis, Fotios Panou, Georgios Athanassopoulos, Themistoclis Maounis, Elias Tsougos, Kallirrhoe Kourea, Dimitrios Th. Kremastinos, Dennis V. Cokkinos, Onassis Cardiac Surgery Center, Athens, Greece, University of Athens, Attikon University Hospital, Athens, Greece

Background. Left atrial (LA) stunning, the transient impairment of LA function, is responsible for an increased thromboembolic risk after cardioversion of atrial fibrillation (AF). Angiotensin receptor blockers (ARBs) could influence LA stunning by attenuation of atrial remodeling. We studied the effect of Irbesartan.

Methods. We prospectively assigned 50 consecutive patients undergoing electrical cardioversion for AF with duration >4 weeks, into two groups: 25 patients were treated with Irbesartan for at least 2 weeks prior to cardioversion (Irbesartan group); 25 patients did not receive ACE-inhibitors or ARBs (control group). LA appendage emptying velocities (LAAEV) and LA spontaneous echo contrast (LASEC) were assessed immediately before and after electrical cardioversion by transesophageal echocardiography.

Results. There were no differences between the two groups concerning age (64±13 vs 63±13 years), AF duration (20±18 weeks vs 20±19 weeks), underlying disease, LA diameter (46±7 vs 47±9 mm), LV dimensions and ejection fraction (47.7±11.6% vs 49.7±14.5%)(p=NS for all parameters). After cardioversion, LAAEV showed no significant reduction in the Irbesartan group (28±9 vs 25±13 cm/s before and afterwards, p=NS), whereas in the control group, LAAEV decreased from 34±15 to 16±6 cm/s (p<0.05). New or increased LASEC occurred in 8 patients (32%) in the Irbesartan vs 16 (64%) in the control group (p=0.048).

Conclusions. Irbesartan significantly attenuates LA stunning after electrical cardioversion of AF. ARBs may represent an important supplementation in these patients.

924-142 Effects of Angiotensin II Type 1 Receptor Antagonist on Atrial Fibrillation Stability in Genetically Identical Goats

Panos E. Vardas, Hercules E. Mavrakis, Stavros I. Chrysostomakis, Heraklion University Hospital, Heraklion, Greece

Background: It has previously been reported that the blockage of angiotensin II prevents the electrical remodeling induced by short term rapid atrial pacing. However, the long-term effects of this blockage on atrial fibrillation (AF) stability are still unclear. We hypothesized that a prospective experimental study that would investigate the effects of angiotensin II blockage on AF maintenance in genetic identical animals would be of importance.

METHODS: Five sets of twin goats divided into two groups were used. The first group was kept in AF by burst pacing for 4 weeks, while the second was kept in AF and received a daily oral dose of 1,5 mg/kg of candesartan starting 1 week before pacing and for a subsequent period of 4 weeks. AF duration was determined by repeat induction of AF at right atrium by burst pacing at baseline and after maintaining AF for 24 hours, 1, 2 weeks, 3 weeks and 1 month respectively.

RESULTS: In the baseline study, the duration of the first induced AF episode was less than 15 seconds both in the candesartan (8±2 sec) and the control (9±3 sec) group. The mean number of bursts needed to induce AF episodes lasting more than 30 seconds were 17±8 bursts in the candesartan group and 6±4 bursts for the control group (p<0.05). Surprisingly, in the first 24 hours of the experiment, AF was not induced at all in 2 of the 5 goats in the candesartan group.

Over time, atrial pacing caused a significant increase in AF duration and a significant decrease in the mean number of bursts needed to induce AF episodes lasting more than 30 seconds in both groups compared to the baseline study. Sustained AF (>1200 ms) that required cardioversion was observed after 1 week in all 5 control goats. On the contrary sustained AF (>1200 ms) was observed during the second week in three goats from the candesartan group and in the third week in the two other goats. The mean duration of induced AF in the candesartan group was significantly shorter compared to control group (1.545±.623 vs. 5.12±.227 sec, p<0.01) after 1 month.

Conclusion: Angiotensin II blockage by candesartan decreases AF stability in genetically identical goats.

804

Atrial Fibrillation: Pharmacology and Epidemiology

Monday, March 13, 2006, 7:00 a.m.-8:30 a.m.
Georgia World Congress Center, Room B406

7:00 a.m.

804-3 Efficacy and Tolerance of RSD1235 in the Treatment of Atrial Fibrillation or Atrial Flutter: Results of a Phase III, Randomized, Placebo-controlled, Multicenter Trial

Craig Pratt, Denis Roy, Steen Juul-Møller, Christian Torp-Pedersen, Egon Toft, D. George Wyse, Tonny Nielsen, Soren Lind Rasmussen, on behalf of the ACT III Investigators, The Methodist Hospital/Methodist DeBakey Heart Center, Houston, TX, Montreal Heart Institute, Montreal, ON, Canada

Background: The efficacy and safety of intravenous RSD1235 in conversion of atrial fibrillation (AF) or atrial flutter (AFL) to sinus rhythm (SR) were assessed. The primary endpoint was the proportion of patients (pts) with AF duration of 3 hours to 7 days with treatment-induced conversion to SR for a minimum of 1 minute within 90 minutes of dosing.

Methods: 276 pts were randomized 1:1 to RSD1235 or placebo and stratified by AF or AFL duration. Pts received placebo or 3 mg/kg RSD1235 for 10 minutes, followed by a 15-minute observation period; a second 10-minute infusion of placebo or 2 mg/kg RSD1235 was given if AF or AFL did not terminate. Incidence of adverse events, serious adverse events (SAE), vital signs, laboratory data, ECG, and Holter monitoring were assessed.

Results: 265 pts (131 placebo, 134 RSD1235) received at least 1 infusion of study drug. 239 pts had AF, 23 had AFL, 11 did not receive study drug, and 3 had unknown baseline arrhythmia. 52% of RSD1235 pts (vs 4% in the placebo group) met the primary endpoint, with a median time to conversion of 8 minutes in the responders.

Duration of AF/AFL	Proportion of RSD1235 Patients Who Converted From AF to SR or had Termination of AF or AFL					
	3 hours to 7 days (p<0.0001)†		3 hours to 45 days* (p<0.0001)		8 to 45 days* (p=NS)‡	
Treatment Group	Placebo	RSD1235	Placebo	RSD1235	Placebo	RSD1235
AF	N=84 3 (3.6%)	N=86 45 (52%)	N=121 5 (4.1%)	N=118 48 (41%)	N=37 1 (2.7%)	N=32 3 (9.4%)
AF/AFL	N=92 3 (3.3%)	N=98 46 (47%)	N=131 5 (3.8%)	N=134 49 (37%)	N=39 1 (2.6%)	N=36 3 (8.3%)

* Termination of AF or AFL (defined as absence of AF or AFL)
† p-value calculated using Cochran-Mantel-Haenszel test.
‡ p-value calculated using Fisher's exact test.

SAEs occurred in 17 (13%) placebo and 14 (10%) RSD1235 pts in the 30-day follow-up; 1 placebo and 3 RSD1235 pts experienced a treatment-related SAE. There were no torsades de pointes in the RSD1235 group. There was 1 death in a pt with critical aortic stenosis who received RSD1235. Transient dysgeusia (22%) and sneezing (19%) were the most common adverse events.

Conclusion: RSD1235 safely achieved a rapid and high rate of conversion of recent-onset AF.

7:15 a.m.

804-4 Procainamide - Propafenone - Amiodarone: A Comparative Study of Their Efficacy And Safety For the Conversion of Recent Onset Atrial Fibrillation

Nikolaos E. Igoumenidis, George E. Kochiadakis, Michael I. Hamilos, Mary E. Marketou, Nick C. Klapsinos, Emmanuel I. Skaliadis, Panos E. Vardas, Heraklion University Hospital, Heraklion, Greece

Background: In a prospective, randomised, single blind, placebo-controlled study, we examined the effectiveness and safety of procainamide, propafenone and amiodarone, administered intravenously, for the restoration of sinus rhythm in recent onset atrial fibrillation.

Methods: We studied 362 patients (183men) aged between 34 and 86 years (average age: 65±10 years) with atrial fibrillation with duration ≤ 48 hrs. Of these, 89 were given procainamide, 91 propafenone, 92 amiodarone and 90 placebo.

Results: The treatment was successful in 61 (68.53%) of the procainamide group (median time 3 hours), in 73 (80.21%) of the propafenone (median time 1 hour), in 82 (89.13%) of the amiodarone (median time 9 hours) and in 55 (61.11 %) of the controls (median time 17 hours) (p<0.05 for all medicated groups compared to those who received placebo, p<0.05 for amiodarone and propafenone compared to the procainamide group).

Treatment was discontinued in one patient on amiodarone because of an allergic reaction and in four patients receiving propafenone because of excessive QRS widening.

Conclusions. All 3 medications, when administered intravenously, are effective in the restoration of sinus rhythm in recent onset atrial fibrillation. Amiodarone and propafenone are more effective, while procainamide and propafenone are faster.

804-5 The Outcomes of Thyrotoxicosis Related New-Onset Atrial Fibrillation

Chung Wah Siu, Man Hong Jim, Annie Kung, Chu Pak Lau, Hung Fat Tse, The University of Hong Kong, Hong Kon SAR, Hong Kong

Introduction: Although thyrotoxicosis (TT) is a common cause for atrial fibrillation (AF), the clinical outcomes of TT related new onset persistent AF remains unclear.

Methods and Results: Over 10-year period, 215 patients (pts) with TT with new onset-AF were studied. 15 pts with pre-existing heart diseases were excluded. Among 200 pts with TT related AF, their mean age was 64±17 years (41% male). At presentation, 14 pts (7%) had concomitant ischemic stroke (IS) and 77 pts (39%) developed congestive cardiac failure (CCF). Pts with IS had a higher prevalence of hypertension (HT) than those without IS (50 vs. 25%, p=0.04), but had no difference in age and sex (p>0.05). After mean follow-up of 45±37 months, 100 pts (50%) had spontaneous cardioversion (CV) at median time of 23 days. The median time to euthyroidism with anti-thyroid drug was 81 days. In univariate analysis, there were no significant differences in pts with or without CV with respect to age, male gender and diabetes (Table). However, pts without CV had a higher prevalence of HT and CCF at the time of presentation, lower usage of beta-blockers, larger left atrial (LA) and left ventricular (LV) size, and lower ejection fraction (EF) than those with CV (Table, P<0.05). Multivariate analysis demonstrated only LA is the independent predictor for CV (OR=3.9, P=0.01).

Conclusion: TT related AF is related to high incidence of IS and CCF at presentation. After control of TT, spontaneous CV can occur in up to 50% pts. The sole independent predictors of CV is smaller LA.

Baseline characteristics

	Pts with CV	Pts with no CV	p-value
Age	64±16	64±17	0.99
Male	36	46	0.15
HT	11	20	0.01
DM	18	35	0.08
CCF	23	54	0.01
LA	4.1±0.7	3.6±0.7	0.01
LVEF	55±17	65±16	0.01

7:45 a.m.

804-6 Are There Gender Differences in Risk of Ischemic Stroke in Patients with Atrial Fibrillation Who Are Anticoagulated? Results from the AFFIRM Trial

Suma H. Konety, Sue A. Joslyn, Brain Olshansky, University of Iowa Hospitals and Clinics, Iowa City, IA, University of Northern Iowa, Cedar Falls, IA

Background: Atrial fibrillation (AF) is a risk factor for ischemic stroke especially in the elderly but it is not clear if warfarin reduces risk of stroke in women with AF to the same extent as it does for men with AF.

Methods: Risk of ischemic stroke was evaluated in all 4,060 patients [men (M) n=2466, women (W) n=1594] enrolled in the AFFIRM trial. An actuarial analysis of time to first ischemic stroke by gender was adjusted for stroke-risk variables namely age, heart failure, diabetes, hypertension, prior stroke, coronary artery disease; international normalized ratio (INR) level at last follow-up visit and randomization group (rate-control vs. rhythm-control).

Results: The randomization and patient follow-up (3.5 years, range 4-6 years) were similar in men and women. Ischemic strokes occurred in 4.2% of the patients (n=171/4060) of which 157 had at least one ischemic stroke. Strokes were more common among women (W=80, M=77; 5.0% vs. 3.1%, p=0.002). While there was no difference in time to ischemic stroke from randomization among men and women (M vs.W: 683 days vs. 782 days, p=0.24), the unadjusted risk for ischemic stroke was higher among women compared to men (Hazard Ratio [HR] = 1.64; 95% confidence interval [CI]=1.19, 2.26). Warfarin was less prescribed in the rhythm-control group compared to the rate-control group (rhythm-control - M vs.W: 68% vs. 71%, p=0.2; rate-control - M vs.W: 86% vs. 87%, p=0.7). After adjusting for the stroke-risk variables women were as likely as men to be prescribed warfarin (Odds Ratio [OR] = 1.12; 95% CI=0.95, 1.32). Even after adjusting for stroke-risk variables and INR levels, the stroke risk for women was higher than for men (HR = 1.59; 95% CI = 1.07, 2.35). **Conclusions:** In the AFFIRM Trial, a study of patients with AF, women were at greater risk for ischemic stroke than men even after adjusting for known stroke-risk variables and INR levels. Prescription of warfarin was similar for men and women.

8:00 a.m.

804-7 Diabetes, Insulin, and the Prevalence of Atrial Fibrillation and Flutter in a Large Heart Failure Population

Somjot S. Brar, In-Lu A. Liu, Steven S. Khan, Adam Kotlewski, Albert Y-J Shen, Kaiser Permanente, Los Angeles, CA, UCLA School of Medicine, Los Angeles, CA

Objective: We sought to determine if differences exist in the prevalence of atrial fibrillation and flutter (AF) between diabetic insulin users, diabetic non-insulin users, and non-diabetics with heart failure.

Background: Insulin is thought to have some influence on atrial electrical activity. Whether there is a significant association between insulin use and AF has not been well studied.

Methods: We identified 28,009 patients with HF using existing care management databases from January 1999 to March 2005. HF was identified by ICD-9 codes and/or

medication records, and AF by ICD-9 codes. Insulin use was obtained from pharmacy databases. Multiple logistic regression was used to explore the independent relationship between groups.

Results: The mean age for the entire cohort was 71 ±13 years. The prevalence of diabetes in the population was 45% (n=12,638). Of these, 37.6% (n=4,754) were insulin users. Ejection fraction was available for 7,350. Mean EF ±SD for non-diabetics, diabetic (-) insulin, and diabetic (+) insulin was 42 ±17%, 43 ±17%, 44 ±17% respectively. Multiple logistic regression models follow.

Odds Ratio of AF by Diabetes Status and Insulin Use				
Model 1	Unadjusted		Adjusted	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Non-Diabetic	1.0	n/a	1.0	n/a
Diabetic (-) Insulin	1.09 (1.00-1.17)	0.04	1.04 (0.96-1.13)	0.36
Diabetic (+) Insulin	0.70 (0.64-0.77)	<0.0001	0.81 (0.74-0.90)	<0.0001
Model 2				
Diabetic (-) Insulin	1.0	n/a	1.0	n/a
Diabetic (+) Insulin	0.80 (0.74-0.87)	<0.0001	0.77 (0.71-0.84)	<0.0001

Adjusted models included: age, gender, HTN, CAD, valvular surgery or valvuloplasty, rheumatic and non-rheumatic valvular disease, thyroid disease, COPD, education, and income.

Conclusions: Diabetic insulin users had significantly less AF compared to diabetic non-insulin users and non-diabetics. These results suggest insulin use may be protective against AF in patients with heart failure.

8:15 a.m.

804-8 A Novel Locus for Familial Atrial Fibrillation on Chromosome 10p11-q21

Qian Zhu, Paul G.A. Volders, Carl Timmermans, Petra Eurlings, Xiaoyan Su, Yvonne Arens, Li Li, Roselie Jongbloed, Min Xia, Luz-Maria Rodriguez, Yi Han Chen, Tongji University Hospital, Shanghai, People's Republic of China, Academic Hospital Maastricht, Maastricht, The Netherlands

Background: Atrial Fibrillation (AF) is the most common cardiac arrhythmia encountered in clinical practice. It is a significant public health problem in the United States, affecting 2.2 million Americans. Familial clustering of AF indicates that the profibrillatory changes in atrial tissue may be, at least partly, genetically determined. Recently, three chromosomal loci (i.e., 5p13, 6q14-16 and 10q22-24) and three K⁺-channel genes (i.e., *KCNQ1*, *KCNE2* and *KCNJ2*) have been found to be associated with familial AF. However, in most other AF cases the genetic basis is still poorly understood.

Methods: We analyzed a four-generation Dutch family in which AF segregated as an autosomal dominant trait. After the exclusion of linkage to 5p13, 6q14-16, 10q22-24, *KCNQ1*, *KCNE2* and *KCNJ2*, a genome-wide linkage scan using 398 microsatellite markers was performed.

Results: Two-point LOD scores >1 at recombination fraction [θ] = 0.00 and a haplotype segregating with disease were demonstrated only across regions of chromosome 10. Subsequent fine mapping gave a maximum two-point LOD score of 4.1982 at D10S568 at [θ] = 0.00. Distinct recombination in several individuals narrowed the shared region among all affected individuals to 16.4 cM on the Genethon map (flanking markers: D10S578 and D10S1652), corresponding to chromosome 10p11-q21. Several candidate genes reside in this region, which could be associated with AF, such as ion-channel regulators, connexins, signal transduction systems, and genes for cell proliferation, hypertrophy, differentiation and migration.

Conclusion: These results provide evidence of a novel gene for AF on chromosome 10p11-q21.

ORAL CONTRIBUTIONS

810

Predicting Cardiac Resynchronization Therapy Benefit

Monday, March 13, 2006, 9:00 a.m.-10:30 a.m.
Georgia World Congress Center, Room B406

9:00 a.m.

810-3 Magnetic Resonance Imaging Based Characterization of Mechanical Dyssynchrony and Cardiac Resynchronization Therapy in Right Bundle Branch Block

Melissa J. Byrne, Robert H. Helm, Nael F. Osman, Marco A. S. Cordeiro, Ronald D. Berger, Henry R. Halperin, David A. Kass, Albert C. Lardo, Johns Hopkins University School of Medicine, Baltimore, MD

Background: Clinical cardiac resynchronization therapy (CRT) studies using bi-ventricular (BiV) pacing suggest it is useful in patients with right bundle branch block (RBBB), even though lateral wall contraction is not typically delayed. However, it is still unclear if the left ventricular (LV) lead is required or if right ventricular (RV) pacing alone is sufficient. The magnitude of CRT benefit in pure RBBB with heart failure (HF) is also unknown. Accordingly, we tested the hypotheses that RBBB generates less dyssynchrony than left bundle branch block (LBBB), that CRT effects are accordingly smaller, and that RV-only pacing is as effective as BiV in RBBB+HF.

Methods: RBBB+HF or LBBB+HF were induced by radiofrequency ablation of the right or left bundle followed by atrial tachypacing (210 bpm) for 3 wks in 12 dogs (6 on each group). Single site and combined (BiV) configurations were randomly tested, and the functional response assessed by dP/dt_{max}. Mechanical dyssynchrony was assessed by MRI-tagging, and reported as a previously validated circumferential uniformity ratio estimate (CURE; 1 = synchronous, 0 = fully dyssynchronous).

Results: RBBB+HF were significantly less dyssynchronous than LBBB+HF hearts (CURE, 0.78±0.03 vs. 0.58±0.09; p<0.05), while still more dyssynchronous than normal ones (CURE, 0.97±0.01; p<0.05). In LBBB+HF, both LV-only and BiV pacing increased dP/dt_{max} and CURE (LV-only, dP/dt_{max} 24.3±1.20%, CURE, 31.1±10.93%; BiV, dP/dt_{max} 26.98±5.22%, CURE, 46.34±12.69%), whereas in RBBB+HF, LV-only decreased function and synchrony (dP/dt_{max} -5.12±1.78%; CURE, -8.69±3.23%). In RBBB+HF hearts, single site RV and BiV pacing similarly improved dp/dt_{max} (RV-only, 3.76±1.12%; BiV, 5.53±1.14%; p=NS). However, CURE was only improved in these animals by single site RV pacing (RV-only, 9.09±4.07%; BiV, 2.93±4.20%; p<0.05).

Conclusions: RBBB+HF generates less mechanical dyssynchrony when compared with LBBB+HF. Both functionally and mechanically, single site and BiV pacing gave less benefit in RBBB+HF as opposed to LBBB+HF. Single site RV pacing reduces RBBB+HF induced dyssynchrony more effectively than BiV pacing, suggesting that an LV lead is not necessary for RBBB+HF CRT.

9:15 a.m.

810-4 Definition of Optimal Left Ventricular Lead Position in Cardiac Resynchronization Therapy Using Myocardial Deformation Imaging

Michael Becker, Theresa Kaminski, Andreas Franke, Peter Hanrath, Rainer Hoffmann, RWTH University Aachen, Aachen, Germany

Background: This study sought to assess if myocardial deformation imaging (MDI) allows definition of an optimal left ventricular (LV) lead position for improved effectiveness of cardiac resynchronization therapy (CRT).

Methods: MDI based on tracking of acoustic markers within 2D echocardiographic images (GE Vingmed Ultrasound) was performed in 42 heart failure patients at baseline, 7 days postoperatively and at 3 months. Ejection fraction (EF) and peak oxygen consumption (VO₂max) were determined before and after CRT. In a 36 segment LV model based on 6 short axis views the segment with latest peak systolic circumferential strain was determined. Additionally, the segment with maximal temporal difference in peak strain on CRT prior to CRT was defined as the segment with greatest benefit of the CRT-system and assumed to be location of the LV-lead. Optimal LV lead position was defined as concordance or immediate neighbouring of the segment with latest myocardial deformation prior to CRT and the segment with maximal temporal difference in peak strain on-off CRT.

Results: 19 patients showed optimal, 23 patients non-optimal position of the LV lead based on this definition. Preoperative EF and Vo2max were similar between patient with optimal and non-optimal LV lead position (EF 31.4±6.1% vs. 30.3±6.5%, VO₂max 14.5±1.8ml/min/kg vs. 14.2±2.1ml/min/kg). With CRT EF increased by 6.7±2.1% in the optimal LV lead position group vs 3.5±2.5% in the non-optimal group (p<0.001). After 3 months there was greater increase of VO₂max in the optimal compared to the non-optimal LV lead position group (2.3±0.9 ml/min/kg vs 1.2±0.6 ml/min/kg, p<0.001).

Conclusions: MDI is a new 2D echocardiography based imaging modality which allows detailed analysis of the myocardial contraction sequence. Optimal LV lead position in CRT defined by MDI with the segment with latest contraction prior to CRT results in greater improvement in EF and Vo2max than non-optimal LV lead position

9:30 a.m.

810-5 Relationship of Tissue Doppler Dyssynchrony and Acute Hemodynamic Response to Later Reverse Remodeling After Resynchronization Therapy

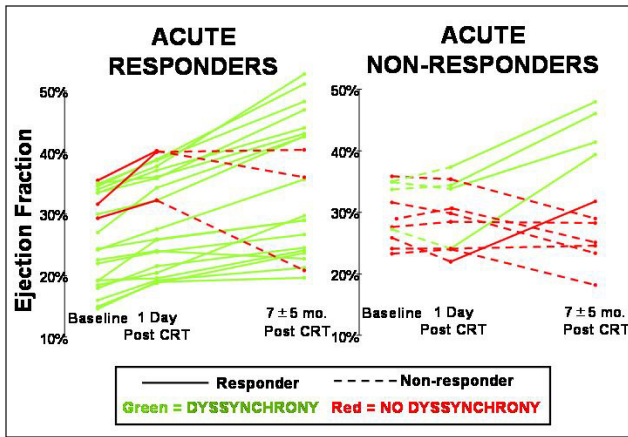
Matthew S. Suffoletto, Maxime Cansseon, Masaki Tanabe, Samir Saba, John Gorcsan, III, University of Pittsburgh, Pittsburgh, PA

Background: Tissue Doppler (TD) dyssynchrony can predict response to resynchronization therapy (CRT), but the relationship of dyssynchrony to acute hemodynamic response and later reverse remodeling in the same patients (pts) remains unclear.

Methods: Thirty-three class III-IV heart failure pts (ejection fraction (EF) 27±7%, QRS duration 156±24 ms) were studied before, the day after, and 7 ± 5 mo. after CRT. Baseline color TD dyssynchrony was defined as ≥ 65 ms difference in opposing wall peak systolic velocities from 12 segments in 3 apical views. Acute hemodynamic response was defined as ≥ 15% increase in Doppler stroke volume the day after CRT and reverse remodeling was defined as ≥ 15% increase in ejection fraction (EF) over baseline.

Results: An acute hemodynamic response occurred in 22 of 33 pts (67%), 19 of whom (86%) went on to show reverse remodeling 7±5 mo. after CRT (EF from 25±7% to 34±11%, p<0.001). The 3 acute responders who had no late EF improvement also had no baseline dyssynchrony. Five of 11 (45%) of acute non-responders still went on to later reverse remodeling (EF from 30±4% to 39±6%, p<0.01). Baseline TD dyssynchrony predicted late EF response with 92% sensitivity and 89% specificity. Specificity improved to 100% when combined with an acute hemodynamic response.

Conclusions: Dyssynchrony by TD is predictive of reverse remodeling after CRT. An acute hemodynamic response is predictive of later reverse remodeling when it occurs following CRT, but underestimates the potential for a later response.



9:45 a.m.

810-6

Effect of Postero-lateral Scar Tissue on Clinical and Echocardiographic Improvement Following Cardiac Resynchronization Therapy

Gabe B. Bleeker, Theodorus AM Kaandorp, Hildo J. Lamb, Paul Steendijk, Albert de Roos, Ernst E. van der Wall, Martin J. Schalij, Jeroen J. Bax, Leiden University Medical Center, Leiden, The Netherlands

Background Currently, one third of patients treated with cardiac resynchronization therapy (CRT) do not respond. Non-response to CRT may be explained by the presence of scar tissue in the postero-lateral left ventricular (LV) segments, which may result in ineffective LV pacing and inadequate LV resynchronization. In the current study the relationship between transmural postero-lateral scar tissue and response to CRT was evaluated.

Methods Forty consecutive patients with end-stage heart failure (New York Heart Association (NYHA) class III/IV), LV ejection fraction (EF) $\leq 35\%$, QRS duration >120 ms, LBBB and chronic coronary artery disease were included. The localization and transmural of scar tissue was evaluated with contrast-enhanced MRI. Next, LV dyssynchrony was assessed at baseline and immediately post-implantation using tissue Doppler imaging (TDI). Clinical parameters, LV volumes and LVEF were assessed at baseline and at 6 months follow-up.

Results Fourteen patients (35%) had a transmural ($>50\%$ of LV wall thickness) postero-lateral scar. In contrast to patients without postero-lateral scar tissue, these patients showed a low response rate (14% vs. 81%, $P < 0.05$) and did not improve in clinical or echocardiographic parameters. In addition, LV dyssynchrony remained unchanged after CRT implantation (84 ± 46 ms vs. 78 ± 41 ms, ns).

Patients without postero-lateral scar tissue and severe baseline dyssynchrony (≥ 65 ms) showed an excellent response rate of 95%, compared to patients with a postero-lateral scar and/or absent LV dyssynchrony (11%).

Conclusion CRT does not reduce LV dyssynchrony in patients with transmural scar tissue in the postero-lateral LV segments, resulting in clinical and echocardiographic non-response to CRT.

10:00 a.m.

810-7

Left Ventricular Lead Positioning Over Infarcted Myocardium Results in Less Improvement in Ejection Fraction in Patients With Ischemic Cardiomyopathy Following Cardiac Resynchronization Therapy

William H. Sauer, Mathew Hutchinson, Sumeet K. Mainigi, Michael Toca, Leonard Ilkhanoff, Paveljit Bindra, Michael P. Riley, Edward P. Gerstenfeld, David J. Callans, Francis E. Marchlinski, Joshua M. Cooper, University of Pennsylvania School of Medicine, Philadelphia, PA

Introduction: Cardiac resynchronization therapy (CRT) reduces interventricular activation time and improves congestive heart failure symptoms. Not all appropriate patients, however, benefit from CRT. We hypothesized that left ventricular (LV) lead positioning over infarcted myocardium would result in less improvement in LV ejection fraction (EF) compared to LV pacing over non-infarcted myocardium in patients with ischemic cardiomyopathy.

Methods: Patients with ischemic cardiomyopathy undergoing CRT were retrospectively analyzed to assess the relationship between lead position and improvement in left ventricular ejection fraction (LVEF). Areas of infarcted LV segments were identified with nuclear imaging and echocardiography prior to the implantation procedure. Final LV lead location was categorized into one of 17 myocardial segments using fluoroscopic images in orthogonal views. Pre- and post-implant LV chamber dimensions and EF were measured by an echocardiographer blinded to the study.

Results: Of the 108 patients included in the analysis, there were 21 patients with LV lead positions located in an infarcted segment. The posterolateral wall was the most frequent site (23.7%), followed by the apical lateral wall (16.5%). The mean LVEF in this group of patients increased less than the remainder of the cohort ($1.4 \pm 0.8\%$ vs. $3.9 \pm 1.1\%$; $P < 0.01$). Other clinical characteristics including age, gender, LV end diastolic dimension, and severity of mitral regurgitation were not associated with pacing-related improvement of the LVEF ($P > 0.05$).

Conclusion: CRT using an LV lead positioned within an infarcted myocardial segment results in less improvement in LVEF compared to an LV lead positioned in a non-infarcted segments. These results hold important implications regarding optimal LV lead positioning and device programming in patients with ischemic cardiomyopathy.

10:15 a.m.

810-8

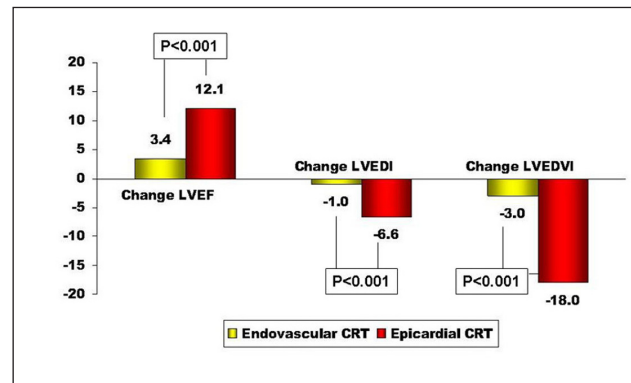
Robotic Epicardial Cardiac Resynchronization Is Superior to Endovascular Implantation in Promoting Reverse Remodelling

Ajay S. Shah, Rawa Sarji, Danny Pudupud, Donna Macmillan-Marotti, Sripal Bangalore, Anand Haridas, Afam Onuora, Sandhya Balam, Joseph DeRose, Jonathan S. Steinberg, Farooq Chaudhry, St Lukes-Roosevelt Hospital Center, New York, NY

Background: Cardiac resynchronization therapy (CRT) has been shown to improve systolic function and cause reverse-remodeling in patients with advanced heart failure (HF). Robotically implanted epicardial lead placement is a rescue therapy in patients with failed endovascular implants. The relative efficacy of robotically implanted epicardial lead placement versus endovascular lead placement has not been examined. A superior lead placement offers the theoretical benefit of ideal site of lead placement.

Methods: Thirty seven patients (54% male) with advanced HF (NYHA-3.4 \pm 0.3, EF-19 \pm 8%) and optimized medical therapy, undergoing CRT (49% endovascular, 51% epicardial) formed the study cohort. Reverse-remodeling was assessed by changes in follow-up (9.7 \pm 4 months) 2D-trans thoracic echocardiographic parameters of left ventricular ejection fraction (LVEF), LV end-diastolic index (LVEDI) and LV end diastolic volume index (LVEDVI) were quantitatively evaluated.

Results: Patients receiving robotically implanted epicardial CRT demonstrated significantly increased LVEF, decreased LVEDI, and decreased LVEDVI compared to patients receiving endovascular CRT (Figure).



Conclusion: Robotically implanted epicardial CRT -LV lead placement is superior to endovascular CRT -LV lead placement in inducing reverse remodeling for patients with advanced heart failure. This observation likely stems from greater flexibility of lead placement by the robotic epicardial procedure.

ORAL CONTRIBUTIONS

813

Prognostic Value of the ECG

Monday, March 13, 2006, 9:00 a.m.-10:30 a.m.
Georgia World Congress Center, Room B312

9:00 a.m.

813-3

Electrogram Features Are Superior to Clinical Characteristics for Predicting Atrial Fibrillation After Coronary Artery Bypass Graft Surgery

Matthew C. Wiggins, Edward P. Gerstenfeld, George Vachtsevanos, Brian Litt, School of Electrical and Computer Engineering, Georgia Institute of Technology, Atlanta, GA, University of Pennsylvania, Philadelphia, PA

Background: Atrial fibrillation (AF) occurs in approximately 30% of coronary artery bypass graft (CABG) patients following surgery, increasing cost and morbidity. We hypothesized that quantitative features extracted from the surface ECG and atrial wire tracing could predict the risk of AF after CABG.

Methods: Patients were monitored with continuous Holter recordings from surface lead II and intracardiac right atrial electrograms for 48 hours following CABG. A single, five-minute segment of ECG at 36 hours following surgery was extracted for analysis. P waves and QRS complexes were annotated and used to extract ECG segments (RR, RP, PR, PP) and heart rate variability measures from which 536 temporal, frequency, and nonlinear domain features were calculated. An evolutionary computing technique was used to train a k-Nearest-Neighbor (kNN) classifier to determine the best features to assess AF risk. For comparison, the patients' age, history of AF, beta-blocker withdrawal, and the presence of pulmonary disease were used as inputs to a linear AF risk score. An AF prediction threshold was assigned as the maximum of the product of the sensitivity and

specificity as found on the data's receiver operating characteristic curve.
Results: Thirty-three patients (21 male, 11 with post-operative AF) were studied. The trained kNN classifier identified two variables, the skewness of heart rate and the minimum of the RP segment's median frequency, as predictors of post-operative AF. The algorithm, validated using a leave-one-out methodology, correctly classifies 90.9% (30 of 33) patients, with a sensitivity of 82% and a specificity of 96%. The clinical AF risk score produced an accuracy of 63.6% (21 of 33), significantly inferior to the kNN classifier.
Conclusions: Two combined indicators, based on surface and intracardiac electrogram, skewness of heart rate and the minimum of the RP segment's median frequency, were superior to clinical characteristics for predicting AF after CABG. These findings, if validated prospectively, may be important for identifying patients at risk of developing AF after CABG.

