

MECHANISMS AND MANAGEMENT OF ATRIAL FIBRILLATION

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UNIVERSITY OF HAWAI'I

2024 ANNUAL UPDATE



HAWAII ACADEMY OF
FAMILY PHYSICIANS

FEBRUARY 16-18

GRAND NANILOA HOTEL

Nothing to Disclose



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FAMILY PHYSICIANS

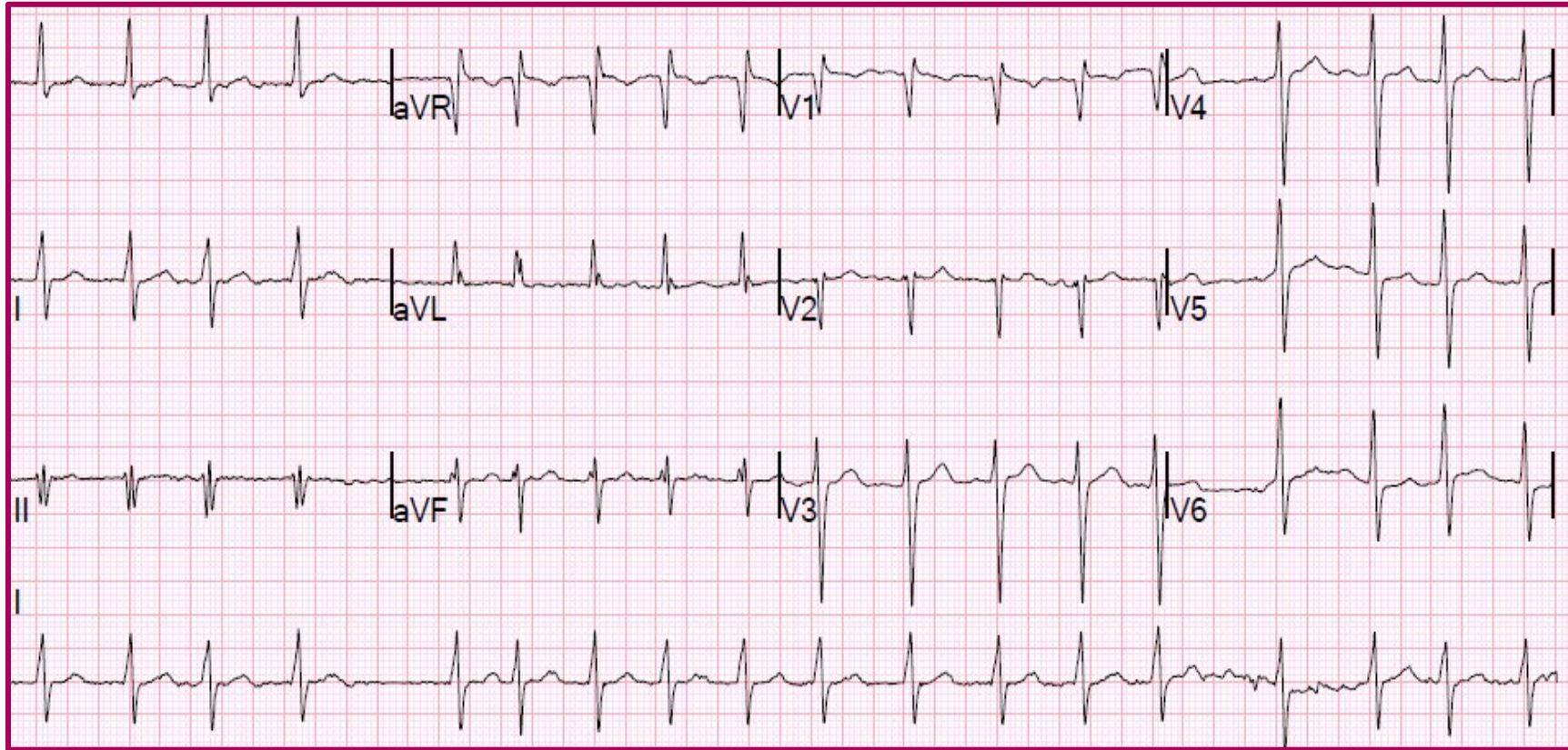
FEBRUARY 16-18

GRAND NANILOA HOTEL

OBJECTIVES

- *Epidemiology and Mechanisms of AF*
- *Role of Lifestyle and Risk Factor Modification*
- *Stroke Prevention*
- *Pharmacotherapy*
- *Ablative therapy*



