FC11 Mechanisms of atrial fibrillation

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Are onset mechanisms consistent in AF patients?

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Objective: The aim of this study was to investigate the onset mechanisms of atrial tachyarrhythmia (AT) in patients implanted for an usual pacing indication with a Selection device (Vitatron).

Methods: The diagnostic functions were programmed with 2 detection rates: 200 and 300 bpm. Underlying rhythm and triggers were analysed and classified in classes: tachycardia, Premature Atrial Complex (PAC) trend increase, restart, no underlying rate and, PAC, multiple PAC, short run, brady-tachy, sudden onset respectively. An onset scenario has been defined as a combination of one trigger and one underlying rhythm.

Results: 23 / 55 pts had AT episodes between implantation and 6 month follow-up. 237 onset mechanisms have been analysed. An increase of the atrial ectopy has been noticed during the trigger [52%]. the underlying rhythm [150%] and the onset scenario [143%] analysis.

Conclusion: Before preventing AF by pacing, onset mechanisms have to be documented to optimize the pacing therapy. Moreover, due to the variety of onset mechanisms, the AF prevention by conventional pacing may require several specific algorithms.

Interatrial conduction index as predictor of atrial fibrillation

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Our aim was to estimate a clinical value of the index PA interval to P wave duration as a predictor of paroxysmal atrial fibrillation (PAF).

Material and methods. P wave duration and PA interval from oesophageal electrode was registered on computerized electrophysiological BardLab System and analyzed by two/three independent observers. 72 patients (42F, 30M; age 44±19 years) were subdivided into two groups. Group 1: pts with PAF (36pts), group 2: pts without PAF (including results of transoesophageal atrial pacing). Index PA/P’ was calculated.

Results. In pts with PAF duration of the P wave ranged from 108ms to 242ms (139±30ms). In control group from 96ms to 166ms (120±19ms) (p=0.003), PA interval ranged in group 1 from 30 to 150ms (69±30ms), in group 2 from 26 to 86ms (46±17ms) (p=0.0002). PA/P index ranged from 24 to 82ms (48±12ms) in pts with PAF and from 25 to 56ms (37,5±10ms) in pts without PAF (p=0.0005).

Conclusion. PA/P index has more Important clinical value in prediction of PAF than P wave duration and PA interval.
Premature atrial contractions immediately after successful direct current conversion in patients with and without subsequent relapse

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Patients and methods: 125 patients (pts) who underwent elective direct current conversion for persistent AF were prospectively studied. A continuous ECG recording was performed during five minutes after direct current conversion. 13 pts remained in AF after conversion attempts and three had relapsed at discharge two hours after the procedure. 31 (97±224) pts (70±8yrs) were in AF at the one week control after successful direct current conversion. These pts were compared with 31 sex- and age-matched pts who were still in SR at one week. The mean coupling interval of PAC's, the PAC density and the prematurity index for the first two minutes immediately after DC conversion were analyzed for each pt and compared between the two groups.

Results: AF duration (ms)
SR at 1 week

<table>
<thead>
<tr>
<th>PAC Type</th>
<th>p-value</th>
</tr>
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<tbody>
<tr>
<td>AF duration (ms)</td>
<td>5.9±3.4 3.8±1.6</td>
</tr>
<tr>
<td>Coupling interval (ms)</td>
<td>571±244 610±265</td>
</tr>
<tr>
<td>Density (1-5 minute) (No)</td>
<td>3.0±1.7 3.6±1.5</td>
</tr>
<tr>
<td>Density (1-2 minute) (No)</td>
<td>6.2±5.8 8.1±5.5</td>
</tr>
<tr>
<td>Preceding RR (ms)</td>
<td>846±390 915±387</td>
</tr>
<tr>
<td>Prematurity Index</td>
<td>62% 60%</td>
</tr>
</tbody>
</table>

Conclusion: Short AF duration was the only significantly different finding between the groups, while no differences in PAC properties during the first two minutes after successful DC conversion were found. PAC's may still be triggers but other factors are likely to decide whether a PAC will initiate an AF episode.

520
Versapamil in atrial fibrillation: effect on trigger or on substrate?
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We analyzed 112 patients (age 70±8yrs) from the VERAF-Study, randomized to standard therapy (STEP) (n=50) or additional versapamil (VER) (n=50), 1 week before and after successful electrical cardioversion (EC) for persistent atrial fibrillation (AF) duration 157±101 days. No antiarrhythmic drugs were given. The incidence of premature atrial beats (PAB's) and their shortest P-P' coupling interval (P-Pmin) during 30 s after sinus rhythm (SR) resumption, were evaluated.

Immediate (within 1 hour) recurrence of AF (IR AF) occurred in 16 patients and early (within 7 days) recurrence (ER AF) in 37 patients. SR persisted 7 days after EC in 57 patients.

