Yalnızca PV izolasyonu yeterlidir

Uzm.Dr. Meryem KARA

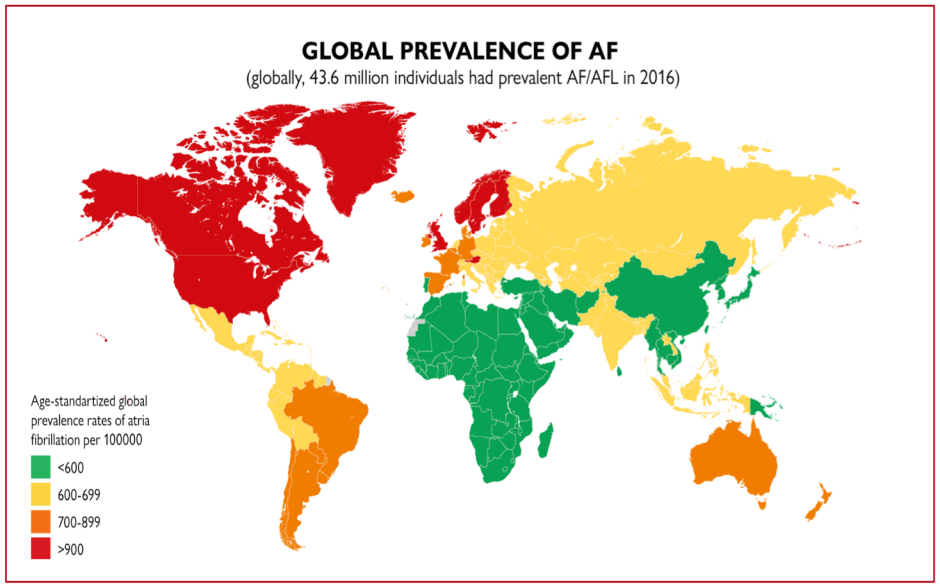
Ankara Şehir Hastanesi

Yüksek İhtisas EPS Ekibi

	Definition
AF	A supraventricular tachyarrhythmia with uncoordinated atrial electrical activation and consequently ineffective atrial contraction. *Electrocardiographic characteristics of AF include:* ● Irregularly irregular R-R intervals (when atrioventricular conduction is not impaired), ● Absence of distinct repeating P waves, and ● Irregular atrial activations.
	Currently used terms
Clinical AF	*Symptomatic* or *asymptomatic* AF that is documented by surface ECG. The minimum duration of an ECG tracing of AF required to establish the diagnosis of clinical AF is at least 30 seconds, or entire 12-lead ECG.[1,2]
AHRE, subclinical AF	Refers to individuals *without symptoms attributable to AF*, in whom *clinical AF is NOT previously detected (that is, there is no surface ECG tracing of AF)*, see also *section 3.3*. **AHRE** - events fulfilling programmed or specified criteria for AHRE that are detected by CIEDs with an atrial lead allowing automated continuous monitoring of atrial rhythm and tracings storage. CIED-recorded AHRE need to be visually inspected because some AHRE may be electrical artefacts/false positives. **Subclinical AF** includes AHRE confirmed to be AF, AFL, or an AT, or AF episodes detected by insertable cardiac monitor or wearable monitor and confirmed by visually reviewed intracardiac electrograms or ECG-recorded rhythm.

Figure 2 (1) Epidemiology of AF: prevalence

ESC European Society of Cardiology



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2020 ESC Guidelines for the diagnosis and management of atrial fibrillation
(European Heart Journal 2020-doi/10.1093/eurheartj/ehaa612)

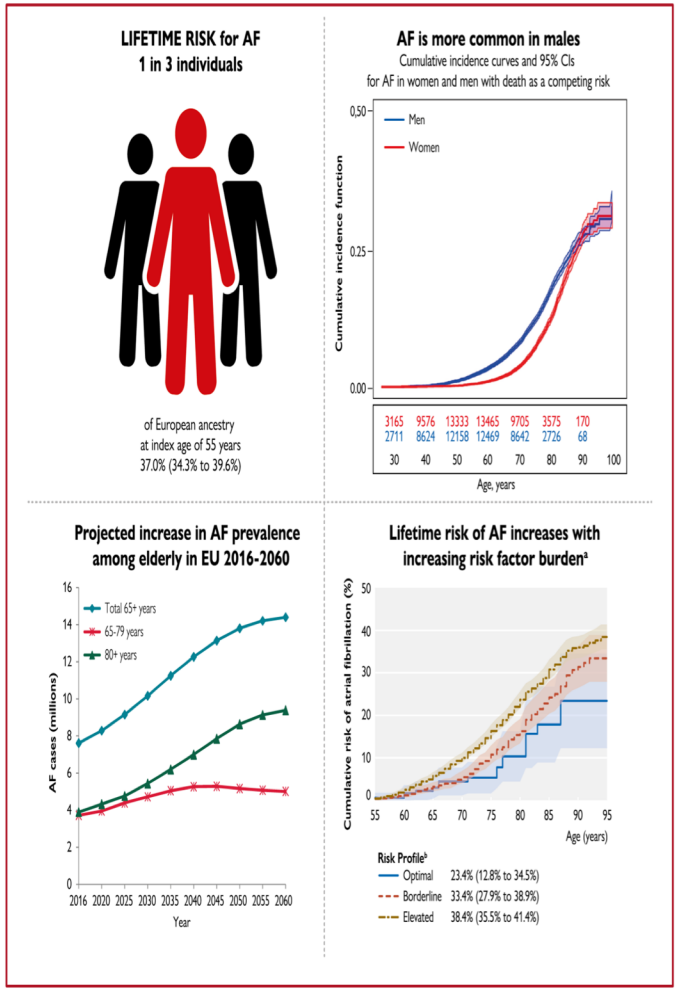

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Figure 2 (2)
Epidemiology of AF: lifetime risk and projected rise in the incidence and prevalence

[a]Smoking, alcohol consumption, body mass index, BP, diabetes mellitus (type 1 or 2), and history of myocardial infarction or heart failure. [b]Risk profile: *optimal* – all risk factors are negative or within the normal range; *borderline* – no elevated risk factors but >1 borderline risk factor; *elevated* – >1 elevated risk factor.

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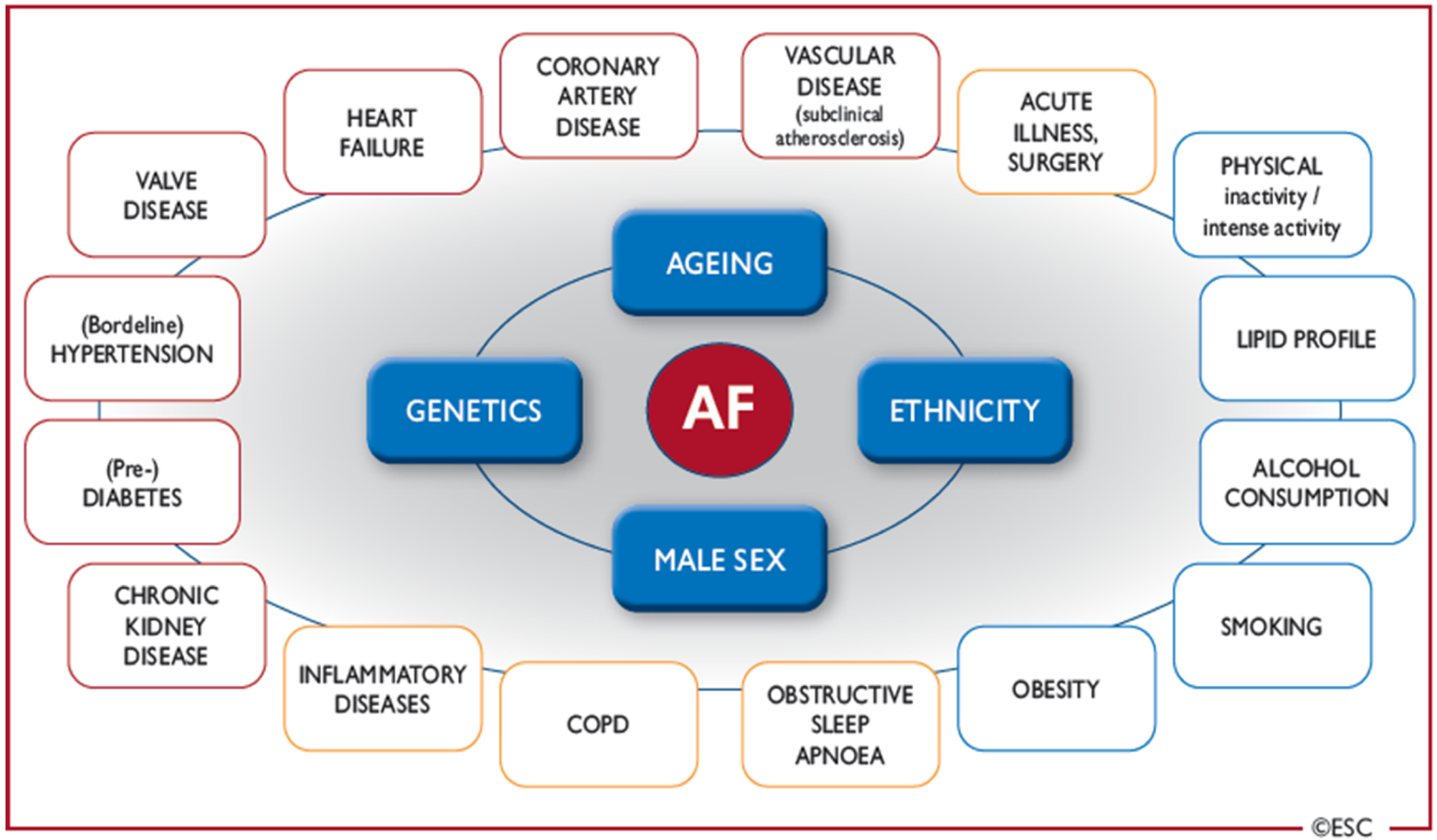
2020 ESC Guidelines for the diagnosis and management of atrial fibrillation
(European Heart Journal 2020-doi/10.1093/eurheartj/ehaa612)

