Atrial fibrillation: 2022 updates

Ali Sheikh DO

Becky Freel, MSN, APRN, FNP-C

Clinical Cardiac Electrophysiology

Sparrow Thoracic & Cardiovascular Institute (TCI): AF Center

Financial disclosure

- None

Objectives

- Definitions
- Mechanism review
- 4 Prong Approach to AF:
  - Stroke risk
  - Rate control
  - Rhythm / symptom control
  - Risk factor modification

Atrial fibrillation (AF)

- AF and AFL can coexist or occur in 30-50% of patients in 5 years
- After treatment/ablation for atrial flutter, risk of AF occurrence should be considered.

AF

- ECG criteria:
  - ‘Absolutely’ irregular R-R interval
  - No distinct ‘P’ waves on surface ECG
  - Atrial rates >300 bpm when visible on ECG (typically 500-600 bpm)

- Bottom line: Chaotic electrical activity that usually originates in the left atrium and spreads to right atrium and then conducts to ventricles with variable rates

TABLE 3 Definitions of AF: A Simplified Scheme

Term	Definition
Paroxysmal AF	• AF that terminates spontaneously or with intervention within 7 d of onset. • Episodes may recur with variable frequency.
Persistent AF	• Continuous AF that is sustained >7 d.
Long-standing persistent AF	• Continuous AF >12 mo in duration.
Permanent AF	• The term "permanent AF" is used when the patient and clinician make a joint decision to stop further attempts to restore and/or maintain sinus rhythm. • Acceptance of AF represents a therapeutic attitude on the part of the patient and clinician rather than an inherent pathophysiological attribute of AF. • Acceptance of AF may change as symptoms, efficacy of therapeutic interventions, and patient and clinician preferences evolve.
Nonvalvular AF	• AF in the absence of rheumatic mitral stenosis, a mechanical or bioprosthetic heart valve, or mitral valve repair.

AF indicates atrial fibrillation.

- Early Persistent AF: AF between 1 week– 1 year

- Terminology: *Lone AF* and *Chronic AF* used to describe young patients with AF, or AF with long duration are non specific and use is no longer favored.

J A C C V O L . 6 4 , N O . 2 1 , 2 0 1 4 January et al.D E C 2 , 2 0 1 4 : 2 2 4 6 – 8 0 Executive Summary: AHA/ACC/HRS Atrial Fibrillation Guideline

AF incidence and burden

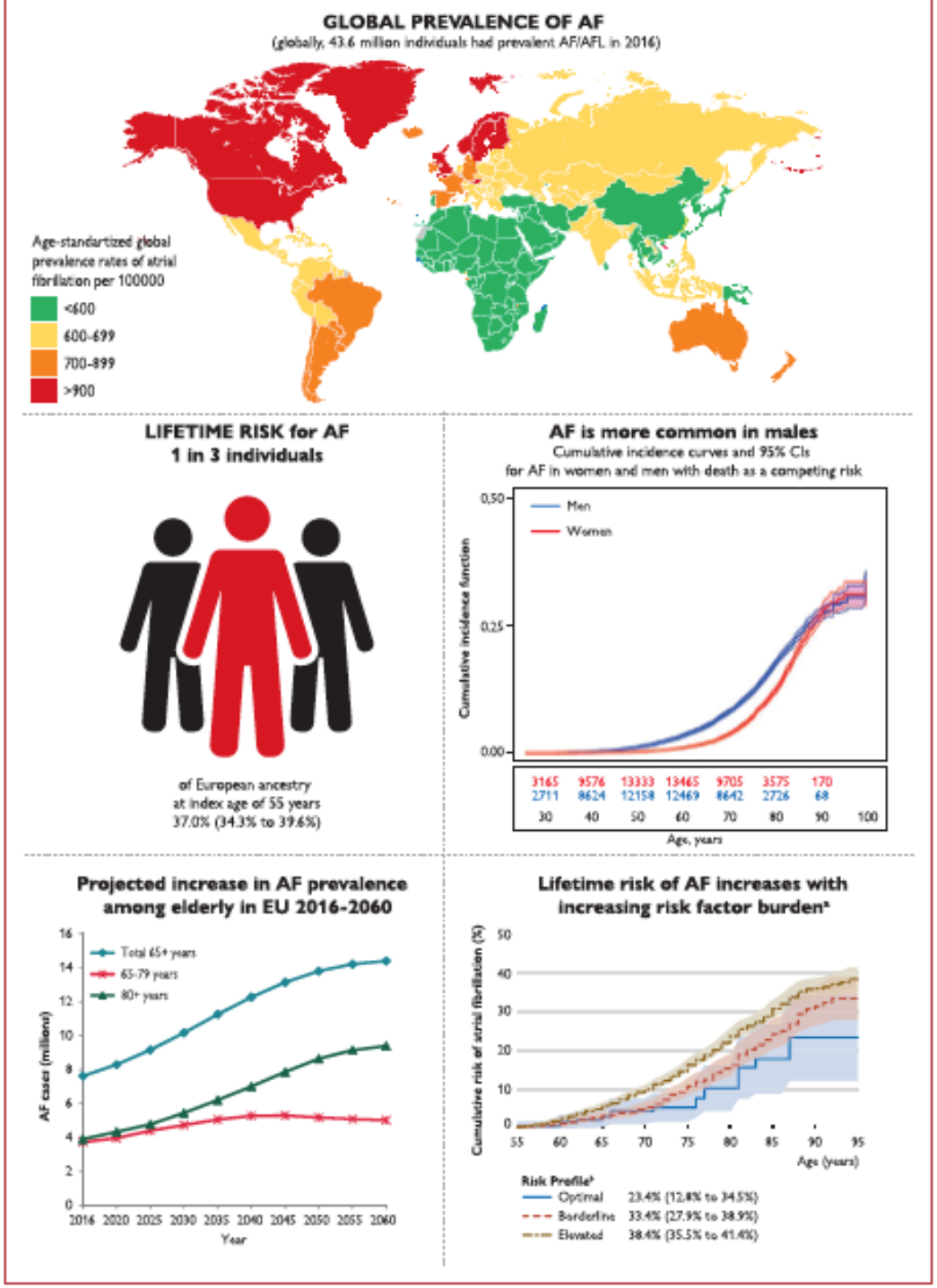
- High health care burden:
  - 33 million world wide
  - 3-5 million in U.S, estimated >8 million by 2050
  - AF increases risk of stroke by 5x, increases mortality and dementia
  - AF accounts for 450,000 hospitalizations and 99,000 deaths and increases health care cost by $8700/pt / $26 billion/yr

AF-related OUTCOMES

AF-Related Outcome	Frequency in AF	Mechanism(s)
Death	1.5 - 3.5 fold increase	Excess mortality related to: • HF, comorbidities • Stroke
Stroke	20-30% of all ischaemic strokes, 10% of cryptogenic strokes	• Cardioembolic, or • Related to comorbid vascular atheroma
LV dysfunction / Heart failure	In 20-30% of AF patients	• Excessive ventricular rate • Irregular ventricular contractions • A primary underlying cause of AF
Cognitive decline / Vascular dementia	HR 1.4 / 1.6 (irrespective of stroke history)	• Brain white matter lesions, inflammation, • Hypoperfusion, • Micro-embolism
Depression	Depression in 16-20% (even suicidal ideation)	• Severe symptoms and decreased QoL • Drug side effects
Impaired quality of life	>60% of patients	• Related to AF burden, comorbidities, psychological functioning and medication • Distressed personality type
Hospitalizations	10-40% annual hospitalization rate	• AF management, related to HF, MI or AF related symptoms • Treatment-associated complications

European Heart Journal (2020) 00, 1125 ESC GUIDELINES
doi:10.1093/eurheartj/ehaa612

Calkin et al. 2017 AF catheter ablation expert consensus statement. Heart Rhythm, Vol 14, No 10, October 2017



European Heart Journal (2020) 00, 1125 ESC GUIDELINES
doi:10.1093/eurheartj/ehaa612

AF: Risk factors

- AF is age related arrhythmia
- Lifetime risk of developing AF in humans of Eu descent >40 yrs
  - Men 26%, Women 23%
- Risk factors for AF development:
  - Non modifiable:
    - **Age: 10% will have AF over age 80
    - Sex, FHx, tall stature, other types of heart dz (Valvular heart disease, Amyloid, HCM)
  - Modifiable risk factors:
    - Obesity
    - Obstructive sleep apnea
    - Hypertension
    - Endurance Exercise
    - ETOH
    - Thyroid disease

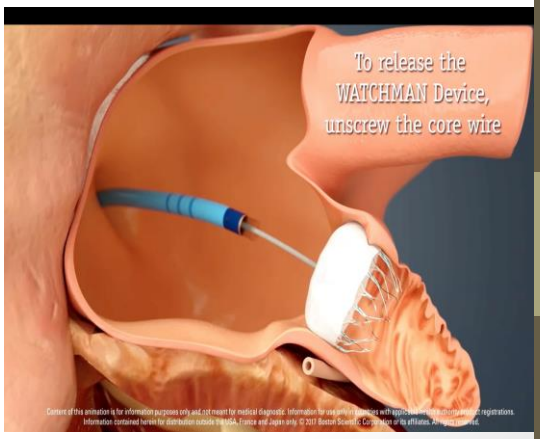
Approach to AF

- Stroke Risk:
  - CHA2DS2-VASc score
  - BMI >40 (AC choice), CKD, hypertrophic/LVNC CM, WPW, valvular AF
- Rate control
  - <110 bpm -> with CM preferably lower (<80 bpm)
- Rhythm control
  - Decision: symptom based, CM/HF, age
- Risk factor modification
  - Non modifiable: Age, genetics (*Titan gene*)
  - Modifiable: Obesity (BMI>30), HTN, OSA, ETOH, VHD

AF: Anticoagulation (AC)

- Same considerations as for Atrial flutter
- Coumadin, Direct oral anticoagulants (DOAC) should be started based on CHA2DS2-VASc score.

- Contraindications to AC: LAA occlusive device (Watchman, Amulet, Atriclip/surgical clips)
- 2 exceptions to anticoagulate regardless of CHA2DS2-VASc score:
  - Hypertrophic CM, LV non compaction CM
  - Moderate to severe Mitral Stenosis



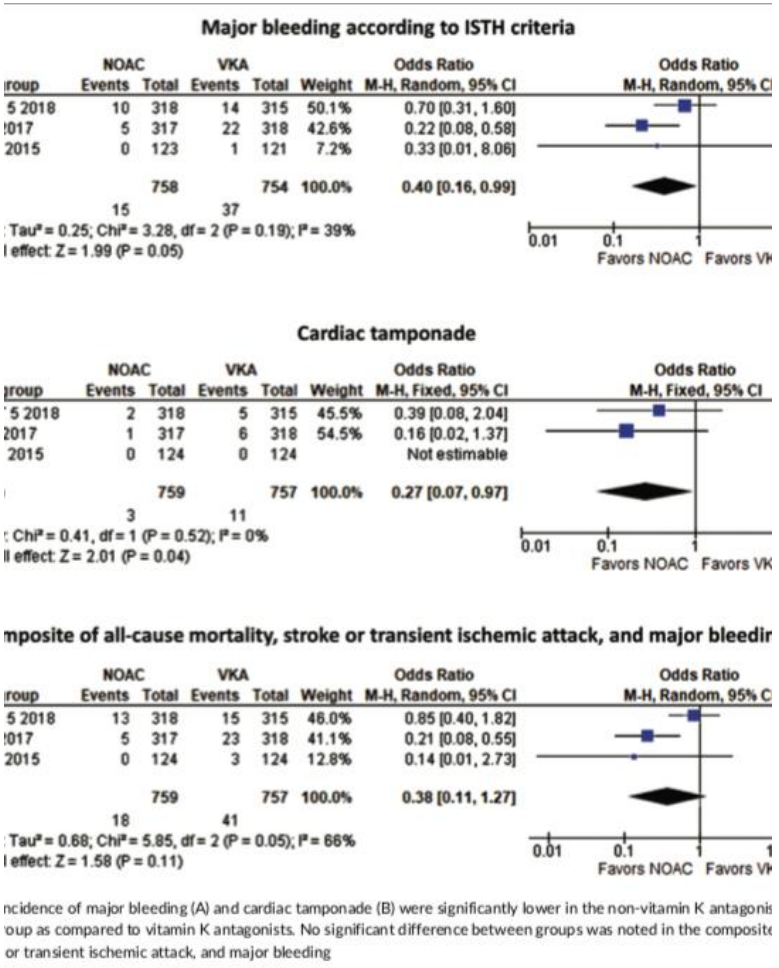
BostonScientific.com

AF: Cardioversion & Anticoagulation (AC)

- Contraindication to AC would contraindicate cardioversion (CV) unless it is emergent
- Start AC >3 weeks before cardioversion if CHA2DS2-VASc >0.
- If CV cannot wait that long (inpatient or symptoms), then TEE/CCTA to r/o LAA thrombus and CV.
- Regardless of CHA2DS2-VASc score, anticoagulation is mandatory for 4 weeks after due to LA stunning and risk of stroke.

AF: Ablation & Anticoagulation

- AC 1 month prior
- Uninterrupted AC for AF ablation
- Atleast 2 month post Ablation
- Beyond 2-3 months: based on stroke risk

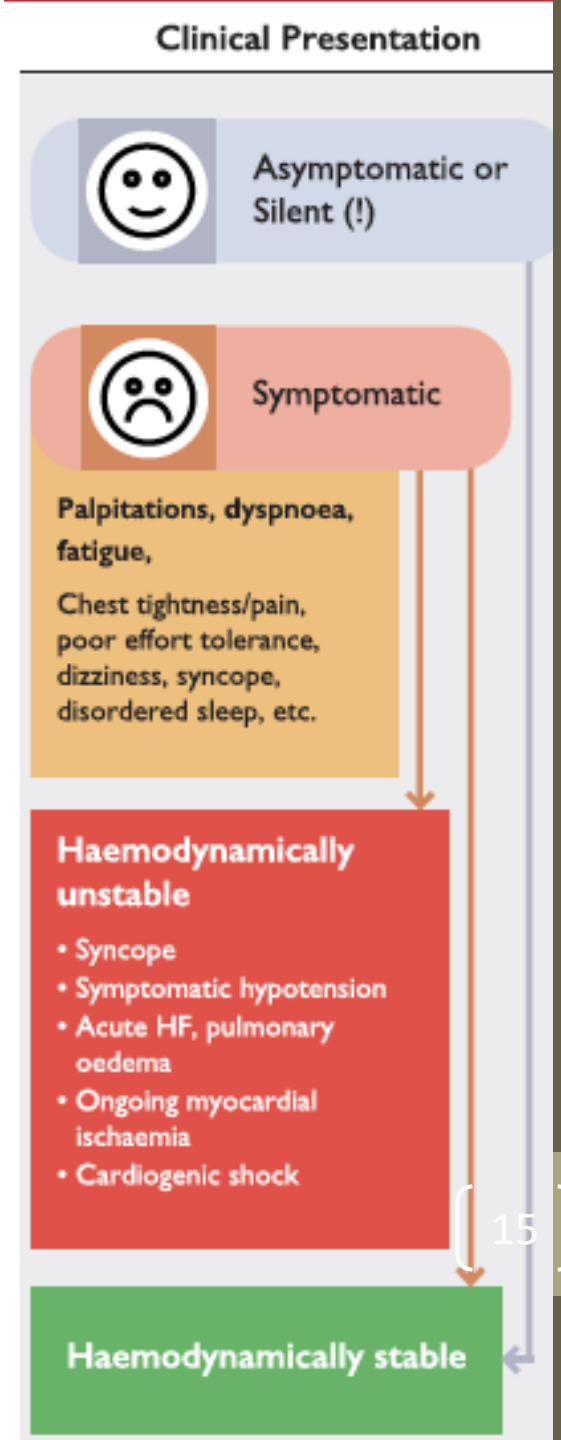


Rate Control strategies

- AVN blockers
  - CCB to be avoid in HF+AF
- Digoxin (in heart failure)
- Amiodarone in acute setting/shock (IIb)
- ‘Pace & Ablate’
- Sick sinus syndrome/Tachy-brady syndrome -> PPM support vs AFA

AF: Symptoms

- Symptoms related to AF are highly variable:
  - Asymptomatic – incidental pick up by PCP, smart watches, BP monitors
  - Strokes (up to 20-30% ischemic strokes, 10% cryptogenic strokes)
  - CHF/Tachycardia induced Cardiomyopathy
  - Fatigue, palpitations, chest pain
  - Post op especially Cardiac surgery, hospitalization for other diagnosis (ICU, infections, anemia triggered)



Mechanism of AF

- Trigger: responsible for initiating AF
  - Focal (pulmonary vein AT, AVNRT, WPW)
  - Role of sympathetic and parasympathetics (ganglionic plexi)?
  - Age related conduction heterogeneity
- Substrate: to maintain AF
  - Atrial tissue remodeling (electrical and structural)
- Perpetuator: progression from paroxysmal to persistent
  - 'AF begets AF'
  - ~11% progression from parox→persis over 12 months
  - Risk factors for AF are perpetuators: LA size, stroke, HTN etc

