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CATHETER ABLATION VERSUS ANTIARRHYTHMIC DRUG THERAPY

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Abstract. Catheter ablation uses either cryoablation (cryotherapy) or radiofrequency ablation (RFA). Pulse-field ablation, another promising energy source, is not yet approved by the United States Food and Drug Administration. AF recurrence, defined as an AF episode >30 seconds in duration on cardiac monitoring, occurs in approximately 20 to 40 percent of patients at one year, although overall AF burden is often markedly decreased [3]. Important complications from catheter ablation include cardiac tamponade (1 percent), pulmonary vein stenosis (<1 percent), phrenic nerve paralysis (up to 3 percent), and rare instances of stroke and atrioesophageal fistula [4-6]. These and other complications are described in detail separately.

A 2017 randomized comparison between cryoablation and RFA showed similar success rates, as did a meta-analysis of observational studies [7,8].

Keywords. Catheter ablation, atrial fibrillation, antiarrhythmic drugs, heart failure

Commonly employed drugs to maintain sinus rhythm are amiodarone, sotalol, dofetilide, dronedarone, flecainide, and propafenone. Approximately 25 to 50 percent of people who receive antiarrhythmic medications will have recurrent AF within one year. Important side effects of antiarrhythmics include proarrhythmia, bradyarrhythmia, and organ toxicity in the case of amiodarone.

Approach — For patients with symptomatic paroxysmal AF in whom a rhythm rather than a rate control strategy is being pursued, either catheter ablation or AAD are reasonable first-line therapies. We suggest catheter ablation as first-line therapy over AAD in younger patients, patients who are poor candidates for AAD therapy, or in those concerned about the potential complications of AADs. Other factors that may impact the safety and efficacy of catheter ablation also need to be considered when deciding between catheter ablation and AAD.

For patients with symptomatic paroxysmal or persistent AF who have failed or become intolerant to one or more AADs, we recommend catheter ablation.

For patients with symptomatic persistent or longstanding persistent AF who have failed or become intolerant of one or more AADs or who choose not to start antiarrhythmic therapy, we suggest catheter ablation.

Patients without prior antiarrhythmic therapy

For patients who have chosen rhythm control and who have not previously received antiarrhythmic drug (AAD) therapy, either AAD or CA may be appropriate. All patients need to be informed of the possibility of recurrence of AF and AF-related symptoms and adverse events with both therapies. Recurrence rates and side effects are discussed in detail elsewhere.

Until recently, catheter ablation (CA) was generally not offered as first-line therapy given the complexity of the procedure and the potential for complications. It was typically offered to patients who had failed AAD therapy. However, evidence suggests that CA is superior to AAD for control of

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symptoms. While CA appears superior to AAD for the prevention of AF recurrence, there is no evidence that the rates of cardiovascular death, myocardial infarction, or stroke differ between the two interventions. In addition, in the studies demonstrating superiority of CA, the procedure was performed by highly expert electrophysiologists. Thus, CA by an experienced operator may be considered as first-line therapy for symptomatic patients who, after a full discussion of the benefits and risks of both approaches, prefer an invasive approach.

This section will review the studies that have directly compared the two approaches as first-line therapy. These studies demonstrate that among the advantages of ablation, there is a greater reduction in AF recurrences, progression to persistent AF, and AF-related symptoms.

In a meta-analysis of six studies in 1200 patients comparing CA with AAD as first-line treatment for paroxysmal AF, CA was associated with [9]:

- Lower rates of recurrent atrial arrhythmias (35 versus 53 percent; risk ratio [RR] 0.64, 95% CI 0.51-0.80) [9].
- Similar risks of serious adverse events (18 versus 21 percent; RR 0.87, 95% CI 0.58-1.30). Adverse events were defined differently across studies and included stroke, tamponade, and death.
- Lower rates of symptomatic atrial arrhythmias.
- Lower healthcare resource utilization.
- Lower rates of crossover to alternative treatment (RR 0.21, 95% CI 0.13-0.32).

Limitations of this study include a moderate degree of heterogeneity among the included studies; one study in particular accounted for most of the heterogeneity (the RAAFT 2 trial) [10].

A randomized study of 303 patients (EARLY-AF) compared initial rhythm-control therapy with catheter ablation with antiarrhythmic therapy in individuals with paroxysmal AF [11]. Over 36 months of follow-up the following findings were noted:

- Patients assigned catheter ablation had less persistent AF compared with patients assigned to AADs (1.9 versus 7.4 percent; hazard ratio [HR] 0.25; 95% CI 0.09-0.70).
- Patients assigned catheter ablation had less recurrent atrial tachyarrhythmia, which occurred in 87 patients in the ablation group (56.5 percent) and in 115 in the AAD group (77.2 percent; 56.5 versus 77.2 percent; HR 0.51; 95% CI 0.38-0.67).
- Serious adverse events occurred in seven patients (4.5 percent) in the ablation group and in 15 (10.1 percent) in the AAD group.

