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2017 HRS/EHRA/ECAS/APHRS/SOLAECE Expert Consensus Statement on Catheter and Surgical Ablation of Atrial Fibrillation

Training Requirements, Surgical Ablation, and Clinical Trial Design

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Training Requirements

Fundamental Principles

1. Appropriate selection of patients
2. Knowledge of the anatomy of the atria and adjacent structures
3. Conceptual knowledge of strategies to ablate AF
4. Technical competence
5. Recognition, prevention, and management of complications
6. Appropriate follow-up and long-term management

Training Requirements

Technical Competence

1. LA access and instrumentation
2. Appropriate use of fluoroscopy, 3D mapping systems, and ICE
3. Principles of radiation safety
4. Interpretation of intracardiac EGMs (PVs)
5. Concomitant atrial arrhythmias
6. Energy sources (RF, Crio and Balloon Ablation)

Training Requirements

Procedural Experience

1. At least 50 AF ablations and 30 macroreentrant ATs
    - 20 isthmus and 10 nonisthmus-dependent / macroreentry
    - Supportive of the 2015 ACC/AHA/HRS Advanced Training Statement
2. Several AF procedures per month to maintain competence
3. Underestimation of the experience required for a high degree of proficiency
4. To perform AF ablation indepedently
    - Aditional training after the standard fellowship if < 50 cases

Surgical and Hybrid AF Ablation

Terminology

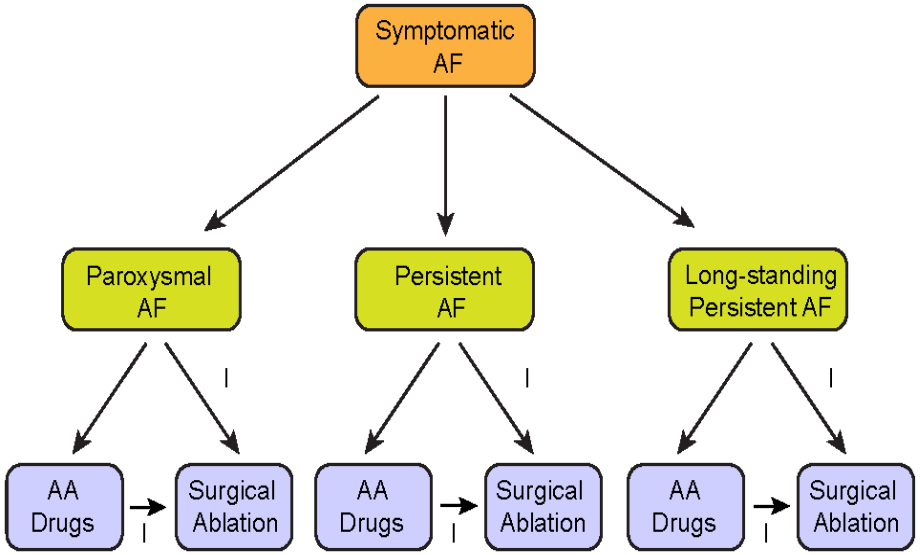
1. Avoid the term “Lone AF” to describe population of AF patients
2. Stand-alone ablation
   - When no concomitant procedure is performed

3. Maze procedure
   - Refer only to the biatrial lesion set of the Cox-Maze surgery

4. Less extension lesion sets
   - Surgical AF ablation procedure (PVI or PVI + lesions)

Surgical AF Ablation

Indications for Concomitant Open (Such as Mitral Valve) Surgical Ablation of AF



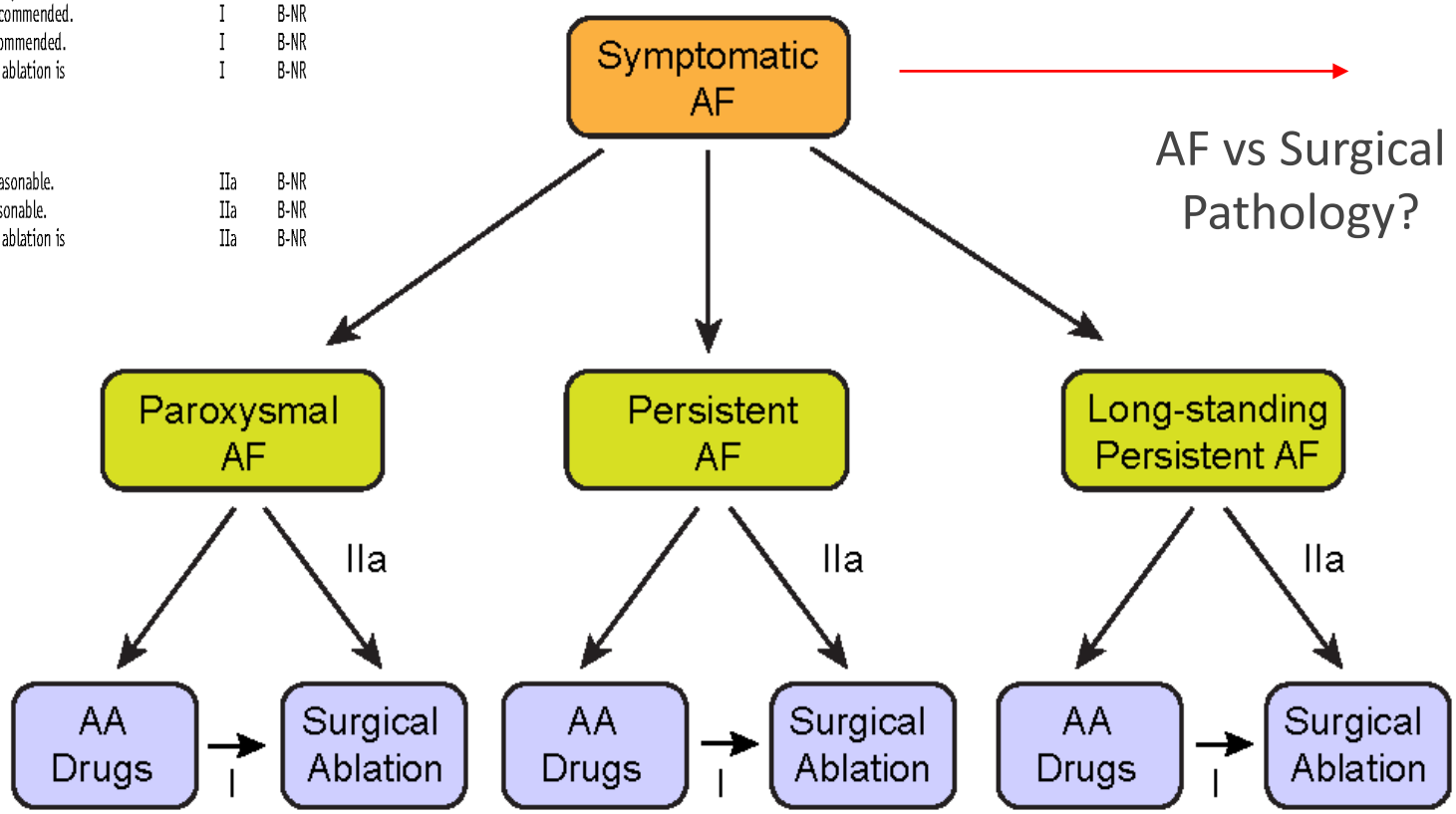
Recommendation		Class	LOE
Indications for surgical ablation of atrial fibrillation			
C. Indications for concomitant open (such as mitral valve) surgical ablation of atrial fibrillation			
Symptomatic AF refractory or intolerant to at least one Class I or III antiarrhythmic medication	Paroxysmal: Surgical ablation is recommended.	I	B-NR
	Persistent: Surgical ablation is recommended.	I	B-NR
	Long-standing persistent: Surgical ablation is recommended.	I	B-NR
Symptomatic AF prior to initiation of antiarrhythmic therapy with a Class I or III antiarrhythmic medication	Paroxysmal: Surgical ablation is recommended.	I	B-NR
	Persistent: Surgical ablation is recommended.	I	B-NR
	Long-standing persistent: Surgical ablation is recommended.	I	B-NR

Surgical AF Ablation

Indications for Concomitant Closed (Such as CABG or AVR) Surgical Ablation of AF

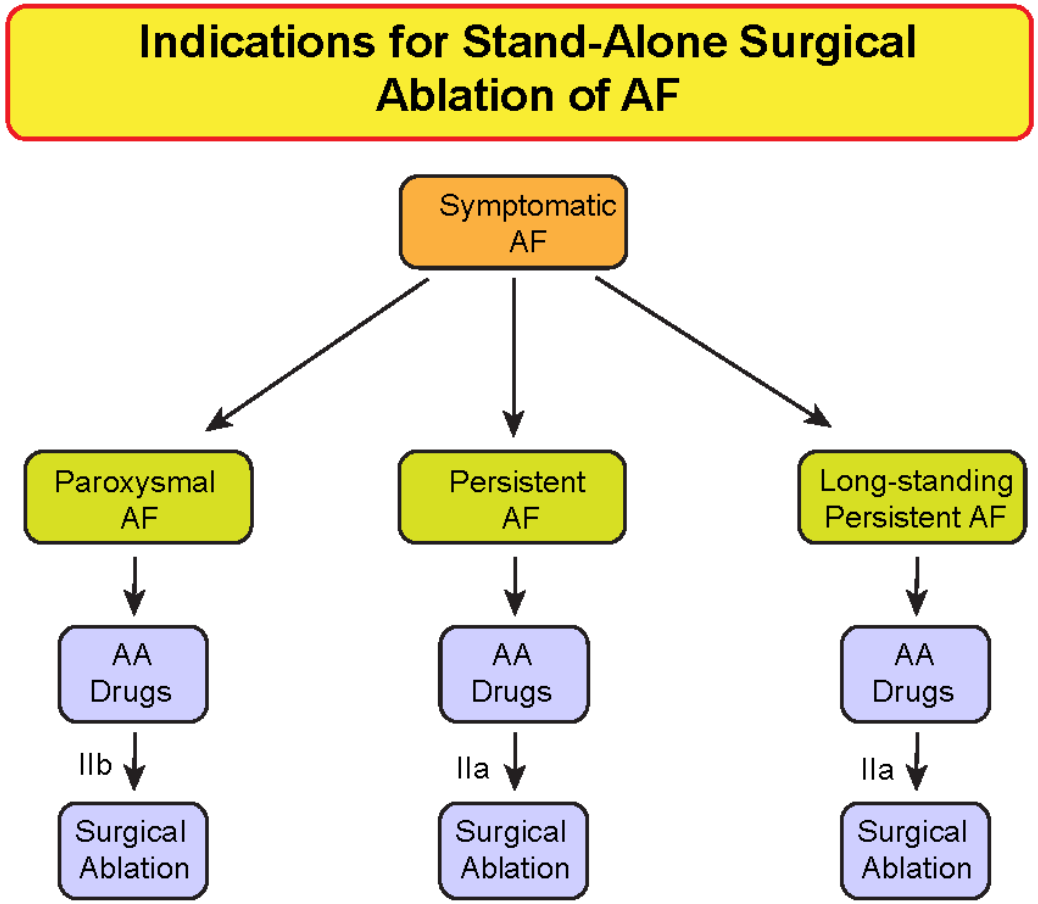
D. Indications for concomitant closed (such as CABG and AVR) surgical ablation of atrial fibrillation

Symptomatic AF refractory or intolerant to at least one Class I or III antiarrhythmic medication	Paroxysmal: Surgical ablation is recommended.	I	B-NR
	Persistent: Surgical ablation is recommended.	I	B-NR
	Long-standing persistent: Surgical ablation is recommended.	I	B-NR
Symptomatic AF prior to initiation of antiarrhythmic therapy with a Class I or III antiarrhythmic medication	Paroxysmal: Surgical ablation is reasonable.	IIa	B-NR
	Persistent: Surgical ablation is reasonable.	IIa	B-NR
	Long-standing persistent: Surgical ablation is reasonable.	IIa	B-NR



Class IIa, LOE B

Surgical AF Ablation



After review of relative safety and efficacy vs catheter ablation

After failed 1 or more attempts at catheter ablation

LOE B

Surgical AF Ablation

Symptomatic AF refractory or intolerant to at least one Class I or III antiarrhythmic medication	Paroxysmal: Stand-alone surgical ablation can be considered for patients who have failed one or more attempts at catheter ablation and also for those who are intolerant or refractory to antiarrhythmic drug therapy and prefer a surgical approach, after review of the relative safety and efficacy of catheter ablation versus a stand-alone surgical approach.	IIb	B-NR
	Persistent: Stand-alone surgical ablation is reasonable for patients who have failed one or more attempts at catheter ablation and also for those patients who prefer a surgical approach after review of the relative safety and efficacy of catheter ablation versus a stand-alone surgical approach.	IIa	B-NR
	Long-standing persistent: Stand-alone surgical ablation is reasonable for patients who have failed one or more attempts at catheter ablation and also for those patients who prefer a surgical approach after review of the relative safety and efficacy of catheter ablation versus a stand-alone surgical approach.	IIa	B-NR
	It might be reasonable to apply the indications for stand-alone surgical ablation described above to patients being considered for hybrid surgical AF ablation.	IIb	C-EO

Hybrid Procedures:

1. Complementary endo + epi ablation
2. Touch-up catheter ablation of surgical endocardial gaps
3. Catheter ablation of ICT, CS, flutters and focal triggers

Class IIb, LOE C

Clinical Trial Design

Clinical Endpoint Considerations

1. Multitude of different endpoints used in trials
    - Efficacy, QOL measures, non-AF recurrence endpoints, complications

2. Consistency in reporting by using standardized definitions
    - Success, complications, minimum monitoring after ablation

Clinical Trial Design

Definitions for Use When Reporting Outcomes and Designing Clinical Trials

Acute procedural success (pulmonary vein isolation)	Acute procedural success is defined as electrical isolation of all pulmonary veins. A minimal assessment of electrical isolation of the PVs should consist of an assessment of entrance block. If other methods are used to assess PVI, including exit block and/or the use of provocative agents such as adenosine or isoproterenol, they should be prespecified. Furthermore, it is recommended that the wait time used to screen for early recurrence of PV conduction once initial electrical isolation is documented be specified in all prospective clinical trials.
Acute procedural success (not related by pulmonary vein isolation)	Typically, this would apply to substrate ablation performed in addition to PVI for persistent AF. Although some have proposed AF termination as a surrogate for acute procedural success, its relationship to long-term success is controversial. Complete elimination of the additional substrate (localized rotational activation, scar region, non-PV trigger, or other target) and/or demonstration of bidirectional conduction block across a linear ablation lesion would typically be considered the appropriate endpoint.
One-year success*	One-year success is defined as freedom from AF/AFL/AT after removal from antiarrhythmic drug therapy as assessed from the end of the 3month blanking period to 12 months following the ablation procedure. Because cavotricuspid isthmus-dependent atrial flutter is easily treated with cavotricuspid isthmus ablation and is not an iatrogenic arrhythmia following a left atrial ablation procedure for AF, it is reasonable for clinical trials to choose to prespecify that occurrence of isthmus-dependent atrial flutter, if confirmed by entrainment maneuvers during electrophysiology testing, should not be considered an ablation failure or primary effectiveness endpoint.
Alternative one-year success	Although the one-year success definition provided above remains the recommended end point that should be reported in all AF ablation trials, and the endpoint for which the objective performance criteria listed below were developed, the Task Force recognizes that alternative definitions for success can be used if the main goal of therapy in the study is to relieve AF-related symptoms and to improve patient QOL. In particular, it is appropriate for clinical trials to define success as freedom from only symptomatic AF/AFL/AT after removal from antiarrhythmic drug therapy as assessed from the end of the 3-month blanking period to 12 months following the ablation procedure if the main goal of therapy in the study is to relieve AF-related symptoms and to improve patient QOL. However, because symptoms of AF can resolve over time, and because studies have shown that asymptomatic AF represents a greater proportion of all AF postablation than prior to ablation, clinical trials need to continue to report freedom from both symptomatic and asymptomatic AF even if this alternative one year success definition is used as the primary trial endpoint.
Clinical/partial success*	It is reasonable for clinical trials to define and incorporate one or more secondary definitions of success that can be referred to as "clinical success" or "partial success." If these alternative definitions of success are included, they should be defined prospectively. In prior Consensus Documents the Task Force has proposed that clinical/partial success be defined as a "75% or greater reduction in the number of AF episodes, the duration of AF episodes, or the % time a patient is in AF as assessed with a device capable of measuring AF burden in the presence or absence of previously ineffective antiarrhythmic drug therapy." Because there is no firm scientific basis for selecting the cutoff of 75% rather than a different cutoff, this prior recommendation is provided only as an example of what future clinical trials may choose to use as a definition of clinical/partial success.
Long-term success*	Long-term success is defined as freedom from AF/AFL/AT recurrences following the 3-month blanking period through a minimum of 36-month follow-up from the date of the ablation procedure in the absence of Class I and III antiarrhythmic drug therapy.
Recurrent AF/AFL/AT	Recurrent AF/AFL/AT is defined as AF/AFL/AT of at least 30 seconds' duration that is documented by an ECG or device recording system and occurs following catheter ablation. Recurrent AF/AFL/AT may occur within or following the post ablation blanking period. Recurrent AF/AFL/AT that occurs within the postablation blanking period is not considered a failure of AF ablation.
Early recurrence of AF/AFL/AT	Early recurrence of AF/AFL/AT is defined as a recurrence of atrial fibrillation within three months of ablation. Episodes of atrial tachycardia or atrial flutter should also be classified as a "recurrence." These are not counted toward the success rate if a blanking period is specified.
Recurrence of AF/AFL/AT	Recurrence of AF/AFL/AT postablation is defined as a recurrence of atrial fibrillation more than 3 months following AF ablation. Episodes of atrial tachycardia or atrial flutter should also be classified as a "recurrence."
Late recurrence of AF/AFL/AT	Late recurrence of AF/AFL/AT is defined as a recurrence of atrial fibrillation 12 months or more after AF ablation. Episodes of atrial tachycardia or atrial flutter should also be classified as a "recurrence."
Blanking period	A blanking period of three months should be employed after ablation when reporting efficacy outcomes. Thus, early recurrences of AF/AFL/AT within the first 3 months should not be classified as treatment failure. If a blanking period of less than 3 months is chosen, it should be prespecified and included in the Methods section.
Stroke screening	A risk-based approach to determine the level of postablation stroke screening in clinical trials is recommended by the Task Force. For ablation devices with a lower risk of stroke and for which a stroke signal has not been reported, a minimum standardized neurological assessment of stroke should be conducted by a physician at baseline and at hospital discharge or 24 hours after the procedure, whichever is later. If this neurological assessment demonstrates new abnormal findings, the patient should have a formal neurological consult and examination with appropriate imaging (i.e., DW-MRI), used to confirm any suspected diagnosis of stroke. For devices in which a higher risk of stroke is suspected or revealed in prior trials, a formal neurological examination by a neurologist at discharge or 24 hours after the procedure, whichever is later, is recommended. Appropriate imaging should be obtained if this evaluation reveals a new neurological finding. In some studies in which delayed stroke is a concern, repeat neurological screening at 30 days postablation might be appropriate.
Detectable AF/AFL/AT	Detectable AF is defined as AF/AFL/AT of at least 30 seconds' duration when assessed with ECG monitoring. If other monitoring systems are used, including implantable pacemakers, implantable defibrillators, and subcutaneous ECG monitoring devices, the definition of detectable AF needs to be prespecified in the clinical trial based on the sensitivity and specificity of AF detection with the particular device. We recommend that episodes of atrial flutter and atrial tachycardia be included within the broader definition of a detectable AF/AFL/AT episode.
AF/AFL/AT burden	It is reasonable for clinical trials to incorporate AF/AFL/AT burden as a secondary endpoint in a clinical trial of AF ablation. In stating this it is recognized that there are no conclusive data that have validated a rate of AF burden reduction as a predictor of patient benefit (i.e. reduction in mortality and major morbidities such as stroke, CHF, QOL, or hospitalization). If AF burden is included, it is important to predefine and standardize the monitoring technique that will be used to measure AF burden. Available monitoring techniques have been discussed in this document. Should AF burden be selected as an endpoint in a clinical trial, the chosen monitoring technique should be employed at least a month prior to ablation to establish a baseline burden of AF.
Entrance block	Entrance block is defined as the absence, or if present, the dissociation, of electrical activity within the PV antrum. Entrance block is most commonly evaluated using a circular multielectrode mapping catheter positioned at the PV antrum. Entrance block can also be assessed using detailed point-by-point mapping of the PV antrum guided by an electroanatomical mapping system. The particular method used to assess entrance block should be specified in all clinical trials. Entrance block of the left PVs should be assessed during distal coronary sinus or left atrial appendage pacing in order to distinguish far-field atrial potentials from PV potentials. It is recommended that reassessment of entrance block be performed a minimum of 20 minutes after initial establishment of PV isolation.

Clinical Trial Design

AF Recurrence Endpoints

1. Freedom from any atrial arrhythmia (AF, AT, or AFL) >30s off AADs
   - Gold standard for reporting efficacy
2. All trials should report single-procedure off AAD efficacy with minimum 12-month follow-up

Clinical Trial Design

30s Cutoff for Arrhythmia Recurrence

1. Stringent and might not accurately reflect more clinically relevant endpoints
   - Reduction in total AF burden, symptom abatement, improvement in QOL = underestimation of true benefits
2. More liberal endpoints suggested
   - Greater than 2 minutes (implantable monitoring technology detection limit)
   - Greater than 6 minutes, greater than 1 hour, or greater than 5-6 hours – stroke relevant duration

Clinical Trial Design

AF Burden

1. More optimal endpoint for assessing efficacy
   - Estimated on long-term monitoring
   - Truly defined only by implantable devices
2. Freedom from relevant AF
   - Low daily AF burden (<1%-2%) – might be an acceptable outcome
3. Reduction in AF burden >75% = clinical success
4. Number of episodes necessitating urgent or emergency care visits
   - Cost-effectiveness of the procedure

Clinical Trial Design

Definitions for Use When Reporting Outcomes and Designing Clinical Trials

Procedural endpoints for AF ablation strategies not targeting the PVs	Procedural endpoints for AF ablation strategies not targeting the PVs: The acute procedural endpoints for ablation strategies not targeting the PVs vary depending on the specific ablation strategy and tool. It is important that they be prespecified in all clinical trials. For example, if a linear ablation strategy is used, documentation of bidirectional block across the ablation line must be shown. For ablation of CFAEs, rotational activity, or non-PV triggers, the acute endpoint should at a minimum be elimination of CFAEs, rotational activity, or non-PV triggers. Demonstration of AF slowing or termination is an appropriate procedural endpoint, but it is not required as a procedural endpoint for AF ablation strategies not targeting the PVs.
Esophageal temperature monitoring	Esophageal temperature monitoring should be performed in all clinical trials of AF ablation. At a minimum, a single thermocouple should be used. The location of the probe should be adjusted during the procedure to reflect the location of energy delivery. Although this document does not provide formal recommendations regarding the specific temperature or temperature change at which energy delivery should be terminated, the Task Force does recommend that all trials prespecify temperature guidelines for termination of energy delivery.
Enrolled subject	An enrolled subject is defined as a subject who has signed written informed consent to participate in the trial in question.
Exit block	Exit block is defined as the inability to capture the atrium during pacing at multiple sites within the PV antrum. Local capture of musculature within the pulmonary veins and/or antrum must be documented to be present to make this assessment. Exit block is demonstrated by a dissociated spontaneous pulmonary vein rhythm.
Nonablative strategies	The optimal nonablative therapy for patients with persistent and long-standing persistent AF who are randomized to the control arm of an AF ablation trial is a trial of a new Class I or III antiarrhythmic agent or a higher dose of a previously failed antiarrhythmic agent. For patients with persistent or long-standing persistent AF, performance of a direct-current cardioversion while taking the new or dose adjusted antiarrhythmic agent should be performed, if restoration of sinus rhythm is not achieved following initiation and/or dose adjustment of antiarrhythmic drug therapy. Failure of pharmacological cardioversion alone is not adequate to declare this pharmacological strategy unsuccessful.
Noninducibility of atrial fibrillation	Noninducibility of atrial fibrillation is defined as the inability to induce atrial fibrillation with a standardized prespecified pharmacological or electrical stimulation protocol. The stimulation protocol should be prespecified in the specific clinical trial. Common stimulation approaches include a high-dose isoproterenol infusion protocol or repeated atrial burst pacing at progressively more rapid rates.
Patient populations for inclusion in clinical trials	It is considered optimal for clinical trials to enroll patients with only one type of AF: paroxysmal, persistent, or long-standing persistent. If more than one type of AF patient is enrolled, the results of the trial should also be reported separately for each of the AF types. It is recognized that "early persistent" AF responds to AF ablation to a similar degree as patients with paroxysmal AF and that the response of patients with "late persistent AF" is more similar to that in those with long-standing persistent AF.
Therapy consolidation period	Following a 3-month blanking period, it is reasonable for clinical trials to incorporate an additional 1- to 3-month therapy consolidation period. During this time, adjustment of antiarrhythmic medications and/or cardioversion can be performed. Should a consolidation period be incorporated into a clinical trial design, the minimum follow-up duration should be 9 months following the therapy consolidation period. Performance of a repeat ablation procedure during the blanking or therapy consolidation period would "reset" the endpoint of the study and trigger a new 3-month blanking period. Incorporation of a therapy consolidation period can be especially appropriate for clinical trials evaluating the efficacy of AF ablation for persistent or long-standing persistent AF. The challenge of this approach is that it prolongs the overall study duration. Because of this concern regarding overall study duration, we suggest that the therapy consolidation period be no more than 3 months in duration following the 3-month blanking period.
Recommendations regarding repeat ablation procedures	It is recommended that all clinical trials report the single procedure efficacy of catheter ablation. Success is defined as freedom from symptomatic or asymptomatic AF/AFL/AT of 30 seconds or longer at 12 months postablation. Recurrences of AF/AFL/AT during the first 3-month blanking period post-AF ablation are not considered a failure. Performance of a repeat ablation procedure at any point after the initial ablation procedure should be considered a failure of a single procedure strategy. It is acceptable for a clinical trial to choose to prespecify and use a multiprocedure success rate as the primary endpoint of a clinical trial. When a multiprocedure success is selected as the primary endpoint, efficacy should be defined as freedom from AF/flutter or tachycardia at 12 months after the final ablation procedure. In the case of multiple procedures, repeat ablation procedures can be performed at any time following the initial ablation procedure. All ablation procedures are subject to a 3-month post blanking window, and all ablation trials should report efficacy at 12 months after the final ablation procedure.
Cardioversion definitions	
Failed electrical cardioversion	Failed electrical cardioversion is defined as the inability to restore sinus rhythm for 30 seconds or longer following electrical cardioversion.
Successful electrical cardioversion	Successful electrical cardioversion is defined as the ability to restore sinus rhythm for at least 30 seconds following cardioversion.
Immediate AF recurrence postcardioversion	Immediate AF recurrence postcardioversion is defined as a recurrence of AF within 24 hours following cardioversion. The most common time for an immediate recurrence is within 30–60 minutes postcardioversion.
Early AF recurrence postcardioversion	Early AF recurrence postcardioversion is defined as a recurrence of AF within 30 days of a successful cardioversion.
Late AF recurrence postcardioversion	Late AF recurrence postcardioversion is defined as recurrence of AF more than 30 days following a successful cardioversion.
Surgical ablation definitions	
Hybrid AF surgical ablation procedure	Hybrid AF surgical ablation procedure is defined as a joint AF ablation procedure performed by electrophysiologists and cardiac surgeons either as part of a single "joint" procedure or performed as two preplanned separate ablation procedures separated by no more than 6 months.
Surgical Maze ablation procedure	Surgical Maze ablation procedure is defined as a surgical ablation procedure for AF that includes, at a minimum, the following components: (1) line from SVC to IVC; (2) line from IVC to the tricuspid valve; (3) isolation of the PVs; (4) isolation of the posterior left atrium; (5) line from MV to the PVs; (6) management of the LA appendage.
Stand-alone surgical AF ablation	A surgical AF ablation procedure during which other cardiac surgical procedures are not performed such as CABG, valve replacement, or valve repair.
Nomenclature for types of surgical AF ablation procedures	We recommend that the term "Maze" procedure is appropriately used only to refer to the biatrial lesion set of the Cox-Maze operation. It requires ablation of the RA and LA isthmuses. Less extensive lesion sets should not be referred to as a "Maze" procedure, but rather as a surgical AF ablation procedure. In general, surgical ablation procedures for AF can be grouped into three different groups: (1) a full biatrial Cox-Maze procedure; (2) PVI alone; and (3) PVI combined with left atrial lesion sets.
Hybrid epicardial and endocardial AF ablation	This term refers to a combined AF ablation procedure involving an off-pump minimally invasive surgical AF ablation as well as a catheter-based AF ablation procedure designed to complement the surgical lesion set. Hybrid ablation procedures may be performed in a single-procedure setting in a hybrid operating room or a cardiac catheterization laboratory environment, or it can be staged. When staged, it is most typical to have the patient undergo the minimally invasive surgical ablation procedure first following by a catheter ablation procedure 1 to 3 months later. This latter approach is referred to as a "staged Hybrid AF ablation procedure."

Clinical Trial Design

Minimum AF Documentation Endpoints. TEE and Success Rates in Clinical Trials

Minimum documentation for paroxysmal AF	The minimum AF documentation requirement for paroxysmal AF is (1) physician's note indicating recurrent self-terminating AF and (2) one electrocardiographically documented AF episode within 6 months prior to the ablation procedure.
Minimum documentation for persistent AF	The minimum AF documentation requirement for persistent AF is (1) physician's note indicating continuous AF >7 days but no more than 1 year and (2) a 24-hour Holter within 90 days of the ablation procedure showing continuous AF.
Minimum documentation for early persistent AF	The minimum AF documentation requirement for persistent AF is (1) physician's note indicating continuous AF >7 days but no more than 3 months and (2) a 24-hour Holter showing continuous AF within 90 days of the ablation procedure.
Minimum documentation for long-standing persistent AF	The minimum AF documentation requirement for long-standing persistent AF is as follows: physician's note indicating at least 1 year of continuous AF plus a 24-hour Holter within 90 days of the ablation procedure showing continuous AF. The performance of a successful cardioversion (sinus rhythm >30 seconds) within 12 months of an ablation procedure with documented early recurrence of AF within 30 days should not alter the classification of AF as long-standing persistent.
Symptomatic AF/AFL/AT	AF/AFL/AT that results in symptoms that are experienced by the patient. These symptoms can include but are not limited to palpitations, presyncope, syncope, fatigue, and shortness of breath. For patients in continuous AF, reassessment of symptoms after restoration of sinus rhythm is recommended to establish the relationship between symptoms and AF.
Documentation of AF-related symptoms	Documentation by a physician evaluating the patient that the patient experiences symptoms that could be attributable to AF. This does not require a time-stamped ECG, Holter, or event monitor at the precise time of symptoms. For patients with persistent AF who initially report no symptoms, it is reasonable to reassess symptom status after restoration of sinus rhythm with cardioversion.
Minimum effectiveness endpoint for patients with symptomatic and asymptomatic AF	The minimum effectiveness endpoint is freedom from symptomatic and asymptomatic episodes of AF/AFL/AT recurrences at 12 months following ablation, free from antiarrhythmic drug therapy, and including a prespecified blanking period.
Minimum chronic acceptable success rate: paroxysmal AF at 12-month follow-up	If a minimum chronic success rate is selected as an objective effectiveness endpoint for a clinical trial, we recommend that the minimum chronic acceptable success rate for paroxysmal AF at 12-month follow-up is 50%.
Minimum chronic acceptable success rate: persistent AF at 12-month follow-up	If a minimum chronic success rate is selected as an objective effectiveness endpoint for a clinical trial, we recommend that the minimum chronic acceptable success rate for persistent AF at 12-month follow-up is 40%.
Minimum chronic acceptable success rate: long-standing persistent AF at 12-month follow-up	If a minimum chronic success rate is selected as an objective effectiveness endpoint for a clinical trial, we recommend that the minimum chronic acceptable success rate for long-standing persistent AF at 12-month follow-up is 30%.
Minimum follow-up screening for paroxysmal AF recurrence	For paroxysmal AF, the minimum follow-up screening should include (1) 12-lead ECG at each follow-up visit; (2) 24-hour Holter at the end of the follow-up period (e.g., 12 months); and (3) event recording with an event monitor regularly and when symptoms occur from the end of the 3-month blanking period to the end of follow-up (e.g., 12 months).
Minimum follow-up screening for persistent or long-standing AF recurrence	For persistent and long-standing persistent AF, the minimum follow-up screening should include (1) 12-lead ECG at each follow-up visit; (2) 24-hour Holter every 6 months; and (3) symptom-driven event monitoring.
Requirements for transesophageal echocardiogram	It is recommended that the minimum requirement for performance of a TEE in a clinical trial should be those requirements set forth in ACC/AHA/HRS 2014 Guidelines for AF Management pertaining to anticoagulation at the time of cardioversion. Prior to undergoing an AF ablation procedure a TEE should be performed in all patients with AF of >48 hours' duration or of unknown duration if adequate systemic anticoagulation has not been maintained for at least 3 weeks prior to AF ablation. If a TEE is performed for this indication, it should be performed within 24 hours of the ablation procedure.