Figure 3 Summary of risk factors for incident AF



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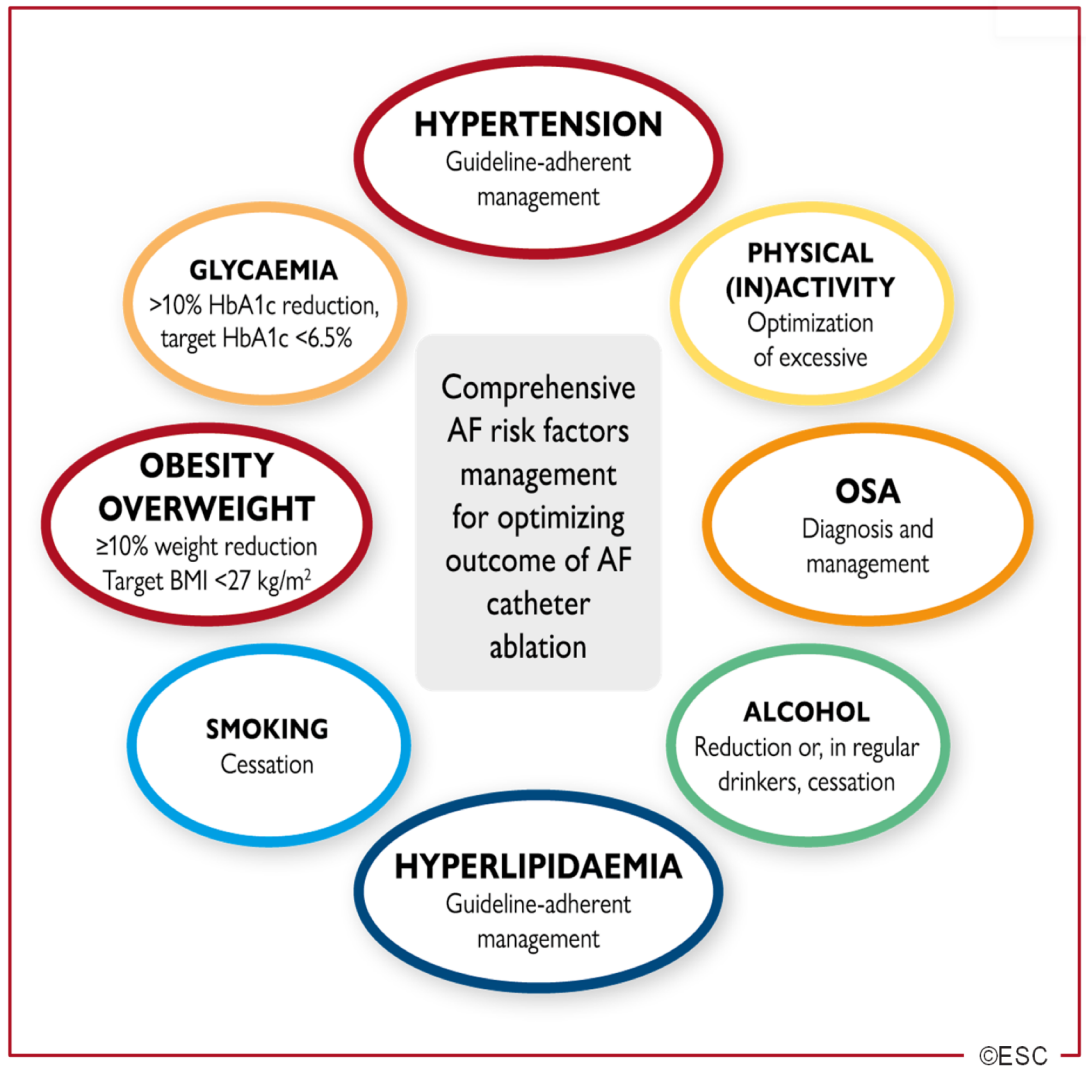

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Figure 18 Contribution of AF risk factors to the development of an abnormal substrate translating into poorer outcomes with rhythm control strategies

Several AF risk factors may contribute to the development of LA substrates and thus affect the outcome of AF catheter ablation, predisposing to a higher recurrence rate. Aggressive control of modifiable risk factors may reduce recurrence rate

2020 ESC Guidelines for the diagnosis and management of atrial fibrillation
(European Heart Journal 2020-doi/10.1093/eurheartj/ehaa612)

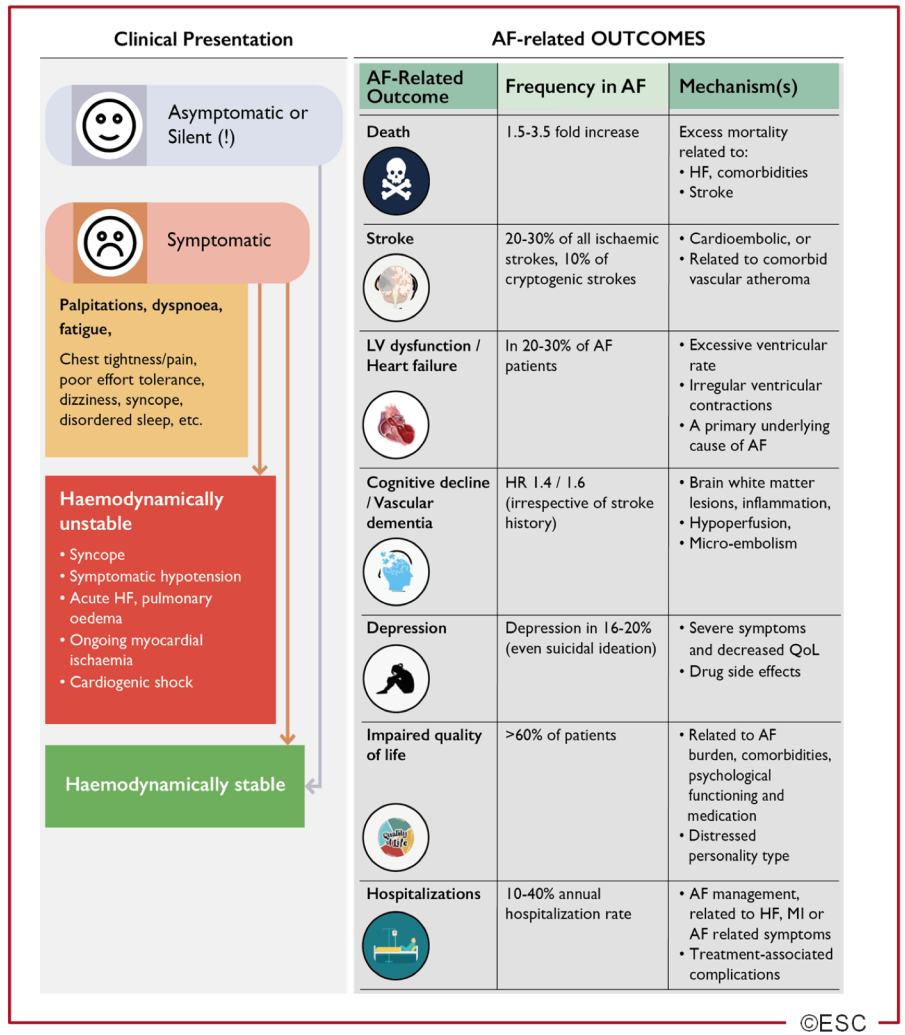

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Figure 4 Clinical presentation of AF and AF-related outcomes

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(European Heart Journal 2020-doi/10.1093/eurheartj/ehaa612)

Table 6 EHRA symptom scale

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Score	Symptoms	Description
1	None	AF does not cause any symptoms
2a	Mild	Normal daily activity not affected by symptoms related to AF
2b	Moderate	Normal daily activity not affected by symptoms related to AF, but patient troubled by symptoms
3	Severe	Normal daily activity affected by symptoms related to AF
4	Disabling	Normal daily activity discontinued

Table 4 Classification of AF (1)

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AF pattern	Definition
First diagnosed	AF not diagnosed before, irrespective of its duration or the presence/severity of AF-related symptoms.
Paroxysmal	AF that terminates spontaneously or with intervention within 7 days of onset.
Persistent	AF that is continuously sustained beyond 7 days, including episodes that are terminated by cardioversion (drugs or direct current cardioversion) after 7 days or more.
Long-standing persistent	Continuous AF of >12 months' duration when decided to adopt a rhythm control strategy.
Permanent	AF that is accepted by the patient and physician, and no further attempts to restore/maintain sinus rhythm will be undertaken. Permanent AF represents a therapeutic attitude of the patient and physician rather than an inherent pathophysiological attribute of AF, and the term should not be used in the context of a rhythm control strategy with antiarrhythmic drug therapy or AF ablation. Should a rhythm control strategy be adopted, the arrhythmia would be re-classified as 'long-standing persistent AF'.

