During our study, one patient without LP and with high grade of QTd (120 ms) died suddenly. The incidence of LP was not different in the two groups of patients. The strong association of increased QTd with VT in HC suggests that patients with life-threatening arrhythmias could be identified by means of this simple parameter.

716 Basic Mechanisms of Atrial Fibrillation

Monday, March 25, 1996, 2:00 p.m.–3:30 p.m.
Orange County Convention Center, Room 314

2:00

716-1 Redistribution of Gap Junction Protein Connexin43 After Radiofrequency Ablation of Dog Atrial Myocardium

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The purpose of this study was to investigate the pattern of connexin43 (Cx43) gap junction distribution in dogs with pacing-induced atrial fibrillation (AF) that underwent radiofrequency catheter ablation (RFA). Complete AV nodal block was produced in three adult dogs by RFA of the AV junction. The atria received atrial pacemakers programmed to pace at 20–30 Hz and ventricular pacemakers programmed at a cycle length of 750 ms. Spontaneous atrial fibrillation was produced after 10–14 weeks of pacing. Dogs then underwent RFA of the atria that terminated AF and were sacrificed. The right atrial roof was fixed in Zn formalin and double labeled with Cx43 and wheat germ agglutinin (WGA). Double labeling with WGA allowed definition of the atrial cell borders and orientation of the immunostained C7x43. Confocal microscopy of optical sections revealed abundant Cx43 expression that was located (as expected) to intercalated discs and to a lesser extent in side to side junctions. RFA of the right atria terminated the AF and resulted in extensive fibrosis with loss of Cx43 staining. In some areas, surviving myocytes clustered as islands surrounded by fibrotic tissue. Hematoxylin and Eosin staining showed normal muscle configuration but Cx43 immunostaining indicated a redistribution of the Cx43 channel protein in these surviving mycocytes. WGA labeling demonstrated defects in the circumferential staining of the surface of the atrial myocytes and redistribution of Cx43 within these surviving myocytes to loci distinct from the intercalated discs. These results suggest that areas of the atrium ablated by RFA may not have normal electrical coupling by Cx43 gap junction channels, even in surviving atrial muscle cells. RFA caused remodeling of Cx43 which very probably affected conduction. In summary, these data suggest that some of the effects of RFA may be mediated by loss or remodeling of gap junction channels.

2:15

716-2 Mechanisms of Termination of Reentrant Wave Fronts in the Atrium: Implications for Prevention of Atrial Fibrillation

James J.C. Ong, John J. Lee, Dustan Hough, Kamyar Kamjoo, Hrayr S. Karagueuzian, Peng-Sheng Chen. *Cedars-Sinai Med Ctr, LA, CA*

The mechanism by which single strong premature stimuli (S_2) induce atrial fibrillation (AF) was studied in 6 open-chest dogs. A plaque electrode array with 480 bipolar electrodes (1.6 mm resolution) was placed epicardially on the right (n = 4) or the left atrium (n = 2). An S2 was given in the center of the plaque scanning diastole following a train of 8 baseline stimuli (S_1) from the edge of the plaque.

Results: In 30 episodes reentrant wave fronts (RWF) were induced (S_1S_2 159 ± 12 ms, 43 ± 26 mA). Earliest activation following S_2 was in the region between S_1 and S_2 and form a single rotor (n = 11) or a "figure of 8" (n = 19) reentry. These RWF (cycle length [CL] 110 ± 11 ms) persisted for 3.1 ± 1.6 cycles (342 ± 199 ms) and terminated: 1) spontaneously without apparent changes in WF characteristics (n = 8), 2) when they meandered out of the mapped region (n = 4), 3) when the leading edge of RWF excited the core of reentry (n = 10), and 4) when critically timed WF from outside the mapped region captured the core (n = 8). Of 30 episodes of RWF, 21 degenerated into AF (CL 110 ± 9 ms) while 9 did not (CL 113 ± 19 ms, p = NS). RWF that degenerated had longer life span than those that did not (3.5 ± 1.7 vs 1.9 ± 1.0 cycles, p < 0.05). When the initial RWF were terminated by direct excitation of the core (n = 18), "late" termination (at 3.7 ± 1.8 cycles) did not prevent development of AF while "early" termination (at 1.1 ± 0.9 cycles, p = 0.07) aborted AF.