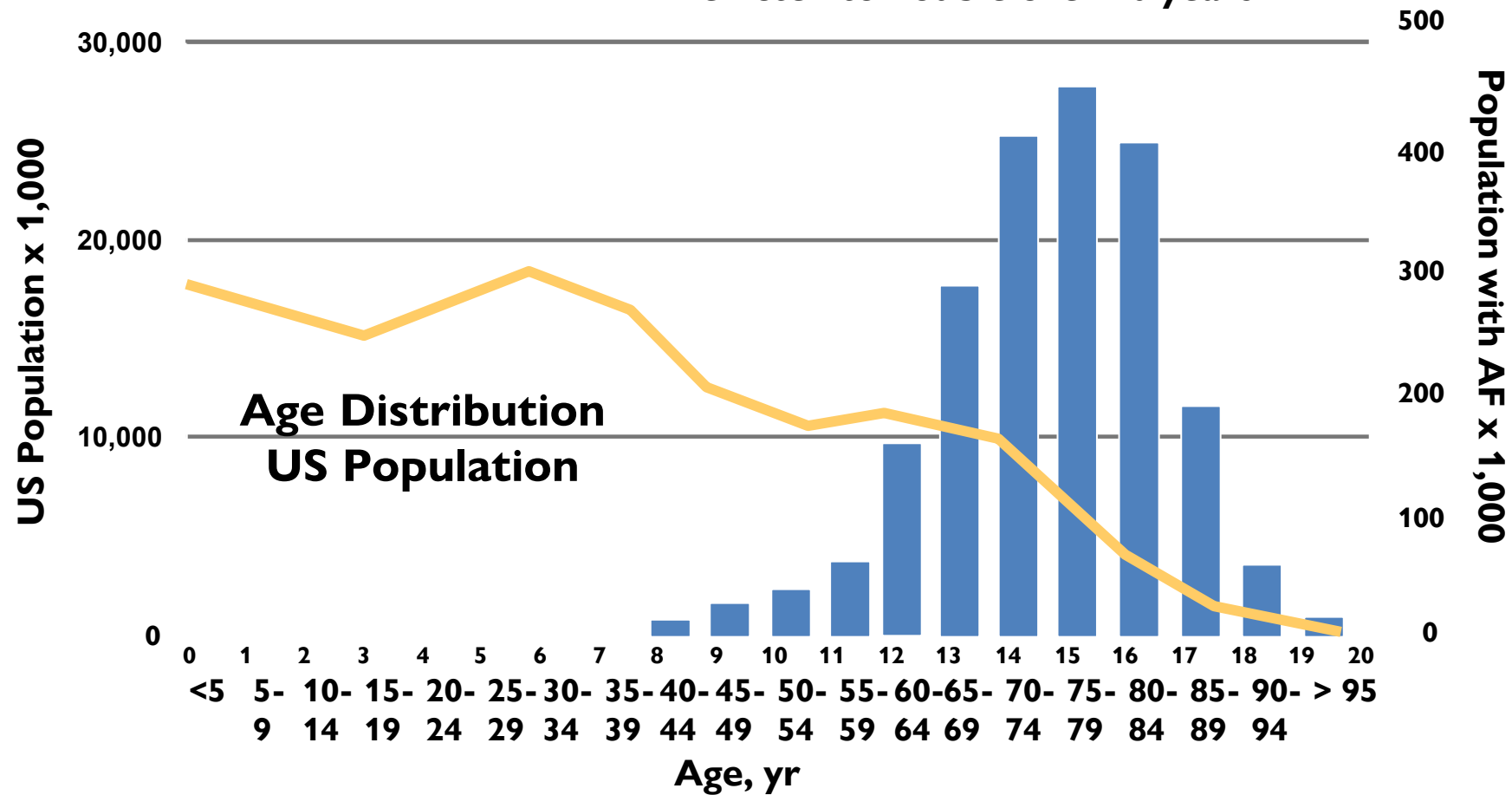


- It is a common sustained arrhythmia
- Important cause of stroke- 20% attributable risk in elderly
- Significant morbidity from symptoms- palpitations, malaise, loss of exercise tolerance , reduced QOL
- Tachy-myopathy from rapid ventricular response may result in congestive heart failure
- Can be associated with increased mortality (1.2- 2 x)



ATRIAL FIBRILLATION PREVALENCE BY AGE

US Population with AF: ~6 Million
Predicted to double over 20 years

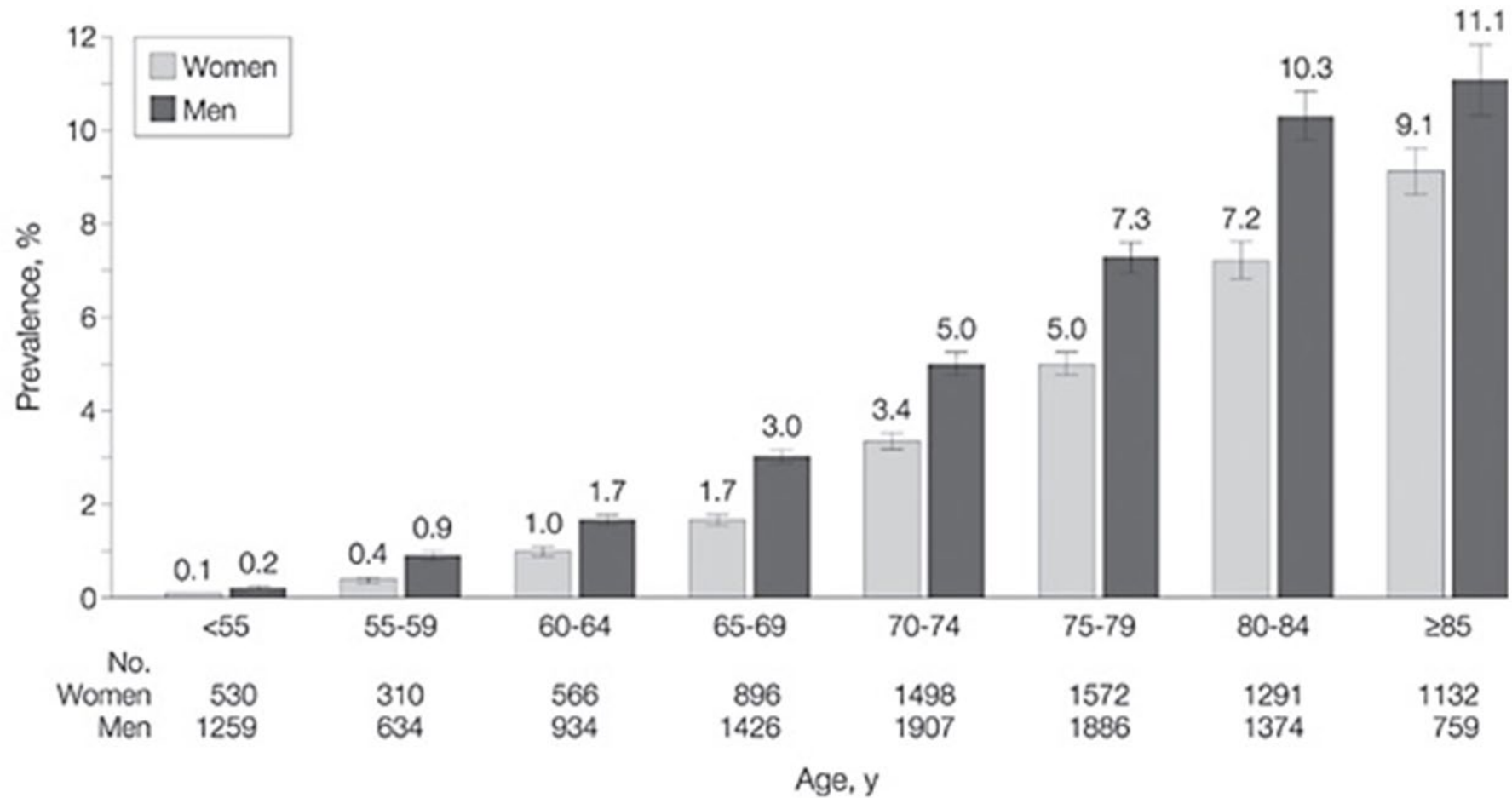


Am J Cardiol. 2009;104(11):1534-1539.



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ATRIAL FIBRILLATION PREVALENCE BY AGE



1 2019 FACILITY-SPECIFIC CLAIMS DATA FOR AFIB AND AFL PATIENTS AT THE QUEENS HOSPITAL

Total number of AFib **Patients:** 4910

Total number of AFib **Claims:** 8107



Total number of AFI Patients: 843

Total number of AFI Claims: 1163

Total number of Cardioversions: 169

¹From IQUVIA. Source file available.



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Non-modifiable

- Age
- Gender
- Family History
- Race (racial paradox)
- Tall Stature
- CV and Valvular Heart Disease

Modifiable

- Hypertension
- Obesity
- Diabetes
- Sleep Apnea
- Thyroid disease
- Alcohol Consumption
- Smoking
- Endurance Exercise

Arch Intern Med, 2006.166(21): p. 2322-8.