Limitations of this study include the sole use of cryoballoon ablation and the exclusion of patients with persistent AF.

Patients with prior antiarrhythmic therapy

For patients with either paroxysmal or persistent (see 'Classification' above) AF who seek to reduce their symptom burden and have received treatment with at least one effective antiarrhythmic drug, the option of continuing AAD or undergoing AF ablation should be based on the success and tolerability of AAD therapy along with patient preference. The patient's choice will be guided by advantages and burdens of each approach

Three early meta-analyses of studies comparing catheter ablation and antiarrhythmic drug therapy found that recurrence of AF occurred less often in patients who received catheter ablation in the 12 months after initiation of therapy [12-14]. The following three randomized trials directly compared catheter ablation with antiarrhythmic drug therapy:

- The ThermoCool AF study randomly assigned 167 symptomatic patients with paroxysmal AF (no episodes lasting more than 30 days) who did not respond to at least one AAD and who experienced at least three episodes of paroxysmal AF within six months before randomization to either catheter ablation (with RFA) or AAD therapy in a 2:1 fashion [15]. Patients with

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significant left ventricular dysfunction, persistent AF, and advanced heart failure were excluded. Catheter ablation included pulmonary vein isolation with confirmation of entrance block, and AAD therapy included flecainide (36 percent), propafenone (41 percent), dofetilide, sotalol, or quinidine at the investigator's discretion. After nine months, there were significantly fewer patients with documented symptomatic paroxysmal AF in the catheter ablation group (16 versus 66 percent; hazard ratio 0.30, 95% CI 0.19-0.47). In addition, major treatment-related adverse events occurred more often with AAD therapy (9 versus 5 percent) at 30 days. Mean quality-of-life scores improved significantly with catheter ablation compared to AAD therapy.

- The STOP AF trial randomly assigned 245 paroxysmal AF patients (in a 2:1 manner) to cryoballoon ablation or drug therapy [16]. Patients had previously failed drug therapy; paroxysmal and early persistent AF were present in 78 and 22 percent, respectively. Treatment success was defined as freedom from chronic treatment failure, as defined by the absence of: any detectable AF after the blanking period; use of a non-study antiarrhythmic drug; and any non-protocol intervention for AF. At 12 months, the primary end point was present in 69.9 and 7.3 percent of the two groups ($p<0.001$). Serious adverse procedure-related events occurred in 3.1 percent. Phrenic nerve palsy occurred in 11.2 percent, but resolved in the majority.
- The Catheter ABlation vs ANtiarrhythmic Drug Therapy in Atrial Fibrillation (CABANA) trial randomly assigned 2204 patients with paroxysmal (43 percent) or persistent AF (57 percent) to catheter ablation or antiarrhythmic drug therapy [17]. Patients were excluded if they had a prior catheter ablation or had failed two or more antiarrhythmic drugs. The following findings were noted:
  - Among the patients who received antiarrhythmic drug therapy, 27.5 percent crossed over to the ablation group.
  - The primary composite end point (death, disabling stroke, serous bleeding, or cardiac arrest) occurred in 8.0 and 9.2 percent of the two groups, respectively (hazard ratio [HR] 0.86, 95% CI 0.65-1.15), during a median follow-up of about four years. There was no difference in all-cause mortality (5.2 versus 6.1 percent; HR 0.85, 95% CI 0.60-1.21). The end point of death or cardiovascular hospitalization occurred less often with catheter ablation (51.7 versus 58.1 percent; HR 0.83, 95% CI 0.74-0.93), as did the rate for AF recurrence (49.9 versus 69.5 percent; HR 0.52, 95% CI 0.45-0.60).
  - Both patient groups achieved significant improvement in quality-of-life scores, and the improvement in the catheter ablation group was significantly greater than in the drug therapy group. Using one quality-of-life tool, the mean score at baseline was approximately 63 points. At 12 months, the scores were 80.9 and 86.4 points, respectively [18].
- The Catheter Ablation compared with optimized Pharmacological Therapy for Atrial Fibrillation (CAPTAF) trial randomly assigned 155 patients with symptomatic persistent or paroxysmal AF to catheter ablation or antiarrhythmic drug therapy [19]. The primary end point, SF-36 General Health score, improved more in the ablation group than the drug therapy group from baseline to 12 months (mean baseline score, 61.8 versus 62.7; mean change 11.9 versus 3.1, respectively; $p = 0.003$).

Patients with heart failure — Mortality and morbidity are higher among patients with atrial fibrillation and heart failure than among those with heart failure alone. Adverse events due to antiarrhythmic drug therapy appear to be higher in patients with heart failure and reduced ejection fraction. Catheter ablation for atrial fibrillation has been proposed as a means of improving outcomes among patients with heart failure who are otherwise receiving appropriate treatment. This issue is discussed separately.

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