9:15 a.m.

813-4 Which ECG Criteria for Left Ventricular Hypertrophy Best Predict Mortality?

Edward P. Havranek, Frederick A. Masoudi, Mori J. Krantz, Rebecca L. Hanratty, Raymond O. Estacio, Caroline Bublitz, John F. Steiner, Denver Health Medical Center, Denver, CO, University of Colorado Health Sciences Center, Denver, CO

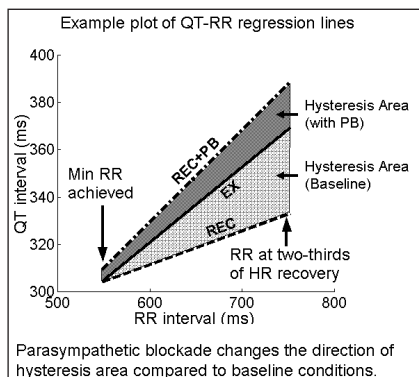
Background: Many criteria have been proposed for assessing for the presence or absence of left ventricular hypertrophy using electrocardiography, but there is no consensus on which criteria are the most clinically meaningful.
Methods: We obtained baseline electrocardiographic data and 5-year mortality rates from the National Health and Nutrition Epidemiologic Survey (NHANES III). For each baseline electrocardiogram, we computed Cornell voltage, Cornell voltage adjusted for age, gender, and body mass, Cornell product, Sokolow-Lyons voltage, and Novacode estimate of left ventricular mass index. We created a correlation matrix among the criteria. For each of these five criteria we computed sensitivity and specificity for subsequent mortality by decile, and constructed receiver-operating characteristic (ROC) curves from these data. We compared the five criteria by c-statistic (the area under the ROC curve).
Results: There were 7,840 subjects with data available to calculate all five of the voltage criteria. Subjects were of mean age 60 years, 47% female, and had a mean systolic blood pressure of 133 mmHg. Correlations among the criteria varied widely, varying from 0.94 for the comparison of the Cornell voltage and the Cornell product, and 0.35 for the comparison of the Cornell product and the Sokolow-Lyons voltage. C-statistics for each of the criteria were modest, but was significantly greater for the adjusted Cornell voltage (0.562) than for the other criteria.
Conclusions: These results suggest that the adjusted Cornell voltage is the best of the electrocardiographic criterion for assessing for the presence of left ventricular hypertrophy among those tested, based on its superior discriminative capacity for the outcome of total mortality.

9:30 a.m.

813-5 Changes in Parasympathetic Tone Result in QT-RR Interval Hysteresis during Exercise and Recovery

Marc K. Lahiri, Jason Ng, Alan H. Kadish, Jeffrey J. Goldberger, Northwestern University Feinberg School of Medicine, Chicago, IL

Background: For matched RR intervals, the QT interval (QT) is shorter in recovery (REC) than in exercise (EX), a phenomenon known as QT hysteresis.
Methods: To evaluate the mechanism of QT hysteresis, 20 subjects (16M; age 61±11 years) underwent continuous ECG monitoring during 16 min of submaximal EX on a stationary bicycle followed by 30 min of REC. Session #1 was performed under normal physiologic conditions; in session #2, parasympathetic blockade (PB) with atropine was performed at end exercise. Beat to beat QT and RR intervals were measured and median filtered. Three QT-RR interval data sets were analyzed: 1) During EX (without PB); 2) During REC without PB; 3) During REC with PB (REC+PB). Hysteresis area was defined as the area between the QT-RR linear regression lines for EX and REC in the range of measured RR intervals. When the REC line was below that of EX, the area was considered negative.
Results: The minimum RR with EX was 522±76ms. QT-RR slope during REC (0.20±0.07) was different than those during both EX (0.33±0.08, p<0.0001) and REC+PB (0.34±0.08, p<0.0001), with no difference between EX and REC+PB. QT hysteresis was present at baseline (area -2.6±3.2 103ms²); after PB, hysteresis area was positive and differed significantly from REC without PB (1.9±3.5 103ms², p<0.0001).
Conclusions: "QT hysteresis" is due to differential parasympathetic effects in EX and REC, rather than an intrinsic ionic mechanism. QT hysteresis may provide an index of parasympathetic effects on cardiac repolarization in REC.



10:15 a.m.

813-6 Three Optimally Placed Electrodes Versus 12-Lead ECG for Detecting Myocardial Occlusion Ischemia by Bayesian Classification

Juhani Dabek, Helena Hänninen, Heikki Väänänen, Matti Stenroos, Mats Lindholm, Ilkka Tierala, Lauri Toivonen, Helsinki University Central Hospital, Laboratory of Biomedical Engineering, Espoo, Finland

Background: Body surface potential mapping (BSPM) was recorded during balloon angioplasty of following coronary arteries: left anterior descending (LAD) in 9, left circumflex (LCX) in 6, and right coronary artery (RCA) in 7 patients. BSPM was applied to find a limited number of leads to differentiate between the culprit coronary arteries.
Methods: Around forty heartbeats during ischemia were used from each patient. ST-segment amplitude was measured 60 ms after the J-point. The classification was based on the multidimensional Bayesian method, assuming a Gaussian distribution. For identification of the best lead sets, the leave-one-out cross-validation method was used. The model was trained by utilizing 21 patients' data whilst using the 1 remaining patient's data for testing. This was repeated 22 times by having each patient's data once in the testing group and the others in the training group. Combinations of 3 leads from the 120 BSPM leads were thus tested, totalling in 280840 combinations. As a criterion for the goodness of a 3 lead set, the average percentage of correctly classified data was used.
Results: For the best test set, the criterion equalled 81,8 %, and the next best one 80,0 %. The electrodes of the optimal lead set were located on the midsternal line 5 cm below the standard leads V1-V2, 10 cm below lead V3, and 5 cm above the dorsal lead V9. From the 12-lead ECG, using 8 independent leads (V1-V6, I, and II), the classification result by the same method was 43,2 %.
Conclusions: Combination of optimally located 3-lead set, identified by Bayesian classification, accurately identified the culprit coronary artery in myocardial occlusion ischemia. Compared to the 12-lead ECG, this optimal lead set covered the inferior frontal chest and the dorsal chest, which represent RCA and LCX supply areas.

10:00 a.m.

813-7 ECG-Based Method for Identifying KvLQT1/KCNE1 or HERG Mutation in Patients With The Long QT Syndrome

Martino Vaglio, Jean-Philippe Couderc, Scott McNitt, Wojciech Zareba, Arthur J. Moss, Heart Research Follow-Up-Program, University of Rochester Medical Center, Rochester, NY

The clinical course and the precipitating risk factors in the congenital long QT syndrome (LQTS) are genotype specific. Among LQTS mutations, KvLQT1/KCNE1 (LQT1) and HERG (LQT2) mutations have the higher likelihood of recurrent cardiac events and their diagnosis is crucial to reduce their associated risk of sudden death. Twelve-lead ECG Holter were recorded in 48 LQT1 (21.6±12.2 yrs, 34 f) and 24 LQT2 genotyped patients (22.4±8.7 yrs, 19 f). The cardiac beats were grouped based on heart rate (HR), scalar and vectorial repolarization factors were compared for principal HR. The QT, QT_{apex} and the T_{peak} to T_{end} interval (T_{pTe}) were measured. Principal Component Analysis (PCA) was computed and early, late and total duration of T-loops was measured. Average RR intervals were similar between LQT1 (906±193 msec) and LQT2 (904±211 msec) patients. The Table provides the results for the repolarization factors.

	level of significance * p<=0.001				
HR: 75 - 77.4 (bpm)	RR (msec)	QT (msec)	TpTe (msec)	Tamp(mV)	LTD(msec)
LQT1 (n=44)	788.3±2.0	443.5±29.6	84.6±9.5	0.41±0.17	27.5±3.6
LQT2 (n=23)	787.9±3.1	453.4±40.8	110.6±33.5*	0.15±0.20*	34.3±9.3*

Binary logistic regression analysis were used to design models for discriminating LQT1 from LQT2 pts. T-wave amplitude and T_{pTe} from lead II were selected. The model correctly identified 93.2% of LQT1 and 82.6 % of LQT2 patients. Adding late T-loop duration (LTD) slightly increased the classification of LQT1 pts to 95.5%. While QT intervals were prolonged in LQT1 and LQT2 patients, T-wave amplitude and transmural dispersion (T_{pTe}) were different between the two groups. Our discriminant model could separate LQT1 from LQT2 patients using the phenotypic expressions of their respective mutation on the surface ECGs.

10:15 a.m.

813-8 Novel Computer Assisted Measurement of Electrocardiographic P Terminal Force to Predict Elevated Left Ventricular End Diastolic Pressure

Eunyoung Lee, Barbara J. Drew, Ronald H. Selvester, Daniel M. Schindler, Andrew D. Michaels, University of California, San Francisco, San Francisco, CA

Background: P terminal force (PTF) in ECG leads V1 or V2 provides a non-invasive measure of left atrial pressure and volume overload. The classic calculation of PTF (PTF_{CL}) involves multiplying peak negative P amplitude with maximal P negative duration, which may over-estimate the actual P negative area. We evaluated a novel calculation of actual P negative area (PTF_{Nov}) using the integral of each point in P terminal negative area. We hypothesized that PTF_{Nov} is superior to PTF_{CL} to distinguish normal (≤15mmHg) vs elevated (>15 mmHg) left ventricular end diastolic pressure (LVEDP).
Methods: Both methods were calculated using computer-assisted measurement software (Inovise Medical, Inc., Portland, OR). PTF_{Nov} and PTF_{CL} were measured in 96 adults in sinus rhythm who underwent left heart catheterization.

Results: Mean age 62 ± 14 (24-90), CAD (71%), acute coronary syndrome (17%), LVEDP >15 mmHg (46%). LVEDP had a higher correlation coefficient with PTF_{Nov} compared to PTF_{CL} (Table, $p < 0.01$ for all values). Using either measurement method, lead V1 was superior to V2 in estimating LVEDP. With 70% sensitivity and 70% specificity, a $PTF_{Nov} > 3000$ μ V-ms was predictive of elevated LVEDP (OR: 5.8, 95% CI: 2.4-14.2, $p < 0.01$).

Conclusions: Computer-assisted measurement of the P negative area is superior to the classic PTF measurement to predict elevated LVEDP. A $PTF_{Nov} > 3000$ μ V-ms is indicative of left ventricular filling pressure overload.

Point biserial correlation between PTF and LVEDP, using two methods of PTF

	PTF_{Nov}			PTF_{CL}		
	V1	V2	V1 or V2	V1	V2	V1 or V2
LVEDP	.435	.310	.409	.355	.277	.330

POSTER SESSION

947

Defibrillation/Implantable Antiarrhythmia Devices

Monday, March 13, 2006, 9:00 a.m.-12:30 p.m.

Georgia World Congress Center, Hall B1

Presentation Hour: 11:00 a.m.-Noon

947-123

Do Ventricular Tachyarrhythmias From a Failing Heart Need More Energy to Convert?

F. Roosevelt Gilliam, Leslie A. Saxon, Emile G. Daoud, Michael A. Lee, Dong Li, Yunlong Zhang, Claudio D. Schuger, Duke University Medical Center, Durham, NC, Guidant CRM, St. Paul, MN

Background: Clinical trials have demonstrated that cardiac resynchronization therapy defibrillators (CRT-D) have improved outcome in heart failure (HF) patients and reduced mortality. However, there is an increasing trend of implanting high-energy (HE) devices due to a concern that ventricular tachycardia (VT) or ventricular fibrillation (VF) in a failing heart may require higher energy to convert. This study compared the conversion rates in patients with CRT-Ds to those with implantable cardioverter defibrillators (ICD).

Methods: This report retrospectively analyzed independently induced VT/VF episodes from 13 recently completed ICD and CRT-D trials. All episodes had a shock programmed as the first therapy. Four most commonly used test energy levels were selected with highest energy level of 21J, which had at least a 10J safety margin for a 31J device. The conversion rate was calculated at each energy level. Chi-square test was used when comparing the conversion rate between ICD and CRT-D groups.

Results: A total of 1257 ICD and 743 CRT-D patients with 6351 and 1686 independently induced VT/VF episodes for each group were analyzed. There were significant differences in age ($p = 0.01$), gender ($p = 0.0026$), NYHA ($p < 0.0001$) and EF ($p < 0.0001$) between groups. There was no difference of arrhythmia types distribution between the groups ($p > 0.05$). The overall conversion rate for all energy levels for the CRT-D group (89%) was higher than the ICD group (86%) ($p = 0.004$). However, there were no differences of the conversion rates between CRT-D and ICD at the 11J (86% vs. 82%), 14J (86% vs. 85%) and 21J (85% vs. 88%) energy levels ($p > 0.05$). Significance was observed only at 17J (88% vs. 92%, $p = 0.002$).

Conclusions: Despite the presence of more advanced HF, there does not appear to be a higher energy requirement for CRT-D recipients, at implant testing, compared to ICD patients to terminate induced VT/VF. A standard energy CRT-D may be sufficient for the majority of HF patients and a HE device may only be required for a proven high DFT patient.

947-124

Practices and Opinions of Morticians Regarding Postmortem Implantable Device Analysis and Retrieval

James N. Kirkpatrick, Susan S. Kim, Subbuh Rajaguru, Michael S. Panutich, Martin C. Burke, Bradley P. Knight, University of Chicago, Chicago, IL

Background: Recent recalls of implantable cardiac rhythm management devices have cast a spotlight on the need for improved postmortem device analysis and retrieval. The purpose of this study was to determine current practices regarding management of implantable devices in deceased persons.

Methods: Funeral home phone numbers were obtained from the yellow pages of a large metropolitan area. The embalmer or funeral director of each funeral home was contacted by phone and asked to complete a survey. Questions involved current practices and opinions regarding postmortem device interrogation and explanation.

Results: Of 56 potential subjects contacted, only 2 declined to participate. Amount of experience averaged 24 years (range = 2-55 years) with an annual volume of 374 deceased persons (range = 25-3000 persons). The mean proportion of deceased persons with an implantable device was 11% (range = < 1 to 38%). Only 4 subjects recall a deceased person undergoing postmortem device interrogation. Among those persons with an implanted device, the mean proportion who had the device removed was 33%. The most common reason for device removal was in preparation for cremation. The subjects routinely handled the explanted devices by placing them in medical waste ($n = 22$), or by donating the devices to an organization involved in refurbishment for animal use or for human use in developing nations ($n = 13$). 5 subjects stored the devices onsite. Only 2 subjects recall returning at least one device to the manufacturer. 83% of respondents thought it would be feasible to interrogate devices in the funeral home routinely; and 93% said it would be possible to remove and return all devices to the manufacturer.

Conclusions: Implantable devices are rarely interrogated or returned to the manufacturer after a patient dies. However, funeral directors and embalmers believe routine interrogation and device retrieval is feasible. There appears to be significant potential for improved postmortem implantable device analysis.

947-125

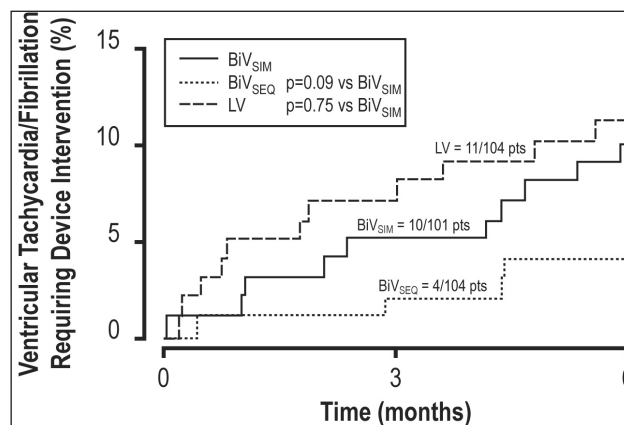
Effect of Different Cardiac Resynchronization Therapy Pacing Modalities on Ventricular Tachycardia/Ventricular Fibrillation Events in Heart Failure Patients

Michael Gold, Michael Mollerus, David De Lurgio, Joseph Strakna, Lindsay Fleming, Clarence Cumming, Medical University of South Carolina, Charleston, SC, Guidant, St. Paul, MN

Background: Studies of cardiac resynchronization therapy (CRT) using simultaneous biventricular (BiV SIM) pacing have demonstrated improved clinical outcomes. While previous BiV SIM studies have reported a neutral effect on ventricular tachycardia/fibrillation (VT/VF), little has been published on the potential for proarrhythmic effects of two investigational CRT modalities [sequential biventricular (BiV SEQ) and left ventricular (LV-CRT)] as studied in the DECREASE-HF clinical trial.

Methods: This clinical trial randomized patients on a 1:1:1 basis to BiV SIM, BiV SEQ, or LV-CRT for a six-month period. Time to first VT/VF event was estimated with the Kaplan-Meier method and the event rates for BiV SEQ and LV-CRT were compared to BiV SIM and tested with the log-rank test.

Results: There were 360 patients enrolled of whom 342 were implanted and 306 were randomized. Patients had a mean age of 67 years, mean LVEF 23%, 67% male, mean QRS of 166 ms, and 64% ischemic with mean follow-up duration of 10.9Y4.2 months. There were no significant differences in baseline characteristics between groups. The Kaplan-Meier curves for each study arm are shown below. There were no statistically significant differences in VT/VF event rates for the alternate CRT modalities when compared to control.



Conclusions:

The BiV SEQ and LV-CRT modalities do not appear to have a proarrhythmic effect when compared to simultaneous BiV SIM CRT. Further prospectively designed studies are necessary to confirm this finding.

947-126

Stepped Defibrillation Waveform Is Substantially More Efficient Than the 50% Tilt Biphasic

Mark W. Kroll, Karlheinz Seidl, Chris Moulder, Gabriel Mouchawar, Christoph Stoeppler, T. Becker, K. Donges, T. Kleeman, U. Weise, E. Anskel, H. Burnett, Russell A. Denman, Herzzentrum, Ludwigshafen, Germany, Prince Charles Hospital, Brisbane, Australia

Introduction: There is a clinical need for a method of reducing the defibrillation threshold (DFT) in the highest DFT patients. The stepped waveform has demonstrated superior defibrillation performance over the biphasic waveform in animal studies and computer modeling. It has three parts: the first portion is positive and equivalent to 2 capacitors in parallel, the second is positive with the capacitors in series, and the last portion is negative, also with the capacitors in series. The increased efficiency is due to the capacitor stepping approximating an ascending waveform that, in turn, couples energy more efficiently with the passive cardiac membrane response.

Method: We measured the delivered energy DFT in 17 patients in a dual-site study with both a control biphasic and the stepped waveform using a Malkin 4-shock protocol. The control waveform was a 50%/50% tilt biphasic in both phases truncated exponential as this is the most commonly implanted waveform today. The stepped waveform had its 3 durations determined by the theoretical cardiac membrane time constant of a 3.5 ms. All shocks were delivered using an arbitrary waveform defibrillator, which was programmed to mimic two 220 μ F capacitors (110 μ F in series).

Results: The median DFT was reduced by 35% from 11.6 J to 7.5 J ($p = .03$). On average, the stepped waveform was able to defibrillate as well as the 50% tilt biphasic with 28% more energy. The shocking resistance was 53.2 ± 8.7 ohms. The benefit of the stepped waveform had a negative correlation with the resistance ($r^2 = 0.21$) suggesting that the capacitance values chosen for the stepped waveform were close to optimal for a 30 ohm resistance but that a smaller capacitance value could give even better DFTs for resistances of > 50 ohms.

Conclusions: The stepped waveform shows significant promise for the clinical problem of high DFT patients in this very preliminary study. Further studies are warranted to guide in the optimization of the usage and parameters of this waveform.

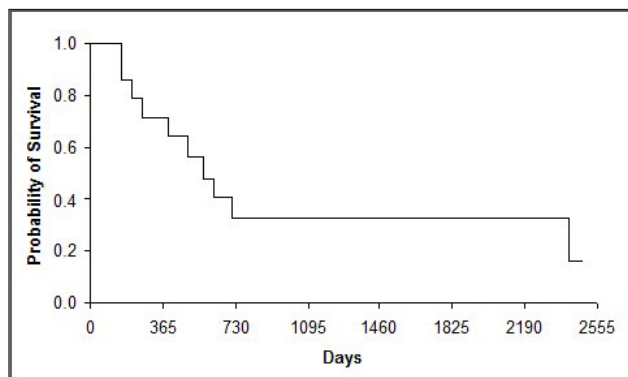
947-127 **Natural History of Hemodialysis Patients Receiving an Implantable Cardioverter Defibrillator for Secondary Prevention**

David P. Dobesh, Kenneth Stein, Suneet Mittal, Sei Iwai, Bindi Shah, James Cheung, Vivian Tan, Dmitry Nemirovsky, Sandhya Dhruvakumar, Bruce Lerman, Stephen Markowitz, New York Presbyterian - Weill Cornell Medical Center, New York, NY

Background: Hemodialysis (HD) patients have increased risk of cardiovascular mortality as compared to the general population. Not infrequently, patients experience either syncope or sudden cardiac death (SCD) at dialysis from which they are revived. The role of an implantable cardioverter-defibrillator (ICD) in these patients is undefined.

Methods: We retrospectively reviewed the data of all patients referred to our electrophysiology laboratory between 1998 and 2005 who experienced syncope or cardiac arrest during or within 6 hours following hemodialysis. Device interrogation strips were reviewed when available. The social security death index was used to obtain mortality data.

Results: We identified 20 patients with cardiac arrest (16) or syncope (3) at hemodialysis. Five received a pacemaker for clear documentation of a bradyarrhythmias and were excluded from analysis. Fifteen received an ICD of whom 7 had documented ventricular tachycardia (VT) and 4 had ventricular fibrillation (VF). Of patients receiving an ICD ten were male, seven had an ejection fraction <=35% and seven had no significant coronary disease. Nine of fifteen patients underwent electrophysiologic testing. Six patients had no inducible VT despite four of them having documented VT or VF. Three were inducible for VT. There was a 63% mortality in the ICD population at 2 years.



Conclusion: Hemodialysis patients who experience syncope or SCD at dialysis have a high mortality despite implantation of an ICD.

947-128 **Impact of Left Ventricular Mass and Diameter on Defibrillation Thresholds in Patients with Implantable Cardioverter Defibrillators**

Dhanunjaya R. Lakkireddy, David J. Burkhardt, Kay Ryschon, Dimpi Patel, Rohit Bhateja, Subramanya Prasad, Sergio Thal, Ashok Kondur, Oussama Wazni, Mohammed Kanj, Kenneth Civallo, Robert Schweikert, Walid Saliba, Mandeep Bhargava, Mauricio Arruda, Mina Chung, Bruce Wilkoff, Patrick Tchou, Andrea Natale, Cleveland Clinic Foundation, Cleveland, OH

Objective: This study studies the impact of LV mass and diameter on defibrillation thresholds (DFT) in patients undergoing implantable cardioverter defibrillator (ICD) surgery.

Methods: Consecutive patients who underwent ICD implantation at the Cleveland Clinic Foundation between 1995 and 2001 were studied. Baseline demographic, clinical characteristics of patients who had high DFTs (≥ 21 J) and low DFTs (≤ 20 J) were compared. DFTs were determined at the end of implantation in a roving fashion until two successful defibrillations are achieved with adequate safety margin of at least 10J. Multivariate regression analysis was performed to identify predictors of high DFTs from this large cohort.

Results: Of the entire study population 13% (305/2430) had high DFTs and 87% (2125/2430) had low DFTs. Patients with high DFTs were younger (64 vs 66 yrs, $p<0.001$), had higher BMI (29 vs 28, $p=0.03$), greater left ventricular internal diastolic and systolic diameters (6.5/6 vs 5.2/4.9, $p<0.001$); thicker interventricular septum/posterior wall (1.3/1.2 vs 1.2/1.1, $p<0.05$); larger left atria (4.8 vs 4.6 cm, $p<0.001$), larger mid descending aortic diameter (3.6 vs 3.3 cm, $p<0.001$), lower EF (24% vs 26%, $p<0.001$), wider QRS (149 vs 134 msec, $p<0.001$), males (92% vs 83%, $p<0.001$) and dilated cardiomyopathy (36% vs 13%, $p<0.001$). A ROC curve demonstrated 655 gm as the cut off which consistently predicted high DFTs. Patients with LV mass >655 gm had higher incidence of high DFTs (75%vs25%, $p=0.001$) compared to those with LV mass ≤ 655 gm. By multivariate analysis LV mass, LVIDD, QRS duration, LVEF & DCM were found to be an independent predictor of high defibrillation thresholds.

Conclusion: Patients with larger and heavier hearts have higher defibrillation thresholds.

947-129 **Does Gender Alter the Efficacy of Implantable Cardioverter Defibrillators?**

Nickole N. Henyan, Effie L. Gillespie, Kara Smith, Jeffrey Kluger, C. Michael White, Craig I. Coleman, Hartford Hospital, Hartford, CT, University of Connecticut, Storrs, CT

Background: Implantable Cardioverter Defibrillators (ICDs) are a life saving therapy for many patients with cardiovascular disease at increased risk of fatal arrhythmias. Since men consistently comprise the majority of the study population (up to 85%) in clinical

trials, the benefit to women is unknown. We conducted a meta-analysis of primary prevention ICD trials to evaluate the benefits in men and women.

Methods: A systematic literature search was conducted from 1966 through September 2005 to identify primary prevention trials of ICDs in patients with cardiovascular disease. The primary outcome measure was death from any cause in males and females. Trials were included if they met the following criteria: 1) randomized controlled trials versus standard of care 2) ICD used as primary prevention in a well-described protocol, and 3) data provided on risk of death for both male and female patients.

Results: Eleven trials were identified, with five satisfying the inclusion criteria. Upon meta-analysis, the risk of death from any cause was reduced by 29% in male patients who received ICD therapy compared to control, adjusted hazard ratio (HR) 0.71 (95% CI 0.54 to 0.94) but not among female patients, HR 0.86 (95% CI 0.66 to 1.12). Since the COMPANION trial evaluated the combination of pacemaker with ICD therapy we conducted a separate analysis without the inclusion of this study. Male patients receiving ICD therapy demonstrated a 28% reduction in risk of death from any cause HR 0.72 (95% CI 0.5 to 1.04) while female patients demonstrated a reduction of only 7% HR 0.93 (95% CI 0.69 to 1.24).

Conclusion: Females do not derive the same degree of mortality benefit from ICDs for primary prevention as their male counterparts.

947-130 **Polynomial Modeling of Ventricular Shock Electrogram for Rhythm Discrimination in Implantable Devices**

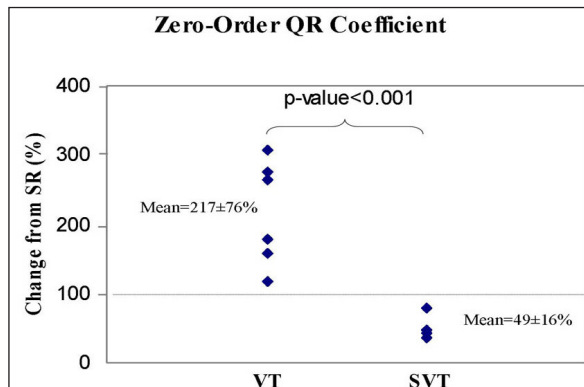
Jeffrey L. Williams, Vladimir Shusterman, Samir Saba, University of Pittsburgh, Pittsburgh, PA

Background: Inappropriate shocks continue to be a problem for patients with implantable defibrillators (ICD). We evaluated a simple polynomial model of ventricular electrograms (EGM) to discriminate between supraventricular (SVT) and ventricular (VT) tachyarrhythmias in low computational power implantable devices.

Methods: Six sets of EGM from patients having both SVT and VT documented during a single ICD interrogation were included. The cardiac cycle was analyzed off-line in 2 parts, QR and RQ segments, which were modeled separately using 3rd-order and 6th-order polynomial equations, respectively.

Results: Eighteen of 24 QR and 25 of 43 RQ coefficients for SR and SVT were found to be significantly ($p<0.05$) different than the corresponding coefficient during VT. Percent change from SR in the zero-order QR coefficient was significantly higher for VT compared to SVT episodes (217 \pm 76% versus 49 \pm 16%, $p<0.001$). Using a cut-off value of 2-fold (100%) change from SR, the zero-order coefficient of the QR segment was able to completely separate VT from SVT in the same patient (Figure). Higher order QR and RQ segment coefficients were less useful for rhythm discrimination.

Conclusions: Our data demonstrate the feasibility of simple polynomial equations that reproduce the depolarization and repolarization phases of human ventricular shock EGM and reliably discriminate between SVT and VT while preserving computational simplicity. This method deserves further testing in a larger number of patients.



947-131 **Risk Factors for Ventricular Arrhythmias in Heart Failure Patients**

David B. De Lurgio, Elyse Foster, Bradley P. Knight, Emory Crawford Long Hospital, Atlanta, GA, Guidant Corporation, St. Paul, MN

Background: Identifying baseline characteristics that indicate which heart failure patients (pts) are at highest risk for ventricular arrhythmias (VT/VF) may be beneficial to physicians in determining treatment options.

Methods: Pts participating in the Device Evaluation of CONTAK® RENEWAL® 2/4/4HE and EASYTRAK® 2: Assessment of Safety and Effectiveness in Heart Failure (DECREASE-HF) Study were included in this retrospective analysis. Univariate and Multivariate Cox Proportional Hazards Regression (PHR) Analyses were used to evaluate baseline characteristics that were related to subsequent VT/VF episodes.

Results: The baseline characteristics of the 360 patients enrolled in the DECREASE-HF study were typical of a CRT-D indicated population (67% male, mean age = 67 yrs, mean LVEF 23%, mean QRS = 166ms, 64% ischemic). Of the 342 patients implanted with a CRT-D device, 45 patients had at least one episode of VT/VF that received appropriate device therapy. Table 1 presents the relationship between baseline characteristics and time to first VT/VF episodes. Significant multivariate predictors of VT/VF are higher LVEDD, lower pulse pressure and history of AF.

Table 1: Cox Proportional Hazards Model for Time to First VT/VF

All patients implanted, N=342

Variable	Hazard Ratio (95% C.I.)	P-value	Multivariate Hazard	P-Value
Age >= 68 years	0.79 (0.44, 1.43)	0.44	-	-
LVEF < 23%	1.84 (1.00, 3.35)	0.05	-	-
LVEDD >= 66 mm	2.54 (1.31, 4.94)	0.006	2.51 (1.28, 4.89)	0.007
LVESD >= 55 mm	2.16 (1.15, 4.08)	0.02	-	-
PR Interval >= 190 ms	1.53 (0.84, 2.78)	0.16	-	-
QRS Duration < 160 ms	0.73 (0.35, 1.51)	0.39	-	-
BSA >= 2 m ²	0.97 (0.54, 1.75)	0.92	-	-
BMI < 28 kg/m ²	1.12 (0.62, 2.01)	0.71	-	-
Systolic BP < 120 mmHg	1.12 (0.62, 2.01)	0.70	-	-
Diastolic BP < 70 mmHg	0.93 (0.52, 1.67)	0.81	-	-
Pulse Pressure < 50 mmHg	1.96 (1.07, 3.58)	0.03	1.97 (1.06, 3.65)	0.031
Mean Arterial Pressure < 86 mmHg	1.00 (0.56, 1.79)	0.99	-	-
Heart Rate < 71 bpm	0.94 (0.52, 1.69)	0.83	-	-
BUN >= 22 mg/dL	0.89 (0.27, 2.93)	0.85	-	-
Creatinine >= 1.2 mg/dL	1.00 (0.55, 1.79)	0.99	-	-
BUN/Creatinine Ratio >= 18	1.16 (0.36, 3.81)	0.80	-	-
QOL >= 56 units	1.06 (0.58, 1.93)	0.85	-	-
Peak VO ₂ < 12.5 ml/kg/min	1.11 (0.61, 2.03)	0.72	-	-
VE/CO ₂ Slope >= 36	1.38 (0.76, 2.48)	0.29	-	-
GFR < 60	0.79 (0.44, 1.42)	0.43	-	-
Male	2.89 (1.29, 6.48)	0.01	-	-
No ACE/ARB	0.98 (0.41, 2.31)	0.96	-	-
No Beta Blocker	1.16 (0.56, 2.42)	0.68	-	-
No ACE/ACB or No Beta Blocker	0.90 (0.44, 1.81)	0.76	-	-
Spirolactone	0.71 (0.38, 1.33)	0.28	-	-
No ACE/ACB or No Beta Blocker or No Spirolactone	1.51 (0.75, 3.06)	0.25	-	-
No Digoxon	0.74 (0.41, 1.34)	0.33	-	-
Diuretic	1.00 (0.42, 2.35)	0.99	-	-
Non-loop Diuretic (with or without Loop)	0.27 (0.04, 1.98)	0.20	-	-
No Loop Diuretic (or Loop and Non-loop)	0.69 (0.31, 1.55)	0.37	-	-
Type III Antiarrhythmic	1.69 (0.81, 3.51)	0.16	-	-
Ischemic	1.59 (0.82, 3.07)	0.17	-	-
Non-Specific Conduction Disorder	2.25 (0.95, 5.32)	0.06	-	-
NYHA IV at Implant	0.66 (0.09, 4.76)	0.68	-	-
Monomorphic VT	1.46 (0.72, 2.95)	0.29	-	-
No Polymorphic VT	1.07 (0.15, 7.76)	0.95	-	-
Non-Sustained VT	2.42 (0.96, 6.15)	0.06	-	-
VF	1.18 (0.47, 3.00)	0.72	-	-
Atrial Tachycardia	1.93 (1.03, 3.63)	0.04	-	-
History of AF	2.02 (1.02, 3.99)	0.04	2.46 (1.23, 4.92)	0.011
Renal Disease	0.99 (0.44, 2.21)	0.97	-	-

Conclusions: In heart failure patients receiving CRT-D, higher end-diastolic dimension, lower pulse pressure, and a history of AF are at greater risk for occurrence of VT/VF.