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Disparities among Asians and Native Hawaiians and Pacific Islanders with ischemic stroke

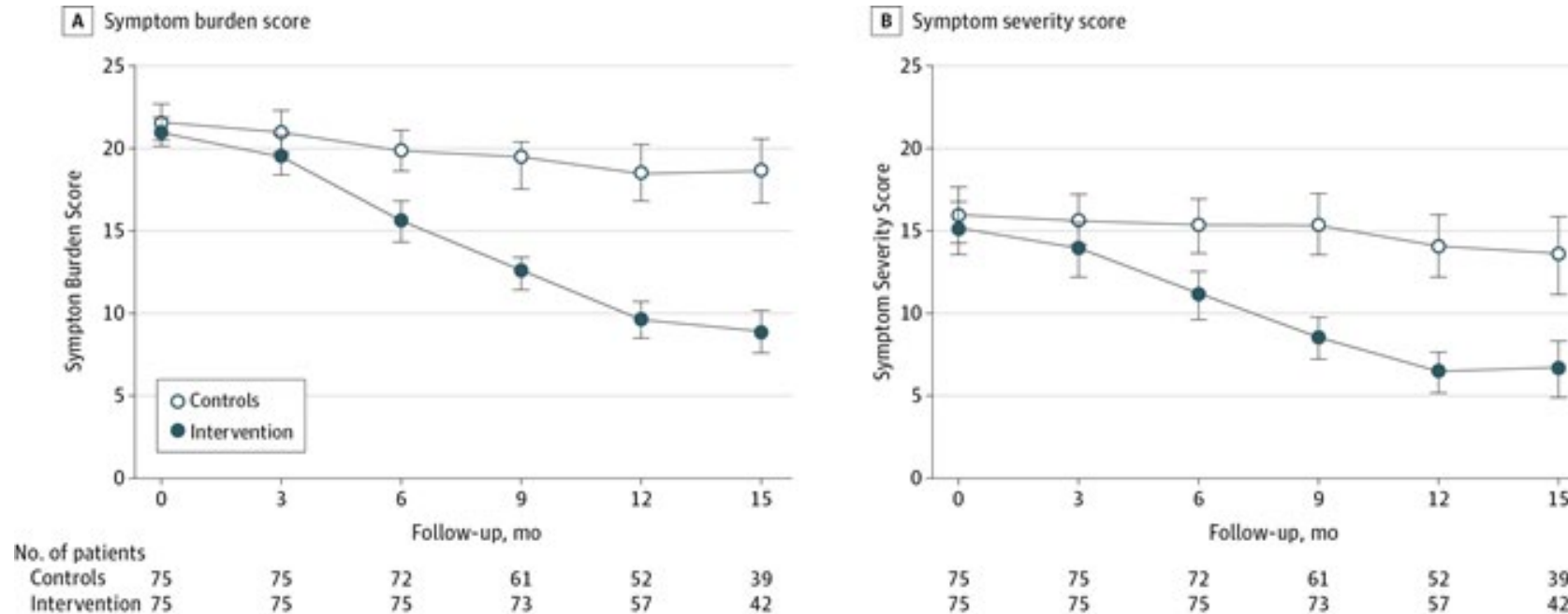
Kazuma Nakagawa, MD,[✉] Matthew A. Koenig, MD, Susan M. Asai, RN, Cherylee W. Chang, MD, and Todd B. Seto, MD, MPH

Table 1 Cardiovascular risk factors among ischemic stroke patients at The Queen's Medical Center: 2004-2010^a

Patient characteristics	NHPI	Asians	Whites
No. of patients	378	1,025	468
Risk factors			
→ Age, y	60 ± 14 ^b	72 ± 14	71 ± 14
Female	190 (50)	504 (49)	217 (46)
→ Diabetes mellitus	200 (53) ^b	349 (34) ^b	104 (22)
→ Hypertension	309 (82) ^b	802 (78) ^b	311 (67)
Atrial fibrillation/atrial flutter	56 (15)	149 (15) ^b	91 (19)
Congestive heart failure	7 (2)	12 (1)	7 (2)
Previous stroke or TIA	112 (30)	237 (23)	115 (25)
Coronary artery disease or prior MI	75 (20)	204 (20)	114 (24)
Smoking	72 (19)	141 (14)	73 (16)
Dyslipidemia	161 (43) ^b	452 (44) ^b	158 (34)
→ Obesity ^c	167 (55) ^b	92 (12) ^b	92 (26)
Total cholesterol, mg/dL	177 ± 51	182 ± 48 ^b	170 ± 43
LDL, mg/dL	114 ± 50 ^b	111 ± 48 ^b	103 ± 45
HDL, mg/dL	38 ± 11 ^b	46 ± 14	45 ± 15
Triglycerides, mg/dL	137 ± 90	139 ± 106 ^b	125 ± 102
→ BMI, kg/m ²	31 ± 7 ^b	24 ± 5 ^b	27 ± 6



Effect of weight reduction and cardiometabolic risk factor management on symptom burden and severity in patients with atrial fibrillation: a randomized clinical trial

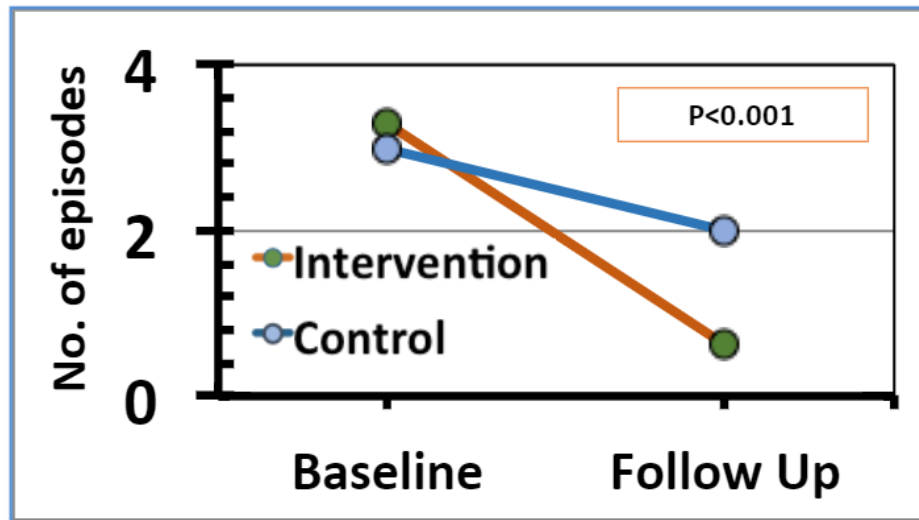


Abed et al. JAMA 2013

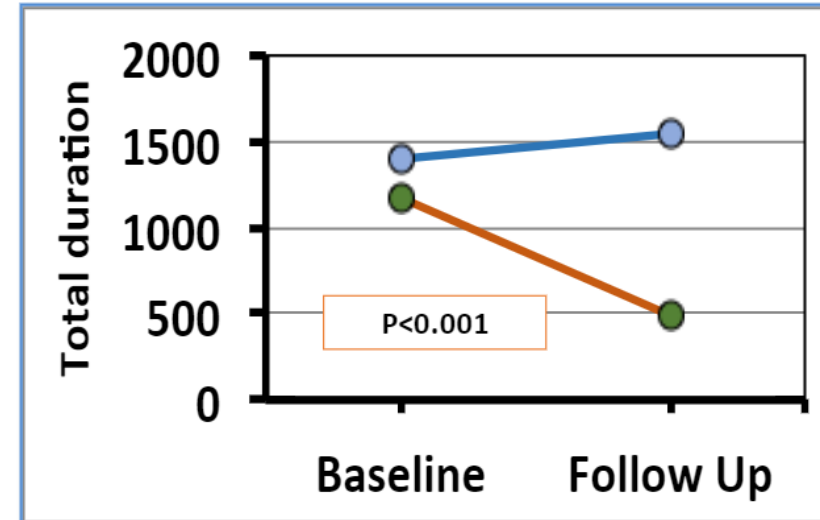


Effect of weight reduction and cardiometabolic risk factor management on symptom burden and severity in patients with atrial fibrillation: a randomized clinical trial