Most patients

HCM, LVNC, WPW

Acute illness – periop/ICU/infectious

Athletes

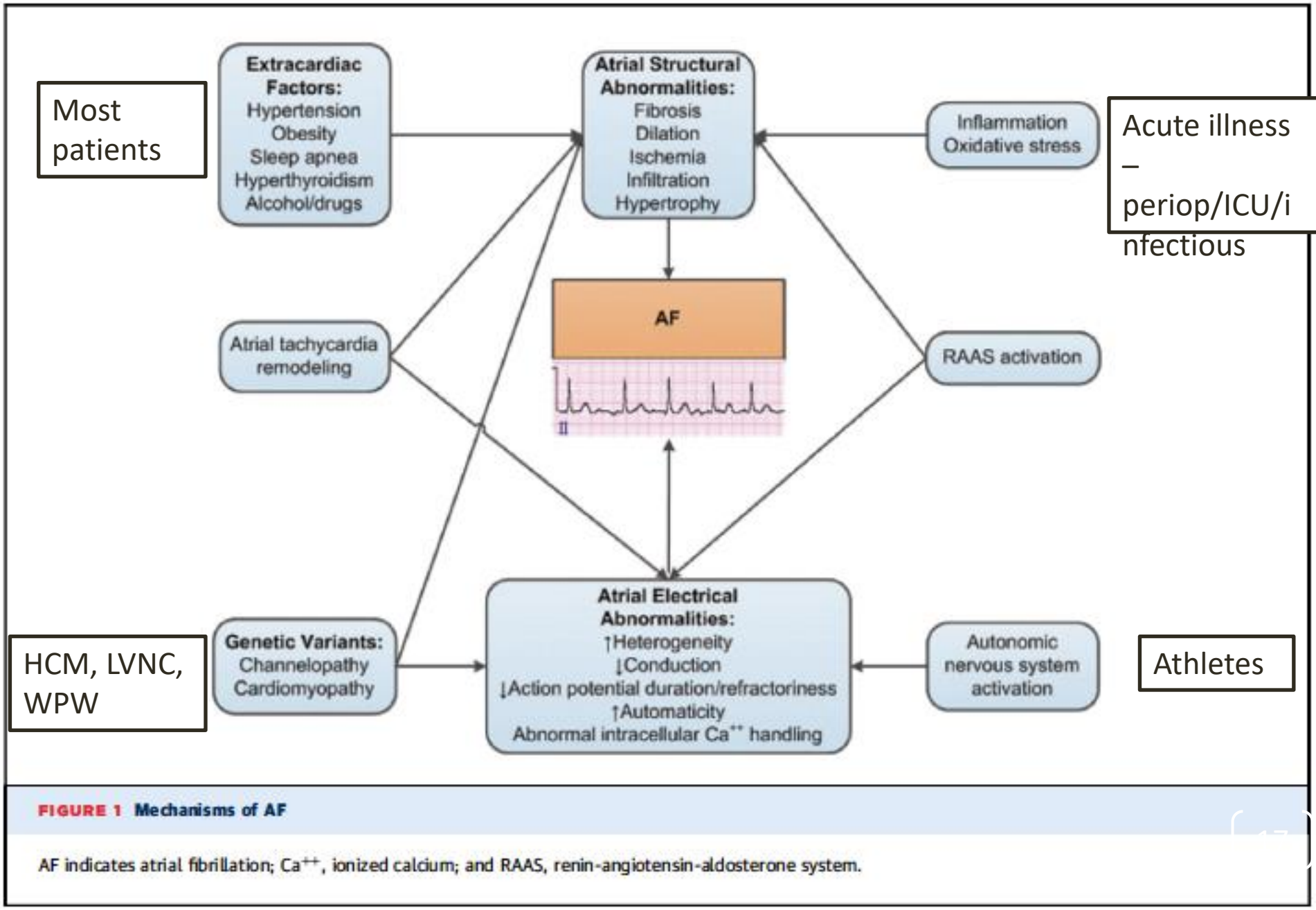
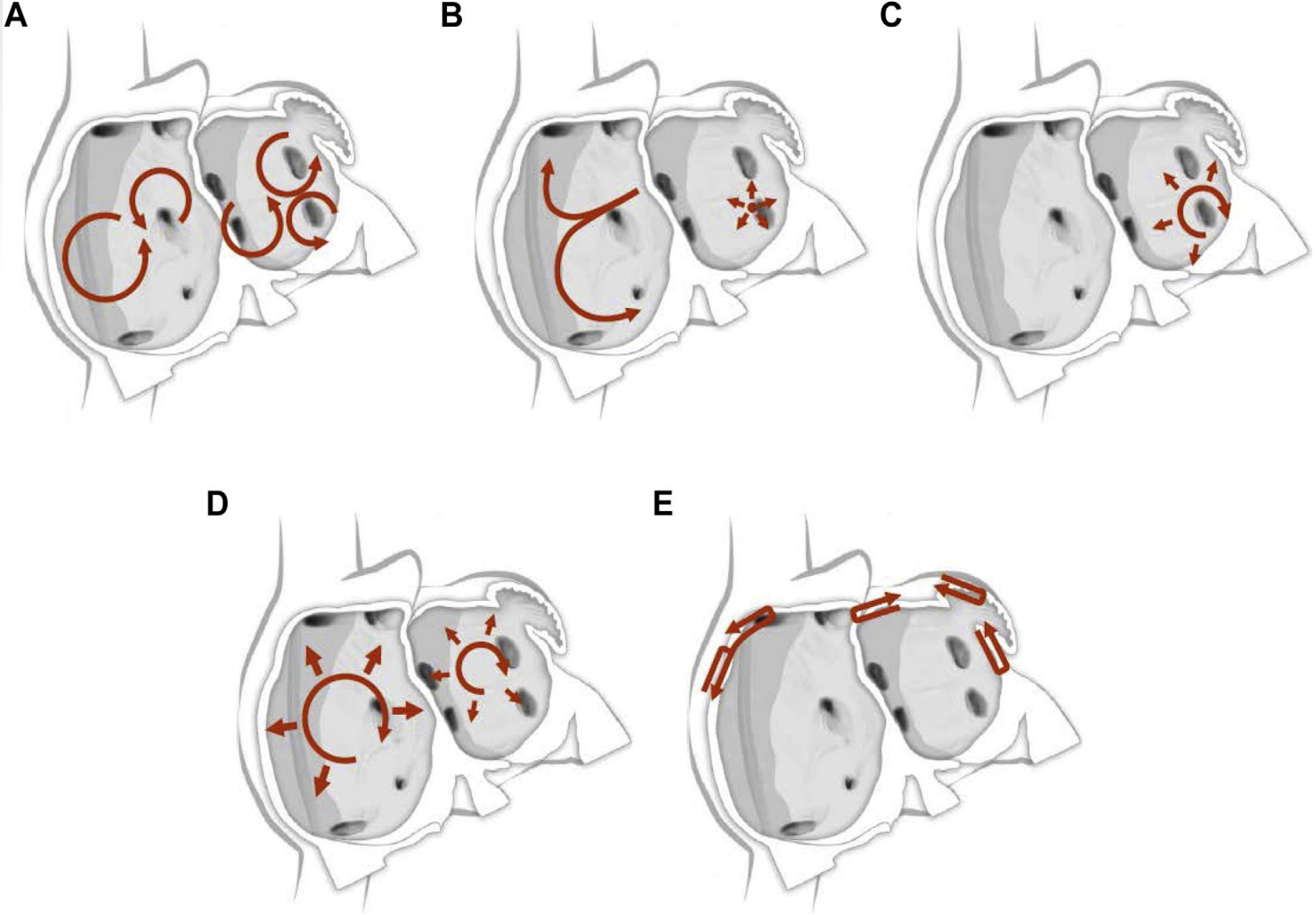


FIGURE 1 Mechanisms of AF

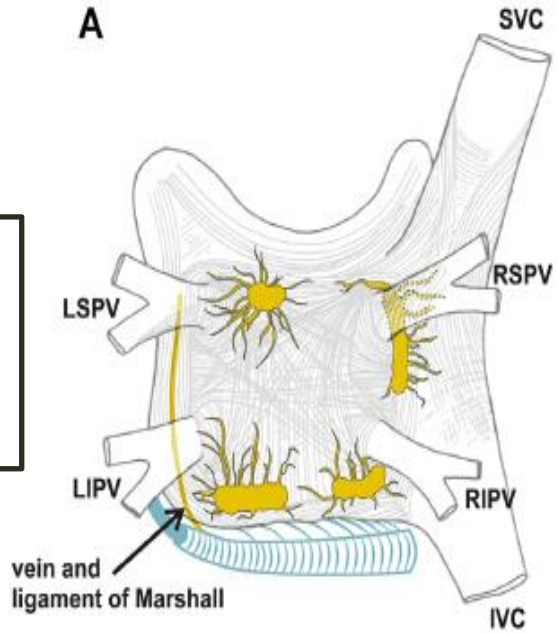
AF indicates atrial fibrillation; Ca^{++}, ionized calcium; and RAAS, renin-angiotensin-aldosterone system.

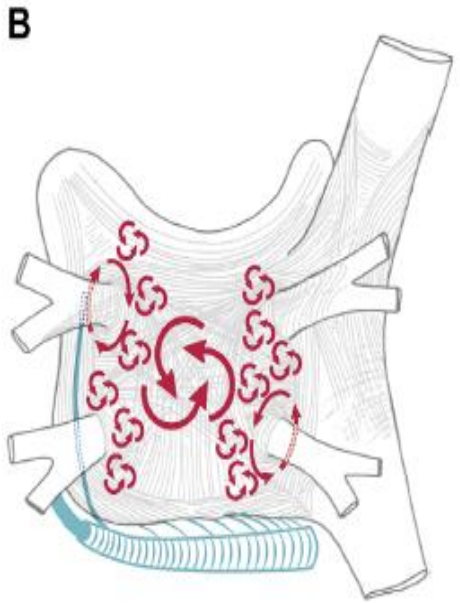


Various hypotheses and proposals concerning the mechanisms of atrial fibrillation. A: Multiple wavelets hypothesis. B: Rapidly discharging automatic foci. C: Single reentrant circuit with fibrillatory conduction. D: Functional reentry resulting from rotors or spiral waves. E: AF maintenance resulting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

2017 AF catheter ablation expert consensus statement. HRJ

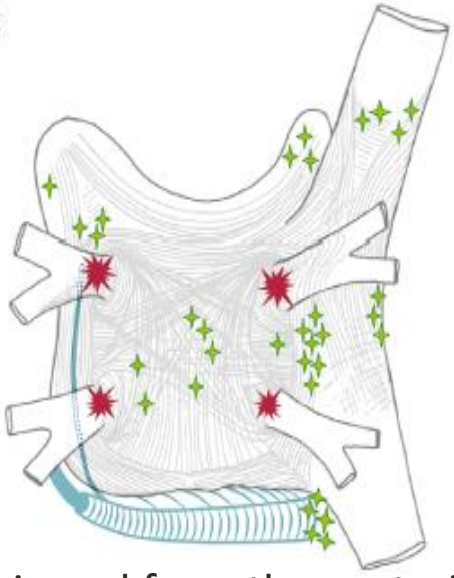
A. 5 ganglionic plexi play potential role in AF trigger

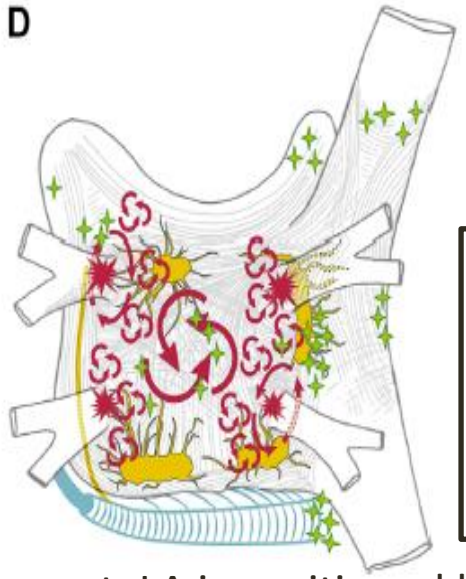




B. Large and small reentrant wavelets initiate and sustain AF

C. Common site of PV (red) and non- (green) for AF Cardiac tissue encroach the PV 1-3 mm





D. Composite of anatomic and arrhythmic mechanism of AF

LEFT ATRIUM viewed from the posterior aspect. LA is positioned left and posterior in the chest. RA is anterior and to the right

Calkins et al. Heart Rhythm 2012; 9:632-696.e21.2

AF: Rhythm control

- If questionable to no symptoms: DCCV & reassess
- If symptomatic and recurrent AF: DCCV +/- AAD
- If patient prefers no AAD: AF ablation (Class IIa indication)
- If patient failed AAD (recurrent AF on atleast 1 AAD) or contraindication to AAD: AF ablation (class I indication)

TABLE 11 Dosage and Safety Considerations for Maintenance of Sinus Rhythm in AF

Drug	Usual Doses	Exclude/Use With Caution	Major Pharmacokinetic Drug Interactions
Vaughan Williams class IA			
Disopyramide	• Immediate release: 100-200 mg once every 6 h • Extended release: 200-400 mg once every 12 h	• HF • Prolonged QT interval • Prostatism, glaucoma • Avoid other QT interval–prolonging drugs	• Metabolized by CYP3A4: caution with inhibitors (e.g., verapamil, diltiazem, ketoconazole, macrolide antibiotics, protease inhibitors, grapefruit juice) and inducers (e.g., rifampin, phenobarbital, phenytoin)
Quinidine	• 324-648 mg every 8 h	• Prolonged QT interval • Diarrhea	• Inhibits CYP2D6: ↑concentrations of tricyclic antidepressants, metoprolol, antipsychotics; ↓efficacy of codeine • Inhibits P-glycoprotein: ↑digoxin concentration
Vaughan Williams class IC			
Flecainide	• 50-200 mg once every 12 h	• Sinus or AV node dysfunction • HF • CAD • Atrial flutter • Infranodal conduction disease • Brugada syndrome • Renal or liver disease	• Metabolized by CYP2D6 (inhibitors include quinidine, fluoxetine, tricyclics; also genetically absent in 7%-10% of population) and renal excretion (dual impairment can ↑↑plasma concentration)
Propafenone	• Extended release: 225-425 mg once every 12 h	• Sinus or AV node dysfunction • HF • CAD • Atrial flutter • Infranodal conduction disease • Brugada syndrome • Liver disease • Asthma	• Metabolized by CYP2D6 (inhibitors include quinidine, fluoxetine, tricyclics; also genetically absent in 7%-10% of population)—poor metabolizers have ↑beta blockade • Inhibits P-glycoprotein: ↑digoxin concentration • Inhibits CYP2C9: ↑warfarin concentration (↑INR 25%)

Rarely used

Preferred use in Structurally normal hearts Should be used with AVN blockers due to risk of 1:1 AV conduction especially in flutter

In general, increase the risk of prolonging QT interval

Vaughan Williams class III			
Amiodarone	• Oral: doses for 2-4 wk; maintenance typically 100–200 mg QD • IV: 150 mg over 10 min; then 1 mg/min for 6 h; then 0.5 mg/min for 18 h or change to oral dosing; after 24 h, consider decreasing dose to 0.25 mg/min	• Infranodal conduction disease • Lung disease • Prolonged QT interval	cause drug interaction: ↑concentrations of warfarin (↑INR 0%–200%), statins, many other drugs • Inhibits P-glycoprotein: ↑digoxin concentration
Dofetilide	• 125-500 mcg once every 12 h	• Renal disease • Hypokalemia • Hypomagnesemia • Diuretic therapy • Avoid other QT interval–prolonging drugs	filtration and active tubular secretion: verapamil, HCTZ, cimetidine, ketoconazole, trimethoprim, prochlorperazine, and megestrol are contraindicated; discontinue amiodarone at least 3 mo before initiation
Dronedaro		• Bradycardia • HF • Long-standing persistent AF/flutter • Liver disease • Prolonged QT interval	• Metabolized by CYP3A: caution with inhibitors (e.g., verapamil, diltiazem, ketoconazole, macrolide antibiotics, protease inhibitors, grapefruit juice) and inducers (e.g., rifampin, phenobarbital, phenytoin) • Inhibits CYP3A, CYP2D6, P-glycoprotein: ↑concentrations of some statins, sirolimus, tacrolimus, beta blockers, digoxin
Sotalol	• 40-160 mg once every 12 h	• Prolonged QT interval • Renal disease • Hypokalemia • Hypomagnesemia • Diuretic therapy • Avoid other QT interval–prolonging drugs • Sinus or AV nodal dysfunction • HF • Asthma	• None (renal excretion)

Reserved for: Inpatient (sick), CHF, when contraindications to other AAD. Risk of lung fibrosis, Liver, thyroid and eye important considerations to chronic use. No renal clearance, just liver. Increases INR- therefore, need lowered dose of Coumadin.

Risk of TdP: Require inpatient drug initiation. Renal clearance

Contraindicated with HF and long standing persistent AF

J A C C V O L . 6 4 , N O . 2 1 , 2 0 1 4 January et al.
D E C E M B E R 2 , 2 0 1 4 : 2 2 4 6 – 8 0 Executive Summary: AHA/ACC/HRS Atrial Fibrillation Guideline

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.