VER(n=50) PABs P-Pmin(mean)

<table>
<thead>
<tr>
<th>VER(n=50)</th>
<th>PABs</th>
<th>P-P min(mean)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IFAF (3/101±17±1)</td>
<td>11±5</td>
<td>313±43</td>
</tr>
<tr>
<td>EFAF (2/104±17±1)</td>
<td>11±5</td>
<td>313±43</td>
</tr>
<tr>
<td>EFAF (2/104±17±1)</td>
<td>11±5</td>
<td>313±43</td>
</tr>
<tr>
<td>RR (39/57±88±1)</td>
<td>6±5</td>
<td>343±111</td>
</tr>
<tr>
<td>RS (39/57±88±1)</td>
<td>6±5</td>
<td>343±111</td>
</tr>
<tr>
<td>p&lt;0.001 vs IFAF</td>
<td>*p&lt;0.003 vs EFAF</td>
<td>p&lt;0.003 vs EFAF and RR</td>
</tr>
<tr>
<td>p&lt;0.02 vs IFAF and RS</td>
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P-Pmin was longer in VER compared to STG (507±116 msec vs 377±47 msec; p=0.001), no differences were found concerning PAB's incidence between the two treatments (7±8 vs 7±6).

Conclusion: A higher number of PAB's together a shorter P-Pmin characterized IFAF. Furthermore P-Pmin prolongation is associated to RS maintenance.

494
Mechanism of the arrhythmogenic activity from pulmonary veins
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Background: Pulmonary veins are important loci of ectopic beats initiating paroxysmal atrial fibrillation. The aim of this study was to investigate the underlying ionic mechanisms of the arrhythmogenic activity from pulmonary vein cardiomyocytes.

Methods: Rabbits cardiomyocytes were isolated by retrograde perfusion (anesthetized through aorta, left ventricle and left atrium) with nominally Ca2+-free Tyrode solution containing digestive enzyme. Dissociation of pulmonary veins yielded a mixture of cardiomyocytes with (71%) or without (29%) spontaneous activity. In beating cardiomyocytes (n=32), perfusion of 10M Isoproterenol significantly accelerated the spontaneous firing rate from 1.0±0.9 to 1.9±0.2 Hz. At the same concentration, Isoproterenol-induced early afterdepolarization In 9 (28%) cells, delayed afterdepolarization in 5 (16%) cells, and both early and delayed afterdepolarization in 5 (16%) cells. Nitric oxide (0.1 uM) suppressed the isoproterenol-induced early afterdepolarization and delayed afterdepolarization. Voltage-clamp studies showed that Isoproterenol increased the slow inward current (I42:20.25 to 1.71:0.29 mA/pF; p<0.05) and the steady-state outward current (I0.52:0.06 to 0.80:0.04 mA/pF; p<0.05).

Conclusions: Pulmonary veins contain cardiomyocytes with pace-making activity. Enhanced automaticity and induction of triggered activity may result in the arrhythmogenic activity of pulmonary veins.

548
Effects of Versapamil and Metoprolol on recovery from atrial electrical remodeling after internal electrical cardioversion of long-lasting atrial fibrillation: relation to immediate and early recurrences
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Background: Restoration of sinus rhythm after atrial fibrillation (AF) is accompanied by the persistence of high vulnerability to AF, which can easily relapse. To date, many reports have demonstrated in animal models and humans that this high vulnerability is related to atrial electrophysiological changes, called atrial electrical remodeling, occurring during AF. The aim of this prospective, randomized study was to investigate the effect of pretreatment with 2 different calcium-lowering drugs (verapamil and metoprolol) on recovery from atrial effective refractory period (AERP) shortening after internal electrical cardioversion (EC) of persistent AF in patients on amiodarone.

Methods: Twenty-one patients were referred to our hospital for internal EC of persistent AF refractory to external EC. They had been on amiodarone for at least 30 days, and were randomized to receive only amiodarone (Gr. PLA, n=7), or amiodarone and verapamil 240 mg/die for at least 14 days before and 7 days after EC (Gr. MET, n=7). In contrast, patients pretreated only with amiodarone had a trend towards a higher incidence of AF relapses. Patients of AF were recovered after 10 minutes, 24 hours and 7 days.

Results: Clinical and echocardiographic data were similar in the 3 study groups. Internal EC at 8 or 15 J was successful in all patients. The AERP after 10 minutes was significantly shorter in Gr. PLA (207±31 ms; p=0.001) and in Gr. MET (203±34 ms; p<0.001) than in controls (249±45 ms; but not in Gr. VER 237±51 ms; p=NS). The AERP after 24 hours was still significantly shorter in Gr. PLA (205±30 ms; p=0.01) than in controls, but not in Gr. MET (225±52 ms; p=NS) or in Gr. VER (250±36 ms; p=NS). Nevertheless, there was a trend towards a higher incidence of AF relapses after 7 days in Gr. VER (57%) than in Gr. PLA (43%) and Gr. MET (14%).

Conclusions: Recovery from AERP shortening in patients pretreated only with amiodarone lasts more than 24 hours; pretreatment with amiodarone and metoprolol accelerates recovery; pretreatment with amiodarone and verapamil prevents AERP shortening, but does not reduce the incidence of early AF relapses.

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