947-132 Predictors of Mortality in Patients Receiving Implantable Defibrillators

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Introduction: Specific risk factors predict mortality of patients with heart disease but clinical outcome predictors for patients at risk for arrhythmic death who receive implantable defibrillators (ICDs) are not known. **Hypothesis:** Clinical characteristics identify risk of death in patients receiving ICDs. **Methods:** The INTRINSIC RV trial enrolled 1528 patients requiring ICD implantation. Logistic regression analysis was used to assess the relationship between 19 clinical variables identified at enrollment and mortality. Associations between clinical characteristics and survival were assessed by univariate and multivariate analyses. **Results:** Univariate attributes: older age, lower mean systolic blood pressure, New York Heart Association functional class, atrial fibrillation, congestive heart failure, and diabetes predicted one-year mortality (p < 0.01 for each). In a multivariate model, older age (p=0.01), atrial fibrillation (p=0.02), lower mean systolic blood pressure (p=0.02), and diabetes (p=0.03) were associated with increased mortality. Functional class and congestive heart failure were not predictors in the multivariate

model. Of note, Body Mass Index (BMI) and presence of coronary artery disease did not predict mortality in either model. **Conclusion:** Clinical characteristics predict mortality in a large ICD database. Remarkably, BMI, coronary artery disease, congestive heart failure and hypertension did not predict mortality in this population.

Mortality Risk Factors

Risk factor	Survivors (n=1472)	Deaths (n=56)	Univariate P-value	Multivariate P-value
Gender, % male	81.2	71.4	0.0720	0.1879
Age, years (mean ± SD)	65.2±11.9	69.8±10.6	0.0048	0.0144
BMI, kg/m ² (mean ± SD)	28.5±6.3	27.9±7.4	0.4899	0.7389
Systolic BP, mm Hg (mean ± SD)	128.3±22.3	118.7±21.3	0.0017	0.0231
NYHA, % III/IV	22.4	41.1	0.0015	0.2963
Dilated cardiomyopathy	69.2	75.0	0.3537	0.2450
Atrial fibrillation	10.9	25.0	0.0017	0.0214
Congestive heart failure	36.6	57.1	0.0024	0.3806
Hypertension	50.4	62.5	0.0783	0.1205
Diabetes	26.8	46.4	0.0016	0.0343
Coronary artery disease	67.1	69.6	0.6855	0.8855

947-133 Defibrillation Thresholds in Patients with Hypertrophic Cardiomyopathy

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Background: Implantable defibrillators (ICD) are used for the prevention of sudden cardiac death (SCD) in high-risk patients with hypertrophic cardiomyopathy (HCM). Defibrillation thresholds (DFT) have been reported to be elevated in this population with older lead systems, presumably due to a high left ventricular mass index.

Methods: We analyzed 38 consecutive patients with HCM who had an ICD implanted with a left pectoral dual coil lead, active can system. Biphasic DFT was determined with a uniform step-down protocol. The control group was 38 patients with left ventricular dysfunction who underwent ICD implantation over the same time period with the same lead system and testing protocol.

Results: The HCM group was 66% male and 87% of patients had undergone alcohol septal ablation for outflow tract obstruction. The HCM group was younger (46±15 vs. 63±14 years, p=0.001) and had more females (34% vs. 17%). Left ventricular mass index (216±56 g/m² vs. 167±62 g/m², p=0.01) and ejection fraction (62±6% vs. 35±13%, p<0.0001) were higher in the HCM group as expected. The mean DFT was similar between the HCM and control groups (10.7±5.4 joules vs. 10.7±5.6 joules) with no perioperative complications or failed defibrillations noted. 97% of patients in both groups had a DFT ≤20 joules.

Conclusions: Increased left ventricular mass index does not predict higher DFT in HCM patients. ICD implantation can be safely performed in this population with normal output devices.

947-134 Utility of Electronic Reprogrammable Vectors in Biventricular Devices

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Background: Cardiac resynchronization therapy (CRT) is often limited by high left ventricular (LV) pacing thresholds or diaphragmatic stimulation. With bipolar LV leads, the pacing configuration can be altered, but the utility of such programmable pacing vectors has not been evaluated previously.

Methods: We prospectively studied 28 consecutive patients with NYHA III symptoms undergoing CRT therapy. Mean age was 65 ± 10 years and 68 % were male. QRS duration was 153 ± 27 milliseconds; LV ejection fraction was 22 ± 7 %. The LV lead was placed in an optimal position fluoroscopically and then all 4 pacing configurations were evaluated using the LV tip, ring, and right ventricular coil as anode. Standard pacing parameters and diaphragmatic stimulation threshold were measured. The nominal Tip-to-ring (TtR) pacing configuration was compared with the best capture threshold configuration.

Results: Pacing parameters are shown in the table. Eleven (39%) patients had evidence of diaphragmatic stimulation at or near capture threshold in one or more pacing configurations, including 5 in the TtR configuration. Diaphragmatic stimulation was prevented in all patients in at least one configuration. Estimated battery life was also prolonged by 0.13 years.

Conclusions: Programmable pacing vectors can facilitate LV lead placement by minimizing diaphragmatic stimulation and reducing pacing thresholds. This results in a modest prolongation of battery life.

	Pacing Threshold (Volt)	Pacing Impedance (Ohm)	Current (milliampere)	R-waves (millivolt)	Estimated Battery Life (years)
Tip to Ring Configuration (control)	2.1±/ 1.1	1061.6 ±/ 344	2.01 ±/ 1.38	19.28 ±/ 13.2	6.5
Best Capture Threshold Configuration	1.1±/ 0.7	588.7 ±/ 174	1.89 ±/ 1.24	14.66 ±/ 8.8	6.63
T-test	P<0.001	P<0.001	P=0.52	P=0.01	

947-135 Cardiac Resynchronization Therapy Reduces the Need for Shocks in Patients With Automated Implantable Cardioverter Defibrillators

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Introduction: Cardiac resynchronization therapy (CRT) improves cardiac performance in heart failure. However, there are conflicting data on the effects of CRT on the frequency of ventricular arrhythmias. We tested the hypothesis that in patients with previously implanted cardioverter defibrillators (ICDs) who meet established criteria for CRT, upgrading to CRT-defibrillators (CRT-Ds) reduces the frequency of ventricular tachyarrhythmias requiring shocks.

Methods: We conducted a retrospective analysis of all patients who had undergone upgrades from ICDs to CRT-Ds at our institution (N=39). We recorded the frequency (before and after upgrade) of ventricular arrhythmias requiring shock from ICD stored diagnostics, and assessed the change in frequency using a nonparametric Wilcoxon signed rank test. Additionally, QRS duration, ejection fraction, and functional class were assessed at the time of upgrade. The use of beta-blockers and antiarrhythmics was ascertained at the time of ICD implantation and at upgrade. All of these variables were analyzed for association with changes in shock frequency using a linear regression model.

Results: Upgrading from ICDs to CRT-Ds reduced the frequency of ventricular tachyarrhythmias requiring shocks by 76%. ICD diagnostic data were assessed for an average of 37 months prior to upgrade and 15 months after upgrade. The mean number of episodes per year decreased from 0.71 before upgrade to 0.17 after (p<0.01). In the linear regression model, QRS duration prolongation (beta=-0.01, p<0.001) and ejection fraction at the time of upgrade (beta=-0.06, p<0.001) demonstrated independent effects on the reduction in shock frequency. Beta-blocker use increased from 24% before ICD implantation to 84% at the time of upgrade, but was not independently associated with the change in shock frequency (p=0.67). The prevalence of antiarrhythmic use did not change (52 vs. 50%).

Conclusions: In patients who meet criteria for CRT, upgrading their ICD to a CRT-D results in a reduction in ventricular tachyarrhythmias requiring shock. Patients with greater QRS prolongation and higher ejection fraction at the time of CRT-D upgrade experienced the greatest reduction.

947-136 Internal Cardiac Defibrillators With Right Ventricular Outflow Tract Lead Do Not Require Defibrillation Threshold Testing At Routine Device Replacement

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Background: The right ventricular outflow tract (RVOT) is increasingly selected for pacing to reduce right ventricular pacing-mediated dyssynchrony in ICD(I) or CRT-D(D) patients. Acute safety of sensing, pacing and defibrillation thresholds (DFT) using RVOT-placed leads has been established. Chronic DFT results of RVOT-placed leads are limited.

Methods: We retrospectively analyzed DFT data from 62 consecutive patients (63% male, Age: 67.3 ± 10.9 years) undergoing routine ICD or CRT-D device replacement. At implant, 58% presented with CAD with mean LVEF of 32%. All patients had the right ventricular lead previously implanted in the RVOT. 50% of patients received a CRT-D device and the remaining 50% received an ICD. The mean duration between implant and replacement is 3.5 ± 1.9 years.

Results:

Acute DFT (J)		N = pts with CHRONIC DFT(J)							
Devices	DFT	N = pts	≤6	≤10	≤12	≤15	≤18	≤20	≥24
CRT-D	≤ 6	12	8	3	1	0	0	0	0
	> 6	10	7	3	0	0	0	0	0
ICD	≤ 6	9	2	5	1	0	1	0	0
	> 6	5	3	0	2	0	0	0	0
CRT-D	≤ 10	4	1	2	0	0	0	1	0
	> 10	5	5	0	0	0	0	0	0
ICD	≤ 10	1	0	1	0	0	0	0	0
	> 10	5	1	3	0	1	0	0	0
CRT-D	≤ 15	2	1	0	0	0	1	0	0
	> 15	2	1	0	0	0	1	0	0
ICD	≤ 15	2	1	0	0	0	1	0	0
	> 15	3	2	1	0	0	0	0	0
CRT-D	≤ 18	3	0	1	0	1	0	1	0
	> 18	0	0	0	0	0	0	0	0
ICD	≤ 18	3	0	1	0	1	0	1	0
	> 18	0	0	0	0	0	0	0	0
CRT-D	≤ 20	0	0	0	0	0	0	0	0
	> 20	1	0	0	0	0	0	1	0
ICD	≤ 20	0	0	0	0	0	0	0	0
	> 20	1	0	0	0	0	0	1	0

Conclusion : Chronic DFT data from 62 consecutive patients suggest that patients with acute DFT ≤24J do not require additional DFT testing at routine device replacement. ICD and CRT-D RVOT lead DFTs are stable through an average follow-up of 3.5 years. Even though 4.8% (<12% with 95% confidence) of DFTs were shown to have increased by > 5J at device replacement, 100% (>95.3% with 95% confidence) of acute DFT < 24J met the 10J safety margin for a 35J device at follow-up. With the recent expansion of indications for use of defibrillators, prospective studies to characterize long-term DFTs are warranted.

947-137 Risk for Early Heart Failure Hospitalization or Death After Cardiac Resynchronization Therapy

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Background: Cardiac resynchronization therapy (CRT) has been associated with reductions in heart failure symptoms, hospitalization, and mortality in numerous previous clinical studies. Nonetheless, even after the addition of CRT to optimal medical therapy, clinical events continue to occur. The reasons are not well characterized. **Methods:** The CRT Renewal Registry is an ongoing study of patients who have received CRT pacing

or defibrillator therapy. Of 1232 patients enrolled and receiving devices, 96 patients experienced a heart failure hospitalization or death within 90 days of enrollment. Clinical factors were evaluated in an attempt to identify predictors of events. **Results:** Descriptive statistics for each group are shown in the table below. Odds ratios are calculated for one standard deviation difference (approximately 11 years for age and 9% for ejection fraction). **Conclusion:** Advanced age and diminished ejection fraction are associated with persistent risk for heart failure hospitalizations and/or death in the short term after CRT therapy. Whether other risk factors will emerge will be examined in longitudinal follow-up in the registry.

	No Early Event (n=1136)	Had Early Event (n=96)
Age (years)	70±11	73±10
Gender (% male)	72	68
BMI	29±6	27±6
Caucasian	81	86
NYHA III/IV	88	88
Prior arrhythmia	16	16
Ejection Fraction (%)	25±9	23±8
Systolic BP	123±19	120±19
Diastolic BP	70±12	67±1
	Odds Ratio	95% CI
Age	1.37	1.09-1.72
Ejection Fraction (%)	0.76	0.59-0.96

947-138 Is Pulmonary Vein Isolation (PVI) a Better Therapeutic Option than Atrioventricular Node Ablation (AVNA) and Direct Current Cardioversion (DCC)? Mortality Differences in Patients with Atrial Fibrillation

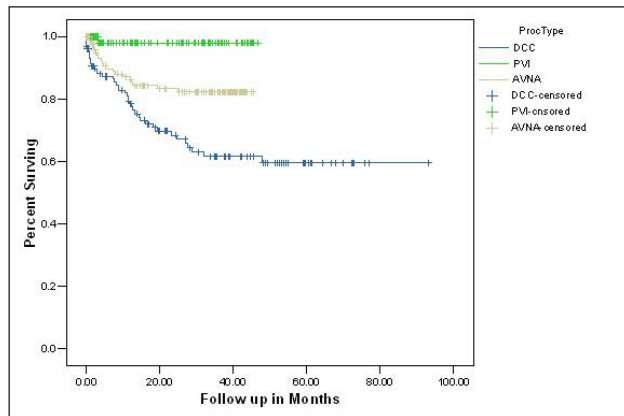
Dhanunjaya R. Lakkireddy, Dimpi Patel, Kay Ryschon, Sergtio Thal, Oussama Wazni, Subramanya Prasad, Mohammed Kanj, Claude Elayi, Atul Verma, Mandeep Bhargava, Robert Schweikert, David Burkhardt, Walid Saliba, Jennifer Cummings, Mina Chung, Mauricio Arruda, Patrick Tchou, Andrea Natale, Cleveland Clinic Foundation, Cleveland, OH

Background: PVI is an effective therapeutic option for the treatment of symptomatic AF who failed medical therapy. The mortality differences between PVI and conventional treatments like AVNA with pacing or DCC with anticoagulation is not known.

Methods: Patients aged 60-80 years who underwent PVI (n=138) were compared to age matched patients who had AVNA (n=133) and DCC (n=139) between 1996 -2004. The baseline clinical characteristics, short-term (< 2 months) and late (>2 to 12 months) recurrence rates and mortality rates were compared for the 3 treatment types. Mortality information was derived from hospital records and national death index.

Results: The mean age of patients who had DCC, PVI and AVNA was 70.2, 70.6 and 70.3 years respectively. The baseline characteristics and comorbidities were comparable. The short-term (13% vs 25% vs 37%, p<0.001), late recurrence rates (9% vs 54% vs 48%, p<0.001), stroke/transient ischemic attacks (4% vs 5% vs 18%, p<0.001) and mortality rates (1.4% vs 31% vs 15%, p<0.001) were significantly lower in PVI group than DCC and AVNA groups respectively. The Kaplan-Meier survival curves for the three types of treatments are shown below. There was a small but significant improvement in LA size (Δ -0.18±0.29cm) and LVEF (Δ 3±9%) in PVI group. Multivariate regression analysis showed low LVEF (p<0.001) and type of treatment (p<0.02) to be predictive of mortality.

Conclusion: PVI has very low mortality, stroke and early/late recurrence rates compared to DCC and AVNA.



947-139 Presence and Type of Provocable Non Pulmonary Triggers for Atrial Fibrillation: Influence of Gender and Arrhythmia Presentation

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Background: In patients (pts) undergoing atrial fibrillation (AF) ablation non pulmonary vein (NPV) triggers can be observed with isoproterenol infusion (ISO) or following

cardioversion of AF. The frequency and type of NPV trigger in patients with paroxysmal (PAF) versus persistent or permanent AF has not been determined.

Methods: Provocative maneuvers were used to identify PV and NPV triggers in 755 consecutive pts referred for PV isolation including 440 pts with PAF, 279 pts with persistent AF, and 36 pts with permanent AF. Provocation attempts before and repeated after AF ablation (PV Isolation and/or focal ablation of NPV triggers) included: 1) ISO to 20 mcg/min, 2) cardioversion of spontaneous or induced AF and 3) cardioversion of AF on 1-3 mcg/min of ISO. Simultaneous multipolar recordings from RA, CS PV ostia and LA confirmed NPV trigger initiating AF. In all pts, programmed atrial stimulation was performed to identify AVN reentrant tachycardia (AVNRT).

Results: NPV triggers were noted in 113 pts (15%) and 34 of 182 women (19%) versus 79 of 573 (14%) of men (p=NS). NPV triggers occurred in 74 pts with PAF (17%), 38 pts with persistent AF (14%) and 1 pt with permanent AF (3%) (p≤0.1). AVNRT as a potential trigger for AF was noted in 27 pts (4%) including 22 (5%) with PAF versus 4 (1.5%) with persistent or 1 (2.7%) with permanent AF (p≤0.05).

Conclusions: NPV triggers for AF provokable by the described maneuvers are 1) seen in ~ 15% of women (18%) and men (14%) undergoing AF ablation and 2) although non PV triggers including AVNRT tend to be more commonly observed in patients with PAF these triggers can also be identified in pts with persistent or even permanent forms of AF. These data have important implications for ablation strategies for AF control.

947-140 Effects of Catheter Ablation for Atrial Fibrillation on Left and Right Atrial Volume and Function

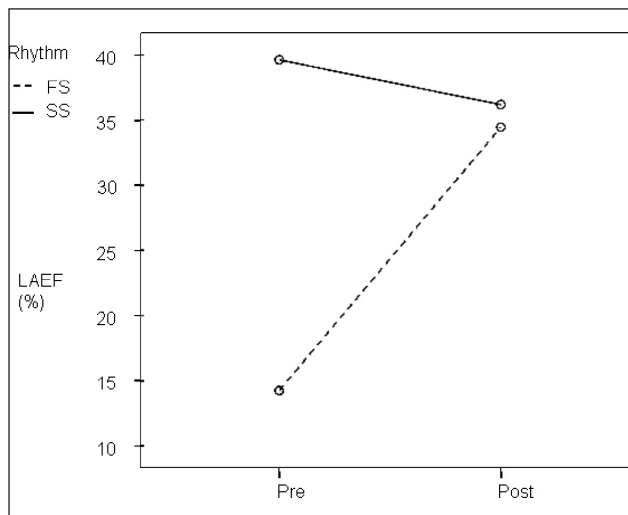
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Background: Atrial fibrillation (AF) may result in atrial enlargement and dysfunction. Effects of AF catheter ablation on LA size and function are unknown.

Methods: Pts referred for AF ablation underwent MRI pre- (MR1) & post-ablation (MR2). Using TrueFISP cine imaging on a 1.5-Tesla Siemens Sonata, contiguous 6-mm slices were acquired in the standard 4-chamber view. Maximum and Minimum LA & RA volumes were measured. Emptying Fraction (EF) was calculated as (Max Volume - Min Volume)/Max Volume.

Results: MR1 & MR2 were obtained 2±4 wks pre- & 15±10 wks post-ablation in 36 pts (54±9 yrs, 31 M, 27 paroxysmal). Ablation was successful in 20 pts who had SR on both MR's (SS) & in 8 pts who had AF on MR1 & SR on MR2 (FS). Ablation was unsuccessful in 5 SS pts, 1 FS pt, & 2 other pts. LAMax decreased with ablation from 118±8 ml to 107±7 ml (p<0.05), with no significant effect of rhythm category or ablation outcome. RAMax tended to decrease with ablation from 114±9 ml to 103±7 ml (p=0.06). Whereas LAEF & RAEF did not significantly change in SS pts, they increased in FS pts (Fig) from 14±3% to 35±4% (p<0.001) & from 9±3% to 36±4% (p<0.001). While pre-ablation LA & RA EF's were lower in FS pts compared to SS pts (p<0.001), they were not significantly different post-ablation.

Conclusions: Catheter ablation for AF results in reduction of LA and RA volumes. Ablation in pts with baseline SR does not adversely impact atrial function. Pts with baseline AF have depressed atrial function that improves after ablation to a similar level as those with baseline SR.



947-141 Characteristics of Cavotricuspid Isthmus-Dependent Flutter Following Left Atrial Ablation of Atrial Fibrillation

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Background: Patients who have previously undergone ablation of atrial fibrillation (AF) may experience cavotricuspid isthmus-dependent (CTI) flutter during follow-up. The purpose of this study was to describe the effects of left atrial (LA) ablation on the characteristics of CTI flutter. **Methods:** Fifteen patients (Age=54±9 years, EF=0.50±0.10, LA=4.4±0.3

cm) underwent ablation of CTI flutter late after LA ablation of AF. The electrocardiogram (ECG), atrial activation patterns, and LA voltage maps during flutter were analyzed. Thirty patients who underwent ablation of CTI flutter without prior LA ablation served as controls. **Results:** The mean cycle lengths of CTI flutter in the study and control groups were 253±26 ms, and 235±29 ms, respectively (p=0.05). In patients with prior LA ablation, mapping revealed counterclockwise (CCW) activation around the tricuspid valve in 12/15 patients (80%) and clockwise (CW) activation in 3/15 patients (20%). In lead aVL, the flutter waves were negative in 9 of the 15 study patients (60%) compared with 1 of the 30 controls (3%; p<0.001). The flutter waves in the inferior leads were upright in 9 of the 15 patients (60%) with prior LA ablation and in none of the controls (p<0.001). The upright flutter waves in the inferior leads in patients with CCW flutter corresponded to craniocaudal activation of the right atrial free wall. LA activation contributed little to the genesis of the flutter waves in these patients because of a significant reduction in bipolar LA voltage (0.44 ± 0.20 mV versus 1.54 ± 0.19 mV in patients with biphasic/negative flutter waves; p<0.001). The earliest LA activation occurred in the inferoposterior region during CCW flutter and in the anterosuperior aspect during CW flutter, consistent with conduction over the coronary sinus and Bachmann's bundle, respectively. Flutter termination and CTI block were achieved in all patients (100%). **Conclusions:** CTI flutter that occurs after LA ablation of AF often has atypical ECG characteristics because of altered LA activation. In patients presenting with atrial flutter following LA ablation, entrainment mapping should be performed at the CTI even if the ECG is uncharacteristic of CTI flutter.

947-142 Microreentry as a Mechanism of Focal Atrial Tachycardia

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Background: Most focal atrial tachycardias (AT) in humans demonstrate characteristics consistent with automaticity or triggered activity, including suppression or termination with adenosine. While microreentry may account for some cases of human AT, this entity remains poorly defined.

Methods: In 56 consecutive pts (28 F, 60±15 yrs), 59 ATs demonstrated focal activation with the CARTO electroanatomical mapping system. Adenosine was administered to each case in incremental doses until the AT terminated or AV block occurred. Electrograms at the sites of origin were characterized in terms of fractionation, morphology, and activation.

Results: Of 59 focal atrial tachycardias, 5 (8%) were insensitive to adenosine (doses 6-12 mg). Pts with adenosine-insensitive focal AT were older (73 vs 60, p<0.05) and more likely to have coexisting AF (5/5 vs 5/51) compared to pts with adenosine-sensitive AT. In all cases of adenosine-insensitive focal AT, highly fractionated, low-amplitude, mid-diastolic potentials were present at the sites of origin, with local electrogram durations of 81-186 msec (comprising 29-64% of the AT cycle length). Concealed entrainment was demonstrated at these sites in 3/3 cases. These tachycardias originated in the posterior wall of the LA or pulmonary veins (N=3) or the RA (N=2). Focal radiofrequency ablation at these sites terminated AT in each case.

Conclusions: Electrogram characteristics and response to adenosine in these ATs are consistent with small reentrant circuits, with dimensions below the resolution of the mapping system. These data provide evidence that microreentry is a mechanism of focal AT and has an electropharmacological profile that differs from AT due to automaticity and triggered activity.

947-143 Effects of Two Different Catheter Ablation Techniques on Spectral Characteristics of Atrial Fibrillation

Kristina Lemola, Michael Ting, Priya Gupta, Jeffrey N. Anker, Aman Chugh, Eric Good, Scott Reich, David Tschopp, Petar Ilgic, Darryl Elmouchi, Krit Jongnarangsin, Frank Bogun, Frank Pelosi, Jr., Fred Morady, Hakan Oral, University of Michigan, Ann Arbor, MI

Background: Circumferential pulmonary vein ablation (CPVA) and electrogram-guided ablation (EGA) are 2 different techniques that have been used to eliminate atrial fibrillation (AF). Spectral analysis may identify rotors that perpetuate AF. The effects of CPVA and EGA on the spectral characteristics of AF have not been described, and whether there is any association between changes in dominant frequency (DF) and clinical outcome is unknown.

Methods: In 71 consecutive patients (age=57±9 years), CPVA (29) or EGA (42) was performed for paroxysmal (42) or persistent (29) AF. During EGA, complex electrograms characterized by a short cycle length, fractionation, and/or continuous electrical activity were targeted. Lead V1 and bipolar electrograms recorded in the left atrium and coronary sinus were analyzed to determine the DF of AF before and after ablation.

Results: The DF in the left atrium was higher in patients with persistent (5.83±0.86 Hz) than paroxysmal AF (5.33±0.76 Hz, P=0.03). There was a frequency gradient from the left atrium (5.51±0.81 Hz) to the coronary sinus (5.20±0.80 Hz, P<0.001). CPVA and EGA resulted in a similar decrease in DF (19±17% vs 17±15%, P=0.5). During a mean follow-up of 10±7 months after a single ablation procedure, the change in DF after CPVA was similar among patients who did and did not have recurrent AF. There was a significant association between an acute decrease in DF after EGA and freedom from recurrent AF, but only in patients with persistent AF (19±14% versus 3±6%, P=0.02).

Conclusions: Both CPVA and EGA decrease the DF of AF, consistent with elimination of rotors. Whereas the efficacy of EGA is associated with a decrease in DF in patients with persistent AF, the efficacy of CPVA is independent of changes in DF. This suggests that CPVA and EGA eliminate different mechanisms operative in the genesis of persistent AF.

ORAL CONTRIBUTIONS

818

Defibrillation and Resynchronization Devices

Monday, March 13, 2006, 11:00 a.m.-12:30 p.m.
Georgia World Congress Center, Room B312

11:00 a.m.

818-3 Comparison of Heart Failure Adverse Event Rates Between Alternative Cardiac Resynchronization Therapy Pacing Modalities

Imran Niazi, Steven Higgins, Satish Goel, Clarence Cumming, Lindsay Fleming, St. Luke's Medical Center, Milwaukee, WI, Guidant, St. Paul, MN

Background: Clinical trials have shown right ventricular pacing to increase heart failure (HF) symptoms while other trials have shown simultaneous biventricular (BiV SIM) decreasing HF related symptoms. The DECREASE-HF trial compared two other investigational methods of Cardiac Resynchronization Therapy (CRT), sequential BiV (BiV SEQ) and LV Only (LV-CRT), to the conventional BiV SIM method. It is unknown whether LV-CRT or BiV SEQ pacing could be associated with an increase in HF related events.

Methods: The data were analyzed retrospectively for the number of pts experiencing a HF related event to determine the impact of pacing modality. In this trial, HF events included dyspnea, hypotension, and weight gain, among others. Fisher's exact test was used to compare differences across arms for each HF related event due to the low rates and a p-value was calculated.

Results: Of the 360 enrolled pts, 342 were implanted and 306 were randomized with mean age of 67 yrs, mean LVEF 23%, mean QRS 166ms, 67% were male, and 64% had an ischemic etiology. Pts were randomized to BiV SIM (101), LV-CRT (101) or BiV SEQ (104). Of these, 16 BiV SIM pts (18 events), 24 LV-CRT pts (39 events), and 19 BiV SEQ (33 events) experienced a HF event. There was no statistically significant difference in the number of pts with a HF related event (p=0.36) though there were more events in the LV-CRT and BiV SEQ arms as several patients had multiple events.

Conclusions: In the DECREASE-HF study, less than 20% of pts experienced a HF related event in the six-month follow-up period. These results suggest that LV-CRT and BiV SEQ when compared to BiV SIM do not significantly increase the risk for HF related events as compared to reports with right ventricular pacing. Thus, when troubleshooting a CRT device, the use of LV-CRT or BiV SEQ pacing should not be associated with an increase in HF symptoms.

11:15 a.m.

818-4 Relationship Between Renal Function, Risk of Sudden Cardiac Death, and Benefit of the Implanted Cardiac Defibrillator in Post Myocardial Infarction Patients With Left Ventricular Dysfunction

Ilan Goldenberg, Arthur J. Moss, Scott McNitt, Mark L. Andrews, Wojciech Zareba, W. Jackson Hall, Henry Greenberg, Robert B. Case, University of Rochester Medical Center, Rochester, NY, Columbia University College of Physicians and Surgeons, New York, NY

Background: The implanted cardioverter defibrillator (ICD) has been shown to reduce the risk of sudden cardiac death (SCD) in patients with ischemic left ventricular dysfunction by 67%. However, data on the relationship between renal function and SCD in this population are limited, and the effect of renal dysfunction on ICD benefit has not been determined.

Methods: We performed a retrospective analysis of the outcome associated with renal dysfunction, as determined by estimated glomerular filtration rate (eGFR), in patients enrolled in the Multicenter Automatic Defibrillator Implantation Trial-II (MADIT-II).

Results: Multivariate analysis in conventionally treated patients showed that for each 10 unit reduction in eGFR the risk of all-cause mortality and SCD increased by 16% (p=0.005) and 17% (p=0.03), respectively. Defibrillator therapy was associated with a survival benefit in each eGFR category ≥ 35 ml per min per 1.73 m^2 (overall risk reduction, all-cause mortality: 32%; p=0.01, SCD: 66%; p<0.001), while no ICD benefit was shown among patients with eGFR <35ml per min per 1.73 m^2 (all-cause mortality: hazard ratio [HR]=1.09; p=0.84, SCD: HR=0.95; p=0.95).

Conclusions: In high-risk cardiac patients enrolled in MADIT-II, there was a significant increase in the risk of SCD with declining renal function. Defibrillator therapy was associated with a significant survival benefit among study patients with mild to moderate or no renal disease, while no benefit was shown among patients with more advanced renal dysfunction.

11:30 a.m.

818-5 Is There a Role for Implantable Cardioverter-Defibrillator Therapy for the Primary Prevention of Sudden Death in Patients With Chronic Kidney Disease?

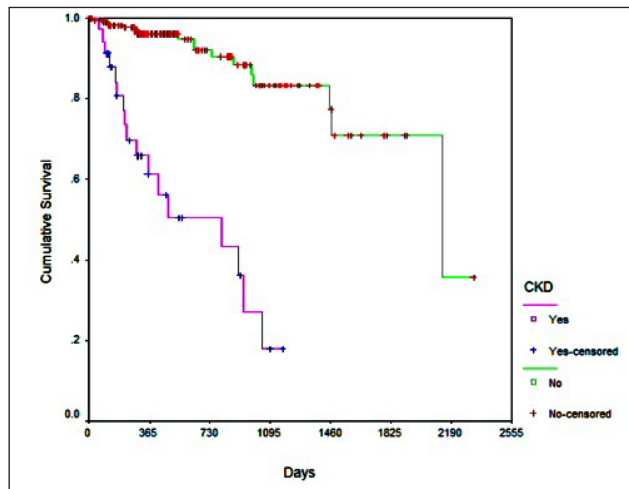
Phillip Cuculich, Jose M. Sanchez, Roger Kerzner, Scott Greenberg, Jay Sengupta, Jane Chen, Mitchell Faddis, Marye Gleva, Bruce Lindsay, Timothy Smith, Barnes-Jewish Hospital; Washington University School of Medicine, Saint Louis, MO

Background: Patients with chronic kidney disease (CKD) are at increased risk for sudden death (SD). Little is known about implantable cardioverter-defibrillator (ICD) use for primary prevention of SD in this large, high-risk population. This retrospective study evaluated the outcome of primary prevention ICD therapy in patients with CKD.

Methods: A total of 229 consecutive patients with ischemic or nonischemic cardiomyopathy

underwent ICD implantation for primary prevention of SD. Patients were stratified by CKD, defined by serum creatinine > 2 mg/dl or dialysis use. End point was mortality.

Results: CKD was identified in 35 of 229 patients (15.3%). Baseline characteristics of patients with and without CKD were similar except for decreased use of angiotensin converting enzyme inhibitors and angiotensin receptor blockers in CKD patients (74.3% vs. 93.3%, p = 0.002). There were 33 deaths during a follow-up period of 55.5 ± 6.3 months: 17 of 35 CKD patients (48.6%) and 16 of 194 control patients (8.2%). Kaplan Meier analysis verified a significant mortality difference (p < 0.00001). Cox regression analysis controlling for age, sex, comorbidities, ejection fraction and medication showed CKD to be the strongest independent predictor of death (hazard ratio = 10.5; confidence interval, 4.8-23.1; p = 0.0001).



Conclusions: In patients receiving an ICD for primary prevention of SD, CKD significantly reduced long-term survival. The impact of primary prevention ICD therapy is markedly reduced in patients with CKD.

11:45 a.m.