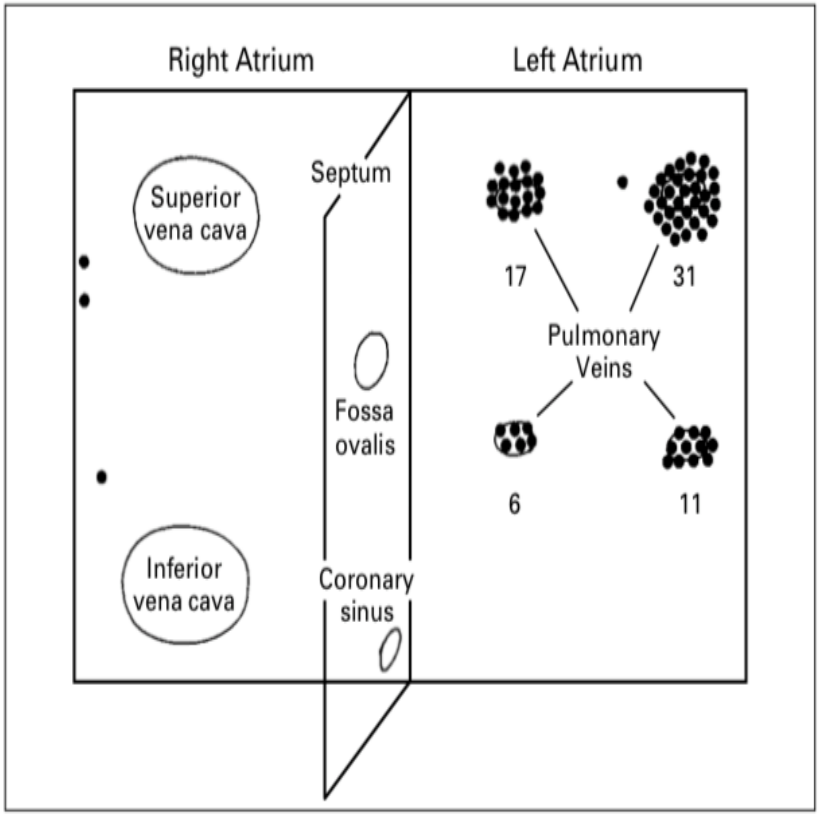
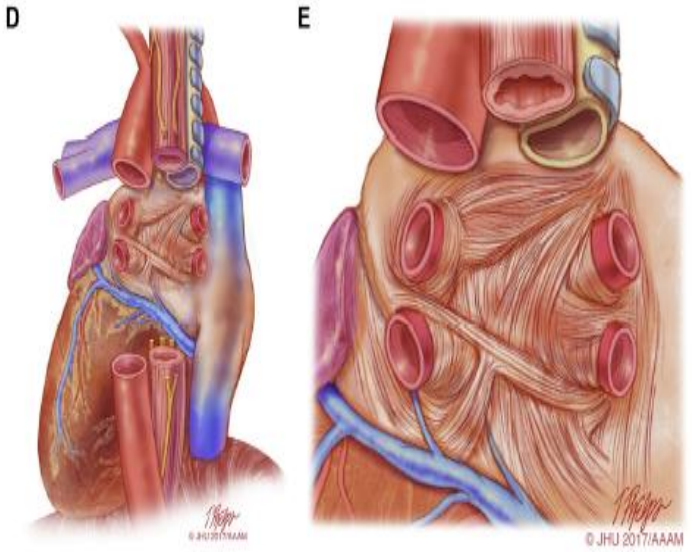
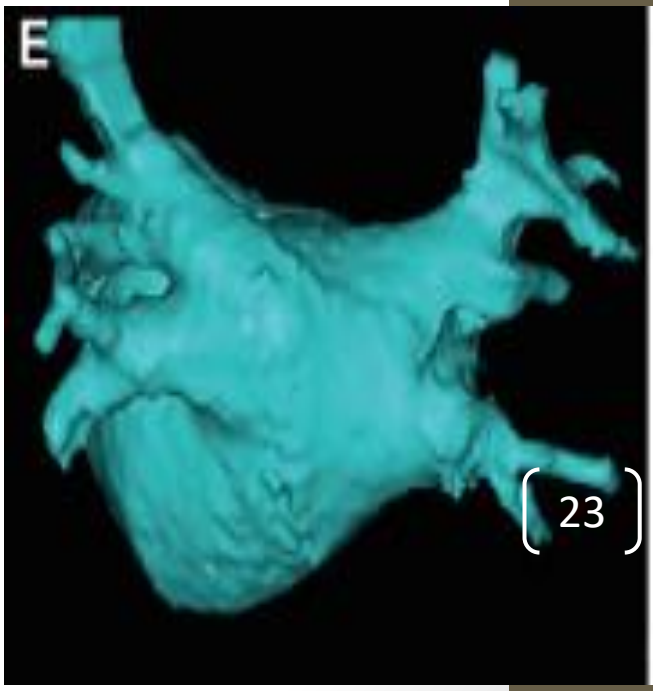


Figure 1. Diagram of the Sites of 69 Foci Triggering Atrial Fibrillation in 45 Patients.
Note the clustering in the pulmonary veins, particularly in both superior pulmonary veins. Numbers indicate the distribution of foci in the pulmonary veins.





1. N Engl J Med 1998;339:659-66.

2. Calkins et al Catheter and Surgical Ablation of Atrial Fibrillation. Heart Rhythm2017

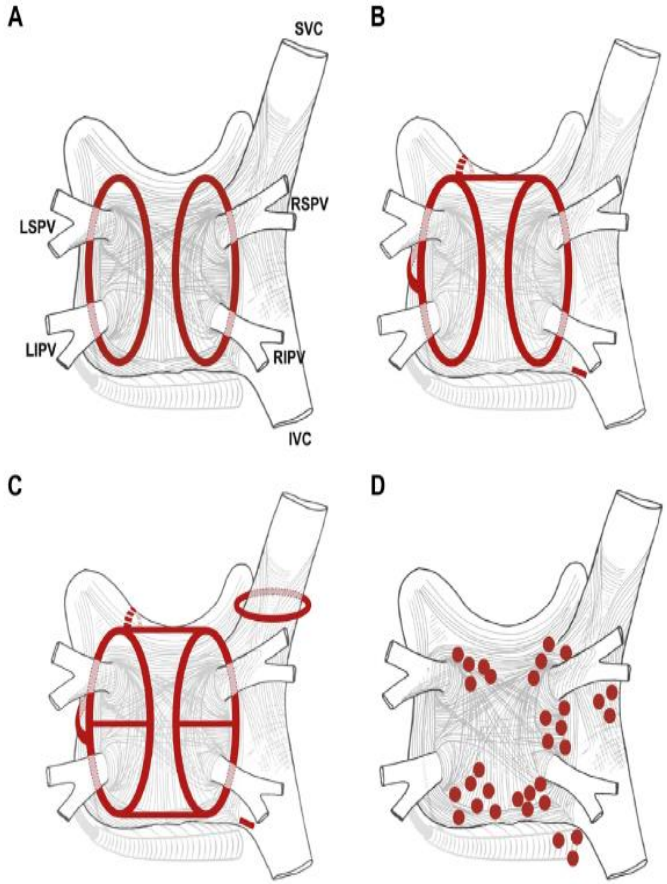
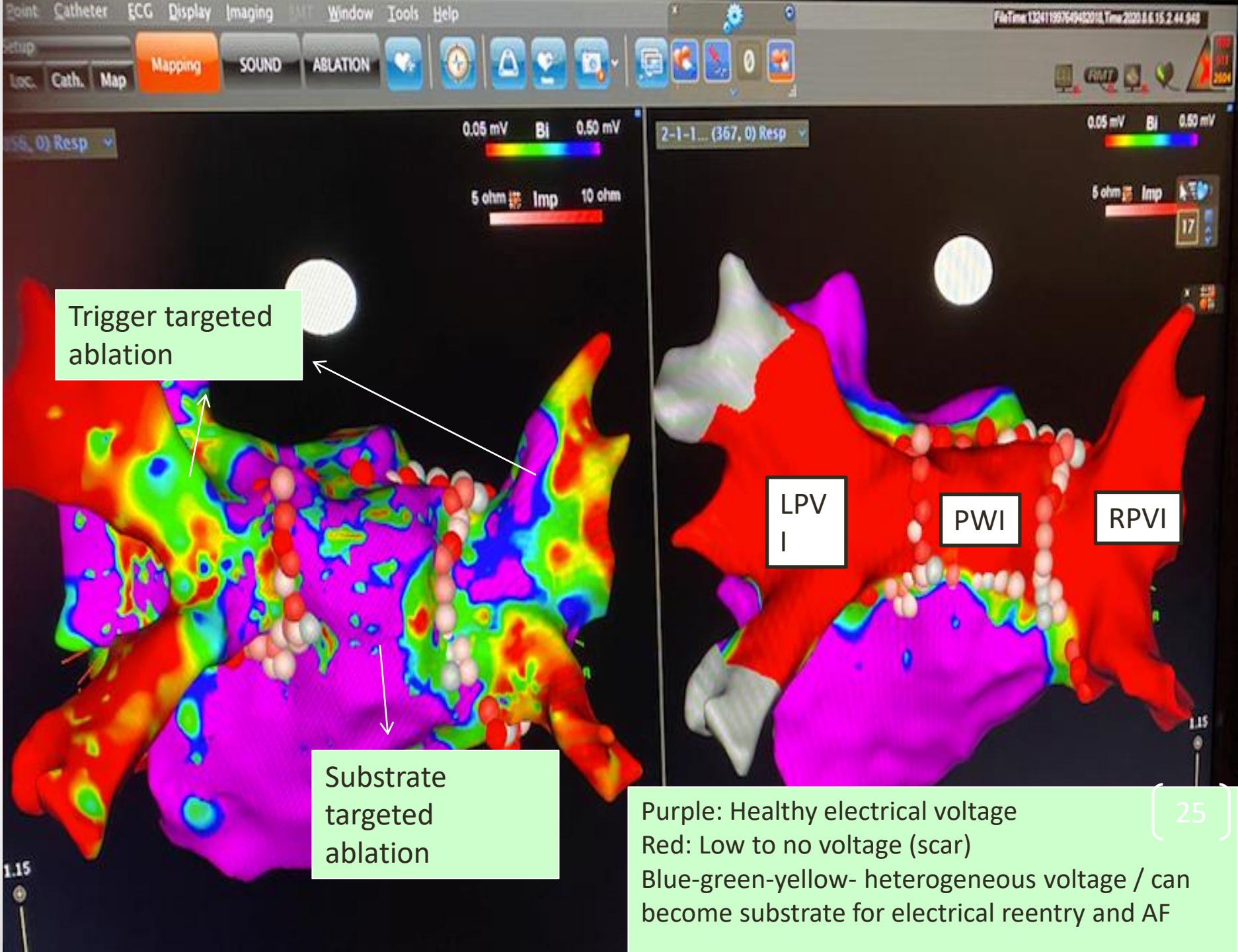
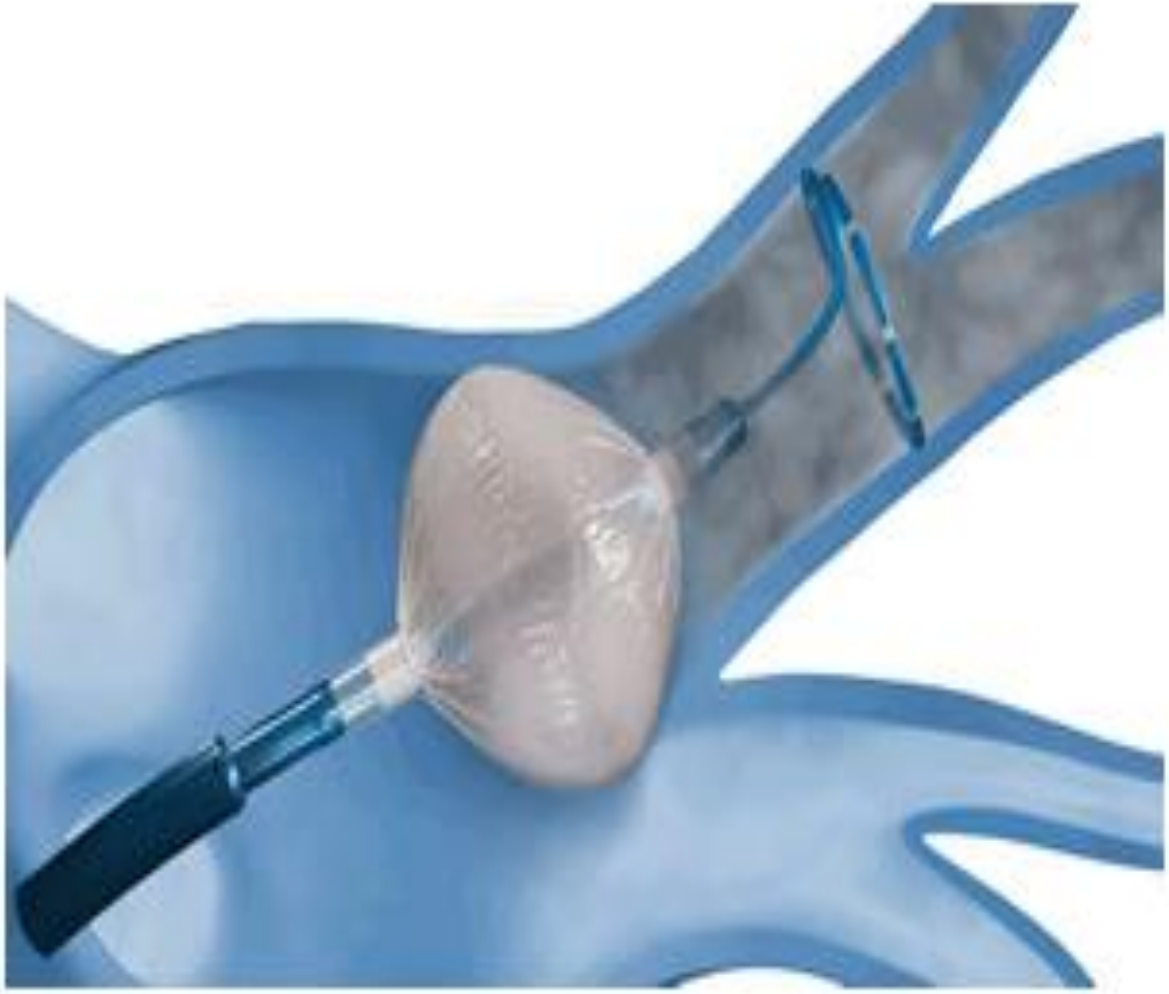


Figure 6 Schematic of common lesion sets employed in AF ablation. **A:** The circumferential ablation lesions that are created in a circumferential fashion around the right and the left PVs. The primary endpoint of this ablation strategy is the electrical isolation of the PV musculature. **B:** Some 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]


Trigger targeted ablation
Substrate targeted ablation
LPV I
PWI
RPVI
Purple: Healthy electrical voltage
Red: Low to no voltage (scar)
Blue-green-yellow- heterogeneous voltage / can become substrate for electrical reentry and AF

Cryoballoon ablation of pulmonary vein



AF: ablation strategy

- Pulmonary vein (PV) ablation/isolation is cornerstone.
- Ablation within PV can cause stenosis. Therefore, ablation lesions are aimed at the antrum of all 4 PV.
- Cryoablation of PV involves use of balloon catheter wedged into each PV and freeze ablate the PV until PV signals are obliterated.
- Radiofrequency (point by point lesion) around the PVs until PV are electrically isolated.
- Other: Surgical (MAZE) ablation, Hybrid (surgical and catheter) ablation, Pulse Field Ablation (PFA)
- Cryoablation vs Radiofrequency ablation carry same success rate (most require more than 1 ablation procedure)
  - Paroxysmal AF: ~87%
  - Persistent AF: ~72%
  - Long persistent AF: 65% (at 4 year follow up)

Winkle, R et al. High-power short duration AF ablation using contact force sensing catheters: Outcomes and predictors of success including posterior wall isolation. Heart Rhythm 2020;17:1223-1231

Can Early Rhythm Control (ERC) improve CV outcomes?

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, K.-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*

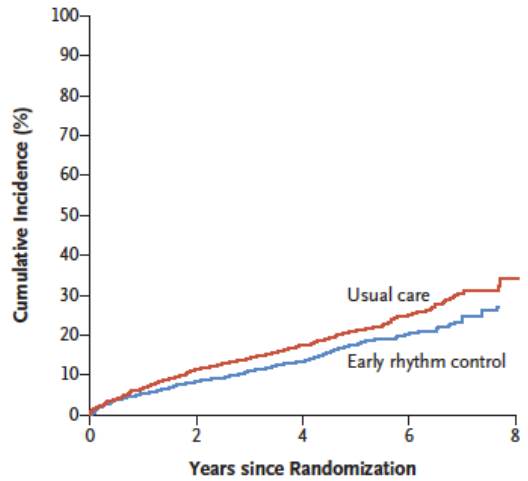


Figure 2. Aalen–Johansen Cumulative-Incidence Curves for the First Primary Outcome.

The first primary outcome was a composite of death from cardiovascular causes, stroke, or hospitalization with worsening of heart failure or acute coronary syndrome.

