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Long-Term Benefits Following Catheter Ablation of Atrial Fibrillation
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Catheter ablation has acquired a prominent role in the management of symptomatic atrial fibrillation (AF). Attempting to accurately assess the benefit of ablation can be quite challenging and is influenced by many variables, including the type of AF, procedural technique, operator experience, and duration and method of follow-up. Equally elusive is the proper definition of a successful ablative outcome. Should a “successful” ablation necessitate complete resolution of AF and AF symptoms documented by long-term monitoring, or does a more clinical approach evaluating for symptomatic improvement constitute a favorable outcome? Furthermore, at what point following an ablation should a recurrence be an acceptable, if not an expected, occurrence and should a significant decrease in AF burden warrant consideration as success? Our goal here will be to explore the current data evaluating outcomes for ablation of AF. We will examine electrophysiologic and other clinical endpoints, and hope to provide long-term expectations following ablation of paroxysmal and persistent AF. (Circ J 2013; 77: 1091–1096)

Key Words: Ablation; Atrial fibrillation; Outcomes

The earliest reports of catheter ablation of atrial fibrillation (AF) in humans date to the early and mid-1990s when ablation to produce linear lesions was performed to emulate portions of the surgical maze procedure. Recognition and targeting of pulmonary vein (PV) drivers in the late 1990s led to a dramatic rise in the efficacy and prominence of catheter ablation, particularly for paroxysmal AF. Since then, with improvements in technology, operator experience, and most importantly, our understanding of the mechanisms of AF, techniques and strategies of ablation have evolved. Older patients and those with persistent and longstanding persistent AF, as well as significant comorbidities including cardiomyopathy and renal dysfunction, are now offered ablation. Ablation technologies have evolved to meet the challenges posed by increasing variability in patient substrates and to improve procedural efficacy and safety.

Over the past decade we have observed considerable variability in patients’ responses to ablation, with some being “cured” by a single procedure without arrhythmia recurrence, but others requiring several repeat ablations before a successful outcome, and still others failing adequate rhythm control despite multiple ablation attempts even with the use of antiarrhythmic drugs (AAD). These differences in outcome may partially be explained by variations in ablation technology and strategy. However, underlying differences in patient substrate and mechanisms of AF likely explain a significant portion of the varying patient outcomes.

In this review, we will begin by analyzing immediate goals for a successful ablation followed by intermediate term outcomes for ablation of both paroxysmal and persistent AF. We will then proceed to evaluate longer-term results (>3 years), focusing on maintenance of sinus rhythm (SR). We will follow this with a description of other clinical outcomes before concluding on the overall benefit and expectations during long-term follow-up for AF ablation.

Procedural Goals and Intermediate Term Outcomes

Immediate procedural success involves completion of the intended goals of ablation. The most common goal, particularly for ablation of paroxysmal AF, is complete PV isolation (PVI) with unidirectional or bidirectional conduction block. The PVs may be challenged with intravenous adenosine following isolation to reveal dormant PV conduction and to prompt further ablation; however, whether this improves long-term outcomes is unclear.

Other potential immediate procedural goals may include successful isolation of sites of non-pulmonary vein triggers such as the superior vena cava or coronary sinus; elimination of sites harboring complex fractionated atrial electrograms (CFAE); linear ablation with bidirectional block; ablation of sites harboring ganglionic plexi; ablation utilizing electrogram analysis to eliminate sites of AF rotors or other drivers; ablation with a goal of conversion to SR during ablation; or ablation until the absence of any atrial arrhythmias during at least one hour following ablation to reveal dormant PV conduction and to prompt further ablation; however, whether this improves long-term outcomes is unclear.

Following PVI, data supporting the addition of linear ablation with bidirectional block in the superior vena cava or coronary sinus is a reasonable strategy to extend durability. An additional benefit from linear ablation in the coronary sinus is elimination of sites harboring CFAE. However, ablation of these sites alone is not associated with improved outcomes.

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and preference.

Most of the available clinical outcome data has evaluated 1–2-year follow-up. Results vary by type and duration of AF, and the different follow-up periods and protocols often limit comparisons of studies. In general, results following ablation of paroxysmal AF are superior to those following persistent AF, with most studies showing freedom from AF following ablation at 1 year in the range of 75–93% off AAD.13–17 Freedom from AF following ablation for nonparoxysmal AF at 1 year is lower, at 63–74% off AAD.4,17–19 A recent meta-analysis (Figure 1) showed an improvement in SR maintenance following multiple procedures, as well as the incremental benefit of AAD. An average follow-up of 14 months with a population of 70% paroxysmal AF and allowing for repeat ablations, overall freedom from AF was 71% without the use of AAD and 77% including AAD.20 The majority of studies used a combination of patient symptoms and remote monitoring to document the absence of recurrent atrial arrhythmias. Whether these results hold up during longer-term follow-up has been the subject of more recent studies.

**Longer-Term Outcomes**

Recently, more data evaluating longer-term outcomes for ablation of both paroxysmal and persistent AF have become available (Table). When allowing for multiple ablations, as well as the concomitant use of AAD in some patients, most studies have demonstrated only mild increases in arrhythmia recurrence for ablation of paroxysmal AF beyond 1–2 years; however, recurrences following ablation of persistent AF are more common.