818-6 Cardiac Resynchronization Device Placement During Hospitalization for Heart Failure is Associated With a Significant Improvement in Early Clinical Outcomes

William T. Abraham, Barry Greenberg, Gregg C. Fonarow, Nancy M. Albert, Karen Chiswell, Wendy Gattis Stough, Mihai Gheorghiadu, Christopher O'Connor, Jie-Lena Sun, Clyde Yancy, James B. Young, OPTIMIZE-HF Investigators and Hospitals, The Ohio State University Heart Center, Columbus, OH

Introduction: CRT devices with or without ICD have demonstrated benefit in heart failure (HF) patients and are recommended by current guidelines. However, little is known about CRT placement during a HF hospitalization and its association with early clinical outcomes.

Methods: OPTIMIZE-HF is a registry/performance improvement program for pts hospitalized with HF. 60-90 day post discharge follow-up (f/u) data were prospectively collected in a pre-specified 10% sample. Multivariable analysis was performed for 60-90 day f/u death and death + rehospitalization.

Results: 5791 pts from 91 hospitals were included in this analysis. 132 pts (2.3%) underwent placement of CRT during hospitalization (1.5% CRT only and 0.8% w/ CRT-D). Pts receiving CRT were of similar age and more likely to be male and have an ischemic etiology. Length of stay (LOS) and in-hospital mortality were 6.4 / 5.6 days and 1.3 / 3.8% in those receiving and not receiving CRT device therapy. During 60-90 day f/u there were significantly less rehospitalizations in CRT pts and a trend for lower mortality (Table 1). After multivariable risk adjustment, CRT placement remained associated with significantly lower rates of death and/or rehospitalization OR 0.38 95% CI 0.23-0.62, P<0.0001.

Conclusions: CRT device placement at the time of HF hospitalization, while associated with a modest increase in LOS, appears to be safe and was associated with a significantly lower risk of death or rehospitalization during the first 60-90 days post hospital discharge.

Parameter	Total Patients N=5791	No CRT N=5659	CRT N=132	P Value
Mean Age (years)	72.1	72.2	71.4	0.2586
Female (%)	48.8	49.1	34.1	0.0006
Ischemic etiology (%)	42.0	41.6	60.6	<0.0001
Mean EF (%)	36.9	37.2	24.3	<0.0001
Creatinine, mean (mg/dL)	1.6	1.6	1.7	0.0004
BNP mean, admission (pg/dL)	1305	1300	1558	0.0616
Death since discharge (%)	8.3	8.3	6.2	0.3735
Rehospitalized since discharge (%)	29.6	29.9	18.2	0.0036
Death or rehospitalization since discharge (%)	36.2	36.6	22.3	0.0008

818-7 Multicenter Experience with 1,355 Failed and Recalled Implantable Cardioverter Defibrillators

Robert G. Hauser, David L. Hayes, Andrew E. Epstein, Stephen C. Vlay, David S. Cannom, Susan L. Song, Minneapolis Heart Institute Foundation, Minneapolis, MN

Background: Despite the widespread and growing use of implantable cardioverter-defibrillators (ICD), little information is available regarding their clinical performance, failure modes, or the impact of advanced pacing functions on ICD reliability and longevity.

Methods: We conducted a 6-year prospective multicenter study of ICD pulse generators that failed or required replacement due to manufacturers recalls. ICD failure (F) was defined as removal from service because the ICD was not functioning according to the manufacturer's specifications. A recalled ICD was a normally functioning device that was prophylactically replaced as the result of a manufacturers recall.

Results: Between 1998-2005, 1,220 ICDs failed and 135 ICDs were recalled and replaced at 9 participating centers. The average implant times (AIT) of failed and recalled ICDs were 4.4+/-1.5 and 1.7+/-0.8 years respectively. AIT for single chamber (SR) and dual chamber (DR) ICDs with rate responsive (RR) and cardiac resynchronization (CRT-D) pacing capabilities were significantly less than single chamber (S) and dual chamber (D) ICDs without RR: SR-2.5+/-1.7; DR-3.4+/-1.3; CRT-D-1.9+/-0.9; S-4.8+/-1.5; D-5.1+/-0.9 (P<0.001). Overall, ICDs were removed for: normal battery depletion (>3 yrs)-73%; premature battery depletion (<3 yrs)-9%; electronic or housing failure-6%, and recalls-10%. Compared to ICDs without RR or CRT-D capabilities, ICDs with RR or CRT-D failed earlier due to battery depletion (P<0.001) and they were significantly more prone to unexpected electronic or housing F (9% vs 5%; P=0.008) and manufacturers recalls (25% vs 1%;P<0.0001). Major device-related adverse events included death (n=2), failure to convert VT/VF (n=6), and inappropriate shocks (n=11).

Conclusions: Based on our analysis of failed and recalled devices, the performance of ICDs, particularly those offering advanced pacing capabilities, has been adversely affected by early battery depletion, electronic or housing failure, and manufacturers recalls. These findings suggest that a national registry is needed to accurately estimate ICD longevity and to determine the incidence of unexpected failure modes.

12:15 p.m.

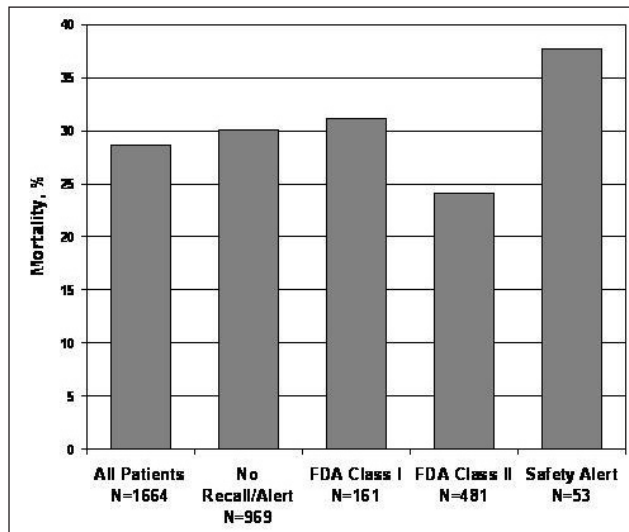
818-8 Implantable Cardioverter-Defibrillator FDA Recalls and Safety Alerts: Prevalence and Impact on Patient Mortality

Arthur C. Kendig, Mohammed Khan, Patrick J. Tchou, David O. Martin, Andrea Natale, Bruce L. Wilkoff, J David Burkhardt, Mandeep Bhargava, Mina K. Chung, Cleveland Clinic Foundation, Cleveland, OH

Background: Recently several implantable defibrillators (ICDs) have been recalled by the FDA. With more ICDs being implanted, recalled or subjected to safety alerts, we studied the impact on patients and mortality associated with ICD recalls/alerts.

Methods: ICDs first implanted 8/96-5/04 at the Cleveland Clinic and subjected to FDA class I, II or III recalls or manufacturer safety alerts were identified. A recall/alert was categorized as potentially life threatening, predictable or with a software indicator or fix. Survival analyses were performed to test association of recall/alert status with mortality.

Results: In 1644 patients (age 63±13, 78% male), 695 (41.8%) had an ICD subject to FDA recall or manufacturer safety alert (Figure). Overall mortality was 28.7% (follow-up 1299±819 days). With FDA class I or II recalls or safety alerts, mortality was 26.8% (p=NS). Compared to 30.1% mortality with no recall/alert, mortality was 31.1% with FDA class I (p=NS) and 24.1% with class II recalls (p=0.016), 37.7% with safety alerts (p=NS), 25.7% with life-threatening recall/alerts (p=0.08), 31.8% with predictable alerts (p=NS), 24.2% with software indicators (p=0.03), and 21.4% with software fixes (p=0.02). Kaplan-Meier analyses comparing no recall/alert to recall/alert groups showed no significant differences in mortality.



Conclusions: CD recalls or safety alerts impact over 40% of patients. However, having an ICD that is recalled or under a safety alert was not associated with higher mortality.

CRT Methods, Results and Prediction of Benefit, Pacing Infections & Other Complications

Monday, March 13, 2006, 1:30 p.m.-5:00 p.m.
Georgia World Congress Center, Hall B1
Presentation Hour: 3:30 p.m.-4:30 p.m.

969-123 Reduced Ventricular Volumes and Improved Systolic Performance with Cardiac Resynchronization Therapy: A Comparison of Simultaneous Biventricular Pacing vs. Sequential Biventricular Pacing vs. Left Univentricular Pacing

Rajni K. Rao, Esperanza Vilorio, Jill Schafer, David De Lurgio, Elyse Foster, University of California, San Francisco, San Francisco, CA

Background: Cardiac resynchronization therapy (CRT) is a proven treatment for systolic heart failure. The DECREASE-HF Trial is the first randomized, double-blind study comparing simultaneous biventricular (SimBiV), sequential (Seq) BiV (left and right ventricular stimulation is offset), and left univentricular (LV) pacing. Seq BiV pacing and LV only pacing are currently under investigation as part of this study.

Methods: 360 patients were enrolled and 342 were successfully implanted with a CRT system. Of these, 306 were randomized to LV, SimBiV, or SeqBiV pacing in a 1:1:1 ratio. Inclusion criteria were: NYHA III or IV HF, EF ≤35%, QRS ≥150 ms, and a life expectancy >6 mo. Exclusions were: prior CRT, other pacing indications, and beta-blocker treatment for <90 days. Data were analyzed using a longitudinal method.

Results: The mean baseline LV end-diastolic volume (LVEDV = 229 ± 4 mL), LV end-systolic volume (LVESV=167 ± 4 mL) and ejection fraction (EF=28% ± 0.4) did not differ among groups. All groups had similar significant improvements in EF and myocardial performance index (MPI) at 6 months. The SimBiV group had the greatest reduction in LVEDV and LVESV although LVESV improved in all groups.

* p-value <0.05 (baseline vs. 6 mo); § p=0.02 for sim BiV vs. LV only

	LV Only	Sequential	Simultaneous
Change in LVEDV (mL)	-5 +/- 5	-8 +/- 5	-20 +/- 5*§
Change in LVESV (mL)	-14 +/- 4*	-19 +/- 4*	-27 +/- 4*§
Change in LVEF (%)	5.7 +/- 0.8*	6.9 +/- 0.8*	7.4 +/- 0.8*
MPI	-0.1 +/- 0.02*	-0.11 +/- 0.02*	-0.13 +/- 0.02*

Conclusions: All groups exhibited a reduction in LV volumes as well as an improvement in systolic performance. The greatest improvement was seen in the simultaneous BiV group. LV only pacing was associated with more modest benefits.

969-124 Radial Artery Pulse Wave Analysis Corresponds to Echo Doppler Measures of Cardiac Function in Patients Undergoing Atrioventricular and Ventriculo-Ventricular Optimization of Biventricular Pacemaker

Asim M. Rafique, Tasneem Z. Naqvi, Cedars-Sinai Medical Center, Los Angeles, CA, UCLA School of Medicine, Los Angeles, CA

Background: Echo-guided optimization of biventricular (Biv) pacemaker post cardiac resynchronization therapy (CRT) has been shown to provide incremental improvement in cardiac function and patient (pt) functional class. Routine application of echo-guided optimization is however limited due to time and expertise required and lack of appropriate reimbursement. SphygmoCor (SCor) device (AtCor Medical) can measure left ventricular (LV) systolic function as ejection duration (ED) via applanation tonometry of the radial artery (aa). We examined whether LV ED by SCor will correspond with echo Doppler parameters of cardiac systolic and diastolic function and synchrony during atrioventricular (AV) and ventriculo-ventricular (VV) pacemaker optimization.

Methods: We performed blinded simultaneous echo Doppler and SCor radial aa tonometry at different AV (40-300 ms), and VV delays (nominal, 20 & 40 ms, LV or RV pre-excited), LV only pacing, A-pacing, A-sensing and during native rhythm in 42 pts (67±14 yrs, 32 M), LVEF 0.38±0.08, 3±5 days post CRT.

Results: 252 measurements (mean of 6/pt) of echo Doppler and SCor radial aa pulse waveform were made at above pacemaker settings. Correlation of SCor radial aa ED with echo Doppler variables was as follows: LV outflow velocity times integral r=0.78, p<0.001, myocardial performance index (MPI) r=0.81, p<0.001, echo systolic ejection period r=0.87, p<0.001, pulsed wave mitral inflow filling time, r=0.50, p<0.001, E-duration(dur), r=0.42, p<0.001 and A-dur, r=0.69, p<0.001. Using MPI as gold standard for cardiac function, the sensitivity and specificity of SCor ED was 83% and 81%. Optimal VV delay was concordant between echo and SCor in all pts. Optimal AV delay was concordant between echo and SCor in 72% of pts and in 28% of pts difference between echo and SCor optimal AV delay was 20±5 ms. Mean SCor ED during native rhythm was 222±50 ms and during bipacing with optimal AV and VV delay was 270±45 ms.

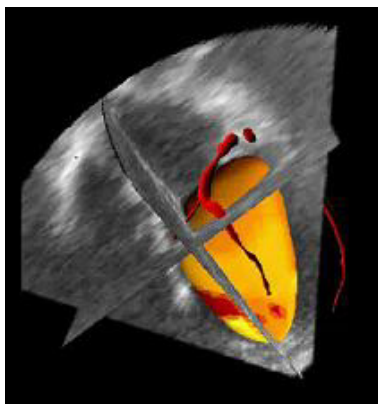
Conclusions: Assessment of cardiac function by SCor radial aa tonometry corresponds to indices of cardiac function derived from echo Doppler. This non-invasive, simple and objective technique may be used for Biv pacemaker programming in pts who have undergone CRT.

969-125

Integration of Three-Dimensional Coronary Venous Angiography with Three-Dimensional Echocardiography for Biventricular Device Implantation

Moussa C. Mansour, Jagmeet Singh MD P. Singh, Anwer Qureishi, Sham Sokka, Robert Manzke, Volker Rasche, Michael H. Picard, Jeremy N. Ruskin, Massachusetts General Hospital, Boston, MA, Philips Medical Systems, Boston, MA

Background: The rate of non-responders after resynchronization therapy (CRT) is 20-30%. While the concept of CRT is a functional one, the choice of the optimal coronary sinus (CS) branch for the left ventricular (LV) lead is anatomical, with most operators targeting a lateral branch. We investigated the feasibility of integrating data from 3D CS angiography, with functional data from 3D echo to help determine the optimal CS branch for LV lead placement. **Methods and Results:** In five patients undergoing CRT device implantation, 3D echo, and a parametric display of time-to-maximum excursion of the LV segments were obtained. During the procedure, a rotational angiogram of the CS was performed followed by a 3D reconstruction of the CS tree. Off-line integration of the 3D echo with the 3D angiogram involved the use of fluoroscopic skin markers to register the 3D angiogram with the patient's chest, and an optical tracking system to register these markers with the echo probe. Retrospective integration of the 3D data was possible in all patients to allow the identification of the CS branch closest to the segment of latest contraction. In-vitro validation studies using a heart model revealed that the resulting error of the registration process is 1.8±1.1 mm. **Conclusion:** Integration of 3D angiography data of the coronary venous tree with 3D ultrasound functional information is feasible. This has the potential to facilitate the choice of the optimal site for LV lead placement and increase the efficacy of biventricular pacing.



969-126

Incidence of Left Ventricular Dysfunction After Pacemaker Implantation for Complete Heart Block

Mark A. Iler, Katherina Tillan, Tingfei Hu, Anthony A. Bavy, Bruce L. Wilkoff, Mina K. Chung, Cleveland Clinic Foundation, Cleveland, OH

Background: Cardiac dyssynchrony caused by right ventricular pacing is of growing concern. The DAVID trial showed that patients with left ventricular dysfunction who are paced from the right ventricle after defibrillator implantation have a worse outcome than those whose pacemakers are programmed to allow intrinsic conduction. The incidence of worsening left ventricular function in patients who receive pacemakers for complete heart block is unknown.

Methods: Patients who underwent pacemaker implantation for complete heart block were identified from a clinical database. Those who had pre-operative and post-operative echocardiograms were then analyzed for the endpoints of worsening left ventricular function and mortality.

Results: A total of 805 patients were identified, of which 486 had an available follow-up echocardiogram and were included for final analysis (age 67 ± 14 yrs, 57% male, 33% coronary disease). Included patients had slightly higher LVEF than those who were excluded (49 vs 48%, p=0.009) but were similar with respect to other characteristics and overall mortality. Mean LVEF decreased from 49 ± 13% to 47 ± 14% after a median of 13 months (p<0.001). A decrease in LVEF (by at least 5%) after implantation occurred in 46% of all patients, including 54% of those who had normal left ventricular function (LVEF ≥ 50%) at baseline. A clinically significant decrease (defined as at least 10%) occurred in 29% of all patients and 33% of those with normal baseline function. Only older age (HR 1.03, 95% CI 1.01-1.05, p=0.004) and lower baseline LVEF (HR 1.03, 95% CI 1.01-1.04, p=0.001) were independent predictors of mortality. While a decrease in LVEF after pacing did not independently predict mortality, patients whose LVEF did not decrease had a better prognosis (HR 0.95, 95% CI 0.92-0.99, p=0.017).

Conclusion: The development of left ventricular dysfunction after pacemaker implantation for complete heart block is common, including a third of patients with normal function at baseline. Careful follow-up of these patients to assess for clinical worsening due to dyssynchrony is warranted.

969-127

Does Left Bundle Branch Block Indicate a Better Response to Cardiac Resynchronization Therapy in Heart Failure Patients with Echocardiographic Evidence of Mechanical Asynchrony?

Qing Zhang, Yat Sun Chan, Jeffrey WH Fung, Chi Kin Chan, Gabriel WK Yip, Leo CC Kum, Eugene B. Wu, Pui Wai Lee, Yat Yin Lam, Skiva Chan, Li Wen Wu, Cheuk Man Yu, The Chinese University of Hong Kong, Hong Kong, People's Republic of China

Background: It is unknown whether patients with pre-existing systolic asynchrony behave differently after CRT if they have different QRS pattern.

Methods: Fifty-three patients receiving CRT were included, who had echocardiographic evidence of systolic asynchrony with "Asynchrony Index" (Ts-SD) ≥32ms by TDI. They were divided into 2 groups: those with baseline LBBB (group 1, N=30) or without (group 2, N=23), and the efficacy of CRT at 3-month was compared.

Results: Reverse remodeling was achieved by reduction of both LVEDV (145±67 vs 182±72cm³) and LVESV (93±54 vs 135±62cm³), and gain in EF (37±9 vs 27±9%) (all p<0.001). Responders were found in 42 patients (81%) where the reduction of LVESV exceeded 15%. Group 1 and group 2 had similar degree of intraventricular asynchrony at baseline reflected by Ts-SD (45±7 vs 43±11ms) and atrioventricular asynchrony by PR interval (192±39 vs 188±36ms) (both p=NS), though the QRS duration was different (168±28 vs 115±24ms, p<0.001). However, more responders were found in group 1 (87 vs 74%, P<0.05), and the degree of reverse remodeling was better in group 1 than group 2 (Table). Clinical improvement was comparable (Table).

Conclusions: LBBB seems to indicate a better response of reverse remodeling after CRT in patients with intraventricular asynchrony assessed by echocardiography. Further investigations are needed in order to help patient selection and response prediction for CRT. Table. Comparison of changes in Echo and Clinical Parameters between Group 1 & 2

Parameters	Group 1	Group 2	P value
LVEDV,%	-26±17	-14±12	0.005
LVESV,%	-36±19	-23±15	0.008
Ejection fraction, %	12±8	8±6	0.07
Ts-SD, ms	-12±14	-10±16	NS
NYHA class	-0.8±0.6	-0.9±0.5	NS
Quality of life score	-16±15	-6±26	NS
6-Min hall walk, m	56±65	30±103	NS

969-128

Ventricular Dyssynchrony Assessment With Equilibrium Radionuclide Angiography Phase Analysis Predicts Outcome After Cardiac Resynchronization Therapy

Jacopo Dalle Mule, Marco Mazzella, Maria Liberata Di Sipio, Eugenio Moro, Baldovino Sponga, Pasquale Perrone Filardi, UO Cardiologia Ospedale del Cadore, Pieve di Cadore, Italy, UO Medicina Nucleare Ospedale San Martino, Belluno, Italy

Background: Electromechanical ventricular conduction disorders worsen the prognosis of heart failure patients. Cardiac resynchronization therapy (CRT) with pacing results in reverse remodeling, improvement in systolic left ventricular (LV) function, clinical response and prognosis of patients with advanced chronic congestive heart failure. However, 20% to 30% of patients are clinically non responders, with avoidable costs and exposure to unnecessary risks. We assessed the prognostic value of residual ventricular dyssynchrony (Dys) in patients who underwent biventricular pacing.

Methods: We evaluated 61 patients (age 65 ± 7 years old) with LV ejection fraction (EF) ≤ 35%, QRS ≥120 ms, NYHA class 3 or 4 despite optimal medical therapy, end diastolic volume 104 ± 14 ml/m²; intraventricular Dys in the LV was 50 ± 17° pre and 41 ± 21° post CRT, interventricular Dys was 32 ± 26° pre and 35 ± 30° post CRT. Patients were assessed with equilibrium gated radionuclide ventriculography and with echocardiography before, and 6 months after CRT. Events (death, hospitalization for worsening heart failure) were appraised during Follow-Up.

Results: During the mean Follow-Up of 27 months, 15 patients were hospitalized and 9 died. The presence of LV intra ventricular (V) but not inter V Dys was identified as an independent predictor of cardiac events (change in -2 Log Likelihood 33,875; p < 0.0001), independent of the LV EF value and QRS width. Multivariate analysis showed that LV end diastolic volume, ischemic etiology and the degree of LV intra V Dys significantly correlated with events. A cut off value of 37° for LV Dys yielded a sensitivity of 80% and specificity of 74% to predict LV reverse remodelling (reduction in EDV >15%) at receiver operator characteristic curve analysis; furthermore, it had a sensitivity of 62% and a specificity of 96% to predict a LV EF improvement (> 5 units). Patients with intra V Dys in the LV ≤ 37° at the 6-month phase analysis after CRT had an excellent prognosis (4% event rate) at the Follow-Up, as compared with a 62% event rate in patients with Dys > 37°.

Conclusions: Patients with dyssynchrony < 37° in the LV after CRT have a favorable response and show an excellent prognosis at Follow-Up.

969-129

Influence of Location of Scar Tissue in Cardiac Resynchronization Therapy

Annemieke H. Jansen, Jan Melle van Dantzig, Frank Bracke, Hans C. Post, Harry van den Bosch, Berry van Gelder, Albert Meijer, Kathinka H. Peels, Catharina Hospital, Eindhoven, The Netherlands

Background: Gadolinium-enhanced CMR can identify myocardial scar tissue. We investigated if a transmural posterolateral (PL) infarction is of influence on the acute hemodynamic effect and occurrence of left ventricular (LV) reverse remodeling after cardiac resynchronization therapy (CRT).

Method: There were 49 pts (36 male, age 69 ± 7 years). QRS duration was 167 ± 28 ms, LV-ejection fraction 22 ± 8 % and LV end diastolic volume 249 ± 97 ml. The

extent of hyperenhanced tissue on MRI with a 17-segment model was graded 0 to 4 (0: 0%; 1:1-25%; 2: 25-50%; 3:50-75%; 4:75-100%). LVdP/dt_{max} (37 pts) was derived invasively with a 0,014"sensor-tipped pressure guide wire to optimize atrio-ventricular and interventricular delay and determine acute response. LV reverse remodeling was measured by echocardiography as LV end-systolic volume decrease (LVESV Δ) after 3 month biventricular pacing.

Results: 13 pts had grade 3 or 4-scar tissue posterolateral. 10 pts had scar tissue at another location and 16 pts had no scar. The hemodynamic benefit and LV reverse remodeling response after CRT is given for the different groups in the table.

	LV dP/dt _{max} Δ (%)	LVESV Δ (%)
PL scar	14 \pm 12 (n=11)	0.2 \pm 8
Non PL scar	33 \pm 17 (n=8)	12 \pm 8
ρ	0.01	0.0009
PL scar	14 \pm 12 (n=11)	0.2 \pm 9
Viable	29 \pm 18 (n=19)	25 \pm 17
ρ	0.02	< 0.0001
Non PL scar	33 \pm 17 (n=8)	12 \pm 8
Viable	29 \pm 18 (n=19)	25 \pm 17
ρ	ns	P=0.02

Conclusion: The acute hemodynamic benefit of CRT measured by invasive LVdP/dt_{max} and the occurrence of LV reverse remodeling after 3 months pacing is strongly influenced by PL scar tissue. Infarct at other location had less influence on LV reverse remodeling in contrast to viable tissue although still significantly reduced the LV volume.

969-130 The Haemodynamic Response to Changes in Atrioventricular and Interventricular Delay of Cardiac Resynchronization Therapy Closely Fits a Parabola, Which May Allow More Efficient Optimization

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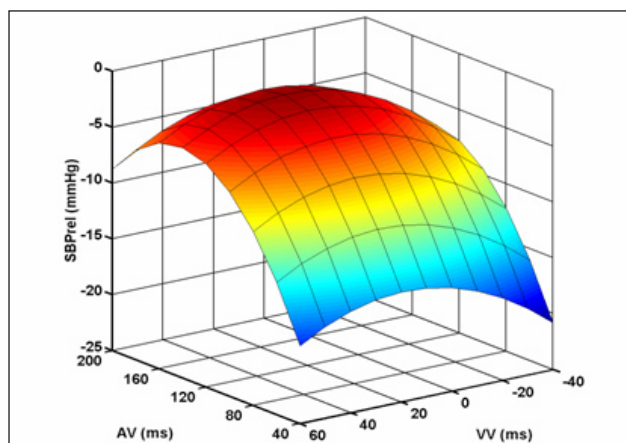
Background: Little is known about the characteristics of the haemodynamic response curves to changes in atrioventricular (AV) and interventricular (VV) delay of cardiac resynchronization therapy. In this study we assess in detail these characteristics and compare the magnitude and relative importance of adjustment in AV and VV delay.

Methods and Results: 36 different combinations of AV and VV delay were tested using digital photoplethysmography (Finometer) with repeated alternations, to measure systolic blood pressure relative to a reference pacing configuration (SBP_{rel}), in fifteen patients with cardiac resynchronisation devices for heart failure.

Changing AV and VV delay both had a curvilinear effect. However, AV delay had a significantly larger effect compared with changes in VV delay (range of SBP_{rel} 21 versus 4.2mmHg p<0.001).

The curve of response to AV delay fitted extremely closely to a parabola (average R²=0.99, average residual variance 0.8mmHg²). The response to VV delay was significantly less curved (quadratic coefficient 67 versus 1194 mmHg·s⁻² p=0.003) and therefore although the residual variance was equally small (0.8mmHg²) the R² value was 0.7.

Conclusions: Changing AV and VV delay results in a curvilinear acute blood pressure response. This shape fits very closely to a parabola, which may be valuable information in developing a streamlined clinical protocol. VV delay adjustment provides an additional, albeit smaller, haemodynamic benefit to AV optimisation.



969-131 Normalization of Left Ventricular Ejection Fraction After Cardiac Resynchronization Therapy Is More Frequent in Patients With Non-Ischemic Cardiomyopathy

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Introduction: Cardiac resynchronization therapy (CRT) reduces interventricular activation time and improves congestive heart failure symptoms. However, only a small portion of

patients will have complete normalization of measured echocardiographic parameters. We sought to characterize these patients.

Methods: The cohort of patients undergoing CRT at the University of Pennsylvania Health System was retrospectively analyzed to assess the potential relationships between lead position, clinical characteristics and normalization of left ventricular ejection fraction (LVEF). Final LV lead location was categorized into one of 17 myocardial segments using fluoroscopic images in orthogonal views. Pre- and post-implant LV chamber dimensions and EF were measured by an echocardiographer blinded to the study.

Results: Of the 163 patients included in the analysis, there were 19 patients (11.7%) with an echocardiogram demonstrating a LVEF > 50% after implantation (pre and post implant: LVEF 24.5 \pm 12.7%, 57.2% \pm 4.8 %). Of these, 16 (88.9%) had non-ischemic cardiomyopathy vs. 33.7% in the remainder of the cohort (P<0.01). The other 3 patients who had normalization of LVEF had infarctions localized to the inferior wall of the LV wall and an average LVEF of >30% prior to implantation. All 19 patients (100%) had an LV lead position on the lateral free wall of the LV vs. 81% of the remaining cohort (P<0.01). There were no other significant clinical predictors of LVEF normalization including age, sex, severity of mitral regurgitation, LV end diastolic dimension, and QRS duration.

Conclusions: Normalization of LVEF is seen in a minority of patients treated with CRT and is almost exclusively observed in patients with non-ischemic cardiomyopathy with lead positions on the lateral wall of the LV.

969-132 Evaluation of Left Ventricle Pressure Derivative Enhanced by Multi Site Pacing in Patients With Heart Failure

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Background: One of the essential point of cardiac resynchronization therapy is improvement of left ventricle (LV) pressure derivative (dP/dt). However, evaluation of dP/dt augmented by pacing multi site is not well-established. We assessed the LV pressure derivative maximum (LV+dP/dt) and minimum (LV-dP/dt) under various pacing modes including biventricular pacing, right ventricle (RV) bifocal pacing and trisite stimulation in heart failure cases.

Methods: Thirty cardiac failure patients were studied by cardiac catheterization. LV+dP/dt and LV-dP/dt were measured during atrial pacing as control atrial-ventricular sequential stimulation at a rate of 80 beats/min. Atrial-ventricular delay was fixed at 100 msec. The measurements of dP/dt during atrial-ventricular sequential stimulation at same rate were made under the following stimulation mode: RV apex, RV outflow, LV lateral, RV bifocal (RV apex + RV outflow), biventricular1 (RV apex + LV lateral), biventricular2 (RV outflow + LV lateral), trisite (RV apex + RV outflow + LV lateral).

Results: The average of baseline LV+dP/dt and LV-dP/dt were 748mmHg/sec and -781mmHg/sec. RV apex pacing decreased LV+dP/dt by 25% significantly (p<0.05). LV+dP/dt during RV outflow pacing showed no change compared with control. LV lateral, RV bifocal, biventricular1, biventricular2 and trisite pacing increased LV+dP/dt by 32%, 24%, 35%, 36% and 34%, respectively (p<0.05). Biventricular1, biventricular2 and trisite pacing increased absolute value of LV-dP/dt by 20%, 19% and 27%, respectively (p<0.05) while other pacing mode decreased these data. Trisite pacing increased absolute value of LV-dP/dt more than biventricular pacing. There was no remarkable difference of data between biventricular1 pacing and biventricular2 pacing.

Conclusions: RV apex stimulation impaired LV function, whereas RV outflow pacing preserved LV function. RV bifocal pacing provided a modest but favorable effect. LV lateral, biventricular and trisite pacing showed better performance in systolic phase than the control equally. Trisite pacing demonstrated additional effect on diastolic function.

969-133 Coronary Sinus Lead Extraction Is Safe Even With Prolonged Lead Implant Duration

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Background: With a continual increase in the implantation of cardiac resynchronization devices for severe left ventricular (LV) dysfunction, the need for extraction of coronary sinus (CS) leads has become more frequent. Published data in this area is sparse; risk of procedure unclear. This study reports our institution's experience in the removal of CS leads.

Methods: We prospectively evaluated extraction of LV CS pacing leads over a 38 month period (8/02 - 10/05). Operators clinically experienced in the lead extraction performed the procedures, using standard extraction tools as required to remove all device hardware.

Results: 29 CS leads were extracted. The patient group included 22 males and 7 females aged 63 to 85 years. Inplant duration ranged from 2 days to 27 months. Indications for lead extraction were: generator and/or lead infection with or without concurrent bacteremia (n = 23), lead malfunction or diaphragmatic pacing (n = 4), pocket erosion (n = 1), and heart transplant (n = 1). Lead models: 25 were unipolar CS leads, 3 were bipolar CS leads, and one was a bipolar model number 4024 lead placed in the CS. All leads had passive fixation mechanisms. Leads were explanted using the superior approach in all patients, except for one lead tip removed femorally from the innominate vein. All CS leads were removed with manual traction alone except for one removed with a locking stylet and Byrd dilating sheath secondary to adherence of the lead tip to the tricuspid valve. Predominate areas of fibrosis occurred in the superior vena cava at crossing points with other leads. There were no complications related to the removal of the CS leads themselves; however, 2 patients experienced transient hypotension during extraction of other leads.

Conclusions: Removing CS leads that have been in place for prolonged periods, even greater than 2 years can be accomplished without complications, usually with direct traction. Rarely, extraction tools may be needed. Main areas of lead fibrosis occurs along the venous walls outside the CS.

969-134

Development of Venous Stenosis and Occlusion After Pacemaker Implantation

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Background: Electrodes in central veins are known to predispose to venous obstruction. Although usually asymptomatic, venous stenosis may render electrode removal or replacement a difficult task. This is the first study to assess changes in venous caliber in a prospective fashion based on contrast venography (Vg) before and after pacemaker (PM) or cardioverter-defibrillator (ICD) implantation.

Methods: 150 (mean age 67; 61% male) consecutive patients referred for implantation of a first PM or ICD were enrolled, and followed for 6 months. A successful ipsilateral Vg was done both at baseline prior to device implantation and at 6-month follow-up in 137 (91%) patients. Measurements of minimum (Dmin) and maximum (Dmax) vessel diameters were obtained from both Vgs. A stenosis was defined as a 50 % diameter reduction in a venous segment. We implanted a total of 232 electrodes: 47 (34.3%) single lead, 85 (62.0%) 2-lead and 6 (4.4%) 3-lead systems.

Results: Mean baseline venous diameters were 10.6 mm (Dmin) and 17.8 (Dmax), which did not change significantly during the follow-up. At six months a stenosis was present in 14 (10 %) patients, whose average venous minimum diameter had reduced to 4.6 mm (38% of the baseline diameter). In 12 of 14 patients the stenosis developed at the same site where the vessel was narrowest at baseline. Complete venous occlusion with collateral vein development was seen in 5 (3.6 %) patients. None of the 19 patients with stenosis or occlusion exhibited any local symptoms. Clinical predictors for the development of stenosis were the presence of atrial fibrillation, obesity, higher NYHA class at baseline and older age among women.