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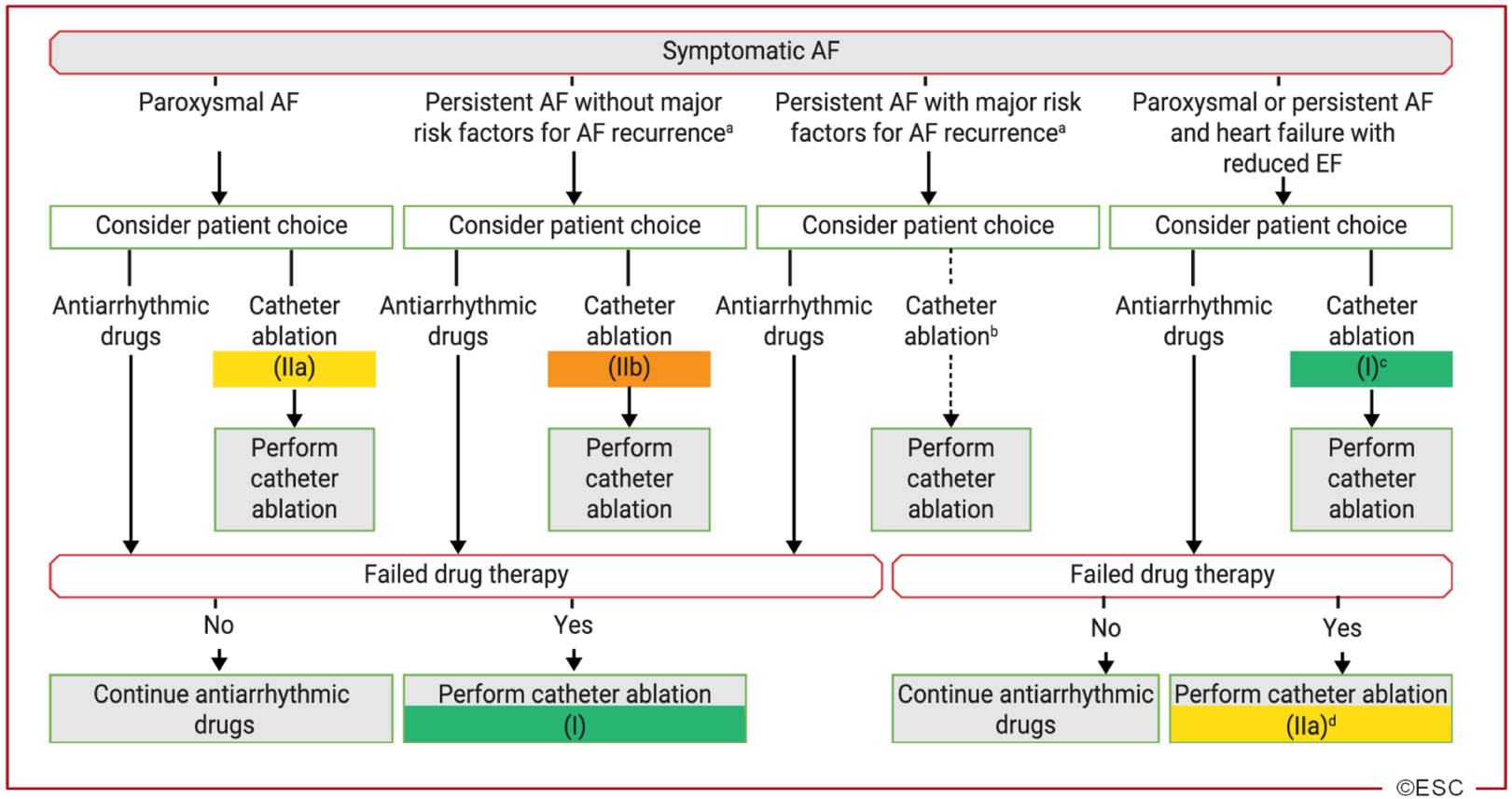
(European Heart Journal 2020-doi/10.1093/eurheartj/ehaa612)

Recommendations for rhythm control

Recommendations	Class	Level
Rhythm control therapy is recommended for symptom and QoL improvement in symptomatic patients with AF.	I	A

Figure 17 Indications for catheter ablation of symptomatic AF



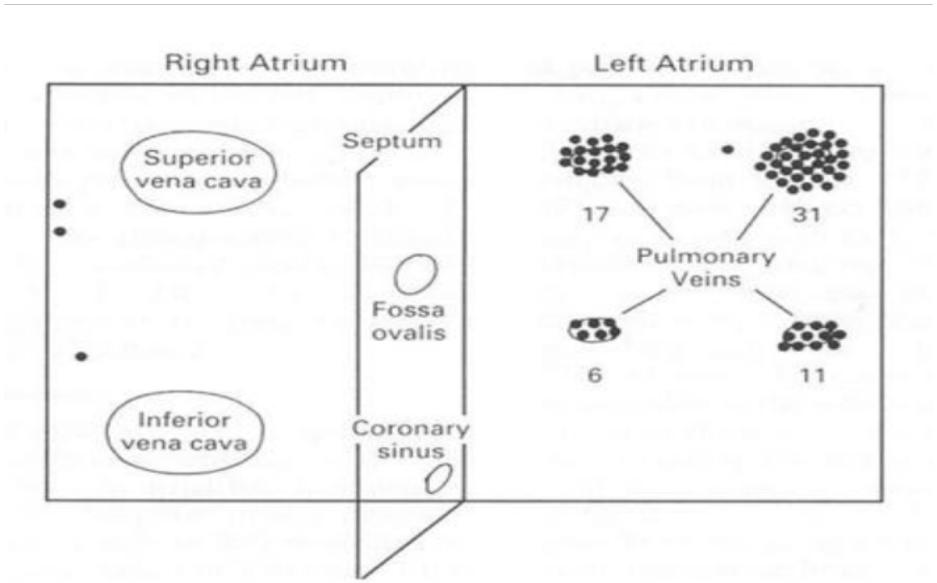
[a]Significantly enlarged LA volume, advanced age, long AF duration, renal dysfunction, and other cardiovascular risk factors. [b]In rare individual circumstances, catheter ablation may be carefully considered as first-line therapy. [c]Recommended to reverse LV dysfunction when tachycardiomyopathy is highly probable. [d]To improve survival and reduce hospitalization.

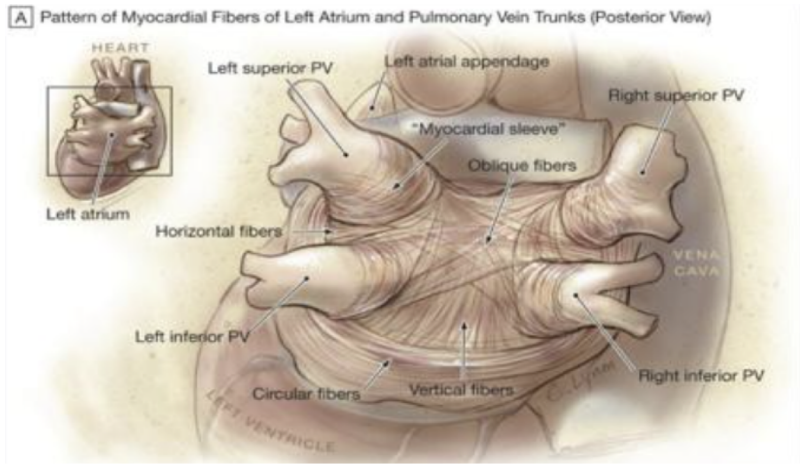
2020 ESC Guidelines for the diagnosis and management of atrial fibrillation
(European Heart Journal 2020-doi/10.1093/eurheartj/ehaa612)

AF catheter ablation for PVI should be considered as a strategy to avoid pacemaker implantation in patients with AF-related bradycardia or symptomatic pre-automaticity pause after AF conversion considering the clinical situation.	**IIa**	**C**

SPONTANEOUS INITIATION OF ATRIAL FIBRILLATION BY ECTOPIC BEATS ORIGINATING IN THE PULMONARY VEINS

MICHEL HAÏSSAGUERRE, M.D., PIERRE JAÏS, M.D., DIPEN C. SHAH, M.D., ATSUSHI TAKAHASHI, M.D., MÉLÈZE HOCINI, M.D., GILLES QUINIOU, M.D., STÉPHANE GARRIGUE, M.D., ALAIN LE MOUROUX, M.D., PHILIPPE LE MÉTAYER, M.D., AND JACQUES CLÉMENTY, M.D.