Ouyang et al.21 followed 161 patients with normal left ventricular function who underwent PVI for paroxysmal AF. At a median follow-up of 4.8 years, 47% were free from atrial tachyarrhythmias after a single procedure and 79.5% after 1–3 procedures, with 15% of those in SR on AAD. The highest rate of recurrence was observed in the first 3 months. During a second ablation, recovered PV conduction was seen in 94% of cases. Only 2.4% of patients progressed to chronic AF during the 5 years and a significant portion of those with recurrence still reported some clinical improvement.

Medi et al.22 reported on 100 patients with paroxysmal AF who underwent antral PVI and were followed for a mean of 39 months. SR maintenance without the use of AAD was seen in 49% of patients after a single ablation, in 57% of patients after a repeat procedure off AAD, and in a total of 82% of patients including those on AAD. Most recurrences in this population were seen in the first year after the index ablation, with a mean time to recurrence of 6 months.

Rates of long-term SR maintenance after ablation of persistent AF are significantly lower. Tilz et al.23 followed 202 patients who underwent ablation for persistent AF who were followed for a median of 56 months. Ablation strategy during the index ablation was PVI alone followed by direct current cardioversion. If AF recurred during a 30-min waiting period, AF triggers, CFAE ablation, or linear ablation to target an atrial tachycardia were performed. Following a single procedure, 20% were maintained in SR. Following multiple procedures, SR maintenance was 45%, including 12% on AAD. Duration of AF >2 years and not being an acute PVI responder were predictive of arrhythmia recurrence.

Sorgente et al.24 followed 103 patients (63 nonparoxysmal, 40 paroxysmal) who underwent ablation by a single operator for a median follow-up of 6 years. Ablation strategy was PVI followed by further ablation of extra-PV triggers or linear ablation based on inducibility. Freedom from AF was 23% following a single procedure and 39% following the last procedure (41% undergoing repeat ablations). Recurrences were

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**Figure 1.** Efficacy of catheter ablation in patients with atrial fibrillation (AF). Results are from a recent meta-analysis and include 70% patients with paroxysmal AF and mean follow-up of 14 months. Number of studies included with number of patients in parentheses. AAD, antiarrhythmic drugs. (Reproduced from Calkins et al with permission.20)
Long-Term AF Ablation Benefits

Paroxysmal) as compared with both a control group that received medical management and the general population. Patients were followed for a mean of 3.1 years from their first ablation. Freedom from AF was 85% for paroxysmal AF (76% off AAD) and 72% for persistent AF (60% off AAD). Freedom from AF following ablation was a strong predictor of stroke-free survival (hazard ratio (HR) 0.3, P<0.001; Figure 3), despite only 29% of these patients continuing oral anticoagulation (vs. 69% continuing anticoagulation with recurrent AF). Furthermore, the ablation group had stroke and mortality rates that were significantly lower than those in the control group and that approached the risk in the general population (Figure 4).

Although this study primarily evaluated patients with baseline lower stroke risk (mean CHADS2 score of 0.7±0.9, mean age 58±11 years), the results were similar in another study evaluating 508 higher risk patients ≥65 years old undergoing ablation (mean CHADS2 score of 1.1±0.9, mean age 70±3 years). Although that study did confirm a higher stroke risk for older patients (age >75 years had odds ratio (OR) 4.9,

**Table.** Studies Evaluating Long-Term Follow-up for SR Maintenance Following Ablation of AF

<table>
<thead>
<tr>
<th>Study</th>
<th>No. of patients, AF type</th>
<th>Primary ablation strategy</th>
<th>Follow-up</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ouyang et al (2010)21</td>
<td>161 paroxysmal</td>
<td>PVI, occasional linear ablation</td>
<td>Median 4.6 years</td>
<td>46.6% SR after 1 ablation; 79.5% after 1–3 ablations, 15% of which were on AAD</td>
</tr>
<tr>
<td>Medi et al (2011)22</td>
<td>100 paroxysmal</td>
<td>PVI</td>
<td>39±10 months</td>
<td>49% SR after 1 ablation off AAD; 57% after repeat ablations off AAD; 82% including AAD</td>
</tr>
<tr>
<td>Weerasooriya et al (2011)24</td>
<td>64 paroxysmal, 22 persistent, 14 longstanding persistent</td>
<td>PVI, CTI ablation, ± linear ablation</td>
<td>Median 54 months</td>
<td>29% SR after 1 ablation, 63% after multiple ablations off AAD</td>
</tr>
<tr>
<td>Sorgente et al (2012)24</td>
<td>40 paroxysmal, 63 nonparoxysmal</td>
<td>PVI, ± linear ablation, ± extra-PV triggers</td>
<td>Median 6 years (4.88–7.27)</td>
<td>23% SR after 1 ablation, 39% after last ablation</td>
</tr>
<tr>
<td>Tiz et al (2012)22</td>
<td>202 longstanding persistent</td>
<td>PVI, ± CFAE, ± targeted ablation</td>
<td>Median 56 months (49–67 months)</td>
<td>20% SR after 1st ablation, 45% after multiple ablations with 12% on AAD</td>
</tr>
</tbody>
</table>

AAD, antiarrhythmic drugs; AF, atrial fibrillation; CFAE, complex fractionated atrial electrograms; CTI, cavo-tricuspid isthmus; PV, pulmonary vein; PVI, pulmonary vein isolation; SR, sinus rhythm.