Conclusions: (1) RWF are present at the initial stage of AF induced by single strong premature stimuli. (2) They have a limited life span and must persist for 3.5 ± 1.7 cycles for AF to occur. (3) They can be terminated by direct excitation of the core. (4) Early termination of these RWF appears to prevent degeneration into AF.

2:30

716-3 Conversion of Non-Stationary to Stationary Reentrant Wave Front With a Critically-Sized Anatomical Obstacle in the Atrium

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Acetylcholine (ACh) destabilizes functional reentrant wave fronts (RWF) by causing them to meander from one atrial site to another. We hypothesized that an obstacle of a critical size stabilizes the wandering RWF by anchoring it to the obstacle. Eight isolated canine right atrial tissues (3.8 by 3.2 cm) were mounted in a tissue bath and the endocardial isochronal activation maps of an S_2-induced reentrant activity constructed using up to 480 bipolar electrodes (1.6 mm interelectrode distance). Consecutive (up to 8 sec) RWF activity was also visualized dynamically on a computer screen. Holes of 2 to 10 mm diameters were created in the center of the tissue with punch biopsies and the dynamics of the induced RWF were evaluated after each test lesion in the presence of ACh (5 μM). ACh shortened the refractory period from 99 ± 14 ms to 58 ± 10 ms. When no lesion was present, the induced RWF meandered in a concentric and irregular manner, which eventually underwent breakup to multiple and/or disorganized wave fronts. Hole sizes of 2–4 mm diameter had no effect on the stability of the RWF. The induced RWF continued to meander and underwent breakups causing the formation of new RWFs. However, when the hole diameter was increased to 6 mm and up to 8 and 10 mm, the RWF became stationary and stable by anchoring to the central hole. No wave breakup or disorganization occurred. We conclude that induced functional RWF in the atrium in the presence of ACh are non-stationary and undergo breakups. Holes of critical size (i.e., ≥ 6 mm) stabilize the RWF and prevent wave front instabilities. These findings may have relevance to lesions created in clinical settings to control atrial fibrillation.

2:45

716-4 Effects of Acute Right Atrial Pressure Load on Conduction and Refractoriness

Ruediger Becker, Kirsten D. Freigang, Alexander Bauer, Frederik Voss, Julia C. Senges, Mustafa Oezbek, Wolfgang Schoels. *Department of Cardiology, University of Heidelberg, Germany*

The increase in atrial pressure associated with the onset of atrial fibrillation might directly affect electrophysiologic properties and thereby favor the sustenance of the arrhythmia. To analyze the effects of acute right atrial pressure load on conduction and refractoriness, a custom-designed electrode array containing 128 bipolar electrodes was placed on the epicardial surface of both atria in 5 normal beagle dogs. Using a computerized multiplexer mapping system, epicardial activation maps were constructed and local effective refractory periods (ERPs) at 13 ± 2 randomly selected right (RA) and left atrial (LA) sites were determined before and after banding of the pulmonary artery. During banding, RA pressure increased by 3 ± 1.7 mmHg, systemic pressure decreased by 20 ± 9 mmHg and heart rate dropped by 11 ± 11 bpm. The epicardial activation pattern remained basically unchanged, RA and LA activation time was 43 ± 9 and 36 ± 4 ms (control) versus 45 ± 8 and 37 ± 7 ms (banding), respectively (p > 0.05, control versus banding). Effects on atrial ERPs are summarized in the table below.

	Control	Banding	p
RA ERP (ms)	129 ± 17	119 ± 16	0.002
LA ERP (ms)	110 ± 18	114 ± 21	0.154

Conclusions: Acute right atrial pressure load results in shortening of ERPs in the RA, but not in the LA. This suggests a direct effect of atrial pressure on local electrophysiologic properties rather than a secondary effect due to autonomic counterregulation. Local changes in ERP might increase the dispersion of refractoriness and thereby favor reentry.

3:00

716-5 Pectinate Muscle Network and Wave Front Curvature Contribute to Slow Conduction and Reentry in the Atrium

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It is uncertain whether the highly complex branching network of pectinate muscles in the atrial subendocardium is involved in the initiation or main-