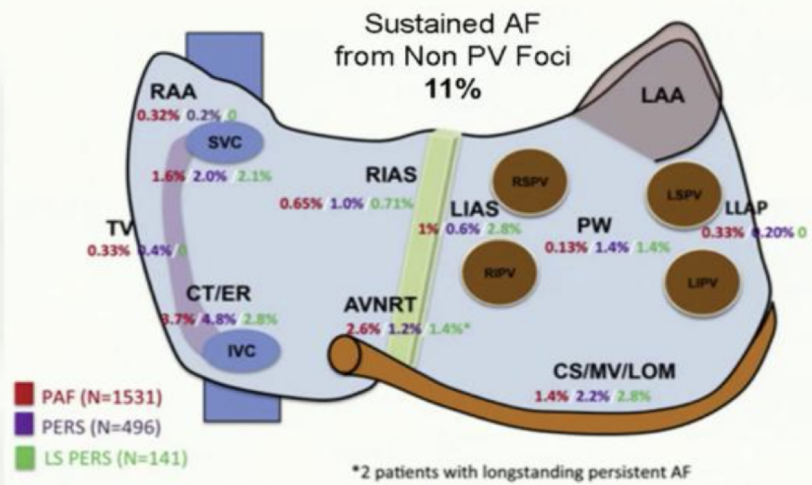


Non PV Triggers: Where are they?

–CS
– SVC
–LAA

–CT
–LoM
–MV/TV Annuli

–Lt persistent SVC
–IVC, RAA…



Santangeli et al. Heart Rhythm 2017;14:1087–1096

Atrial Fibrillation Mechanisms:
It is not so clear

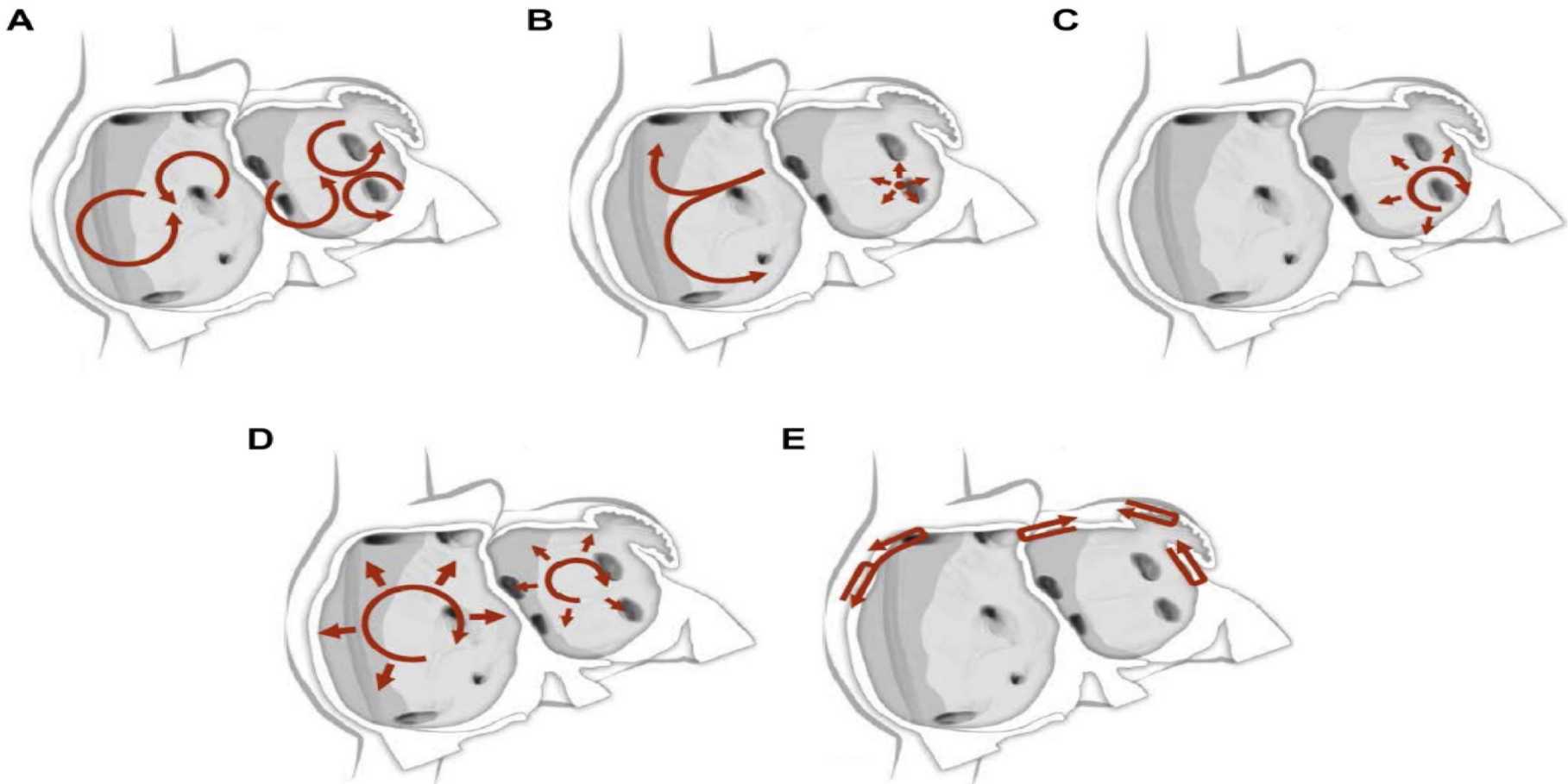


Figure 3 Schematic drawing showing various hypotheses and proposals concerning the mechanisms of atrial fibrillation. **A:** Multiple wavelets hypothesis. **B:** Rapidly discharging automatic foci. **C:** Single reentrant circuit with fibrillatory conduction. **D:** Functional reentry resulting from rotors or spiral waves. **E:** AF maintenance resulting from dissociation between epicardial and endocardial layers, with mutual interaction producing multiplying activity that maintains the arrhythmia.

