Catheter ablation of paroxysmal atrial fibrillation: long-term follow-up and the inevitability to fibrillate

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This editorial refers to ‘Outcome of anatomic ganglionated plexi ablation to treat paroxysmal atrial fibrillation: a 3-year follow-up study’ by E. Mikhaylov et al., on page 362.

Paroxysmal atrial fibrillation has been defined as atrial fibrillation that is self-terminating and lasting <7 days.1 The majority of patients with such conditions typically consists of individuals (mostly men aged <70 years) with a CHADS score of ≤2. Although precipitating factors may occur, most patients have recurrent episodes of atrial fibrillation that eventually (not always) require treatment. The treatment of underlying risk factors for atrial fibrillation, such as hypertension, diabetes, and sleep apnoea, may help reduce the burden of atrial fibrillation, but the elimination of atrial fibrillation using this strategy is infrequent. The natural history of atrial fibrillation has shown that atrial fibrillation will inevitably recur in a substantial number of patients.1,2

Trials evaluating anti-arrhythmic drug treatment have typically been evaluated by the length of time without atrial fibrillation. The safety profile of anti-arrhythmic agents has limited their clinical use, but generally, especially in healthier patients, the majority of patients will have a significant increase in the duration of atrial fibrillation free episodes. In a recent study that compared dronedarone with placebo, this new class-3 anti-arrhythmic agent was shown to increase the duration of time in sinus rhythm from 41 days to 96 days, P < 0.01.2 However, in spite of the daily intake of a potent anti-arrhythmic agent, the majority of patients inevitably develop recurrence of atrial fibrillation.

Catheter ablation of paroxysmal atrial fibrillation

There are generally four methods to eliminate atrial fibrillation.1 Segmental isolation of the pulmonary veins and circumferential left atrial ablation in the antral region of the pulmonary veins combine strategies to eliminate both the triggers and substrate to fibrillate.1 Targeting complex fractionated atrial electrograms and ablation of ganglionated plexuses are often performed in superimposed regions.1,3–6 These latter strategies appear to directly aim at the fuel or milieu required to fibrillate, which can be extensive; pulmonary and non-pulmonary sites of fibrillation result in difficult comprehensive sets of ablation lesions and precise endpoints.

The consensus document of 2007 on ablation of atrial fibrillation was an attempt to review the different methodologies of ablation that developed over the last decade, and propose that isolation of the pulmonary veins should become the standard for ablation in patients with paroxysmal atrial fibrillation.1 Several workers have provided excellent outcomes that do not result in the isolation of the pulmonary veins.3,4 However, the majority of centres performing ablation of atrial fibrillation have attempted to isolate the pulmonary veins, partly due to the relative simplicity of the technique and its very distinct endpoints, and in part, due to the strong tide resulting from the consensus document.

Long-term clinical outcome following ablation of paroxysmal atrial fibrillation

The consensus document emphasized the need for patient follow-up to evaluate the long-term effectiveness of ablation of atrial fibrillation. However, it has become apparent that a 1-year follow-up is inadequate at truly evaluating long-term elimination of atrial fibrillation. Table 1 summarizes the recent reports7–12 on the long-term follow-up of patients with paroxysmal atrial fibrillation who underwent isolation of the pulmonary veins, including the report from Mikhaylov et al.12 These reports involved different strategies of ablation to isolate the pulmonary veins (with or
was initially reported in 1998 still remains technically challenging of the patients, or the unfavourable view that a technique that results, including the favourable outcome in approximately half atrial fibrillation. There can be different viewpoints to these and endpoints, directed at patients that all had self-terminating large variation for a technique that involved similar power-sources atrial fibrillation was effective in 41–78% of patients, a rather with less than satisfactory results for long term. Inevitably again, radiofrequency ablation in the anatomic group (86 curiously was associated with significantly more applications of mal atrial fibrillation, while another 35 patients underwent a cir- regions of the ganglionated plexuses in 35 patients with paroxys- et al. All of these different approaches to ablation of atrial fibrillation

Table 1 Long term success rates in 1894 patients of a single radiofrequency catheter ablation procedure for paroxysmal atrial fibrillation that includes circumferential ablation of the pulmonary veins with or without non-PV sites of ablation