Number of AF episodes



Duration of AF

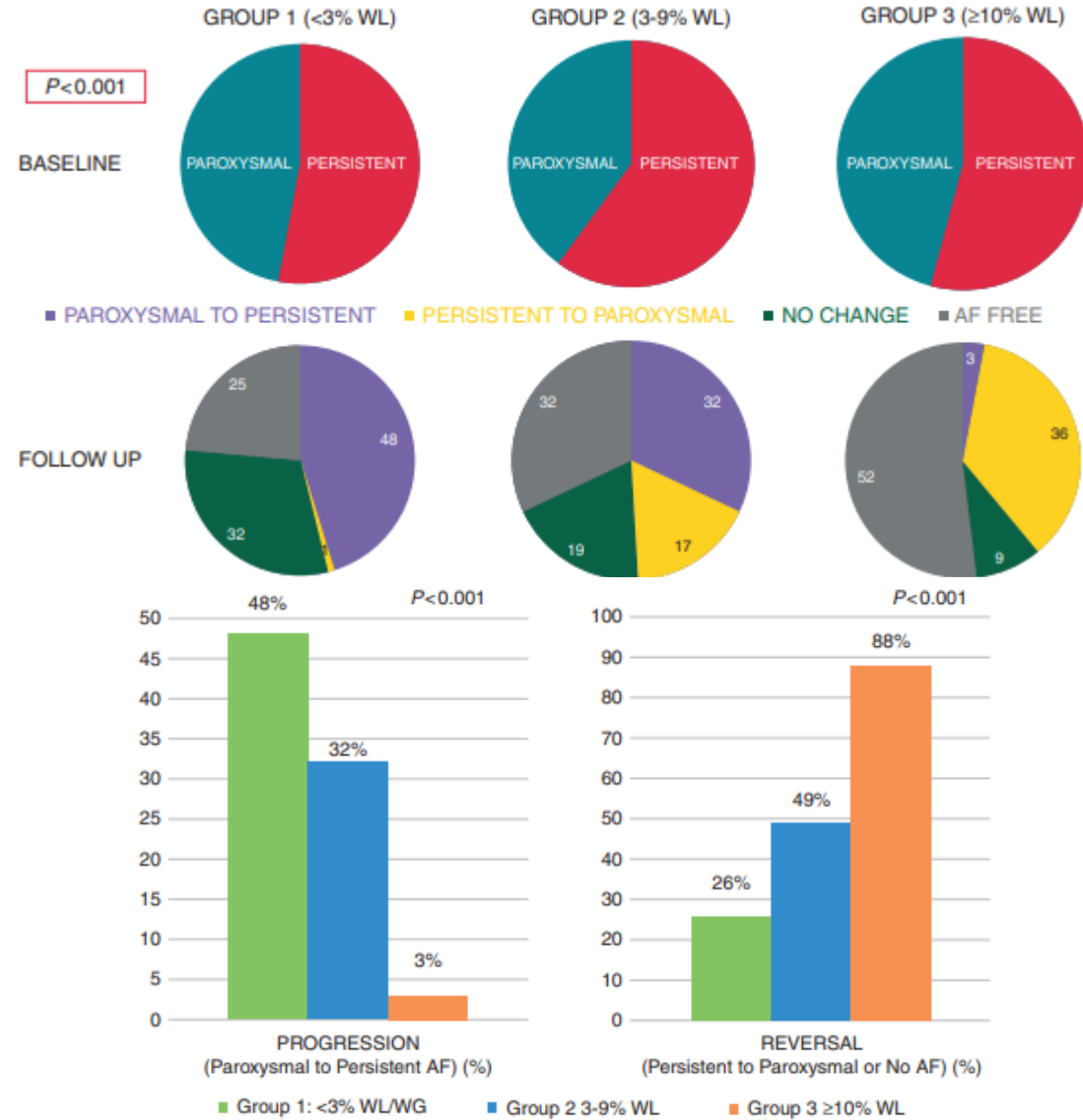


Abed et al. JAMA 2013



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PREvention and regReSSive Effect of weight-loss and risk factor modification on Atrial Fibrillation: the REVERSE-AF study



2023 ACC/AHA/ACC/P/HRS GUIDELINE FOR THE DIAGNOSIS AND MANAGEMENT OF ATRIAL FIBRILLATION

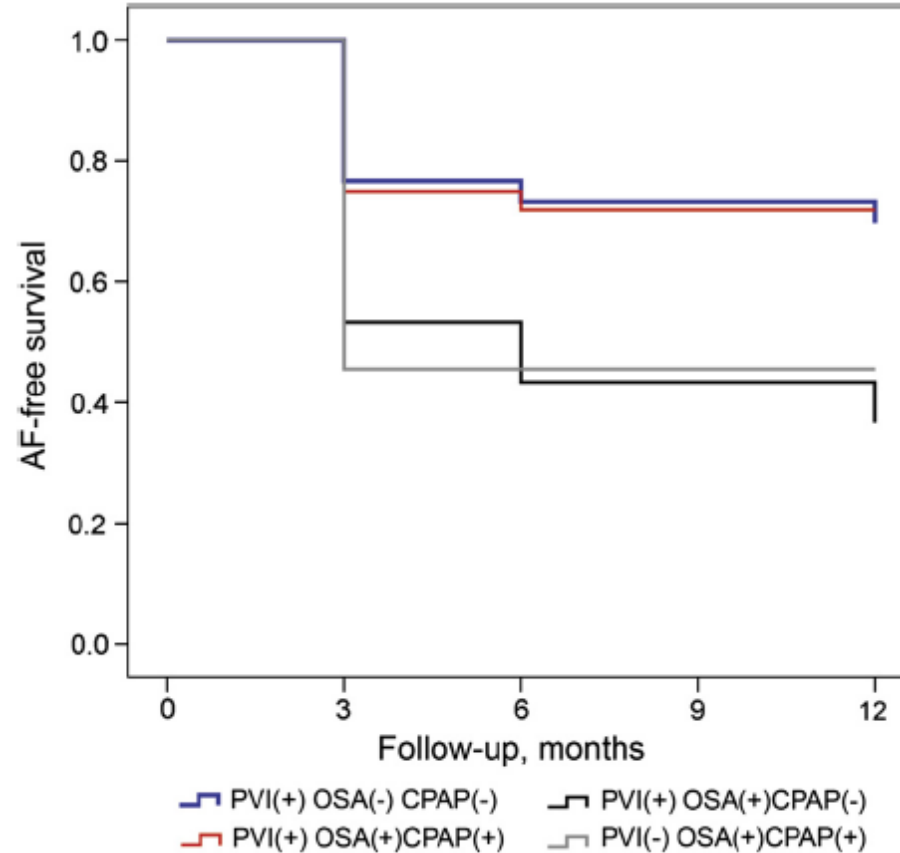
Recommendation for Weight Loss in Individuals Who Are Overweight or Obese

Referenced studies that support the recommendation are summarized in the [Online Data Supplement](#).