Clinical Trial Design

QOL Scales, Definitions, and Strengths

Scale	Definition/Details	Strengths/Weaknesses
Short Form (36) Health Survey (SF36)38 (General)	Consists of 8 equally weighted, scaled scores in the following sections: vitality, physical functioning, bodily pain, general health perceptions, physical role functioning, emotional role functioning, social role functioning, mental health. Each section receives a scale score from 0 to 100. Physical component summary (PCS) and mental component summary (MCS) is an average of all the physically and mentally relevant questions, respectively. The Short Form (12) Health Survey (SF12) is a shorter version of the SF-36, which uses just 12 questions and still provides scores that can be compared with SF-36 norms, especially for summary physical and mental functioning. Gives more precision in measuring QOL than EQ-5D but can be harder to transform into cost utility analysis.	Advantages: extensively validated in a number of disease and health states. Might have more resolution than EQ-50 for AF QOL. Disadvantages: not specific for AF, so might not have resolution to detect AF-specific changes in QOL.
EuroQol Five Dimensions Questionnaire (EQ-5D)39 (General)	Two components: Health state description is measured in five dimensions: mobility, self-care, usual activities, pain/discomfort, anxiety/depression. Answers may be provided on a three-level (3L) or five-level (5L) scale. In the Evaluation section, respondents evaluate their overall health status using a visual analogue scale (EQ-VAS). Results can easily be converted to quality-adjusted life years for cost utility analysis.	Advantages: extensively validated in a number of disease and health states. Can easily be converted into quality-adjusted life years for cost-effectiveness analysis. Disadvantages: might not be specific enough to detect AF-specific changes in QOL. Might be less specific than SF-36.
AF effect on Quality of Life Survey (AFEQT)40 (AF specific)	20 questions: 4 targeting AF-related symptoms, 8 evaluating daily function, and 6 assessing AF treatment concerns. Each item scored on a 7-point Likert scale.	Advantages: brief, simple, very responsive to AF interventions. Good internal validity and well validated against a number of other global and AF-specific QOL scales. Used in CABANA. Disadvantages: validation in only two published studies (approximately 219 patients).
Quality of Life Questionnaire for Patients with AF (AF-QoL)41 (AF specific)	18-item self-administered questionnaire with three domains: psychological, physical, and sexual activity. Each item scores on a 5-point Likert scale.	Advantages: brief, simple, responsive to AF interventions; good internal validity; used in SARA trial. Disadvantages: external validity compared only to SF-36; formal validation in 1 study (approximately 400 patients).
Arrhythmia-Related Symptom Checklist (SCL) 42 (AF specific)	16 items covering AF symptom frequency and symptom severity.	Advantages: most extensively validated in a number of arrhythmia cohorts and clinical trials. Disadvantages: time-consuming and uncertain generalizability.
Mayo AF Specific Symptom Inventory (MAFSI)43 (AF specific)	10 items covering AF symptom frequency and severity. Combination of 5- point and 3-point Likert scale responses. Used in CABANA trial.	Advantages: validated in an AF ablation population and responsive to ablation outcome; used in CABANA trial. Disadvantages: external validity compared only to SF-36; 1 validation study (approximately 300 patients).
University of Toronto Atrial Fibrillation Severity Scale (AFSS) (AF specific)44	10 items covering frequency, duration, and severity. 7-point Likert scale responses.	Advantages: validated and reproducible; used in CTAF trial. Disadvantages: time-consuming and uncertain generalizability.
Arrhythmia Specific Questionnaire in Tachycardia and Arrhythmia (ASTA)45 (AF specific)	Records number of AF episodes and average episode duration during last 3 months. 8 symptoms and 2 disabling symptoms are recorded with scores from 1–4 for each.	Advantages: validated in various arrhythmia groups; external validity compared with SCL, EQ5D, and SF-36; used in MANTRA-PAF; brief; simple. Disadvantages: one validation study (approximately 300 patients).
European Heart Rhythm Association (EHRA)46 (AF specific)	Like NYHA scale. I = no symptoms, II = mild symptoms not affecting daily activity, III = severe symptoms affecting daily activity, and IV = disabling symptoms terminating daily activities.	Advantage: very simple, like NYHA. Disadvantages: not used in studies and not well validated; not very specific; unknown generalizability.
Canadian Cardiovascular Society Severity of Atrial Fibrillation Scale (CCS-SAF)47 (AF specific)	Like NYHA scale. 0 = asymptomatic, I = AF symptoms have minimal effect on patient's QOL, II = AF symptoms have minor effect on patient QOL, III = symptoms have moderate effect on patient QOL, IV= AF symptoms have severe effect on patient QOL.	Advantages: very simple, like NYHA; validated against SF-36 and University of Toronto AFSS. Disadvantages: poor correlation with subjective AF burden; not very specific.

Clinical Trial Design

Non-AF Recurrence–Related Endpoints for Reporting in AF Ablation Trials

Stroke and bleeding endpoints	Definitions/Details
Stroke (2014 ACC/AHA Key Data Elements)	An acute episode of focal or global neurological dysfunction caused by brain, spinal cord, or retinal vascular injury as a result of hemorrhage or infarction. Symptoms or signs must persist ≥24 hours, or if documented by CT, MRI or autopsy, the duration of symptoms/signs may be less than 24 hours. Stroke may be classified as ischemic (including hemorrhagic transformation of ischemic stroke), hemorrhagic, or undetermined. Stroke disability measurement is typically performed using the modified Rankin Scale (mRS).
Transient ischemic attack (2014 ACC/AHA Key Data Elements)	Transient episode of focal neurological dysfunction caused by brain, spinal cord, or retinal ischemia without acute infarction and with signs and symptoms lasting less than 24 hours.
Major bleeding (ISTH definition)	Fatal bleeding AND/OR symptomatic bleeding in a critical area or organ, such as intracranial, intraspinal, intraocular, retroperitoneal, intraarticular, pericardial, or intramuscular with compartment syndrome AND/OR bleeding causing a fall in hemoglobin level of 2 g/dL (1.24 mmol/L) or more, or leading to transfusion of two or more units of blood.
Clinically relevant nonmajor bleed (ISTH definition)	An acute or subacute clinically overt bleed that does not meet the criteria for a major bleed but prompts a clinical response such that it leads to one of the following: hospital admission for bleeding; physician-guided medical or surgical treatment for bleeding; change in antithrombotic therapy (including interruption or discontinuation).
Minor bleeding (ISTH definition)	All nonmajor bleeds. Minor bleeds are further divided into clinically relevant and not.
Incidence and discontinuation of oral anticoagulation	The number of patients receiving oral anticoagulation and the type of oral anticoagulation should be documented at the end of follow-up. If patients have their oral anticoagulation discontinued, the number of patients discontinuing, the timing of discontinuation, and the reasons for discontinuation of oral anticoagulation, as well as the clinical characteristics and stroke risk profile of the patients should be reported.

Clinical Trial Design

Advantages and Disadvantages of AF-Related Endpoints

Endpoint	Advantages	Disadvantages	Relevance and Comments
Freedom from AF/AFL/AT recurrence "gold standard" is 30 seconds	- Has been in use for many years - Can be used to compare results of new trials with historical trials - Sets a high bar for AF elimination	- Can systematically underestimate the efficacy of AF ablation, particularly for persistent AF, if 30-second cutoff is used	- Particularly well suited for paroxysmal AF outcomes - Reporting of cutoffs other than 30 seconds encouraged as secondary endpoints to better contextualize results - May be reported as proportion of patients free from arrhythmia or time to recurrence
Freedom from stroke-relevant AF/AFL/AT-duration cutoff of 1 hour	- Useful for trials in which interest is more for prognostic change conferred by ablation rather than elimination of all arrhythmias	- No consistent definition of what a stroke-relevant duration of AF is: ranges from 6 minutes to 24 hours in literature	- More than 1 hour could be a useful cutoff based on results of 505 trial - May be reported as proportion of patients free from arrhythmia or time to recurrence
Freedom from AF/AFL/AT requiring intervention (emergency visits, cardioversion, urgent care visit, reablation, etc.)	- Can provide an endpoint more relevant to systemic costs of AF recurrence - Clinically relevant	- Will overestimate efficacy of ablation by ignoring shorter episodes not requiring intervention that still might be important to quality of life or stroke	- Determination of what is an "intervention" must be prespecified in protocol and biases mitigated to avoid over- or underintervention in the trial
Freedom from persistent AF/AFL/AT-duration cutoff of 7 days	- Useful for trials assessing additional substrate modification in persistent AF	- Can systematically overestimate the efficacy of AF ablation, particularly for persistent AF	- Can require continuous monitoring to definitively assess if episode is >7 days
Freedom from AF/AFL/AT on previously ineffective antiarrhythmic therapy	- If patient maintains sinus rhythm on previously ineffective drug therapy, this may be considered a clinically relevant, successful outcome	- Will increase the success rate compared with off-drug success - May not be relevant to patients hoping to discontinue drug therapy	- Postablation drug and dosage of drug should be identical to preablation drug and dosage
Significant reduction in AF burden: >75% reduction from pre- to postablation and/or total postablation burden <12%	- Can be useful in persistent AF studies, but might not be suited for early, paroxysmal AF studies	- Ideally requires continuous monitoring using an implantable device - No scientific basic exists showing that a 75% reduction in AF burden impacts hard endpoints, including heart failure, stroke, and mortality	- AF burden can be estimated by intermittent monitoring and reporting of patient symptoms and recurrences like a "time in therapeutic range" report for oral anticoagulation; see text - Could also see 75% reduction in number and duration of AF episodes - Because there is no firm scientific basis for selecting the cutoff of 75%, this prior recommendation is provided only as an example of what future clinical trials may choose to use as a definition of clinical/partial success
Prevention in AF progression: time to first episode of persistent AF (>7 days)	- Does not assume that total elimination of AF is required - Well suited for paroxysmal or "early" AF studies in which goal is to prevent progression to persistent AF	- Prevention in progression might be irrelevant for stroke or thromboembolic outcomes - Long follow-up time might be required unless population is "enriched" - Can ideally require continuous implantable monitoring	- Might be useful for specific populations such as heart failure or hypertrophic cardiomyopathy, in which progression to persistent AF can lead to increased hospitalization
Regression of AF: reduction in burden to a given threshold or conversion of persistent to paroxysmal AF	- Does not assume that total elimination of AF is required - Well suited for persistent "late" AF studies in which goal is to regress to paroxysmal AF, which might be easier to control with drug therapy	- Regression endpoint will overestimate efficacy of AF ablation - Might ideally require continuous implantable monitoring - Patients will require ongoing drug therapy	- Could be particularly useful for long-standing persistent AF populations with structural heart disease, heart failure, etc.
Acute AF termination during ablation procedure	- Could provide indication of successful modification of substrate responsible for maintaining AF, most relevant to persistent or long-standing persistent AF - Limited studies have linked acute AF termination to long-term success	- Relevance of acute AF termination has not consistently been shown to correlate to long-term success - Endpoint might not be relevant to paroxysmal AF patients in whom AF might terminate spontaneously - Some studies employ administration of intravenous or oral antiarrhythmics during ablation that could cause spontaneous termination - Studies consider termination as reversion to sinus rhythm, whereas others consider reversion to any regular tachycardia as termination	- Intraprocedural administration of preprocedural oral antiarrhythmics or intraprocedural intravenous antiarrhythmics are discouraged - If antiarrhythmics are used, their use and dosage before and during the ablation should be clearly documented - Termination to sinus rhythm and termination to another regular tachycardia (AT or AFL) should be separately reported

2017 HRS/EHRA/ECAS/APHRS/SOLAECE Expert Consensus Statement on Catheter and Surgical Ablation of Atrial Fibrillation

Young-Hoon Kim, MD, PhD

FOLLOW-UP CONSIDERATIONS

1. Monitoring for Complications in the First Months After AF Ablation
   Signs and Symptoms of Complications Within 1 Month Postablation
   Signs and Symptoms of Complications More Than a Month Postablation
2. ECG Monitoring Pre- and Postablation
3. Available Methods for Arrhythmia Monitoring
4. Follow-up and Monitoring Guidelines for Routine Clinical Care

EARLY RECURRENCE AFTER ABLATION

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Signs and Symptoms Following AF Ablation

	Differential	Suggested evaluation
Signs and symptoms of complications within a month postablation		
Back pain	Musculoskeletal, retroperitoneal hematoma	Physical exam, CT imaging
Chest pain	Pericarditis, pericardial effusion, coronary stenosis (ablation related), pulmonary vein stenosis, musculoskeletal (after cardioversion), worsening reflux	Physical exam, chest X-ray, ECG, echocardiogram, stress test, cardiac catheterization, chest CT
Cough	Infectious process, bronchial irritation (mechanical, cryoballoon), pulmonary vein stenosis	Physical exam, chest X-ray, chest CT
Dysphagia	Esophageal irritation (related to transesophageal echocardiography), AE fistula	Physical exam, chest CT or MRI
Early satiety, nausea	Gastric denervation	Physical exam, gastric emptying study
Fever	Infectious process, pericarditis, AE fistula	Physical exam, chest X-ray, chest CT, urinalysis, laboratory blood work

	Differential	Suggested evaluation
Signs and symptoms of complications within a month postablation		
Fever, dysphagia, neurological symptoms	Atrial esophageal fistula	Physical exam, laboratory work, chest CT or MRI; avoid endoscopy with air insufflation
Groin pain at site of access	Pseudoaneurysm, AV fistula, hematoma	Ultrasound of the groin, laboratory blood work; consider CT if ultrasound negative
Headache	Migraine (related to anesthesia or transseptal access, hemorrhagic stroke), effect of general anesthetic	Physical exam, brain imaging (MRI)
Hypotension	Pericardial effusion/tamponade, bleeding, sepsis, persistent vagal reaction	Echocardiography, laboratory blood work
Hemoptysis	PV stenosis or occlusion, pneumonia	CXR, chest CT or MR scan, VQ scan
Neurological symptoms	Cerebral embolic event, AE fistula	Physical exam, brain imaging, chest CT or MRI
Shortness of breath	Volume overload, pneumonia, pulmonary vein stenosis, phrenic nerve injury	Physical exam, chest X-ray, chest CT, laboratory blood work

Signs and symptoms of complications more than a month postablation

Fever, dysphagia, neurological symptoms	Atrial esophageal fistula	Physical exam, laboratory blood work, chest CT or MRI; avoid endoscopy with air insufflation
Persistent cough, atypical chest pain	Infectious process, PV stenosis	Physical exam, laboratory blood work, chest X-ray, chest CT or MRI
Neurological symptoms	Cerebral embolic event, atrial esophageal fistula	Physical exam, brain imaging, chest CT or MRI
Hemoptysis	PV stenosis or occlusion, pneumonia	CT scan, VQ scan

ECG Monitoring Pre- and Postablation

The two main reasons to perform arrhythmia monitoring following catheter ablation are clinical care and as part of a clinical research trial.

Complaints of palpitations often result from atrial or ventricular premature beats and are not an accurate predictor of recurrent AF.

Arrhythmia monitoring can also be of value in asymptomatic patients and can influence decision making regarding anticoagulant therapy after ablation.

Multiple studies have demonstrated that asymptomatic AF commonly occurs in patients following catheter ablation.

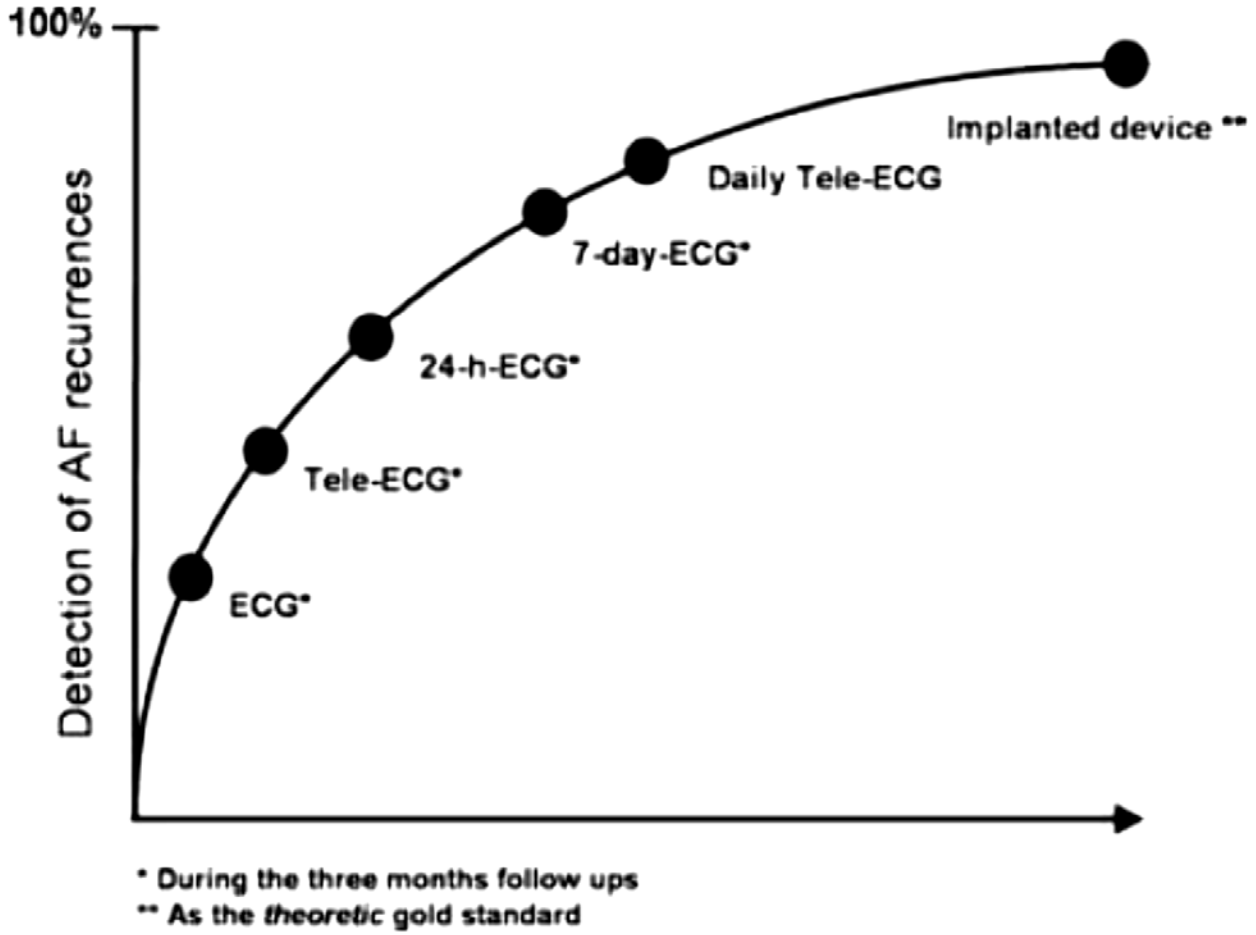
Detection of these asymptomatic episodes of AF impact the characterization of the procedure as “successful.”

Types of Ambulatory Cardiac Monitoring Devices

Type of recorder	Typical monitoring duration	Continuous recording	Event recording	Auto trigger	Unique features
Holter monitor	24–48 hours, approximately 7–30 days	Yes	Yes	N/A	Short term, provides quantitative data on arrhythmia burden
Patch monitor	1–3 weeks	Yes	Yes	N/A	Intermediate term, can provide continuous data for up to several weeks; improved patient compliance without lead wires
External loop recorder	1 month	Yes	Yes	Variable	Good correlation between symptoms and even brief arrhythmias
External nonloop recorder	Months	No	Yes	No	May be used long term and intermittently; will not capture very brief episodes
NEW **Smartphone monitor**	Indefinite	No	Yes	No	Provides inexpensive long-term intermittent monitoring; dependent on patient compliance; requires a smartphone
NEW **Mobile cardiac telemetry**	30 days	Yes	Yes	Yes	Real time central monitoring and alarms; relatively expensive
Implantable loop recorder	Up to 3 years	Yes	Yes	Yes	Improved patient compliance for long-term use; not able to detect 30-second episodes of AF due to detection algorithm; presence of AF needs to be confirmed by EGM review because specificity of detection algorithm is imperfect; expensive
Pacemakers or ICDs with atrial leads	Indefinite	Yes	Yes	Yes	Excellent AF documentation of burden and trends; presence of AF needs to be confirmed by ECG tracing review because specificity of detection algorithms is imperfect; expensive
NEW **Wearable multisensor ECG monitors**	Indefinite	Yes	Yes	Yes	ECG 3 leads, temp, HR, HRV, activity tracking, respiratory rate, galvanic skin response

Types of Ambulatory Cardiac Monitoring Devices

Different Monitoring Methods to Detect AF
The more you look, the more you find!



Pacing Clin Electrophysiol 2007;30:458-462

The proportion of asymptomatic compared with symptomatic events might be higher after AF ablation.

1. Asymptomatic AF was 11%–35% prior to and 53%–65% after ablation
2. Asymptomatic AF was 53.8%, with an increase in asymptomatic episodes changing from the acute to the chronic period after ablation.

Follow-up and Monitoring Guidelines for Routine Clinical Care

There is a consensus among the writing group members that all patients who undergo catheter ablation of AF, regardless of whether they are enrolled in a clinical trial, should be seen in “follow-up a minimum of 3 months” following the ablation procedure.

There is also consensus that all patients who undergo catheter ablation should be seen by some type of physician (family physician, internist, cardiologist, or electrophysiologist) on an annual basis thereafter.

“2012 Document”

> There is consensus among the Task Force that all patients who undergo catheter ablation of AF, regardless of whether or not they are enrolled in a clinical trial, should be seen in follow-up at a minimum of three months following the ablation procedure, and then every six months for at least two years (Table 5).

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Very Late Recurrence (More Than 1 Year) After AF Ablation

Early recurrences of AF after AF ablation :

Recurrence of AF >30 seconds during the first 3 months of follow-up.
Late recurrence (LR): recurrence of AF >30 seconds between 3 and 12 months after AF.

The pathophysiological mechanisms

1. Incomplete isolation of the PVs
2. Acute inflammatory changes owing to energy delivery
3. Recovery of conduction in a previously isolated PV
4. Modification of the ANS
5. Changes in the atrial substrate
6. Delayed effect of RF ablation due to lesion consolidation

The occurrence of atrial arrhythmias early after ablation does not necessarily indicate treatment failure later during follow-up.
Nevertheless, early recurrences have been shown to predict arrhythmia recurrences late after catheter ablation of AF in some patients.

Management of Early Recurrences

1. AADs

The 5A study

Usefulness of initiation or discontinuation of AAD therapy during the postablation healing phase in an effort to improve long-term outcomes is unclear (Class IIb, LOE C-LD, Table 3).

2. Corticosteroid

Two different results, negative vs. positive effect of prevention of late recurrence of AF (125 patients vs. 138 patients undergoing PV ablation)

3. Colchicine

has been shown to reduce postoperative AF following cardiac surgery.

Two studies were positive; however, 94% of the writing group members do not routinely administer colchicine.

Deleted “The impact of ARB/ACEI and statin on outcome of AF ablation” from 2012 document.

4. Early Cardioversion

"CV within 30 days of arrhythmia recurrence"
An aggressive approach with early DC CV after LA catheter ablation appears important to maintain SR in order to minimize late arrhythmia recurrences, reduce chronic AAD use, and prevent reablation procedures.
CV ≥3 times was a predictor of ablation failure (*n* = 40).

5. Early Reablation

Early reablation was associated with greater freedom from LR. Although the clinical benefit of early reablation was demonstrated, the first month following the procedure might not be the optimal time for a repeat intervention. Reablation is not recommended in an early recurrence of AF that might be a transient phenomenon.

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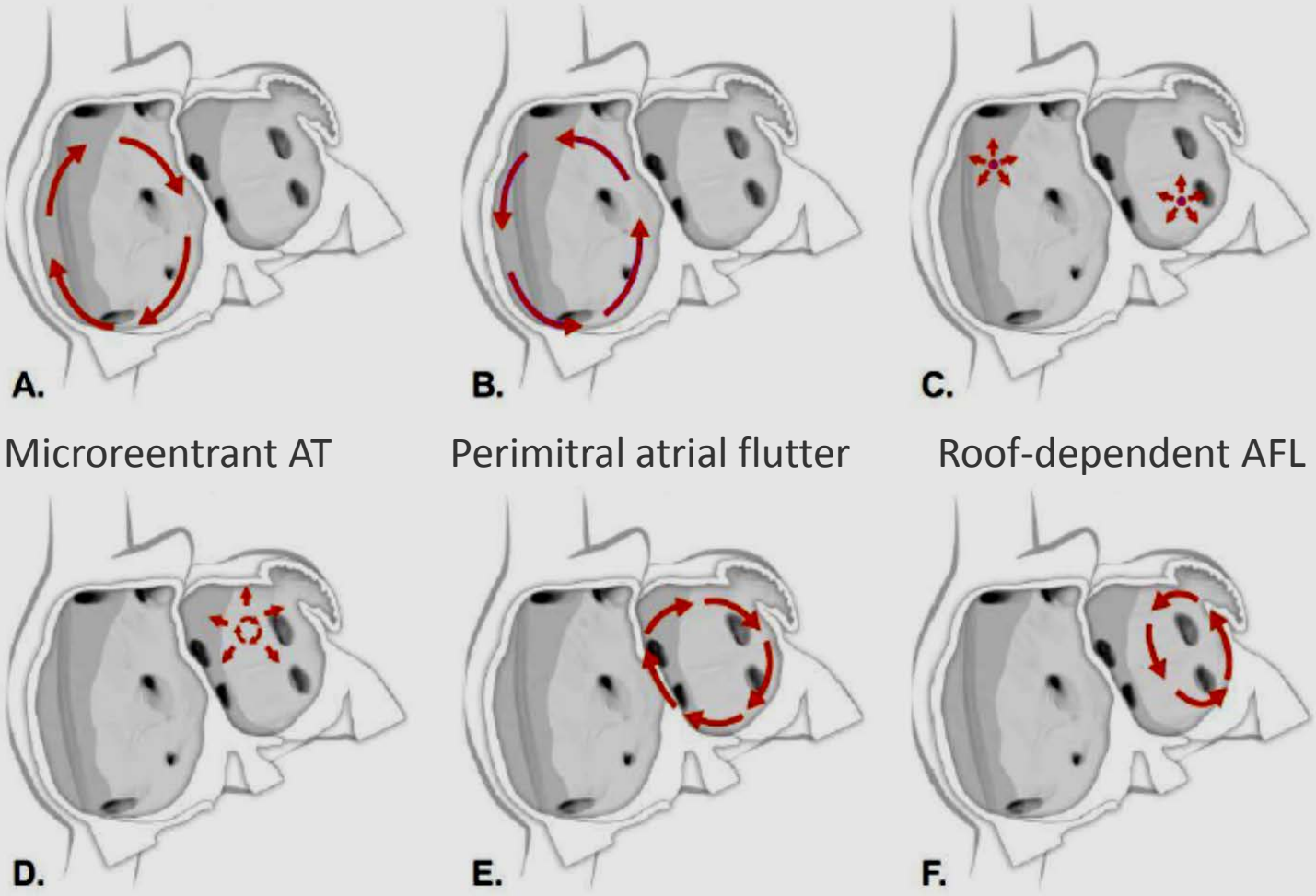
Atrial Tachycardias After AF Ablation

NEW

Figure 5 (A-F)



Atrial Tachycardias After AF Ablation

1. Antiarrhythmic and Other Pharmacological Therapy

#1. AADs have been used unsuccessfully prior to ablation; include flecainide, propafenone, sotalol, dofetilide, dronedarone, and amiodarone.

The short-term use of AADs after AF ablation decreased early recurrences of atrial arrhythmias and need for hospitalization or CV, but had no effect on the prediction or prevention of arrhythmia recurrence at 6 and 12 months.

#2. Corticosteroids/PPIs or H2 blockers/ARB or ACEI: remains unproven.

2. Later-Term Repeat Ablation Procedures

The first step in second AF ablation procedure is to check each PV for reconduction. If, however, there is no evidence of PV reconduction, ablation can be guided by

1. LA substrate mapping
2. Electrogram voltage
3. CFAEs
4. Non-PV triggers or sites commonly associated with non-PVs triggers such as the SVC
5. Focal impulse and rotational activity mapping
6. Dormant PV conduction unmasked by adenosine

Atrial Tachycardias After AF Ablation

1. **Antiarrhythmic and Other Pharmacological Therapy**
2. **Later-Term Repeat Ablation Procedures**
3. **Autonomic Alterations**

Most autonomic alterations associated with AF ablation were self-terminating and asymptomatic. However, severe symptomatic periesophageal vagal nerve injury can occur after LA posterior wall ablation (25–30 W).

Very Late Recurrence (More Than 1 Year) After AF Ablation

Despite of late recurrence, a low incidence of progression (0.3% per year) from paroxysmal to persistent AF as well as stroke rates <1% have been reported. More likely to have sporadic episodes and a better response to AADs and repeat ablation procedures than those with earlier recurrences.