**Figure 2.** Kaplan-Meier arrhythmia-free survival curve after final catheter ablation of atrial fibrillation (AF). Patients followed included 63 with nonparoxysmal AF and 40 with paroxysmal AF. (Reproduced from Sorgente et al with permission.24)

**Thromboembolic Risk**
A recent study25 reviewed the stroke risk following ablation in 1,273 patients who underwent catheter ablation for AF (56% paroxysmal) as compared with both a control group that received medical management and the general population. Patients were followed for a mean of 3.1 years from their first ablation. Freedom from AF was 85% for paroxysmal AF (76% off AAD) and 72% for persistent AF (60% off AAD). Freedom from AF following ablation was a strong predictor of stroke-free survival (hazard ratio (HR) 0.3, P<0.001).

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thermore, although all ablation patients as a group showed an improvement in stroke risk, the majority of benefit was driven by those who remained in SR.

**Symptomatic Improvement**

Although most trials evaluate success of ablation in terms of long-term maintenance of SR, patients often show clinical im-

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Figure 3. Kaplan-Meier curve showing stroke-free survival for patients who remained free from atrial fibrillation (AF) following ablation compared with those with recurrent AF. Comparison of curves was by log-rank test. (Reproduced from Hunter et al with permission.)

Figure 4. Outcome after catheter ablation of atrial fibrillation (AF) compared with medical treatment in the Euro Heart Survey and controls without AF in the general population. Bars show rates of stroke, death, or a composite of both as a percentage of patients per 100 years of patient follow-up. (Reproduced from Hunter et al with permission.)
provement despite recurrence of atrial arrhythmias. This clinical improvement may be attributed to a decreased AF burden, alteration in the severity of AF, or changes in overall cardiac function. In the previously described study by Ouyang et al., in addition to the 79.5% of patients who achieved stable SR, an additional 13% of patients experienced clinical improvement, bringing the total to 92% of patients who experienced some clinical benefit at 5 years.

In the study described by Medi et al., a mean AF symptom score was calculated for each patient based on both subjective symptoms and objective measurements of AF burden, hospitalizations, and cardioversions. Among the 13 patients with recurrent paroxysmal AF at long-term follow-up, the majority still reported clinical benefit and the composite score improved from 17±2 to 10±6 (P<0.0001).

This symptomatic improvement is not limited to patients with recurrent paroxysmal AF. Oral et al reported that patients undergoing ablation for persistent AF who had recurrent atrial arrhythmias at 12 months still experienced a reduction in symptom severity score (17±4 vs. 12±4, P=0.02), albeit less of an improvement than in patients without recurrence. Similarly, Pappone et al reported that patients with both paroxysmal and persistent AF had significantly fewer hospitalizations following ablation, regardless of whether or not AF recurred. These results suggest that success rates for ablation that focus purely on strict criteria for documented AF recurrence may be underestimating the overall potential clinical effect of ablation.

Mortality Benefit

AF is a known independent risk factor for mortality (OR 1.5, 95% confidence interval (CI) 1.2–1.8 in men; OR 1.9, 95% CI 1.5–2.2 in women). Medical management has not been shown in clinical trials to decrease mortality risk and may actually increase this risk with the use of some AADs. Subgroup analyses from some trials, however, have shown an associated improvement in outcomes and mortality among patients who maintained AF.

Whether catheter ablation can effect mortality remains to be seen and published trials thus far have lacked the power to clearly substantiate such a claim. The superiority of ablation to medical management in maintaining SR for both paroxysmal and persistent AF suggests such a benefit may exist. This current is being explored in ongoing clinical trials such as Catheter Ablation vs. Antiarrhythmic Drug Therapy for Atrial Fibrillation (CABANA).

Conclusions

Following an initial period of early recurrences, SR maintenance following ablation of paroxysmal AF seems to show a steady but gradual decline over the next several years. A 1-year efficacy of approximately 80% can be maintained, but may necessitate repeat ablations or the use of AAD. Ablation in these patients does appear to significantly curtail progression from paroxysmal to persistent AF, with a <3% reported progression over 2–5 years. This is significantly lower than the 11–26% 1-year progression reported in patients selected to medical management with rhythm or rate control strategies. Ablation of persistent AF has not produced as durable a result in terms of SR maintenance, with rates likely in the 40–50% range at 5 years following ablation. However, in paroxysmal and persistent AF patients, other clinical parameters, including symptomatic improvement and fewer hospitalizations, were noted even in patients with recurrence following ablation. A decrease in long-term stroke risk is also seen following ablation, particularly in patients successfully maintained in SR.

Disclosures

No authors have any relevant relationships or conflicts of interest to disclose.

References