COR	LOE	Recommendation
1	B-R	1. In patients with AF who are overweight or obese (with body mass index [BMI] >27 kg/m ²), weight loss is recommended, with an ideal target of at least 10% weight loss to reduce AF symptoms, burden, recurrence, and progression to persistent AF. ¹⁻⁴



TREATMENT OF OBSTRUCTIVE SLEEP APNEA REDUCES RISK OF A-FIB RECURRENCE AFTER CATHETER ABLATION



- In OSA patients, CPAP resulted in higher freedom from AF
 - 71.9% vs 36.7% (p 0.01)

- AF recurrence in CPAP users was similar to patients without OSA

- AF recurrence in CPAP non-users was similar to OSA patients managed medically without ablation

JACC Vol. 62, No. 4, 2013

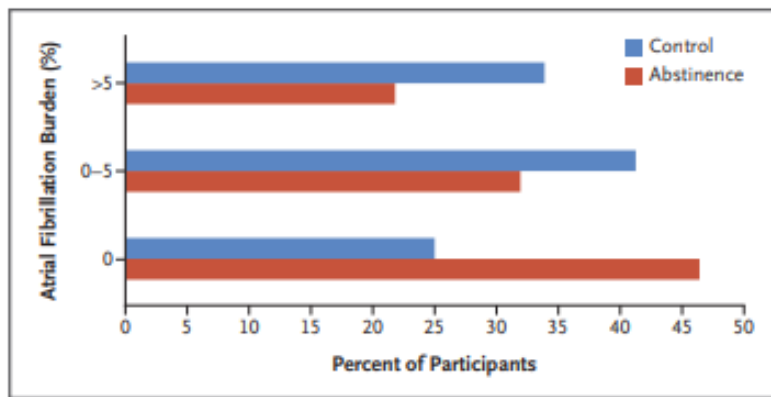
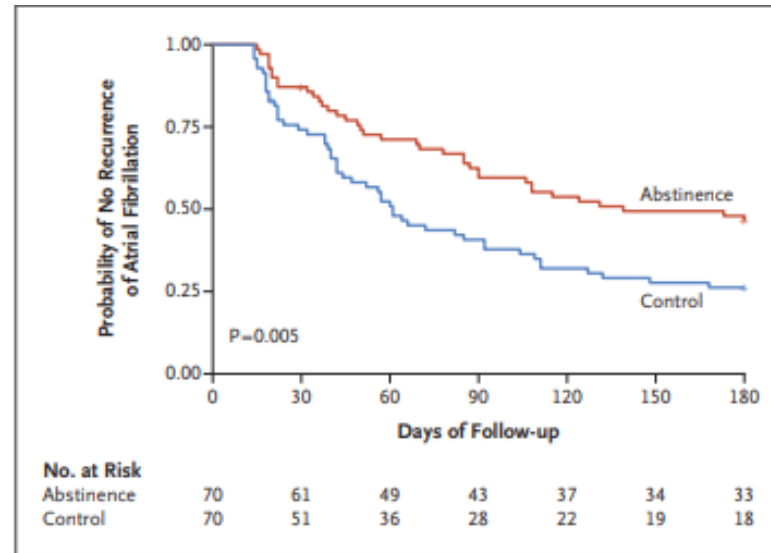


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Alcohol Abstinence in Drinkers with Atrial Fibrillation



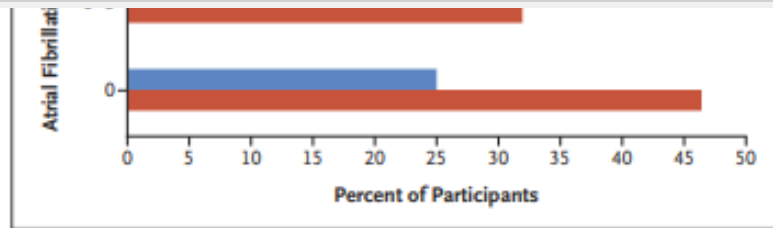
N Engl J Med 2020;382:20-8



Alcohol Abstinence in Drinkers with Atrial Fibrillation

Recommendation for Alcohol Consumption
Referenced studies that support the recommendation are summarized in the [Online Data Supplement](#).

COR	LOE	Recommendation
1	B-R	1. Patients with AF seeking a rhythm-control strategy should minimize or eliminate alcohol consumption to reduce AF recurrence and burden. ¹⁻³



Aggressive Risk Factor Reduction Study for Atrial Fibrillation and Implications for the Outcome of Ablation

The ARREST-AF Cohort Study

281 consecutive patients undergoing AF ablation in Australia

165 had BMI > 27 AND one additional risk factor (HTN, OSA, Dyslipidemia, DM/glucose intolerance, smoking or EtOH excess)

61 – Risk Factor Management

- Amb BP monitoring with goal <130/80 (<200/100 exercise)
- Sleep studies and CPAP titration
- Diet/Nutrition counseling, support groups, goal >10% loss
- RFM, then statins for goal LDL < 100 mg/dl
- HBA1c goal < 6.5%, DM clinic referral if > 7

88 – Control Group

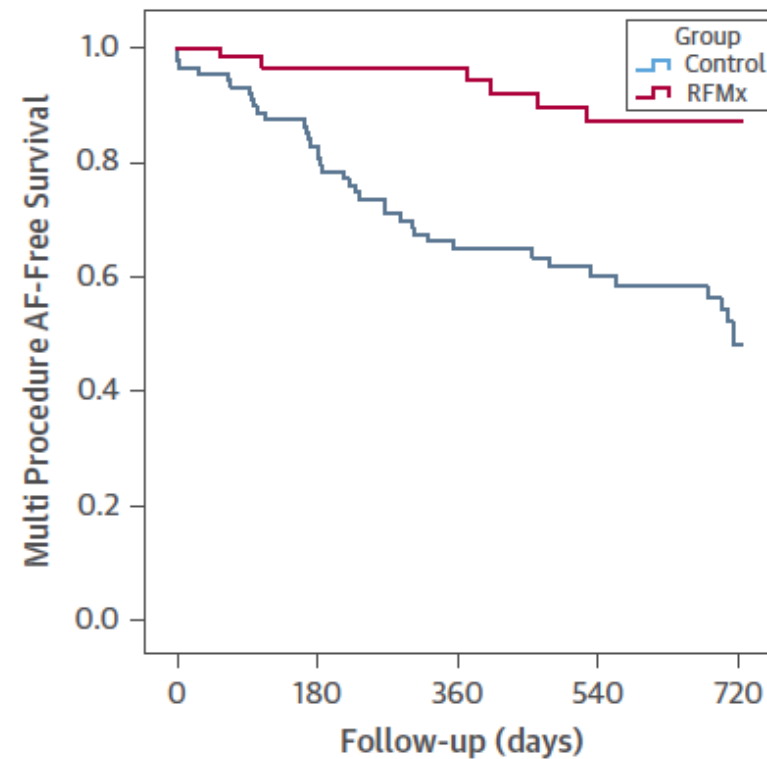
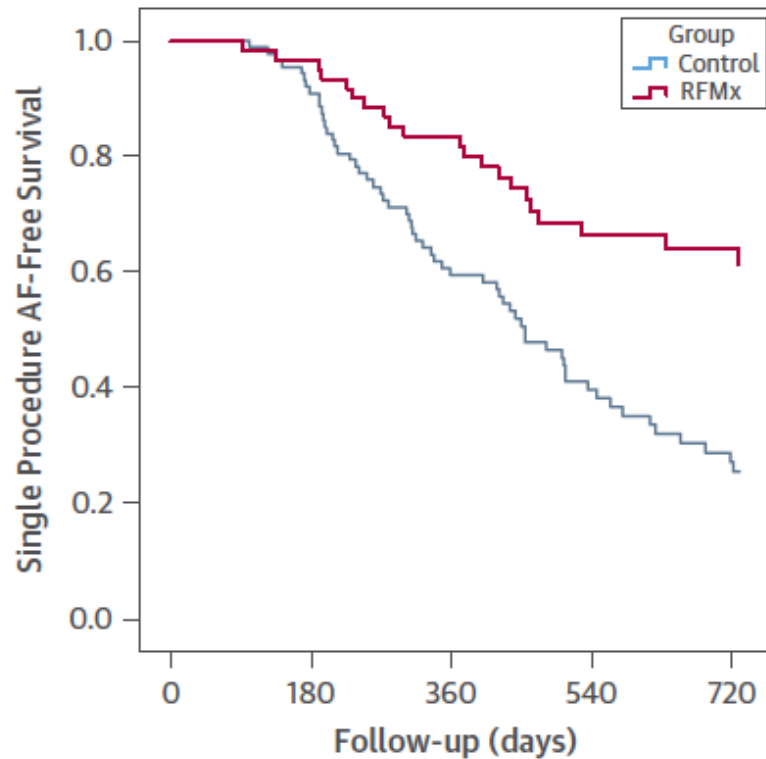
JACC Vol. 64, No. 21, 2014