The most consistent predictor of late recurrence

#1. Persistent AF

#2. Hypertension, age, LA size, diabetes, VHD and
LV dysfunction, and higher thromboembolic risk scores

#3. PV reconnection, non-PV foci, and gaps in prior ablation lines,
non-PV triggers from LAA and LA posterior wall

OUTCOMES AND EFFICACY

Overview/ Published Literature Review: Clinical Trials Performed for FDA Approval

1. AF Ablation as Second-Line Rhythm Control Therapy
2. Outcomes and Efficacy of Catheter Ablation of AF as First-Line Rhythm Control Therapy

NEW Published Literature Review: Survey Results

OUTCOMES OF AF ABLATION IN POPULATIONS NOT WELL REPRESENTED IN CLINICAL TRIALS

1. Outcomes of Catheter Ablation of Persistent and Long-Standing Persistent AF
2. Outcomes of AF Ablation in Elderly Patients
3. Outcomes of AF Ablation in Patients with Congestive Heart Failure and the Impact of Ablation on Left Ventricular Function

NEW 4. Outcomes of AF Ablation in Patients with Hypertrophic Cardiomyopathy

NEW 5. Outcomes of AF Ablation in Young Patients

NEW 6. Outcomes of AF Ablation in Women

7. Outcomes of Cryoballoon Ablation

NEW 8. Outcome of Rotational Activity Ablation for AF

NEW 9. Outcomes of Laser Balloon Ablation

10. Long-Term Ablation Efficacy
11. Impact of Catheter Ablation of AF on QOL
12. Impact of Catheter Ablation of AF on LA Size and Function

NEW 13. Impact of Catheter Ablation on Stroke Risk

Predictors of Success Following AF Ablation

Cost-Effectiveness of AF Ablation

Selected Clinical Trials of Catheter Ablation of AF and/or for FDA Approval

Clinical Trials Performed for FDA Approval

Trial	Year	Type	*N*	AF type	Ablation strategy	Initial time frame
JAMA 2010; 303; 333-340 (ThermoCool AF)	2010	Randomized to RF ablation or AAD, multicenter	167	Paroxysmal	PVI, optional CFAEs and lines	12 months
JACC 2013; 61: 1713-1723 (STOP AF)	2013	Randomized to cryoballoon ablation or AAD, multicenter	245	Paroxysmal	PVI	12 months
Heart Rhythm 2014; 11: 202-209 (TTOP)	2014	Randomized to phased RF ablation or AAD/cardioversion, multicenter nonirrigated circumferential multielectrode ablation catheters with duty cycled phased RF energy	210	Persistent	PVI + CFAEs	6 months
JACC 2014; 64: 647-656 (SMART-AF)	2014	Nonrandomized multicenter study of CF sensing RF catheter, comparing to performance goals	172	Paroxysmal	PVI, optional CFAEs and lines	12 months
Circulation 2015; 132: 907-915 (TOCCASTAR)	2015	Randomized to CF sensing RF catheter or approved RF catheter, multicenter	300	Paroxysaml	PVI, optional triggers, CAFEs and lines in both arms	12 months
JACC 2015; 66: 1350-1360 (HeartLight)	2015	Randomized to laser balloon or approved RF catheter, multicenter	353	Paroxysmal	PVI ± CTI ablation vs. PVI, optional CFAEs, and Lines	12 months

Selected Clinical Trials of Catheter Ablation of AF and/or for FDA Approval

Clinical Trials Performed for FDA Approval

Trial	Effectiveness endpoint	Ablation success	Drug/Control success	*P* value for success	Ablation Cxs	Drug/Control Cxs	FDA
JAMA 2010; 303; 333-340 (ThermoCool AF)	Freedom from symptomatic PAF, acute procedural failure, or changes in specified drug regimen	66%	16%	< 0.001	4.9%	8.8%	Approval (+)
JACC 2013; 61: 1713-1723 (STOP AF)	Freedom from any detectable AF, use of nonstudy AAD, or non-protocol intervention for AF	70%	7%	< 0.001	3.1%	NA	Approval (+)
Heart Rhythm 2014; 11: 202-209 (TTOP)	Acute procedural success, ≥90% reduction in AF burden, off AAD nonirrigated circumferential multielectrode ablation catheters with duty cycled phased RF energy	56%	26%	<0.001	12.3% 4 strokes (2.9%)	NA	Approval (-)
JACC 2014; 64: 647-656 (SMART-AF)	Freedom from symptomatic AF, flutter, tachycardia, acute procedural failure, or changes in AAD	72.5%	N/A	<0.0001	7.5%	NA	Approval (+)
Circulation 2015; 132: 907-915 (TOCCASTAR)	Acute procedural success + freedom from symptomatic AF/flutter/tachycardia off AAD	67.8%	69.4%	0.0073 for noninferiority	7.2%	9.1%	Approval (+)
JACC 2015; 66: 1350-1360 (HeartLight)	Freedom from symptomatic AF/flutter/tachycardia, acute procedural failure, AAD, or nonprotocol intervention	61.1%	61.7%	0.003 for noninferiority	5.3%	6.4%	Approval (+)

As in the past, future studies might compare novel ablation systems against medical management because, at this point, no ablation system is expressly approved for persistent or long-standing persistent AF in the United States.

Alternatively, a novel ablation system could be evaluated in single-arm trials with prespecified OPCs.

Objective Performance Criteria (OPC)

First-Line Therapy Trials

Trial	Year	Type	*N*	AF type	Ablation strategy	Initial time frame
JAMA 2005; 293: 2634-264 (RAAFT)	2005	Randomized to drug, multicenter	70	PAF (*N*=67), PeAF (*N*= 3)	PVI	12 Ms
NEJM 2012; 367:1587-1595 (MANTRA-PAF)	2012	Randomized to drug, multicenter	294	PAF	PVI, roof line, optional mitral and CTI	24 Ms
JAMA 2014; 311: 692-700 (RAAFT-2)	2014	Randomized to drug, multicenter	127	PAF	PVI + optional Non-PVI targets	24 Ms

First-Line Therapy Trials

Trial	Effectiveness endpoint	Ablation success	Drug/Control success	*P*	Ablation Cxs	Drug /Control Cxs
JAMA 2005; 293: 2634-2640 (RAAFT)	Freedom from detectable AF	84%	37%	<0.01	9%	11%
NEJM 2012; 367:1587-1595 (MANTRA-PAF)	Cumulative AF burden	13% AF burden	19% AF burden	NS	17%	15%
JAMA 2014; 311: 692-700 (RAAFT-2)	Freedom from detectable AF, flutter, tachycardia	45%	28%	0.02	9%	4.9%

MANTRA-PAF negative result might be explained by the ablation techniques with discretional circumferential ablation without confirmation of PVI with a circular mapping catheter as well as by the choice of reduction in AF burden on 7-day Holter as a primary endpoint.

RAAFT: Whether such benefits extend to elderly patients with PAF, patients with associated SHD or non-PAF, is still controversial.

Other Paroxysmal AF Ablation Trials

Trial	Year	Type	*N*	AF type	Ablation strategy	Initial time frame
JACC 2006; 48: 2340-2347 (APAF)	2006	Randomized to drug single center	198	PAF	PVI, mitral line and tricuspid line	12 months
Circulation 2008; 118: 2498-2505 (A4)	2008	Randomized to drug	112	PAF	PVI (optional LA lines, CTI, focal)	12 months
NEJM 2016; 374: 2235-2245 (FIRE AND ICE)	2016	Randomized RF vs Cryo, multicenter	762	PAF	PVI	12 months
JACC 2016; 68: 2747-2757	2016	Randomized to hot balloon or drug, multicenter	100	PAF	PVI	12 months

Other Paroxysmal AF Ablation Trials

Trial	Effectiveness endpoint	Ablation success	Drug/Control success	*P* for success	Ablation Cxs	Drug/Control Cxs
JACC 2006; 48: 2340-2347 (APAF)	Freedom from detectable AF, flutter, tachycardia	86%	22%	<0.001	1%	23%
Circulation 2008; 118: 2498-2505 (A4)	Freedom from AF	89	23	<0.0001	5.7%	1.7%
NEJM 2016; 374: 2235-2245 (FIRE AND ICE)	Freedom from detectable AF, flutter, tachycardia	64.1% (RF)	65.4% (cryo)	NS	12.8%	10.2%
JACC 2016; 68: 2747-2757	Freedom from AF	59%	5%	< 0.001	10.4%	4.7%

Other Persistent AF Ablation Trials

Trial	Year	Type	*N*	AF type	Ablation strategy	Initial time frame
NEJM 2006; 354: 934-941	2006	Randomized to RF ablation or to CV and short-term amio	146	PeAF	PVI, roof, mitral line	12 months
EHJ 2014; 35: 501-507 (SARA)	2014	Randomized to drug (2:1 ablation to drug), multicenter	146	PeAF	PVI (optional LA lines, CFAEs)	12 months
NEJM 2015; 372: 1812-1822 STAR AF II	2015	Randomized ablation strategies, multicenter	589	PeAF	PVI alone vs. PVI & CFAEs or PVI & lines	18 months

Other Persistent AF Ablation Trials

Trial	Effectiveness endpoint	Ablation success	Drug/Control success	*P*	Ablation Cxs	Drug/Control Cxs
NEJM 2006; 354: 934-941	No AF or flutter month 12	74%	58%	0.05	1.3%	1.4%
EHJ 2014; 35: 501-507 (SARA)	Freedom from AF/ flutter lasting >24h	70%	44%	0.002	6.1%	4.20%
NEJM 2015; 372: 1812-1822 STAR AF II	Freedom from AF with or without drugs	59% (PVI alone)	49% and 46%	NS	6%	4.3% and 7.6%

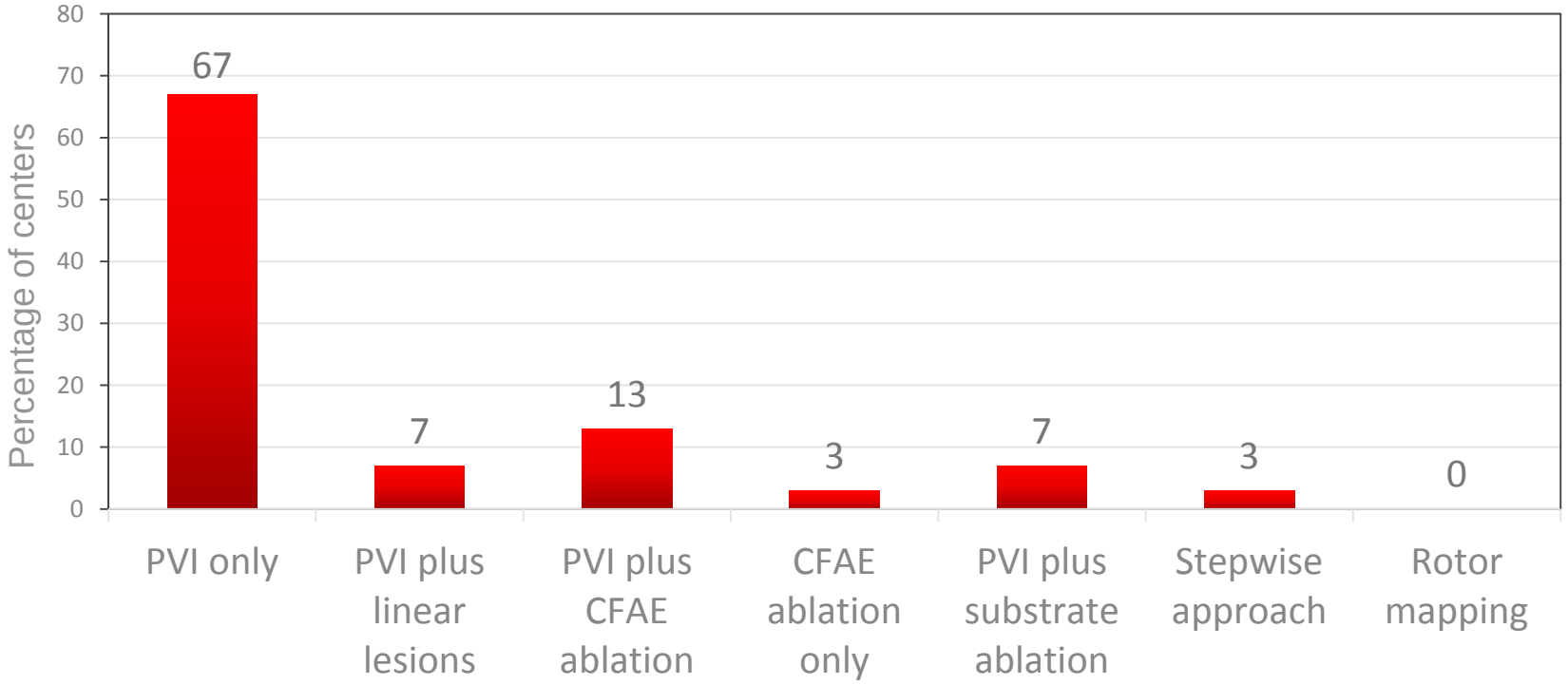
Other Mixed Paroxysmal and Persistent AF Ablation Trials

Trial	Year	Type	*N*	AF type	Ablation strategy	Initial time frame
J Med Assoc Thai 2003; 86 (Suppl 1): S8-S16	2003	Randomized to RF ablation or amiodarone	30	Paroxysmal (70%), Persistent (30%)	PVI, mitral line, CTI, SVC to IVC	12 months
EHJ 2006; 27: 216-221	2006	Randomized to RF ablation or drug, multicenter	137	Paroxysmal (67%), Persistent (33%)	PVI, mitral line, CTI	12 months
JCVEP 2009, 20: 22-28	2009	Randomized to RF ablation or drug, multicenter	70	Paroxysmal (41%), Persistent (59%) and Type 2 DM	PVI, CTI, optional mitral line and roof line	12 months

Other Mixed Paroxysmal and Persistent AF Ablation Trials

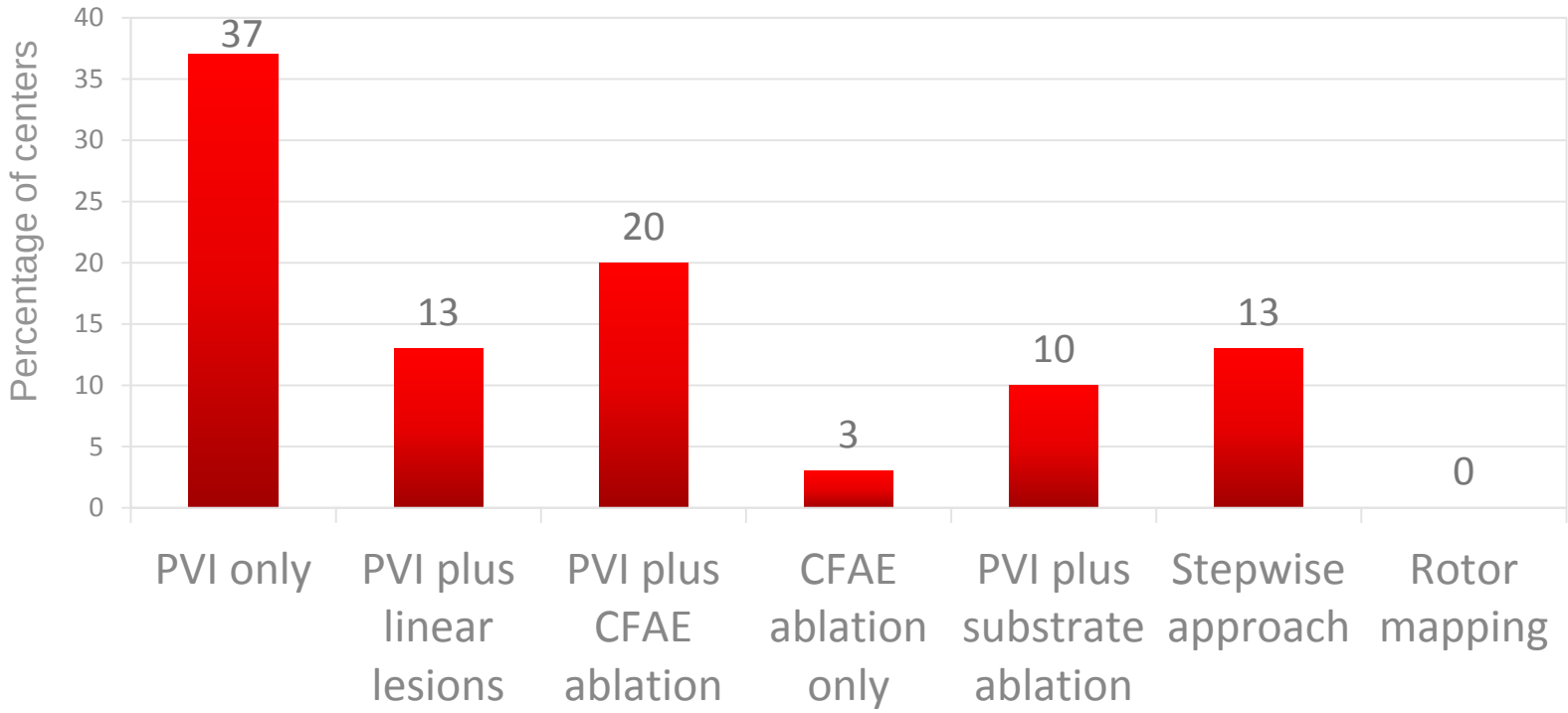
Trial	Effectiveness endpoint	Ablation success	Drug/Control success	P	Ablation Cxs	Drug/Control Cxs
J Med Assoc Thai 2003; 86(Suppl. 1): S8-S16	Freedom from AF	79%	40%	0.018	6.70%	47%
EHJ 2006; 27: 216-221	Freedom from AF, flutter, tachycardia	66%	9%	< 0.001	4.40%	2.90%
JCVEP 2009, 20: 22-28	Freedom from AF and atypical atrial flutter	80%	43%	0.001	2.90%	17%

Ablation Concepts in Persistent AF



Europace 2015;17:1596-1600

Ablation Concepts in Persistent AF



Europace 2015;17:1596-1600

OUTCOMES AND EFFICACY

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Cost-Effectiveness of AF Ablation

OUTCOMES OF AF ABLATION IN POPULATIONS NOT WELL REPRESENTED IN CLINICAL TRIALS

1. Outcomes of Catheter Ablation of Persistent and Long-Standing Persistent AF

PVI remains the cornerstone.

Several new ablation strategies: mapping and ablation of rotational activity, ablation of areas of low voltage, ablation of areas identified on MRI as showing fibrosis, ablation of non-PV triggers, as well as LAA focal ablation, isolation, and/or ligation.

A single-procedure efficacy of stepwise approach was 35% at 1 year, falling to 17% at year 5, and the 5-year outcome after repeated procedures was 63%.

2. Outcomes of AF Ablation in Elderly Patients

Similar success rates with catheter ablation for AF in older patients compared with younger patients, with comparable complication rates. A consistent finding is that older patients are less likely to undergo a second procedure if the index procedure fails to eliminate the arrhythmia.

3. Outcomes of AF Ablation in Patients with CHF and the Impact of Ablation on LV Function

Randomized Trials of AF Ablation in Patients with Heart Failure

Trial	Year	Type	*N*	AF type	Ablation strategy	Initial time frame
NEJM 2008; 359: 1778-1785 (PABA-HF)	2008	Randomized to RF ablation of AVJ abl and BiV pacing	81	PeAF (50%), PAF(50%), EF 27% abl, 29% AVJ	PVI, optional linear abl, and CFAEs	6 months
Heart 2011; 97: 740-747	2011	Randomized to RF ablation or pharmacological rate control	41	Persistent , EF 20% abl, 16% rate control	PVI, roof line, CFAEs	6 months
JACC 2013; 61: 1894-1903	2013	Randomized to RF ablation or pharmacological rate control	52	Persistent AF (100%), EF 22% abl, 25% rate control	PVI, optional linear abl, and CFAEs	12 months
Circ A and E 2014; 7: 31-38	2014	Randomized to RF ablation or pharmacological rate control	50	Persistent AF (100%), EF 32% abl, 34% rate control	PVI, optional linear abl, and CFAEs	6 months

Randomized Trials of AF Ablation in Patients with Heart Failure

Trial	Effectiveness endpoint	Ablation success	Drug/Control success	*P*	Ablation Cxs	Drug/C Cxs
NEJM 2008; 359: 1778-1785 (PABA-HF)	Composite EF, 6 min walk, MLWHF score; freedom from AF (secondary, mult proc, +/- AA drugs)	88% AF free, EF 35% abl, 28% AVJ (*P* <.001), > QOL and 6 min walk increase with abl		< 0.001	14.60%	17.50%
Heart 2011; 97: 740-747	Change in LVEF, sinus rhythm at 6 months (secondary)	50% in NSR, LVEF increase 4.5%	0% in NSR, LVEF increase 2.8%	0.6 (for EF increase)	15%	Not reported
JACC 2013; 61: 1894-1903	Change in peak O_2 consumption (also reported single procedure off drug ablation success)	Peak O_2 consumption increase greater with abl, 72% abl success		0.018	15%	Not reported
Circ A and E 2014; 7: 31-38	Change in LVEF at 6 months, multiple procedure freedom from AF also reported	LVEF 40% with abl, 31% rate control, 81% AF free with abl		0.015	7.70%	

Di Biase L et al. Ablation versus amiodarone for treatment of persistent atrial fibrillation in patients with congestive heart failure and an implanted device: results from the AATAC multicenter randomized trial. Circulation 2016;133(17):1637–1644. CA was more effective than amiodarone in preventing recurrent AF (70% after a mean of 1.4 procedures vs. 34%) and was associated with a lower rate of unplanned hospitalization.

OUTCOMES OF AF ABLATION IN POPULATIONS NOT WELL REPRESENTED IN CLINICAL TRIALS

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3. Outcomes of AF Ablation in Patients with CHF and the Impact of Ablation on LV Function

It is reasonable to use similar indications for AF ablation in selected patients with heart failure as in patients without heart failure.

4. Outcomes of AF Ablation in Patients with Hypertrophic Cardiomyopathy

The risk of procedure-related adverse events was low. Even though the likelihood of recurrence is twofold higher, catheter ablation can be effective in patients with HCM and AF, particularly in patients with PAF and smaller atria.

5. Outcomes of AF Ablation in Young Patients

The largest study on AF ablation in younger patients was a multicenter German registry in which 593 patients aged ≤45 years were compared with 6650 patients aged >45 years. The younger patients had lower rates of complication, shorter hospital stays, and lower rates of AF recurrence and AAD than older patients.

6. Outcomes of AF Ablation in Women

Studies have not shown a significant sex-related difference in outcomes with AF ablation in women compared with men, but complication rates are consistently higher in women.

7. Outcomes of Cryoballoon Ablation

FREEZE-AF (2015): 70.7% in the RF vs. 73.6% in the CB. Complications occurred in CB (12.2% vs 5.0% in RF), which was largely due to 9 transient PN injuries (5.8%) in CB arm.

FIRE AND ICE trial (2016)

CB appears to be associated with a favorable long-term outcome in patients with persistent AF, with arrhythmia-free survival ranging from 56% to 82%. In one nonrandomized study, arrhythmia-free survival off AADs was similar between CB and RF (60% vs 50%).

8. Outcome of Rotational Activity Ablation for AF

"64-pole basket catheter/body-surface high-density mapping/Phase mapping"
The usefulness of ablation of rotational activity as an initial or repeat ablation strategy for persistent and long-standing persistent AF is not well established.

9. Outcomes of Laser Balloon Ablation

The laser balloon is effective in achieving PVI, from 98% to 100%.
The freedom from AF at follow-up ranged from 60% to 88%, which is comparable to the outcome of PVI using RF energy in similar populations.

10. Long-Term Ablation Efficacy

The predictors of late recurrence: persistent AF + comorbid conditions.
Despite the low single-procedure, long-term success rate reported in virtually all of these clinical trials, they also reveal that with the use of repeat AF ablation procedures and/or AAD therapy, much higher rates of freedom from recurrent AF as well as concomitant reductions in AF burden can be achieved.

11. Impact of Catheter Ablation of AF on QOL

Substantial improvements in QOL with ablation; can more accurately reflect ablation efficacy. However, there is currently no general agreement that any of the "AF-specific" QOL instruments are superior to others or to the "general" QOL instruments.

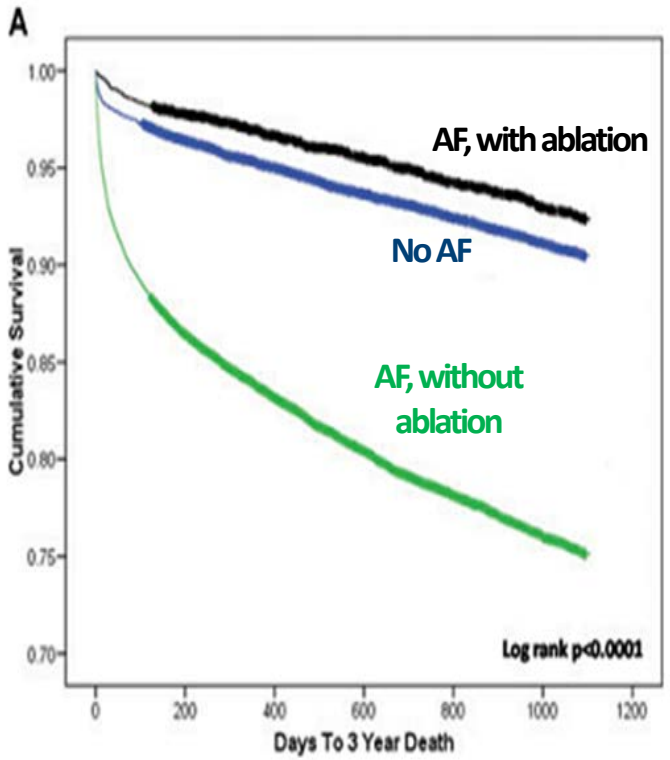
12. Impact of Catheter Ablation of AF on LA Size and Function

The reverse remodeling of LA was more pronounced when SR had been successfully restored. It appears consistent with reverse remodeling due to the decreased burden of AF and scar formation from the ablation procedure. Restoration of SR in patients with persistent AF improves atrial function if SR is maintained. Ablation-related scarring with the risk of causing persistent atrial dysfunction still remains a major concern after extensive ablation for persistent AF.

13. Impact of Catheter Ablation on Stroke Risk

13. Impact of Catheter Ablation on Stroke Risk

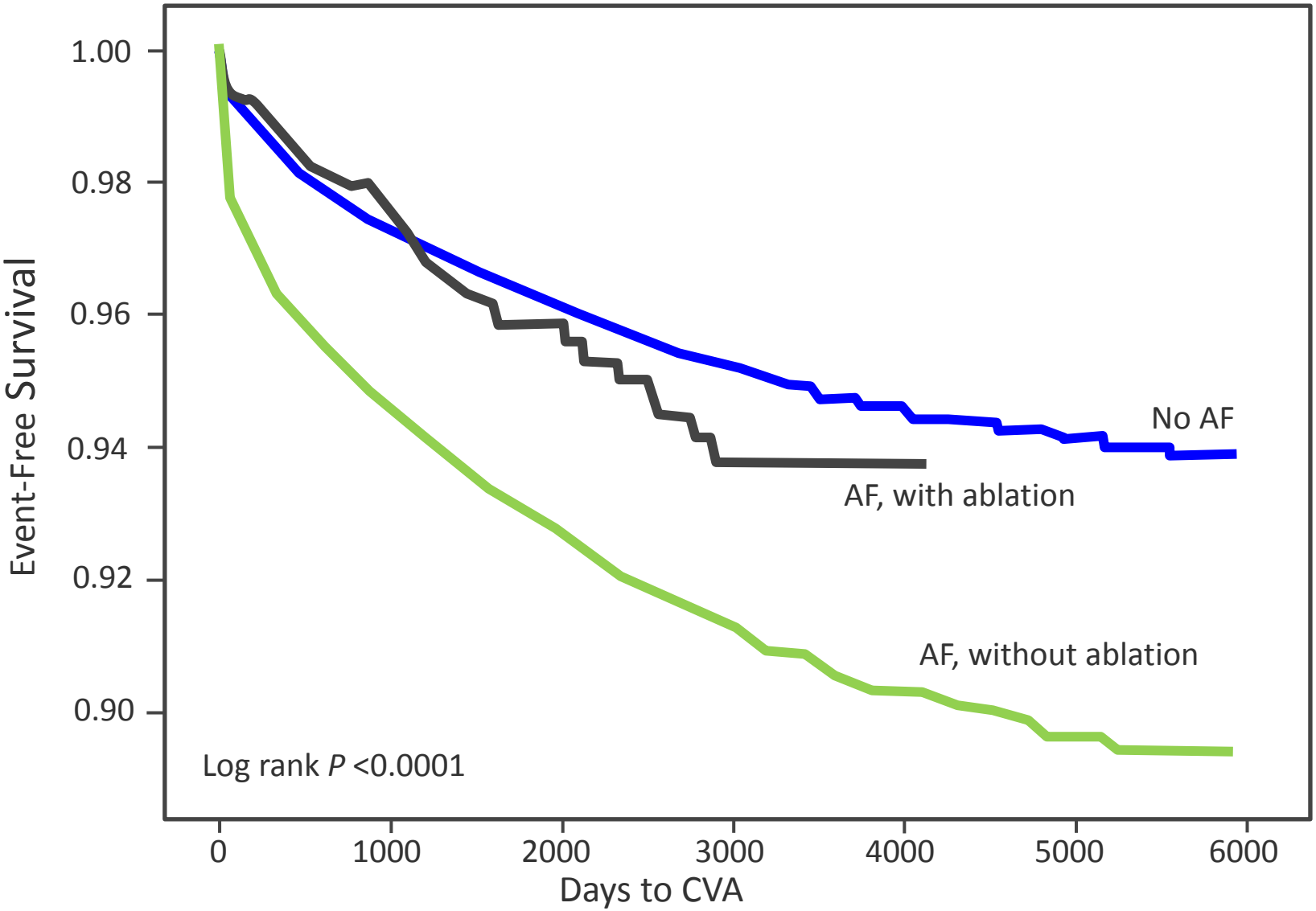
Long-Term Survival Free of Death



J Cardiovasc Electrophysiol 2011;22:839-845

13. Impact of Catheter Ablation on Stroke Risk

Long-Term Survival Free of CVA



Impact of Catheter Ablation on Stroke Risk

To date, there are no RCTs verifying the hypothesis that ablation lowers the long-term incidence of stroke or TIA.

1. The Intermountain Healthcare Database in Utah (4,212 ablated patients)
2. MarketScan Research Database (*n* = 805 in each group)
3. Taiwanese national health insurance claims database (846 ablated patients)
4. Swedish health registries (*n* = 2836 in each group)

Ablation was associated with a lower incidence of ischemic stroke than in nonablated patients.
Ablation-treated patients without AF recurrence had a lower incidence of ischemic strokes and TIAs compared with patients with AF recurrence or medically treated patients.

It is recognized that the retrospective nature of these studies makes them prone to bias.

Therefore, the above findings cannot be viewed as definitive and do not provide sufficient evidence that ablation reduces stroke risk. Instead, they reinforce the hypothesis behind studies such as the CABANA trial or the EAST trial, which will provide more definitive evidence.

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Predictors of Success Following AF Ablation

Cost-Effectiveness of AF Ablation

Predictors of Success Following AF Ablation

Predictors of a poorer outcome, at least in some studies, include

(1) non-PAF and particularly long-term persistent AF
(2) LV dysfunction
(3) sleep apnea and obesity
(4) increased LA size
(5) increased age
(6) hypertension
(7) LA fibrosis as detected by cardiac MRI

Cost-Effectiveness of AF Ablation

Most formal cost-effectiveness studies have not found AF ablation to be cost neutral or cost saving in the short to intermediate term.

"Second-line" therapy in patients with PAF vs. "first-line" setting or in patients with persistent or long-term persistent AF.

AF ablation might only be cost-effective as first-line therapy in younger patients.

COMPLICATIONS

- Overview
- Cardiac Tamponade
- Pulmonary Vein Stenosis
- Atrial Esophageal Fistula, Atrial pericardial Fistula, and Esophageal Hematoma
- Gastric Hypomotility and Periesophageal Vagal Nerve Injury
- Phrenic Nerve Palsy
- Stroke, TIA, and Silent Microemboli
- Air Embolism
- Vascular Complications
- Acute Coronary Artery Occlusion and Stenosis
- Radiation Exposure During Catheter Ablation of AF
- Pericarditis
- Mitral Valve Trauma and Curvilinear Catheter Entrapment
- Mortality Risk with AF Ablation

COMPLICATIONS

Stiff Left Atrial Syndrome

Cough

Increase in Heart Rate and/or Sinus Tachycardia

Definitions of Complications Associated with AF Ablation

Asymptomatic cerebral embolism	Asymptomatic cerebral embolism is defined as an occlusion of a blood vessel in the brain due to an embolus that does not result in any acute clinical symptoms. Silent cerebral embolism is generally detected using a diffusion weighted MRI.
Atrioesophageal fistula	An atrioesophageal fistula is defined as a connection between the atrium and the lumen of the esophagus. Evidence supporting this diagnosis includes documentation of esophageal erosion combined with evidence of a fistulous connection to the atrium, such as air emboli, an embolic event, or direct observation at the time of surgical repair. A CT scan or MRI scan is the most common method of documentation of an atrioesophageal fistula.
Bleeding	Bleeding is defined as a major complication of AF ablation if it requires and/or is treated with transfusion or results in a 20% or greater fall in hematocrit.
Bleeding following cardiac surgery	Excessive bleeding following a surgical AF ablation procedure is defined as bleeding requiring reoperation or ≥2 units of PRBC transfusion within any 24 hours of the first 7 days following the index procedure.
Cardiac perforation	We recommend that cardiac perforation be defined together with cardiac tamponade. See “Cardiac tamponade/perforation.”
Cardiac tamponade	We recommend that cardiac tamponade be defined together with cardiac perforation. See “Cardiac tamponade/perforation.”
Cardiac tamponade/ perforation	Cardiac tamponade/perforation is defined as the development of a significant pericardial effusion during or within 30 days of undergoing an AF ablation procedure. A significant pericardial effusion is one that results in hemodynamic compromise, requires elective or urgent pericardiocentesis, or results in a 1-cm or more pericardial effusion as documented by echocardiography. Cardiac tamponade/perforation should also be classified as “early” or “late” depending on whether it is diagnosed during or following initial discharge from the hospital.

