

HRS / EHRA / ECAS Expert Consensus Statement on Catheter and Surgical Ablation of Atrial Fibrillation:

Recommendations for Personnel, Policy, Procedures and Follow-Up

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Presenter Disclosure Information

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AF Ablation: Clinical Trial Considerations

- What are the long-term efficacy outcomes for ablation?
- What are the comparative success rates of various drug and ablative techniques?
- What are the outcomes of AF ablation in patients with persistent and longstanding AF?
- Does symptom state at enrollment contribute to trial outcomes?
- What is the impact of ablation on atrial size, morphology, and function?
- What is the benefit of AF ablation in patients with varying types of underlying cardiac and noncardiac disease?
- Do these interventions have an impact on long-term occurrence of stroke / peripheral thrombo-embolic events?

AF Ablation: Clinical Trial Considerations

- In which patients can warfarin be safely discontinued following the ablation?
- Is there acceptable rationale for ablation applied as first line therapy for AF?
- Is ablative intervention cost-effective, or is drug therapy more economically efficient?
- Beyond placebo effect, what is the relative quality of life benefit of ablation vs. drug therapy?
- What is the optimal ablative strategy for treatment of persistent and long standing AF?
- What are the safety and efficacy outcomes of newer ablation technologies such as cryo, ultrasound, and laser ablation, and
- What is the ultimate utility of ablation targeting complex fractionated electrograms or autonomic ganglia?

Incentive For Investigational Studies: Current and Future

1. Sufficiently powered, randomized mortality studies
2. Multi-center clinical outcome trials
3. Carefully constructed single and multi-center registry studies.
4. Industry-sponsored device approval studies,

AF Ablation Mortality Trials

1. Large, multi-center randomized clinical trials are expensive
2. Take years for completion
3. Critical to establish the impact of therapy on mortality and other long-term outcomes.
4. Randomized design to provide an unbiased understanding of the outcomes of ablative intervention
5. These studies are appropriately held to a higher clinical trial standard
6. Should require the comparison of ablative therapy against best available drug therapy.

Mortality Trials

The Catheter Ablation versus Anti-arrhythmic Drug for Atrial Fibrillation (CABANA) Trial, which is currently in pilot phase, is designed to enroll a sufficiently large number of patients, and continue for a long enough period of time to determine if there is a mortality benefit to catheter ablation of AF. In addition, the CABANA study will investigate other outcomes of AF ablation and drug therapy including cardiovascular death, occurrence of disabling stroke, serious bleeding and cardiac arrest. Rather than comparing any specific drug therapy against an individual ablative intervention, this trial will examine pharmacologic rate and rhythm control strategies and ablative intervention with the intention of eliminating AF. It is hoped that this study will collect mortality information and will expand our understanding of the role of drug and non-drug therapy in those with advancing age, underlying heart disease, and more established AF, which will be applicable to a broader range of patients commonly seen in real life clinical practice. Finally, this trial will gather information needed for assessing the impact of therapy on quality of life and health care resource utilization.

Multi-Centered Outcomes Trials

1. Smaller, more agile
2. Quickly provide answers to more specific questions
3. Further evaluate the safety and efficacy of RF catheter ablation as first line therapy
4. Relevant to patients with various types of AF or underlying disease
5. Could provide outcomes data more applicable to a wider range of patients
6. Without limitations of single center studies or requisite randomization against drug therapy.

Industry-Sponsored Device Approval Studies

1. Evaluate the safety and efficacy of AF ablation using investigational catheters / systems
2. Part of FDA and other regulatory agency approval processes
3. Enrollment limited to patients with paroxysmal AF without underlying disease
4. Should provide important insight into the safety and efficacy of catheter ablation
5. Limited by short follow-up durations, and restrictive inclusion and exclusion criteria
6. Could be streamlined by the elimination of randomized comparisons to drug therapy

AF Ablation Registry Studies

1. Provide an insightful look at ablation outcomes outside of the largest academic centers
2. Format discloses outcomes as ablation therapy as it is actually performed, rather than the way guidelines suggest it should be.
3. Provide efficacy and safety information in the setting of less common underlying disease, such as hypertrophic cardiomyopathy or valvular heart disease
4. Data unlikely to be generated in any single center
5. Extended understanding of uncommon complications such as pulmonary vein stenosis and atrial esophageal fistula formation

Recommendations for Reporting Outcomes of Clinical Studies

Limitations of Current Literature

1. Highly variable definitions and endpoints
2. Substantial differences in treatment modalities,
3. Definitions of acute and long-term success
4. Variability of post-ablation blanking periods, follow-up, redo and cross-over treatments
5. Variability in accounting for asymptomatic AF
6. Incomplete accounting of adverse events occurring beyond the first week of therapy

AF Ablation Task Force - Recommended Minimum Reporting

Study Design Considerations

1. Study design should depend on the questions to be answered
2. Trials assessing ablation outcomes should not necessarily require randomization against drug therapy
3. Randomization against an accepted standard-of-care ablation catheter may be sufficient for efficacy and safety assessment
4. Sham procedures as a part of these studies are ill advised.

