Assessment of Arrhythmogenic Potential in Brugada Syndrome: Comparison Between Two Configurations of ST Segment Elevation

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Background: Two-ST segment configurations (i.e., coved and saddle-back shape) have been described in Brugada-type electrocardiograms (ECGs), but it is controversial which one would have stronger arrhythmogenic potential. On the other hand, we recently proposed that configuration of ST segment elevation per se is arrhythmogenic in Brugada syndrome. The aim of this study was to examine which configuration is highly associated with life-threatening arrhythmic events and suggests a stronger conduction disturbance.

Methods: Consecutive 48 patients (aged ±15 years, 42 men) with Brugada-type ECG, undergoing signal-averaged ECG (SAECG), were enrolled. Marked ST segment elevation (>0.1 mV) of either the coved type or saddle-back type (≥2 mm) at the right chest leads was seen in all patients. No patients had structural heart disease. The incidence of history of life-threatening events defined as syncope and aborted sudden death and the value of SAECG were compared between two groups. In this study, late potentials (LP) were considered as positive when both criteria (RMS450 < 20 uV and LAS40 < 38 ms) were met.

Results: Life-threatening events: A total of 24 patients had a history of life-threatening events. The incidence of life-threatening events was 17 patients (88%) in group A and 7 patients (33%) in group B (P = 0.02). SAECG: Although QRS duration did not differ between two groups (117.0±12.5 ms vs. 111.0±10.2 ms), RMS40 and LAS40 of group A were significantly longer and lower, respectively than those of group B (RMS40: 13.4±6.8 μV vs. 27.7±12.0 μV; P < 0.0001, and LAS40: 45.7±7.9 ms vs. 30.7±7.0 ms; P < 0.0001). The discriminative power in group A was significantly greater than that in group B (22 patients 88%) and 4 patients (19%) (P < 0.0001).

Conclusion: Life-threatening events were highly observed in patients with coved type ST-segment elevation. Moreover these patients have stronger conduction disturbances compared to patients with saddle-back type ST-segment elevation. When assessing risk for sudden death in patients with Brugada-type ECG, the configuration of ST-segment elevation should be taken into consideration.

Lateral Atrial Dimension Is Associated With Atrial Fibrillation Recurrence: Four-Year Echo Follow-Up Data

Kazama Satoh, Martin S. Green, Charles R. Karr, Stuart J. Connolly, George J. Klein, Robert S. Sheldon, Maria Teleja, Xiaohua Wang, Paul Donahue, Karen Humphries, University of Ottawa Heart Institute, Ottawa, Ontario, Canada.

The Canadian Registry of Atrial Fibrillation (CARAF) enrolled subjects with atrial fibrillation (AF) at the first ECG confirmed diagnosis. We have previously found a relationship between LA dimension (LA dim) and recurrence of AF at 2 years. 899 patients with newly diagnosed non-surgical AF were enrolled beginning in 1990 from 6 Canadian centers. Baseline and 4 year (14) echocardiographic data were available on 403 patients. Participants were followed at 3 months, and then annually for AF status. Patients were classified at 4 years as: no recurrent AF (No AF, n=137) or recurrent AF (RAF, n=266) based on clinical symptoms or ECG documentation. The Raf patients were subdivided into paroxysmal (P) AF, n=123, chronic AF (CAF, n=140) and other (n=3). The mean age was 52±12 years, 73% were women, history of MI 15%, mitral valve disease 12%, hypertension 39%, diabetes 7%, CHF 14%, left ventricular fractional shortening 36%±10%. For the 403 patients, the mean LA dim was 39.0±7.6 mm at baseline, and increased to 41.8±8.6 mm at 4 years. Compared to the No AF group, the RAF group had a larger LA dim at baseline (P<0.001) and a trend toward a larger increase in LA dim over 4 years (P=0.03)$. Those who had developed CAF by 4 years had a larger LA dim baseline and a larger increase in LA dim over 4 years when compared to PAF (P=0.001). See Table.

Conclusion: Larger baseline LA dim is associated with AF recurrence. Patients who progressed to CAF had the largest baseline LA dim and the greatest increase in LA size over 4 years.