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Aggressive Risk Factor Reduction Study for Atrial Fibrillation and Implications for the Outcome of Ablation

The ARREST-AF Cohort Study



JACC Vol. 64, No. 21, 2014



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AF PREVENTION

- **Cardiac Risk Factor Reduction**
 - Treat hypertension, diabetes, dyslipidemia
 - Smoking cessation
- **Weight loss- diet and exercise**
- **Moderate/elimination of alcohol**
- **Identify and treat hyperthyroidism (1%)**
- **Identify and treat sleep apnea**



POLL QUESTION 1

Which of the following has not been shown to reduce symptom burden, severity and duration of AF episodes, as well as improve outcomes of AF catheter ablation?

1. Alcohol cessation
2. Weight loss program in obese patients
3. Caffeine cessation



POLL QUESTION 1

Which of the following has not been shown to reduce symptom burden, severity and duration of AF episodes, as well as improve outcomes of AF catheter ablation?

1. Alcohol cessation
2. Weight loss program in obese patients
- 3. Caffeine cessation**



Recommendation for Caffeine Consumption

Referenced studies that support the recommendation are summarized in the [Online Data Supplement](#).

COR	LOE	Recommendation
3: No Benefit	B-NR	1. For patients with AF, recommending <u>caffeine abstinence</u> to prevent AF episodes <u>is of no benefit</u> , although it may reduce symptoms in patients who report caffeine triggers or worsens AF symptoms. ¹⁻⁹



1	2	3				4
At risk for AF	Pre-AF	AF				Permanent AF
Presence of modifiable and nonmodifiable risk factors associated with AF. Modifiable risk factors: <ul style="list-style-type: none"> • Obesity • Lack of fitness • Hypertension • Sleep apnea • Alcohol • Diabetes Nonmodifiable risk factors: <ul style="list-style-type: none"> • Genetics • Male sex • Age 	Evidence of structural or electrical findings further predisposing a patient to AF: <ul style="list-style-type: none"> • Atrial enlargement • Frequent atrial ectopy • Short bursts of atrial tachycardia <ul style="list-style-type: none"> • Atrial flutter • Other high AF risk scenarios* 					No further attempts at rhythm control after discussion between patient and clinician
	Consider heightened surveillance					



José A. Joglar. Circulation. 2023 ACC/AHA/ACCP/HRS Guideline for the Diagnosis and Management of Atrial Fibrillation: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines, Volume: 149, Issue: 1, Pages: e1-e156, DOI: (10.1161/CIR.0000000000001193)

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1	2
At risk for AF	Pre-AF
<p>Presence of modifiable and nonmodifiable risk factors associated with AF.</p> <p>Modifiable risk factors:</p> <ul style="list-style-type: none"> • Obesity • Lack of fitness • Hypertension • Sleep apnea • Alcohol • Diabetes <p>Nonmodifiable risk factors:</p> <ul style="list-style-type: none"> • Genetics • Male sex • Age 	<p>Evidence of structural or electrical findings further predisposing a patient to AF:</p> <ul style="list-style-type: none"> • Atrial enlargement • Frequent atrial ectopy • Short bursts of atrial tachycardia • Atrial flutter • Other high AF risk scenarios*
	<p>Consider heightened surveillance</p>

3 AF			4
<p>transition among different substages of AF</p>			<p>Permanent AF</p>
<p>Persistent AF (3B) AF is continuous and requires intervention</p>	<p>Long-standing persistent AF (3C) AF that is continuous for >12 mo in duration</p>	<p>Successful AF ablation (3D) Freedom from AF after percutaneous or surgical intervention to eliminate AF</p>	<p>No further attempts at rhythm control after discussion between patient and clinician</p>
<p>Modifiable Risk Factors</p>			
<p>Treat as clinically appropriate for AF burden</p>			
<p>AF associated with pathophysiological changes?</p>			
<p>Perform risk assessment and therapy if appropriate</p>			
<p>Treat symptoms</p>			