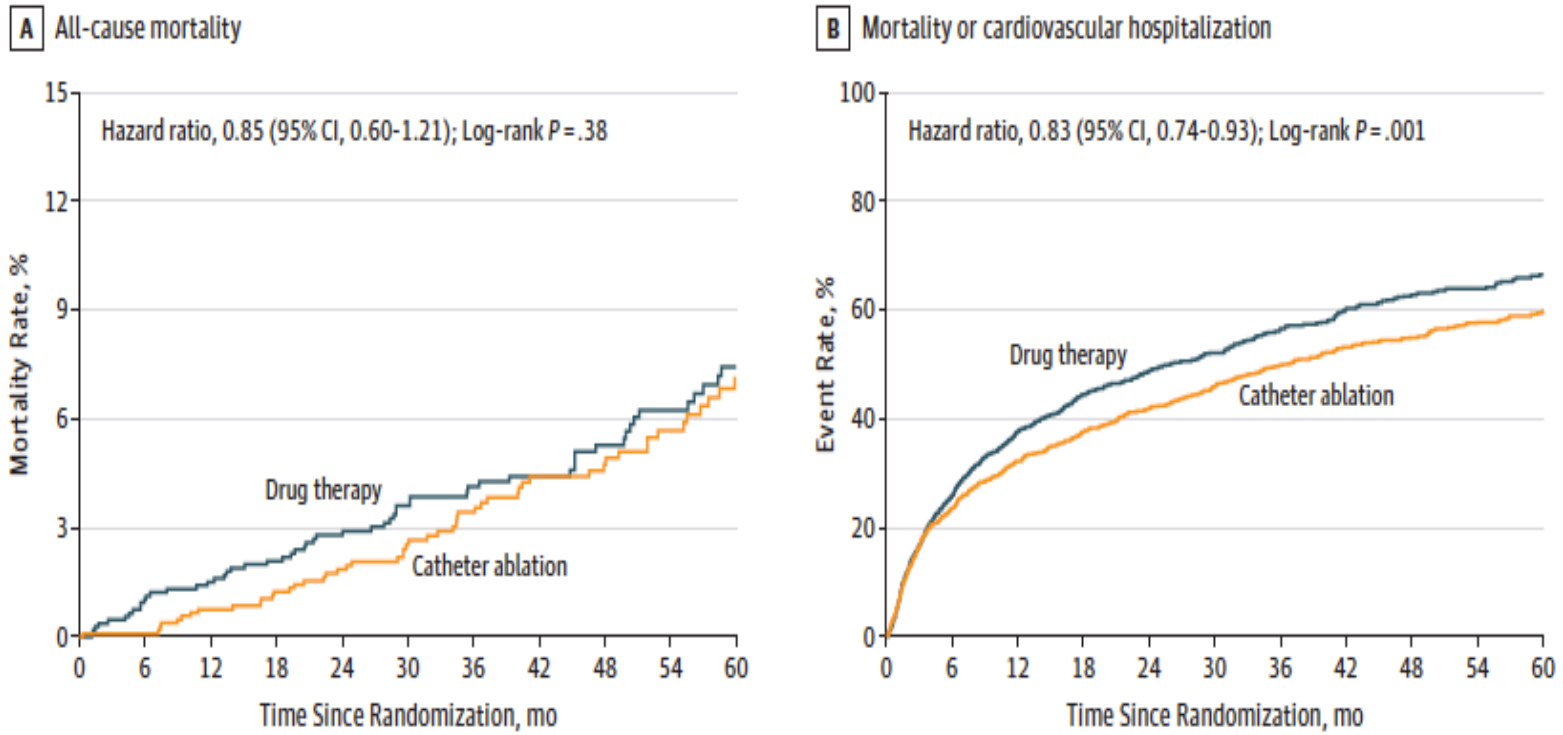
Dx: < 1yr
ERC: AAD or AFA VS symptom related tx
1^0: CV death, CVA, CHF, ACS
2^0: hospital nights

N= 2789
Stopped at 5 yrs
$1^{0:}$ 249 vs 316 ($p<0.005$)
2^0: \

CONCLUSIONS

Early rhythm-control therapy was associated with a lower risk of adverse cardiovascular outcomes than usual care among patients with early atrial fibrillation and cardiovascular conditions. (Funded by the German Ministry of Education and

Figure 3. Kaplan-Meier Estimates of All-Cause Mortality and Mortality or Cardiovascular Hospitalization by Intention-to-Treat Analysis



No. at risk

Drug therapy	1096	1046	1023	992	903	783	679	606	527	445	334
Catheter ablation	1108	1058	1035	1013	933	814	724	632	555	455	332

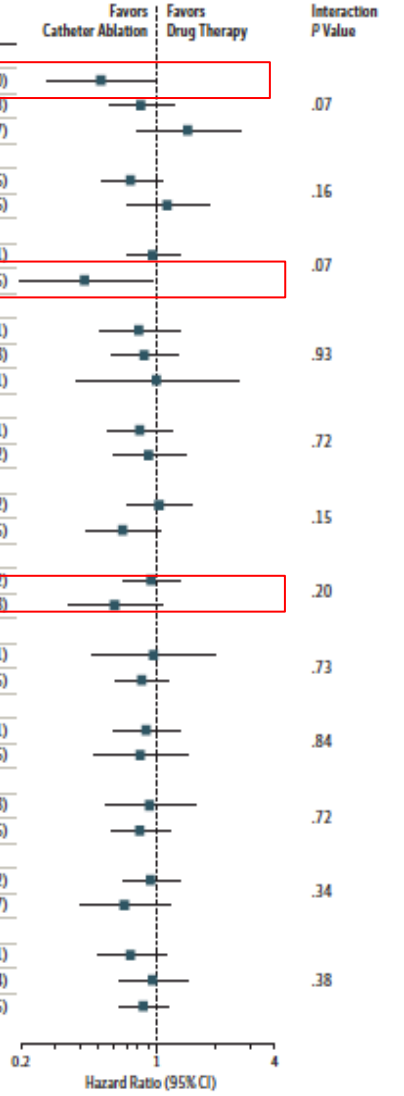
1096	778	643	563	474	387	302	244	197	165	112
1108	807	708	643	558	450	372	307	261	207	137

A, The median (25th, 75th percentiles) length of patient follow-up was 4.1 years (2.5, 5.1) in the catheter ablation group and 4.0 years (2.5, 5.2) in the drug therapy group. B, The median (25th, 75th percentiles) length of patient follow-up was 4.1 years (2.5, 5.1) in the catheter ablation group and 4.0 years (2.5, 5.2) in the drug therapy group.

CABANA trial (2019): In all-comers AF ablation did not improve mortality or hospitalization

Figure 4. Primary End Point Subgroup Analysis (Intention to Treat)

Source	No. of Events/Patients (Person-Years) Catheter Ablation	Drug Therapy	Hazard Ratio (95% CI)	Interaction P Value
Age, y				
<65	14/375 (1483)	27/391 (1498)	0.52 (0.27-1.00)	
≥65 and <75	50/577 (2159)	56/553 (2019)	0.84 (0.57-1.23)	.07
≥75	25/156 (514)	18/152 (529)	1.46 (0.80-2.67)	
Sex				
Male	54/695 (2670)	71/690 (2591)	0.74 (0.52-1.06)	.16
Female	35/413 (1485)	30/406 (1456)	1.14 (0.70-1.86)	
Minority status				
White	80/995 (3721)	82/984 (3654)	0.96 (0.71-1.31)	.07
Minority[a]	9/113 (434)	19/112 (393)	0.43 (0.20-0.95)	
Atrial fibrillation type[b]				
Paroxysmal	31/470 (1756)	38/476 (1761)	0.82 (0.51-1.31)	
Persistent	49/524 (1922)	55/518 (1860)	0.87 (0.59-1.28)	.93
Long-standing persistent	9/114 (477)	8/101 (426)	1.01 (0.39-2.61)	
Time since onset of atrial fibrillation, y				
≤1	50/540 (1922)	58/523 (1835)	0.83 (0.57-1.21)	.72
>1	39/560 (2207)	42/562 (2177)	0.92 (0.59-1.42)	
Baseline NYHA class[c]				
No heart failure or class I	55/719 (2735)	52/689 (2657)	1.04 (0.71-1.52)	.15
≥ Class II	34/378 (1396)	49/400 (1372)	0.68 (0.44-1.05)	
History of congestive heart failure				
No	68/934 (3506)	72/931 (3500)	0.95 (0.68-1.32)	.20
Yes	21/174 (650)	29/163 (547)	0.61 (0.35-1.08)	
Hypertension				
Absent	15/232 (857)	14/195 (761)	0.97 (0.47-2.01)	.73
Present	74/876 (3298)	87/900 (3287)	0.85 (0.62-1.15)	
Hypertension with LVH				
Absent	53/632 (2391)	51/544 (2022)	0.89 (0.61-1.31)	.84
Present	22/286 (1126)	27/301 (1152)	0.83 (0.47-1.46)	
CHA_2DS_2-VASc score[d]				
≤2 (Less risk)	26/481 (1861)	28/478 (1859)	0.93 (0.54-1.58)	.72
>2 (More risk)	63/627 (2295)	73/618 (2188)	0.83 (0.59-1.16)	
Sleep apnea				
Absent	65/846 (3129)	69/849 (3106)	0.94 (0.67-1.32)	.34
Present	24/262 (1027)	32/246 (941)	0.69 (0.41-1.17)	
Body mass index[e]				
<30 (Not obese)	42/541 (2012)	53/523 (1886)	0.74 (0.49-1.11)	.38
≥30 (Obese)	45/545 (2088)	48/561 (2122)	0.96 (0.64-1.44)	
All patients	89/1108 (4155)	101/1096 (4047)	0.86 (0.65-1.15)	



The squares represent the hazard ratios and the bars indicate the 95% CIs. AF indicates atrial fibrillation; CHA_2DS_2-VASc, congestive heart failure, hypertension, age ≥75 years (doubled), diabetes, stroke/transient ischemic attack/thromboembolism (doubled), vascular disease (prior myocardial infarction, peripheral artery disease, or aortic plaque), age 65-75 years, sex category (female); LVH, left ventricular hypertrophy; NYHA, New York Heart Association.

[a] Minority = Hispanic or Latino or nonwhite race. Minority status was determined by the site investigator in conjunction with the patient based on predefined categories as required by the National Institutes of Health (NIH) using NIH-specified categories.

[b] Paroxysmal = AF episodes lasting ≥1 hour in duration that terminate spontaneously within 7 days or cardioversion is performed within 48 hours of AF onset. Persistent = AF episode sustained for ≥7 days or cardioversion is performed more than 48 hours after AF onset. Long-standing persistent = continuous AF >1 year in duration.

[c] On a scale of I to IV, with I indicating the least severe and IV, the most severe symptoms of heart failure.

[d] On a scale of 0 to 9, with 0 indicating the lowest risk of stroke and 9, the highest risk of stroke.

[e] Calculated as weight in kilograms divided by height in meters squared.

CABANA subgroup analysis: Young age (<65), hx of CHF and minority benefited the most.

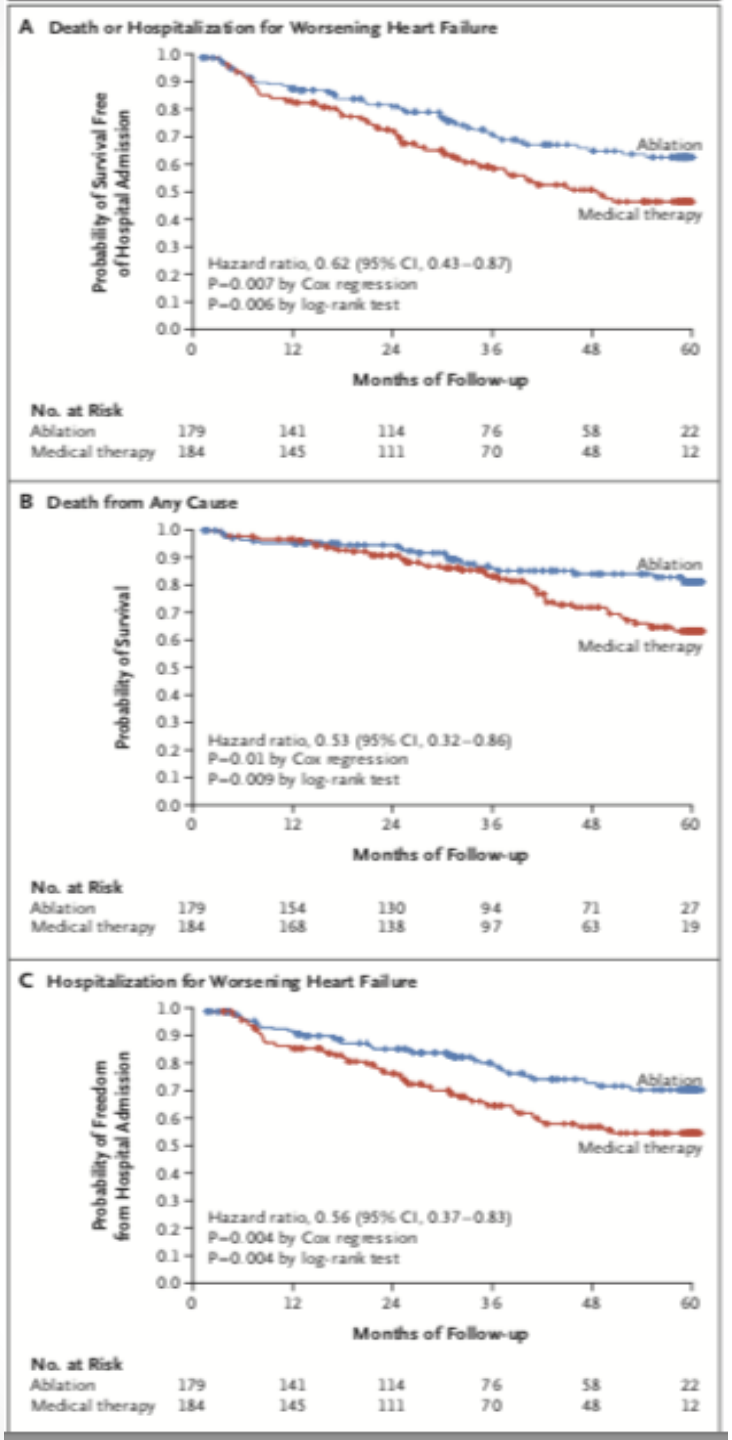
The NEW ENGLAND JOURNAL of MEDICINE

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*

Can AFA in CHF improve Death / CHF hospitalization?



N= 179/184
pAF / persis AF + CHF (II-IV)
EF ≤ 35+ICD
AFA vs med tx (AAD/Rate control)
1^0: Death or CHF hospitalization

1^0: 28.5% vs 44.6%
Death (any): 13 % vs 25%
Death (CV): 11 % vs 22%
CHF hosp: 21% vs 36%

CASTLE AF trial: Improvement in mortality and hospitalization from CHF with AF ablation in patients with LVEF <35%

N Engl J Med 2018;378:417-27.

Early Rhythm Control Therapy in Patients With Atrial Fibrillation and Heart Failure

Andreas Rillig, MD; Christina Magnussen, MD; Ann-Kathrin Ozga, PhD; Anna Suling, PhD; Axel Brandes, MD; Günter Breithardt, MD; A. John Camm, MD; Harry J.G.M. Crijns, MD; Lars Eckardt, MD; Arif Elvan, MD; Andreas Goette, MD; Michele Gulizia, MD; Laurent Haegeli, MD; Hein Heidbuchel, MD; Karl-Heinz Kuck, MD; Andre Ng, MD; Lukasz Szumowski, MD; Isabelle van Gelder, MD; Karl Wegscheider, MD; Paulus Kirchhof, MD

BACKGROUND: Even on optimal therapy, many patients with heart failure and atrial fibrillation experience cardiovascular complications. Additional treatments are needed to reduce these events, especially in patients with heart failure and preserved left ventricular ejection fraction.

METHODS: This prespecified subanalysis of the randomized EAST-AFNET4 trial (Early Treatment of Atrial Fibrillation for Stroke Prevention Trial) assessed the effect of systematic, early rhythm control therapy (ERC; using antiarrhythmic drugs or catheter ablation) compared with usual care (allowing rhythm control therapy to improve symptoms) on the 2 primary outcomes of the trial and on selected secondary outcomes in patients with heart failure, defined as heart failure symptoms New York Heart Association II to III or left ventricular ejection fraction [LVEF] <50%.