Mean LA dim (mm) in AF groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Baseline (SD)</th>
<th>Year 4 (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All N=403</td>
<td>39.52 (7.98)</td>
<td>41.18 (8.60)*</td>
</tr>
<tr>
<td>NoAF N=137</td>
<td>37.59 (7.41)</td>
<td>37.96 (7.91)</td>
</tr>
<tr>
<td>RAF N=266</td>
<td>41.12 (7.87)</td>
<td>42.84 (8.49)*</td>
</tr>
<tr>
<td>PAF N=103</td>
<td>39.06 (7.35)</td>
<td>39.00 (7.50)</td>
</tr>
<tr>
<td>CAF N=140</td>
<td>43.13 (7.73)</td>
<td>46.63 (7.98)*</td>
</tr>
</tbody>
</table>

*P<0.001

Effects of Class III Drugs on Prophylaxis of Atrial Fibrillation After Cardioversion in High Risk Patients for Recurrence Predicted by P Wave Signal-Averaged ECG

Koichi Mizumaki, Akira Fujiki, Hidehiko Nagasawa, Masao Sakabe, Kunihiro Nishida, Robert S. Sheldon, Marie Talajic, Xiaohua Wang, Paul Dorian, Karin Humphries, THRIRD Department of Internal Medicine Toho University Ohashi Hospital, Tokyo, Japan.

Though P wave signal-averaged ECG (P-SAE) may predict recurrence of atrial fibrillation (AF) after cardioversion (CV) for AF in high risk patients (paroxysmal AF and abnormal P-SAE), the effect of class III antiarrhythmic drugs in high risk pts for AF recurrence after CV predicted by P-SAE has not been determined. In this study, criteria for AF recurrence were: death, hospitalization, and new onset AF. Class III drugs was defined as: amiodarone (7.1±2.2 ms), tocainide (6 ms), mexiletine (11 ms), procainamide (12 ms), disopyramide (14 ms), sotalol (8 ms). P wave parameters were measured continuously as follows: P peak, P duration, P amplitude. The cohort had a mean age of 65±10 years, mean ejection fraction of 27±8 % and 89% had symptomatic heart failure. The mean duration of follow-up was 493±395 days. There were no significant differences in baseline characteristics or treatment between the atrial pacing and exercise groups. Cox survival analysis in subjects with determinate results revealed that exercise TWA was an independent predictor of arrhythmogenic events (HR 2.5, 95% CI 1.2 - 5.3, p = 0.02). In contrast, pacing TWA did not predict outcome events (HR=1.9, 95% CI 0.6 - 1.9, p = 0.8). In the subgroup that had both tests performed, pacing TWA yielded more positive tests (73% vs 47%) and fewer indeterminate results (7% vs 27%, p = 0.02); the concordance between pacing and exercise TWA results was only 56%.

Conclusion: Exercise TWA is useful for risk stratification of patients with ischemic cardiomyopathy. PACING TWA does not have prognostic value in this population.

Abnormal QT Prolongation and Psychotropic Drug Therapy in Psychiatric Patients: Significance of Bradycardia-Dependent QT Prolongation

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Background: Sudden unexplained death in psychiatric patients might be associated with drug-induced arrhythmias. Since many psychotropic drugs have electrophysiologic properties similar to class I antiarrhythmic drugs, they might lengthen QT interval and cause torsades de pointes. Methods: Electrocardiograms (ECG) were obtained in 409 psychiatric patients (228 men, 180 women) receiving psychotropic drugs at the Kyushu National Hospital. QTc was calculated by the Bazett's formula. In order to elucidate the heart rate dependence of QT prolongation, QT intervals and the preceding R-R intervals (50-100 beats) were measured at various heart rates (50-100/min) by 24-hour Holter ECG (CM5 lead) in 77 patients. We estimated the QT intervals at the heart rates of 30 and 50/min (QT30, QT50). Results: Mean QTc interval (longest in 12 ECG leads) was prolonged to 444±32 ms (men, 437±32 ms, women, 453:±9 ms, mean heart rate 82±15/min). QTc interval >460 ms was observed in 43 (22%) patients (16% in men and 31% in women). QTc interval >500 ms was observed in 19 (5%) patients (3% in men and 7% in women). Mean QT30 and QT50 were 385±27 and 466±42 ms, which were significantly longer than those in healthy reference group (QT30 and QT50, 370±15 and 440±20 ms, n=95). QTc > 400 ms (mean=2SD of the reference group) was observed in 16 (21%) patients. In the remaining 61 patients whom QTc < 400 ms, the bradycardia-dependent QT prolongation was prominent and QT50 exceeded 480 ms (mean=2SD) in 12 patients. Accordingly, QTc > 400 ms was observed in 28 (36%) patients. Therefore, we need to pay additional attention to the bradycardia-dependent QT prolongation even when the QT interval was not prolonged at usual heart rates (around 800ms). Since torsades de pointes is prone to occur at slower heart rates,
**POSTER SESSION**

**1041**

**Autonomic and Central Nervous System Regulation of the Heart**

Sunday, March 17, 2002, Noon-2:00 p.m.

Georgia World Congress Center, Hall G

Presentation Hour: 1:00 p.m.-2:00 p.m.