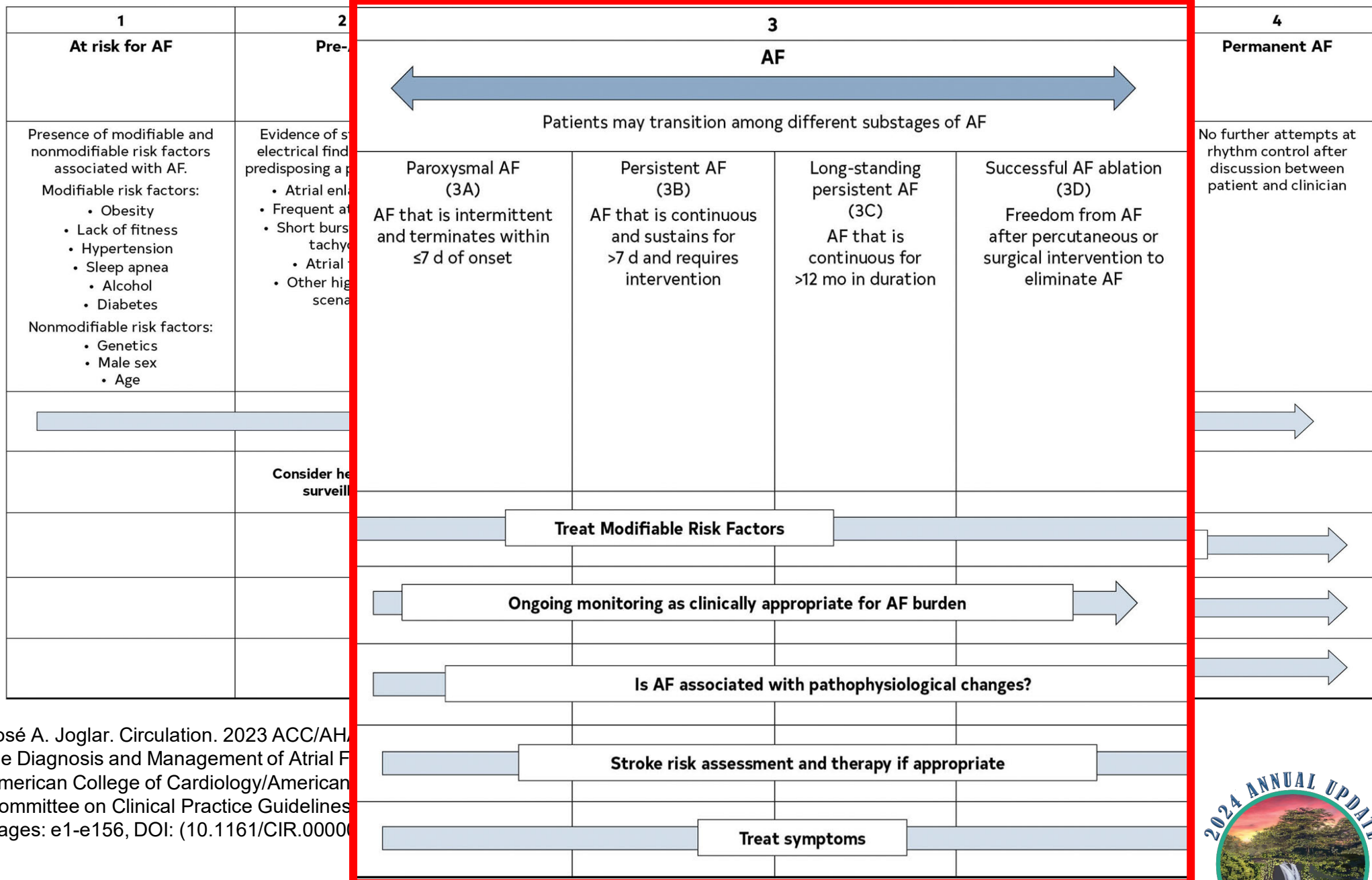


Journal of the American College of Physicians

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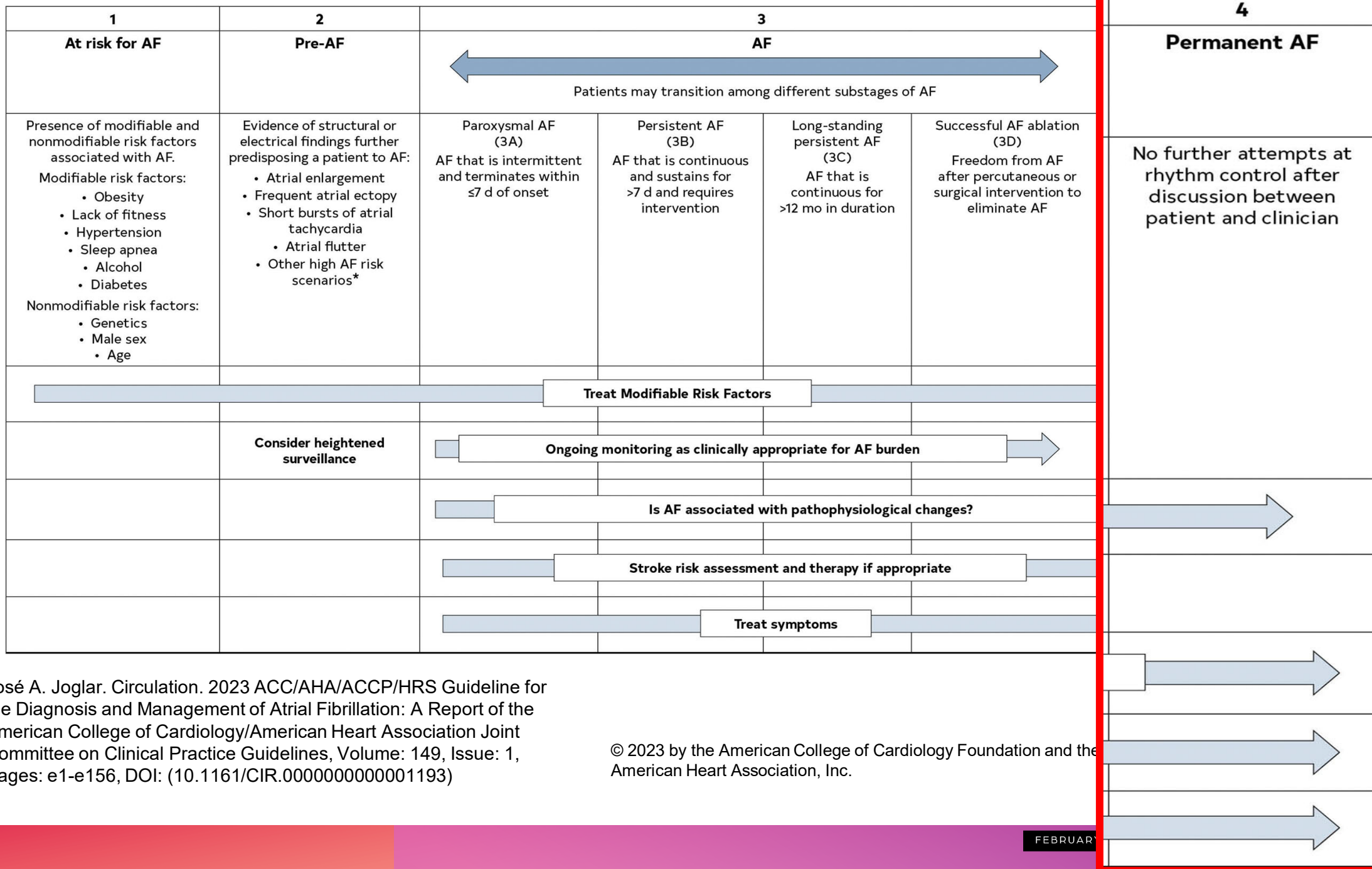
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José A. Joglar. Circulation. 2023 ACC/AHA/AHA/ACC/HRS Guideline for the Diagnosis and Management of Atrial Fibrillation: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Pages: e1-e156, DOI: (10.1161/CIR.0000000000001156)



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José A. Joglar. Circulation. 2023 ACC/AHA/ACCP/HRS Guideline for the Diagnosis and Management of Atrial Fibrillation: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines, Volume: 149, Issue: 1, Pages: e1-e156, DOI: (10.1161/CIR.0000000000001193)

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1	2	3			4
At risk for AF	Pre-AF	AF			Permanent AF
Presence of nonmodifiable risk factors associated with AF: Modifiable risk factors: <ul style="list-style-type: none"> • Obesity • Lack of physical activity • Hypertension • Sleep apnea • Alcohol • Diabetes Nonmodifiable risk factors: <ul style="list-style-type: none"> • Genetics • Male sex • Age 	Risk factors for AF: <ul style="list-style-type: none"> • Atrial flutter • Other high AF risk scenarios* 	Paroxysmal AF (3A) AF that is intermittent and terminates within ≤7 d of onset	Persistent AF (3B) AF that is continuous and sustains for >7 d and requires intervention	Long-standing persistent AF (3C) AF that is continuous for >12 mo in duration	Attempts at control after treatment by a clinician
<div style="border: 2px solid red; padding: 5px; display: inline-block; margin: 5px;"> Avoid terms: “Chronic AF” and “Lone AF” </div> <div style="border: 2px solid red; padding: 5px; display: inline-block; margin: 5px; margin-left: 200px;"> Non-valvular vs. Valvular AF </div>					