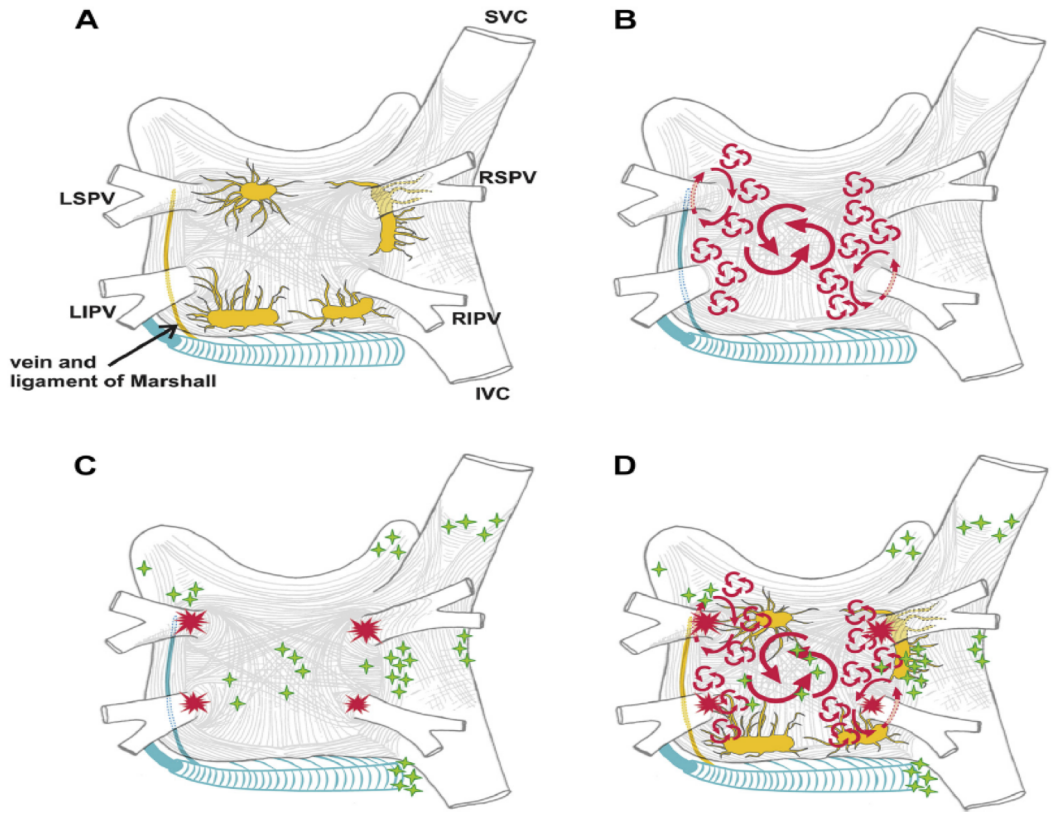
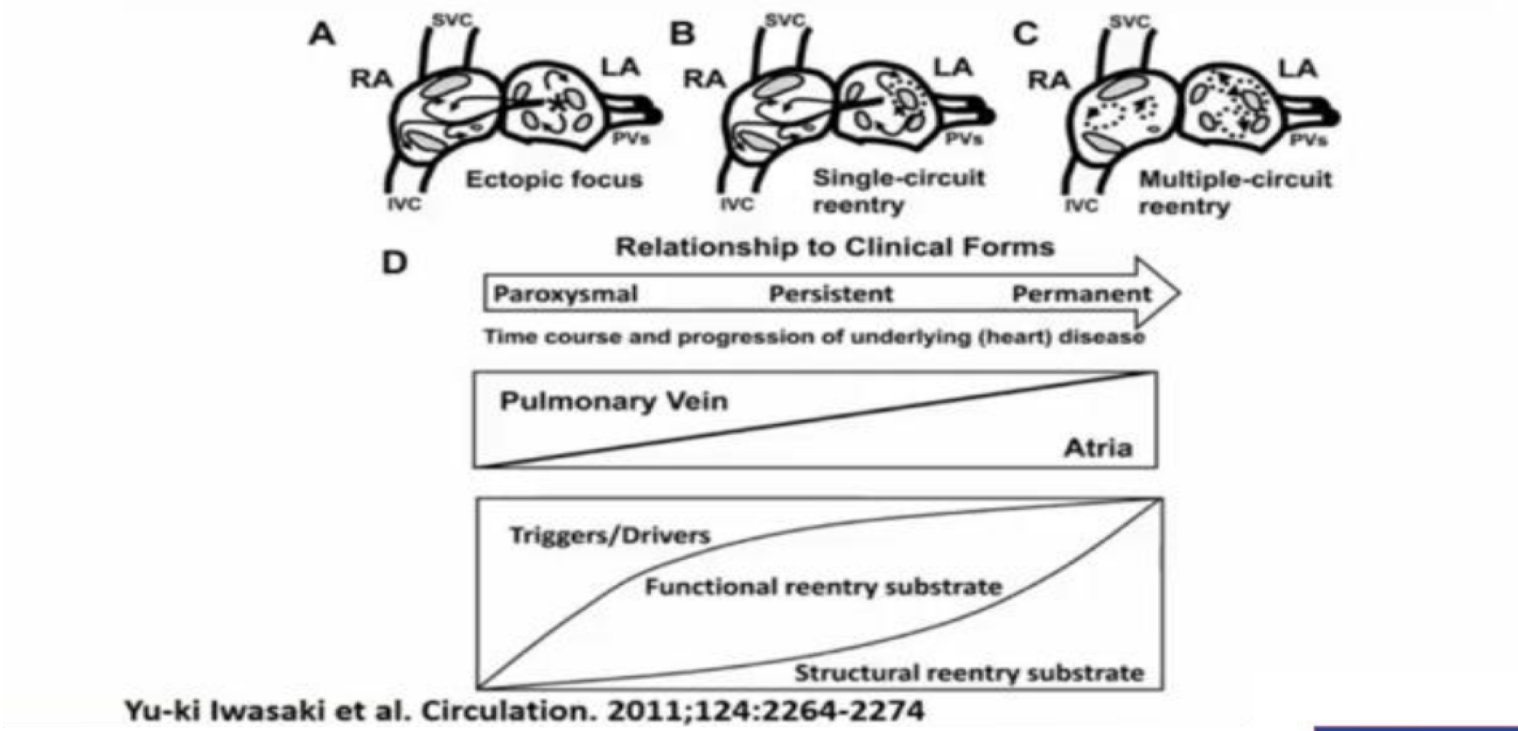
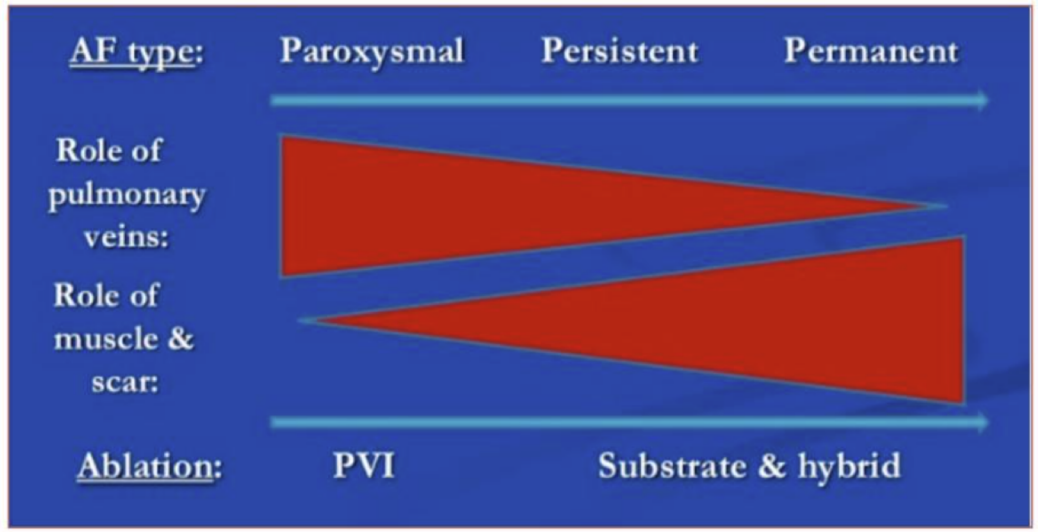
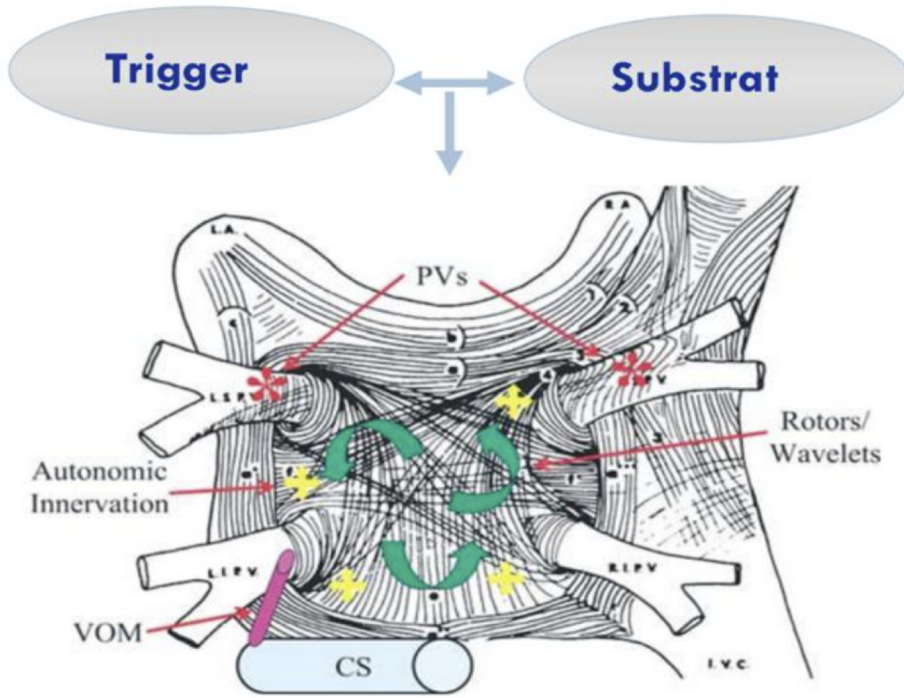


Figure 4 Structure and mechanisms of atrial fibrillation. **A:** Schematic drawing of the left and right atria as viewed from the posterior perspective. The extension of muscular fibers onto the PVs can be appreciated. Shown in yellow are the five major left atrial autonomic ganglionic plexi (GP) and axons (superior left GP, inferior left GP, anterior right GP, inferior right GP, and ligament of Marshall). Shown in blue is the coronary sinus, which is enveloped by muscular fibers that have connections to the atria. Also shown in blue is the vein and ligament of Marshall, which travels from the coronary sinus to the region between the left superior PV and the left atrial appendage. **B:** The large and small reentrant wavelets that play a role in initiating and sustaining AF. **C:** The common locations of PV (red) and also the common sites of origin of non-PV triggers (shown in green). **D:** Composite of the anatomic and arrhythmic mechanisms of AF. Adapted with permission from Calkins et al. Heart Rhythm 2012; 9:632–696.e21.[2]



Yu-ki Iwasaki et al. Circulation. 2011;124:2264-2274

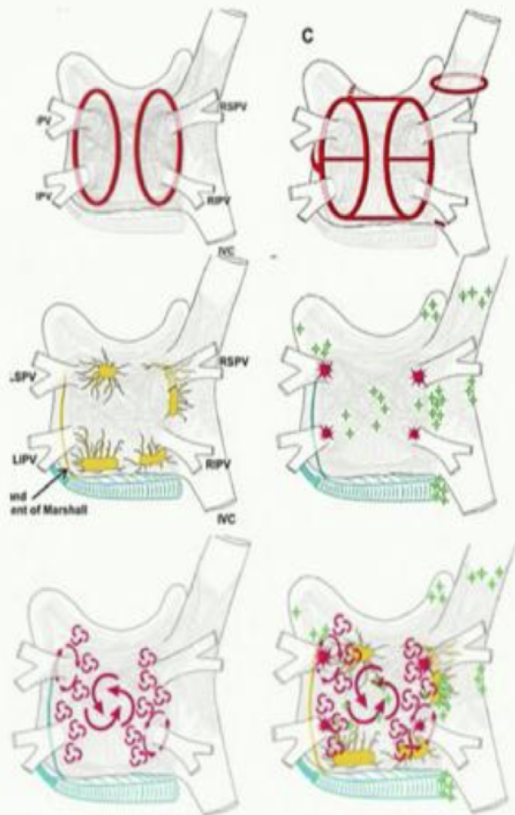



Trigger
Substrat
PVs
Rotors/
Wavelets
Autonomic
Innervation
VOM
CS

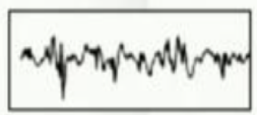
- PVI
- LA Roof line
- Mitral Isthmus line
- Ligament of Marshall ablation
- Coronary sinus ablation
- SVC Isolation