Deep sternal wound infection/mediastinitis following cardiac surgery	Deep sternal wound infection/mediastinitis following cardiac surgery requires one of the following: (1) an organism isolated from culture of mediastinal tissue or fluid; (2) evidence of mediastinitis observed during surgery; (3) one of the following conditions: chest pain, sternal instability, or fever (>38°C), in combination with either purulent discharge from the mediastinum or an organism isolated from blood culture or culture of mediastinal drainage.
Esophageal injury	Esophageal injury is defined as an erosion, ulceration, or perforation of the esophagus. The method of screening for esophageal injury should be specified. Esophageal injury can be a mild complication (erosion or ulceration) or a major complication (perforation).
Gastric motility/pyloric spasm disorders	Gastric motility/pyloric spasm disorder should be considered a major complication of AF ablation when it prolongs or requires hospitalization, requires intervention, or results in late disability, such as weight loss, early satiety, diarrhea, or GI disturbance.
Major complication	A major complication is a complication that results in permanent injury or death, requires intervention for treatment, or prolongs or requires hospitalization for more than 48 hours. Because early recurrences of AF/AFL/AT are to be expected following AF ablation, recurrent AF/AFL/AT within 3 months that requires or prolongs a patient's hospitalization should not be considered to be a major complication of AF ablation.
Mediastinitis	Mediastinitis is defined as inflammation of the mediastinum. Diagnosis requires one of the following: (1) an organism isolated from culture of mediastinal tissue or fluid; (2) evidence of mediastinitis observed during surgery; (3) one of the following conditions: chest pain, sternal instability, or fever (>38°C), in combination with either purulent discharge from the mediastinum or an organism isolated from blood culture or culture of mediastinal drainage.
Myocardial infarction in the context of AF ablation	The universal definition of myocardial infarction cannot be applied in the context of catheter or surgical AF ablation procedures because it relies heavily on cardiac biomarkers (troponin and CPK), which are anticipated to increase in all patients who undergo AF ablation as a result of the ablation of myocardial tissue. Similarly, chest pain and other cardiac symptoms are difficult to interpret in the context of AF ablation both because of the required sedation and anesthesia and also because most patients experience chest pain following the procedure as a result of the associated pericarditis that occurs following catheter ablation. We therefore propose that a myocardial infarction, in the context of catheter or surgical ablation, be defined as the presence of any one of the following criteria: (1) detection of ECG changes indicative of new ischemia (new ST-T wave changes or new LBBB) that persist for more than 1 hour; (2) development of new pathological Q waves on an ECG; (3) imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.

Pericarditis	Pericarditis should be considered a major complication following ablation if it results in an effusion that leads to hemodynamic compromise or requires pericardiocentesis, prolongs hospitalization by more than 48 hours, requires hospitalization, or persists for more than 30 days following the ablation procedure.
Phrenic nerve paralysis	Phrenic nerve paralysis is defined as absent phrenic nerve function as assessed by a sniff test. A phrenic nerve paralysis is considered to be permanent when it is documented to be present 12 months or longer following ablation.
Pulmonary vein stenosis	Pulmonary vein stenosis is defined as a reduction of the diameter of a PV or PV branch. PV stenosis can be categorized as mild <50%, moderate 50%–70%, and severe ≥70% reduction in the diameter of the PV or PV branch. A severe PV stenosis should be considered a major complication of AF ablation.
Serious adverse device effect	A serious adverse device effect is defined as a serious adverse event that is attributed to use of a particular device.
Stiff left atrial syndrome 	Stiff left atrial syndrome is a clinical syndrome defined by the presence of signs of right heart failure in the presence of preserved LV function, pulmonary hypertension (mean PA pressure >25 mm Hg or during exercise >30 mm Hg), and large V waves ≥10 mm Hg or higher) on PCWP or left atrial pressure tracings in the absence of significant mitral valve disease or PV stenosis.
	• No other readily identifiable nonstroke cause for the clinical presentation (e.g., brain tumor, trauma, infection, hypoglycemia, peripheral lesion, pharmacological influences).^ • Confirmation of the diagnosis by at least one of the following: neurology or neurosurgical specialist; neuroimaging procedure (MRI or CT scan or cerebral angiography); lumbar puncture (i.e., spinal fluid analysis diagnostic of intracranial hemorrhage)

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Stroke or TIA postablation	Stroke definitions • Transient ischemic attack: new focal neurological deficit with rapid symptom resolution (usually 1 to 2 hours), always within 24 hours; neuroimaging without tissue injury • Stroke: (diagnosis as above, preferably with positive neuroimaging study); Minor—Modified Rankin score <2 at 30 and 90 days† Major—Modified Rankin score >2 at 30 and 90 days ^Patients with nonfocal global encephalopathy will not be reported as a stroke without unequivocal evidence based on neuroimaging studies. †Modified Rankin score assessments should be made by qualified individuals according to a certification process. If there is discordance between the 30- and 90-day modified Rankin scores, a final determination of major versus minor stroke will be adjudicated by the neurology members of the clinical events committee.
Unanticipated adverse device effect	Unanticipated adverse device effect is defined as complication of an ablation procedure that has not been previously known to be associated with catheter or surgical ablation procedures.
Vagal nerve injury	Vagal nerve injury is defined as injury to the vagal nerve that results in esophageal dysmotility or gastroparesis. Vagal nerve injury is considered to be a major complication if it prolongs hospitalization, requires hospitalization, or results in ongoing symptoms for more than 30 days following an ablation procedure.
Vascular access complication	Vascular access complications include development of a hematoma, an AV fistula, or a pseudoaneurysm. A major vascular complication is defined as one that requires intervention, such as surgical repair or transfusion, prolongs the hospital stay, or requires hospital admission.

AF = atrial fibrillation; CT = computed tomography; MRI = magnetic resonance imaging; PRBC = packed red blood cell; AFL = atrial flutter; AT = atrial tachycardia; CPK = creatine phosphokinase; ECG = electrocardiogram; LBBB = left bundle branch block.

Incidence, Prevention, Diagnosis, and Treatment of Selected Complications of AF Ablation

Complication	Incidence	Selected prevention techniques	Diagnostic testing	Selected treatment options
Air embolism	<1%	Sheath management	Nothing or cardiac catheterization	Supportive care with fluid, oxygen, head down tilt, hyperbaric oxygen
Asymptomatic cerebral emboli (ACE)	2% to 15%	Anticoagulation, catheter and sheath management, TEE	Brain MRI	None
Atrial esophageal fistula	0.02% to 0.11%	Reduce power, force, and RF time on posterior wall, monitor esophageal temp, use PPIs; avoid energy delivery over esophagus	CT scan of chest, MRI; avoid endoscopy with air insufflation	Surgical repair
Cardiac tamponade	0.2% to 5%	Cather manipulation, transseptal technique, reduce power, force, and RF time	Echocardiography	Pericardiocentesis or surgical drainage
Coronary artery stenosis/occlusion	<0.1%	Avoid high-power energy delivery near coronary arteries	Cardiac catheterization	PTCA
Death	<0.1% to 0.4%	Meticulous performance of procedure, attentive postprocedure care	NA	NA
Gastric hypomotility	0% to 17%	Reduce power, force, and RF time on posterior wall	Endoscopy, barium swallow, gastric emptying study	Metoclopramide, possibly intravenous erythromycin

Cardiac Tamponade

The incidence of pericardial complications increased from 0.74% in 2000 to 2.24% in 2010.

Causes:

(1) Misdirected transseptal punctures
(2) Direct mechanical trauma
(3) Overheating during RF energy delivery

Excessive power, temperatures, and CF might also be contributory.

Re-Circuit Study

Comparison of uninterrupted dabigatran vs. uninterrupted warfarin: Lower major bleeding events during and up to 8 weeks postablation (*n* = 635) dabigatran than with warfarin (1.6% vs. 6.9%; RR reduction 77%).

Recent introduction of CF catheters would reduce the rate of tamponade—this has not been confirmed in clinical trials.

Incidence, Prevention, Diagnosis, and Treatment of Selected Complications of AF Ablation

Complication	Incidence	Selected prevention techniques	Diagnostic test	Selected treatment options
Mitral valve entrapment	<0.1%	Avoid circular catheter placement near or across mitral valve; clockwise torque on catheter	Echocardiography	Gentle catheter manipulation, surgical extraction
Pericarditis	0% to 50%	None proven	Clinical history, ECG, sedimentation rate, echocardiogram	NSAID, colchicine, steroids
Permanent phrenic nerve paralysis	0% to 0.4%			
Pulmonary vein stenosis	<1%			
Radiation injury	<0.1%	Minimize fluoroscopy exposure, especially in obese and repeat ablation patients, X-ray equipment	None	Supportive care, rarely skin graft
Stiff left atrial syndrome	<1.5%	Limit extent of left atrial ablation	Echocardiography, cardiac catheterization	Diuretics

NEW

NEW

Permanent PN palsy resulting from CB ablation is far less common, with an incidence of 0.3% in the recently completed FIRE AND ICE trial. In the HeartLight study of the laser balloon, PN injury occurred in 3.6% of the patients and was more common than with RF ablation. Persistent PN paralysis at 1 year occurred in 1.8% of the patients.

Complication	Incidence	Selected prevention techniques	Diagnostic test	Selected treatment options
Stroke and TIA	0% to 2%	Pre-, post-, and intraprocedure anticoagulation, catheter and sheath management, TEE	Head CT or MRI, cerebral angiography	Thrombolytic therapy, angioplasty
Vascular complications	0.2% to 1.5%	Vascular access techniques, US guided access, anticoagulation management	Vascular ultrasound CT scan	Conservative treatment, surgical repair, transfusion

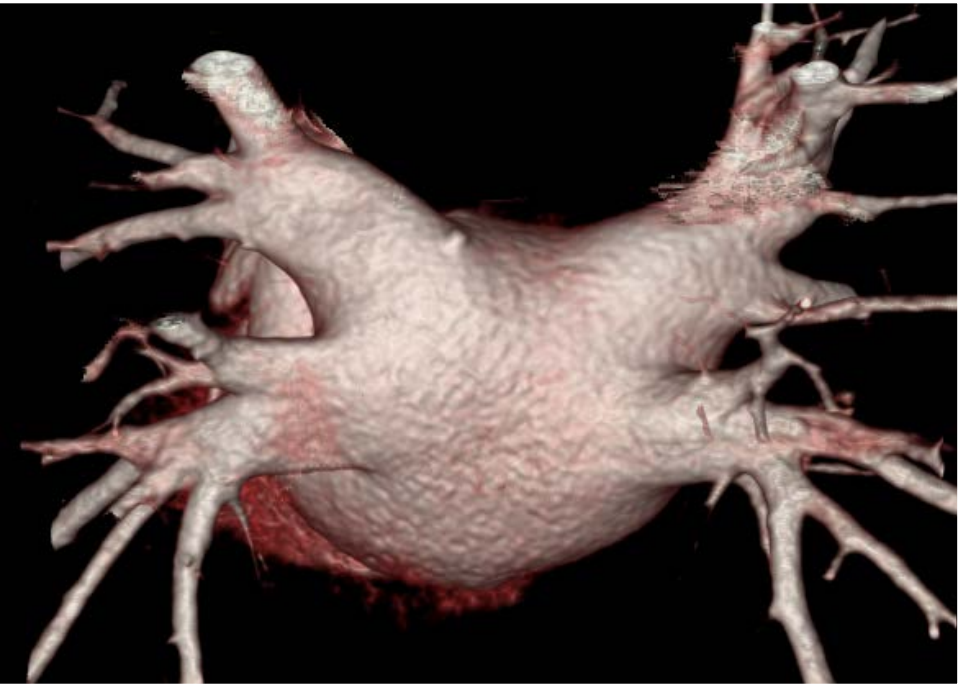
The overall incidence of complications was 6.29%—increasing from 5.3% in 2000 to 7.5% in 2010. The in-hospital mortality was 0.46%.

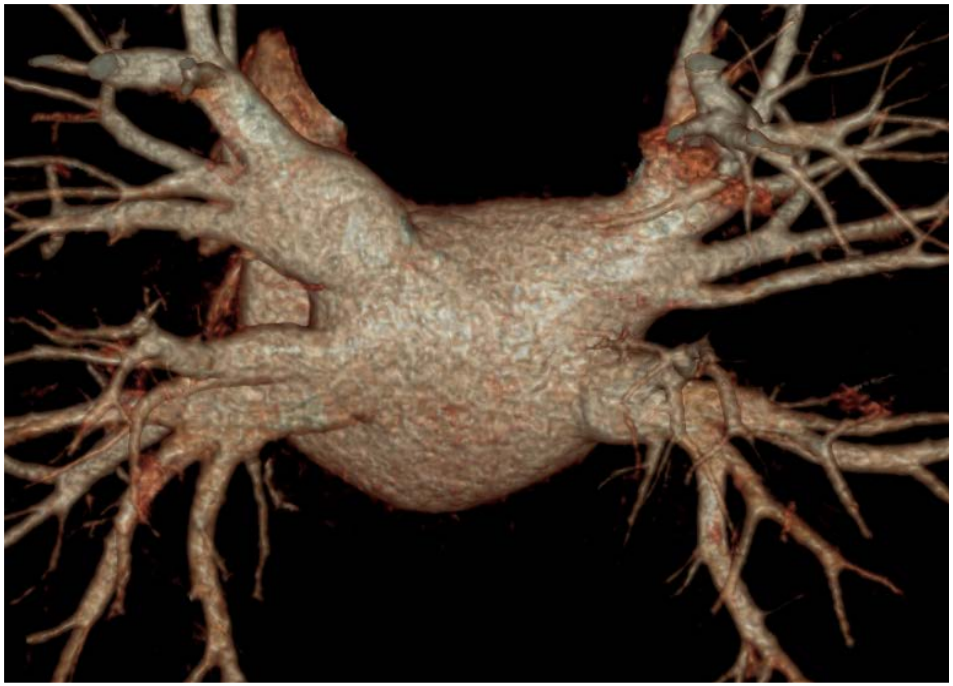
Not surprisingly, lower operator and hospital procedure volume was an important predictor of complications.

These data are a stark reminder that our efforts to eliminate complications associated with AF ablation are incomplete and there is more work to do.

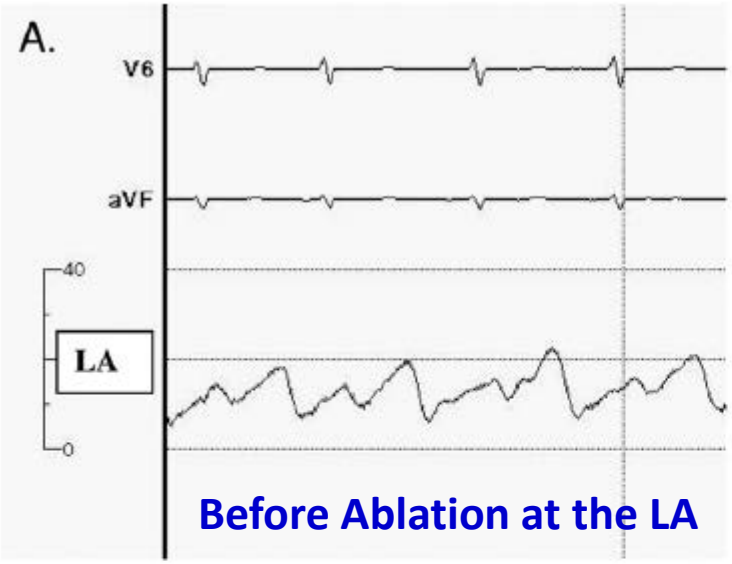
M/40, PeAF

	De Novo	Redo
LA Size:	44 mm	42 mm
LA volume:	108 ml	78 ml

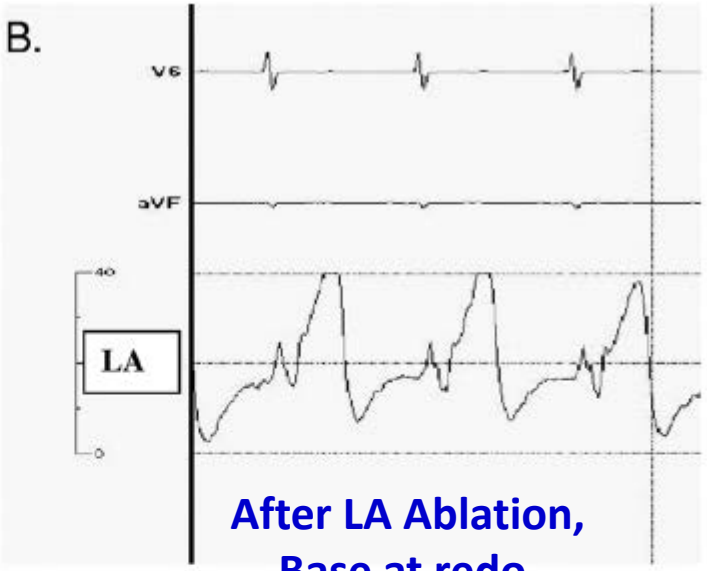




“Stiff LA Syndrome” After LA Ablation

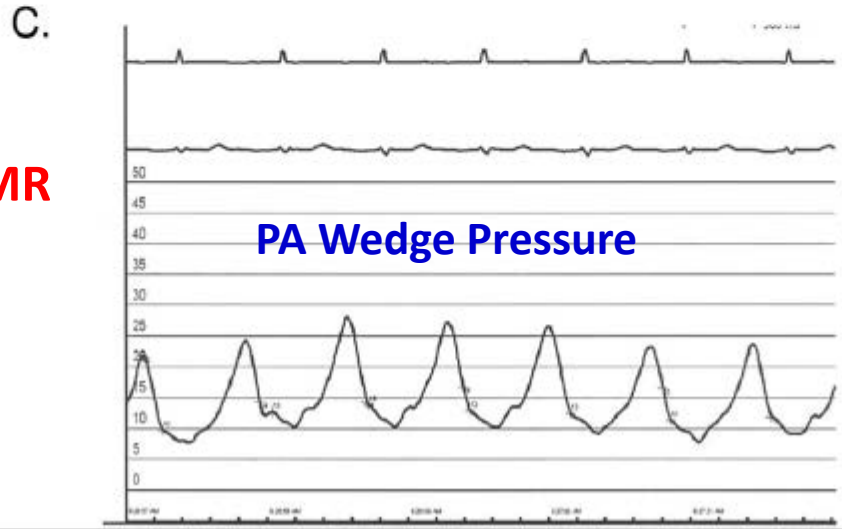


Before Ablation at the LA



After LA Ablation,
Base at redo

*No significant MR



PA Wedge Pressure

Pilote L, Hüttner I, Marpole D, Sniderman A.
Stiff left atrial syndrome. Can J Cardiol 1988;4:255–257

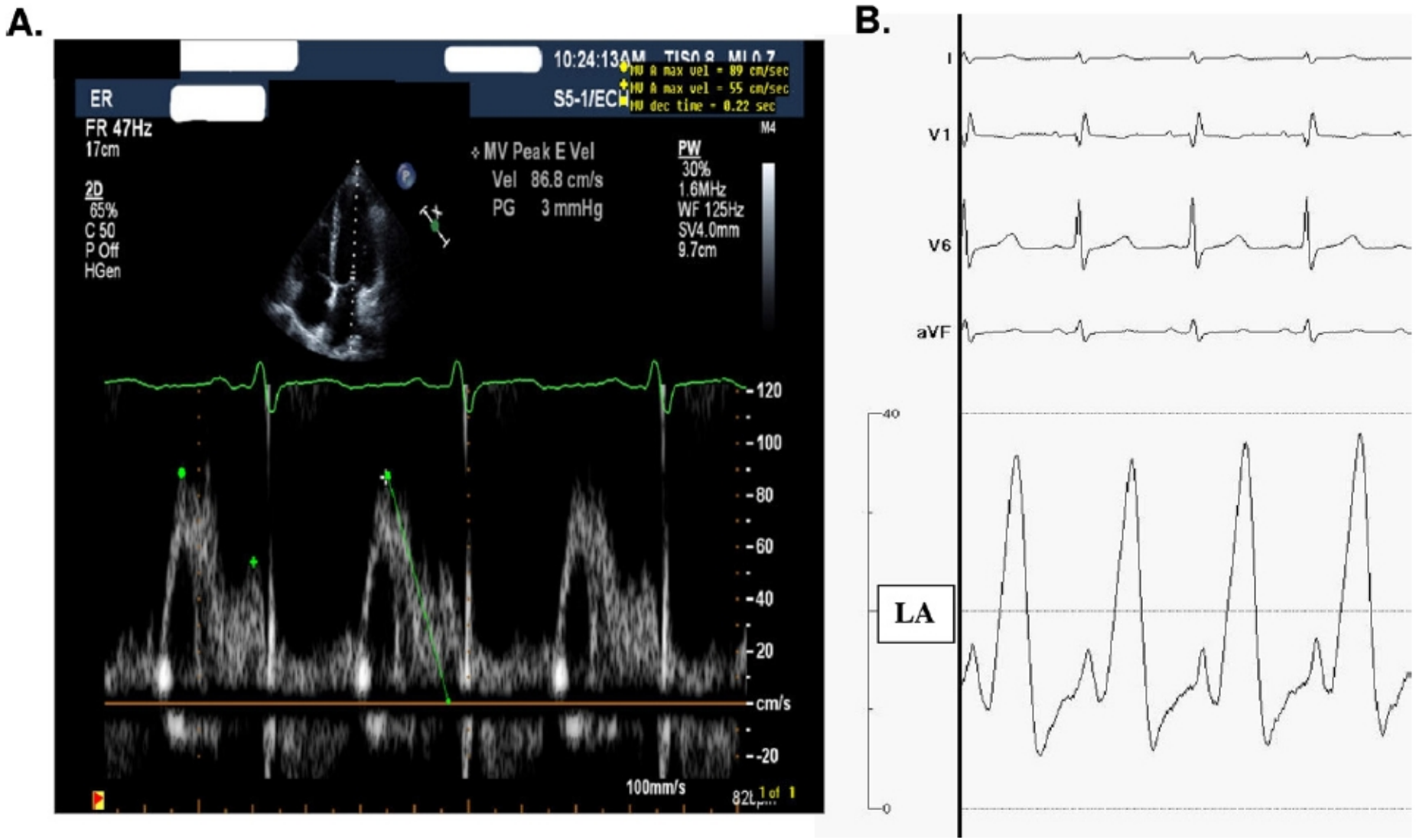
Mehta S, Charbonneau F, Fitchett DH, Marpole DG, Patton R, Sniderman AD.
The clinical consequences of a stiff left atrium.
Am Heart J 1991;122:1184–1191

Gibson DN, Di Biase L, Mohanty P, Patel JD, Bai R, Sanchez J, Burkhardt JD, Heywood JT, Johnson AD, Rubenson DS, Horton R, Gallinghouse GJ, Beheiry S, Curtis GP, Cohen DN, Lee MY, Smith MR, Gopinath D, Lewis WR, Natale A.

Stiff left atrial syndrome after catheter ablation for atrial fibrillation: clinical characterization, prevalence, and predictors.

Heart Rhythm 2011;8:1364–1371

Atrial Diastolic Dysfunction with Preserved Atrial Systole

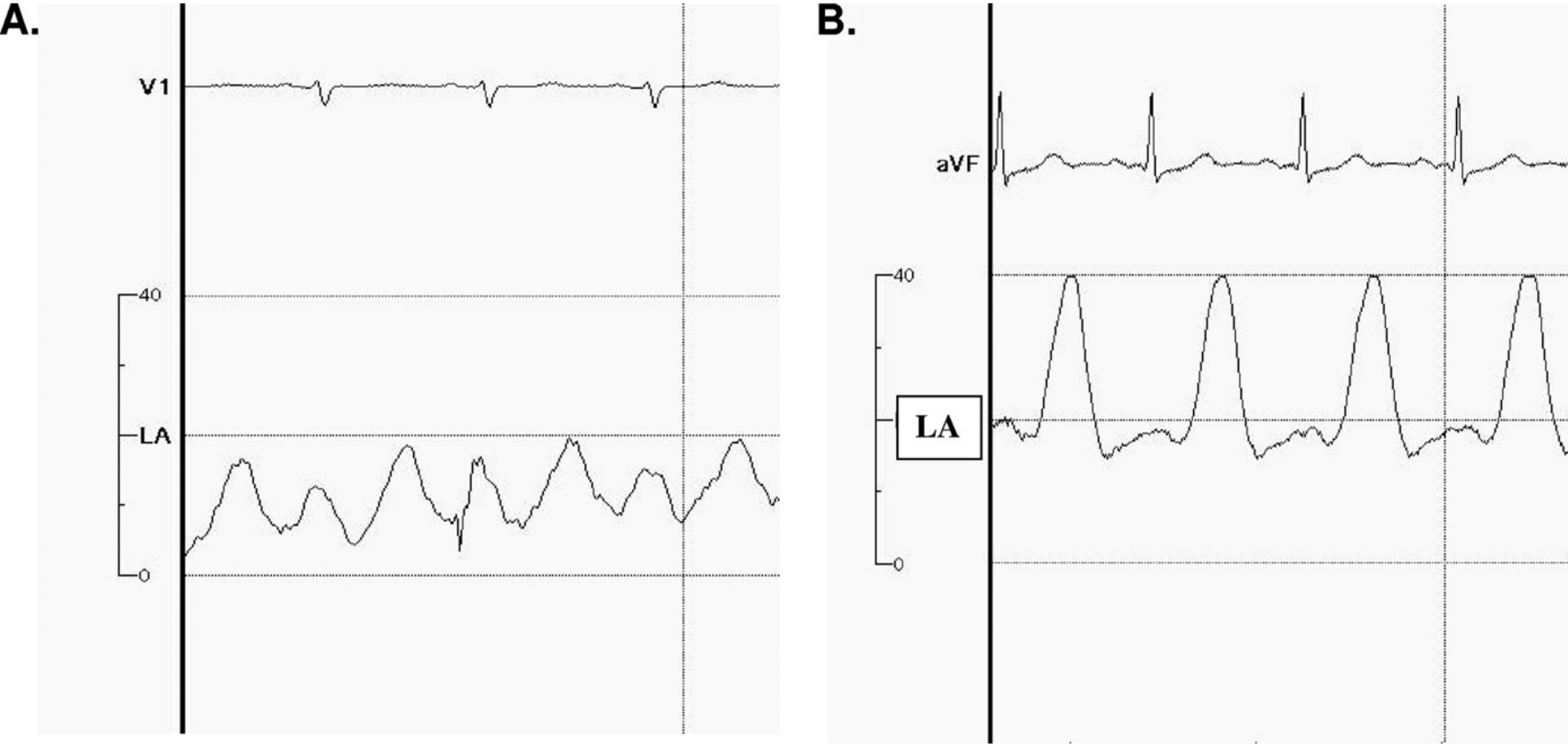


Heart Rhythm 2011;8:1364–1371

Atrial Diastolic Dysfunction Along with Systolic Dysfunction

Before Ablation at the LA

After LA Ablation,
Base at redo



Heart Rhythm 2011;8:1364–1371

Table 3 Univariate analysis comparing patients with and without PH

	No PH postablation (n = 1,361, 98.6%)	Patients with PH (n = 19, 1.4%)	*P*-value
Age, year			.850
Male			.900
AF type			
PAF			.612
Persistent			.509
Longstanding			1.000
AF duration, mo			.895
BMI			.970
Hypertension			1.000
Coronary artery			.554
LA scarring, n			<.001
Dyslipidemia			.646
Diabetes			.026
OSA			.006
Redo			1.000
LA appendage is			.749
Complex fraction			.212
Coronary sinus is			.141
Baseline LA size,			.036
Baseline LVEF, %			.809
LV diastolic dysfunction	268 (20)	3 (16)	1.000
A wave, cm/s	58 ± 18	53 ± 22	.462
A wave VTI, s	7.6 ± 3.6	6.8 ± 2.4	.163
Fluoroscopy time, minutes	75 ± 18	66 ± 22	.146
Procedure time, minutes	168 ± 57	170 ± 53	.791
RF time, minutes	81 ± 38	74 ± 13	.518

Table 4 Predictors of pulmonary arterial hypertension (n = 1,058)

	Odds ratio	95% CI	*P*-value
Diabetes mellitus	9.49	2.0–44.2	.004
OSA	6.23	1.6–24.4	.009
LA size ≤45 mm	6.13	1.2–32.5	.033
Mean LA pressure	1.14	1.1–1.4	.025
Atrial scarring (severe)	4.4	1.1–22.2	.046

Heart Rhythm 2011;8:1364–1371

Stiff LA syndrome may be unrecognized if the clinician does not suspect it.

Predictors

1) Small LA
2) OSA
3) DM
4) Atrial scarring (>60%)
5) High LA pressure

Heart Rhythm 2011;8:1364–1371

Stiff LA syndrome

Fortunately responds well to diuretics, furosemide.

There was a case who was refractory to diuretics, but responded to “sildenafil.”

Wong GR et al. Novel use of sildenafil in the management of pulmonary hypertension due to post-catheter ablation ‘stiff left atrial syndrome.’ Int J Cardiol 2015;181:55–56.

Cough

It might be a sign of underlying PV stenosis, PN injury, direct bronchial injury, stiff LA syndrome, gastroesophageal reflux, pulmonary embolism, pericarditis, or other iatrogenic respiratory complications such as ventilator-associated pneumonia or postprocedure aspiration pneumonia.

Cough following CBA is more frequent.

1. CBA-induced PN injury (up to 11%)
2. Direct upper airway irritation during CBA
3. Direct and acute bronchial inflammation, bleeding, and mucosal injury
4. Ice formation within the left main-stem bronchus

Increase in Heart Rate and/or Sinus Tachycardia

This phenomenon is related to shifts in autonomic tone following ablation and is predictive of ablation success.

This shift in autonomic tone results from ablation of GP that are commonly located near the PV antra, and these signs have been associated with improved procedural outcomes.

Although the increase in heart rate and reduction in HRV after ablation typically follow a transient time course, with resolution within 3 months, some studies have shown that the long-term persistence of these autonomic changes is associated with improved clinical outcomes.

FOLLOW-UP CONSIDERATIONS
OUTCOMES AND EFFICACY
COMPLICATIONS

Up-to-date review with a large number of recently published randomized trials, non-RCT, and consensus of writing group.

Provide data and evidence with well-organized tables.

Many unanswered questions in AF ablation are described for future investigation and consensus statement.