RESULTS: This analysis included 798 patients (300 [37.6%] female, median age 71.0 [64.0, 76.0] years, 785 with known LVEF). The majority of patients (n=442) had heart failure and preserved LVEF (LVEF≥50%; mean LVEF 61±6.3%), the others had heart failure with midrange ejection fraction (n=211; LVEF 40%–49%; mean LVEF 44 ± 2.9%) or heart failure with reduced ejection fraction (n=132; LVEF<40%; mean LVEF 31±5.5%). Over the 5.1-year median follow-up, the composite primary outcome of cardiovascular death, stroke, or hospitalization for worsening of heart failure or for acute coronary syndrome occurred less often in patients randomly assigned to ERC (94/396; 5.7 per 100 patient-years) compared with patients randomly assigned to usual care (130/402; 7.9 per 100 patient-years; hazard ratio, 0.74 [0.56–0.97]; *P*=0.03), not altered by heart failure status (interaction *P* value=0.63). The primary safety outcome (death, stroke, or serious adverse events related to rhythm control therapy) occurred in 71 of 396 (17.9%) patients with heart failure randomly assigned to ERC and in 87 of 402 (21.6%) patients with heart failure randomly assigned to usual care (hazard ratio, 0.85 [0.62–1.17]; *P*=0.33). LVEF improved in both groups (LVEF change at 2 years: ERC 5.3±11.6%, usual care 4.9±11.6%, *P*=0.43). ERC also improved the composite outcome of death or hospitalization for worsening of heart failure.

CONCLUSIONS: Rhythm control therapy conveys clinical benefit when initiated within 1 year of diagnosing atrial fibrillation in patients with signs or symptoms of heart failure.

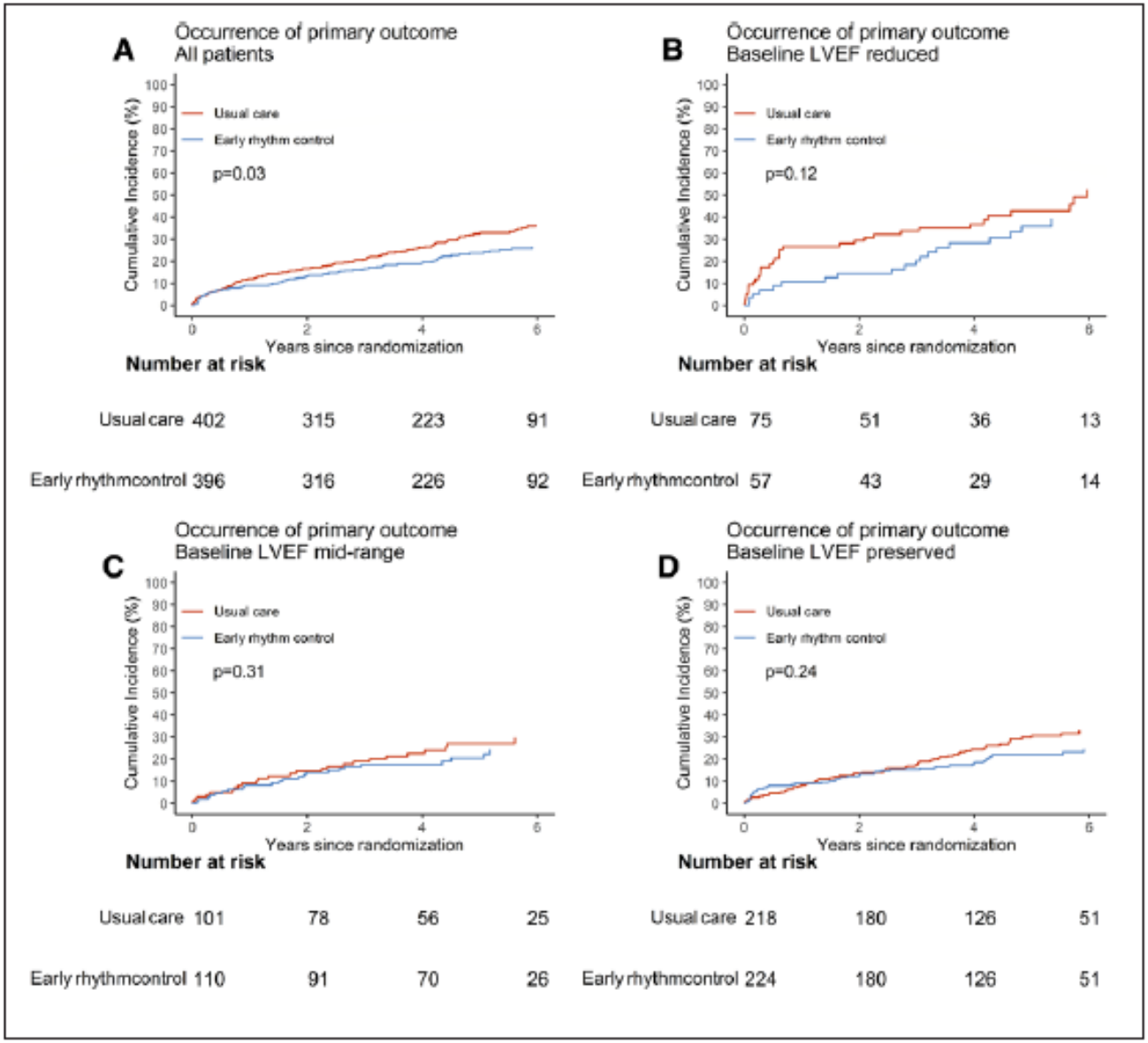


Figure 2. Primary outcome in EAST-AFNET4 patients with heart failure by randomized groups.
Aalen-Johansen cumulative-incidence curves for the effects of early rhythm control on the primary outcome. Primary outcome is defined as a composite of death from cardiovascular causes, stroke, or hospitalization with worsening of heart failure or acute coronary syndrome. **A**, All patients with heart failure. **B**, Heart failure with reduced ejection fraction. **C**, Heart failure with midrange ejection fraction. **D**, Heart failure with preserved ejection fraction. EAST-AFNET4 indicates Early Treatment of Atrial Fibrillation for Stroke Prevention Trial; and LVEF, left ventricular ejection fraction.

Paroxysmal AF – AF ablation first line therapy – IIa -> ? Class I indication

- STOP AF: NEJM 2021. Wasni et al.
  - Cryoballoon Ablation as Initial Therapy for Atrial fibrillation

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Cryoballoon Ablation as Initial Therapy for Atrial Fibrillation

Oussama M. Wazni, M.D., Gopi Dandamudi, M.D., Nitesh Sood, M.D., Robert Hoyt, M.D., Jaret Tyler, M.D., Sarfraz Durrani, M.D., Mark Niebauer, M.D., Kevin Makati, M.D., Blair Halperin, M.D., Andre Gauri, M.D., Gustavo Morales, M.D., Mingyuan Shao, Ph.D., Jeffrey Cerkvenik, M.S., Rachelle E. Kaplon, Ph.D., and Steven E. Nissen, M.D., for the STOP AF First Trial Investigators*

ABSTRACT

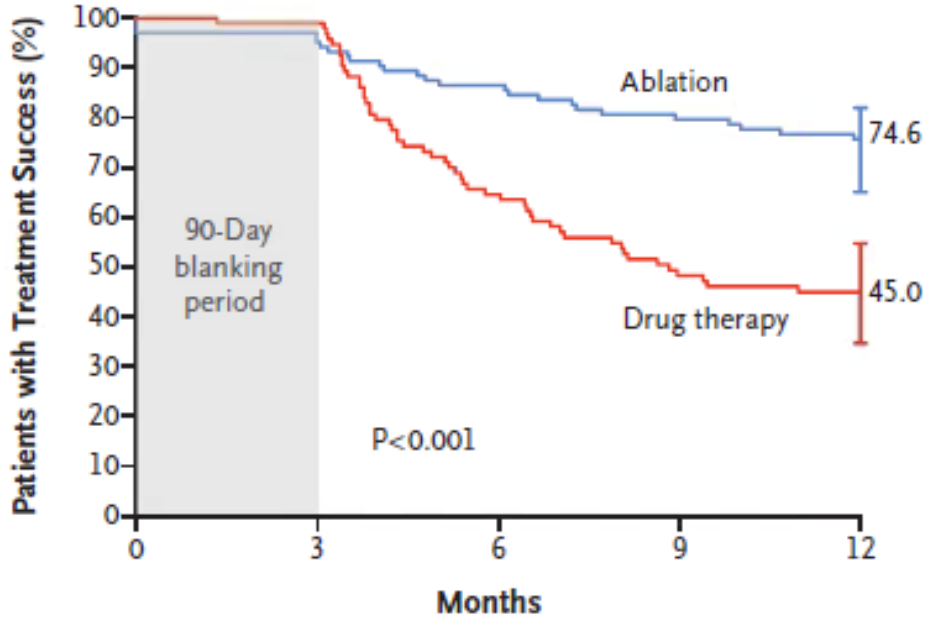
BACKGROUND

In patients with symptomatic paroxysmal atrial fibrillation that has not responded to medication, catheter ablation is more effective than antiarrhythmic drug therapy for maintaining sinus rhythm. However, the safety and efficacy of cryoballoon ablation as initial first-line therapy have not been established.

METHODS

We performed a multicenter trial in which patients 18 to 80 years of age who had paroxysmal atrial fibrillation for which they had not previously received rhythm-control therapy were randomly assigned (1:1) to receive treatment with antiarrhythmic drugs (class I or III agents) or pulmonary vein isolation with a cryoballoon. Arrhythmia monitoring included 12-lead electrocardiography conducted at baseline and at 1, 3, 6, and 12 months; patient-activated telephone monitoring conducted weekly and when symptoms were present during months 3 through 12; and 24-hour ambulatory monitoring conducted at 6 and 12 months. The primary efficacy end point was treatment success (defined as freedom from initial failure of the procedure or atrial arrhythmia recurrence after a 90-day blanking period to

N=203



No. at Risk

Ablation	104	99	88	81	70
Drug therapy	99	93	60	44	39

Figure 1. Treatment Success at 12 Months.

Treatment success was defined as freedom from any of the following events: initial failure of the procedure; any subsequent atrial fibrillation surgery or ablation in the left atrium; or atrial arrhythmia recurrence, cardioversion, or use of class I or III antiarrhythmic drugs (ablation group only) outside the 90-day blanking period. The median time from randomization to treatment initiation was 24 days in the ablation group and 2 days in the drug-therapy group. During the blanking period, three patients in the ablation group had treatment failure as a result of initial failure of the procedure, and one patient in the drug-therapy group had treatment failure because the patient underwent an ablation. Because the assumption of proportional hazards was not met, a hazard ratio is not presented. I bars indicate 95% confidence intervals.

Table 1. Characteristics of the Patients.*

Characteristic	Ablation (N=104)	Drug Therapy (N=99)
Age — yr	60.4±11.2	61.6±11.2
Male sex — no. (%)	63 (61)	57 (58)
Time since paroxysmal atrial fibrillation onset — yr	1.3±2.5†	1.3±2.3‡
Left atrial diameter — mm	38.7±5.7	38.2±5.4‡
Left ventricular ejection fraction — %	60.9±6.0	61.1±5.9‡
Medical characteristics — no. (%)		
Cardioversions in the previous 12 mo		
Electrical	19 (18)	15 (15)
Pharmacologic	8 (8)	14 (14)

STOP AF. Wasni 2021
NEJM

Paroxysmal AF – AF ablation first line therapy – IIa -> ? Class I indication

- STOP AF: NEJM 2021. Wasni et al.
  - Cryoballoon Ablation as Initial Therapy for Atrial fibrillation
- EARLY AF: NEJM 2021. Andrade et al.
  - Cyoablation or Drug therapy for initial treatment of Atrial Fibrillation

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 28, 2021 VOL. 384 NO. 4

Cryoablation or Drug Therapy for Initial Treatment of Atrial Fibrillation

Jason G. Andrade, M.D., George A. Wells, Ph.D., Marc W. Deyell, M.D., Matthew Bennett, M.D., Vidal Essebag, M.D., Ph.D., Jean Champagne, M.D., Jean-Francois Roux, M.D., Derek Yung, M.D., Allan Skanes, M.D., Yaariv Khaykin, M.D., Carlos Morillo, M.D., Umjeet Jolly, M.D., Paul Novak, M.D., Evan Lockwood, M.D., Guy Amit, M.D., Paul Angaran, M.D., John Sapp, M.D., Stephan Wardell, M.D., Sandra Lauck, Ph.D., Laurent Macle, M.D., and Atul Verma, M.D., for the EARLY-AF Investigators*

ABSTRACT

BACKGROUND

Guidelines recommend a trial of one or more antiarrhythmic drugs before catheter ablation is considered in patients with atrial fibrillation. However, first-line ablation may be more effective in maintaining sinus rhythm.

METHODS

We randomly assigned 303 patients with symptomatic, paroxysmal, untreated atrial fibrillation to undergo catheter ablation with a cryothermy balloon or to receive antiarrhythmic drug therapy for initial rhythm control. All the patients received an implantable cardiac monitoring device to detect atrial tachyarrhythmia. The follow-up period was 12 months. The primary end point was the first documented recurrence of any atrial tachyarrhythmia (atrial fibrillation, atrial flutter, or atrial tachycardia) between 91 and 365 days after catheter ablation or the initiation of an antiarrhythmic drug. The secondary end points included freedom from symptomatic arrhythmia, the atrial fibrillation burden, and quality of life.

RESULTS

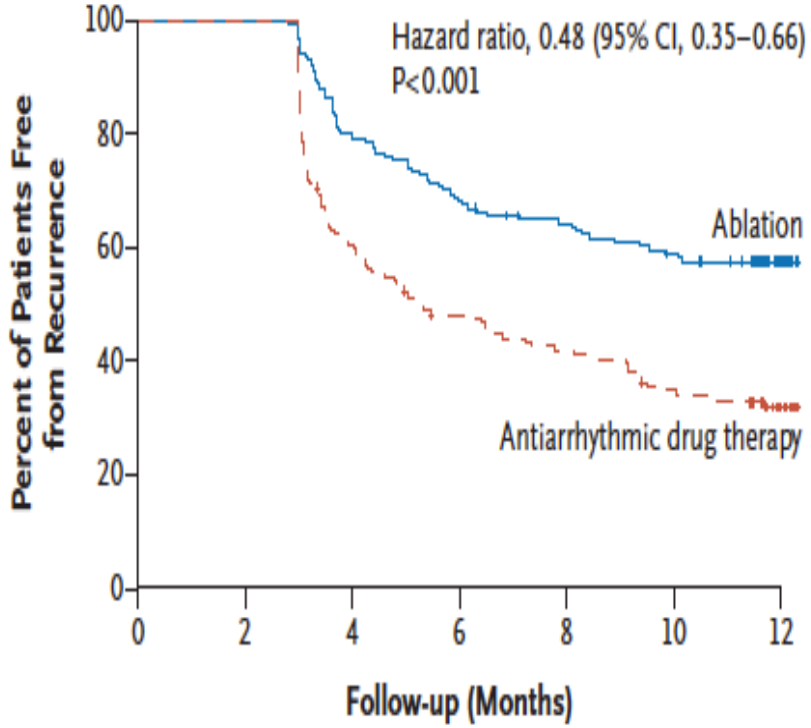
At 1 year, a recurrence of atrial tachyarrhythmia had occurred in 66 of 154 patients (42.9%) assigned to undergo ablation and in 101 of 149 patients (67.8%) assigned to receive antiarrhythmic drugs (hazard ratio, 0.48; 95% confidence interval [CI], 0.35 to 0.66; P<0.001). Symptomatic atrial tachyarrhythmia had recurred in 11.0% of the patients who underwent ablation and in 26.2% of those who received antiarrhythmic drugs (hazard ratio, 0.39; 95% CI, 0.22 to 0.68). The median percentage of time in atrial fibrillation was 0% (interquartile range, 0 to 0.08) with ablation and 0.13% (interquartile range, 0 to 1.60) with antiarrhythmic drugs. Serious adverse events occurred in 5 patients (3.2%) who underwent ablation and in 6 patients

From Vancouver General Hospital (J.G.A., M.B.), the University of British Columbia (J.G.A., M.W.D., M.B., S.L.), and the Centre for Cardiovascular Innovation (J.G.A., M.W.D.), Vancouver, Montreal Heart Institute, Université de Montréal (J.G.A., L.M.) and McGill University Health Centre (V.E.), Montreal, the University of Ottawa Heart Institute, Ottawa (G.A.W.), Université Laval, Quebec, QC (J.C.), Université de Sherbrooke, Sherbrooke, QC (J.-F.R.), Rouge Valley Centenary Hospital, Scarborough, ON (D.Y.), Western University, London, ON (A.S.), Southlake Regional Health Centre, University of Toronto, Newmarket, ON (Y.K., A.V.), Libin Cardiovascular Institute, University of Calgary, Calgary, AB (C.M.), St. Mary's General Hospital, Kitchener, ON (U.J.), Royal Jubilee Hospital, Victoria, BC (P.N.), Royal Alexandra Hospital, Edmonton, AB (E.L.), McMaster University, Hamilton, ON (G.A.), St. Michael's Hospital, University of Toronto, Toronto (P.A.), Dalhousie University, Halifax, NS (J.S.), and the University of Saskatchewan, Saskatoon, SK (S.W.) — all in Canada. Address reprint requests to Dr. Andrade at Vancouver General Hospital, Rm. 9159, 9th Fl. Cardiology, 2775 Laurel St., Vancouver, BC V5Z 1M9, Canada, or

N=303
ILR monitoring

Table 1. Characteristics of the Patients at Baseline.*

Characteristic	Ablation Group (N=154)	Antiarrhythmic Drug Group (N=149)
Age — yr	57.7±12.3	59.5±10.6
Male sex — no. (%)	112 (72.7)	102 (68.5)
BMI†	30.9±14.2	29.7±9.3
Obesity — no. (%)‡	56 (36.4)	53 (35.6)
Tobacco use	8 (5.2)	10 (6.7)
Blood pressure — mm Hg		
Systolic	129.1±18.1	129.3±15.7
Diastolic	78.4±10.6	78.0±9.8
Median yr since diagnosis of atrial fibrillation (IQR)	1 (0–3)	1 (0–4)
Paroxysmal atrial fibrillation — no. (%)	147 (95.5)	140 (94.0)
Symptomatic atrial fibrillation episodes/mo — median (IQR)	3 (1–10)	3 (1–10)
Previous cardioversion — no. (%)	56 (36.4)	63 (42.3)
Left atrial diameter — mm	39.5±5.0	38.1±6.5
Left atrial volume — ml/m^2	35.6±15.2	35.4±12.5
Left ventricular ejection fraction — %	59.6±7.0	59.8±7.5



No. at Risk

Ablation	154	154	123	105	96	86	55
Antiarrhythmic drug therapy	149	149	89	69	60	49	27

Figure 1. Freedom from Recurrence of Atrial Tachyarrhythmia over Time.