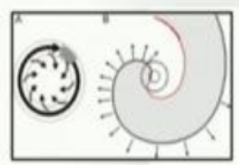
- Posterior wall Isolation
- LA Appendage isolation
- CFAE
- Ganglionated Plexus ablation
- Focal Impulse and Rotor modification
- MRI guided low voltage area (LVA) ablation

Ablation Therapy beyond PVI



- Lines Flutter: Roof, Mitral, CTI, other (GP's)
- Non PV Triggers
  - LAPW; SVC; Septum
  - LAA; CS;
  - LoM; Crista; IVC
- Substrate Modification
  - CFAE's
  - Scar
  - Focal sources, Rotors …





	Par AF	Pers AF
Definition	<7 days	>= 7 days
AF Mechanism	PV or non-PV triggers	Reentry and Wavelet
LA size	Usually normal	Usually enlarged
LA Voltage	Usually normal	Often abnormal
Pharmacological Rx	Class IC/ III AAD	Class III AAD
Risk Factor Reduction	Useful	Useful ++
Ablation Target	PV	PV +/- ??????????????

Catheter Ablation for Atrial Fibrillation

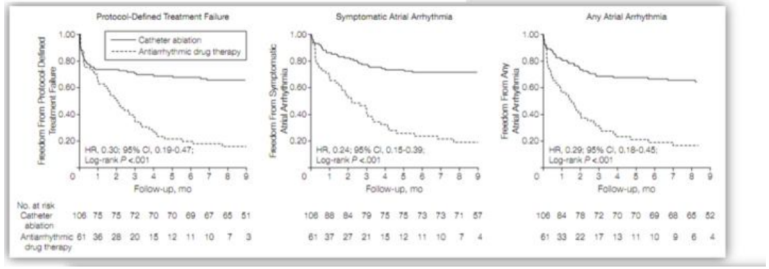
Are Results Maintained at 5 Years of Follow-Up?

Rukshen Weerasooriya, BMEDSC(HONS), MBBS,*† Paul Khairy, MD, PHD,‡ Jean Litalien, MD,* Laurent Macle, MD,‡ Meleze Hocini, MD,* Frederic Sacher, MD,* Nicolas Lellouche, MD,* Sebastien Knecht, MD,* Matthew Wright, PHD, MD,* Isabelle Nault, MD,* Shinsuke Miyazaki, MD,* Christophe Scavee, MD,* Jacques Clementy, MD,* Michel Haissaguerre, MD,* Pierre Jais, MD*

Bordeaux-Pessac, France; Crawley, Western Australia; and Montreal, Quebec, Canada

Comparison of Antiarrhythmic Drug Therapy and Radiofrequency Catheter Ablation in Patients With Paroxysmal Atrial Fibrillation

A Randomized Controlled Trial



ORIGINAL ARTICLE

Cryoballoon or Radiofrequency Ablation for Paroxysmal Atrial Fibrillation

Karl-Heinz Kuck, M.D., Josep Brugada, M.D., Alexander Fürnkranz, M.D., Andreas Metzner, M.D., Feifan Ouyang, M.D., K.R. Julian Chun, M.D., Arif Elvan, M.D., Ph.D, Thomas Arentz, M.D., Kurt Bestehorn, M.D., Stuart J. Pocock, Ph.D., Jean-Paul Albenque, M.D., Ph.D., and Claudio Tondo, M.D., Ph.D., for the FIRE AND ICE Investigators*

ORIGINAL ARTICLE

Approaches to Catheter Ablation for Persistent Atrial Fibrillation

Atul Verma, M.D., Chen-yang Jiang, M.D., Timothy R. Betts, M.D., M.B., Ch.B., Jian Chen, M.D., Isabel Deisenhofer, M.D., Roberto Mantovan, M.D., Ph.D., Laurent Macle, M.D., Carlos A. Morillo, M.D., Wilhelm Haverkamp, M.D., Ph.D., Rukshen Weerasooriya, M.D., Jean-Paul Albenque, M.D., Stefano Nardi, M.D., Endrj Menardi, M.D., Paul Novak, M.D., and Prashanthan Sanders, M.B., B.S., Ph.D., for the STAR AF II Investigators*

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OCTOBER 1, 2020 VOL. 383 NO. 14

Early Rhythm-Control Therapy in Patients with Atrial Fibrillation

P. Kirchhof, A.J. Camm, A. Goette, A. Brandes, L. Eckardt, A. Elvan, T. Fetsch, I.C. van Gelder, D. Haase, L.M. Haegeli, F. Hamann, H. Heidbüchel, G. Hindricks, J. Kautzner, C.-H. Kuck, L. Mont, G.A. Ng, J. Rekosz, N. Schoen, U. Schotten, A. Suling, J. Taggeselle, S. Themistoclakis, E. Vettorazzi, P. Vardas, K. Wegscheider, S. Willems, H.J.G.M. Crijns, and G. Breithardt, for the EAST-AFNET 4 Trial Investigators*

EAST – AFNET 4 Hypothesis and setting

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 1, 2018 VOL. 378 NO. 5

Catheter Ablation for Atrial Fibrillation with Heart Failure

Nassir F. Marrouche, M.D., Johannes Brachmann, M.D., Dietrich Andresen, M.D., Jürgen Siebels, M.D., Lucas Boersma, M.D., Luc Jordaens, M.D., Béla Merkely, M.D., Evgeny Pokushalov, M.D., Prashanthan Sanders, M.D., Jochen Proff, B.S., Heribert Schunkert, M.D., Hildegard Christ, M.D., Jürgen Vogt, M.D., and Dietmar Bänsch, M.D., for the CASTLE-AF Investigators*

AFNET

east
early treatment of atrial fibrillation for stroke prevention trial

EHRA
European Heart Rhythm Association
European Society of Cardiology

Does early rhythm control therapy improve outcomes compared to usual care in patients with early, recently diagnosed atrial fibrillation at risk of stroke?

EAST- AFNET 4 is a multi-centre, investigator-initiated trial. Sponsor is AFNET,

supported by AFNET, BMBF, DHS, DZHK, EHRA, Sanofi, St Jude Medical/Abbott.