Hugh Calkins, MD (Chair)

Gerhard Hindricks, MD (Vice-Chair); Riccardo Cappato, MD (Vice-Chair); Young-Hoon Kim, MD, PhD (Vice-Chair); Eduardo B. Saad, MD, PhD (Vice-Chair)

Section Chairs

Definitions, Mechanisms, and Rationale for AF Ablation: **Shih-Ann Chen, MD, Taiwan**
Modifiable Risk Factors for AF and Impact on Ablation: **Jonathan M. Kalman, MBBS, PhD, Australia**
Indications: **Claudio Tondo, MD, PhD, Italy**
Strategies, Techniques, and Endpoints: **Karl Heinz Kuck, MD, PhD, Germany**
Technology and Tools: **Andrea Natale, MD, USA**
Technical Aspects of Ablation to Maximize Safety and Anticoagulation: **David E. Haines, MD, USA**
Follow-up Considerations: **Francis E. Marchlinski, MD, USA**
Outcomes and Efficacy: **Matthew R. Reynolds, MD, MSc, USA**
Complications: **D. Wyn Davies, MD, United Kingdom**
Training Requirements: **Bruce D. Lindsay, MD, USA**
Surgical and Hybrid AF Ablation: **James R. Edgerton, MD, USA**
Clinical Trial Design: **Atul Verma, MD, Canada**

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Definitions for Use When Reporting Outcomes of AF Ablation and in Designing Clinical Trials of Catheter or Surgical Ablation of AF

Acute procedural success (pulmonary vein isolation)	Acute procedural success is defined as electrical isolation of all pulmonary veins. A minimal assessment of electrical isolation of the PVs should consist of an assessment of entrance block. If other methods are used to assess PVI, including exit block and/or the use of provocative agents such as adenosine or isoproterenol, they should be prespecified. Furthermore, it is recommended that the wait time used to screen for early recurrence of PV conduction once initial electrical isolation is documented be specified in all prospective clinical trials.
Acute procedural success (not related by pulmonary vein isolation)	Typically, this would apply to substrate ablation performed in addition to PVI for persistent AF. Although some have proposed AF termination as a surrogate for acute procedural success, its relationship to long-term success is controversial. Complete elimination of the additional substrate (localized rotational activation, scar region, non-PV trigger, or other target) and/or demonstration of bidirectional conduction block across a linear ablation lesion would typically be considered the appropriate endpoint.
One-year success*	One-year success is defined as freedom from AF/AFL/AT after removal from antiarrhythmic drug therapy as assessed from the end of the 3month blanking period to 12 months following the ablation procedure. Because cavotricuspid isthmus-dependent atrial flutter is easily treated with cavotricuspid isthmus ablation and is not an iatrogenic arrhythmia following a left atrial ablation procedure for AF, it is reasonable for clinical trials to choose to prespecify that occurrence of isthmus-dependent atrial flutter, if confirmed by entrainment maneuvers during electrophysiology testing, should not be considered an ablation failure or primary effectiveness endpoint.

Alternative one-year success	Although the one-year success definition provided above remains the recommended end point that should be reported in all AF ablation trials, and the endpoint for which the objective performance criteria listed below were developed, the Task Force recognizes that alternative definitions for success can be used if the main goal of therapy in the study is to relieve AF-related symptoms and to improve patient quality of life. In particular, it is appropriate for clinical trials to define success as freedom from only symptomatic AF/AFL/AT after removal from antiarrhythmic drug therapy as assessed from the end of the 3-month blanking period to 12 months following the ablation procedure if the main goal of therapy in the study is to relieve AF-related symptoms and to improve patient quality of life. However, because symptoms of AF can resolve over time, and because studies have shown that asymptomatic AF represents a greater proportion of all AF postablation than prior to ablation, clinical trials need to continue to report freedom from both symptomatic and asymptomatic AF even if this alternative one year success definition is used as the primary trial endpoint.
Clinical/partial success*	It is reasonable for clinical trials to define and incorporate one or more secondary definitions of success that can be referred to as “clinical success” or “partial success.” If these alternative definitions of success are included, they should be defined prospectively. In prior Consensus Documents the Task Force has proposed that clinical/partial success be defined as a “75% or greater reduction in the number of AF episodes, the duration of AF episodes, or the % time a patient is in AF as assessed with a device capable of measuring AF burden in the presence or absence of previously ineffective antiarrhythmic drug therapy.” Because there is no firm scientific basis for selecting the cutoff of 75% rather than a different cutoff, this prior recommendation is provided only as an example of what future clinical trials may choose to use as a definition of clinical/partial success.
Long-term success*	Long-term success is defined as freedom from AF/AFL/AT recurrences following the 3-month blanking period through a minimum of 36-month follow-up from the date of the ablation procedure in the absence of Class I and III antiarrhythmic drug therapy.

*When reporting outcomes of AF ablation, the development of atrial tachycardia or atrial flutter should be included in the broad definition of recurrence following AF ablation. All studies should report freedom from AF, atrial tachycardia, and atrial flutter. These endpoints can also be reported separately. All studies should also clearly specify the type and frequency of ECG monitoring as well as the degree of compliance with the prespecified monitoring protocol.

Recurrent AF/AFL/AT	Recurrent AF/AFL/AT is defined as AF/AFL/AT of at least 30 seconds' duration that is documented by an ECG or device recording system and occurs following catheter ablation. Recurrent AF/AFL/AT may occur within or following the post ablation blanking period. Recurrent AF/AFL/AT that occurs within the postablation blanking period is not considered a failure of AF ablation.
Early recurrence of AF/AFL/AT	Early recurrence of AF/AFL/AT is defined as a recurrence of atrial fibrillation within three months of ablation. Episodes of atrial tachycardia or atrial flutter should also be classified as a "recurrence." These are not counted toward the success rate if a blanking period is specified.
Recurrence of AF/AFL/AT	Recurrence of AF/AFL/AT postablation is defined as a recurrence of atrial fibrillation more than 3 months following AF ablation. Episodes of atrial tachycardia or atrial flutter should also be classified as a "recurrence."
Late recurrence of AF/AFL/AT	Late recurrence of AF/AFL/AT is defined as a recurrence of atrial fibrillation 12 months or more after AF ablation. Episodes of atrial tachycardia or atrial flutter should also be classified as a "recurrence."
Blanking period	A blanking period of three months should be employed after ablation when reporting efficacy outcomes. Thus, early recurrences of AF/AFL/AT within the first 3 months should not be classified as treatment failure. If a blanking period of less than 3 months is chosen, it should be prespecified and included in the Methods section.
Stroke screening	A risk-based approach to determine the level of postablation stroke screening in clinical trials is recommended by the Task Force. For ablation devices with a lower risk of stroke and for which a stroke signal has not been reported, a minimum standardized neurological assessment of stroke should be conducted by a physician at baseline and at hospital discharge or 24 hours after the procedure, whichever is later. If this neurological assessment demonstrates new abnormal findings, the patient should have a formal neurological consult and examination with appropriate imaging (i.e., DW-MRI), used to confirm any suspected diagnosis of stroke. For devices in which a higher risk of stroke is suspected or revealed in prior trials, a formal neurological examination by a neurologist at discharge or 24 hours after the procedure, whichever is later, is recommended. Appropriate imaging should be obtained if this evaluation reveals a new neurological finding. In some studies in which delayed stroke is a concern, repeat neurological screening at 30 days postablation might be appropriate.

Detectable AF/AFL/AT	Detectable AF is defined as AF/AFL/AT of at least 30 seconds' duration when assessed with ECG monitoring. If other monitoring systems are used, including implantable pacemakers, implantable defibrillators, and subcutaneous ECG monitoring devices, the definition of detectable AF needs to be prespecified in the clinical trial based on the sensitivity and specificity of AF detection with the particular device. We recommend that episodes of atrial flutter and atrial tachycardia be included within the broader definition of a detectable AF/AFL/AT episode.
AF/AFL/AT burden	It is reasonable for clinical trials to incorporate AF/AFL/AT burden as a secondary endpoint in a clinical trial of AF ablation. In stating this it is recognized that there are no conclusive data that have validated a rate of AF burden reduction as a predictor of patient benefit (i.e., reduction in mortality and major morbidities such as stroke, CHF, QOL, or hospitalization). If AF burden is included, it is important to predefine and standardize the monitoring technique that will be used to measure AF burden. Available monitoring techniques have been discussed in this document. Should AF burden be selected as an endpoint in a clinical trial, the chosen monitoring technique should be employed at least a month prior to ablation to establish a baseline burden of AF.
Entrance block	Entrance block is defined as the absence, or if present, the dissociation, of electrical activity within the PV antrum. Entrance block is most commonly evaluated using a circular multielectrode mapping catheter positioned at the PV antrum. Entrance block can also be assessed using detailed point-by-point mapping of the PV antrum guided by an electroanatomical mapping system. The particular method used to assess entrance block should be specified in all clinical trials. Entrance block of the left PVs should be assessed during distal coronary sinus or left atrial appendage pacing in order to distinguish far-field atrial potentials from PV potentials. It is recommended that reassessment of entrance block be performed a minimum of 20 minutes after initial establishment of PV isolation.
Procedural endpoints for AF ablation strategies not targeting the PVs	Procedural endpoints for AF ablation strategies not targeting the PVs: The acute procedural endpoints for ablation strategies not targeting the PVs vary depending on the specific ablation strategy and tool. It is important that they be prespecified in all clinical trials. For example, if a linear ablation strategy is used, documentation of bidirectional block across the ablation line must be shown. For ablation of CFAEs, rotational activity, or non-PV triggers, the acute endpoint should at a minimum be elimination of CFAEs, rotational activity, or non-PV triggers. Demonstration of AF slowing or termination is an appropriate procedural endpoint, but it is not required as a procedural endpoint for AF ablation strategies not targeting the PVs.

Esophageal temperature monitoring	Esophageal temperature monitoring should be performed in all clinical trials of AF ablation. At a minimum, a single thermocouple should be used. The location of the probe should be adjusted during the procedure to reflect the location of energy delivery. Although this document does not provide formal recommendations regarding the specific temperature or temperature change at which energy delivery should be terminated, the Task Force does recommend that all trials prespecify temperature guidelines for termination of energy delivery.
Enrolled subject	An enrolled subject is defined as a subject who has signed written informed consent to participate in the trial in question.
Exit block	Exit block is defined as the inability to capture the atrium during pacing at multiple sites within the PV antrum. Local capture of musculature within the pulmonary veins and/or antrum must be documented to be present to make this assessment. Exit block is demonstrated by a dissociated spontaneous pulmonary vein rhythm.
Nonablative strategies	The optimal nonablative therapy for patients with persistent and long-standing persistent AF who are randomized to the control arm of an AF ablation trial is a trial of a new Class 1 or 3 antiarrhythmic agent or a higher dose of a previously failed antiarrhythmic agent. For patients with persistent or long-standing persistent AF, performance of a direct-current cardioversion while taking the new or dose adjusted antiarrhythmic agent should be performed, if restoration of sinus rhythm is not achieved following initiation and/or dose adjustment of antiarrhythmic drug therapy. Failure of pharmacological cardioversion alone is not adequate to declare this pharmacological strategy unsuccessful.
Noninducibility of atrial fibrillation	Noninducibility of atrial fibrillation is defined as the inability to induce atrial fibrillation with a standardized prespecified pharmacological or electrical stimulation protocol. The stimulation protocol should be prespecified in the specific clinical trial. Common stimulation approaches include a high-dose isoproterenol infusion protocol or repeated atrial burst pacing at progressively more rapid rates.
Patient populations for inclusion in clinical trials	It is considered optimal for clinical trials to enroll patients with only one type of AF: paroxysmal, persistent, or long-standing persistent. If more than one type of AF patient is enrolled, the results of the trial should also be reported separately for each of the AF types. It is recognized that “early persistent” AF responds to AF ablation to a similar degree as patients with paroxysmal AF and that the response of patients with “late persistent AF” is more similar to that in those with long-standing persistent AF.

Therapy consolidation period	Following a 3-month blanking period, it is reasonable for clinical trials to incorporate an additional 1- to 3-month therapy consolidation period. During this time, adjustment of antiarrhythmic medications and/or cardioversion can be performed. Should a consolidation period be incorporated into a clinical trial design, the minimum follow-up duration should be 9 months following the therapy consolidation period. Performance of a repeat ablation procedure during the blanking or therapy consolidation period would "reset" the endpoint of the study and trigger a new 3-month blanking period. Incorporation of a therapy consolidation period can be especially appropriate for clinical trials evaluating the efficacy of AF ablation for persistent or long-standing persistent AF. The challenge of this approach is that it prolongs the overall study duration. Because of this concern regarding overall study duration, we suggest that the therapy consolidation period be no more than 3 months in duration following the 3-month blanking period.
Recommendations regarding repeat ablation procedures	It is recommended that all clinical trials report the single procedure efficacy of catheter ablation. Success is defined as freedom from symptomatic or asymptomatic AF/AFL/AT of 30 seconds or longer at 12 months postablation. Recurrences of AF/AFL/AT during the first 3-month blanking period post-AF ablation are not considered a failure. Performance of a repeat ablation procedure at any point after the initial ablation procedure should be considered a failure of a single procedure strategy. It is acceptable for a clinical trial to choose to prespecify and use a multiprocedure success rate as the primary endpoint of a clinical trial. When a multiprocedure success is selected as the primary endpoint, efficacy should be defined as freedom from AF/flutter or tachycardia at 12 months after the final ablation procedure. In the case of multiple procedures, repeat ablation procedures can be performed at any time following the initial ablation procedure. All ablation procedures are subject to a 3-month post blanking window, and all ablation trials should report efficacy at 12 months after the final ablation procedure.
Cardioversion definitions	
Failed electrical cardioversion	Failed electrical cardioversion is defined as the inability to restore sinus rhythm for 30 seconds or longer following electrical cardioversion.
Successful electrical cardioversion	Successful electrical cardioversion is defined as the ability to restore sinus rhythm for at least 30 seconds following cardioversion.

Immediate AF recurrence postcardioversion	Immediate AF recurrence postcardioversion is defined as a recurrence of AF within 24 hours following cardioversion. The most common time for an immediate recurrence is within 30–60 minutes postcardioversion.
Early AF recurrence postcardioversion	Early AF recurrence postcardioversion is defined as a recurrence of AF within 30 days of a successful cardioversion.
Late AF recurrence postcardioversion	Late AF recurrence postcardioversion is defined as recurrence of AF more than 30 days following a successful cardioversion.
Surgical ablation definitions	
Hybrid AF surgical ablation procedure	Hybrid AF surgical ablation procedure is defined as a joint AF ablation procedure performed by electrophysiologists and cardiac surgeons either as part of a single "joint" procedure or performed as two preplanned separate ablation procedures separated by no more than 6 months.
Surgical Maze ablation procedure	Surgical Maze ablation procedure is defined as a surgical ablation procedure for AF that includes, at a minimum, the following components: (1) line from SVC to IVC; (2) line from IVC to the tricuspid valve; (3) isolation of the PVs; (4) isolation of the posterior left atrium; (5) line from MV to the PVs; (6) management of the LA appendage.
Stand-alone surgical AF ablation	A surgical AF ablation procedure during which other cardiac surgical procedures are not performed such as CABG, valve replacement, or valve repair.
Nomenclature for types of surgical AF ablation procedures	We recommend that the term "Maze" procedure is appropriately used only to refer to the biatrial lesion set of the Cox-Maze operation. It requires ablation of the RA and LA isthmuses. Less extensive lesion sets should not be referred to as a "Maze" procedure, but rather as a surgical AF ablation procedure. In general, surgical ablation procedures for AF can be grouped into three different groups: (1) a full biatrial Cox-Maze procedure; (2) PVI alone; and (3) PVI combined with left atrial lesion sets.
Hybrid epicardial and endocardial AF ablation	This term refers to a combined AF ablation procedure involving an off-pump minimally invasive surgical AF ablation as well as a catheter-based AF ablation procedure designed to complement the surgical lesion set. Hybrid ablation procedures may be performed in a single-procedure setting in a hybrid operating room or a cardiac catheterization laboratory environment, or it can be staged. When staged, it is most typical to have the patient undergo the minimally invasive surgical ablation procedure first following by a catheter ablation procedure 1 to 3 months later. This latter approach is referred to as a "staged Hybrid AF ablation procedure."

Minimum AF documentation, endpoints, TEE performance, and success rates in clinical trials	
Minimum documentation for paroxysmal AF	The minimum AF documentation requirement for paroxysmal AF is (1) physician's note indicating recurrent self-terminating AF; and (2) one electrocardiographically documented AF episode within 6 months prior to the ablation procedure.
Minimum documentation for persistent AF	The minimum AF documentation requirement for persistent AF is (1) physician's note indicating continuous AF >7 days but no more than 1 year; and (2) a 24-hour Holter within 90 days of the ablation procedure showing continuous AF.
Minimum documentation for early persistent AF	The minimum AF documentation requirement for persistent AF is (1) physician's note indicating continuous AF >7 days but no more than 3 months; and (2) a 24-hour Holter showing continuous AF within 90 days of the ablation procedure.
Minimum documentation for long-standing persistent AF	The minimum AF documentation requirement for long-standing persistent AF is as follows: physician's note indicating at least 1 year of continuous AF plus a 24-hour Holter within 90 days of the ablation procedure showing continuous AF. The performance of a successful cardioversion (sinus rhythm >30 seconds) within 12 months of an ablation procedure with documented early recurrence of AF within 30 days should not alter the classification of AF as long-standing persistent.
Symptomatic AF/AFL/AT	AF/AFL/AT that results in symptoms that are experienced by the patient. These symptoms can include but are not limited to palpitations, presyncope, syncope, fatigue, and shortness of breath. For patients in continuous AF, reassessment of symptoms after restoration of sinus rhythm is recommended to establish the relationship between symptoms and AF.
Documentation of AF-related symptoms	Documentation by a physician evaluating the patient that the patient experiences symptoms that could be attributable to AF. This does not require a time-stamped ECG, Holter, or event monitor at the precise time of symptoms. For patients with persistent AF who initially report no symptoms, it is reasonable to reassess symptom status after restoration of sinus rhythm with cardioversion.
Minimum effectiveness endpoint for patients with symptomatic and asymptomatic AF	The minimum effectiveness endpoint is freedom from symptomatic and asymptomatic episodes of AF/AFL/AT recurrences at 12 months following ablation, free from antiarrhythmic drug therapy, and including a prespecified blanking period.

Minimum chronic acceptable success rate: paroxysmal AF at 12-month follow-up	If a minimum chronic success rate is selected as an objective effectiveness endpoint for a clinical trial, we recommend that the minimum chronic acceptable success rate for paroxysmal AF at 12-month follow-up is 50%.
Minimum chronic acceptable success rate: persistent AF at 12-month follow-up	If a minimum chronic success rate is selected as an objective effectiveness endpoint for a clinical trial, we recommend that the minimum chronic acceptable success rate for persistent AF at 12-month follow-up is 40%.
Minimum chronic acceptable success rate: long-standing persistent AF at 12-month follow-up	If a minimum chronic success rate is selected as an objective effectiveness endpoint for a clinical trial, we recommend that the minimum chronic acceptable success rate for long-standing persistent AF at 12-month follow-up is 30%.
Minimum follow-up screening for paroxysmal AF recurrence	For paroxysmal AF, the minimum follow-up screening should include (1) 12-lead ECG at each follow-up visit; (2) 24-hour Holter at the end of the follow-up period (e.g., 12 months); and (3) event recording with an event monitor regularly and when symptoms occur from the end of the 3-month blanking period to the end of follow-up (e.g., 12 months).
Minimum follow-up screening for persistent or long-standing AF recurrence	For persistent and long-standing persistent AF, the minimum follow-up screening should include (1) 12-lead ECG at each follow-up visit; (2) 24-hour Holter every 6 months; and (3) symptom-driven event monitoring.
Requirements for transesophageal echocardiogram	It is recommended that the minimum requirement for performance of a TEE in a clinical trial should be those requirements set forth in ACC/AHA/HRS 2014 Guidelines for AF Management pertaining to anticoagulation at the time of cardioversion. Prior to undergoing an AF ablation procedure a TEE should be performed in all patients with AF of >48 hours' duration or of unknown duration if adequate systemic anticoagulation has not been maintained for at least 3 weeks prior to AF ablation. If a TEE is performed for this indication, it should be performed within 24 hours of the ablation procedure.

AF = atrial fibrillation; DW-MRI = diffusion-weighted magnetic resonance imaging; CHF = congestive heart failure; QOL = quality of life; ECG = electrocardiogram; CABG = coronary artery bypass graft; PV = pulmonary vein; SVC = superior vena cava; IVC = inferior vena cava; CFAE = complex fractionated atrial electrogram; PVI = pulmonary vein isolation; AFL = atrial flutter; AT = atrial tachycardia; ACC = American College of Cardiology; AHA = American Heart Association; HRS = Heart Rhythm Society.

Quality of Life Scales, Definitions, and Strengths

Scale	Definition/Details	Strengths/Weaknesses
Short Form (36) Health Survey (SF36) (General)	Consists of 8 equally weighted, scaled scores in the following sections: vitality, physical functioning, bodily pain, general health perceptions, physical role functioning, emotional role functioning, social role functioning, mental health. Each section receives a scale score from 0 to 100. Physical component summary (PCS) and mental component summary (MCS) is an average of all the physically and mentally relevant questions, respectively. The Short Form (12) Health Survey (SF12) is a shorter version of the SF-36, which uses just 12 questions and still provides scores that can be compared with SF-36 norms, especially for summary physical and mental functioning. Gives more precision in measuring QOL than EQ-5D but can be harder to transform into cost utility analysis.	Advantages: extensively validated in a number of disease and health states. Might have more resolution than EQ-50 for AF QOL. Disadvantages: not specific for AF, so might not have resolution to detect AF-specific changes in QOL.

Quality of Life Scales, Definitions, and Strengths

EuroQol Five Dimensions Questionnaire (EQ-5D)39 (General)	Two components: Health state description is measured in five dimensions: mobility, self-care, usual activities, pain/discomfort, anxiety/depression. Answers may be provided on a three-level (3l) or five-level (SL) scale. In the Evaluation section, respondents evaluate their overall health status using a visual analogue scale (EQ-VAS). Results can easily be converted to quality-adjusted life years for cost utility analysis.	Advantages: extensively validated in a number of disease and health states. Can easily be converted into quality adjusted life years (QALY) for cost-effectiveness analysis. Disadvantages: might not be specific enough to detect AF-specific changes in QOL. Might be less specific than SF-36.
AF effect on Quality of Life Survey (AFEQT)40 (AF specific)	20 questions: 4 targeting AF-related symptoms, 8 evaluating daily function, and 6 assessing AF treatment concerns. Each item scored on a 7-point Likert scale.	Advantages: brief, simple, very responsive to AF interventions. Good internal validity and well validated against a number of other global and AF-specific QOL scales. Used in CABANA. Disadvantages: validation in only two published studies (approximately 219 patients).
Quality of Life Questionnaire for Patients with AF (AF-QoL)41 (AF specific)	18-item self-administered questionnaire with three domains: psychological, physical, and sexual activity. Each item scores on a 5-point Likert scale.	Advantages: brief, simple, responsive to AF interventions; good internal validity; used in SARA trial. Disadvantages: external validity compared only to SF-36; formal validation in 1 study (approximately 400 patients).
Arrhythmia-Related Symptom Checklist (SCL)42 (AF specific)	16 items covering AF symptom frequency and symptom severity.	Advantages: most extensively validated in a number of arrhythmia cohorts and clinical trials. Disadvantages: time-consuming and uncertain generalizability.

Mayo AF Specific Symptom Inventory (MAFSI)43 (AF specific)	10 items covering AF symptom frequency and severity. Combination of 5- point and 3-point Likert scale responses. Used in CABANA trial.	Advantages: validated in an AF ablation population and responsive to ablation outcome; used in CABANA trial. Disadvantages: external validity compared only to SF-36; 1 validation study (approximately 300 patients).
University of Toronto Atrial Fibrillation Severity Scale (AFSS)44 (AF specific)	10 items covering frequency, duration, and severity. 7-point Likert scale responses.	Advantages: validated and reproducible; used in CTAF trial. Disadvantages: time-consuming and uncertain generalizability.
Arrhythmia Specific Questionnaire in Tachycardia and Arrhythmia (ASTA)45 (AF specific)	Records number of AF episodes and average episode duration during last 3 months. 8 symptoms and 2 disabling symptoms are recorded with scores from 1–4 for each.	Advantages: validated in various arrhythmia groups; external validity compared with SCL, EQ5D, and SF-36; used in MANTRA-PAF; brief; simple. Disadvantages: one validation study (approximately 300 patients).
European Heart Rhythm Association (EHRA)46 (AF specific)	Like NYHA scale. I = no symptoms, II = mild symptoms not affecting daily activity, III = severe symptoms affecting daily activity, and IV = disabling symptoms terminating daily activities.	Advantage: very simple, like NYHA. Disadvantages: not used in studies and not well validated; not very specific; unknown generalizability.

Canadian Cardiovascular Society Severity of Atrial Fibrillation Scale (CCS-SAF)47 (AF specific)	Like NYHA scale. O = asymptomatic, I = AF symptoms have minimal effect on patient's QOL, II = AF symptoms have minor effect on patient QOL, III = symptoms have moderate effect on patient QOL, IV= AF symptoms have severe effect on patient QOL.	Advantages: very simple, like NYHA; validated against SF-36 and University of Toronto AFSS. Disadvantages: poor correlation with subjective AF burden; not very specific.

AF = atrial fibrillation; QOL = quality of life; CABANA = Catheter Ablation vs Anti-arrhythmic Drug Therapy for Atrial Fibrillation; SARA = Study of Ablation Versus antiaRrhythmic Drugs in Persistent Atrial Fibrillation; CTAF = Canadian Trial of Atrial Fibrillation; MANTRA-PAF = Medical ANtiarrhythmic Treatment or Radiofrequency Ablation in Paroxysmal Atrial Fibrillation; NYHA = New York Heart Association; AFSS = atrial fibrillation severity scale.

Non-AF Recurrence–Related Endpoints for Reporting in AF Ablation Trials

Stroke and bleeding endpoints	Definitions/details
Stroke (2014 ACC/AHA Key Data Elements)	An acute episode of focal or global neurological dysfunction caused by brain, spinal cord, or retinal vascular injury as a result of hemorrhage or infarction. Symptoms or signs must persist ≥24 hours, or if documented by CT, MRI or autopsy, the duration of symptoms/signs may be less than 24 hours. Stroke may be classified as ischemic (including hemorrhagic transformation of ischemic stroke), hemorrhagic, or undetermined. Stroke disability measurement is typically performed using the modified Rankin Scale (mRS).
Transient ischemic attack (2014 ACC/AHA Key Data Elements)	Transient episode of focal neurological dysfunction caused by brain, spinal cord, or retinal ischemia without acute infarction and with signs and symptoms lasting less than 24 hours.
Major bleeding (ISTH definition)	Fatal bleeding AND/OR symptomatic bleeding in a critical area or organ, such as intracranial, intraspinal, intraocular, retroperitoneal, intraarticular, pericardial, or intramuscular with compartment syndrome AND/OR bleeding causing a fall in hemoglobin level of 2 g/dL (1.24 mmol/L) or more, or leading to transfusion of two or more units of blood.
Clinically relevant nonmajor bleed (ISTH definition)	An acute or subacute clinically overt bleed that does not meet the criteria for a major bleed but prompts a clinical response such that it leads to one of the following: hospital admission for bleeding; physician-guided medical or surgical treatment for bleeding; change in antithrombotic therapy (including interruption or discontinuation).

Stroke and bleeding endpoints	Definitions/details
Minor bleeding (ISTH definition)	All nonmajor bleeds. Minor bleeds are further divided into clinically relevant and not.
Incidence and discontinuation of oral anticoagulation	The number of patients receiving oral anticoagulation and the type of oral anticoagulation should be documented at the end of follow-up. If patients have their oral anticoagulation discontinued, the number of patients discontinuing, the timing of discontinuation, and the reasons for discontinuation of oral anticoagulation, as well as the clinical characteristics and stroke risk profile of the patients should be reported.

AF = atrial fibrillation; CT = computed tomography; MRI = magnetic resonance imaging.

Advantages and Disadvantages of AF-Related Endpoints in AF Ablation Trials

Endpoint	Advantages	Disadvantages	Relevance and comments
Freedom from AF/AFL/AT recurrence "gold standard" is 30 seconds	-Has been in use for many years -Can be used to compare results of new trials with historical trials -Sets a high bar for AF elimination	-Can systematically underestimate the efficacy of AF ablation, particularly for persistent AF, if 30-second cutoff is used	-Particularly well suited for paroxysmal AF outcomes -Reporting of cutoffs other than 30 seconds encouraged as secondary endpoints to better contextualize results -May be reported as proportion of patients free from arrhythmia or time to recurrence
Freedom from stroke-relevant AF/AFL/AT-duration cutoff of 1 hour	-Useful for trials in which interest is more for prognostic change conferred by ablation rather than elimination of all arrhythmias	-No consistent definition of what a stroke-relevant duration of AF is: ranges from 6 minutes to 24 hours in literature	-More than 1 hour could be a useful cutoff based on results of 505 trial -May be reported as proportion of patients free from arrhythmia or time to recurrence
Freedom from AF/AFL/AT requiring intervention (emergency visits, cardioversion, urgent care visit, reablation, etc.)	-Can provide an endpoint more relevant to systemic costs of AF recurrence -Clinically relevant	-Will overestimate efficacy of ablation by ignoring shorter episodes not requiring intervention that still might be important to quality of life or stroke	-Determination of what is an "intervention" must be prespecified in protocol and biases mitigated to avoid over- or underintervention in the trial
Freedom from persistent AF/AFL/AT-duration cutoff of 7 days	-Useful for trials assessing additional substrate modification in persistent AF	-Can systematically overestimate the efficacy of AF ablation, particularly for persistent AF	-Can require continuous monitoring to definitively assess if episode is >7 days

Endpoint	Advantages	Disadvantages	Relevance and Comments
Freedom from AF/AFL/AT on previously ineffective antiarrhythmic therapy	-If patient maintains sinus rhythm on previously ineffective drug therapy, this may be considered a clinically relevant, successful outcome	-Will increase the success rate compared with off-drug success -May not be relevant to patients hoping to discontinue drug therapy	-Postablation drug and dosage of drug should be identical to preablation drug and dosage
Significant reduction in AF burden: >75% reduction from pre- to postablation and/or total postablation burden <12%	-Can be useful in persistent AF studies, but might not be suited for early, paroxysmal AF studies	-Ideally requires continuous monitoring using an implantable device -No scientific basic exists showing that a 75% reduction in AF burden impacts hard endpoints, including heart failure, stroke, and mortality	-AF burden can be estimated by intermittent monitoring and reporting of patient symptoms and recurrences like a “time in therapeutic range” report for oral anticoagulation; see text -Could also see 75% reduction in number and duration of AF episodes -Because there is no firm scientific basis for selecting the cutoff of 75%, this prior recommendation is provided only as an example of what future clinical trials may choose to use as a definition of clinical/partial success
Prevention in AF progression: time to first episode of persistent AF (>7 days)	-Does not assume that total elimination of AF is required -Well suited for paroxysmal or “early” AF studies in which goal is to prevent progression to persistent AF	-Prevention in progression might be irrelevant for stroke or thromboembolic outcomes -Long follow-up time might be required unless population is “enriched” -Can ideally require continuous implantable monitoring	-Might be useful for specific populations such as heart failure or hypertrophic cardiomyopathy, in which progression to persistent AF can lead to increased hospitalization

Endpoint	Advantages	Disadvantages	Relevance and Comments
Regression of AF: reduction in burden to a given threshold or conversion of persistent to paroxysmal AF	-Does not assume that total elimination of AF is required -Well suited for persistent “late” AF studies in which goal is to regress to paroxysmal AF, which might be easier to control with drug therapy	-Regression endpoint will overestimate efficacy of AF ablation -Might ideally require continuous implantable monitoring -Patients will require ongoing drug therapy	-Could be particularly useful for long-standing persistent AF populations with structural heart disease, heart failure, etc.
Acute AF termination during ablation procedure	-Could provide indication of successful modification of substrate responsible for maintaining AF, most relevant to persistent or long-standing persistent AF -Limited studies have linked acute AF termination to long-term success	-Relevance of acute AF termination has not consistently been shown to correlate to long-term success -Endpoint might not be relevant to paroxysmal AF patients in whom AF might terminate spontaneously -Some studies employ administration of intravenous or oral antiarrhythmics during ablation that could cause spontaneous termination -Studies consider termination as reversion to sinus rhythm, whereas others consider reversion to any regular tachycardia as termination	-Intraprocedural administration of preprocedural oral antiarrhythmics or intraprocedural intravenous antiarrhythmics are discouraged -If antiarrhythmics are used, their use and dosage before and during the ablation should be clearly documented -Termination to sinus rhythm and termination to another regular tachycardia (AT or AFL) should be separately reported

AF = atrial fibrillation; AFL = atrial flutter; AT = atrial tachycardia

2017 HRS/EHRA/ECAS/APRHS/SOLAECE Expert Consensus Statement on Catheter and Surgical Ablation of Atrial Fibrillation

Gerhard Hindricks, MD

www.HRSonline.org

Presenter Disclosure Information

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No personal financial relations to disclose.