Conclusions: This is the first systematic prospective study to assess the changes in venous caliber after pacemaker or ICD implantation. The incidence of significant venous narrowing or complete obstruction was 14 % in this material.

969-135

Antibiotic Prophylaxis is Essential in Surgical Procedures of Cardiac Implantable Devices

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Background: Antibiotic prophylaxis in artificial cardiac stimulation (ACS) surgical procedures is an unsolved question. There are few published data, once definitive conclusions require a large population protocol. Conflicting results of small studies are not enough to establish an evidence-based clinical orientation. The aim of this study was to evaluate the effects of preventive antibiotic administration previous to surgical procedures concerning ACS and also to determine eventual predictive correlations.

Methods: Patients with pacemaker or cardioverter-defibrillator surgical procedures indication were selected in a large-scale, double blind, randomized (1:1) trial. Two groups were compared: GI- Cefazolin (1,0g- single dose) versus GII- placebo. Venous administration was performed immediately before surgery. Follow-up was performed 10 days, 1, 3 and 6 months after hospital discharge. Primary end point was infectious signals at pulse generator pocket or systemic infection related to the procedure. Estimated sample size was of 1000 patients, considering infection incidence of 2% (α -error of 5%, power of 90%). Statistical analysis used the following tests: χ^2 -square, Fischer's exact, Wilcoxon and logistic regression.

Results: The security committee interrupted the trial after inclusion of 649 patients due to differences between groups in favor of the antibiotic arm (GI: 2 patients infected - 0.63%; GII: 11 patients infected - 3.28%; RR=0.19; $p=0.016$). Clinical features were similar between both groups and the following markers were identified by univariate analysis: non-use of preventive antibiotic; implant procedures (versus generator replacement); presence of post-operative haematoma and procedure duration (all with $p<0.05$). Multivariate analysis identified the non-use of antibiotic ($p=0.03$) and the post-operative haematoma ($p=0.02$) as independent predictors of infection. Occurred 15 deaths being none related to infections.

Conclusions: Antibiotic prophylaxis reduces significantly infectious complications in ACS procedures. The presence of local haematoma identifies patients with high risk of post-operative infections.

969-136

Device Erosions Are Not Associated With Systemic Infections

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Background: Implantable pacemakers (PPM) and defibrillators (ICD) can be complicated by infection and device erosion. It is unclear if the clinical features of patients who have device erosion differ from those without erosion.

Methods: We retrospectively examined the records of all patients who had explantation of a pacemaker or defibrillator from January 2000 to May 2005. We examined demographic variables including age, gender and body mass index (BMI) as well clinical variables related to the erosion and procedural variables. Chi square analysis was used to compare the distribution of discrete variables.

Results: 74 patients had infected PPM or ICDs. The mean age was 68 years, the majority (n=54) were male. Of the 74 cases, 30 (41%) developed infection complicated by erosion, of which 8/26 (31%) cases were related to AICDs and 22/46 (48%) related to pacemakers. Device erosion was significantly associated with absence of a systemic infection (3/30(10%)) as opposed to patients without erosion (21/44 (48%)) $p=0.007$. All other variables were similar between the two groups.

Conclusions: Infections associated with erosion appear to be associated with a decreased risk of systemic infection, as compared to those without erosion. This finding may have implications in the timing of device re-implantation.

Characteristics of patients with device erosion and non-erosion

	Erosion (n=30)	Non-Erosion (n=44)	p value
Fever	0 (0%)	4 (9%)	NS
Elevated WBC	2 (7%)	10 (23%)	NS
Positive blood cultures	3 (10%)	21 (48%)	$p=0.007$

969-137

A Comparison of Bleeding Complications Associated With Warfarin and Coumadin Among Patients Undergoing Device Implantation

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BACKGROUND: The management of patients on chronic anticoagulation (AC) undergoing device implantation is controversial. Common strategies include discontinuing warfarin, bridging with heparin until oral anticoagulation can be restarted or maintaining chronic warfarin therapy. Little is known regarding the risk of bleeding complications with these different approaches. **METHODS:** All patients who underwent device implantation over a 33 month period were retrospectively reviewed. These patients were categorized into 3 groups: heparin (continuous heparin administration initiated within 24 hours of device implantation), continued warfarin or no AC. Bleeding complications were defined as hematoma or bleeding requiring evacuation, transfusion or hospitalization prolongation. **RESULTS:** The study included 1,355 consecutive patients (908 men, 447 females, mean age 66) who underwent device implantation. This included 75 patients bridged with heparin, 134 maintained on warfarin (mean INR 2.0, +/- 0.55) and 1,146 on no AC. There were 12 bleeding complications in the heparin group (16%), 6 in the warfarin group (4.5%) and 2 in the absence of AC (<0.2%) during the immediate postoperative period, yielding statistically significant differences between groups (Table). **CONCLUSION:** If AC cannot be stopped safely, then maintaining warfarin is preferred to bridging with heparin.

Bleeding Complications

	Heparin	Warfarin	Neither
Bleeding Complications % (N)	16%*	4.5%*	0.2%
Notes	$p<0.007$ vs warfarin, $p<0.001$ vs neither	$*p<0.001$ vs neither	NA

969-138

Permanent His Bundle Pacing Does Not Induce Dyssynchrony. An Inpatient Comparison

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Background: Benefits of A-V synchrony during DDD right ventricular apical (RVA) pacing are neutralized by induction of ventricular dyssynchrony (VD). Only a few data are reported about Direct His Bundle pacing (DHP) influence on ventricular synchronism. Aim was to assess the capability of DHP to prevent pacing-induced VD comparing DDD- (or VVI- in case of AF) RVA pacing with DDD-(or VVI-) DHP in the same pts cohort.

Methods: 20 pts (mean age 77±7.8 yrs) with narrow QRS (<120 ms) and HV interval (<65 ms) underwent permanent DHP for "brady-tachy syndrome" (11) or suprahissian I/III-degree AV Block (permanent AF 5, AVN ablation 1). In 10 pts a back-up RVA pacing lead was used; pts were alternatively paced using either permanent DHP or RVA pacing. In the remaining 10 pts temporary DDD-(or VVI-) RVA pacing was performed through a femoral vein. A 4.1 F screw-in lead (Medtronic, Select Secure) was fixed in His position, guided by endocardial pacemapping and unipolar HB potentials. Echocardiographic (E) and PW tissue Doppler imaging (TDI) analysis assessed VD during either DHP or RVA pacing: interventricular mechanical delay (IVD) between the onset of each systolic flow, septal to left posterior wall motion delay (SPWD), and maximal difference between the longest and the shortest segmental electromechanical delay (defined as the time to onset of the systolic TDI wave), among the left ventricle basal segments (TDIMD). In 6 pts higher voltage pacing (2.34±1.32 V vs 1.2±0.54 V; x 0.5ms) resulted both in DHP and adjacent ventricular inflow septum pacing (DH+SP). A-V interval was optimized for each pacing site, using the same pacing rate.

Results: Permanent DHP was obtained in all 20 pts. Indexes of D were drastically reduced during DHP (or DH+SP) in comparison to RVA pacing ($p<0.05$). TDI-DHP, TDI-RVA and TDI-DH+SP were 18.3±11.1, 42.5±26.2 and 16±6.7 ms respectively. IVD-DHP, IVD-RVA and IVD-DH+SP were 1.3±14.5, 40.7±12.4, and 9.4±9.1 ms respectively. SPWD-DHP, SPWD-RVA and SPWD-DH+SP were 51.4±39.2, 152.5±70.5 and 67±39.3 ms respectively. No difference was observed between DHP and combined DH+SP.

Conclusions: DHP (also fused with adjacent septum capture) prevents pacing-induced VD.

969-139

Avoidance of Left Ventricular Dyssynchrony Detected by Tissue Doppler Echocardiography by Permanent Right Ventricular Septal Pacing in Patients With High-Grade Atrioventricular Block

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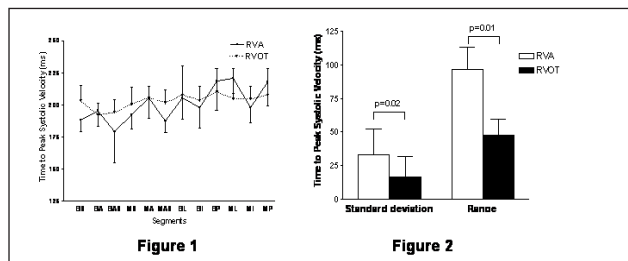
Background: Prior studies suggested that permanent right ventricular apical (RVA) pacing induced left ventricular (LV) dyssynchrony and impaired LV function. Whether alternative right ventricular septal (RVS) pacing can avoid this long-term deleterious effects of permanent pacing remain unclear.

Methods: We randomised 26 pts with high-grade atrioventricular block (AVB) without

structural heart diseases to receive either RVA (n=13) or RVS (n=13) pacing during DDD pacemaker implantation. Radionuclide ventriculography (MUGA scan) and tissue Doppler echocardiography were performed at 24 months after pacemaker implantation to assess LV function and LV mechanical synchrony. LV synchrony was assessed by a 6-basal, 6-mid segmental model and measure the time to peak sustained systolic velocity (TS).

Results: Pts with RVS pacing had a significantly narrow QRS duration than those with RVA pacing (145±4 vs. 165±5 ms, P=0.04), but a similar baseline LV ejection fraction on MUGA scan (56±5 vs. 54±3%, P=0.7). At 24 months, RVS pacing is associated with a significantly higher LV ejection fraction (55±3 vs. 47±5%, P=0.03) and more homogeneous LV contraction as shown by closing time of TS among all 12 segments (Figure 1, P<0.05) and a lower range and standard deviation of TS (Figure 2, P<0.05).

Conclusions: The results of this study demonstrated that long-term RVS pacing can avoid LV dyssynchrony as observed in RVA pacing and preserve LV function in pts with high grade AVB.



969-140 Atrial Versus Dual Chamber Pacing in Sinus Node Disease

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Background: Sinus Node Disease (SND) is a common indication for implantation of a permanent pacemaker. There is a good evidence to support atrial pacing rather than ventricular based pacing but there is some risk of subsequent atrioventricular block development. In such cases upgrade of atrial pacemaker (AAI) to dual-chamber (DDD) is necessary, what creates additional costs of therapy. The aim of the study was to compare costs of primary DDD pacing system implantation to primary AAI implantation, in pts without DDD indications at the time of first implantation, taking into account the future necessity of AAI to DDD upgrade in some cases.

Methods: The data of 752 patients with SND who had AAI implanted between 1993 and 1997 were identified. The records of patients were examined to find cases that required further procedure to upgrade AAI to dual chamber. Observational period: 5.0 - 10.0 (mean 7.4 y). The cost comparison analysis was based on deterministic model in the time window of 10 years. Model assumptions: Pacemaker battery longevity: AAI - 8 y; DDD - 6 y; linear pacing costs depreciation; discount rate 5%. The costs were calculated from the public health care payer perspective. Sensitivity analysis was performed for upgrade to DDD rate and procedure costs.

Results: The rate of upgrade to DDD was 19.1% within mean 7.4 y. period in the studied population. The projected to 10 years rate of upgrade was 25.8%. Cost of primary DDD strategy was 4719 USD PPP (Purchasing Power Parity). Cost of current strategy (primary AAI) was 3804 USD PPP, and cost of hypothetical (ideal) strategy in which all patients that would need upgrade in the future were identified before implantation was 3505 USD PPP. Primary DDD would become equal to primary AAI strategy if upgrade rate was 56% or more. The lower relative DDD costs the lower was the equality upgrade rate, and the higher absolute differences the more beneficial was AAI strategy.

Conclusions: Implantation of AAI pacemaker in patients with SND without DDD indications is cost saving comparing to DDD implantation in each patient. Better identification of patients who will need future upgrade to DDD may bring additional savings.

969-141 Evolution of Left Ventricular Function in Pediatric Patients With Permanent Right Ventricular Pacing for Isolated Congenital Heart Block: A Medium Term Follow-Up

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Background: RVA pacing can be detrimental on LV function in a significant number of adults. Effects in children are still controversial. We aimed to assess the evolution of left ventricular (LV) systolic function in children with right ventricular apical (RVA) pacing for isolated congenital heart block (ICHB) and to identify possible predictors of LV function deterioration.

Methods: LV shortening fraction (LV SF) and QRS width were retrospectively assessed in 45 children with RVA pacing for ICHB: before pacemaker (PM) implantation, immediately after and then regularly during a follow-up of 58.69±45.23 months. Patients were categorized as stable and deteriorator according to an arbitrarily chosen cut-off point of ≥7% decrease in LV SF.

Results: Overall LV SF did not change significantly (41.42%±8.21 before pacing, 39.77%±7.03 immediately after PM implant, 37.43%±9.91 with chronic pacing, p=NS). Deteriorators (n=13) had significantly higher baseline heart rate (57.5±8.7 bpm vs 46.9±10.5 bpm, p<0.05) and baseline LV SF (46.17±8.13% vs. 38.4±6.4%; p<0.05), a significantly higher proportion of them being implanted before 2 years of age: 8 of 13 (61.5%) vs 5 of 25 (20%) in the stable group (p<0.05). Deteriorators had a higher

incidence of an initial epicardial lead and narrower native QRS.

Conclusions: Permanent RVA pacing for ICHB does not necessarily affect LV function in children. The risk for deterioration of LV function seems to be higher in children with higher baseline heart rate and better baseline LV SF, especially with pacing at a younger age, a narrower native QRS and RVA epicardial pacing site.

969-142 Baseline Systolic Blood Pressure Predicts Response to Cardiac Resynchronization Therapy in Heart Failure Patients

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Background: Despite the use of specific selection criteria, about one-third of patients with chronic heart failure (HF) do not benefit from cardiac resynchronization therapy (CRT). Systolic blood pressure (SBP) is a simple measurement, and serves as a major prognostic indicator in HF which is used to determine patient tolerability and eligibility for specific therapy. The effect of baseline SBP on subsequent response to CRT in HF patients has not been previously described.

Methods: We studied 126 patients enrolled in a prospective, multicenter, randomized double-blind controlled trial, the Resynchronization for Hemodynamic Treatment for Heart Failure Management (RHYTHM) study. Patients were required to have NYHA Class III/IV HF, LVEF ≤ 35%, QRS ≥ 150ms, and an indication for an ICD. They were divided into two groups based on pretreatment SBP: Group 1 (n=47) with SBP ≤ 110mmHg and group 2 (n=79) with SBP>110mmHg. The effect of CRT on six-month study endpoints of peak oxygen consumption (VO₂), exercise duration, and quality of life was evaluated within each group.

Results: Baseline characteristics were similar between the CRT OFF and CRT ON groups within groups 1 and 2. At 6 months, patients in group 1 with CRT ON had a significant increase in SBP compared with CRT OFF (13 mmHg, p=0.002), while patients in group 2 had no significant change in SBP compared to baseline. Patients in group 1 with CRT ON also had a significant improvement in peak VO₂ (1.6 ml/kg/min, p=0.01), exercise time (3.3 min, p=0.004) and quality of life (19 points, p=0.03) compared with those with CRT OFF. In contrast, group 2 patients with CRT ON or CRT OFF showed no significant difference in any of these endpoints.

Conclusion: Patients with severe HF and low pretreatment SBP show a greater functional benefit from CRT than those with high pretreatment SBP. Baseline SBP can potentially identify responders to CRT.

969-143 Lack of Association Between QRS Duration and Cardiac Asynchrony in Candidates for Cardiac Resynchronization Therapy

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Background: Although QRS duration has been widely used for the selection of candidates for cardiac resynchronization therapy (CRT), echocardiographic markers of cardiac dyssynchrony (CD) have been demonstrated to accurately identify CRT responders. We evaluated the association of QRS duration with CD in a cohort of consecutive patients, hospitalized for refractory to medical treatment heart failure.

Methods: We studied 52 consecutive patients who were candidates for CRT based on clinical criteria. The majority of the studied patients were males (83%) and suffered from ischemic cardiomyopathy (56%). The maximum QRS duration was measured by four experienced cardiologists and the inter- and intraventricular electromechanical delay (ED) were estimated by Doppler and TDI echocardiography.

Results: In univariate analysis, patients with prolonged QRS duration (≥130ms) had significantly higher interventricular ED and lower LVEF. However, the septal to lateral intraventricular ED did not differ significantly between the two study groups. In multivariate analysis adjusted for age, gender, LVEF, LVDD, NYHA stage and the existence of LBBB, prolonged QRS duration was not found to be significantly and independently associated with either interventricular or intraventricular ED.

Conclusions: In this study population of consecutive patients hospitalized for refractory heart failure, who were candidates for CRT, prolonged QRS duration was not an independent predictor of cardiac asynchrony.

Baseline characteristics in relation to QRS duration

	QRS<130ms (n=19)	QRS≥130ms (n=33)	p value
QRS (ms)	112±10	163±25	<0.001
Age (yrs)	67±13	65±10	0.625
NYHA	2.7±0.8	2.9±0.7	0.242
LVDD (mm)	59±5	64±10	0.058
LVEF (%)	35±8	28±8	0.009
Interventricular delay	4±16	27±31	0.004
Intraventricular delay	80±43	65±33	0.174

826

Arrhythmias: Models and Basic Science

Monday, March 13, 2006, 4:00 p.m.-5:00 p.m.
Georgia World Congress Center, Room B407

4:00 p.m.

826-3

High-Septal Pacing Reduces Electrical Remodeling and Arrhythmogeneity in the Chronic Atrioventricular Block Dog

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Background: Ventricular electrical remodeling (VER) in chronic AV block has 3 contributors: bradycardia, altered activation, and lack of AV synchrony. Studies in AV block rabbits paced from the right ventricular apex suggest that the extent of rate drop is the main factor in VER. With high-septal pacing (HSP) in AV block dogs, the relevance of preserved activation in VER was elucidated. **Methods:** AV block dogs were either paced from the high ventricular septum near the His-bundle at the lowest captured rate (n=7, HSP) or kept at idioventricular rate with uncontrolled activation (n=14, C). Measurements under anaesthesia at 0 and 4 weeks were: left and right ventricular monophasic action potential duration (LV and RV MAPD), RR, and RT-time. Arrhythmogenic response was tested at 4 weeks by 25 µg/kg I_{Kr} blocker dofetilide iv. **Results:** At 0 weeks both groups were comparable (table), but not after 4 weeks of similar bradycardia: values increased more in C than HSP. RT increased 34±23% in C, but only 15±15% in HSP, P<0.05. Interventricular dispersion of repolarization (LV-RV MAPD) increased only in C. Torsade de Pointes arrhythmias were induced in 29% in HSP vs 78% in C, P=0.14. Enhanced arrhythmogenesis was also seen using variables like the mean number of arrhythmias per dog: C 13±16 vs HSP 1±2 arrhythmias/10min, P<0.05. **Conclusion:** HSP reduces the magnitude of VER and arrhythmogeneity in AV block dogs, suggesting that altered activation has a larger role in generation of VER than previously assumed.

Table:

Data: means ± SD (ms)		0 weeks	4 weeks		
Ctrl n=14	RR	1190 ± 300	1344 ± 262	*	
	RT	273 ± 19	363 ± 61	*	
	LV MAPD	262 ± 23	369 ± 54	*	
	RV MAPD	239 ± 19	310 ± 52	*	
	LV-RV MAPD	17 ± 10	60 ± 31	*	
HSP n=7	RR	1173 ± 203	1406 ± 205	*	
	RT	278 ± 22	317 ± 36	*	\$
	LV MAPD	269 ± 20	302 ± 36	*	\$
	RV MAPD	241 ± 17	275 ± 17	*	\$
	LV-RV MAPD	28 ± 11	27 ± 10		\$
		* P<0.05 vs 0 weeks	\$ P<0.05 vs C		

4:15 p.m.

826-4

Heat Shock Proteins Prevent Atrial Tachycardia Remodeling and Atrial Fibrillation Promotion

Bianca J.J.M. Brundel, Akiko Shiroshita-Takeshita, Xiao Yan Qi, Denis Chartier, Robert H. Henning, Harm H. Kampinga, Stanley Nattel, Montreal Heart Institute, Montreal, PQ, Canada, University of Groningen, The Netherlands

Background: There is evidence that heat shock proteins (HSPs) protect against atrial fibrillation (AF) in a variety of clinical paradigms. We evaluated the effect of HSP induction in a paced atrial cell-line (HL-1) model of tachycardia-remodeling and on AF-promotion by atrial tachycardia-induced remodeling in dogs. **Methods:** We studied the effects of tachypacing in HL-1 cells (3 Hz, 0-4 hrs) on Ca²⁺ transients (CaT) and cell shortening (CS), with and without HSP-inducing pre-treatments using a mild heat shock (20 min 43°C + 16 h 37°C) or the heat shock stress response co-inducer geranylgeranylacetone (GGA, 10 µM, 2 hrs before and during pacing). *In vivo*, dogs were subjected to atrial tachypacing at 400 bpm for 7 days in the absence (n=5) and presence of GGA treatment (120 mg/kg/day, n=5), starting 3 days before and continued throughout tachypacing. Results were compared to a non-paced control group (n=5). **Results:** In HL-1 cells *in vitro*, tachypacing significantly and progressively reduced CaT up to 79% after 4 hours of pacing. In parallel, CS was reduced to 68% at 4 hours. Either HS pre-treatment or GGA treatment before and during pacing almost completely prevented tachycardia-induced reductions in CaT and CS. In dogs *in vivo*, atrial tachypacing increased the mean duration of induced AF from 23±13 seconds to 816±402 seconds (*P<0.01) and increased atrial vulnerability (% of atrial sites inducing AF by single extrastimuli) from 10 to 56%, while decreasing the atrial effective refractory period (ERP) from 121±7 to 67±7 ms*. *In vivo* treatment with GGA increased HSP expression and suppressed all these tachypacing-induced changes: with GGA, the mean duration of AF after 7-day tachypacing was 35±11 seconds, atrial vulnerability was 18±5 %, and ERP was 101±2 ms. **Conclusions:** Augmentation of HSP expression protects against tachycardia-induced reductions in cell shortening and Ca²⁺ transients *in vitro* and prevents the electrophysiological and AF-promoting consequences of atrial tachycardia *in vivo*. These findings support the hypothesis that HSP may be an important endogenous suppressor of AF-promoting remodeling and provide a rationale for HSP system manipulation for therapeutic prevention of AF.

826-5

Possibility of Electrical Bridging over AV Groove by the Artificial Epicardiac Accessory Pathway in a Rat Model of Atrio-Ventricular Block

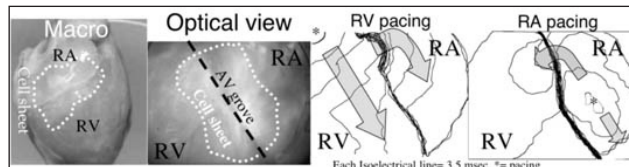
Toshiaki Sato, Shunichiro Miyoshi, Koutarou Fukumoto, Akira Furuta, Yuji Itabashi, Shinichiro Kira, Nobuhiro Nishiyama, Seiji Takatsuki, Kyoko Soejima, Tatsuya Shimizu, Teruo Okano, Satoshi Ogawa, Keio University, School of Medicine, Tokyo, Japan, Tokyo Women's Medical University, Institute of Advanced Biomedical Engineering and Science, Tokyo, Japan

Background: Regenerated cardiomyocytes can be derived from stem cell *in vitro*. Lately novel technology has enabled to make transplantable cell-sheet grafts from cultured cardiomyocytes in fibrin polymer dishes. We have already shown electrical communication from this graft to host-ventricle. Therefore, we implanted the graft as an artificial accessory pathway in rats with complete atrio-ventricular block (CAVB) to treat bradycardia.

Methods: Subjects were 7 nude rats. After making CAVB by ethanol injection, grafts were implanted and bridged over Rt. AV groove. Seven days after that, surface ECG was recorded and electrical conduction was studied on 6 perfused hearts by optical mapping system.

Results: Whereas 2 rats died due to severe bradycardia and AV-node conduction was recovered in 2 rats, CAVB was maintained in 3 rats with wide-QRS waves of inferior axis, LBBB and slurred beginning. The wide-QRS wave followed P-wave intermittently in 1 rat and appeared during slow rate of escape beats with different morphology in 2 rats. Optical mapping system revealed that ventricle activation was spread from the ridge of Rt. atrial appendage during A pacing in 2 rats and atrial activation was propagated from there during V pacing in 1 rat.

Conclusions: In a rat model of CAVB with artificial accessory pathway, ventricle can be driven with specific wide-QRS waves. Activation pulse may be propagated over AV groove through implanted graft. This may suggest a therapeutic potential of cell-sheet graft for CAVB.



4:45 p.m.

826-6

A Common Polymorphism H558R in SCN5A is Associated with Lone Atrial Fibrillation

Lin Y. Chen, Jeffrey D. Ballew, Kathleen J. Herron, Timothy M. Olson, Mayo Clinic College of Medicine, Rochester, MN

Background We have shown that mutations in the cardiac sodium channel gene (*SCN5A*), predicted to reduce sodium current, can cause a syndrome of dilated cardiomyopathy (DCM) and atrial fibrillation (AF). The minor allele of the common polymorphism H558R in *SCN5A* is associated with reduced sodium current. We hypothesized that either *SCN5A* mutations or presence of the minor R558 allele may increase susceptibility to lone AF.

Methods We recruited 157 unrelated probands with lone AF for genetic analysis. The 28 translated exons of *SCN5A* were scanned for DNA sequence variation using D-HPLC heteroduplex analysis. Samples that formed heteroduplexes were analyzed further by sequencing. H558R was genotyped by restriction fragment length polymorphism analysis. We compared the allele frequencies in the AF cohort with 314 age and gender matched normal Caucasian controls. Categorical and continuous variables were tested using the χ^2 test and rank-sum test, respectively.

Results Our AF cohort was 100% Caucasian (77% males, mean age at diagnosis 44 ± 10 yrs). DNA scanning and sequence analyses did not identify mutations that altered splice junctions or protein sequence. The genotype frequencies in the AF cohort vs. normal controls were: HH, 50% vs. 63%; HR, 40% vs. 33%; and RR, 10% vs. 4%; p=0.008. The R558 allele was more common in our cohort than in controls (30% vs. 21%, p=0.002) and compared with the H558 allele, conferred an odds ratio for AF of 1.6 (95% CI 1.2 - 2.2). The mean age at diagnosis in AF males with HR or RR genotype was earlier than HH homozygotes (42 vs 46 yrs, p=0.03). In AF males, RR homozygotes had longer QRS duration (msec) (median, interquartile range: 108, 102 - 118) than HH (98, 90 - 108) or HR (96, 88 - 106) (p=0.02).

Conclusions Mutations in *SCN5A* can cause a syndrome of DCM and AF, but are not a common cause for lone AF. However, there was an increased frequency of the R558 allele among lone AF patients compared with normal controls. The R558 allele was associated with younger age at diagnosis in males. RR homozygote males had a prolonged QRS duration that may suggest reduced sodium current. We conclude that the R558 allele, associated with reduced sodium current, may confer susceptibility to lone AF.

POSTER SESSION

992

Noninvasive Risk Stratification

Tuesday, March 14, 2006, 8:30 a.m.-Noon
 Georgia World Congress Center, Hall B1
 Presentation Hour: 11:00 a.m.-Noon

992-123 **Do ECG Abnormalities Pose the Same Risk for Women and Men?**

Kavita V. Ernst, Swee Y. Tan, Marcus Sandri, Gregory Engel, Jonathan Myers, Victor F. Froelicher, Stanford University School of Medicine, Stanford, CA, VA Palo Alto Health Care System, Palo Alto, CA

Background: There is controversy regarding the relative prognostic value of the resting ECG in women vs men.

Objectives: To compare the diagnostic criteria of computerized ECG measurements in men and women in a large Veteran outpatient with follow up for cardiovascular death.

Methods: Since 1987, digitized ECGs were recorded and analyzed using the GE/Marquette computerized ECG system. ECGs were ordered at physician discretion for usual clinical indications. Through 2000, 45,855 resting ECGs were available for consideration. After removal of inpatients and those with pacemakers and WPW, 33,312 patients (29,320 men and 3,992 women) remained. Limited demographics were available (age, gender, race, weight, height, recording location) and the population was followed until 2002 as to cause of death using the California death index. ECG criteria considered included bundle branch block, left ventricular hypertrophy (LVH), atrial fibrillation (AF), ST depression, diagnostic Q waves, left atrial abnormality (LAA) and QT prolongation. Kaplan Meyer survival curves were plotted and age and heart rate adjusted Cox Hazard analyses performed.

Results: The mean age and BMI were (55.9±/0.1) years and (27.5±/0.1) for males and (56.9±/0.1) years and (26.2±/0.1) for females (p<0.001). With the exception of left bundle branch block (LBBB), right ventricular hypertrophy, QT prolongation and left atrial abnormality, all ECG abnormalities were at least twice as prevalent in males compared to females. After a mean follow up of 7.5 years, the annual mortality was 1.1% for males and 0.6% for females (P< 0.001). All ECG abnormalities had significant hazard ratios (HR) in men. The HRs were greater than 2 or more in all except right bundle branch block, AF and left axis deviation. In females, only LVH and ST depression were associated with significant HR of 2 while LBBB demonstrated a HR of 1.2.

Conclusion: In this veteran population, there were significant differences between men and women in the prevalence and prognostic value of classic ECG criteria. While LVH was associated with a similarly high HR (2 to 3 fold increase), LBBB, RVH and prolonged QT only had a significant HR (greater than 2) in men.

992-124 **QTc Variability in Patients With Long QT Syndrome: The Importance of the Maximum QTc Value From Follow-Up Electrocardiograms in Predicting Cardiac Events**

Jehu Mathew, Ilan Goldenberg, Arthur J. Moss, Wojciech Zareba, Derick R. Peterson, Scott McNitt, Mark L. Andrews, Brian Morray, Jeseia Benhorin, International Long QT Syndrome Registry, University of Rochester School of Medicine and Dentistry, Rochester, NY

Background: A baseline corrected QT interval (QTc) value ≥ 500 msec has been shown to be associated with an increased risk of subsequent cardiac events among Long QT Syndrome (LQTS) patients. However, the value of follow-up electrocardiograms (ECGs) in risk assessment has not been determined.

Methods: A multivariate Cox survivorship model was used to assess the probability of a cardiac event (syncope, aborted cardiac arrest, or LQTS-related sudden cardiac death) between the ages of 10-20 years in 375 patients enrolled in the International LQTS Registry in whom two or more ECGs were recorded before the age of 10.

Results: The mean \pm SD difference between the maximum and minimum mean values of the QTc measures was 47 ± 40 msec. Multivariate analysis demonstrated that the maximum QTc interval recorded before the age of 10 was associated with the highest risk of cardiac events (HR=4.09, p=0.002) during adolescence, whereas other follow-up QTc parameters, including the most recent QTc (HR =2.81, p=0.01), the mean QTc (HR=2.80, p=0.02), and the baseline QTc (HR=1.72, p=0.20) were associated with a lower risk of cardiac events. When the baseline QTc and the maximum QTc during follow-up were entered into the same model, a baseline QTc ≥ 500 msec was no longer predictive of cardiac events (HR= 0.82; p=0.72).

Conclusions: In LQTS patients, there is considerable variability in QTc measures on follow-up ECGs. The maximum QTc interval provides incremental prognostic information over a baseline measurement. We suggest that risk stratification in LQTS patients should include follow-up ECG data.

992-125 **Repolarization Complexity is Increased in Left Ventricular Hypertrophy: The Strong Heart Study**

Peter M. Okin, Marek Malik, Katerina Hnatkova, Elisa T. Lee, James Galloway, Lyle G. Best, Barbara V. Howard, Richard B. Devereux, Cornell Medical Center, New York, NY

Background: ECG measures of ventricular repolarization complexity and heterogeneity have been shown to predict cardiovascular (CV) and all-cause mortality. Left ventricular hypertrophy (LVH) has been associated with an increased risk of ventricular arrhythmias and with arrhythmic, CV and total mortality. However, whether these T-wave descriptors are independently related to ECG LVH has not been examined.

Methods: The relationship of QTc and novel ECG variables characterizing the T-wave loop to ECG LVH was assessed in 2113 American Indian participants in the first Strong Heart Study exam. T-loop morphology was quantified by the ratio of the second to

first eigenvalues of the T-wave vector (PCA ratio), total cosine R to T (TCRT), T-wave morphology dispersion (TMD) and by the sum of the squares of the 4th to 8th eigenvalues, the T-wave residuum (TWR). ECG LVH was measured using gender-adjusted Cornell product (CP) criteria: (RaVL+SV3 [+6 mm in women])*QRS duration >2440 mm*msec, and was present in 307 (14.5%).

Results: CP LVH was associated with a prolonged QTc (445±28 vs 430±24 ms/sec/1/2), higher PCA ratio (22.3±12.5 vs 18.3±11.3%), greater TMD (31.3±24.6 vs 17.7±15.5 degrees) and TWR (67.1±128.1 vs 37.9±53.2 technical units x 10⁻³), and with a lower TCRT (-0.13±0.56 vs 0.40±0.51, all p<0.001). In a step-wise linear regression analysis that included age, sex, blood pressure, and all ECG variables, TCRT, sex, systolic pressure, QTc, TMD, the PCA ratio and TWR all significantly correlated with the magnitude of CP LVH. In a step-wise multivariate logistic regression model that included the same variables, TCRT, TMD, TWR, QTc, systolic pressure and female gender all remained significant predictors of the presence of LVH by CP criteria, with lower TCRT being the strongest predictor (odds ratio 2.42 [per 1 SD of mean decrease in TCRT], 95% CI 2.05-2.87, chi-square=105.2, p<0.001).

Conclusions: ECG measures of repolarization complexity are increased in CP LVH and independently associated with the presence and severity of LVH by CP. These findings suggest that abnormalities of ventricular repolarization may contribute to the increased mortality associated with LVH.