Atrial Fibrillation Ablation Strategies

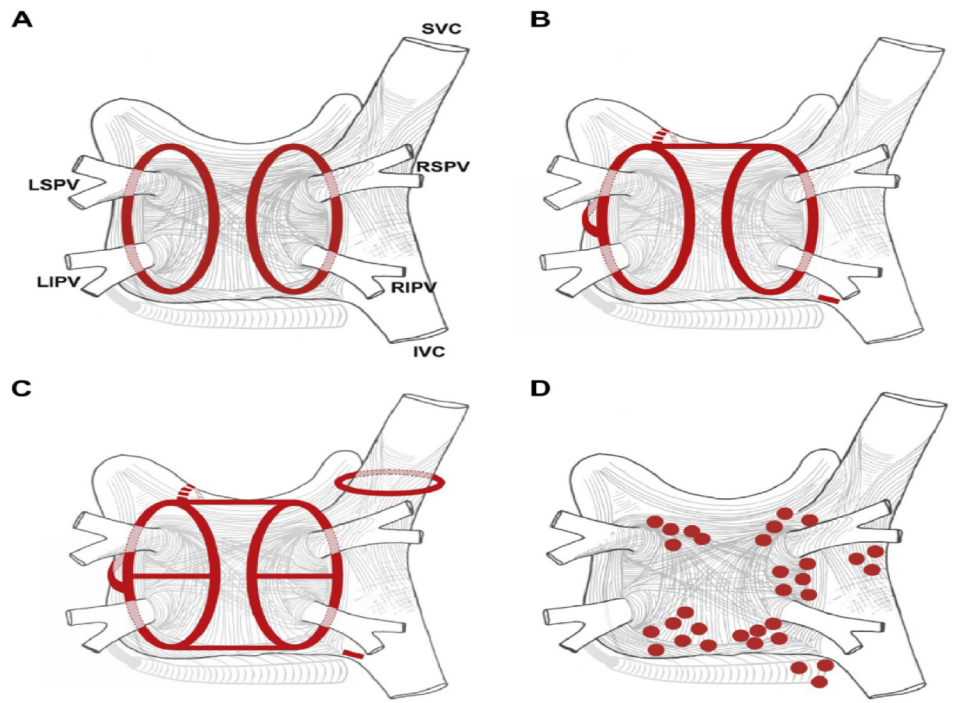


Figure 6 Schematic of common lesion sets employed in AF ablation. **A:** The circumferential ablation lesions that are created in a circumferential fashion around the right and the left PVs. The primary endpoint of this ablation strategy is the electrical isolation of the PV musculature. **B:** Some of the most common sites of linear ablation lesions. These include a "roof line" connecting the lesions encircling the left and/or right PVs, a "mitral isthmus" line connecting the mitral valve and the lesion encircling the left PVs at the end of the left inferior PV, and an anterior linear lesion connecting either the "roof line" or the left or right circumferential lesion to the mitral annulus anteriorly. A linear lesion created at the cavotricuspid isthmus is also shown. This lesion is generally placed in patients who have experienced cavotricuspid isthmus-dependent atrial flutter clinically or have it induced during EP testing. **C:** Similar to 6B, but also shows additional linear ablation lesions between the superior and inferior PVs resulting in a figure of eight lesion sets as well as a posterior inferior line allowing for electrical isolation of the posterior left atrial wall. An encircling lesion of the superior vena cava (SVC) directed at electrical isolation of the SVC is also shown. SVC isolation is performed if focal firing from the SVC can be demonstrated. A subset of operators empirically isolates the SVC. **D:** Representative sites for ablation when targeting rotational activity or CFAEs are targeted. Modified with permission from Calkins et al. Heart Rhythm 2012; 9:632–696.e21.[2]

Atrial Fibrillation Ablation Strategies for Paroxysmal Patients

Randomized Comparison Between Different Techniques

Luigi Di Biase, MD; Claude S. Elayi, MD; Tamer S. Fahmy, MD; David O. Martin, MD; Chi Keong Ching, MD; Conor Barrett, MD; Rong Bai, MD; Dimpi Patel, DO; Yaariv Khaykin, MD; Richard Hongo, MD; Steven Hao, MD; Salwa Beheiry, RN; Gemma Pelargonio, MD; Antonio Dello Russo, MD; Michela Casella, MD; Pietro Santarelli, MD; Domenico Potenza, MD; Raffaele Fanelli, MD; Raimondo Massaro, MD; Paul Wang, MD; Amin Al-Ahmad, MD; Mauricio Arruda, MD; Sakis Themistoclakis, MD; Aldo Bonso, MD; Antonio Rossillo, MD; Antonio Raviele, MD; Robert A. Schweikert, MD; David J. Burkhardt, MD; Andrea Natale, MD

Background—Whether different ablation strategies affect paroxysmal atrial fibrillation (AF) long-term freedom from AF/atrial tachyarrhythmia is unclear. We sought to compare the effect of 3 different ablation approaches on the long-term success in patients with paroxysmal AF.

Methods and Results—One hundred three consecutive patients with paroxysmal AF scheduled for ablation and presenting in the electrophysiology laboratory in AF were selected for this study. Patients were randomized to pulmonary vein antrum isolation (PVAI; n=35) versus biatrial ablation of the complex fractionated atrial electrograms (CFAEs; n=34) versus PVAI followed by CFAEs (n=34). Patients were given event recorders and followed up at 3, 6, 9, 12, and 15 months postablation. There was no statistical significant difference between the groups in term of sex, age, AF duration, left atrial size, and ejection fraction. At 1 year follow-up, freedom from AF/atrial tachyarrhythmia was documented in 89% of patients in the PVAI group, 91% in the PVAI plus CFAEs group, and 23% in the CFAEs group ($P<0.001$) after a single procedure and with antiarrhythmic drugs.

Conclusion—No difference in terms of success rate was seen between PVAI alone and PVAI associated with defragmentation. CFAEs ablation alone had the smallest impact on AF recurrences at 1-year follow-up. These results suggest that antral isolation is sufficient to treat most patients with paroxysmal AF. **(*Circ Arrhythmia Electrophysiol.* 2009;2:113-119.)**

Long-Term Results of Catheter Ablation in Paroxysmal Atrial Fibrillation

Lessons From a 5-Year Follow-Up

Feifan Ouyang, MD*; Roland Tilz, MD*; Julian Chun, MD; Boris Schmidt, MD; Erik Wissner, MD; Thomas Zerm, MD; Kars Neven, MD; Bulent Köktürk, MD; Melanie Konstantinidou, MD; Andreas Metzner, MD; Alexander Fuernkranz, MD; Karl-Heinz Kuck, MD

Background—Paroxysmal atrial fibrillation (AF) naturally progresses toward chronic AF at an estimated rate of 15% to 30% over a 1- to 3-year period. Pulmonary vein (PV) isolation is increasingly performed for the treatment of drug-refractory paroxysmal AF. The long-term data on clinical outcome after circumferential PV isolation are limited.

Methods and Results—From 2003 to late 2004, 161 patients (121 men; age, 59.8±9.7 years) with symptomatic paroxysmal AF and normal left ventricular function underwent circumferential PV isolation guided by 3-dimensional mapping and double Lasso technique. Right-sided and left-sided continuous circular lesions encircling the ipsilateral PVs were placed with irrigated radiofrequency energy. The procedure end point was the absence of all PV spikes for at least 30 minutes after PV isolation verified by 2 Lasso catheters placed within the ipsilateral PVs. Sinus rhythm was present in 75 patients (46.6%) after the initial procedure during a median follow-up period of 4.8 years (0.33 to 5.5 years). A second procedure was performed in 66 and a third procedure in 12 patients. Recovered PV isolation conduction was observed in 62 of 66 patients (94.0%) during the second and in 8 of 12 patients (66.7%) during the third procedure. After a median of 1 (1 to 3) procedure, stable sinus rhythm was achieved in 128 of 161 patients (79.5%), whereas clinical improvement occurred in an additional 21 of 161 patients (13.0%) during a median follow-up of 4.6 years (0.33 to 5.5 years). Four patients in stable sinus rhythm died during follow-up. Progression toward chronic AF was observed in 4 patients (2.4%); however, only 2 patients reported symptoms.

Conclusion—In patients with paroxysmal AF and normal left ventricular function, circumferential PV isolation results in stable sinus rhythm in the majority of patients, and low incidence of chronic AF was observed after ablation during up to 5 years of follow-up. **(*Circulation*. 2010;122:2368-2377.)**

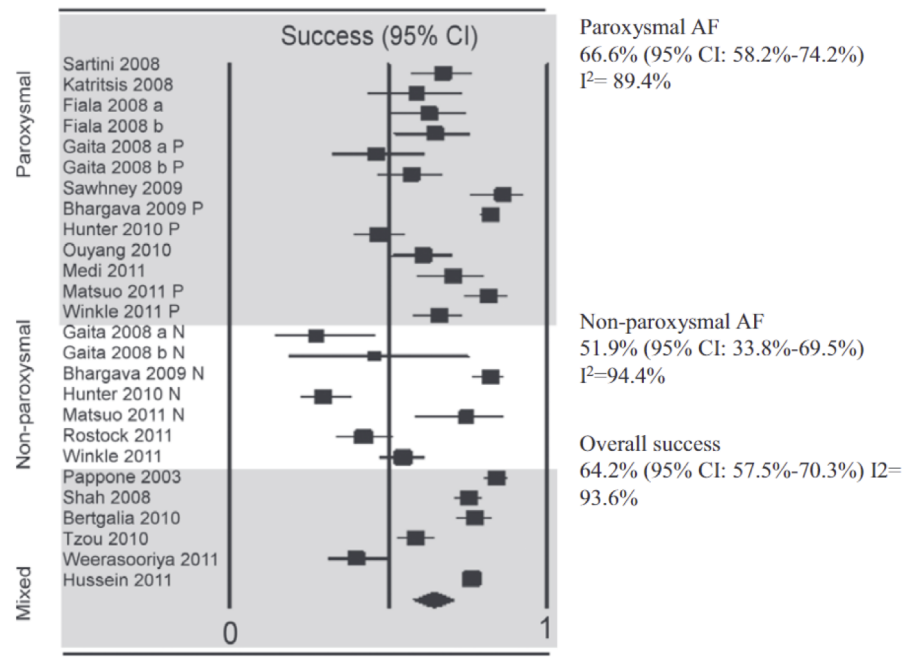
Long-term Outcomes of Catheter Ablation of Atrial Fibrillation: A Systematic Review and Meta-analysis

Anand N. Ganesan, MBBS, PhD; Nicholas J. Shipp, PhD; Anthony G. Brooks, PhD; Pawel Kuklik, PhD; Dennis H. Lau, MBBS, PhD; Han S. Lim, MBBS, PhD; Thomas Sullivan, BMa, CompSc; Kurt C. Roberts-Thomson, MBBS, PhD; Prashanthan Sanders, MBBS, PhD

***Background*—**In the past decade, catheter ablation has become an established therapy for symptomatic atrial fibrillation (AF). Until very recently, few data have been available to guide the clinical community on the outcomes of AF ablation at ≥3 years of follow-up. We aimed to systematically review the medical literature to evaluate the long-term outcomes of AF ablation.