Shown are Kaplan–Meier estimates of the primary end point, freedom from recurrence of any atrial tachyarrhythmia (atrial fibrillation, atrial flutter, or atrial tachycardia) lasting 30 seconds or longer between 91 and 365 days after the initiation of an antiarrhythmic drug or catheter ablation. Tick marks indicate censored data. CI denotes confidence interval.

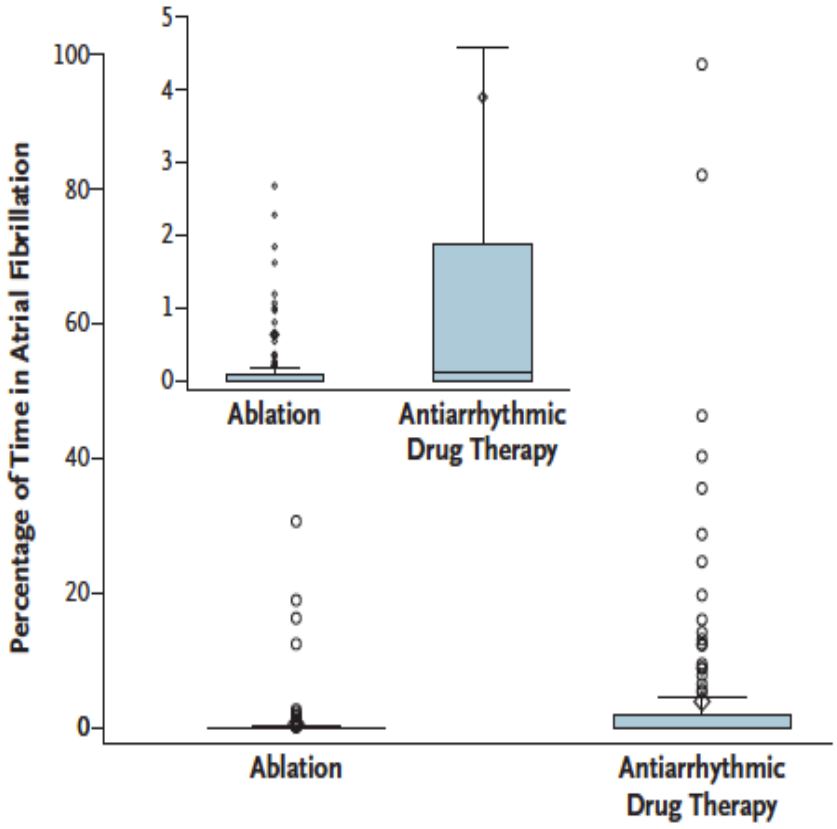


Figure 2. Atrial Fibrillation Burden in the Ablation and Antiarrhythmic Drug Groups.

Shown are box and whisker plots of atrial fibrillation burden expressed as the percentage of time in atrial fibrillation. The inset plots show the data on an expanded y axis. The upper whisker indicates the 90th percentile, the top of the blue box the 75th percentile, the horizontal line within the blue box the 50th percentile, and the bottom of the blue box the 25th percentile. The bottom whisker is too compressed to be shown but is meant to indicate the 10th percentile (0% in both groups). The circles beyond the upper whisker are individual data points for individual patients and are the outliers (beyond the 90th percentile). The diamond indicates the mean atrial fibrillation burden for the treatment group.

JAMA Cardiology | Original Investigation

Assessment of Catheter Ablation or Antiarrhythmic Drugs for First-line Therapy of Atrial Fibrillation
A Meta-analysis of Randomized Clinical Trials

Mohit K. Turagam, MD; Daniel Musikantow, MD; William Whang, MD; Jacob S. Koruth, MD; Marc A. Miller, MD; Marie-Noelle Langan, MD; Aamir Sofi, MD; Subbarao Choudry, MD; Srinivas R. Dukkipati, MD; Vivek Y. Reddy, MD

Figure 2. Primary Clinical Outcome

Study	Ablation Events	Ablation Total	Drug therapy Events	Drug therapy Total	Risk ratio (95% CI)
RAAFT-1[17]	4	32	22	35	0.20 (0.08-0.51)
CRYO-FIRST[23]	19	107	36	111	0.55 (0.34-0.89)
STOP-AF[22]	21	104	35	99	0.57 (0.36-0.91)
EARLY AF[21]	65	154	101	149	0.62 (0.50-0.77)
MANTRA-PAF[18]	53	146	83	148	0.64 (0.49-0.84)
RAAFT-2[19]	36	66	44	61	0.76 (0.58-0.99)
Total (95% CI)		609		603	0.62 (0.51-0.74)
Total events	198		321		

Heterogeneity: $\tau^2 = 0.02$; $\chi^2_6 = 8.37$; $P = .14$; $I^2 = 40\%$

Total overall effect: $z = 5.17$; $P < .001$

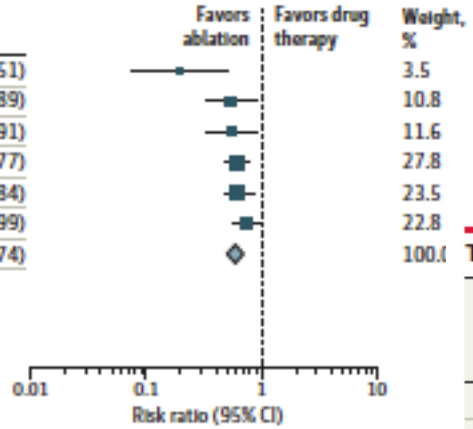


Table 2. Aggregate Complications During Ablation vs Drug Therapy

Complication	No. (%) Ablation group (n = 609)	No. (%) Drug group (n = 603)
Vascular puncture site complications[a]	3 (0.5)	0
Pericardial effusion[b]	8 (1.3)	1 (0.1)
Phrenic nerve palsy	3 (0.5)	0
Pulmonary venous stenosis	4 (0.7)	0
Thromboembolic events[c]	3 (0.5)	1 (0.1)
Bradycardia	3 (0.5)	7 (1.1)
Atrial flutter with 1:1 conduction	0	3 (0.5)
Syncope	2 (0.3)	5 (0.8)
Composite of major adverse events	26 (4.2)	17 (2.8)

[a] Composite of groin hematoma, pseudoaneurysm, and groin infection.

[b] With or without cardiac tamponade physiology.

[c] Composite of all thromboembolic events including stroke and transient ischemic attack.

Can early AF management delay progression of pAF to pers AF?

Catheter ablation or medical therapy to delay progression of atrial fibrillation: the randomized controlled atrial fibrillation progression trial (ATTEST)

Karl-Heinz Kuck [1]*, **Dmitry S. Lebedev** [2], **Evgeny N. Mikhaylov** [2],

Received 16 July 2020; editorial decision 3 September 2020; accepted after revision 28 September 2020; online publish-ahead-of-print 17 December 2020

Aims Delay of progression from paroxysmal to persistent atrial fibrillation (AF) is an important measure of long-term success of AF treatment. However, published data on the impact of catheter ablation on AF progression are limited. This study evaluates whether radiofrequency (RF) catheter ablation delays the progression of AF compared with antiarrhythmic drug (AAD) treatment using current AF management guidelines.

Methods This prospective, randomized, controlled, two-arm, open-label trial was conducted at 29 hospitals and medical centres across 13 countries. Patients were randomized 1 : 1 to RF ablation or AAD treatment. The primary endpoint was the rate of persistent AF/atrial tachycardia (AT) at 3 years.

Results After early study termination following slow enrolment, 255 (79%) of the planned 322 patients were enrolled (RF ablation, $n = 128$, AAD, $n = 127$); 36% of patients in the RF ablation group and 41% in the AAD group completed 3 years of follow-up. For the primary endpoint, the Kaplan–Meier estimate of the rate of persistent AF/AT at 3 years was significantly lower with RF ablation [2.4% (95% confidence interval (CI), 0.6–9.4%)] than with AAD therapy [17.5% (95% CI, 10.7–27.9%); one-sided $P = 0.0009$]. Patients ≥65 years were ~4 times more likely to progress to persistent AF/AT than patients <65 years, suggesting RF ablation can delay disease progression [hazard ratio: 3.87 (95% CI, 0.88–17.00); $P = 0.0727$]. Primary adverse events were reported for eight patients in the RF ablation group.

Conclusions Radiofrequency ablation is superior to guideline-directed AAD therapy in delaying the progression from paroxysmal to persistent AF.

CATHETER ABLATION DELAYS PROGRESSION OF ATRIAL FIBRILLATION

ATTEST: MULTICENTRE, RANDOMISED CONTROLLED TRIAL

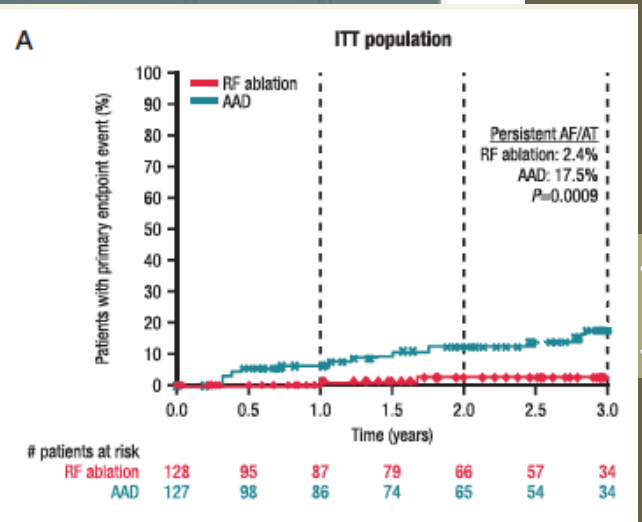
255
PATIENTS ≥ 60 YRS WITH DRUG-REFRACTORY, SYMPTOMATIC PAROXYSMAL ATRIAL FIBRILLATION

29
HOSPITALS

13
COUNTRIES

	RADIOFREQUENCY CATHETER ABLATION	ANTIARRHYTHMIC DRUG
	(N=128)	(N=127)
Rate of progression to persistent Atrial Fibrillation/Atrial Tachycardia at 3 years (P=0.0009)	**2.4%** (95% CI: 0.6-9.4%)	**17.5%** (95% CI: 10.7-27.9%)

Patients with RF ablation were **10x** less likely to develop persistent AF/AT (HR: 0.107; 95% CI: 0.024-0.47; P=0.0031)
Patients ≥65 years were nearly **4x** more likely to develop persistent AF/AT (HR: 3.87; 95%



Strategy for Persistent and long persistent AF

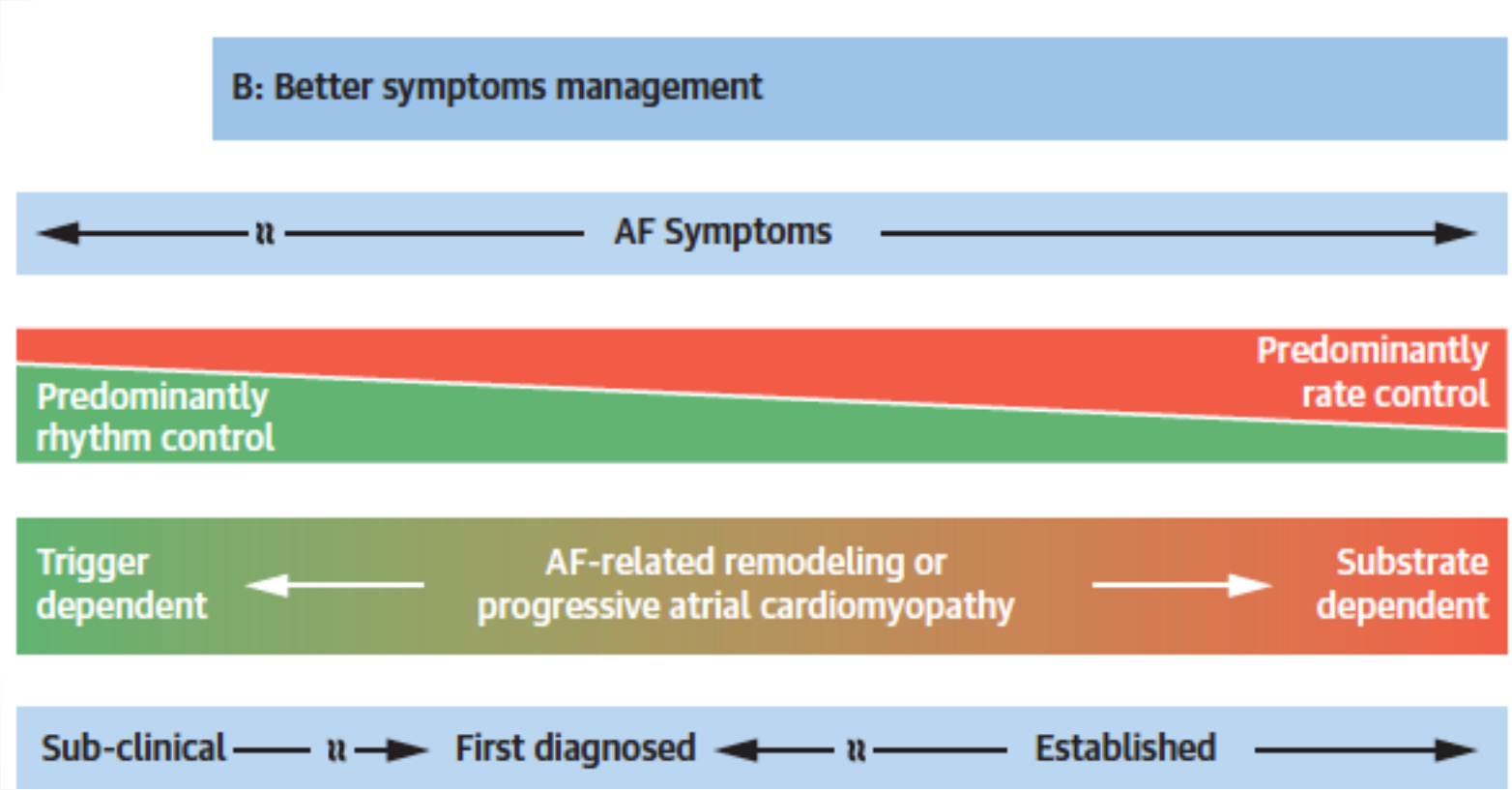
TABLE 3 Definitions of AF: A Simplified Scheme

Term	Definition
Paroxysmal AF	• AF that terminates spontaneously or with intervention within 7 d of onset. • Episodes may recur with variable frequency.
Persistent AF	• Continuous AF that is sustained >7 d.
Long-standing persistent AF	• Continuous AF >12 mo in duration.
Permanent AF	• The term "permanent AF" is used when the patient and clinician make a joint decision to stop further attempts to restore and/or maintain sinus rhythm. • Acceptance of AF represents a therapeutic attitude on the part of the patient and clinician rather than an inherent pathophysiological attribute of AF. • Acceptance of AF may change as symptoms, efficacy of therapeutic interventions, and patient and clinician preferences evolve.
Nonvalvular AF	• AF in the absence of rheumatic mitral stenosis, a mechanical or bioprosthetic heart valve, or mitral valve repair.

AF indicates atrial fibrillation.