992-126 **Heart Rate Turbulence Onset After Atrial Premature Complexes Does Not Reflect Cardiac Autonomic Regulations in Postinfarction Patients**

Dan Wichterle, Maria T. La Rovere, Peter J. Schwartz, Marek Malik, First Medical School, Charles University, Prague, Czech Republic, St. George's Hospital Medical School, London, United Kingdom

Background: The purpose of the study was to assess the relationship between Turbulence Onset after atrial premature complexes (APCs) and other indices of cardiac autonomic modulation.

Methods: Analysis was performed in Holter recordings (n = 1085) of ATRAMI (The Autonomic Tone and Reflexes After Myocardial Infarction) population. Heart rate turbulence described by Turbulence Onset and Turbulence Slope after ventricular premature complexes (VPCs) and after APCs was correlated with low- and high-frequency spectral indices of heart rate variability (HRV) and baroreflex sensitivity assessed by the phenylephrine method.

Results: All heart rate turbulence indices except Turbulence Onset after APCs significantly correlated (Spearman rank correlation) with spectral HRV and baroreflex sensitivity.

	Turbulence Onset after VPCs	Turbulence Slope after VPCs	Turbulence Onset after APCs	Turbulence Slope after APCs
Baroreflex sensitivity	-0.32	0.49	-0.08	0.39
Low-frequency HRV	-0.44	0.65	-0.07	0.59
High frequency HRV	-0.37	0.58	-0.02	0.55

Conclusions: Unlike other descriptors of heart rate turbulence, Turbulence Onset after APCs does not reflect cardiac autonomic regulations. It was previously demonstrated that early RR interval dynamics after APCs is substantially modified by the suppression of sinus nodal automaticity due to direct effect of APC. Consequently, Turbulence Onset after APCs reflects the sinus node dysfunction rather than vagal modulation.

992-127 **Heart Rate Turbulence as a Marker of Severity of Congestive Heart Failure**

Ilona Cygankiewicz, Wojciech Zareba, Montserrat Vallverdu, Rafael Vazquez, Jesus Almandral, Miguel Fiol, Juan Cino, Pere Caminal, Antoni Bayes de Luna, on behalf of MUSIC Trial Investigators, Hospital St Pau, Barcelona, Spain, University of Rochester, Rochester, NY

Background: The aim of our study was to determine whether heart rate turbulence (HRT) could be considered as a marker of congestive heart failure (CHF) advancement and progression giving insight into hemodynamic changes as well as changes of the autonomic nervous system.

Methods: Clinical evaluation, 12-lead ECG, echocardiography, chest X-ray, series of laboratory tests (electrolytes, creatinine, troponine, and proBNP) and 24-hour Holter monitoring with HRT (turbulence slope -TS and turbulence onset- TO) and HRV parameters analyses were performed in consecutive CHF patients (pts) with NYHA class II and III and sinus rhythm.

Results: The study population consisted of 589 pts (425 men) with mean age 65 yrs, mean LVEF of 37±14%, with majority of pts (82%) in NYHA class II. Abnormal HRT parameters (HRT1 or HRT2) were found in 64% of studied pts. Both HRT parameters, but especially TS significantly correlated with clinical indices of heart failure as the third tone, peripheral oedemas, jugular distension and pulmonary congestion (on chest X-ray). Patients with NYHA class III has significantly lower TS and higher TO values than those in class II (TS 1.59 vs 3.09 ms/RR, p<0.001). Significant correlations were found between HRT parameters and LVEF (r=-0.27, p<0.001 for TS) as well as with left ventricle diameters and mitral regurgitation degree. Increased levels of blood markers of advanced CHF stage (proBNP, creatinine, troponine) were associated with more abnormal HRT measures. Pts with more abnormal HRT indices had more advanced abnormalities of autonomic nervous system assessed as reduced HRV parameters. Multivariate analyses testing the association between abnormal HRT and NYHA class and low ejection fraction (<40%) showed that abnormal HRT parameters: HRT2, HRT1, abnormal TS, abnormal

TO are independent predictors of NYHA class III or LVEF<40%.

Conclusions: Our findings indicate that in CHF patients HRT reflects well the severity of heart failure and associated left ventricular dysfunction, which were verified in this study by a series of established clinical, echocardiographic and biochemical parameters.

992-128 Evolution of the Paced and Nonpaced QRS Duration With Chronic Right Ventricular Pacing in Pediatric Patients With and Without Structural Heart Disease

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Background: Currently QRS duration is a selection parameter for cardiac resynchronization therapy (CRT) in adults. Criteria for CRT in pediatric patients are not yet implemented.

Aim: Right ventricular (RV) pacing creates artificial left ventricular dyssynchrony and thus can be used as a surrogate for left bundle branch block. Our aim was to assess the evolution of the QRS width in chronically paced pediatric patients with and without structural heart disease (HD) and to compare the data to the cut-off value for cardiac resynchronization in adults.

Methods: A group of 99 pediatric patients (56 males) with a previously implanted pacemaker was studied retrospectively. Forty-three patients had isolated AV block (IAVB), 24 patients had complex congenital malformations and the remaining 32 had isolated congenital HD. Patients were followed up for an average of 50.6±41.3 months. QRS width was measured in lead V5 or II on ECG recordings with paper speed of 50 or 25 mm/sec. Data on QRS width were analyzed in six age groups (group I: <1 yr, group II: 1-2 yrs, group III: 3-4 yrs, group IV: 5-7 yrs, group V: 8-11 yrs, group VI: 12-15 yrs).

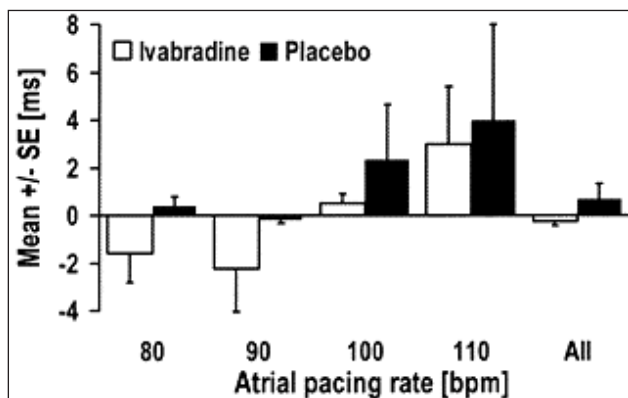
Results: Paced QRS duration showed progressive widening during the follow-up (group I: 109.3±23.4 ms, group VI: 152.8±25.7 ms, p<0.05). Similar increase in non-paced QRS duration was observed (group I: 58.8±16.7 ms, group VI: 95.5±30.2 ms, p<0.05). Patients with structural HD reached the widest paced QRS (age group VI - complex congenital HD: 160±21.9 ms, isolated structural HD: 154.3±32.5 ms, IAVB: 147.5±18.1 ms).

Conclusions: 1) Chronic RV pacing in pediatric patients with or without structural HD does not cause widening of the QRS complex over 120 ms until the age of 2 years. 2) Current adult cut-off value of 130 ms for CRT is not reached until the age of 4 years and cannot be used within this age frame as a parameter for selecting the optimal pediatric patients for CRT. 3) Paced QRS width of 150 ms, beyond which ECG identifies more reliably left ventricular dyssynchrony, is not reached until the age of 12-15 years. 4) The presence of an either isolated or complex congenital HD results in a wider paced QRS complex.

992-129 Noninvasive Electrophysiological Study of Ivabradine (NES) in Patients With Dual Chamber Pacemakers: Effects on Ventricular Repolarization

Irina Savelieva, Sue Jones, Kate Dougal, Marek Malik, John Camm, St George's University of London, London, United Kingdom

Ivabradine (IVA) is a selective inhibitor of the I_c current with potential antiarrhythmic actions. IVA-induced heart rate (HR) reduction is associated with QT prolongation; no changes were observed when QT was corrected for HR. The aim of this study was to investigate if QT prolongation is entirely due to bradycardia or to a direct effect of IVA on ventricular repolarization (VR). **Methods:** To avoid limitations of invasive EP testing, we studied 25 pts (63±10 yrs; M/F 16/9; sinus node disease [SND], 14; 1°-2° AV block [AVB], 11, incl. AVB+bundle branch block [BBB], 5) with DDD pacemakers with non-invasive programmed stimulation (NIPS) in the prospective randomized, double blind, placebo controlled study of oral IVA 5 (n=8) or 10 (n=8) mg bd. Atrial pacing (AP) at 80, 90, 100, 110 bpm and ventricular ERP (VERP) measurements were performed before and after 3½ days of treatment. AP at fixed rates allows for direct QT comparisons at the same HR, with no need for HR correction. A continuous 12-lead digital Holter recording was used for QT analysis. **Results:** IVA did not prolong QT during AP compared with placebo (Figure). The subgroup analysis in SND and AVB±BBB showed identical results. IVA 10 mg bd slightly increased VERP vs baseline (274±21 vs 264±20 ms; p=0.033; IVA 5 mg bd: 271±16 vs 267±17 ms; p=0.36; placebo: 266±36 vs 258±36 ms; p=0.055). **Conclusions:** The study demonstrated the feasibility of NIPS for assessing the EP effects of oral agents. Direct QT comparisons during AP showed no direct pharmacologic effect of IVA on VR.



992-130 Determination of Atrial Flutter Type Using Interactive ECG Analysis

Carl W. Musser, Jr., Stephen C. Hammill, Mayo Clinic College of Medicine, Rochester, MN

Background: The morphology of the 12-lead electrocardiogram (ECG) can give important insights into atrial flutter activation patterns. Commonly used criteria to distinguish between cavotricuspid isthmus (CTI) dependent and non-CTI dependent atrial flutter are often insufficient. An interactive ECG interpretative process may identify flutter wave characteristics that improve the ability to make this distinction.

Methods: A custom software application was developed for computer-assisted ECG interpretation that functioned interactively with a user that directed the interpretive process. The software displayed digital 12-lead ECG data followed by user identification of flutter wave onset and offset in a single lead. The software then calculated simultaneous characteristics in all leads including flutter wave amplitude and cycle length. The study population consisted of 28 patients with documented atrial flutter referred for ablation. An ECG tracing demonstrating atrial flutter was analyzed for each patient prior to electrophysiologic study. Flutter wave activation sequence was confirmed by intracardiac mapping.

Results: In CTI-dependent (typical) atrial flutter (20 patients), 19 tracings (95%) demonstrated flutter wave polarity transition in lead I. The maximum limb and precordial lead flutter wave amplitudes occurred most often in lead II and V4, respectively. In non-CTI-dependent (atypical) atrial flutter (8 patients), only one tracing (12%) showed flutter wave polarity transition in lead I. The maximum limb and precordial lead peak-to-peak voltages occurred most often in lead III and V1, respectively. The mean flutter waveform cycle length was significantly longer and the mean waveform amplitudes significantly were larger for typical flutter as compared to atypical flutter.

Conclusions: Computer-assisted ECG analysis that allows a user to direct the interpretive process identified previously unrecognized differences between CTI and non-CTI dependent atrial flutter.

992-131 ST-Elevation in Lead aVR During Exercise Testing Should Not Be Ignored

Johnne Neill, Amanda Morton, Joanne Shannon, Alison Muir, Mark Harbinson, Jennifer A. Adgey, Royal Victoria Hospital, Belfast, United Kingdom

Background: The diagnostic significance of ST elevation (STE) in lead aVR during exercise is controversial. Lead aVR is directed towards the left ventricular (LV) cavity and so changes may indicate LV dysfunction on exercise. We aimed to assess the diagnostic value of STE in aVR during exercise prior to Tc^{99m}-sestamibi scanning and its predictive value in identifying ischemic territory and angiographic findings.

Methods: Consecutive patients attending for Tc^{99m}-sestamibi perfusion imaging between April 2004 and Aug 2004 were enrolled. Patients completed a treadmill protocol. Peak exercise ECGs of these patients were coded by 2 blinded investigators. STE ≥ 0.5mm in lead aVR was considered significant. Perfusion imaging results including gated images assessing LV function were recorded. A proportion of the images were double reported by a blinded investigator. Findings at angiography were assessed.

Results: Of the 605 patients recruited, mean age was 62 SD 11 years. STE in lead aVR occurred in 23% (138) of the patients. More patients with STE in aVR had a reperfusion defect on imaging compared with those that had no STE in aVR (41% 56/138 vs 28% 132/467 p=0.006). The presence of STE in aVR did not indicate a more severe reperfusion defect as determined by myoquant index (median 7.1 at stress compared with 6.6 in the non STE aVR group p=NS). Significant coronary artery stenosis (>70%) was more likely when STE in aVR occurred (73% 27/37 vs 66% 62/94, p=0.011) but there was no association between its presence and the arteries diseased.

Logistic regression analysis demonstrates that STE in aVR (OR 1.3 p=0.244) is not an independent predictor of reperfusion abnormality when adjusted for ST depression (STD) (OR 1.6 p=0.02)

On further regression analysis with anterior wall reperfusion defect as an endpoint, STE in aVR (OR 1.8 p=0.049) was a predictor despite adjustment for STD (OR 1.1 p=0.7).

Conclusions: STE in aVR during exercise occurs frequently. It does not diagnose significantly more reperfusion abnormalities than STD alone. However, unlike STD which is not predictive of a territory of ischemia, STE in aVR is associated with an anterior wall reperfusion defect.

992-132 Characteristics of Heart Rate Changes in Response to Sleep-Disordered Breathing among Cardiac Patients

Phyllis K. Stein, Eric Lundequam, William Howells, Stephen P. Duntley, Peter P. Domitrovich, Kenneth E. Freedland, Robert M. Carney, Washington University School of Medicine, St. Louis, MO

Background: Repeated HR arousals (HRAs) occur due to obstructive apnea (OA) and hypopneas (H) during sleep.

Method: To explore characteristics of HRAs and factors influencing their magnitude among cardiac patients, data were analyzed from N=123 patients with known cardiovascular disease (age 58±10 yrs, 76M, 47F, 55% post-MI, 55% on beta-blockers) recruited for a study of depression and sleep apnea. ECGs from the 2nd night of polysomnography were extracted and scanned on a Holter analyzer. HRAs from N=4582 OA events and N=7548 H events were measured and integrated with sleep stages and respiratory event type. Regression analysis identified the determinants of HRA characteristics including: event type (OA, H), sleep stage (REM, non-REM), age group (≥60 yrs), gender, BMI (30), Hx of MI, depression and beta-blocker use.

Results: Both HR increases and HRA durations were greater during REM than non-REM (15±10 bpm, 35±16s for REM; 14±8 bpm, 30±13s for non-REM). HRA acceleration was greater for OA compared to H events during both REM and non-REM, but the difference was greatest during REM (OA:0.98±0.05 vs. H:0.64±0.04, p<0.001). In contrast, HRA accelerations were less during H events in REM than in non-REM (p= 0.005). Greater HRA accelerations were seen in patients <60 and were most marked in REM (0.96±0.06 for younger vs. 0.66±0.06 bpm/s for older pts) and during OA (1.08±0.06 for younger

vs. 0.77 ± 0.06 bpm/s for older pts, all $p < 0.001$. HRA accelerations were also greater among overweight patients (BMI 25-30), although also higher in obese than normal weight patients. Females had smaller HRA accelerations during REM and greater HRA accelerations during non-REM, than males, but no difference in H events. There was no effect of Hx of MI, depression or β -blocker use.

Conclusions: Rapid, potentially dangerous HR accelerations suggesting dramatic changes in autonomic tone and not affected by beta-blockade, are seen, especially in association with obstructive apnea during REM sleep in cardiac patients, supporting the importance of screening for sleep-disordered breathing. Lesser accelerations seen in older patients suggest a loss of autonomic sensitivity with aging or possible habituation to sleep apnea.

992-133

Heart Rate Variability Response to Dynamic Exercise Testing: Implications for Interpretation of Spectral Analysis Parameters During Periods of Less Oscillatory Autonomic Function

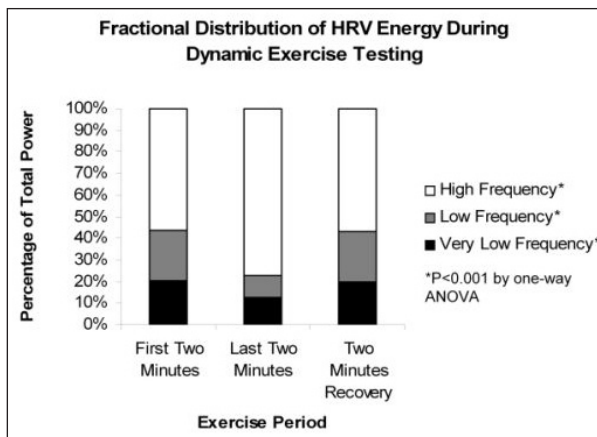
Frederick E. Dewey, James V. Freeman, Gregory Engel, Raul Pinovieo, Natasha Ahmed, Johnathan Myers, Victor F. Froelicher, Stanford University, Palo Alto, CA, Palo Alto VA Health Care System, Palo Alto, CA

Background: Spectral analysis parameters of heart rate variability (HRV) are thought to reflect cardiovascular (CV) response to autonomic function. At rest, the very low frequency (VLF) and low frequency (LF) components are thought to reflect CV response to sympathetic input while the high frequency (HF) component is believed to reflect CV response to vagal function. We evaluated spectral analysis parameters of HRV during and after dynamic exercise testing to characterize the HRV response to exercise.

Methods: Spectral analysis was performed on de-trended R-R interval data taken from the first and last two minutes of, and first two minutes after exercise treadmill testing of 1302 subjects (95% male, mean age 58) at the Palo Alto Veterans Affairs Medical Center.

Results: The fractional distribution of HRV energy is shown in the figure. Relative to the start of exercise, the percentage of VLF and LF power significantly decreased during the last two minutes of testing when sympathetic modulation of heart rate predominates. Relative to peak exercise, the percentage of HF power was observed to decrease during the first two minutes of recovery when parasympathetic modulation of heart rate predominates.

Conclusions: Current models for the frequency domain components of HRV are inadequate to describe the changes we observed in the fractional distribution of HRV energy during and after dynamic exercise testing. We hypothesize that less oscillatory autonomic function or non-neuronal influences must be implicated.



992-134

Prognostic Value of Signal Average Electrocardiogram in Predicting the Occurrence of Atrial Fibrillation. A Meta-Analysis

Manish Undavia, Davendra Mehta, Trong Duong, J. Anthony Gomes, Mount Sinai Medical Center, New York, NY

Background: Prior studies evaluating the role of signal average ECG (SAECG) in stratifying patients at high risk for developing atrial fibrillation (AF) have been limited by small sample size and disparate populations.

Methods: Prospective studies evaluating the role of SAECG in predicting AF published between January 1988 and September 2005 were retrieved. Studies were included if data on cut-off value of an abnormal filtered P wave duration (fPWD) was available and the primary endpoint was occurrence of AF. The combined primary endpoint of interest was the first occurrence of AF (paroxysmal, PAF) or progression of PAF to chronic AF (CAF). The odds ratios (OR) and the 95% confidence intervals (CI) of the individual trials were pooled using a random effects model. A separate sub-group meta-analysis was performed on patients who were post CABG surgery.

Results: A total of 973 pts from 8 studies met our pre-specified criteria (75% M, age range: 46-67 yrs, follow-up: 5 days to 40 months). 17% of the patients had a prior episode of PAF. SAECG was done to evaluate progression of PAF to CAF in 13%; occurrence of AF in the post CABG setting in 51%; in the post MI period in 23%; left ventricular dysfunction (EF<40%) in 8% and post WPW syndrome ablation in 5% of the pts. An abnormal fPWD as defined in individual studies ranged from 126 msec to 155 msec. In the pooled meta-analysis, an abnormal fPWD was present in 32% of the pts. 52% of pts

with an abnormal fPWD met the primary endpoint as compared to 11% pts with normal fPWD (OR=9.3, CI=5.1-17.1, P=0.000). Overall, the positive and negative predictive value (PPV, NPV) of abnormal fPWD for development of AF was 52% and 88% respectively. In the CABG subgroup, post-operative in-hospital AF occurred in 57% of the patients with an abnormal SAECG as compared to 16% with a normal SAECG (OR 7.75, CI 3.5-17.6, P=0.000; PPV=57%, NPV=84%).

Conclusion: fPWD on a SAECG has a significant value in predicting AF across a wide spectrum of patients including those who have had a recent CABG surgery. The critical task remains in standardizing the cut-off value for defining an abnormal fPWD. Further studies are warranted to evaluate the incremental value of SAECG over conventional markers for AF.

992-135

Long History and Frequent Episodes of Paroxysmal Atrial Fibrillation in Patients Without Structural Heart Disease Do Not Lead to Deterioration of Atrial Electrophysiology

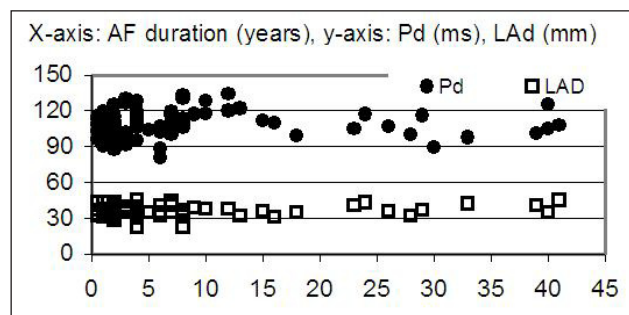
Raija Koskinen, Heikki Väänänen, Jouni Kuusisto, Hannu Parikka, Markku Mäkijärvi, Lauri Toivonen, Helsinki University Hospital, Helsinki, Finland

Background: Long lasting atrial fibrillation (AF) can cause electrophysiological and structural changes in atria. Atrial SAECG has predicted progression of paroxysmal AF to chronic.

Methods: 81 patients with paroxysmal lone AF (aged 43±12 years) and 81 matched controls were examined. P-on-T atrial complexes and fast atrial tachycardias, signifying focally-triggered AF, were demonstrated in 57 patients (69%). The length of AF history was 9±10 years. AF episodes occurred >1/wk in 56%, 1/wk to 1/mo in 29% and <1/mo in 15% of patients. Atrial electromagnetic signals were averaged and high-pass filtered (40 Hz) and atrial wave duration (Pd) and RMS amplitude of the last 40 ms were automatically analyzed. Pd was 109 ms in patients and 104 ms in controls (p=0.004), but RMS (75±29 fV 74 ± 35 fV, p=n.s.), PR interval, QRS duration and left atrial diameter (LAd, 36 ± 5 mm) were normal.

Results: The length of AF history did not correlate with Pd (r=0.02, p=n.s.), LAd (r=0.19, p=n.s., Figure), or atrial wave RMS. None of these correlated either with the frequency of AF episodes. Patients with focal AF had more frequent episodes (72% vs. 17% >1/wk) and normal atrial RMS (80 ± 31 vs. 62 ± 18 fV; p=0.001) compared to those without focal triggers.

Conclusions: Paroxysmal lone AF does not lead to atrial electrical or mechanical remodeling even over prolonged time, particularly the focal type of AF. These observations favor the concept that lone atrial fibrillation can be cured by successful elimination of the local arrhythmic substrate.



992-136

Abnormal Heart Rate Variability is a Powerful Independent Predictor of Long-Term Cardiovascular Mortality in the Elderly: The Cardiovascular Health Study

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Background: Abnormal heart rate variability (HRV) has predicted mortality in patients with a variety of cardiac disorders over a relatively short follow up. Less is known about HRV and cardiovascular (CV) mortality in the general population over a longer follow-up.

Methods: The association of 24-hr time and frequency domain HRV, non-linear HRV and heart rate turbulence (HRT) with CV mortality was determined in 1384 community-dwelling older adults in the Cardiovascular Health Study (CHS), a multi-center, population-based study of the epidemiology of CV disease the elderly. CV as underlying cause of death was adjudicated by an expert panel. Multivariate proportional hazards models, adjusted for a large number of previously-identified independent predictors of CV mortality in the CHS, determined the association of HRV parameters with CV mortality.

Results: Subjects were 71.9 ± 4.9 (65-93) yrs, 53% female. Median FU was 12.3 years. For time domain HRV-eligible recordings (N=1273, 190 CV deaths), after adjustment for covariates, decreased SDANN [(Risk ratio (RR)=0.993, 95% CI (0.989-0.998), p=0.006] combined with abnormal HRT [either turbulence slope (TS) abnormal [RR=1.93 (95% CI (1.31-2.84), p=0.001, or both TS and onset abnormal (RR=3.14, 95% CI (2.03-4.86), p<0.001)] strongly predicted CV mortality. Model chi-sq was 361 without and 401 with HRV. For frequency domain-eligible recordings (N=1198, 175 CV deaths), the combination of decreased ln total power [(RR=0.79, 95% CI (0.54-0.91), p=0.009] with increases in the non-linear measure SD12 [ratio of the axes of an ellipse fitted to the Poincaré plot of N-N intervals, RR=12.9, 95% CI (3.6-45.6), p<0.001] and abnormal HRT [TS abnormal RR=2.02, 95% CI (1.34-3.05), p=0.001, both TS and onset abnormal RR=2.82, 95% CI (1.73-4.58), p<0.001] had the strongest association with CV mortality. Model chi-sq was 331 without and 390 with HRV.

Conclusions: In the elderly, abnormal HRV is a powerful risk factor for long-term CV mortality. Instead of finding a single best HRV predictor, results show that the combination

of multiple HRV predictors, including traditional and non-linear HRV and heart rate turbulence, has the strongest association with mortality.

992-137 Validation of an Electrocardiographic Predictive Regression Model for the Differential Diagnosis of Paroxysmal Junctional Tachycardias in Patients Without Preexcitation

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Background: In patients (P) without preexcitation, the differential diagnosis of paroxysmal junctional tachycardias consists mainly of atrioventricular nodal reentry tachycardias (AVNRT) and orthodromic reciprocating tachycardias (ORT) through a concealed accessory pathway. The objective of this study was to validate the diagnostic accuracy of a multiple logistic regression model using classical electrocardiographic criteria in that diagnosis.

Methods: We included 360 consecutive patients (231 females; 45±18 yrs) who underwent an electrophysiologic (EP) study for paroxysmal, regular, narrow-QRS complex tachycardias without preexcitation in sinus rhythm. Atrial tachycardias were excluded. The ECG recordings during tachycardia were reviewed by 2 independent observers for the presence of the following criteria: a) pseudo r' deflection in V1 and/or pseudo s waves in inferior leads, b) P wave separate from the QRS complex, c) QRS alternans, and d) ST segment depression (≥2 mm) and/or T wave inversion during tachycardia. We performed a cross-validation method using the first 230 patients to develop a multiple logistic model to predict the tachycardia diagnosis (derivation group). The model was validated through the remaining 130 patients (validation group).

Results: EP study demonstrates AVNTR in 241 P and ORT in 119 P. The presence of pseudo r' deflection in V1 and/or pseudo s waves in inferior leads (adjusted OR: 13, 95% CI: 4-39; p=0.0001), a P wave separate from the QRS (adjusted OR: 0.21, 95% CI: 0.11-0.4; p=0.0001), and QRS alternans (adjusted OR: 0.32; 95% CI: 0.13-0.8; p=0.015) were selected by stepwise multiple logistic regression analysis as independent predictors for the diagnosis of AVNRT (vs. ORT) in the derivation group. The application of the obtained model in the validation group showed a shrinkage prediction factor of only 1% of the cases.

Conclusion: The presence of pseudo r' deflection in V1 and/or pseudo s waves in inferior leads, a P wave separate from the QRS, and QRS alternans during tachycardia permit derivation of a reliable logistic model for predicting the mechanism of paroxysmal junctional tachycardias in patients without preexcitation during sinus rhythm.

992-138 Methodological Issues of QRS Duration Measurements in Candidates for Cardiac Resynchronization Therapy

Dimosthenis Avramidis, George K. Andrikopoulos, Stylianos Tzeis, Vassiliki Tsagou, Konstantinos Triantafyllou, Panagiotis Politis, Konstantinos Kappos, Antonis S. Manolis, Evangelismos Hospital, Athens, Greece

Background: Although cardiac dyssynchrony (CD) may exist despite a normal QRS duration, prolonged QRS duration has been extensively used as a surrogate marker of CD. However, there is limited information on interobserver variability of QRS duration measurements, which may delineate its role in the selection of candidates for cardiac resynchronization therapy (CRT).

Methods: We studied 52 consecutive patients (mean age 66±11 years, 83% males, 56% suffering from ischemic cardiomyopathy, and 64% in NYHA stage III-IV) admitted due to worsened heart failure. Maximum QRS duration was measured by four experienced cardiologists using : a) conventionally measured paper 12-lead ECGs, b) on screen measurements of computerised ECGs, and c) measurements of the filtered QRS duration of the signal-averaged ECGs (CS 200, Schiller, CH).

Results: The average value of the maximum QRS duration differed significantly with the three methods (145±33, 144±35 and 131±32 ms respectively, P<0.001). Interventricular electromechanical delay was correlated better to the filtered QRS duration obtained from SAECG (R=0.460, P<0.001) compared to the values obtained from conventional (R=0.359, P=0.010) or from the computerised ECGs (R=0.311, P=0.026). QRS duration measured conventionally differed substantially between the four observers (137±35, 143±33, 155±34 and 142±34 ms respectively, P<0.001). Consequently, significant discrepancies were observed when the studied patients were classified in two groups using the cut-off value of 130 ms. Thus, 28(54%), 33(64%), 33(64%) and 26(50%) patients were classified as having prolonged (≥130 ms) QRS duration by the four observers, respectively.

Conclusions: In a cohort of unselected patients, candidates for CRT, the filtered QRS duration measurements were more reproducible and better correlated to interventricular delay compared to both the conventionally measured QRS duration or to onscreen measurements using computerised methods. Interobserver variability in QRS duration measurements may partly explain inappropriate identification of patients as candidates for CRT in studies of biventricular pacing using QRS duration as the main inclusion criterion.

992-139 Open Irrigated-tip Technology Versus Intracardiac Echo Guided Energy Delivery Using an 8 Mm Tip Catheter For Pulmonary Vein Isolation in Patients With Atrial Fibrillation: A Randomized Comparison

Jens Guenther, Georg Noelke, Klaus Gutleben, Johannes Brachmann, Nassir F. Marrouche, Klinikum Coburg, Coburg, Germany

Background: Radiofrequency energy (RF) delivery for pulmonary vein isolation (PVI) utilizing both irrigated tip and an 8 mm tip catheter under intracardiac echo (ICE) guidance have been proven to be safe and efficient. This study was initiated to prospectively compare the 2 ablation modalities.

Methods and results: 56 patients (40 men; mean age 56±12 years) presenting for PVI for treatment of symptomatic AF were randomized to ablation using one of the following ablation modality: RF delivery using an open irrigated-tip catheter (Group 1); or RF energy delivery under ICE guidance using an 8 mm tip catheter (Group 2). In group

1 temperature and power (with a saline pump flow rate of 30 ml/min) were set at 50° and 45W, respectively. In group 2 patients power delivery was initiated at 25 W and was titrated upwards until scattered microbubbles were observed, then the power was titrated downwards to subside the MB formation. Only if MB formation subsided energy delivery was continued for 25-35 seconds. Table 1 demonstrates patients characteristics and outcome in both study groups. No major complications were observed at follow up in both groups. Conclusion: From the preliminary results of this study open irrigated tip ablation catheter technology is as efficient as ICE guided RF energy delivery in patients presenting for PVI. Nevertheless, open irrigation ablation technology seems to be superior in terms of rapid achievement of isolation, fluoroscopy exposure and procedure time.

	Group 1	Group 2	P value
Patients	26	27	ns
Age (years)	53±8	54±8	ns
Left atrial size (cm)	4.4±0.8	4.3±0.7	ns
Duration of AF (years)	5.1±3.4	5±3.5	ns
Paroxysmal AF	16	17	ns
Persistent/permanent AF	10	10	ns
Follow-up (months)	6±2	6±4	ns
Fluoroscopy exposure (µGy ²)	7560±2	12240±4	0.008
Procedure time (minutes)	164±32	204±47	0.005
Mean duration of RF energy delivery /PV antrum (min)	5.1±2.2	9.2±3.2	0.03
AF Recurrence	18 %	21 %	ns

992-140 First Experience With Cryoballoon Technique and Long-Term Success of Pulmonary Vein Isolation With Cryotechnique Only

Juergen Vogt, Anja Dorszewski, Johannes Heintze, Lam Luong Thanh, Helga Buschler, Peter Schwartz, Dieter Horstkotte, Heart Center North Rhine-Westphalia, Ruhr University Bochum, Bad Oeynhausen, Germany

Background: Segmental isolation of pulmonary veins (PV) with radiofrequency ablation is associated with reconnection in 90% and risk of PV stenosis. A new risk of esophageal left atrial fistulas with RF technique for PV encircling and linear lesions has been reported worldwide. This study reports on the efficacy of circumferential PV isolation using cryotechnique only and first results with a new cryoballoon.

Methods: The PV isolation was performed with the max. 30-mm self-expanding Arctic Circler (AC) over 4 minutes (min) of 3-4 cryoimpulses (CI) down to - 85°C with N₂O. Gaps were closed using a 6-/8-mm tip cryocatheter (Freezor extra / -max). The last patients (P) were treated with a new steerable over the wire cryoballoon with 28 mm diameter.