***Methods and Results*—**A structured electronic database search (PubMed, Embase, Web of Science, Cochrane) of the scientific literature was performed for studies describing outcomes at ≥3 years after AF ablation, with a mean follow-up of ≥24 months after the index procedure. The following data were extracted: (1) single-procedure success, (2) multiple-procedure success, and (3) requirement for repeat procedures. Data were extracted from 19 studies, including 6167 patients undergoing AF ablation. Single-procedure freedom from atrial arrhythmia at long-term follow-up was 53.1% (95% CI 46.2% to 60.0%) overall, 54.1% (95% CI 44.4% to 63.4%) in paroxysmal AF, and 41.8% (95% CI 25.2% to 60.5%) in nonparoxysmal AF. Substantial heterogeneity (I^2>50%) was noted for single-procedure outcomes. With multiple procedures, the long-term success rate was 79.8% (95% CI 75.0% to 83.8%) overall, with significant heterogeneity (I^2>50%).The average number of procedures per patient was 1.51 (95% CI 1.36 to 1.67).

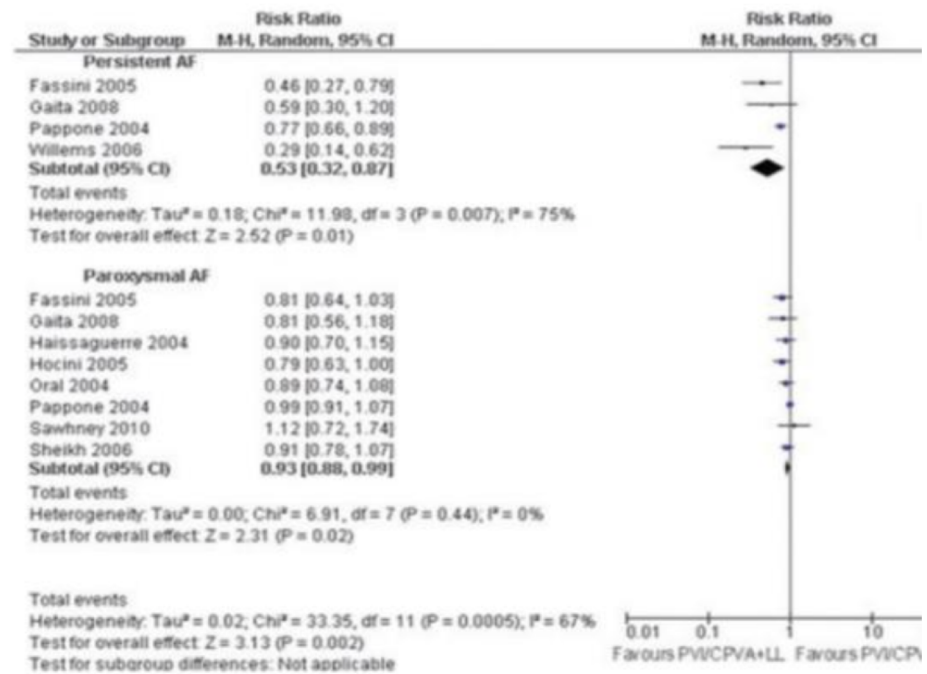
***Conclusions*—**Catheter ablation is an effective and durable long-term therapeutic strategy for some AF patients. Although significant heterogeneity is seen with single procedures, long-term freedom from atrial arrhythmia can be achieved in some patients, but multiple procedures may be required. **(*J Am Heart Assoc.* 2013;2:e004549 doi: 10.1161/JAHA.112.004549)**



Approach to the Catheter Ablation Technique of Paroxysmal and Persistent Atrial Fibrillation: A Meta-Analysis of the Randomized Controlled Trials

RATIKA PARKASH, M.D., M.Sc.,* ANTHONY S.L. TANG, M.D.†
JOHN L. SAPP, M.D.,* and GEORGE WELLS, PH.D.‡

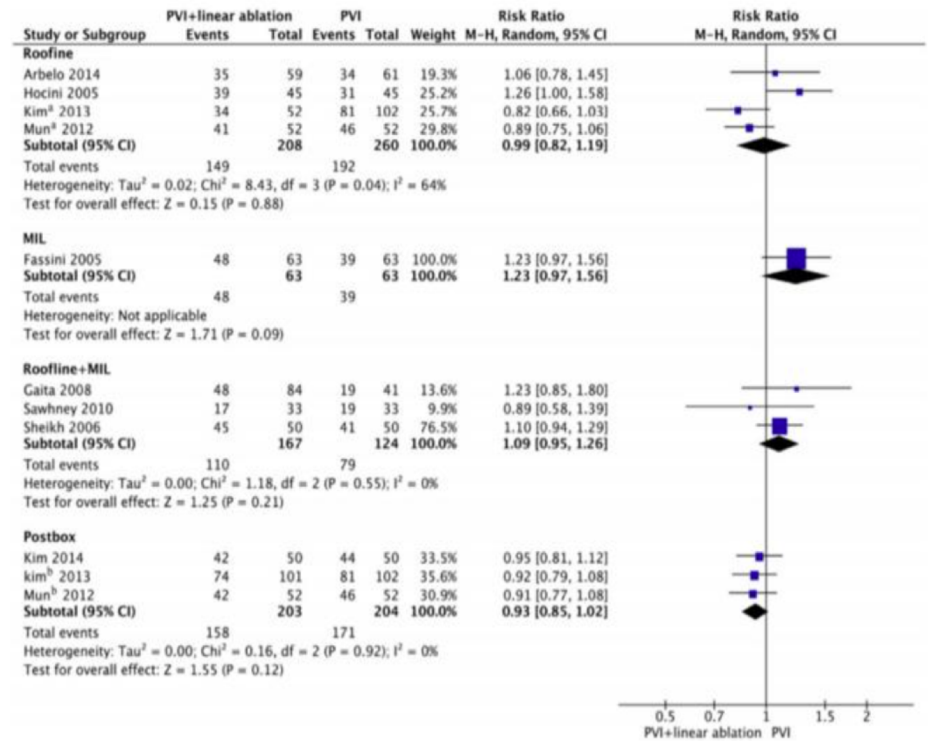
From the *Queen Elizabeth II Health Sciences Centre, Halifax, Canada; †Royal Jubilee Hospital, Victoria, Canada; and ‡University of Ottawa Heart Institute, Ottawa, Canada



Is there still a role for additional linear ablation in addition to pulmonary vein isolation in patients with paroxysmal atrial fibrillation? An Updated Meta-analysis of randomized controlled trials☆

Xiaoliang Hu [1], Jingzhou Jiang [1], Yuedong Ma [1], Anli Tang [*,1]

Department of Cardiology, First Affiliated Hospital of Sun Yat-sen University, Guangzhou, Guangdong, People's Republic of China



Systematic Review

Comparing Efficacy and Safety in Catheter Ablation Strategies for Paroxysmal Atrial Fibrillation: A Network Meta-Analysis of Randomized Controlled Trials

Emmanouil Charitakis [1,*], Silvia Metelli [2], Lars O. Karlsson [1], Antonios P. Antoniadis [3], Ioan Liuba [1], Henrik Almroth [1], Anders Hassel Jönsson [1], Jonas Schwieler [4], Skevos Sideris [5], Dimitrios Tsartsalis [6], Elena Dragioti [7,8], Nikolaos Fragakis [3] and Anna Chaimani [2]

The main findings of this NMA were:

- Based on the existing evidence, non-PVI strategies appear to be inferior in efficacy compared with the majority of PVI strategies.
- Different PVI strategies were found to be similarly effective.
- Different ablation strategies seem to be similar in terms of safety.
- Performing additional ablation to PVI is time-consuming, while there is no difference concerning procedural duration between the most used PVI strategies.
- All CA strategies except for non-PVI strategies and LBA appear to be superior to AADs.

What we have learned: is pulmonary vein isolation still the cornerstone of atrial fibrillation ablation?

Andreas Metzner [1]*, Karl-Heinz Kuck[2,3], and Julian K.R. Chun[4]

[1]Department of Cardiology, University Heart and Vascular Center Hamburg-Eppendorf, Hamburg, Germany; [2]LANS Cardio, Hamburg, Germany; [3]University Heart Center Lübeck, Division of Electrophysiology, Medical Clinic II (Department of Cardiology, Angiology and Intensive Care Medicine), University Hospital Schleswig-Holstein, Luebeck, Germany; and [4]Cardioangiologisches Centrum Bethanien, Agaplesion Markus Krankenhaus, Frankfurt am Main, Germany

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Atrial fibrillation ablation strategies and technologies: past, present, and future

Thomas J. Buist[1] · Douglas P. Zipes[2] · Arif Elvan[1]

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Table 3 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

Recommendations	Class	Level
Techniques and technologies		
Complete electrical isolation of the pulmonary veins is recommended during all AF catheter-ablation procedures.	I	A
If patient has history of CTI-dependent AFL or if typical AFL is induced at the time of AF ablation, delivery of a CTI lesion may be considered.	IIb	B
Use of additional ablation lesions beyond PVI (low voltage areas, lines, fragmented activity, ectopic foci, rotors, and others) may be considered but is not well established.	IIb	B

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