Agenda

- Definitions, mechanisms, and rationale for ablation
- Modifiable risk factors for AF and implications for catheter ablation
- Indications
  - catheter ablation of AF
  - surgical ablation of AF

Significance of AF

- 33 million people have AF world wide
- 3–5 million people in the United States
- By 2050, app. 8 million people will be affected in the United States
- AF increases risk of stroke on average 5-fold
- AF increases heart failure, dementia, and total mortality

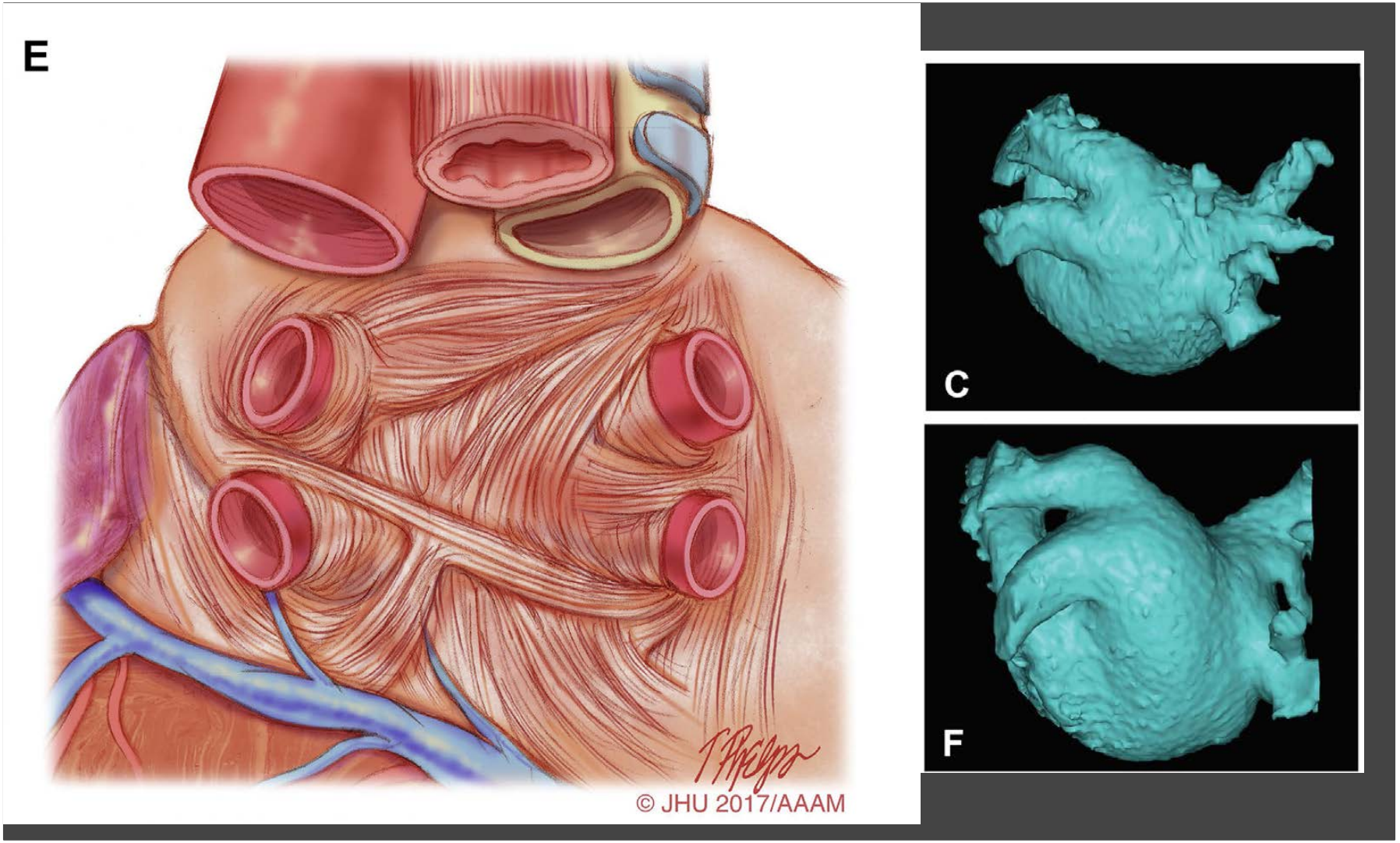
- 450000 hospitalizations in the United States
- 90000 deaths related to AF in the United States

AF Definitions: Speaking the Same Language…

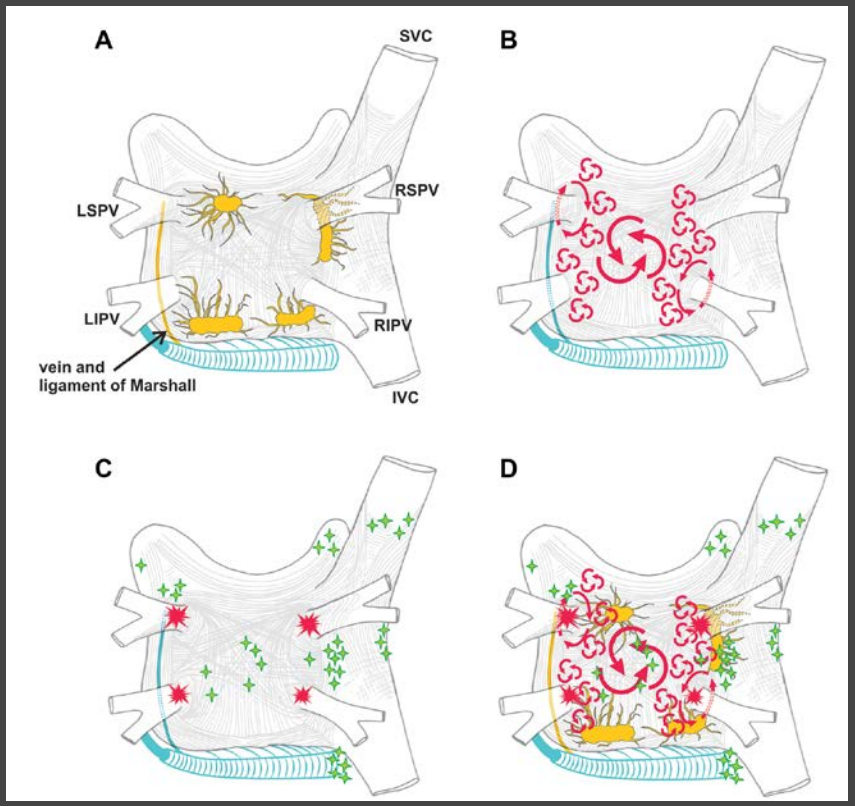
AF episode	An AF episode is defined as AF that is documented by ECG monitoring or intracardiac electrogram monitoring and has a duration of at least 30 seconds, or if less than 30 seconds, is present throughout the ECG monitoring tracing. The presence of subsequent episodes of AF requires that sinus rhythm be documented by ECG monitoring between AF episodes.
Chronic AF	Chronic AF has variable definitions and should not be used to describe populations of AF patients undergoing AF ablation.
Early persistent AF	Early persistent AF is defined as AF that is sustained beyond 7 days but is less than 3 months in duration.
Lone AF	Lone AF is a historical descriptor that is potentially confusing and should not be used to describe populations of patients with AF undergoing AF ablation.
Long-standing persistent AF	Long-standing persistent AF is defined as continuous AF of greater than 12 months duration.
Paroxysmal AF	Paroxysmal AF is defined as AF that terminates spontaneously or with intervention within 7 days of onset.
Permanent AF	Permanent AF is defined as the presence of AF that is accepted by the patient and physician, and for which no further attempts to restore or maintain sinus rhythm will be undertaken. The term "permanent AF" represents a therapeutic attitude on the part of the patient and physician rather than an inherent pathophysiological attribute of AF. The term "permanent AF" should not be used within the context of a rhythm control strategy with antiarrhythmic drug therapy or AF ablation.
Persistent AF	Persistent AF is defined as continuous AF that is sustained beyond 7 days.
Silent AF	Silent AF is defined as asymptomatic AF diagnosed with an opportune ECG or rhythm strip.

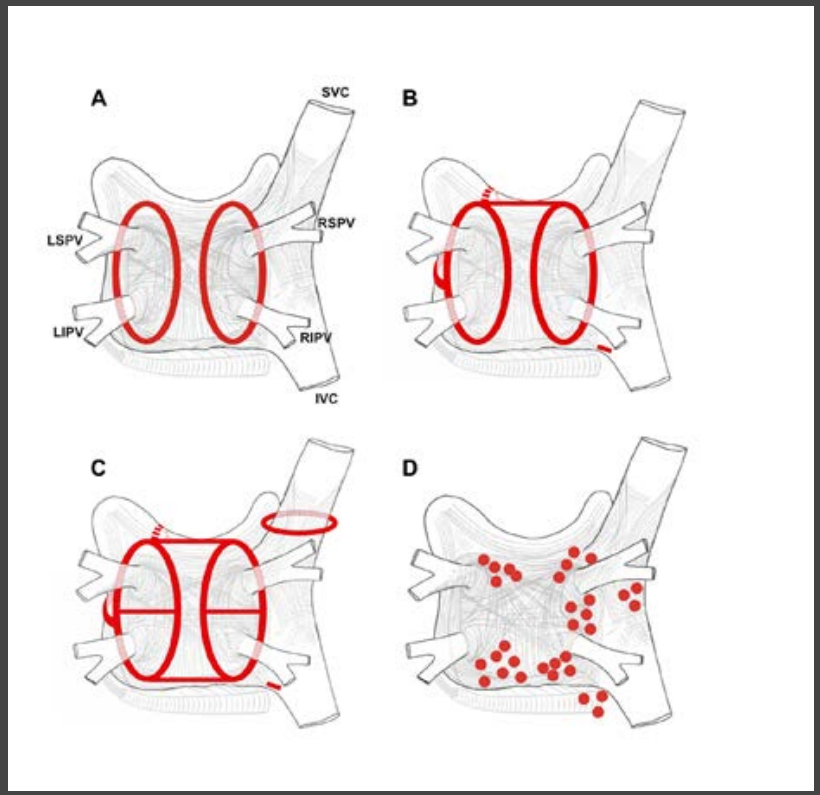
AF = atrial fibrillation; ECG = electrocardiogram

Anatomy of the LA and AF

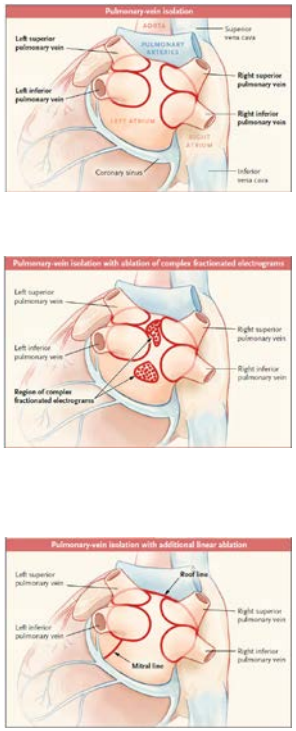


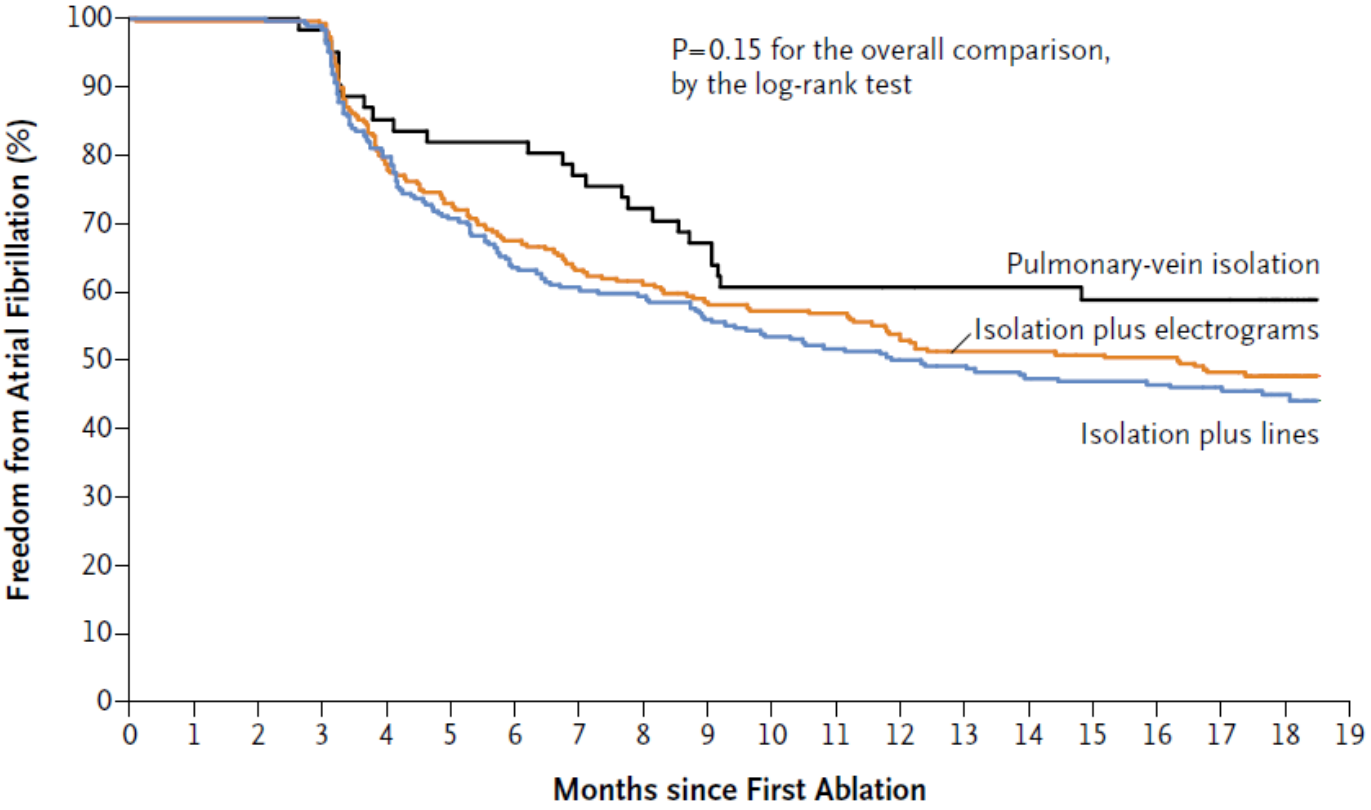
AF Mechanisms and Ablation Concepts





Catheter Ablation of Persistent AF



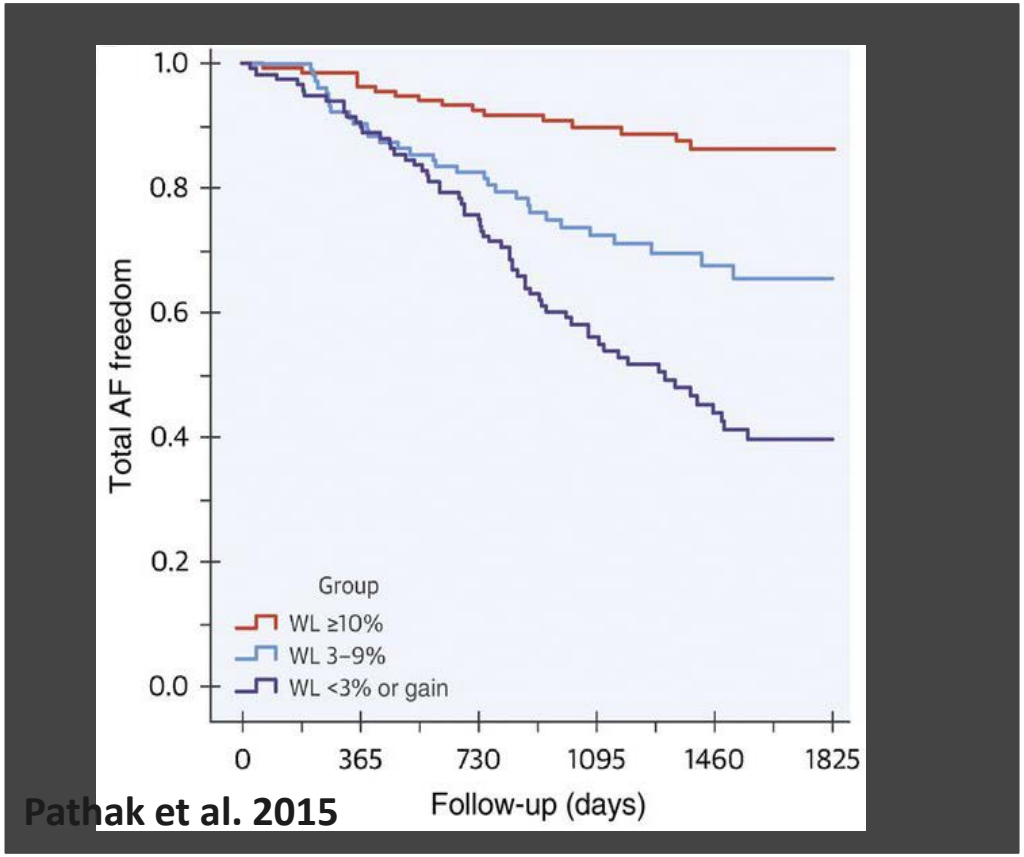


No. at Risk

Pulmonary-vein isolation	61	60	50	41	36	23
Isolation plus electrograms	244	242	161	137	124	72
Isolation plus lines	244	240	152	133	115	57

Risk Factors and Their Interaction with AF

- Obesity
- Sleep apnea
- Hypertension
- Diabetes
- Alcohol
- Exercise



Pathak et al. 2015

- Control of risk factors has a significant impact on AF burden

Risk Factors and Their Interaction with AF

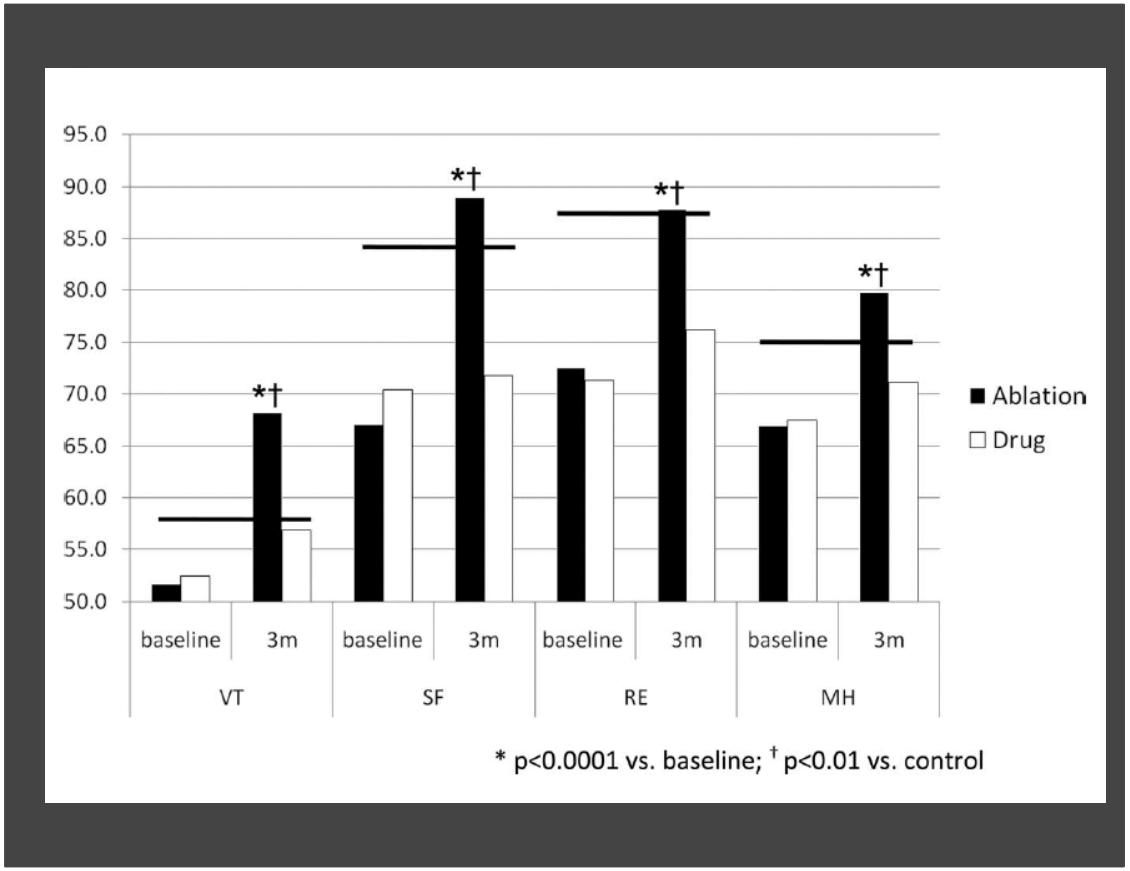
- Obesity
- Sleep apnea
- Hypertension
- Diabetes
- Alcohol
- Exercise

Comorbidity	Association with AF
Heart failure vs. none	HR 1.43 (95% CI 0.85–2.40)
Hypertension (treated) vs. none	HR 1.32 (95% CI 1.08–1.60)
Obesity None (BMI <25 kg/m²) Overweight (BMI 25–30 kg/m²) Obese (BMI ≥31 kg/m²)	HR: 1.00 (reference) 1.13 (95% CI 0.87–1.46) 1.37 (95% CI 1.05–1.78)
Diabetes mellitus vs. none	HR 1.25 (95% CI 0.98–1.60)
Obstructive sleep apnea vs. none	HR 2.18 (95% CI 1.34–3.54)
Chronic obstructive pulmonary disease FEV1 ≥80% FEV1 60–80% FEV1 <60%	RR: 1.00 (reference) 1.28 (95% CI 0.79–2.06) 2.53 (95% CI 1.45–4.42)

- Control of risk factors has a significant impact on AF burden

Benefits of AF Ablation

- quality of life
- hospitalizations
- dementia
- stroke
- mortality



Reynolds et al. Circ Cardiovasc Qual Outcomes 2010;3:615-623

Benefits of AF Ablation

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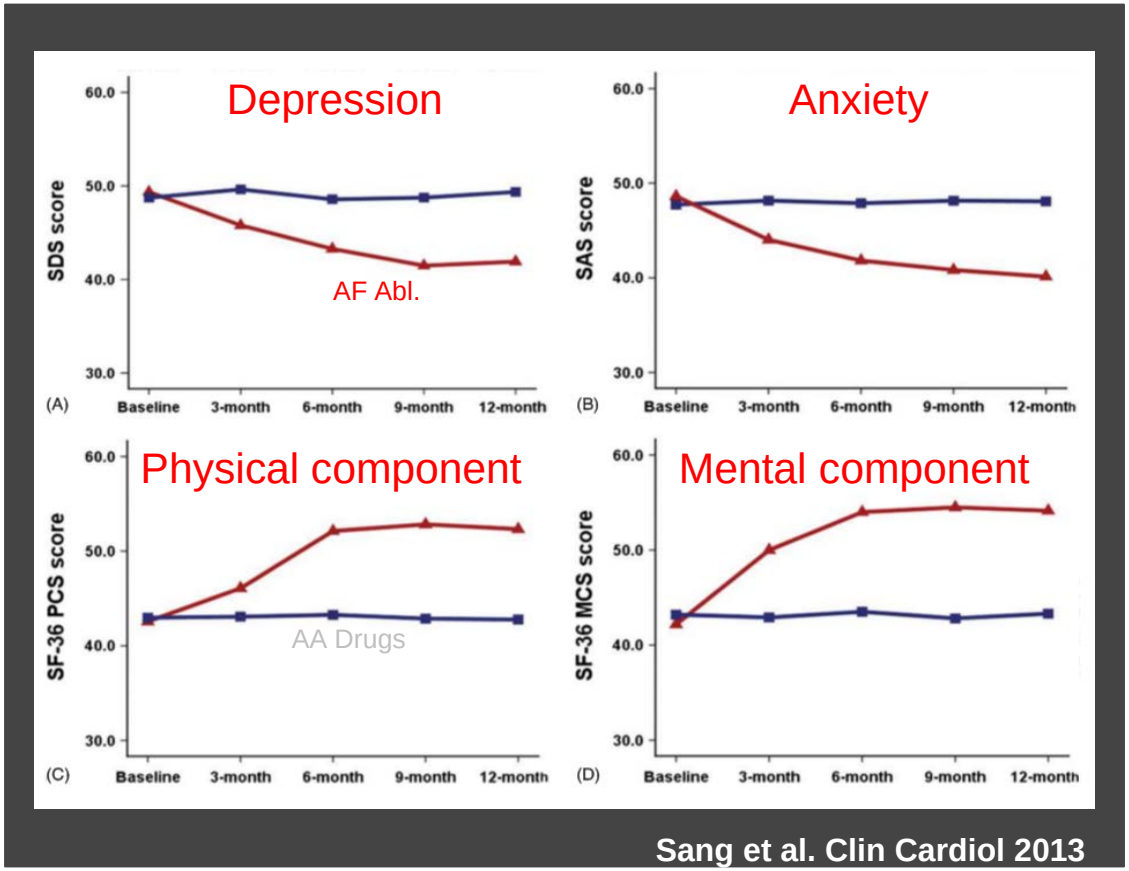
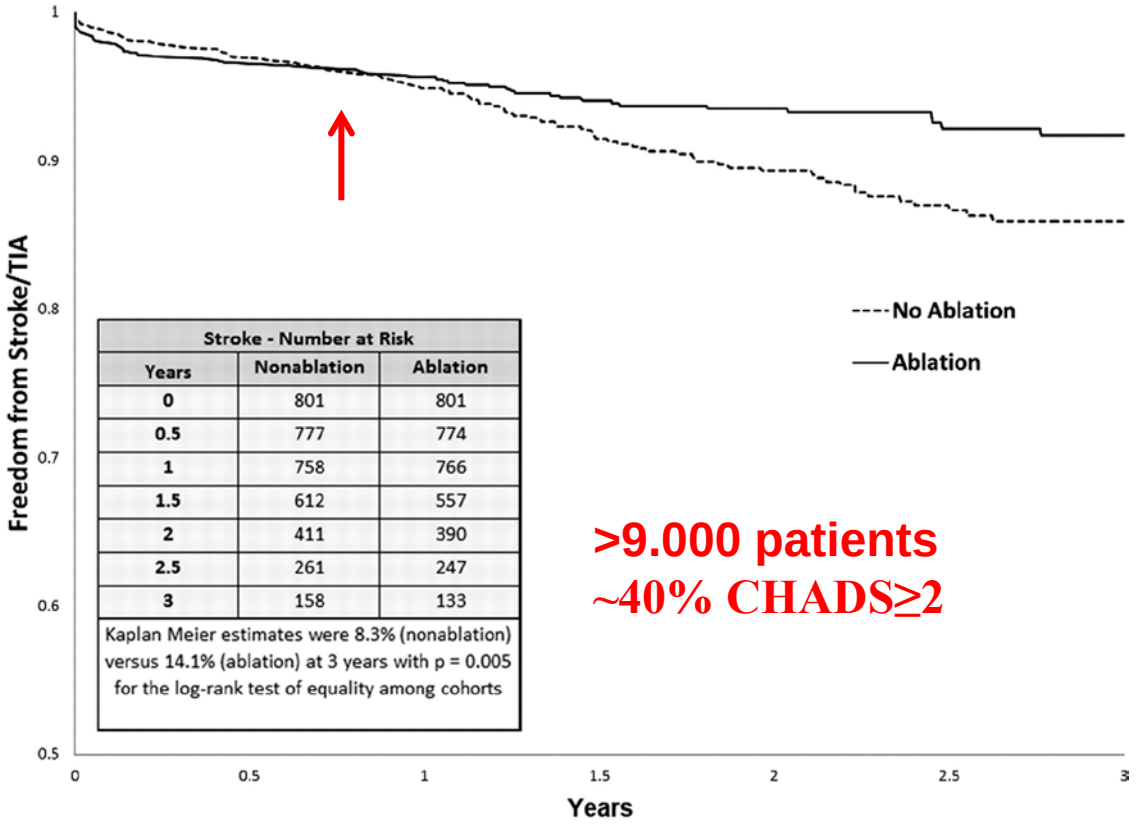


Sang et al. Clin Cardiol 2013

Benefits of AF Ablation

- quality of life
- hospitalizations
- dementia
- stroke
- mortality



Stroke - Number at Risk		
Years	Nonablation	Ablation
0	801	801
0.5	777	774
1	758	766
1.5	612	557
2	411	390
2.5	261	247
3	158	133

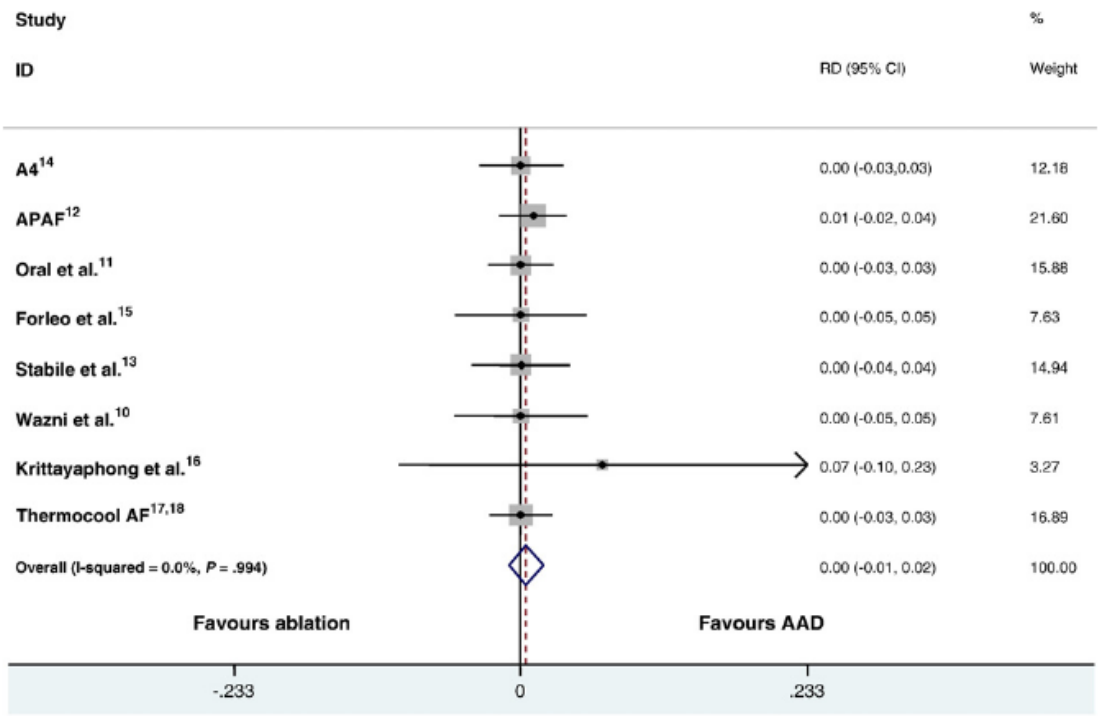
Kaplan Meier estimates were 8.3% (nonablation) versus 14.1% (ablation) at 3 years with p = 0.005 for the log-rank test of equality among cohorts