Results: 68 P (22 female, mean age 61±9 years, 62 with paroxysmal, 6 with persistent AF, left atrium 43±5 mm, 37 with lone AF, 21 with hypertension, 10 with structural heart disease) were treated with the AC. 8% of 263 PV were segmentally isolated. 92 PV (35%) were isolated with the AC only, 56% (148 PV) with additional gap closing. In 21 redos, we observed 27% of 82 PV isolated and 73% with reconducting sleeves. All reconducting veins were reisolated. During a mean follow-up of 16±9 months (mo) and 1.4 procedures per P, 28 of 52 P (52%) had no recurrent AF, 28% a significant reduction of AF burden. 20% remained unchanged. The clinical efficacy was 80%, excluding persistent AF 88%! Due to simultaneous isolation with two AC in 31 P, the procedure time was reduced to 198±44 min (p<0.01) and the X-ray burden to 43±11 min (p=0.021). In 5 P with large PV (22±4 mm), 70% of these veins including parts of the antrum could be isolated with the new balloon during 3 freezes over 4 to 8 min per vein. Only in P with thick muscle layers at the antrum due to hypertensive heart disease, additional segmental freezing was necessary.

Conclusions: The new cryotechnique to eliminate the pulmonary vein triggers only is highly effective during long-term course in paroxysmal AF. Recurrence of AF develops mainly because of reconducting veins. The risk of PV stenoses is definitely eliminated. The new cryoballoon is encouraging in primarily isolating the most veins without additional mapping and ablation catheters.

992-141 Persistence of Iatrogenic Atrial Septal Defect after Pulmonary Vein Isolation with Transseptal Puncture - an Underestimated Risk?

Christoph Hammerstingl, Kyung-Mi Jeong, Clemens Troatz, Klaus Tiemann, Berndt Luederitz, Lars Lickfett, University of Bonn, Bonn, Germany, St. Marien Hospital Bonn, Bonn, Germany

Objective: We sought to determine the risk of persistent iatrogenic atrial septal defect (IASD) after pulmonary vein isolation (PVI) with transseptal puncture.

Background: The number of PVI in patients (pts) with paroxysmal atrial fibrillation is increasing. Until now, there are inconsistent data in what percentage of pts iASD with interatrial shunting persists after long-term follow up (FU).

Methods: 36 pts with AF underwent PVI, thereof 27 pts with single respectively 9 pts with double transseptal puncture. Serial transesophageal echocardiography (TEE) was performed before the intervention and thereafter at long-term FU (FU-time 266.7 ± 37.9 days). Interatrial shunt was characterized by echocardiographic parameters; right-to-left-shunting (RLS) was quantified by contrast echocardiography.

Results: In 8 of 27 pts with single transseptal puncture iASD occurred after PVI, thereof 6 pts with distinct RLS. We saw no iASD in 9 pts after double transseptal puncture during follow up, this difference was statistical significant (p= 0,046; CI 0,89 to 0,014). In pts with RLS and iASD preprocedural pulmonary artery pressure (PAP) was significant higher compared to pts with iASD and no RLS (23.75±0.50 vs 17.59±5.82 ; p=0.0483, CI 0.048 to 12.27).

Conclusion: Persistence of iatrogenic atrial septal defect with right-to-left-shunting after pulmonary vein isolation with single transeptal puncture is a common finding. The results of this study suggest that double transeptal puncture is less traumatic than single puncture with double access. Increasing PAP seems to be a risk-factor for the development of iASD with RLS. Adverse effects of interatrial shunting should be subject of further investigation.

992-142

Early Experience Of Pulmonary Vein Antral Isolation Using an Open Irrigation Ablation Catheter for the Treatment of Atrial Fibrillation: Immediate Short Term Results of a Randomized Study

Mohamed H. Kanj, Oussama M. Wazni, Mauricio Arruda, Dhanunjaya Lakkireddy, Sergio Thal, Walid Saliba, Robert Schweikert, David Burkhardt, David O. Martin, Gemma Pelargonio, Antonio Dello Russo, Pietro Santarelli, Domenico Potenza, Raffaele Fanelli, Raimondo Massaro, Giovanni Forleo, Andrea Natale, Cleveland Clinic Foundation, Cleveland, OH, Casa Sollievo Della Sofferenza, San Giovanni, Rotondo, Italy

Background: An open irrigation catheter allows radiofrequency current delivery at a higher power while maintaining the tip electrode-tissue interface at lower temperatures resulting in larger RF lesions and importantly avoiding coagulum formation. We investigated the efficacy and safety of irrigated-tip catheters in a consecutive series of patients with atrial fibrillation presenting for pulmonary vein antrum isolation (PVI). We hypothesized that this approach is safe and may shorten the left atrial instrumentation and fluoroscopy times.

Methods: Patients were randomized to either Celsius™ (8mm Tip) or Celsius™ ThermoCool® diagnostic/ablation deflectable tip catheters (Biosense Webster, Diamond Bar, CA). The procedure endpoint was isolation of all the pulmonary vein antra. A circular Lasso shaped catheter was used for mapping. Study endpoints were: 1) procedural success, 2) cardiac or thromboembolic complication, and 3) fluoroscopy time and left atrial instrumentation time. The latter was defined as the total clock time where catheters are present in the left atrium.

Results: A total of 62 patients were randomized to this study (32 using Celsius™ ThermoCool® catheter and 30 using Celsius™ 8mm tip catheter). Pulmonary vein antral isolation was achieved in all of the patients at the end of the procedure. The mean fluoroscopy time needed for PVI was significantly lower in the Celsius™ ThermoCool® compared to the Celsius™ catheter (26 +/- 2 minutes vs 39 +/- 2 minutes, p < 0.01). Additionally, the mean left atrial instrumentation time was significantly lower in the Celsius™ ThermoCool® compared to the Celsius™ catheter (60 +/- 3 minutes vs 86 +/- 6 minutes, p < 0.01) time. There were no cases of cardiac perforation, esophageal injury or thromboembolic complications in either group.

Conclusion: Open-irrigation catheters can safely be used for PVI procedures. It minimizes radiation exposure and LA instrumentation time. Avoidance of impedance rise (commonly associate with coagulum formation) is possible without compromising power delivery. This may result in more effective lesions thus improving long term success rates.

838-4

Catheter Ablation of Atrial Fibrillation or Left Atrial Flutter Under Uninterrupted Oral Anticoagulation

Sergio L. Pinski, Marcelo E. Helguera, Cleveland Clinic Florida, Weston, FL

Background: Embolic events are a complication of catheter ablation for atrial fibrillation (AF) or left atrial flutter (Afl). The standard of practice consists of interrupting oral anticoagulation several days in advance of the procedure and to use heparin or enoxaparin as a bridge. It was our hypothesis that catheter ablation without interruption of warfarin is feasible and safe.

Methods: For the last 18 months, we routinely performed catheter ablation of AF or left Afl without interrupting oral anticoagulation. Depending on the baseline INR, warfarin was held for one night or not at all, aiming at an INR between 2 and 3 the day of the procedure. A TEE was obtained within 24 hours of the procedure. All venous access was femoral, and included an 11F introducer for intracardiac echocardiography (ICE) probe. We monitored intraarterial blood pressure via a radial line. Transeptal puncture was performed under ICE guidance. For AF, we performed left atrial circumferential ablation or left pulmonary vein antral isolation, often combined with cavotricuspid isthmus ablation. Intravenous heparin was given during left atrium instrumentation to maintain the ACT between 250 and 300 seconds. Enoxaparin was given if needed after the procedure until the INR was ≥ 2 .

Results: We analyzed 63 ablation procedures (60 AF, 3 left Afl) in 55 pts (47 males, age 57 \pm 9) The INR the day of the procedure was 2.3 \pm 0.5 (range 1.4 to 3.6). Three procedures had to be rescheduled due to an unexpected INR ≥ 4 . The INR had inadvertently dropped below 1.8 in 8 pts. ICE monitoring did not disclose formation of thrombus in the left atrial catheters or sheaths in any case. The INR the morning after was 2.4 \pm 0.6 (range 1.2 to 3.8). More than 1 dose of enoxaparin was required after 9 cases (14 %). One pt (1.5 %) developed a large thigh hematoma that required transfusion. There were no thrombotic or embolic events, cardiac perforation or tamponade. The median hospital stay was 1 day.

Conclusion: Catheter ablation of AF under uninterrupted oral anticoagulation appears safe. It prevents lapses in anticoagulation while minimizing the need for postprocedural enoxaparin. A randomized comparison of this strategy against the standard of practice appears desirable.

9:30 a.m.

838-5

Intraoperative Cooled-tip Radiofrequency Linear Atrial Ablation to Treat Permanent Atrial Fibrillation

Thomas Deneke, Krishna Khargi, Peter H. Grewe, Thomas Lawo, Andreas Mügge, Axel Laczkovics, Bernd Lemke, Medical Clinic II, BG Kliniken Bergmannsheil, University Hospital Bochum, Bochum, Germany, Clinic for Cardio-Thoracic Surgery, BG Kliniken Bergmannsheil, Univ, Bochum, Germany

Atrial fibrillation (AF) surgery has become more engaged in every-day practise of specified cardio-surgical centres. The cut-and-sew technique still remains the gold standard with superior efficacy. Is an intraoperative approach using cooled-tip radiofrequency energy to induce linear atrial lesions (SICTRA) safe and effective in treating AF?

Methods: 180 patients (mean EUROSCORE 6.2, AF duration 7years) presenting with permanent AF (>1 year, 1 failed cardioversion) and the need for cardiac surgery were consecutively included. In addition to the cardio-surgical procedure SICTRA was performed. In 80 patients the ablation pattern was restricted to the left atrium alone. Follow-up constituted of ECG, holter-ECG and Doppler echocardiography.

Results: Concomitant cardio-surgical procedures were mitral valve surgery in 74, aortic valve replacement in 23, bypass surgery in 67 including 24 patients with additional mitral valve surgery and combined procedures in 16. During follow-up 141 patients (78%) converted to sinus rhythm (SR). At discharge (0.5months post operatively) 31% of patients, at 3 months 65%, at 6 months 78% and after 12 months 79% of patients were in SR. Batrial contraction was documented in 82% of patients in SR at 6 month follow-up. In patients with a left atrial procedure conversion rates were not significantly different compared to a batrial approach (80% versus 78%, p=0.47). The type of cardio-surgical procedure did not influence 12-month conversion.

30-day-mortality was found to be 5% (9/180) mainly due to cardiac insufficiency (78%) and histopathology revealed 24% of all lesions to be histologically non-transmural. 4% of patients developed sustained regular atrial arrhythmia (2.8% right atrial arrhythmia) needing invasive therapy (catheter ablation long-term success 75%).

Conclusions: SICTRA is safe and produced stable SR in 80% of patients undergoing open heart surgery with permanent AF. A batrial contraction can be restored in 80% of these patients. Rhythm conversion is not influenced by treatment of the right atrium or the performed cardio-surgical procedure. Sustained regular atrial arrhythmia with the need for invasive treatment strategies occur in 4%.

9:45 a.m.

838-6

Autonomic Heart Plexus Localization With Epicardial and Endocardial Cardioneurostimulation

Cristiano F. Pisani, Barbara D. Oliveira, Sissy Lara, Fernando A. Vidal, Francisco Darrioux, Ivani C. Trombetta, Denise Hachul, Carlos Eduardo Negrão, Maurício Scanavacca, Eduardo Sosa, Heart Institute - InCor, São Paulo, Brazil

Background: Autonomic nervous system modifies electrophysiologic properties of both atria, predisposing the appearance of atrial fibrillation (AF). Autonomic heart innervations are composed of parasympathetic ganglia and sympathetic post-ganglionic fibers over epicardial surface.

Objective: Evaluate if parasympathetic ganglia can be identified by direct electrophysiologic stimulation over epicardium and endocardium, owing to radiofrequency catheter ablation of this structure.

ORAL CONTRIBUTIONS

838

Atrial Fibrillation: Ablative Techniques

Tuesday, March 14, 2006, 9:00 a.m.-10:30 a.m.

Georgia World Congress Center, Room B206

9:00 a.m.

838-3

Circumferential Pulmonary Vein Ablation. Early Experience on Remote Magnetic Navigation Versus Standard Technique

Carlo Pappone, Gabriele Vicedomini, Nicoleta Sora, Simone Sala, Maria Avitabile, Enrico Frigoli, Cristiano Ciaccio, Laura Livolsi, Giuseppe Augello, Stefania Sacchi, Alessandra Marzi, Vincenzo Santinelli, San Raffaele University Hospital, milan, Italy

Background: Continuous stability of ablation catheters may be obtained by the combination of the external magnetic field and flexibility of magnetic soft catheters.

Methods: We evaluated the safety and feasibility of remote catheter guidance using the NIOBE II system (Stereotaxis, Inc) in 40 patients undergoing circumferential pulmonary vein ablation (CPVA) for symptomatic atrial fibrillation (AF). Ablation was performed with a 4-mm tip, magnetic catheter (65°C, maximum 50 W, 15 seconds). The catheter tip was guided by a uniform magnetic field (0.08 T), and a motor drive (Cardiodrive unit, Stereotaxis, Inc) advanced or retracted the catheter to the predefined targets. The left atrium map was created using an integrated CARTO-RMT system. End point of ablation was voltage abatement > 90% of bipolar electrogram amplitude.

Results: Remote navigation was successful in 38/40 patients without complications. The overall median mapping and ablation time was 152.5 minutes (Min-Max, 90-380 minutes) but was much longer in the first 12 patients (192.5 minutes versus 148 minutes; P=0.012). Median ablation time was 49.5 minutes (Min-Max, 17-154) but it was much shorter in the last 28 patients than in the first 12 patients (49 minutes versus 70 minutes; P=0.021). Compared with controls, remote ablation had longer procedure times (p<0.001) with similar mapping time but shorter ablation time on right-sided PVs. Much more mapping points regardless of their location were collected remotely (p<0.001).

Conclusions: Remote magnetic navigation for AF ablation is safe and feasible with a short learning curve suggesting that AF ablation can be performed even by less experienced operators, reducing in all cases fluoroscopic exposure time for the operator.

Methods: Ten patients with isolated paroxysmal AF with history suggesting vagal mechanism of origin were selected. Nine were male with 42.5 ± 10.6 years old. Cardioneurostimulation was performed (20Hz, 100V, 4ms, 3 sec, Grass 70 stimulator) on pulmonary veins (PV) antrum and left atrium posterior wall (LAPW) on epicardial and endocardial surface that could elicit an important vagal response (pause of more than 1.5 seconds). Subxyphoid puncture was performed to access epicardium space. Five fixed points of stimulation (RSPV, LSPV, RIPV, LIPV and LAPW) were selected during the procedure.

Results: No vagal response was observed in 3 patients. Epicardial response was observed at LSPV in 4 patients, at RSPV in 5 and at LIPV, RIPV and LAPW in 6, 5 and 5 patients respectively. Endocardial stimulation response was observed in 2 patients at LSPV, RSPV, RIPV and LAPW and at LIPV vagal response was observed in 4 patients. Vagal response was observed in 23 of 50 points in epicardial surface and 12 of 50 points ($p=0.021$) in endocardial surface.

Conclusion: Parasympathetic ganglia mapping is possible to be done with cardioneurostimulation. Area of response is wider at epicardial surface stimulation.

10:00 a.m.

838-7

Clinical Significance of Early Recurrences of Atrial Fibrillation or Atrial Flutter After Pulmonary Vein Antrum and Superior Vena Cava Isolations

Sakis Themistoclakis, Robert A. Schweikert, Walid I. Saliba, Jennifer E. Cummings, Aldo Bonso, Antonio Rossillo, Ouassama Wazni, William A. Belden, Michelle Williams-Andrews, Dhanumjaya Lakkireddy, Antonio Raviele, Andrea Natale, Umberto I Hospital, Mestre-Venice, Italy, Cleveland Clinic Foundation, Cleveland, OH

Purpose: this multicenter study evaluate the long-term outcome of a large population of patients (Pt) with early recurrences of atrial fibrillation (ERAF) or atrial flutter (ERAFL) after pulmonary vein antrum and superior vena cava isolations (PVAI).

Methods: ERAF and ERAFL that occur within 3 months after PVAI were observed in 489 of 1495 (33%) consecutive pts (male 386, mean age 57 ± 11 years) with symptomatic drug refractory paroxysmal-persistent (58%) and permanent (42%) atrial fibrillations (AF). ERAF and ERAFL were observed in 444 (30%) and 45 (3%) pts respectively. The mean duration of AF was 89 ± 77 months, structural heart disease were present in 105 pt (46%) (mean left ventricular ejection fraction $55 \pm 9\%$, mean left atrium diameter 45 ± 6 mm). The PVAI was guided by intracardiac echocardiography and the end point of the procedure was defined as the ablation of all PV potentials on the circular mapping catheter at the antrum of all PVs. All pts were followed with history, ecg and Holter recordings at 1, 3, 6 and than every 6 month follow up (FU). An event recorder was given to 1364 pts for the first two months after PVAI and repeated at the third month and fourth month FU. In case of symptom recurrences ECG and Holter recordings were also performed. Complete success was defined as the persistence of sinus rhythm in the FU without antiarrhythmic drugs (AAD). Only single procedures were considered.

Results: the end point of the procedure was achieved in all pts. After a mean follow up of 22 ± 9.8 months sinus rhythm was maintained in 222 (50%) pts with ERAF and 22 (49%) pts with ERAFL without AAD.

Conclusions: approximately half of pts with ERAF and ERAFL have no further arrhythmic recurrences in a long term follow up. Therefore early repeat ablation should not be considered in pts with early recurrence of AF or AFL.

10:15 a.m.

838-8

Three-Dimensional Electroanatomical Image Integration Versus Phased Array Intracardiac Echocardiography for Left Atrial Mapping Procedure: Operator Blinded Accuracy Study

Jens Guenther, Georg Noelke, Klaus Gutleben, Johannes Brachmann, Nassir F. Marrouche, Klinikum Coburg, Coburg, Germany

We performed a prospective study to assess the mapping accuracy of the 3D image integration mapping system (CARTOMERGE (CM)) when compared to intracardiac echocardiography (ICE) as a real-time imaging modality.

In 14 patients (9 men, mean age 57 ± 9 years) presenting for pulmonary vein isolation (PVI) for treatment of atrial fibrillation (AF) the CM system was utilized, and registration of the left atrial CT-scan image with the electroanatomical map was performed without ICE guidance. The operator was asked to position the mapping catheter at 5 left atrial pre-defined sites after the CM map (CMM) was completed: right upper PV ostium (RUPO), right lower PV ostium (RLPO), left upper PV ostium (LUPO), left lower PV ostium (LLPO), and left atrial appendage (LAA)- left PVs carina (LC). The operator, blinded to the CMM, first targeted the 5 sites under ICE guidance. The corresponding CMM points were tagged (TS) and the difference between the PS and TS (Δ cm) was measured. Then, the operator was asked to target the 5 sites using the CMM (TS2), blinded to ICE, and the corresponding ICE points (PS2) were marked on CMM. The difference between PS2 and TS2 ($\Delta 2$ cm) was measured. Results of Δ and $\Delta 2$ are listed in table 1. **Conclusion:** From the preliminary results of this study integration of 3D CT images with electroanatomical mapping to guide left atrial mapping seems to be lacking accuracy when compared with ICE. Integrating a real-time imaging modality to the image integration process might improve the mapping accuracy of this system.

	Δ	$\Delta 2$
RUPV	0.5 ± 0.2 cm	0.5 ± 0.2 cm
RLPV	0.5 ± 0.4 cm	0.4 ± 0.3 cm
LUPV	0.6 ± 0.3 cm	0.5 ± 0.3 cm
LLPV	0.4 ± 0.4 cm	0.6 ± 0.3 cm
Carina-LAA/LPV	0.9 ± 0.5 cm	0.9 ± 0.6 cm

POSTER SESSION

1015

Clinical Electrophysiology: Supraventricular Arrhythmias

Tuesday, March 14, 2006, 12:30 p.m.-4:00 p.m.
Georgia World Congress Center, Hall B1
Presentation Hour: 2:30 p.m.-3:30 p.m.

1015-123

Cardiac Resynchronization Therapy (CRT) In Patients With Left Ventricular Dysfunction and Narrow QRS Complex: Sequential Echocardiographic Dyssynchrony Analysis and Correlation with Improvements in Heart Failure Symptoms

Bischan Hassunizadeh, Denise Cunningham, Christian Machado, Providence Hospital and Medical Center, Southfield, MI

Background: Current guidelines recommend CRT for patients with left ventricular EF $\leq 35\%$, refractory, severe heart failure despite optimal medical therapy, and QRS duration > 120 ms. Mechanical dyssynchrony has shown to be a better predictor of response to CRT than QRS prolongation on the electrocardiogram.

Methods: CRT was performed in 14 patients with severe LV dysfunction ($EF \leq 35\%$) and normal QRS duration ≤ 120 ms. Echocardiographic dyssynchrony analysis was performed before CRT and after a mean of 217 ± 24 days including right ventricular electromechanical delay (EMD) and LV EMD as assessed by Pulsed Wave Doppler to calculate interventricular dyssynchrony (IVD, difference between right and left ventricular EMD) and septal wall EMD, lateral wall EMD, anterior wall EMD and inferior wall EMD assessed by Tissue Doppler Imaging to determine intraventricular dyssynchrony (maximal difference of EMDs of the four myocardial walls). Additionally, Minnesota Living with Heart Failure Questionnaire Score (MHFQ-S) and LV EF were assessed at both time points.

Results: Mean age of patients was 57 ± 11 years. Mean QRS duration was significantly longer at follow-up compared to before CRT (150 ± 26 ms vs. 102 ± 16 ms, $p < 0.005$). IVD was significantly shorter at follow-up compared to before CRT (40 ± 29 ms vs. 20 ± 11 ms, $p = 0.04$). Significant reduction in MHFQ-S (43 ± 24 points vs. 64 ± 27 points, $p = 0.003$) was noted at follow-up and also improvement in LV EF compared to before CRT (26 ± 12 vs. 18 ± 8 , $p = 0.01$). Additionally, the reduction in IVD significantly correlated with improvements in MHFQ-S by Pearson correlation ($p = 0.008$). Intraventricular delay times were similar before CRT and at follow-up (93 ± 76 ms vs. 69 ± 25 ms, $p = 0.346$).

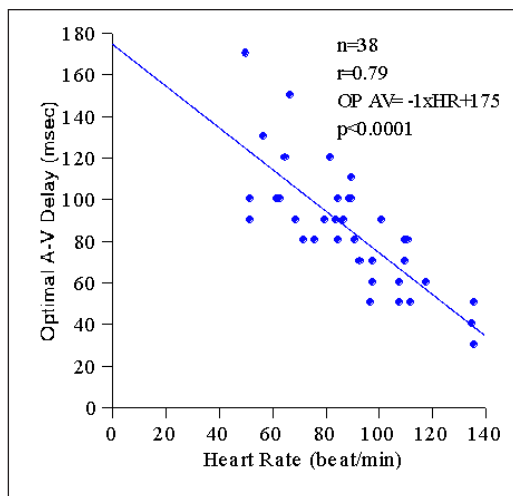
Conclusions: 1) Patients with reduced LV EF ($\leq 35\%$) and narrow QRS show significant clinical improvement (MHFQ-S and LV EF) after CRT. 2) IVD but not intraventricular delay time is significantly decreased after CRT in this patient cohort. 3) The improvements in IVD correlate significantly with reduction of MHFQ-S. Parameters of interventricular dyssynchrony may be better predictors of response to CRT than parameters of intraventricular dyssynchrony in patients with LV dysfunction and narrow QRS complex.

1015-124

An Evaluation of Optimal AV Delays During Exercise in Heart Failure Patients Receiving Cardiac Resynchronization Therapy

Jing Ping Sun, Edward Chinchoy, George Perlic, Deborah Agler, Zouying Hu, James D. Thomas, Bruce L. Wilkoff, Richard A. Grimm, The Cleveland Clinic Foundation, Cleveland, OH

Background: Cardiac Resynchronization Therapy (CRT) procedures are currently performed with patients (pts) at rest. Because of improved exercise tolerance following CRT, the suitability of optimized atrio-ventricular (AV) delay at rest for an active lifestyle remains largely unknown. We hypothesized that exercise-induced increase in heart rate (HR) would necessitate different AV delay than that at rest, to maintain optimal left ventricular (LV) filling. **Methods:** Heart failure pts with CRT who were capable of exercising were studied. Various parameters including end-diastolic and systolic volumes, ejection fraction (EF), pulsed and color Doppler were recorded at rest and during exercise in supine position. After recording baseline Echo, pts were then exercised to target HR of 20 and 40 beats/minute above their intrinsic rates, and the AV interval optimization procedures repeated at each of the elevated HR. **Results:** Fifteen pts (6 male, 9 female, 57 ± 16 years; 12 NYHA II, 3 NYHA III; mean QRS of 151 ± 20 msec) with an average LV EF of $37 \pm 15\%$ (pacing off) and $43 \pm 14\%$ (pacing on) were studied. The correlation between optimal AV delay and heart rate was shown in figure.



Conclusion: This study indicated that CRT pts required a shorter AV delay that is proportionate to HR during exercise, to maintain an optimal LV filling duration. Further analysis and understanding of the relationship between LV filling and increased HR during CRT would allow rate related algorithms to be implemented in these devices more routinely.

1015-125 Comparison of Reverse Ventricular Remodeling Between Surgical Direct Epicardial and Transvenous Coronary Sinus Lead Placement for Cardiac Resynchronization Therapy

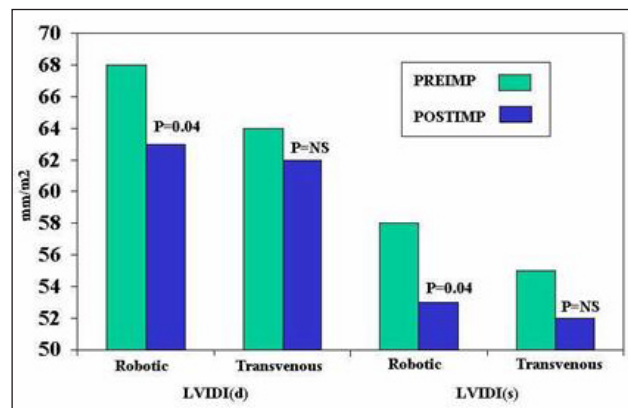
Sandeep Joshi, Joseph J. DeRose, Jr., Devi S. Gopinath, Ajay Shah, Jonathan S. Steinberg, St. Luke's-Roosevelt Hospital Center, New York, NY

Introduction: Cardiac resynchronization therapy (CRT) has been shown to promote reverse ventricular remodeling in patients with heart failure, however inconsistent venous anatomy has limited this. Robotic surgical CRT implants the lead on the left ventricle (LV) epicardial surface with no limitations on lead positioning. A comparison of reverse remodeling between surgical and transvenous CRT hasn't been studied.

Methods: A retrospective case-control comparison was performed with patients matched for age, gender, medications, heart failure etiology, New York Heart Association Class (NYHA) and LV ejection fraction. 16 patients underwent robotically-assisted epicardial LV lead implantation and 16 underwent transvenous CRT. Reverse remodeling was assessed at a follow-up echocardiogram 6-12 months post-implant.

Results: The 32 patients (68 ± 8 yrs, 22 males, 50% ischemic cardiomyopathy, LV ejection fraction 0.22 ± 9 , NYHA 3.3 ± 0.5) were well matched in all variables between groups. Following a mean 9 ± 2 months, the surgical group demonstrated significant reductions in LV internal dimension index, systolic (LVIDI(s)) [-9%, $P=0.04$] and diastolic (LVIDI(d)) [-7%, $P=0.04$] vs. lesser nonsignificant changes (LVIDI(s)-5% $P=NS$, LVIDI(d)-3% $P=NS$) (see figure) in transvenous CRT.

Conclusions: Robotic surgical CRT was more effective in promoting reverse remodeling than transvenous CRT. Given these results, direct epicardial surgical lead placement warrants further analysis as the initial approach for CRT.



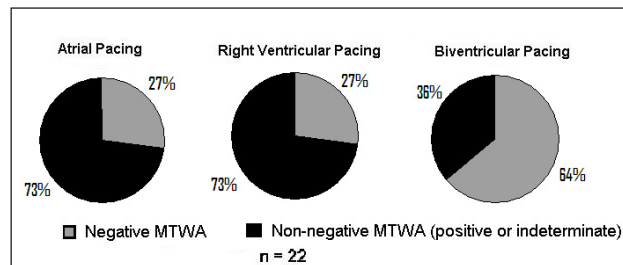
1015-126 Biventricular Pacing Reduces Incidence of Microvolt T Wave Alternans in Patients With Congestive Heart Failure

Safwat A. Gassis, Fernando Mera, David B. DeLurgio, Paul F. Walter, Jonathan J. Langberg, Angel R. Leon, Carlyle Fraser Heart Center, Emory University, Atlanta, GA

Background: Microvolt T-wave alternans (MTWA) is a useful non-invasive tool to assess risk for malignant ventricular arrhythmias. Cardiac resynchronization (CRT) with biventricular pacing (BiV) has been shown to improve hemodynamics and may reduce the risk of sudden cardiac death. The purpose of the current study was to determine the effect of CRT on MTWA.

Methods: Twenty two patients underwent implantation of a CRT device (9 ischemic, mean ejection fraction $18 \pm 7\%$). MTWA was measured during atrial pacing, DDD pacing with only right ventricular (RV) activation, and during DDD pacing with biventricular pacing in an integrated bipolar configuration.

Results: MTWA during atrial pacing was positive in 55%, negative in 27% and indeterminate in 18% of patients. MTWA results were dichotomized into negative and non-negative categories. BiV pacing increased the incidence of negative MTWA from 27% with atrial pacing to 64%. Overall MTWA concordance between atrial and BiV pacing was 55% whereas concordance between atrial and RV pacing was 73%. Concordance of atrial or RV pacing with BiV pacing was 44% for positive or indeterminate tests compared to 83% for negative MTWA tests.



Conclusion: MTWA measurement during BiV pacing is feasible and reduces the proportion of positive or indeterminate results whereas atrial and RV pacing is more likely to lead to non-negative results. Whether the shift to a negative MTWA test during BiV pacing truly represents a decrease in risk for ventricular arrhythmia remains to be determined.

1015-127 Attenuation of Cardiac Remodeling After Recent Myocardial Infarction Through Biventricular Pacing

Eugene S. Chung, Santosh Menon, Raul Weiss, Edward Schloss, Theodore Chow, Dean Kereiakes, Joseph Pastore, Christ Hospital, Cincinnati, OH, Riverside Hospital, Columbus, OH

Background: Dilatation of the left ventricle (LV) after a myocardial infarction (MI) is associated with poor clinical outcomes. Furthermore, treatments that attenuate LV remodeling typically improve outcomes. One possible mechanism for LV remodeling after MI is increased LV stress resulting from an area of delayed activation. We present the results of a randomized feasibility study to test the hypothesis that chronic biventricular pacing with leads placed near the MI location can attenuate LV remodeling.

Methods: 16 patients with recent (within 30-45 days) MI, LV ejection fraction (EF) $\leq 30\%$, narrow QRS (<120 ms), and heart failure were enrolled in the Ohio Pacing post-Infarction Study (OPIS) and randomized to receive an implantable defibrillator (ICD) or atrially-synchronized biventricular pacing with defibrillator (BIV) between day 30-60 post MI. Clinical evaluation, laboratory studies, and echocardiogram (ECHO) were obtained at enrollment, 6 months, and 12 months. ECHO's were analyzed for LV volumes.

Results: 8 patients in the BIV arm (V-paced >95%) were compared with 7 patients in the ICD (0% V-pacing) arm. At 12 months, all patients in both groups were alive and none had received shock therapy for ventricular arrhythmia. There were no unanticipated adverse events in either group.

At baseline, the two groups were similar with regard to major demographics (age, sex, medication use), cardiac structure (LV volumes, EF, sphericity index) and clinical status (NYHA, quality of life, 6 minute walk). At 1, 6, and 12 months, there were no significant differences in NYHA, QOL, 6 minute walk between two groups. Sphericity index rose from 0.38 at baseline to 0.53 at 12 months in the ICD group but remained stable in the BIV group (0.45 at baseline and at 12 months). At 12 months, LV end-diastolic volume and LV end systolic volume increased in the ICD group ($24 \pm 21\%$ and $20 \pm 24\%$, respectively), but remained largely unchanged in the BIV group ($1 \pm 17\%$ and $-6 \pm 18\%$, respectively). LVEF was not different between the two groups.

Conclusions: Chronic application of BIV pacing appears to be feasible in patients with recent MI. Trends in these pilot data suggest that BIV pacing may attenuate post-MI remodeling.

1015-128 Effects of Different Pacing Modes on Right Ventricular Function in Cardiac Resynchronization Patients

Erwan Donal, Sr., Noelle Vignat, Sr., Christian de Place, Sr., Christophe Crocq, Sr., Philippe Mabo, Sr., Claude Daubert, Sr., Christophe Leclercq, Sr., University Hospital, Rennes, France

Cardiac resynchronization therapy (CRT) is a recognized treatment in advanced heart failure patients (pts) with left ventricular (LV) dysfunction and wide QRS. The impact of CRT in right ventricular (RV) function, remains non established. The aim of the study was to evaluate the acute effects of different pacing modes in CRT pts on RV function.

Methods: 15 pts (age 67 years) implanted with a CRT device underwent an echocardiographic evaluation 6 months after device implantation in sinus rhythm (SR), RV/LV, and biventricular (BiV) pacing modes (in random order) to assess RV systolic and diastolic functional parameters (tricuspid annulus peak velocity (Sa); tricuspid annulus plan systolic excursion (TASPE), right myocardial performance index (MPI), pulmonary output and tricuspid flow).

Results: The median LV ejection fraction was 20% with a median LV end-diastolic diameter of 78mm. RV function was impaired as with a fractional shortening of RV surfaces of 36%.

With BiV, Sa was significantly improved as compared to SR, RV and LV pacing modes (table 1). There was a trend to an improvement in TASPE and right MPI with biventricular pacing as compared to the other modes (Table 1). No significant difference was observed between the different pacing modes for pulmonary arterial pressures, indices of right diastolic parameters and pulmonary output.

Conclusion: This acute study showed that right systolic function was significantly improved with biventricular pacing as compared to SR, RV or LV pacing modes in CRTpts.