70% of AF

Paroxysmal AF: ~87% **** with >1 procedures
Persistent AF: ~72%
Long persistent AF: 65% (at 4 year follow up)



The Increasing Role of RhythmControl
in Patients With Atrial Fibrillation

JACC State-of-the-Art ReviewCamm et al. J Am Coll Cardiol 2022;79:1932–1948)

Hybrid Convergent Procedure Vs Endocardial Catheter Ablation for the Treatment of Drug Refractory Persistent and Longstanding Persistent AF (CONVERGE Trial)

PROSPECTIVE RANDOMIZED CONTROLLED MULTICENTER TRIAL

27

US & UK Sites

153

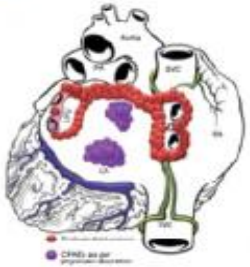
Patients with drug refractory symptomatic persistent and longstanding persistent AF

LESION SET

HYBRID CONVERGENT arm

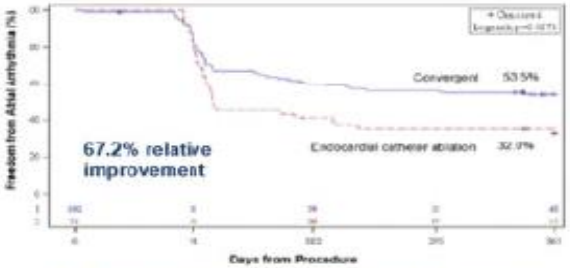
2:1 randomization

Endocardial catheter ablation arm

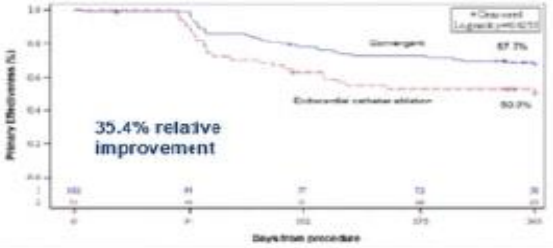


OUTCOMES THROUGH 12 MONTHS

21.5 % absolute improvement (P = 0.013) – Off AADs



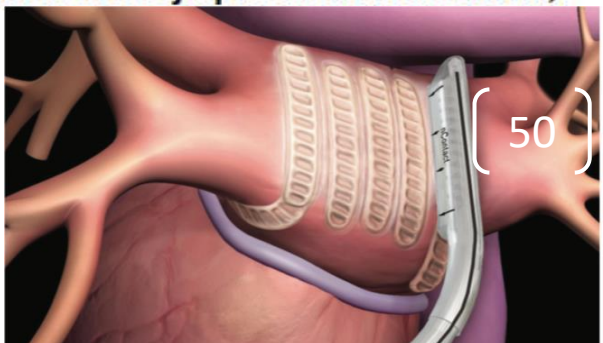
17.7% absolute improvement (P = 0.036) off new/increased dose of failed AADs



Safety rate of 2.9% through 7days & 7.8% through 30 days

Figure 1. CONVERGE trial (Convergence of Epicardial and Endocardial Ablation for the Treatment of Symptomatic Persistent AF). AADs indicates antiarrhythmic drugs; and AF, atrial fibrillation.

Median duration of AF – 4.4 years
Mean age 65, BMI 32-35
LA size 4.4 cm but up to 6 cm allowed
2-3 DCCV in the year prior to Hybrid AFA



- Hypothesis: Hybrid superior to endocardial catheter ablation alone in achieving primary effectiveness
- Primary effectiveness: Freedom from AF/AFL/AT without Class I/III AAD after 3mo blanking period up to 12 month
- Recurrence definition: >30 sec by holter or documentation by EKG (research standard for AF catheter ablation trials)

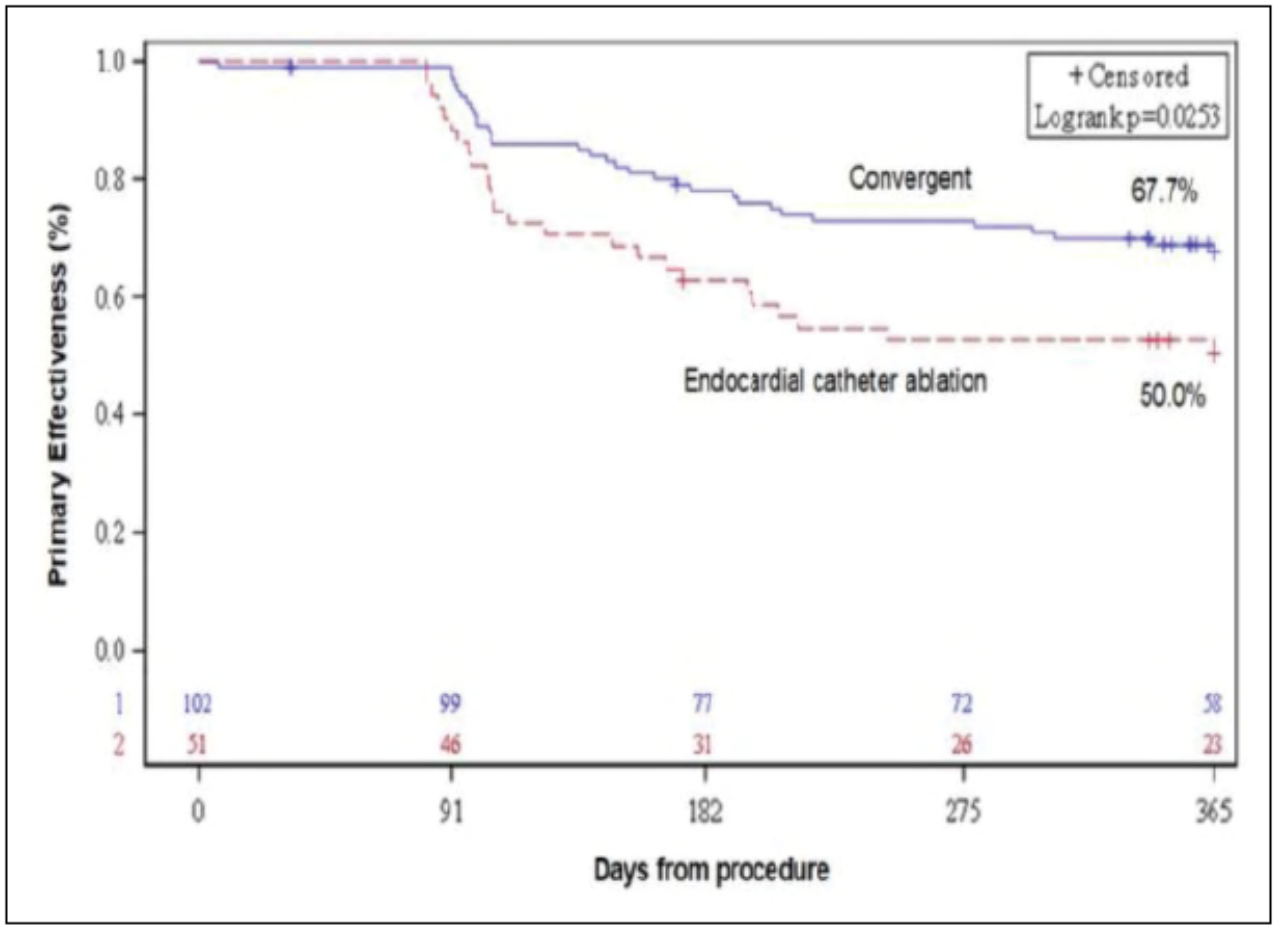


Figure 3. Primary effectiveness comparison between Hybrid Convergent and endocardial catheter ablation groups on or off previously failed class I/III antiarrhythmic drug.

AF: risk factor modification

- Age related AF, no cure. AAD, ablation, DCCV to suppress AF.
- Treatment of HTN, OSA, ETOH, CHF are bedrock of suppressing AF.
- OSA is unrecognized risk factor and requires evaluation and treatment to control AF.
- AF ablation can suppress AF. Shown to reduce mortality in CHF (EF<35%) and patients <65 y/o. Rest improves quality of life.

Long-Term Effect of Goal-Directed Weight Management in an Atrial Fibrillation Cohort

A Long-Term Follow-Up Study (LEGACY)

Rajeev K. Pathak, MBBS,* Melissa E. Middeldorp,* Megan Meredith,* Abhinav B. Mehta, MAcrSr,†
Rajiv Mahajan, MD, PhD,* Christopher X. Wong, MBBS, PhD,*‡ Darragh Twomey, MBBS,* Adrian D. Elliott, PhD,*§
Jonathan M. Kalman, MBBS, PhD,¶ Walter P. Abhayaratna, MBBS, PhD,# Dennis H. Lau, MBBS, PhD,*
Prashanthan Sanders, MBBS, PhD*

ABSTRACT

BACKGROUND Obesity and atrial fibrillation (AF) frequently coexist. Weight loss reduces the burden of AF, but whether this is sustained, has a dose effect, or is influenced by weight fluctuation is unknown.

OBJECTIVES This study sought to evaluate the long-term impact of weight loss and weight fluctuation on rhythm control in obese individuals with AF.

METHODS Of 1,415 consecutive patients with AF, 825 had a body mass index ≥27 kg/m^2 and were offered weight management. After screening for exclusion criteria, 355 were included in this analysis. Weight loss was categorized as group 1 (≥10%), group 2 (3% to 9%), and group 3 (<3%). Weight trend and/or fluctuation was determined by yearly follow-up. We determined the impact on the AF severity scale and 7-day ambulatory monitoring.

RESULTS There were no differences in baseline characteristics or follow-up among the groups. AF burden and symptom severity decreased more in group 1 compared with groups 2 and 3 ($p < 0.001$ for all). Arrhythmia-free survival with and without rhythm control strategies was greatest in group 1 compared with groups 2 and 3 ($p < 0.001$ for both). In multivariate analyses, weight loss and weight fluctuation were independent predictors of outcomes ($p < 0.001$ for both). Weight loss ≥10% resulted in a 6-fold (95% confidence interval: 3.4 to 10.3; $p < 0.001$) greater probability of arrhythmia-free survival compared with the other 2 groups. Weight fluctuation >5% partially offset this benefit, with a 2-fold (95% confidence interval: 1.0 to 4.3; $p = 0.02$) increased risk of arrhythmia recurrence.

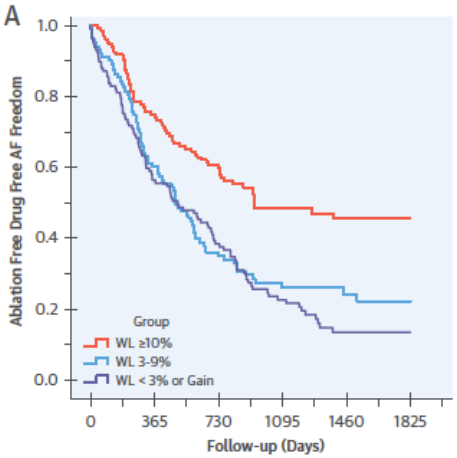
CONCLUSIONS Long-term sustained weight loss is associated with significant reduction of AF burden and maintenance of sinus rhythm. (Long-Term Effect of Goal directed weight management on Atrial Fibrillation Cohort: A 5 Year follow-up study [LEGACY Study]; ACTRN12614001123639) (J Am Coll Cardiol 2015;65:2159–69) © 2015 by the American College

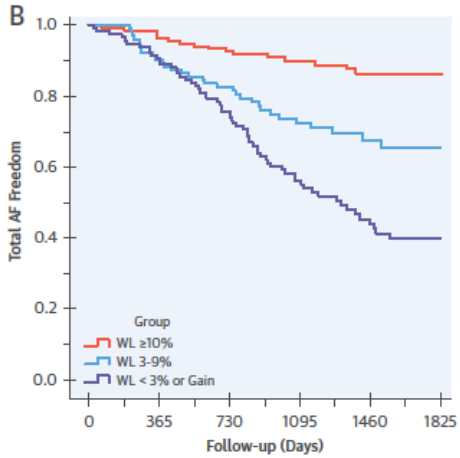
(J Am Coll Cardiol 2015;65:2159–69)

TABLE 1 Baseline Characteristics

	≥10% WL Group 1 (N = 135)	3%-9% WL Group 2 (N = 103)	<3% WL Group 3 (N = 117)	p Value
Age, yrs	65 ± 11	63 ± 11	61 ± 11	0.06
Male	86 (64)	65 (63)	83 (71)	0.37
WL clinic attendance	114 (84)	59 (57)	35 (30)	<0.001
Anthropometric measures and blood pressure				
Weight, kg	101.3 ± 17.0	98.7 ± 16.4	100.2 ± 16.8	0.52
BMI, kg/m^2	33.6 ± 4.7	32.7 ± 4.4	32.9 ± 4.8	0.24
SBP, mm Hg	147 ± 17	144 ± 17	146 ± 17	0.33
Atrial fibrillation				
Paroxysmal	71 (53)	57 (55)	60 (52)	0.86
Nonparoxysmal	64 (47)	46 (45)	45 (56)	
Metabolic risk factors				
Hypertension	109 (81)	75 (73)	90 (78)	0.30
DM	41 (30)	28 (27)	34 (29)	0.35
IGT	18 (13)	8 (8)	8 (7)	
Hyperlipidemia	66 (49)	45 (44)	56 (48)	0.70
Coronary artery disease	21 (16)	12 (12)	11 (9)	0.31
Valvulopathy	8 (6)	3 (3)	8 (7)	0.41
AHI >30	69 (51)	52 (50)	61 (52)	0.97
Alcohol excess (>30 g/week)	42 (31)	35 (34)	34 (29)	0.73
Smoker	50 (37)	41 (40)	47 (40)	0.86
Medication use				
Antiarrhythmic	1.1 ± 0.7	1.0 ± 0.7	0.9 ± 0.8	0.10
Antihypertensive	1.0 ± 0.9	1.0 ± 0.8	1.1 ± 1.0	0.08
Serology and lipid profile				
hsCRP, mg/l	5.1 ± 9.2	4.4 ± 5.8	4.1 ± 2.9	0.70
Fasting insulin level, mU/l	18.1 ± 6.7	16.6 ± 6.3	18.1 ± 7.0	0.10
LDL level, mg/l	112 ± 38	116 ± 35	104 ± 35	0.20
HDL level, mg/l	46 ± 15	46 ± 15	42 ± 12	0.11
TG level, mg/l	141 ± 62	141 ± 53	141 ± 62	0.78
Total cholesterol, mg/l	189 ± 37	185 ± 42	181 ± 42	0.50
Echocardiographic measures				
LA volume indexed, mls/m^2	37.6 ± 5.4	38.5 ± 6.2	39.0 ± 3.8	0.20
LV IVS, mm	11.7 ± 2.0	11.5 ± 2.0	11.5 ± 2.0	0.24
LVEDD, cm	5.0 ± 0.6	5.0 ± 0.6	5.0 ± 0.6	0.92
E/E' ratio	12.7 ± 4.2	12.0 ± 4.6	11.3 ± 3.7	0.06

FIGURE 2 Atrial Fibrillation Freedom Outcome According to Group



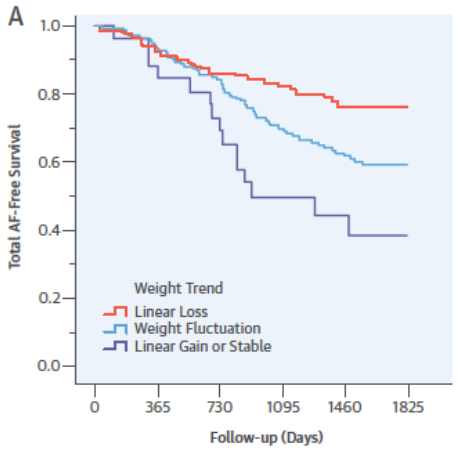


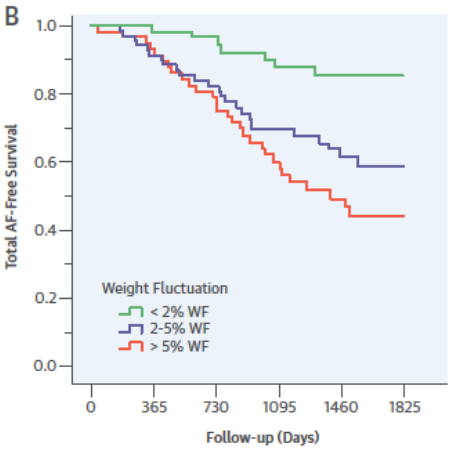
Time (Days)	0	365	730	1095	1460	1825
≥10 WL	135	101	72	42	31	18
3-9% WL	103	62	36	22	13	7
<3% WL or gain	117	66	44	22	11	9

0	365	730	1095	1460	1825
135	130	114	86	67	36
103	93	83	57	35	22
117	105	85	53	32	22

(A) Kaplan-Meier curve for AF-free survival without the use of rhythm control strategies. **(B)** Kaplan-Meier curve for AF-free survival for total AF-free survival (multiple ablation procedures with and without drugs). Abbreviations as in Figure 1.