>9.000 patients
~40% CHADS≥2

Reynolds et al. Circ Cardiovasc Qual Outcomes 2012;5:171-181

Benefits of AF Ablation

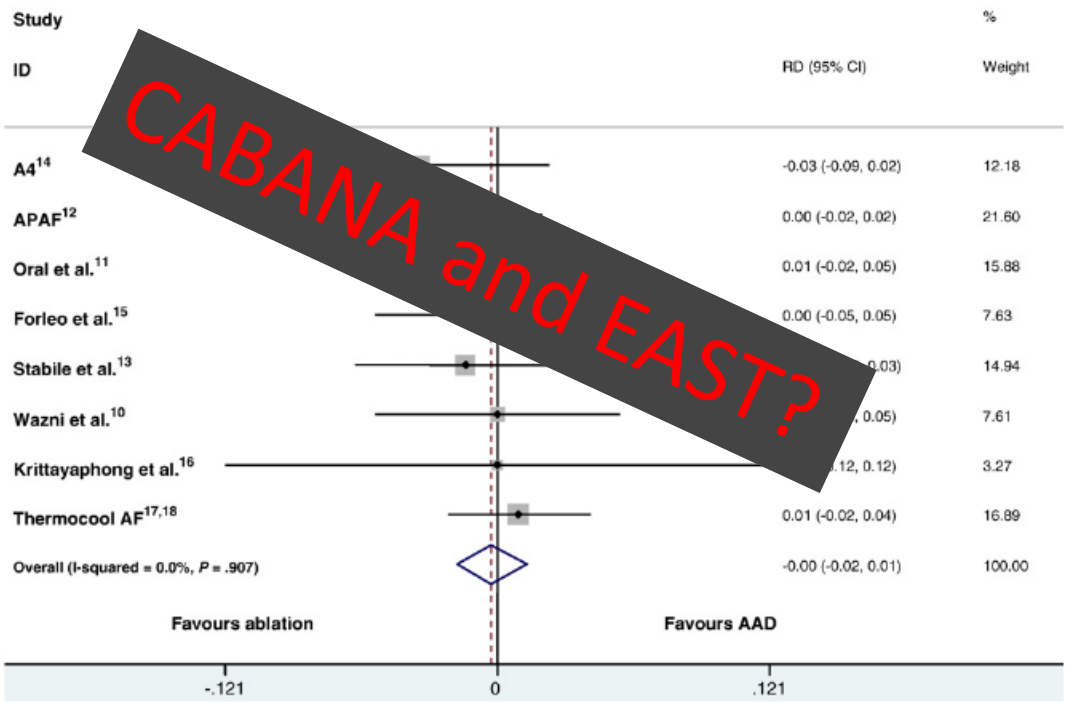
- quality of life
- hospitalizations
- dementia
- stroke
- mortality



Dagres et al. Am Heart J 2009;158:15-20

Benefits of AF Ablation

- quality of life
- hospitalizations
- dementia
- stroke
- mortality



Dagres et al. Am Heart J 2009;158:15-20

Indications for AF Ablation

	Recommendation	Class	LOE
Indications for catheter ablation of atrial fibrillation			
A. Indications for catheter ablation of atrial fibrillation			
Symptomatic AF refractory or intolerant to at least one Class I or III antiarrhythmic medication	Paroxysmal: Catheter ablation is recommended.	I	A
	Persistent: Catheter ablation is reasonable.	IIa	B-NR
	Long-standing persistent: Catheter ablation may be considered.	IIb	C-LD
Symptomatic AF prior to initiation of antiarrhythmic therapy with a Class I or III antiarrhythmic medication	Paroxysmal: Catheter ablation is reasonable.	IIa	B-R
	Persistent: Catheter ablation is reasonable.	IIa	C-EO
	Long-standing persistent: Catheter ablation may be considered.	IIb	C-EO

Indications for AF Ablation

Catheter ablation of AF after failed AA drugs

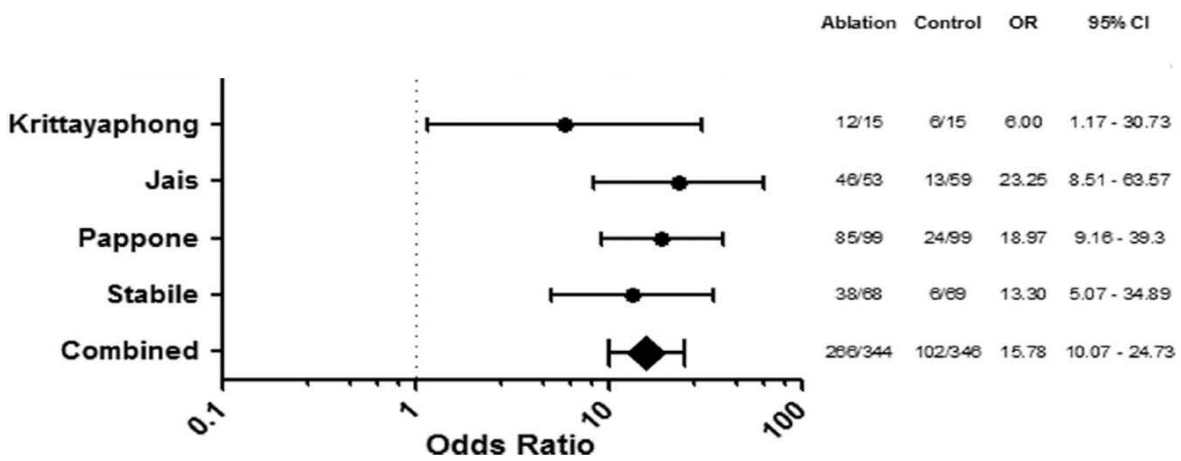
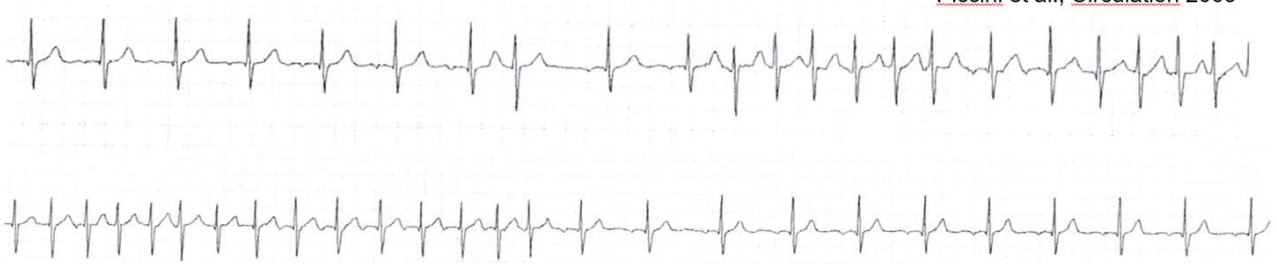
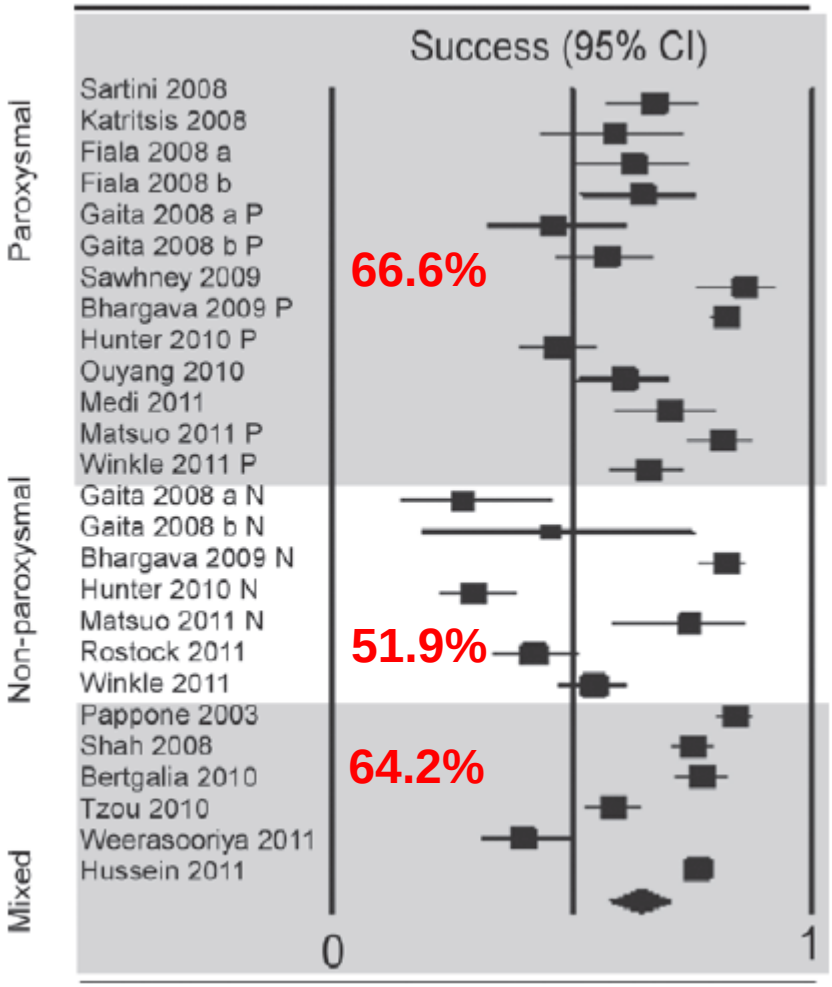


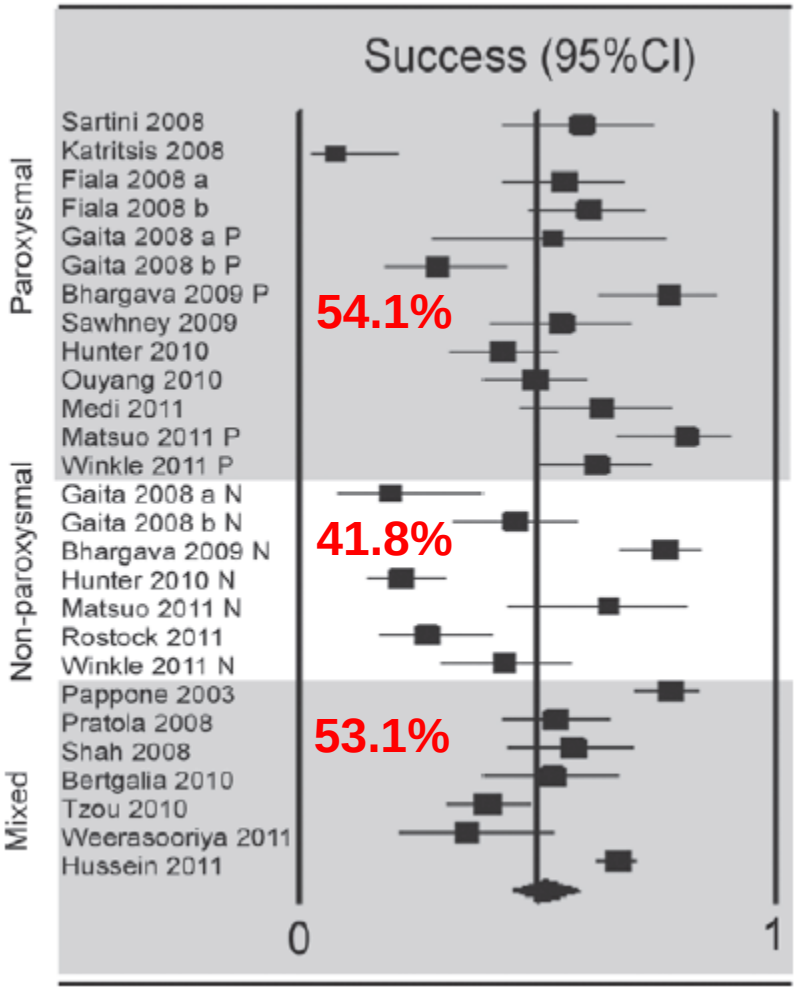
Figure 2. ORs (ablation versus control) for freedom from atrial fibrillation at 12 months.

Piccini et al., Circulation 2009



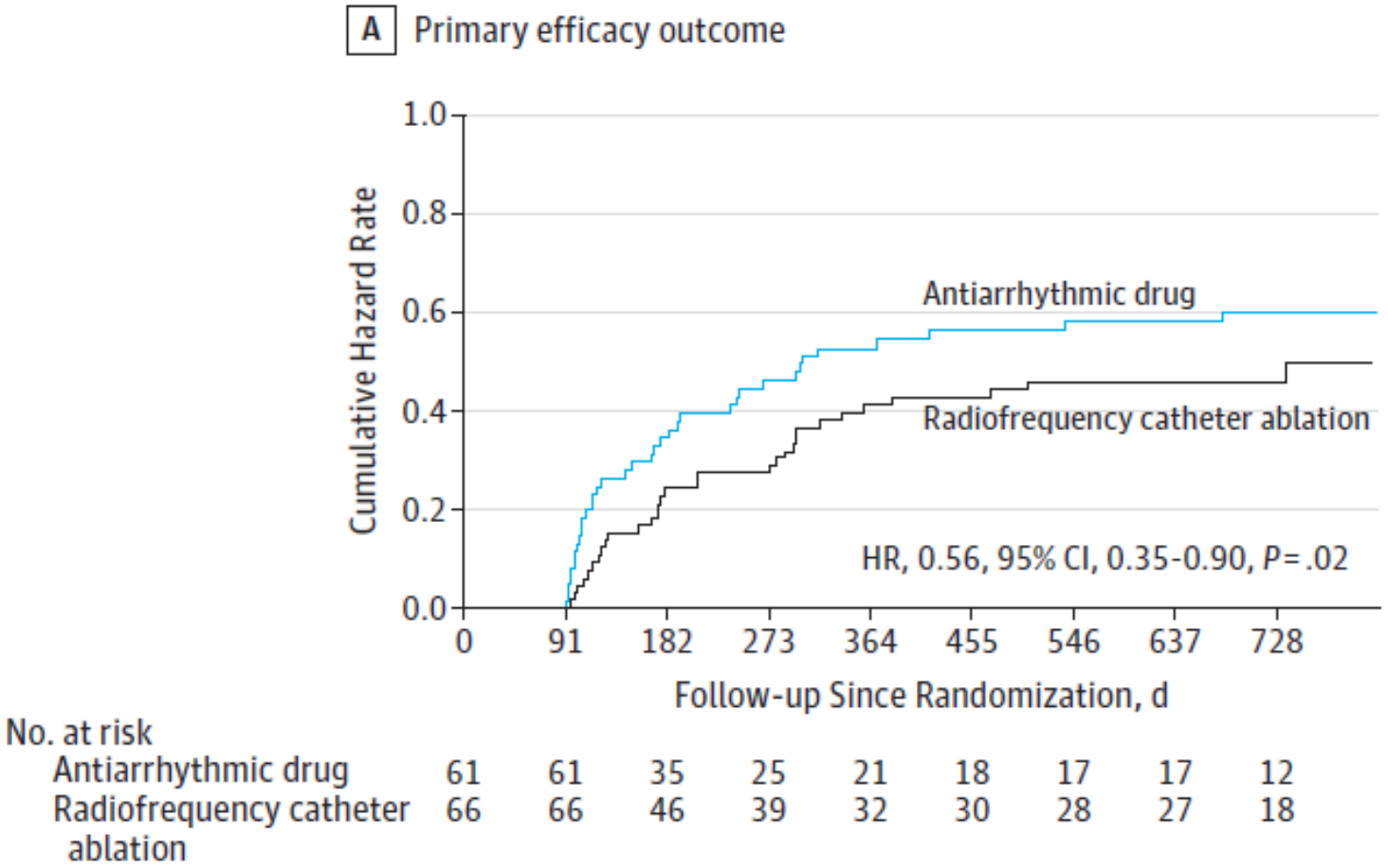
Ablation Outcome: “Early” and “Late” Procedural Success





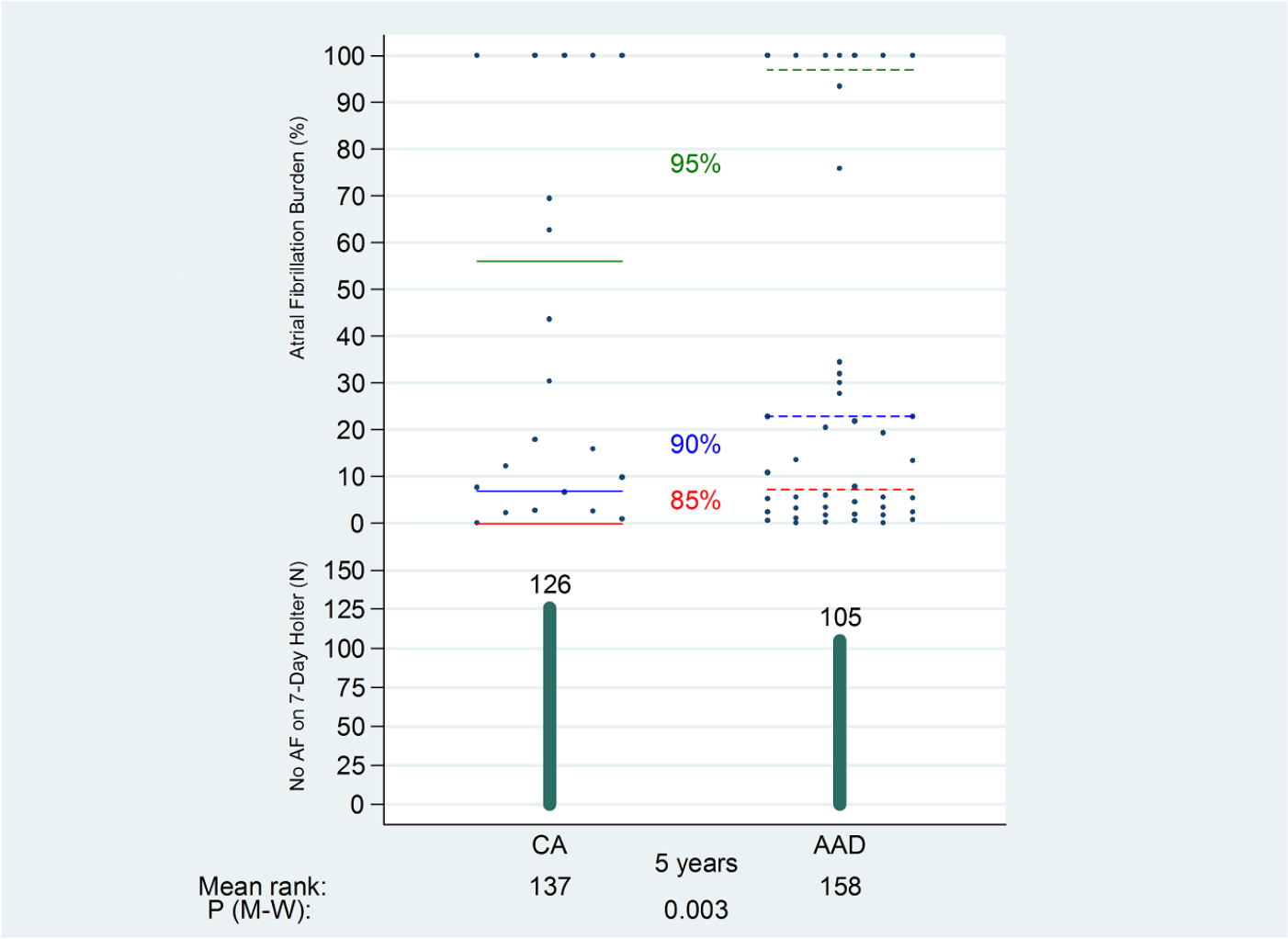
Ganesan et al. J Am Heart Assoc 2013

First-Line AF Catheter Ablation: RAAFT-2



Natale and colleagues. JAMA 2014

Catheter Ablation of AF: MANTRA-PAF Trial at 5 yrs



Nielsen et al. 2016

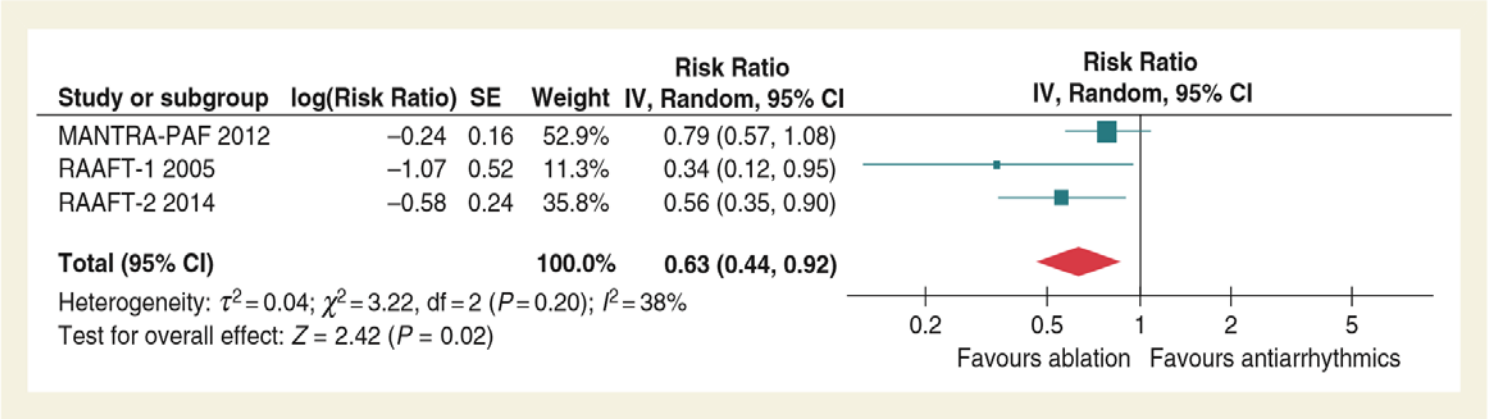
Catheter Ablation of AF: MANTRA-PAF Trial at 5 yrs.

- Freedom from any AF:
  - RFA group: 126/146 (86%)
  - AAD group: 105/148 (71%)

p=0.001

- Freedom from symptomatic AF:
  - RFA group: 137/146 (94%)

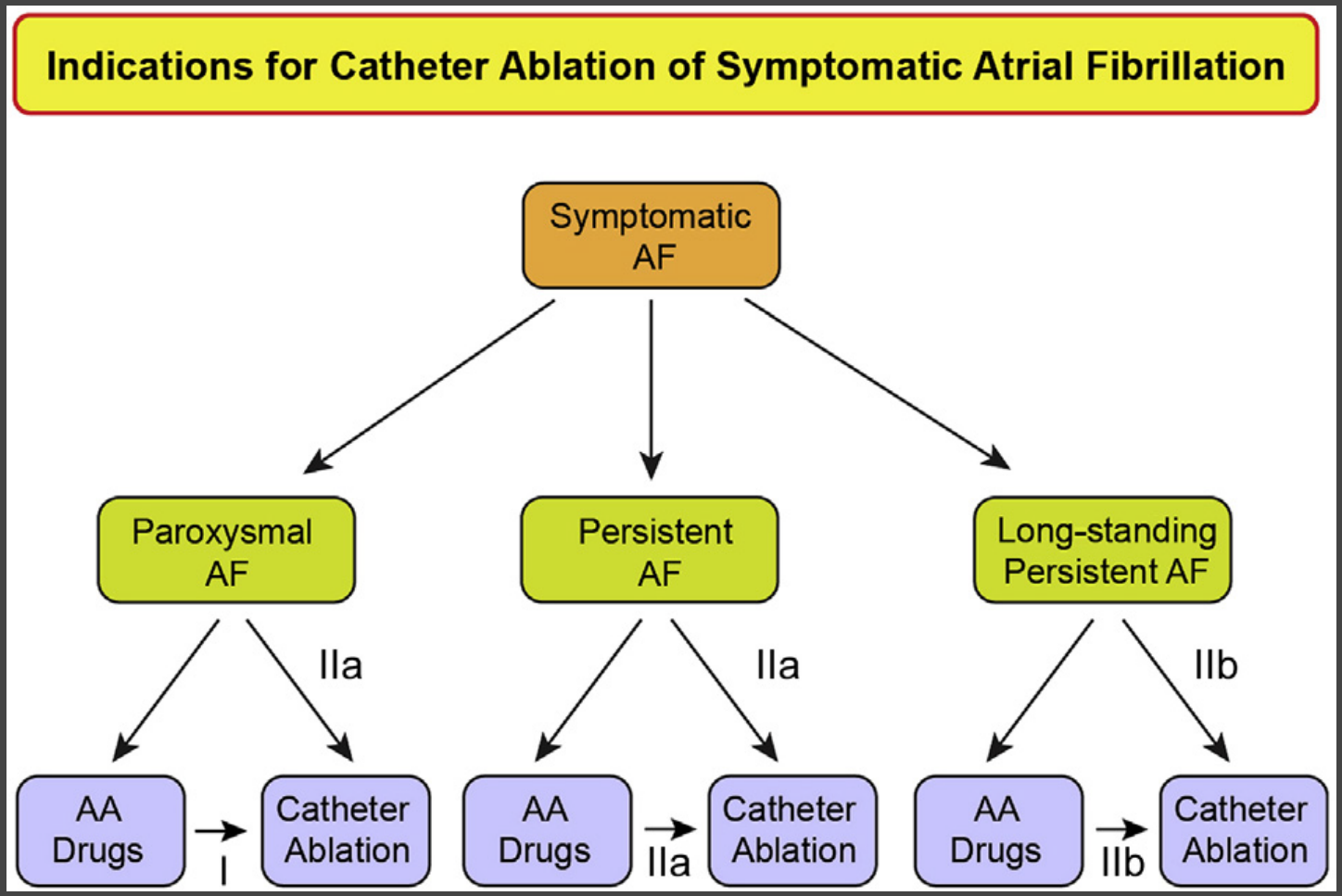
p=0.015



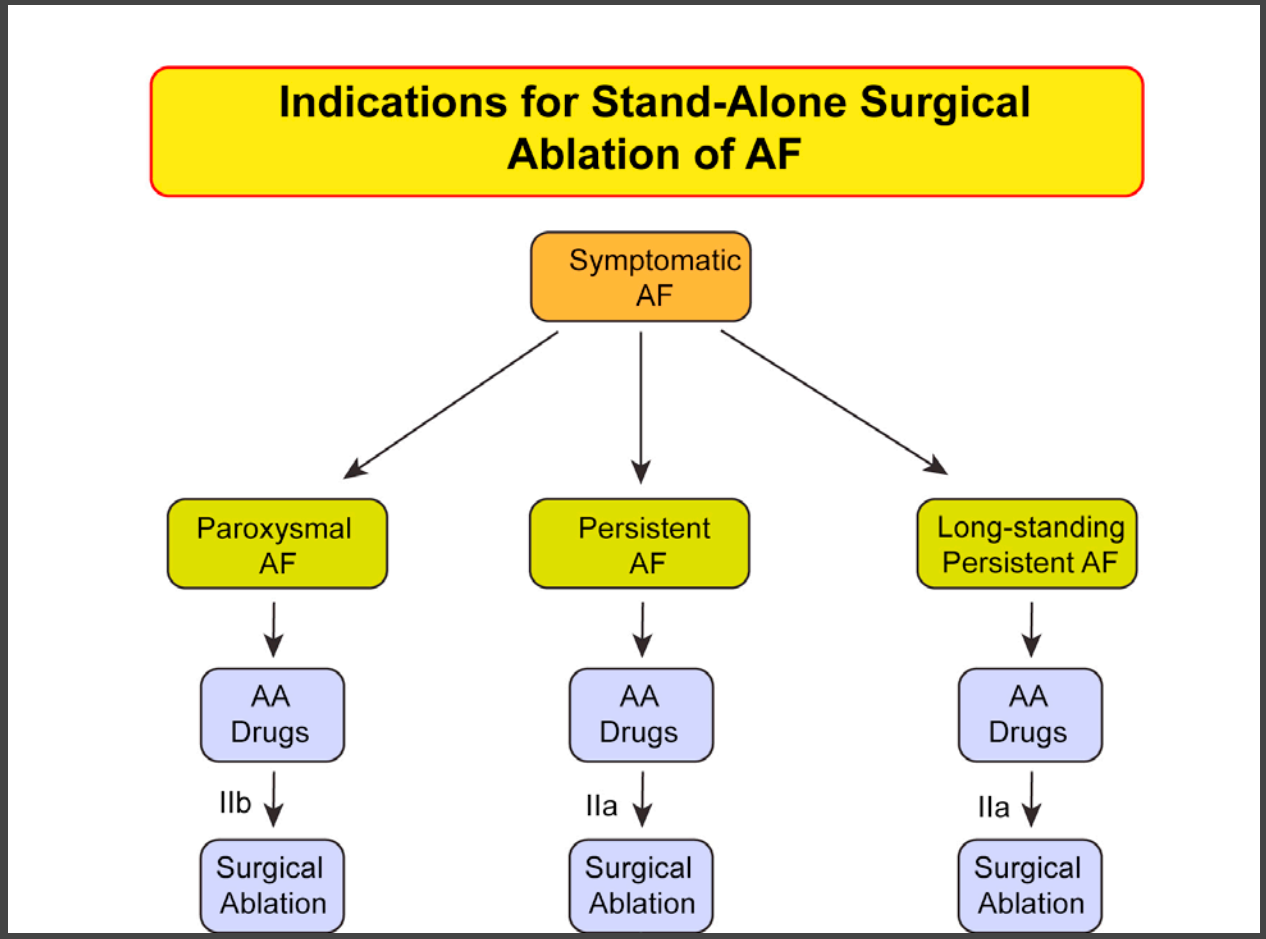
Hakalahti A et al.; Europace 2015

Nielsen et al. 2016

Indications for AF Ablation



Indications for Surgical AF Ablation



Indications for AF Ablation

Indications for catheter atrial fibrillation ablation in populations of patients not well represented in clinical trials			
Congestive heart failure	It is reasonable to use similar indications for AF ablation in selected patients with heart failure as in patients without heart failure.	IIa	B-R
Older patients (>75 years of age)	It is reasonable to use similar indications for AF ablation in selected older patients with AF as in younger patients.	IIa	B-NR
Hypertrophic cardiomyopathy	It is reasonable to use similar indications for AF ablation in selected patients with HCM as in patients without HCM.	IIa	B-NR
Young patients (<45 years of age)	It is reasonable to use similar indications for AF ablation in young patients with AF (<45 years of age) as in older patients.	IIa	B-NR
Tachy-brady syndrome	It is reasonable to offer AF ablation as an alternative to pacemaker implantation in patients with tachy-brady syndrome.	IIa	B-NR
Athletes with AF	It is reasonable to offer high-level athletes AF as first-line therapy due to the negative effects of medications on athletic performance.	IIa	C-LD
Asymptomatic AF**	Paroxysmal: Catheter ablation may be considered in select patients.**	IIb	C-EO
	Persistent: Catheter ablation may be considered in select patients.	IIb	C-EO

**A decision to perform AF ablation in an asymptomatic patient requires additional discussion with the patient because the potential benefits of the procedure for the patient without symptoms are uncertain.

Evidence for a Better Prognosis after Catheter Ablation of Atrial Fibrillation in Heart Failure Patients?

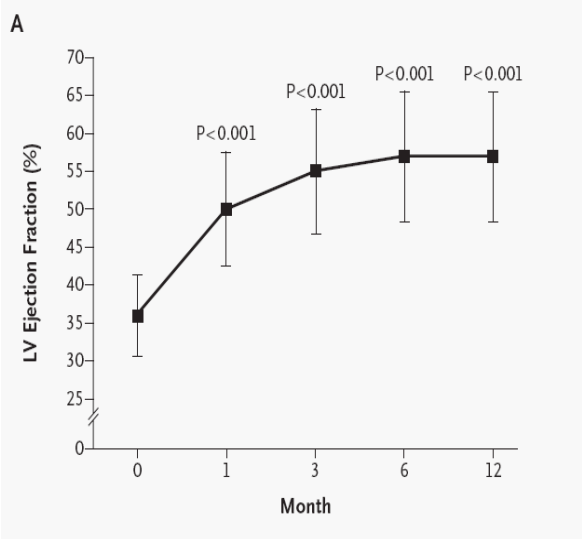
- Rationale:

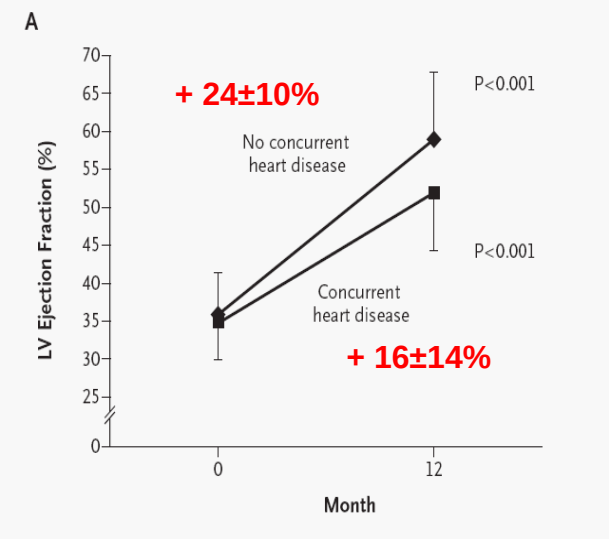
- Patients with atrial fibrillation, heart failure, and highly reduced ejection fraction have a poor prognosis.