Results (* = p<0.01)

	AAI	RV	LV	BiV
Tricuspid Sa (cm/s)	9.9	10	11.7	12.6*
TASPE (cm/s)	17.2	17.6	18	18.6
IMP	0.49	0.44	0.56	0.38
Pulmonary output (l.min)	4.1	4.2	4.2	4.6

1015-129 Impact of Pulmonary Hypertension on Left Ventricular Reverse Remodeling and Long-term Outcome in Patients with Cardiac Resynchronization Therapy

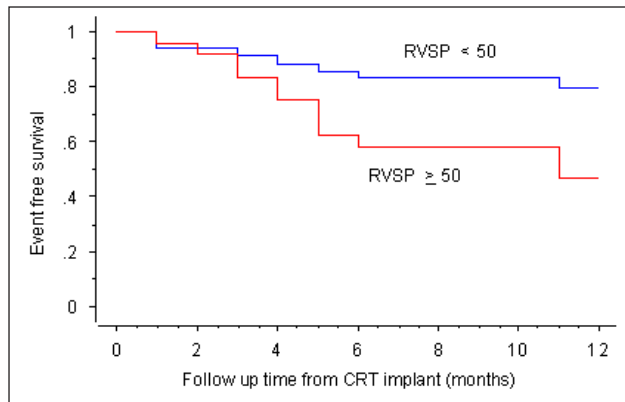
Joshua D. Stern, Lorne Murray, Jeffrey Chung, Michael H. Picard, Marc J. Semigran, Jeremy N. Ruskin, Jagmeet P. Singh, Massachusetts General Hospital, Boston, MA

Background: Many patients with heart failure remain non-responsive to Cardiac resynchronization therapy (CRT). There is a paucity of information on the impact of baseline pulmonary hypertension (PH) on clinical outcome and on left ventricular reverse remodeling (LV-RR) after CRT.

Methods: 59 subjects with standard indications for CRT were followed for a 12-month period. Subjects were stratified into 2 groups based on the echocardiographic estimation of right ventricular systolic pressure (RVSP) i.e. RVSP \geq 50 mm Hg (n=24) and RVSP < 50 mm Hg (n=35). Long-term response was measured as a combined endpoint of heart failure hospitalizations and all cause mortality at 12 months (see Figure). Follow up echocardiograms to assess for LV-RR were available in 41 subjects (mean duration 6.7 months). LV-RR was defined as any improvement in global systolic function and reduction in left ventricular internal diameter.

Results: The study population was comprised of 15 women and 44 men; (age, mean \pm SD; 70 \pm 11 years), with a decreased left ventricular ejection fraction (24 \pm 8%) and a wide QRS (174 \pm 57 ms). There were no significant differences in the clinical features between the high and low RVSP group. Baseline RVSP was not predictive of LV-RR (p=0.32). Subjects with RVSP \geq 50, had a significantly worse outcome (Hazard ratio (95% CI), 2.9 (1.2-7.7), p=0.02).

Conclusion: In patients receiving CRT, although PH (RVSP \geq 50 mm Hg) does not significantly impact LV reverse remodeling, it is associated with an adverse long-term outcome.



1015-130 Blacks Are Less Susceptible to Atrial Fibrillation Despite an Adverse Risk Profile: A Meta-Analysis

Gian M. Novaro, Craig R. Asher, Sergio L. Pinski, Deepak L. Bhatt, Cleveland Clinic Florida, Weston, FL, Cleveland Clinic Foundation, Cleveland, OH

Background: Development of atrial fibrillation (AF) in cardiac patients (pts) is multifactorial, including not well defined genetic factors. We sought to determine if race was associated with the development of AF in pts with coronary disease.

Methods: We conducted a meta-analysis of 7 prospective randomized clinical trials coordinated by the Cleveland Clinic Clinical Coordinating Center that prospectively collected data on the development of AF: 4 trials in patients with acute myocardial infarction (GUSTO I, IIb, III, V), and 3 trials in pts with acute coronary syndromes (PURSUIT, IMPACT II, PARAGON A). Follow-up periods ranged from 6-12 months.

Results: A total of 95,787 pts were identified (93,050 white, 2737 black). At baseline, black pts were younger, had greater body mass index, and a greater prevalence of hypertension, diabetes, tobacco use, and prior infarction compared to white pts. Development of AF was lower in black than in white pts (4.3% vs. 7.6%; OR 0.52; 95% CI 0.43-0.63; p<0.001), while rates of ventricular tachycardia and fibrillation were similar in both groups. There was no significant heterogeneity in the effect among the individual trials (p=0.46; Breslow-Day test). In multivariate logistic analysis, white race was associated with significantly higher rates of AF (OR 1.55; 95% CI 1.39-1.74; p<0.001) compared to black race.

Conclusions: Despite an adverse risk profile, black race appears to be protective against

the development of AF. Further study is needed to investigate the mechanisms and potential genetic underpinning behind this association.

1015-131 Does Hormone Therapy Impact Stroke Risk Among Women With Atrial Fibrillation? Results from the AFFIRM trial

Suma H. Konety, Mitchell Barnett, Brian Olshansky, University of Iowa Hospitals and Clinics, Iowa City, IA

Background: Atrial fibrillation (AF) is a well established risk factor for stroke. It is unclear if there is any impact of hormone therapy (HT) on the risk of ischemic stroke among women with AF.

Methods: Risk of ischemic stroke was evaluated in 1594 women enrolled in the AFFIRM trial, 98% of whom had HT data (estrogen or estrogen-progesterone). An actuarial analysis of time to first ischemic stroke by HT use was adjusted for age, heart failure, diabetes, hypertension, prior stroke, randomization group (rate-control vs. rhythm-control) and international normalized ratio (INR) level at last follow-up visit.

Results: Women taking HT (n=350) were younger but otherwise, had similar baseline characteristics compared to women not taking HT (n=1213) [Table 1]. The unadjusted risk for ischemic stroke was significantly lower in women taking HT compared to those not taking HT (Hazard Ratio [HR] =0.38; 95% confidence interval [CI]= 0.18, 0.79). The interaction between age and HT was not significant (p=0.98). After adjusting for potential confounding variables and INR levels, the stroke rate in women taking HT remained lower compared to women not taking HT (HR=0.45; 95% CI= 0.21, 0.96).

Conclusions: In the AFFIRM Trial, women with AF taking HT were at lower risk for ischemic stroke compared to women with AF who were not taking HT even after adjusting for age, INR levels and other stroke-risk variables. These data highlight the need to consider the impact of HT in similar populations of women with AF.

Baseline Characteristics of Women According to Hormone Therapy

Patient characteristics	Women on HT	Women not on HT	p value
Age, y*	69 \pm 7	72 \pm 7	<0.01
BMI*	28 + 6	29 \pm 7	0.05
Congestive heart failure, %	19	23	0.16
Hypertension, %	73	73	0.99
Diabetes, %	17	20	0.20
Coronary artery disease, %	30	29	0.78
Prior Stroke, %	15	13	0.45
Time to stroke, y*	2.2 + 1.4	2.1 + 1.4	0.84

* = mean \pm standard deviation; y = years

1015-132 Typical Atrial Flutter is Associated with Obstructive Sleep Apnea

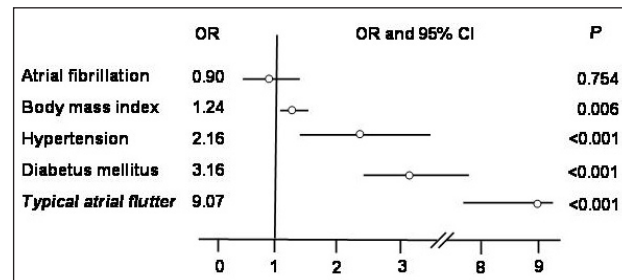
Dai Yumino, Katsuya Kajimoto, Koichi Takeuchi, Eriko Ushikubo, Tetsuyuki Manaka, Koichiro Ejima, Kohei Tanizaki, Atsushi Takagi, Yukio Tsurumi, Morio Shoda, Nobuhisa Hagiwara, Tokyo Women's Medical university, Tokyo, Japan

Background Recently, it is suggested that a strong association exists between arrhythmias and obstructive sleep apnea (OSA). Furthermore, OSA influences right heart morphology and function, and then may contribute to arrhythmogenesis. Therefore, we tested the hypothesis that the prevalence of typical atrial flutter (AFL), a macro-reentrant rhythm in right atrium, is associated with OSA.

Methods and Results: We prospectively studied consecutive patients who underwent the cavotricuspid isthmus ablation for typical AFL (n=52, except for congenital heart disease) and consecutive cardiovascular disease patients without past or current AFL referred to a general cardiology practice (n=198). Pts with an apnea hypopnea index \geq 10/hr by polysomnography was considered as OSA.

The proportion of pts with OSA in the AFL group was significantly higher than that of the general cardiology group (79% versus 36%, P<0.001). By multivariate analysis, AFL, in addition to body mass index, hypertension, and diabetes mellitus remained significantly associated with OSA, showing largest OR for AFL (OR 9.07, P<0.001; Figure). However, there was no significant relationship between OSA and atrial fibrillation (OR 0.90, P=0.754).

Conclusions: This study suggests that there is a strong association between OSA and the prevalence of AFL arising from the right atrium. Interestingly, we did not find significant relationship between OSA and prevalence of atrial fibrillation in our population.



1015-133 Do Endurance Exercise-Induced Sinus Node Dysfunction and Arrhythmias Persist? A Case-Matched Long-Term Follow-Up Study of 62 Former Professional Cyclists

Sylvette Baldesberger, Christine H. Attenhofer Jost, Reto Candinas, Burkhardt Seifert, Michel Zuber, Manfred Ritter, Erwin Oechslin, Pia Luethi, Christoph Scharf, Urs Bauersfeld, HerzGefasszentrum Zurich, Zurich, Switzerland

Background: Significant brady- and tachyarrhythmias may occur in active endurance athletes. It is controversial whether these arrhythmias persist after cessation of competitive endurance training.

Methods: 62 (46 %) of all 134 former Swiss professional cyclists (PC) participating $\geq 1x$ in the professional bicycle race Tour de Suisse in 1955-1975 could be recruited for a prospective study. The PC were screened with history, clinical exam, ECG, 24 hour ECG and echocardiography. The control group consisted of 62 golfers matched for age, gender, weight, hypertension and cardiac medication.

Results: Mean time since the last bicycle race as a PC was 38 ± 6 years. Mean age at exam was 66 ± 6 years in controls and 66 ± 7 in PC ($p=0.77$). There was no difference in coronary risk factors; only smoking was more prevalent in controls ($p<0.0001$). The percentage of study participants with more than 4 hours sports activity per week was identical. Left ventricular ejection fraction was higher in controls (65 ± 8 %) than PC (62 ± 8 %, $p=0.02$), left ventricular muscle mass index tended to be higher in PC than controls (110 ± 34 g/m² versus 100 ± 18 g/m², $p=0.07$).

QRS duration (101 ± 20 versus 95 ± 13 ms, $p=0.03$) was longer in PC. There was no difference in the number of atrial or ventricular premature complexes, or supraventricular tachycardias in the 24 hour ECG. Average heart rate was lower in PC with 66 ± 9 versus 70 ± 8 beats per minute (bpm), $p=0.01$. Minimal heart rate was 49 ± 8 in PC versus 51 ± 6 bpm in controls ($p=0.08$). Ventricular tachycardias tended to occur more often in PC than in controls (13 % versus 3 %, $p=0.10$). There was no difference in atrioventricular blockage ($p>0.99$).

Signs of sinus node dysfunction (SNC) with bradycardia of <40 bpm/min (10 % versus 2 %), atrial flutter (5 % versus 0 %), pacemaker for bradyarrhythmias (3 % versus 0 %) and/or maximal RR interval of >2.5 sec (6 % versus 0 %) were more common in PC (18 %) than controls (2 %, $p=0.004$).

Conclusions. Among former PC, SND occurs significantly more often compared to matched controls. There is a trend towards more frequent ventricular tachycardias in former PC. Further studies have to evaluate the impact on follow-up and management of arrhythmias in former competitive endurance athletes.

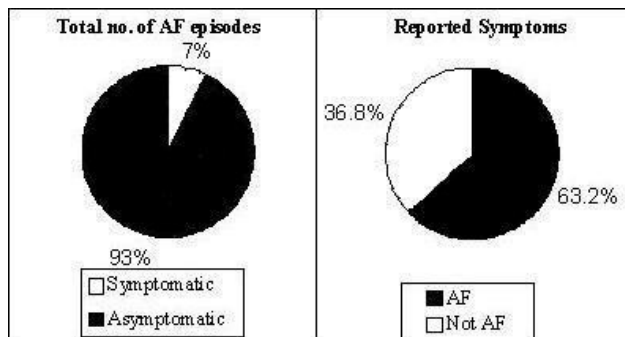
1015-134 Do Symptoms Predict Atrial Fibrillation Episodes in Patients With Paroxysmal Atrial Fibrillation?

Rick A. Veasey, John Silberbauer, John Vrahimides, Wasing Taggu, Vince Paul, Neil Sulke, Eastbourne District General Hospital, Eastbourne, United Kingdom

Background: Using diary cards in conjunction with beat to beat pacemaker Holters, correlation between symptoms and atrial fibrillation (AF) episodes and duration is possible.

Methods: 87 symptomatic paroxysmal atrial fibrillation (PAF) patients with AF burden of 1 to 50% were assessed. 46 pts were excluded due to incomplete diary cards or sensing aberrancy. Holters and corresponding symptom diary cards were analysed from the 41 remaining patients (age 71 ± 9 , 58.5% male). Patients accurately documented time and duration of their symptoms and this was correlated with device Holter AF episodes. Symptoms without corresponding AF, asymptomatic AF, and symptomatic AF could then be described.

Results: 1,960 days (5.4 years) of corresponding Holter and symptom diaries were analysed. 194 symptom episodes without AF, 333 symptom episodes with AF, and 4,274 episodes of asymptomatic AF were recorded. 92.8% of AF was asymptomatic. 36.8% of reported symptoms were not AF related. 63.2% of symptoms exactly correlated with episodes of AF (see figure).



Conclusions: In highly symptomatic PAF patients the majority of symptoms are due to AF episodes. However, the majority of AF detected by the devices was asymptomatic. Thus trials suggesting therapeutic efficacy of drugs and other interventions must be interpreted with caution, without complete beat to beat information.

1015-135 Do Implantable Cardioverter-Defibrillator Patients Have Adequate Rate Control During Atrial Tachyarrhythmias? Results From a New Continuous Long-Term Monitoring System

Kevin T. Ousdigian, Daniel Weiss, Charles J. Lanzarotti, Jodi Koehler, Bruce L. Wilkoff, Medtronic, Inc., Minneapolis, MN

Background: Poor ventricular (V.) rate control during atrial tachyarrhythmias (AT/AF) has been associated with worse clinical outcomes, including cardiovascular hospitalizations. Implantable cardioverter-defibrillators (ICDs) shocks have been associated with diminished quality of life. Some newer ICDs have a feature (Cardiac Compass™) which records the daily time in AT/AF and the daily mean V. rate during AT/AF for up to 425 days. The objective of this study was to characterize the long-term AT/AF burden and V. rate control in ICD patients (pts) and determine if poor rate control was associated with shocks for supra-ventricular tachycardias (SVTs).

Methods: A retrospective analysis was conducted on pts enrolled in the large, worldwide EMPIRIC trial. Pts were included if they had ≥ 30 trend days. A pt was considered to have poor rate control if they had at least one day with ≥ 6 hours AT/AF duration and a mean V. rate >100 bpm during the AT/AF. All episodes with electrograms were adjudicated by at least two reviewers. The proportion of pts with poor rate control and SVT shocks were computed. Fisher's exact test was used to determine significance.

Results: A total of 900 pts received a dual chamber ICD (Marquis DR Model 7274) and were enrolled in the EMPIRIC trial. Of these, 845 pts had ≥ 30 trend days with a mean of 340 ± 76 days. The mean age was 64.7 ± 12.5 , EF = 32.3 ± 12.7 , and 25.2% of pts had a history (hx) of AT/AF. There were 142 pts (17%) with ≥ 6 hrs AT/AF on at least one day, including 41% (88/213) of pts with a hx of AT/AF and 9% (54/632) of pts without a hx of AT/AF. Of the 142 pts with ≥ 6 hours AT/AF, 52% had poor rate control (mean V. rate >100 bpm during the ≥ 6 hrs AT/AF) on at least one day. The proportion of pts with inappropriate SVT shocks increased from 12% (8/68) in pts with adequate rate control to 28% (21/74) in pts with poor rate control ($p=0.02$).

Conclusions: About half (52%) of ICD patients with longer duration AT/AF have poor V. rate control. Poor rate control in these pts is associated with an increased probability of receiving an inappropriate SVT shock. The long-term trends of AT/AF burden and V. rate during AT/AF may help identify pts who require more vigilant monitoring or interventions

1015-136 Prognostic Significance of Interleukin-2 for the Pharmacological Cardioversion of Recent Onset Atrial Fibrillation

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Background: Several recent studies have provided clues of a relation between atrial fibrillation (AF) and inflammation. This relation is not fully understood in terms of cause and effect. IL-2, IL-6 and hs-CRP are inflammatory mediators released in serum at various stages of the inflammatory cascade. Aim of this study is to investigate the significance of these serum markers for the success of pharmacological cardioversion of recent onset AF. **Methods:** We studied 65 patients with recent onset AF (<24 hrs, mean 6 ± 4 hrs) who were admitted for cardioversion with amiodarone. Exclusion criteria were: active inflammatory disease, recent trauma or surgery, acute coronary syndromes, pulmonary embolism, heart failure NYHA>II, chronic airway disease, hepatic or renal failure, hyperthyroidism, recent use of corticosteroids or anti-inflammatory drugs. Patients underwent thorough physical examination, ECG, routine laboratory evaluation, thyroid hormone measurement, echocardiography and measurement of IL-2, IL-6 and hs-CRP on admission and at 48 hrs. Anticoagulation was given according to guidelines. Amiodarone was given (5mg/kg iv bolus in 20 mins and then 500-900 mg iv in 12 hrs) and the ECG was monitored for 48 hours.

Results: Within 48 hrs 55/65 patients (84.6%) had successful cardioversion to sinus rhythm (responders), whereas 10/65 (15.4%) remained in AF (nonresponders). IL-2 on admission was significantly higher in nonresponders than in responders (1.2 ± 1.3 vs 0.45 ± 0.55 U/ml respectively, $p=0.004$). On the contrary the difference of the two groups for IL-6 (5.23 ± 4.25 vs 6.62 ± 13.6 pg/ml $p=0.75$) and hs-CRP (5.39 ± 3.6 vs 8.81 ± 21.3 mg/l $p=0.6$) on admission, was nonsignificant. At 48 hrs nonresponders had a significant rise in both IL-6 (5.23 ± 4.2 vs 36 ± 37 pg/ml, $p=0.026$) and hs-CRP (5.39 ± 3.6 vs 25.21 ± 13.75 mg/l $p=0.001$) and a decline in IL-2 (1.184 ± 1.3 vs 0.306 ± 0.29 U/ml $p=0.04$). Responders at 48 hrs showed nonsignificant changes of the measured parameters.

Conclusion: In patients with recent onset of AF IL-2 is increased in non-responders to pharmacological cardioversion, whereas it remains normal in responders. These findings emphasize the crucial role of inflammation and in particular IL-2 in AF.

1015-137 Biochemical Markers of Collagen Turnover in Atrial Fibrillation

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Background: Fibrosis of atrium is associated with the initiation or perpetuation of atrial fibrillation (AF). Serum concentration of collagen marker is related to myocardial fibrosis in hypertensive patients. **Methods:** We determined levels of pyridinoline cross-linked carboxyterminal telopeptide of type I collagen (ICTP), a marker of collagen type I degradation, and procollagen type III aminoterminal peptide (PIIINP), a marker of collagen type III synthesis, in 21 control subjects, 12 paroxysmal AF patients and 12 chronic AF patients, and we also measured ANP and BNP levels. We determined left ventricular mass index (LVMI) and left atrial volume (LAV) /body surface area (BSA) by echocardiography, and investigated the relationship between serological markers (BNP, ANP, ICTP, PIIINP) and echocardiographic parameters. **Results:** ICTP level in chronic AF was significantly higher than that in control group ($p<0.05$). Moreover, ICTP level

in AF was correlated with BNP ($r=0.68$, $p<0.001$), ANP ($r=0.42$, $p<0.05$) and LAV/BSA ($r=0.45$, $p<0.05$), but not with LVMI. ANP was correlated with LAV/BSA ($r=0.55$, $p<0.01$). **Conclusions:** The present study demonstrated that collagen turnover was accelerated in chronic AF, suggesting that the maintenance of AF is associated with atrial fibrosis. In addition, ICTP level in AF reflected LA remodeling independently of left ventricular hypertrophy in AF. Collagen markers have a possibility to indicate the atrial fibrosis as well as the atrial remodeling in AF.

Correlations

		PIIINP	ANP	BNP	LAV/BSA	LVMI
ICTP	r	0.524	0.415	0.676	0.449	0.255
	p	0.001	0.049	0.001	0.028	0.229
PIIINP	r		0.311	0.320	0.203	0.136
	p		0.149	0.028	0.340	0.527
ANP	r			0.681	0.550	0.088
	p			0.001	0.007	0.688
BNP	r				0.571	0.238
	p				0.004	0.262
LAV/BSA	r					0.253
	p					0.233

1015-138 Anatomical Remodeling of Left Atria in Subjects with Chronic and Paroxysmal Atrial Fibrillation Evaluated by Multislice Computed Tomography

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Background: We used ECG-gated enhance multislice computed tomography (MSCT) to evaluate and compare anatomical change to left atria (LA) including left atrial appendage (LAA) in subjects with chronic and paroxysmal atrial fibrillation (CAF and PAF, respectively). **Methods:** Retrospective ECG-gated MSCT (Light Speed Ultra 16, General Electric) was performed in 16 subjects with CAF (10 male, median age 68/period of CAF 6 years, 3 severe or moderate mitral stenosis (MS), 3 mitral regurgitation (MR)) and 17 with PAF (11 male, median age 62/period of PAF 3 years, one MS, one MR) 30 seconds and 8 minutes after injection of contrast. We evaluated: qualified observed morphology of pectinate muscles (PM) in LAA (well/poorly/non- developed); absolute thickness of LA anterior wall; presence of abnormal late enhancement (LE) of LA wall suggesting fibrotic changes; defect of contrast in LAA only in early phase and LAA enlargement; comparison of LA diameter evaluated by 4-chamber view obtained by transthoracic echocardiogram. **Results:** CAF group: well-developed PM (19% subjects), poor PM (44%), no PM (38%). PAF group: well-developed PM (41%), poor PM (47%), no PM (12%). Incidences of well- and non-developed PM were significantly less and more in CAF group, respectively. CAF subjects with no PM had longer periods of CAF and larger LA diameter than those with developed PM ($P<0.01$). By contrast, there was no relation between PM morphology and PAF periods or LA diameter. Incidence and mean thickness of abnormal LE of LA wall was similar in both groups (2.6mm): 25% (CAF); 24% (PAF). There was a negative correlation in the CAF group between thickness of LA wall and LA diameter ($R^2=0.19$), but not in the PAF group. Contrast defect in LAA only in early phase and enlargement of LAA were observed in 56%, 88% (CAF) and 24%, 41% (PAF); ratios were significantly higher in CAF group ($p<0.01$). **Conclusions:** There were anatomical differences between CAF and PAF groups in MSCT. In CAF group, depending on the period of CAF or degree of LA diameter enlargement, anatomical remodeling (e.g. recession of PM, thinning of LA wall, enlargement of LAA) may appear, which may cause blood flow stagnation, seen as contrast defect in LAA in early phase.

1015-139 Effect of Left Atrial Decompression by Percutaneous Mitral Commissurotomy on Atrial Electrophysiologic Properties

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Background and objective : Atrial dilatation contributes to the inducibility of atrial fibrillation(AF) by changing atrial electrophysiological properties. None of the data was collected from the left atrium(LA), where the most significant electrophysiological impact might be expected to occur in case of mitral stenosis(MS). We investigated electrophysiological changes after reduction of LA pressure in patients undergoing percutaneous balloon mitral commissurotomy (PBMC).

Methods : Twenty-six patients(21 women, 50±12 years) with MS including seven sinus rhythm(SR) patients were studied. Effective refractory period (ERP), monophasic action potential duration (MAPD₉₀), and conduction time (CT) were determined simultaneously in both atrium at 600, 500, 400, and 300 ms of drive cycle length (DCL). Restitution slope(RS) was also calculated by S₁S₂ method. Atrial fibrillation cycle length (AFCL) and dominant Frequency (DF) in case of AF were calculated and all measurements were repeated after PBMC.

Results : Mean LA pressure was significantly reduced after PBMC in both AF and SR patients (17.0±5.5 mmHg vs 10.4±4.0mmHg, $P<0.01$; 17.6±7.1mmHg vs 9.0±2.8mmHg, $P<0.01$). A significant increases of ERP was observed in the LA (212±32ms vs 241±41ms; $P=0.1$) after PBMC, but not in the right atrium(RA). The increase of MAPD₉₀ after PBMC was significant in the LA at all tested DCL, but not in the RA. The CT also decreased significantly at all the tested DCLs after PBMC. RS in the LA decreased from 1.71±0.82 to 0.76±0.33 after PBMC($P=0.028$) AF induced in 3 of 7 SR patients by single atrial stimulation, which was abolished after PBMC. However, no significant change of AFCL, DF and RS after PBMC were observed in AF group.

Conclusion : Chronic atrial stretch altered atrial electrophysiological milieu, especially of the LA, which was partially reversible in SR patients . This result support the theoretical basis for early intervention to reduce atrial pressure overload

1015-140 Risk of Ischemic Stroke in Atrial Fibrillation: Is There an Ethnic Difference in Its Incidence and in the Efficacy of Warfarin?

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Background Studies showing that warfarin reduces atrial fibrillation (AF) related strokes have included predominantly Caucasians and African Americans (AA). We sought to assess whether there is an ethnic difference in stroke incidence and warfarin efficacy in reducing stroke.

Methods We identified all first time hospitalizations for non-rheumatic AF in patients without prior or acute stroke from 1995 to 2000 for all 2 million plus Southern California Kaiser adult members. Average follow-up was 3.5 years. Warfarin use was obtained from pharmacy records, while AF, type of stroke, and other comorbidities were based on hospital discharge ICD-9 codes. We recorded the event rate of each ethnicity while on or not on warfarin.

Results We identified 20,835 AF hospitalizations, of which 15,860 (76%) were Caucasian, 1,650 (8%) were AA, 1,952 (9.4%) were Hispanics and 786 (3.8%) were Asians. There were 1448 ischemic stroke events. Treatment with warfarin reduced stroke rate by over half in all ethnicities except AA. After adjusting for age, gender, warfarin use, hypertension, diabetes, and heart failure, the hazard ratio for ischemic stroke with Caucasians as referent is shown.

	On warfarin	Not on warfarin	
# of Ischemic Strokes /Total Person-Years	176 / 16039	1272 / 56725	
Ischemic Stroke/100 Person-Years			Rate Ratio (95% CI)
All	1.10	2.24	0.49 (0.42 - 0.57)
Caucasian	0.99	2.21	0.45 (0.37 - 0.54)
AA	2.33	3.03	0.77 (0.52 - 1.14)
Hispanic	1.09	2.34	0.47 (0.28 - 0.78)
Asian	0.88	2.07	0.42 (0.17 - 1.06)
	Adjusted Hazard Ratio	95% CI	
Caucasian	1		
AA	1.61	1.40 - 1.90	
Hispanic	1.33	1.12 - 1.59	
Asian	1.16	0.88 - 1.53	

Conclusions In a large, multiethnic cohort of AF patients, the risk reduction for ischemic stroke with warfarin was statistically significant for Caucasians and Hispanics, but not significant for AA and Asians. After adjustment for risk factors and warfarin use, AA and Hispanics were at significantly greater stroke risk than Caucasians.

1015-141 Nadroparin Versus Unfractionated Heparin for Anticoagulation of All Cause Atrial Fibrillation: Final Results of the NADROPAF Trial

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Background: Few studies were conducted to test the safety and efficacy of low molecular weight heparin (LMWH) as an anticoagulation modality in new onset atrial fibrillation (AF) and most of those studies excluded high risk patients (pts) particularly those with valvular heart disease.

Methods: The NADROPAF trial (Nadroparin for Atrial Fibrillation) is a prospective randomized open label multicenter study comparing Nadroparin versus unfractionated heparin (UH) in pts with all cause atrial fibrillation of more than 48 hours duration. From October 2001 to June 2005, 540 pts were included: 270 pts in each group. The demographic characteristics were similar between the 2 groups as shown in the table below.

	LMWH	UH	p
Age (yrs)	60.3±12.2	60.3±12.4	NS
Sex (Female)	189 (70%)	186 (68.9%)	NS
AF Etiology			
Valvular Disease	59 (21.9%)	71 (26.3%)	NS
Hypertension	97 (35.9%)	101 (37.4%)	NS
Other	30 (11.1%)	28 (10.4%)	NS
Lone	84 (31.1%)	70 (25.9%)	NS

In hospital clinical events (death, hemorrhagic or ischemic events) were compared between the 2 groups.

Results: There was only 1 death that occurred in the UH group. There was no major stroke in either group. However, transient ischemic attack was observed in 2 pts of the UH group. Major hemorrhagic event (gastro-intestinal bleeding) occurred in 1 pt of each group. Minor hemorrhage was observed in 2 pts of LMWH group and in 1 pt of UH group. The composite endpoint including death, embolic or hemorrhagic event was 1.1% in the LMWH group and 1.8% of UH group ($p=0.65$).

Conclusions: Anticoagulation of AF from all cause including valvular heart disease can be safely and effectively accomplished by LMWH. These findings need to be confirmed by other studies before recommending an outpatient management of all pts with AF.

1015-142 Long-Term Follow-Up in Patients With Percutaneous Left Atrial Appendage Transcatheter Occlusion System (PLAATO): Risk of Thrombus Formation and Development of Pulmonary Venous Obstruction After Percutaneous Left Atrial Appendage Occlusion

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Background: A new interventional occlusion system for the left atrial appendage (PLAATO) has been introduced as an alternative treatment in patients with increased thromboembolic risk due to atrial fibrillation (AF) and contraindications for oral anticoagulation (OAC). Occlusion of the left atrial appendage (LAA) may compress the left pulmonary vein and carries the risk of thrombus formation on the surface of the device. During the procedure the interatrial septum is punctured to access the left atrium. The aim of this prospective study was to evaluate the morphological and hemodynamical changes following the procedure by means of serial transthoracic and transesophageal echocardiographic examinations.

Methods: Since 2001 48 patients with persistent AF were included in the study (84 patient years) Echocardiographic examinations were performed 24 hours prior to the procedure, during the occlusion procedure, prior to discharge of the hospital, after 1, 3, 6, 12, 24, 36 and 48 months. The echocardiographic analysis included the following parameters: morphology of the interatrial septum, peak pulmonary vein flow and presence of thrombi on the surface of the device and in the left atrium.

Results: Small atrial septum defects are present in all patients immediately after the procedure and disappear within 6 months usually. ASD was still present in only 3 patients after 6 months. Presence of thrombi could be documented in two cases in the follow up period. In one patient a parietal thrombus was detected on the surface of the occluding device, another patient showed a thrombus at the interatrial septum. Under continued combined therapy of Clopidogrel and ASS for three months both thrombi disappeared. Peak flow velocities of the pulmonary veins were not significantly higher after positioning of the device (0.60 ± 0.15 prior versus 0.67 ± 0.14 m/s after the occlusion, $p = ns$).

Conclusion: Long term complications after percutaneous left atrial appendage occlusion are rare. Thrombotic appositions may occur rarely and disappear under continued antiplatelet therapy. The risk of remaining ASD is low.

1015-143 Stroke Prevention Technology for Patients With Non-Valvular AF - Worldwide Experience with the New WATCHMAN LAA System

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Background: Multiple studies have confirmed the presence of thrombus in the left atrial appendage (LAA) in more than 90% of patients with stroke related to atrial fibrillation (AF).

Methods: The WATCHMAN LAA system (Atritech, Inc., Minneapolis, MN) is placed in the LAA via transseptal puncture to prevent the occurrence of thromboembolism. The implant has a 160 micron polyethylene membrane on the proximal face of a nitinol cage and incorporates a row of fixation bars around the mid perimeter. The WATCHMAN device is available in 5 sizes (from 21 to 33 mm). Since August 2002, implantation was started in Europe, in October 2003 also in the US. Patients were assessed at 45 days and 6 months with TEE and chest x-ray and annual clinical assessments thereafter. Clinical endpoint was rate of ischemic stroke, systemic embolism and major bleedings.

Results: In 66 patients worldwide the device has been implanted successfully with a 101.4 cumulative implant years. Mean age was 69.2 years (47-85), 66% were male. Baseline CHAD-Score was 1.7 (0-5) and mean procedure time 59 min (35-157). Two patients experienced device embolization, both successfully retrieved percutaneously. No further embolizations have occurred, since the fixation bars were enhanced. Five pericardial effusions, two of them needing percutaneous puncture, one major air embolism, all without long term sequelae and one delivery system issue (first generation design) have been reported. In 97.1% of patients warfarin was ceased at 6 months. Four patients, however, had a flat thrombus on the device at 6 months, one of these patients developed a transient ischemic attack (TIA). So warfarin was restarted in these patients but again stopped after removal of thrombus. Another patient with a history of TIA experienced a TIA without LAA-thrombus visible. No ischemic stroke or systemic embolism have occurred. One patient died after 9 months due to an ascending aortic dissection. Autopsy documented a stable, well endothelialized device.

Conclusions: Preliminary data suggest the WATCHMAN LAA system to be safe and feasible. Further randomized study is ongoing to determine the long term effect of this technology on stroke reduction in comparison with warfarin.