FIGURE 3 Outcomes of Atrial Fibrillation Freedom According to Weight Trend and Weight Fluctuation





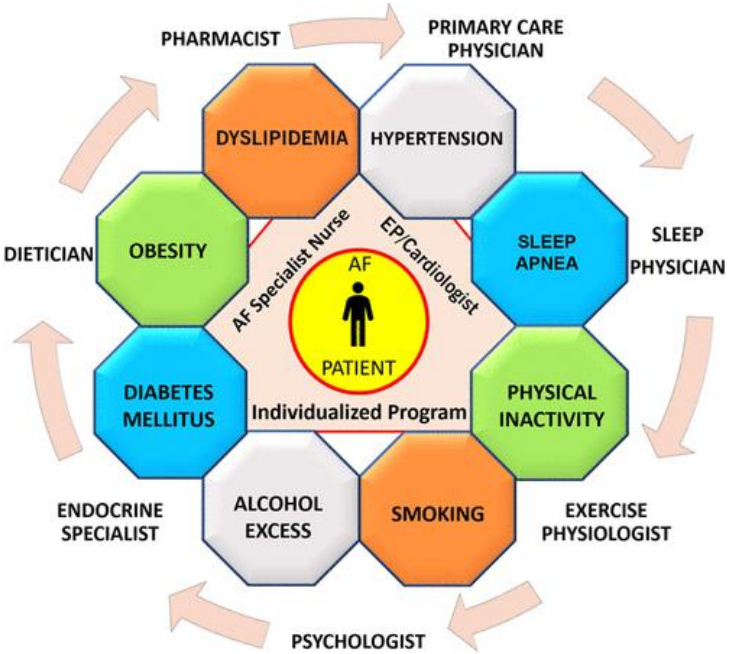
Time (Days)	0	365	730	1095	1460	1825
Linear Loss	141	130	122	80	52	29
Fluctuation	179	165	140	99	71	44
Linear Gain	24	20	18	12	8	5

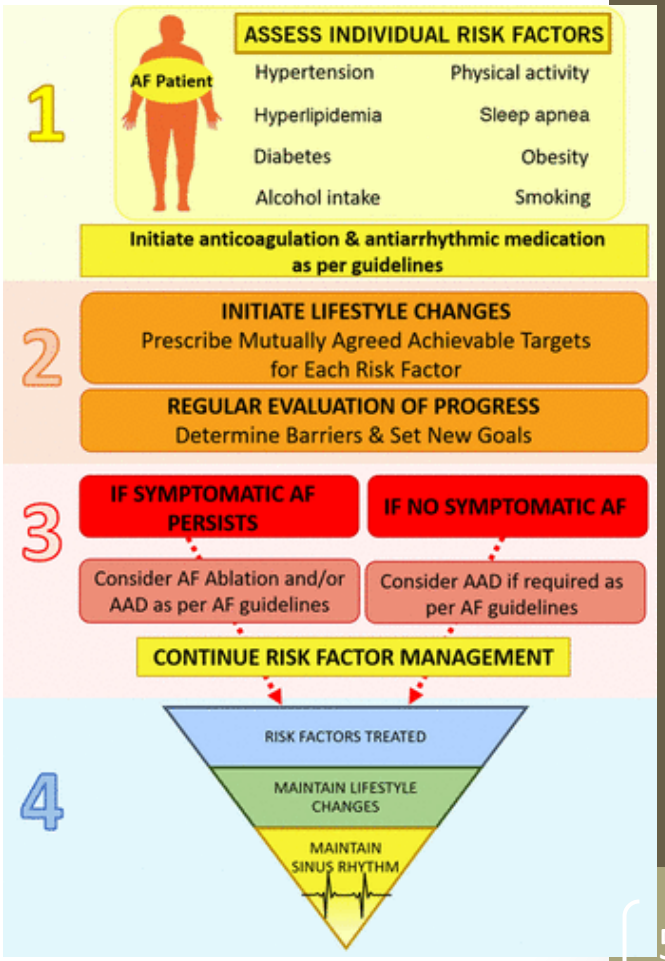
Time (Days)	0	365	730	1095	1460	1825
< 2% WF	54	52	49	39	33	19
2-5% WF	68	62	54	39	27	15
> 5% WF	57	53	45	31	19	14

(A) Kaplan-Meier curve for total AF-free survival (multiple ablation procedures with and without drugs) according to weight trend. **(B)** Kaplan-Meier curve for total AF-free survival (multiple ablation procedures with and without drugs) according to weight fluctuation. Abbreviations as in Figure 1.

Risk Factors

- Hypertension: independent factor for AF recurrence post ablation
- Obesity
- OSA: BiPAP
- Physical inactivity/ Cardiorespiratory fitness
- Diabetes mellitus
- Dyslipidemia
- Alcohol: <30g/wk
- Smoking





Risk Factors

- Lifestyle Modification as Initial Treatment for AF
  - BMI reduce
  - Exercise
  - ETOH

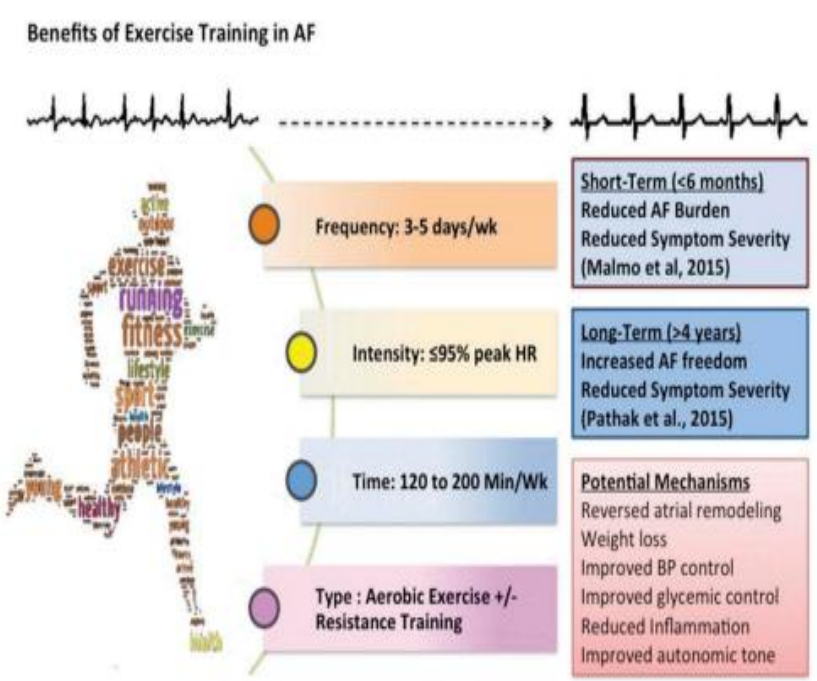
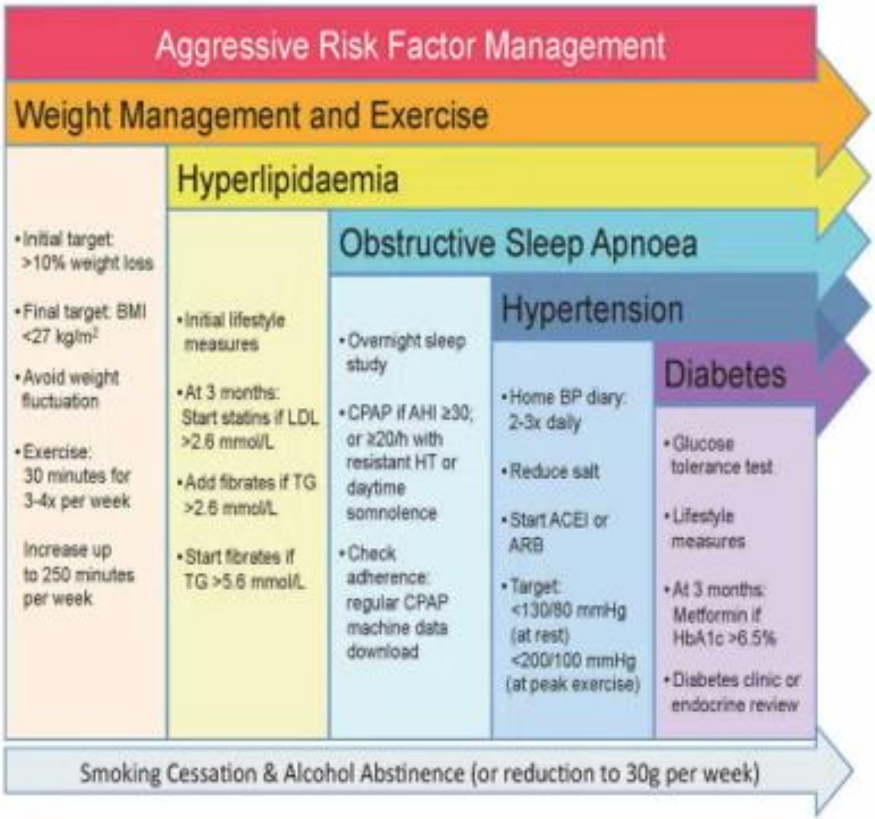
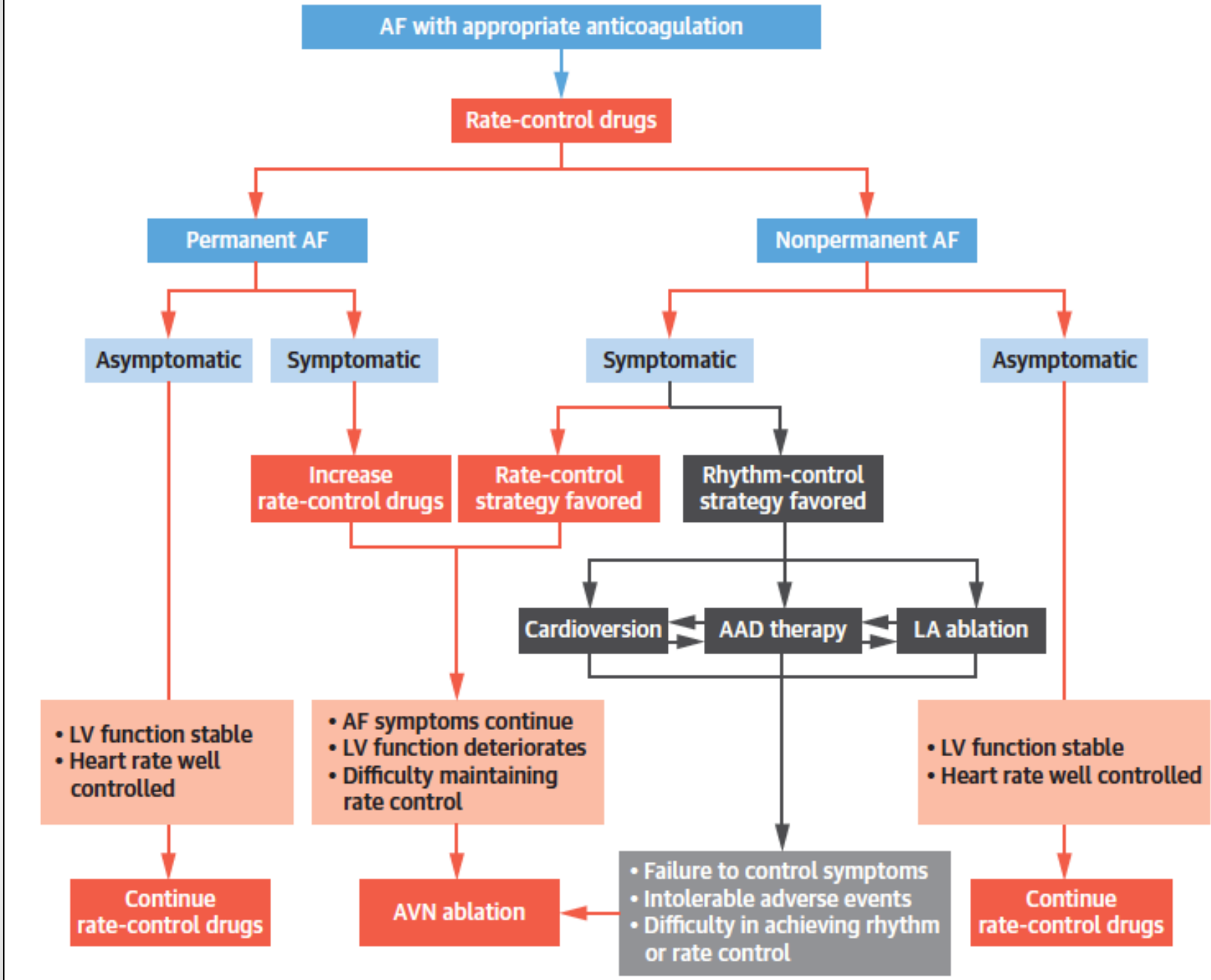


Figure 2. Exercise training and AF. Current concepts with suggested recommendations. Used with permission from Elliott et al. [61]. (BP – blood pressure; HR – heart rate).

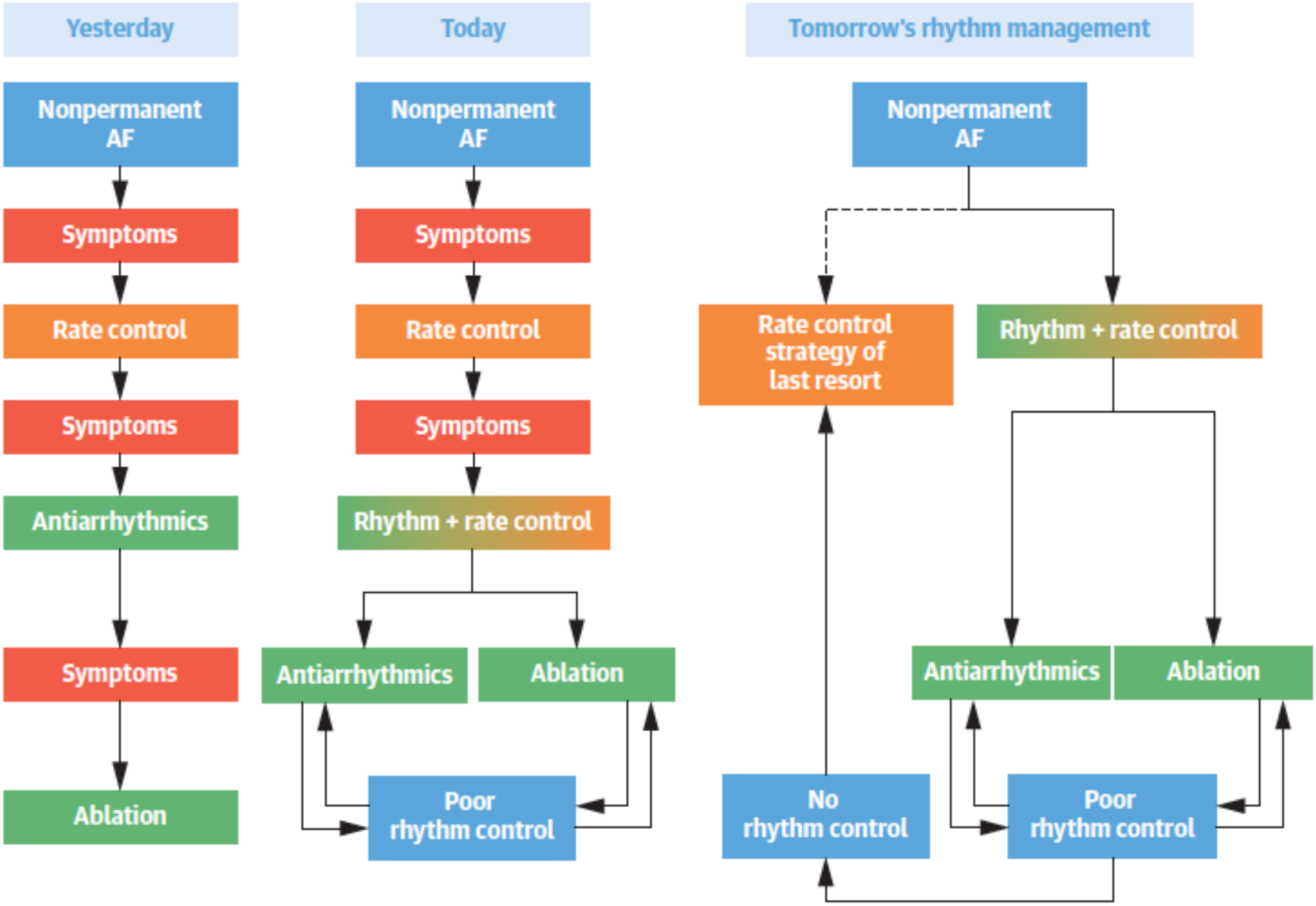
Risk Factors

- Lifestyle Modification to Improve Success of Rhythm Control
  - Weight loss
  - OSA




AF with appropriate anticoagulation
Rate-control drugs
Permanent AF
Nonpermanent AF
Asymptomatic
Symptomatic
Symptomatic
Asymptomatic
Increase rate-control drugs
Rate-control strategy favored
Rhythm-control strategy favored
Cardioversion
AAD therapy
LA ablation
• LV function stable
• Heart rate well controlled
• AF symptoms continue
• LV function deteriorates
• Difficulty maintaining rate control
• LV function stable
• Heart rate well controlled
Continue rate-control drugs
AVN ablation
• Failure to control symptoms
• Intolerable adverse events
• Difficulty in achieving rhythm or rate control
Continue rate-control drugs

CENTRAL ILLUSTRATION Summary of the Evolution of Atrial Fibrillation Rhythm Management



Camm AJ, et al. J Am Coll Cardiol. 2022;79(19):1932-1948.

Summary

- AF is inevitable in our aging population
- PVs are mains triggers in paroxysmal state
- Early Rhythm Control (ERC) is KEY :
  - AFA is superior to AAD therapy
  - reduces progression to persistent AF
  - reduces heart failure hospitalization
  - improves CV outcomes in young patients
- Persistent and long persistent AF carry low catheter ablation and AAD success rates – if symptomatic, then hybrid ablation approach is superior to catheter ablation alone
- Modifiable risk factors such as weight loss, hypertension treatment and OSA diagnosis and treatment can reduce progression

Thank you!