AF Ablation Task Force - Recommended Minimum Reporting

Demographic Issues

5. Clear description of baseline demographics, AF type and duration, and occurrence of cardioversion
6. Adoption of the amended definitions of paroxysmal, persistent, and longstanding persistent AF
7. Extent of underlying heart disease including atrial size and ventricular function
8. Clear delineation of extent of underlying cardiac *and* non-cardiac disease.
9. Reporting of data based on a consistent initial post-ablation blanking period of three months, even if other blanking periods are chosen and reported.
10. Additional reporting of recurrences or events during the post-ablation blanking period as "early events."

AF Ablation Task Force - Recommended Minimum Reporting

Monitoring on Follow-Up

11. Requisite electrocardiogram documentation of recurrent AF in patients with persistent symptoms.
12. Event monitor recordings in patients with intermittent symptoms thought to be arrhythmia related
13. Search for asymptomatic AF at six months intervals thereafter using one of the following:
 - Trans-telephonic monitoring for four weeks around the follow-up interval for symptom-prompted recording and a minimum of weekly transmissions to detect asymptomatic events
 - 24-72 hour Holter monitoring
 - Thirty-day patient or auto-triggered event monitoring or mobile cardiac outpatient telemetry.

AF Ablation Task Force - Recommended Minimum Reporting

•Consistent monitoring techniques should be employed

•Indication of percentage compliance with monitoring requirements should be included

•Duration of recommended monitoring may vary depending on the type of AF that was ablated.

•For paroxysmal AF, multiple 24-hour Holter monitors, and/or four weeks of monitoring, with an auto-triggered event monitor or by mobile outpatient cardiac telemetry to identify asymptomatic episodes

•Monitoring tools are a "work in progress" and may not be uniformly available or practical for all patients

AF Ablation Task Force - Recommended Minimum Reporting

13. A minimum follow-up duration of 12 months
14. Recurrences should include both AF and atrial flutter or atrial tachycardia
15. Any episode of AF, atrial flutter, or tachycardia of at least 30 seconds duration that occurs after the blanking period should be classified as a recurrence
16. The primary efficacy endpoint of ablation should be freedom from AF *and* atrial flutter /tachycardia in the absence of anti-arrhythmic drug therapy.
17. Follow-up period for reporting purposes should begin 5 half lives after the antiarrhythmic drug has been stopped or at least three months after stopping amiodarone.

AF Ablation Task Force - Recommended Minimum Reporting

End Point Considerations

18. Secondary endpoint of freedom from AF and atrial flutter/tachycardia in the presence of previously ineffective antiarrhythmic therapy
19. AF burden, should be considered separately from the primary efficacy endpoint
20. Standardized quality of life assessment
21. All studies of AF ablation should include a complete reporting of major complications.

Final Notes From The AF Task Force

Clinical Trials are critical to provide a solid evidence base upon which to formulate practice guidelines of the future.

Funding of translational and clinical studies provide the critical means of extending and applying basic science to the patient care arena.

Industry, Medical Associations, Third Party Payers and the NIH should be strongly encouraged to provide the increasingly critical dollars needed to conduct these trials.

Final Notes From The AF Task Force

Recommendations and Level of Evidence

Level of Evidence	Definition	Characteristics	Recommendations
Level 1	Randomized controlled trial	Randomized controlled trial with low risk of bias	Strongly recommended
Level 2	Quasi-randomized controlled trial	Quasi-randomized controlled trial with low risk of bias	Recommended
Level 3	Retrospective cohort study	Retrospective cohort study with low risk of bias	Recommended
Level 4	Case-control study	Case-control study with low risk of bias	Recommended
Level 5	Case series	Case series with low risk of bias	Recommended
Level 6	Expert opinion	Expert opinion with low risk of bias	Recommended
Level 7	Case report	Case report with low risk of bias	Recommended
Level 8	Case series	Case series with high risk of bias	Not recommended
Level 9	Case report	Case report with high risk of bias	Not recommended
Level 10	Expert opinion	Expert opinion with high risk of bias	Not recommended