**1041-103** Induction of Cardiac Nerve Sprouting and Sympathetic Hyperinnervation by Subthreshold Electrical Stimulation of the Left Stellate Ganglion in Dogs

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Background: Subthreshold electrical stimulation in the brain can induce nerve sprouting and the kindling model of epilepsy. Whether or not subthreshold electrical stimulation can induce cardiac nerve sprouting is unclear.

Methods: Six dogs were used in the study. The chest was opened from the left 4th intercostal space. An active fixation pacemaker lead was screwed into the left stellate ganglion (LSG). The lead was connected to a Madtronic Medtronic neurostimulator (N=3) or a modified Guidant Discovery pacemaker (N=2) to give rapid stimulation at 20 Hz (0.45 ms pulse width) and 1 Hz (1.9 ms pulse width), respectively. We first determined the stimulation threshold (the lowest voltage output that produced an abrupt increase of heart rate of > 20% from the baseline). The pacemaker output was then programmed to 25% of the stimulation threshold for continuous subthreshold electrical stimulation for 41±9 days. The atrial and ventricular tissues were than harvested and stained for nerve markers tyrosine hydroxylase (TH), synaptophysin (SYN) and growth-associated protein 43 (GAP43) by immunocytochemical techniques. Tissues from 6 healthy dogs were used as controls.

Results: The densities (mm² per mm²) of nerves that stained for TH, SYN and GAP43 was significantly (P<0.01) higher in dogs with LSG subthreshold electrical stimulation compared to matched controls (1657±64, 6516±609, 4482±1955 versus 512±76, 2033±340, 359±236 for left ventricle; 2343±1415, 2186±791, 2579±1123 versus 502±68, 263±340, 263+340 for right ventricle; 12334±1128, 11270±7245, 15300±6473 versus 82±64, 170±267 for left atrium and 1616±1533, 20040±10730, 26388±11012 versus 2343±1128, 263±340, 650±1122 for right atrium, respectively). The nerve sprouting magnitude was significantly higher in the atrium compared to the ventricles (P<0.02). Furthermore, the heart weight of LSG group was 19±14% greater than the control dogs (P=0.02).

Conclusions: LSG subthreshold electrical stimulation induces cardiac hypertrophy and sympathetic nerve sprouting. These effects are more prominent in the atrium than the ventricles.

**1041-104** Catheter Stimulation of Cardiac Parasympathetic Nerves in Man: A Novel Technique

Karl Mischo, Patrick Schauerer, Christian Knackstedt, Markus Zarse, And Sinha, Thomas Schimpf, Christoph Stallbrink, Peter Hanrath, Rheinisch-Westfälische Technische Hochschule, Aachen, Germany

Background: Cardiac parasympathetic nerves run alongside the superior vena cava (SVC) and accumulate epidurally adjacent to the coronary sinus (CS) orifice. In animals transvascular catheter stimulation of these nerves results in a negative chronotropic and dromotropic effect without negative inotropy. The present study reports on the first experience with transvascular human parasympathetic nerve stimulation (PS) in the SVC and CS.

Methods: During electrophysiological studies of 23 patients PS was performed in the SVC (n=13) or in the proximal CS (n=10). A deflectable multipolar electrode catheter was positioned in the SVC just above the atrial junction or into the proximal CS. PS in the SVC was performed with a frequency of 20 Hz and stimulation voltages of 10, 20 and 30V during sinus rhythm and during incremental atrial pacing with a nerve stimulation voltage of 30V. During PS in the proximal CS, atrial myocardial tissue stimulation by high frequency nerve stimuli had to be avoided. We therefore applied trains of nerve stimuli (200 Hz, 50 ms train duration) within the atrial refractory period. The antegrade Wenckebach period was determined to assess a negative dromotropic effect.

Results: PS in the SVC caused a significant increase in heart rate depending on the stimulation voltage as well as a significant increase of the antegrade Wenckebach cycle length. PS in the CS lead to a voltage-dependent increase of the antegrade Wenckebach cycle length until AP-blocking it occurred in 7 patients. The negative chronotropic and dromotropic effects started/ceased immediately after the on/off phase of nerve stimulation and were abolished by atropine. Patients reported on moderate chest discomfort during nerve stimulation.

Conclusions: Transvascular electrical stimulation of cardiac parasympathetic nerves can be achieved with conventional electrode catheters positioned in the SVC or CS. Using this novel stimulation technique, readily reversible negative chronotropic and dromotropic effects can be obtained. PS may be used for acute ventricular rate slowing during supraventricular tachycardias in patients with congestive heart failure or as a diagnostic tool during electrophysiological studies.