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Pts (n)</th>
<th>Approach</th>
<th>Follow-up (years)</th>
<th>Follow-up method</th>
<th>Success (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bharwana et al.</td>
<td>2009</td>
<td>728</td>
<td>PVAI</td>
<td>4.8 ± 1.4</td>
<td>48h Holter 3, 6, 9 and 12 months, event monitor during the first 5 months</td>
<td>77.6</td>
</tr>
<tr>
<td>Hunter et al.</td>
<td>2010</td>
<td>151</td>
<td>WACA</td>
<td>3.3</td>
<td>Holter at 3 and 6 months, event monitor if symptomatic, 12-lead ECG at late follow-up</td>
<td>40.6</td>
</tr>
<tr>
<td>Mirowski et al.</td>
<td>2010</td>
<td>452</td>
<td>EPVI</td>
<td>2.5 ± 1.2</td>
<td>Holter at 2, 6, 10, 14, 24, 36, 48 weeks and every 3 months, event monitor if symptomatic</td>
<td>67.3</td>
</tr>
<tr>
<td>Medi et al.</td>
<td>2010</td>
<td>100</td>
<td>PVAI</td>
<td>3.3 ± 0.8</td>
<td>12-lead ECG and Holter at 3, 6, 9 and 12 months, event monitor every 6 months</td>
<td>49.0</td>
</tr>
<tr>
<td>Wokhlu et al.</td>
<td>2010</td>
<td>428</td>
<td>PVI/HECA</td>
<td>3.0</td>
<td>24h Holter at 3 months, 12-lead ECG at 12 months, event monitor if symptomatic after 12 months</td>
<td>62.0%</td>
</tr>
<tr>
<td>Mikhaylov et al.</td>
<td>2010</td>
<td>35</td>
<td>CPVI</td>
<td>3.0 ± 0.2</td>
<td>24h Holter at 3, 6, 9 and 12 months, event monitor if symptomatic</td>
<td>65.7</td>
</tr>
</tbody>
</table>

CPVI, circumferential pulmonary vein isolation; CTI, cavo tricuspid isthmus ablation; EPVI, extensive pulmonary vein isolation; PVAI, pulmonary vein antral isolation; PVI, pulmonary vein isolation; SVC, superior vena cava; WACA, wide area circumferential ablation.

without a double-trans-septal approach or the use of a circumferential catheter). The minimum follow-up period of these studies is 2 years, extending to a mean of nearly 4 years. The methodology during follow-up to document the recurrence of atrial fibrillation is imperfect in most studies, and could underestimate the actual number of patients who have recurrence of atrial fibrillation.

As a single procedure, ablation for patients with paroxysmal atrial fibrillation was effective in 41–78% of patients, a rather large variation for a technique that involved similar power-sources and endpoints, directed at patients that all had self-terminating atrial fibrillation. There can be different viewpoints to these results, including the favourable outcome in approximately half of the patients, or the unfavourable view that a technique that was initially reported in 1998 still remains technically challenging with less than satisfactory results for long term. Inevitably again, atrial fibrillation recurs in a substantial number of patients.

Ablation of ganglionated plexuses

All of these different approaches to ablation of atrial fibrillation have demonstrated various amounts of denervation. Mikhaylov et al. performed an anatomic approach of ablation in the presumed regions of the ganglionated plexuses in 35 patients with paroxysmal atrial fibrillation, while another 35 patients underwent a circumferential approach. In this non-randomized study, which curiously was associated with significantly more applications of radiofrequency ablation in the anatomic group (86 ± 5) than in the pulmonary vein circumferential group (74 ± 6, P < 0.05), there were no significant differences in the clinical outcome at 12 months.

The authors followed up their patients for another 2 years, and after a mean follow-up of 36 ± 2 months, there was a significant difference in the recurrence of atrial fibrillation, favouring the circumferential approach. As shown in Table 1, the patients who underwent isolation of the pulmonary veins had 66% ablation success, whereas in the anatomic group, the recurrences increased substantially over time, with 34% success long term. These results suggest that recurrence of atrial fibrillation associated with rein- nervation could possibly be reduced by maintaining entrance block into the pulmonary veins. We do not know whether combining both approaches (circumferential ablation and anatomic ablation of ganglionated plexuses) could have further reduced the recurrence of atrial fibrillation.

Towards reducing the inevitability to fibrillate

The next few years will witness significant new technical innovations, including the expanded use of circumferential balloons and catheters to isolate the pulmonary veins. The focus of ablation strategies will continue to be directed at the triggers and substrate that are associated with paroxysmal atrial fibrillation in the majority of patients. Until we can demonstrate a long-term persistence of entrance block in the pulmonary veins, we could continue to observe recurrences of atrial fibrillation.

Novel approaches such as epicardial ablation to eliminate atrial fibrillation, either by expanding on regions of ganglionated plexuses or by isolating the posterior left atrium, could be developed. However, the mechanisms associated with the initiation of paroxysmal atrial fibrillation that appear to predominantly involve autonomic changes remain extremely complex. In this context, the work by Mikhaylov et al. could be viewed favourably, either for a
subgroup of patients or as an evolving approach to modify and reduce the autonomic tone and the inevitability to fibrillate.

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References