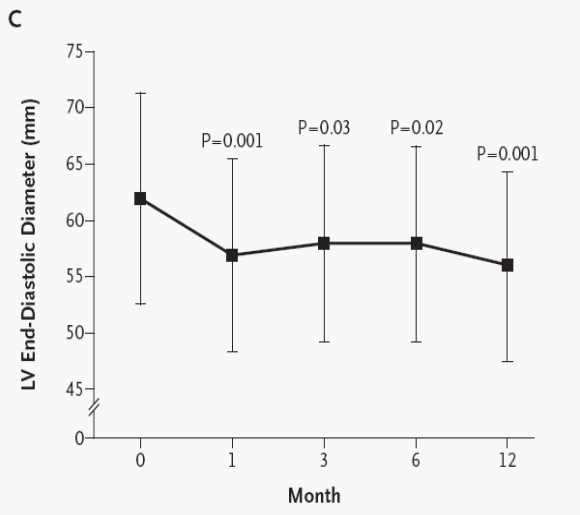
- Nonpharmacological restoration of sinus rhythm with catheter ablation may improve ejection fraction.

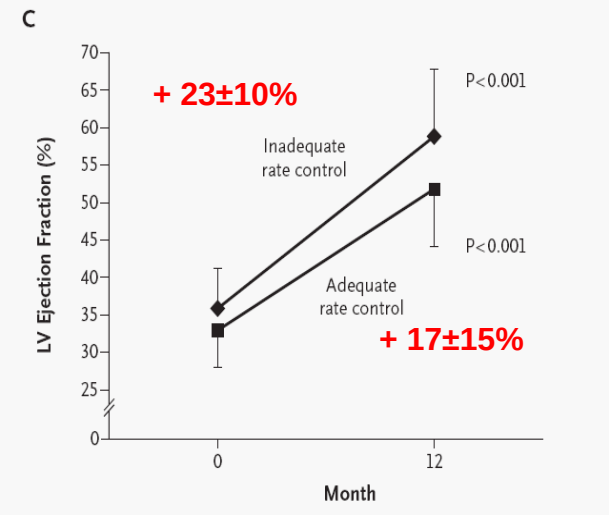
- Improvement of ejection fraction may reduce mortality.

AF Ablation for Rhythm Control in CHF Patients



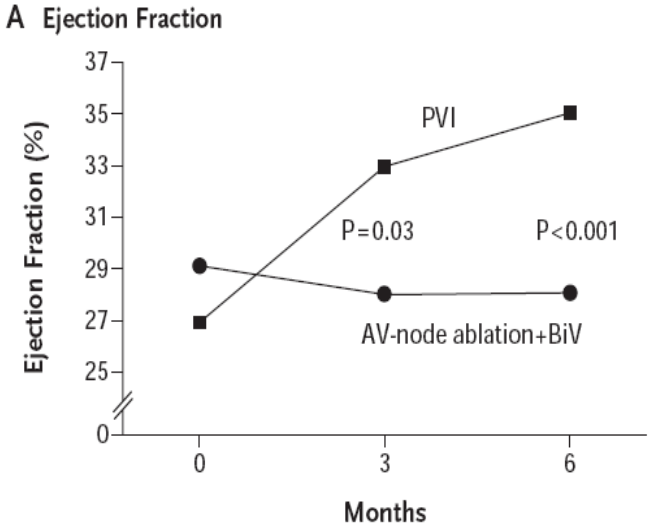


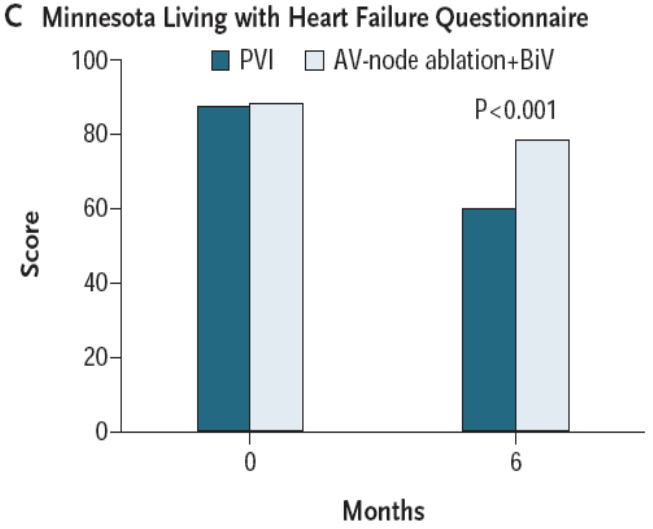


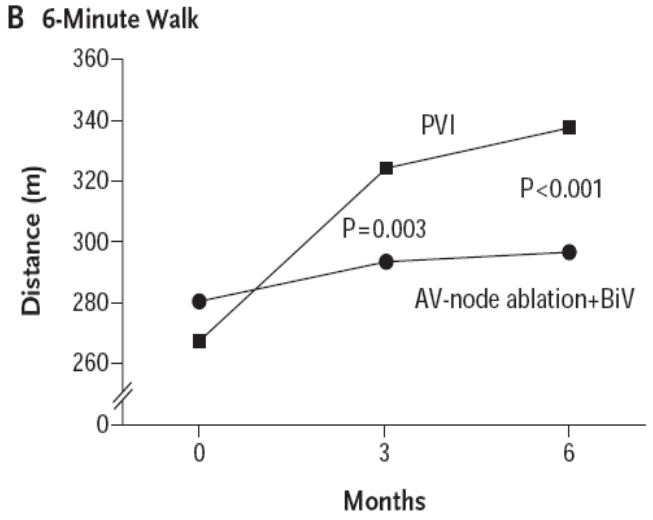


N Engl J Med 2004;351:2373-2383

PABA – CHF





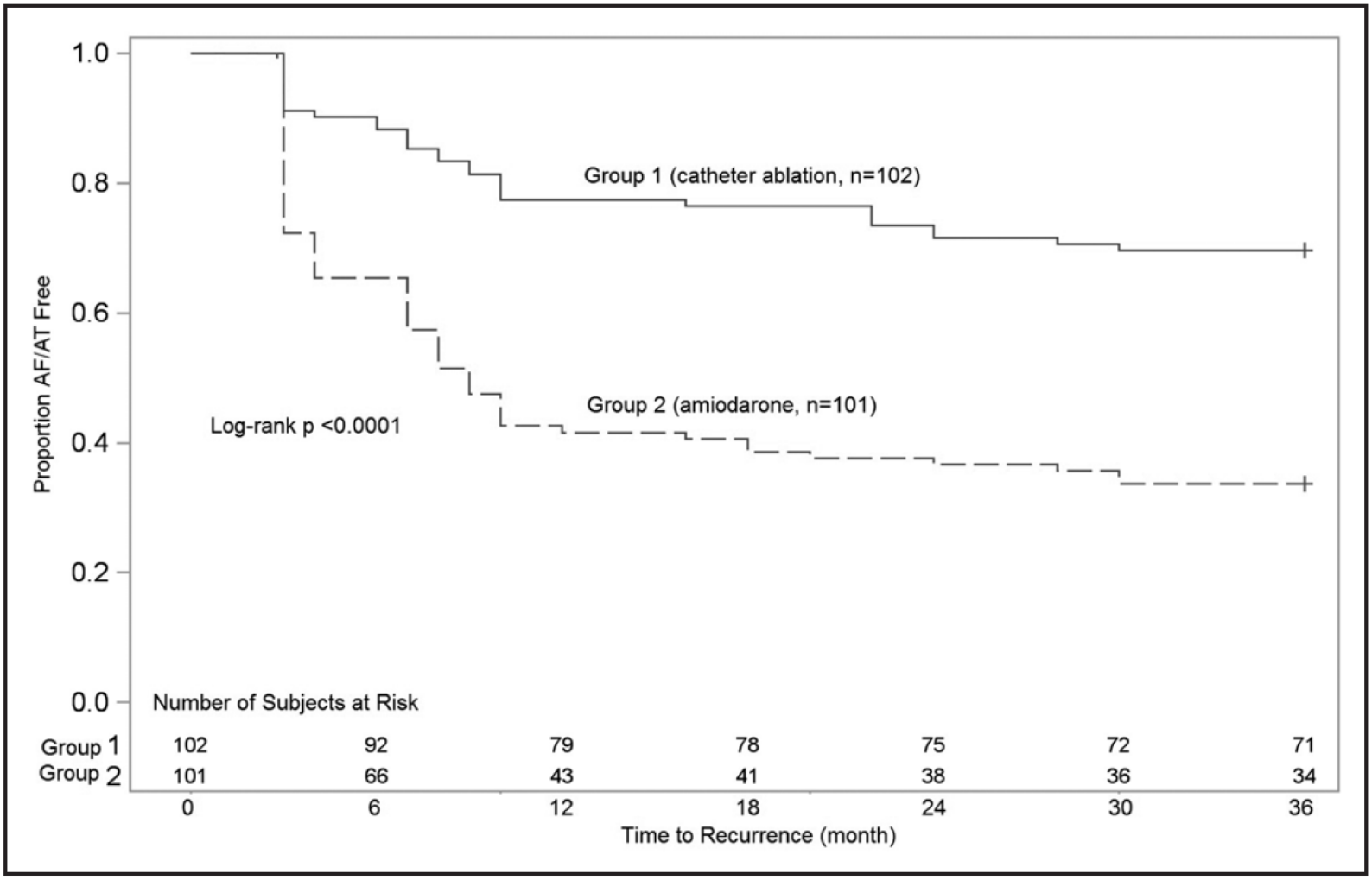


→ **Adverse effects of AA drugs and AV nodal blocking agents minimized !**

→ **Rhythm control by PVI is superior to best possible rate-control strategy !**

N Engl J Med 2008;359:1778-1785

Randomized Controlled Trial on CA of AF in HF: AATAC



Di Biase et al. Circulation 2016

Randomized Controlled Trial on CA of AF in HF: AATAC

- LVEF improved 9.6±7.4%, vs. 4.2±6.2% (p<0.001),
- 6MWD changed 27±38 vs. 8±42 (p<0.001),
- MLHFQ score reduced 14±18 vs. 2.9±15 (p<0.001) in recurrence-free versus patients with recurrence

- Over the 2 year follow-up:
  - Hospitalization rate substantially lower in Group 1 (32 [31%] vs. 58 [57%] in group 2, p <0.001)
  - All-cause Mortality in
  - Group 1 (8 [8%]) and 18 [18%] group 2, log-rank p=0.037);

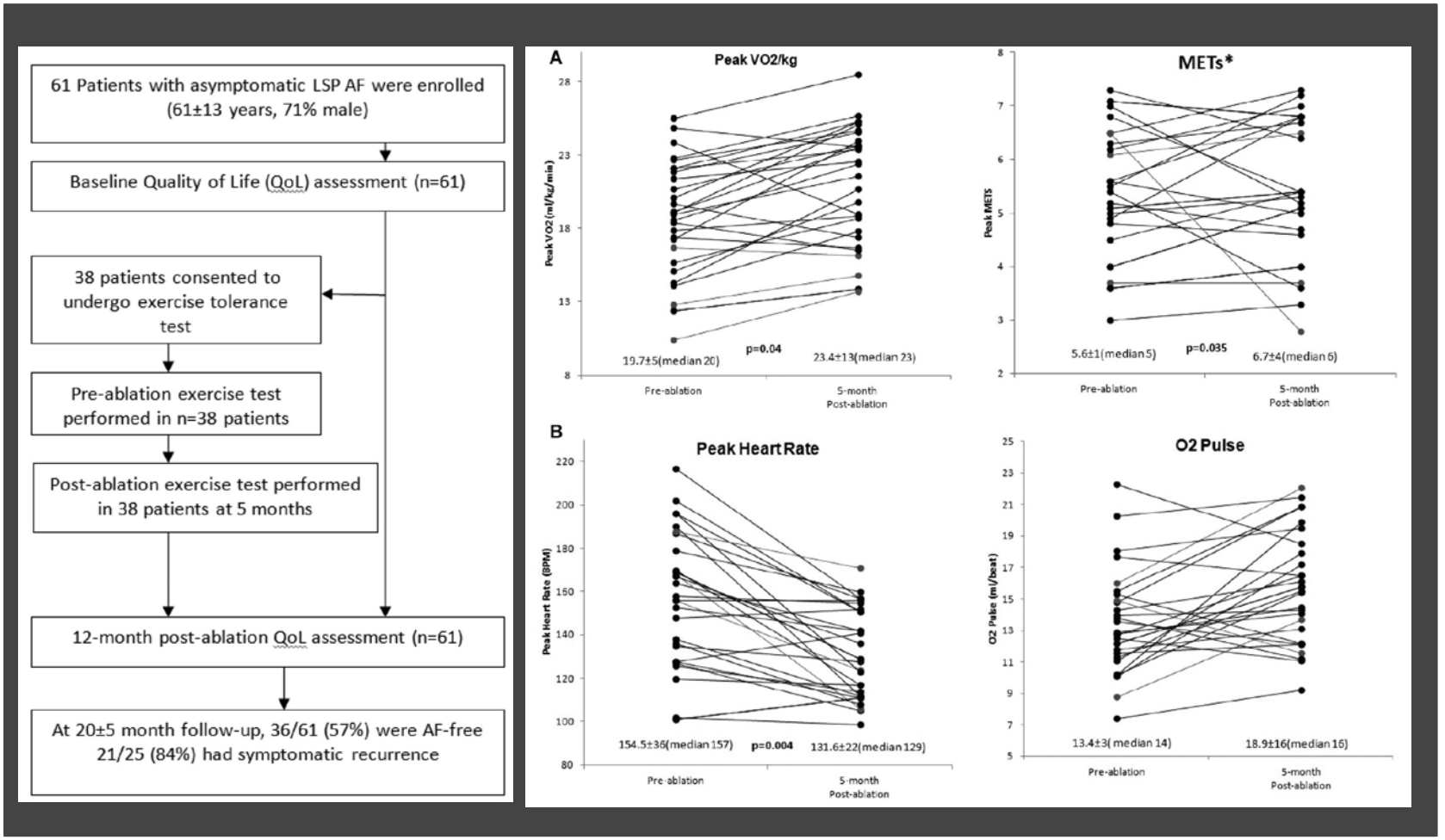
Di Biase et al. Circulation 2016

Catheter Ablation of Asymptomatic AF?

What is the benefit?

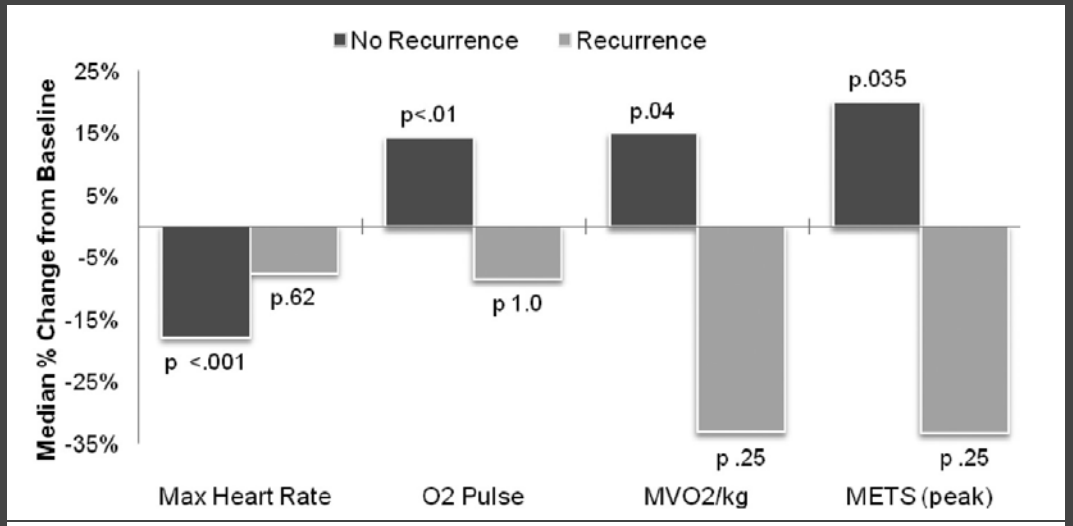
- 1. Will you live better?
- 2. You will live longer!
- 3. You will live longer and better!

Catheter Ablation of Asymptomatic Persistent AF



Mohanty et al. J Cardiovasc Electrophysiol 2014

Catheter Ablation of Asymptomatic Persistent AF



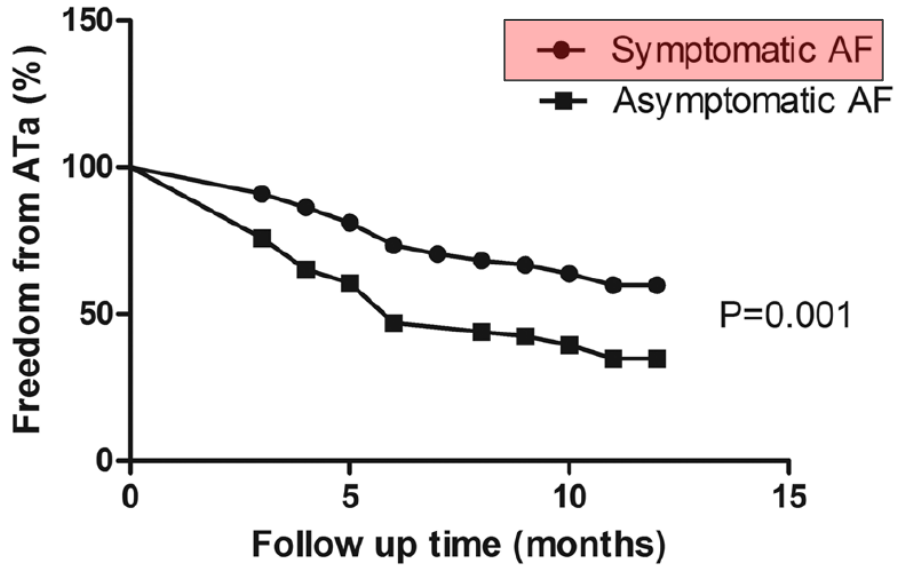
Arrhythmia Status and Heart Rate According to Symptom Status Among Patients with Recurrence

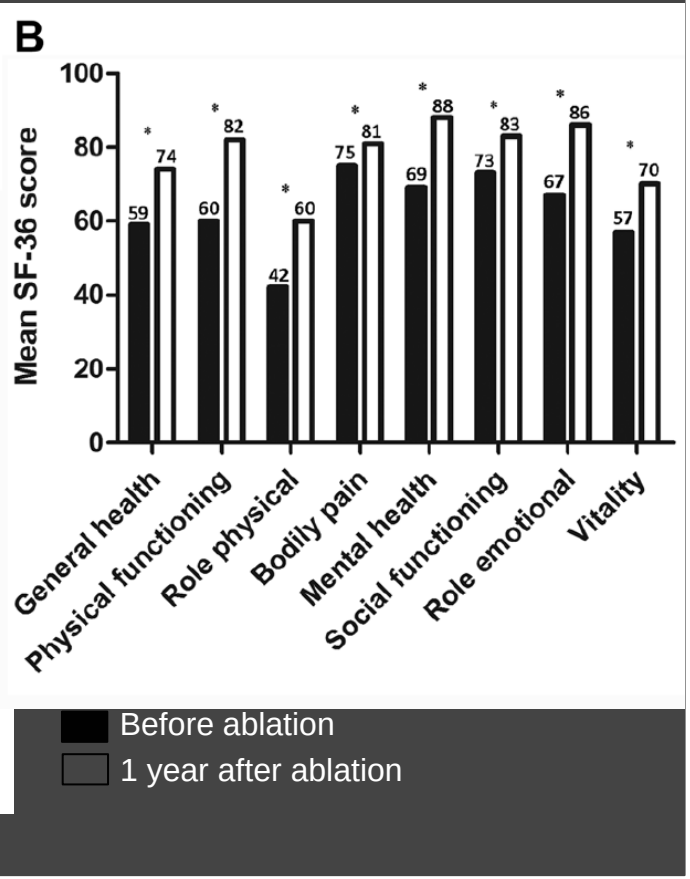
	Symptomatic		Asymptomatic	
	n	Heart Rate Range (Holter)	n	Heart Rate range (Holter)
AF	4 (57%)	110–150	3 (43%)	90–130
Atrial flutter	16 (94%)	140–164	1 (6%)	120–150
Atrial tachycardia	1 (100%)	154	0 (0%)	

Mohanty et al. J Cardiovasc Electrophysiol 2014

Catheter Ablation of Asymptomatic Persistent AF

66 pts with asymptomatic persistent AF compared with 132 matched controls with *symptomatic* persistent AF



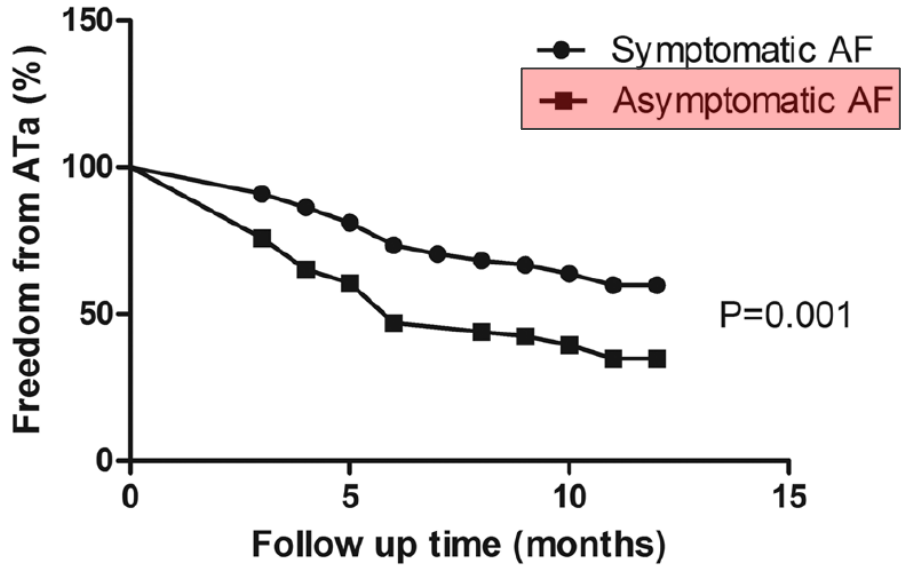


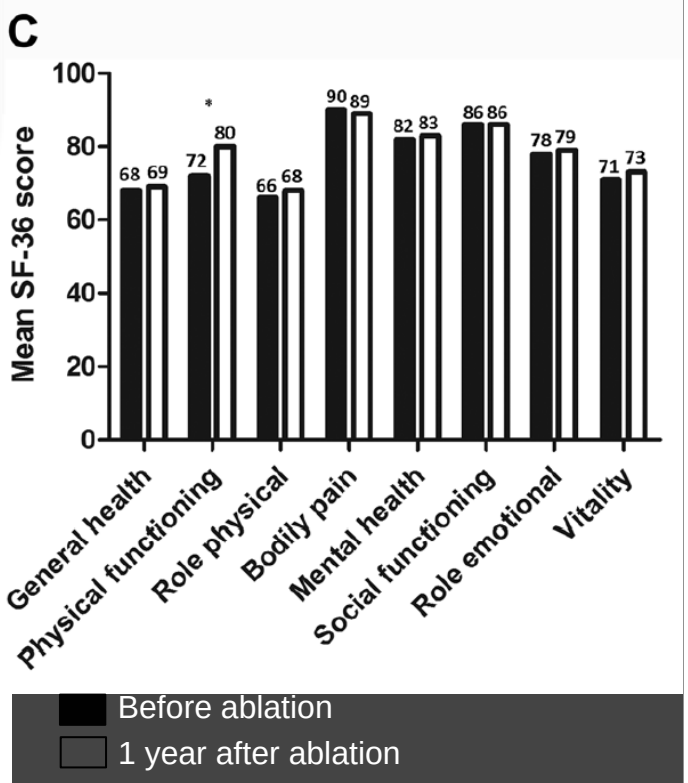
Wu et al. J Cardiovasc Electrophysiol 2016

Catheter Ablation of Asymptomatic Persistent AF

Conclusion

Our study revealed that current catheter ablation techniques are associated with a worse outcome in asymptomatic AF patients than in those with symptoms. This is mainly due to post-ablation AT that can cause significant symptoms in previously asymptomatic patients.





Wu et al. J Cardiovasc Electrophysiol 2016

Perspective

- **AMICA** (NCT00652522)
  Atrial Fibrillation Management In Congestive Heart Failure with Ablation
- **ARC-HF** (NCT00878384)
  Catheter Ablation versus Medical Rate Control for Atrial Fibrillation in Patients with Heart Failure
- **CASTLE-AF** (NCT00643188)
  Catheter Ablation versus Standard Conventional Treatment in Patients with LEft Ventricular Dysfunction and Atrial Fibrillation
- **CABANA** (NCT00578617)
  Catheter ABlation versus ANtiarrhythmic Drug Therapy for Atrial Fibrillation

2017 HRS/EHRA/ECAS/APRHS/SOLAECE Expert Consensus Statement on Catheter and Surgical Ablation of Atrial Fibrillation

Riccardo Cappato, MD

Disclosure Statement of Financial Interest

- Consultant to: Boston Scientific, Medtronic, St. Jude, Biosense Webster, ELA Sorin, Boehringer Ingelheim, Bayer HealthCare, Abbott, Pfizer
- Speaker's Bureau: Boston Scientific, Medtronic, St. Jude, Biosense Webster, BARD, Sanofi, Boehringer Ingelheim, Bayer HealthCare, Abbott
- Investigator: Medtronic, Biosense Webster, Sanofi, Cameron Health, BARD, Bayer HealthCare, Abbott, Pfizer
- Grants: Boston Scientific, Medtronic, St. Jude, Biosense Webster, BARD, ELA Sorin
- Equity and Intellectual Property Rights: Cameron Health

Expert Consensus Statement on AF Ablation

Introduction

- Definition, risk factors, and indications
- Strategies, technology, and technical aspects
- Follow-up, outcomes, and complications
- Training, surgical ablation, and clinical trial design

Expert Consensus Statement on AF Ablation

Technology and Tools

Ablation

- Radiofrequency energy
- Contact force
- Cryoablation
- Laser balloon technology
- Other balloon technologies
- Multielectrode circumferential ablation catheters (PVAC)

Expert Consensus Statement on AF Ablation

Technology and Tools

Mapping

- Electroanatomic
  - CARTO
  - NavX
  - Rhythmia
- Robotic and magnetic navigation system
- Ultrasound (ICE)
- PV venography
- CT and/or MRI scans and rotational angiography
- MRI of atrial fibrosis and RF lesions and MRI-guided ablation

Expert Consensus Statement on AF Ablation

Atrial Fibrillation Ablation: Strategies, Techniques, and Endpoints

	Recommendation	Class	LOE
PV isolation by catheter ablation	Electrical isolation of the PVs is recommended during all AF ablation procedures.	I	A
	Achievement of electrical isolation requires, at a minimum, assessment and demonstration of entrance block into the PV.	I	B-R
	Monitoring for PV reconnection for 20 minutes following initial PV isolation is reasonable.	IIa	B-R
	Administration of adenosine 20 minutes following initial PV isolation using RF energy with reablation if PV reconnection might be considered.	IIb	B-R
	Use of a pace-capture (pacing along the ablation line) ablation strategy may be considered.	IIb	B-R
	Demonstration of exit block may be considered.	IIb	B-NR

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Expert Consensus Statement on AF Ablation

Atrial Fibrillation Ablation: Strategies, Techniques, and Endpoints

Ablation strategies to be considered for use in conjunction with PV isolation	If a patient has a history of typical atrial flutter or typical atrial flutter is induced at the time of AF ablation, delivery of a cavotricuspid isthmus linear lesion is recommended.	I	B-R
	If linear ablation lesions are applied, operators should use mapping and pacing maneuvers to assess for line completeness.	I	C-LD
	If a reproducible focal trigger that initiates AF is identified outside the PV ostia at the time of an AF ablation procedure, ablation of the focal trigger should be considered.	IIa	C-LD
	When performing AF ablation with a force-sensing RF ablation catheter, a minimal targeted contact force of 5 to 10 grams is reasonable.	IIa	C-LD
	Posterior wall isolation might be considered for initial or repeat ablation of persistent or long-standing persistent AF.	IIb	C-LD

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Expert Consensus Statement on AF Ablation

Atrial Fibrillation Ablation: Strategies, Techniques, and Endpoints

Ablation strategies to be considered for use in conjunction with PV isolation	Administration of high-dose isoproterenol to screen for and then ablate non-PV triggers may be considered during initial or repeat AF ablation procedures in patients with paroxysmal, persistent, or long-standing persistent AF.	IIb	C-LD
	DF-based ablation strategy is of unknown usefulness for AF ablation.	IIb	C-LD
	The usefulness of creating linear ablation lesions in the right or left atrium as an initial or repeat ablation strategy for persistent or long-standing persistent AF is not well established.	IIb	B-NR
	The usefulness of linear ablation lesions in the absence of macroreentrant atrial flutter is not well established.	IIb	C-LD

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Expert Consensus Statement on AF Ablation

Atrial Fibrillation Ablation: Strategies, Techniques, and Endpoints

Ablation strategies to be considered for use in conjunction with PV isolation	The usefulness of mapping and ablation of areas of abnormal myocardial tissue identified with voltage mapping or MRI as an initial or repeat ablation strategy for persistent or long-standing persistent AF is not well established.	IIb	B-R
	The usefulness of ablation of complex fractionated atrial electrograms as an initial or repeat ablation strategy for persistent and long-standing persistent AF is not well established.	IIb	B-R
	The usefulness of ablation of rotational activity as an initial or repeat ablation strategy for persistent and long-standing persistent AF is not well established.	IIb	B-NR
	The usefulness of ablation of autonomic ganglia as an initial or repeat ablation strategy for paroxysmal, persistent, and long-standing persistent AF is not well established.	IIb	B-NR

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Expert Consensus Statement on AF Ablation

Atrial Fibrillation Ablation: Strategies, Techniques, and Endpoints

Nonablation strategies to improve outcomes	Weight loss can be useful for patients with AF, including those who are being evaluated to undergo an AF ablation procedure, as part of a comprehensive risk factor management strategy.	IIa	B-R
	It is reasonable to consider a patient's BMI when discussing the risks, benefits, and outcomes of AF ablation with a patient being evaluated for an AF ablation procedure.	IIa	B-R
	It is reasonable to screen for signs and symptoms of sleep apnea when evaluating a patient for an AF ablation procedure and to recommend a sleep evaluation if sleep apnea is suspected.	IIa	B-R
	Treatment of sleep apnea can be useful for patients with AF, including those who are being evaluated to undergo an AF ablation procedure.	IIa	B-R
	The usefulness of discontinuation of antiarrhythmic drug therapy prior to AF ablation in an effort to improve long-term outcomes is unclear.	IIb	C-LD
	The usefulness of initiation or continuation of antiarrhythmic drug therapy during the postablation healing phase in an effort to improve long-term outcomes is unclear.	IIb	C-LD

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Expert Consensus Statement on AF Ablation

Atrial Fibrillation Ablation: Strategies, Techniques, and Endpoints

Strategies to reduce the risks of AF ablation	Careful identification of the PV ostia is mandatory to avoid ablation within the PVs.	I	B-NR
	It is recommended that RF power be reduced when creating lesions along the posterior wall near the esophagus.	I	C-LD
	It is reasonable to use an esophageal temperature probe during AF ablation procedures to monitor esophageal temperature and help guide energy delivery.	IIa	C-EO

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Access the Consensus Statement and Summary Tools

To access the complete clinical document and related summary tools, please visit http://www.hrsonline.org/Policy-Payment/Clinical-Guidelines-Documents

- Executive Summary
- Full document
- Presentation slides