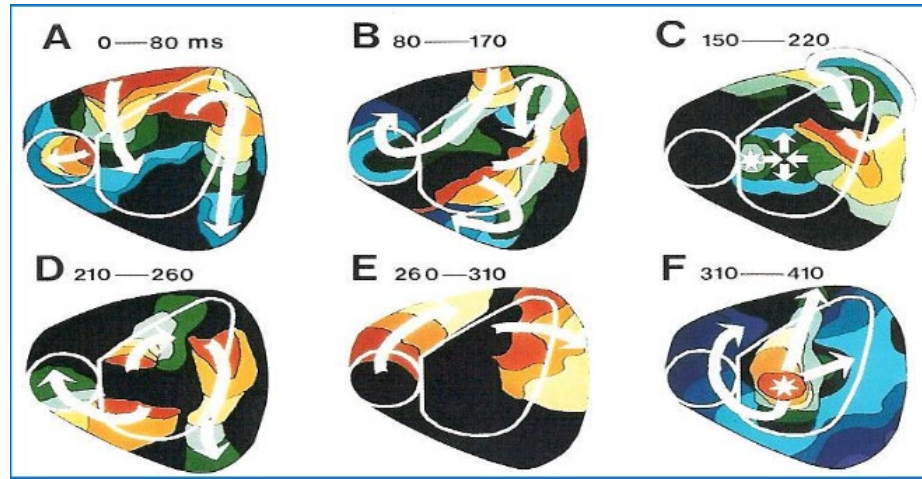
José A. Joglar. Circulation. 2023 ACC/AHA/ACCP/HRS Guideline for the Diagnosis and Management of Atrial Fibrillation: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines, Volume: 149, Issue: 1, Pages: e1-e156, DOI: (10.1161/CIR.0000000000001193)

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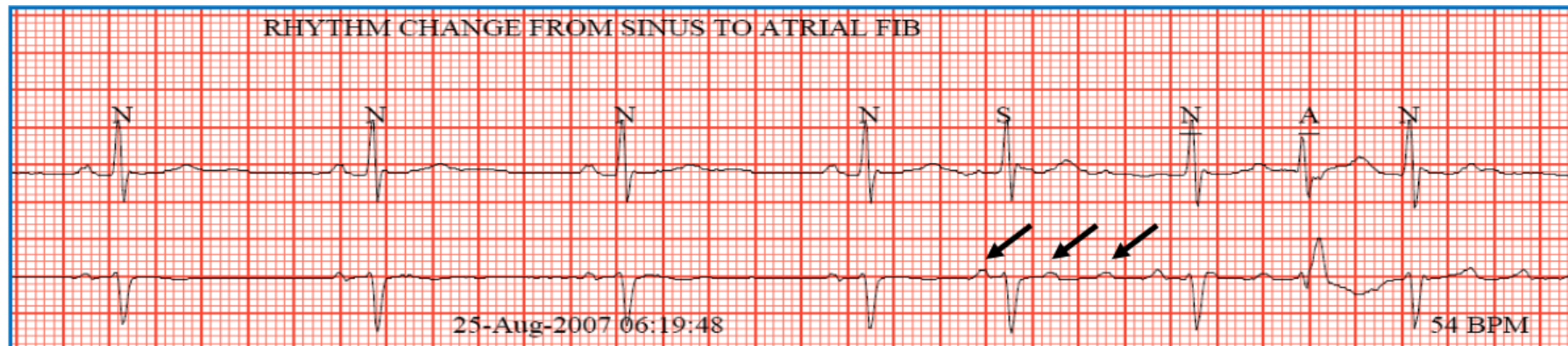
MECHANISMS OF AF



Multiple wavelet hypothesis

“Chaotic” atrial activation

Role of triggers
– Esp. PV ectopy

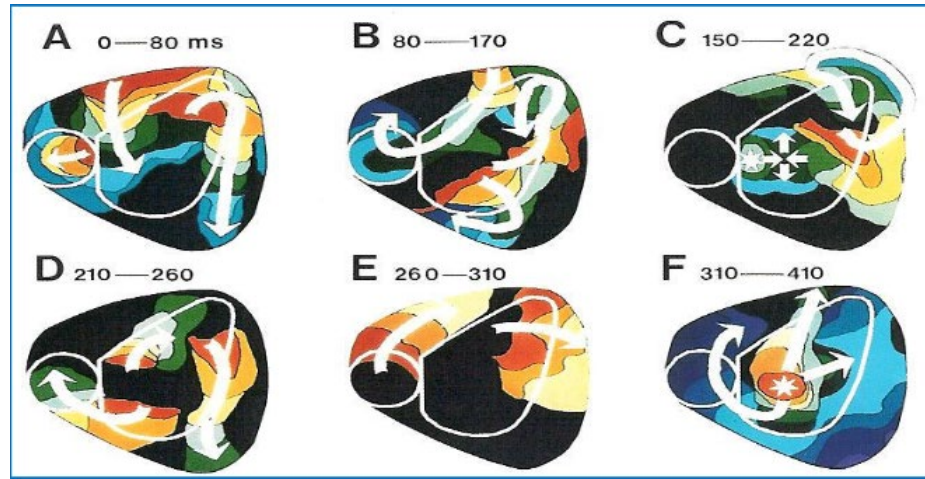


Allessie MA. *Cardiac Electrophysiology and Arrhythmias* 1985:265



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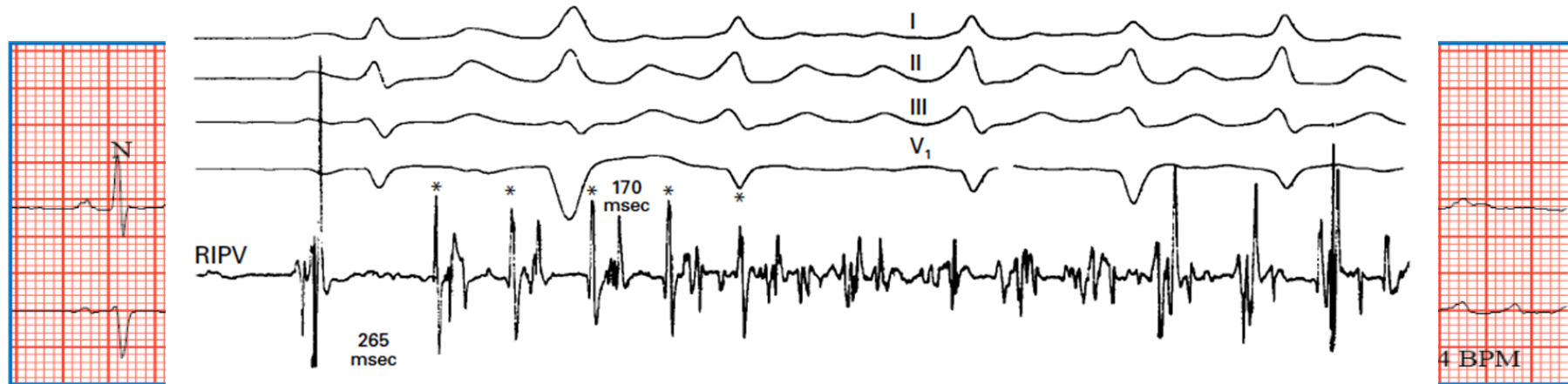
MECHANISMS OF AF



Multiple wavelet hypothesis

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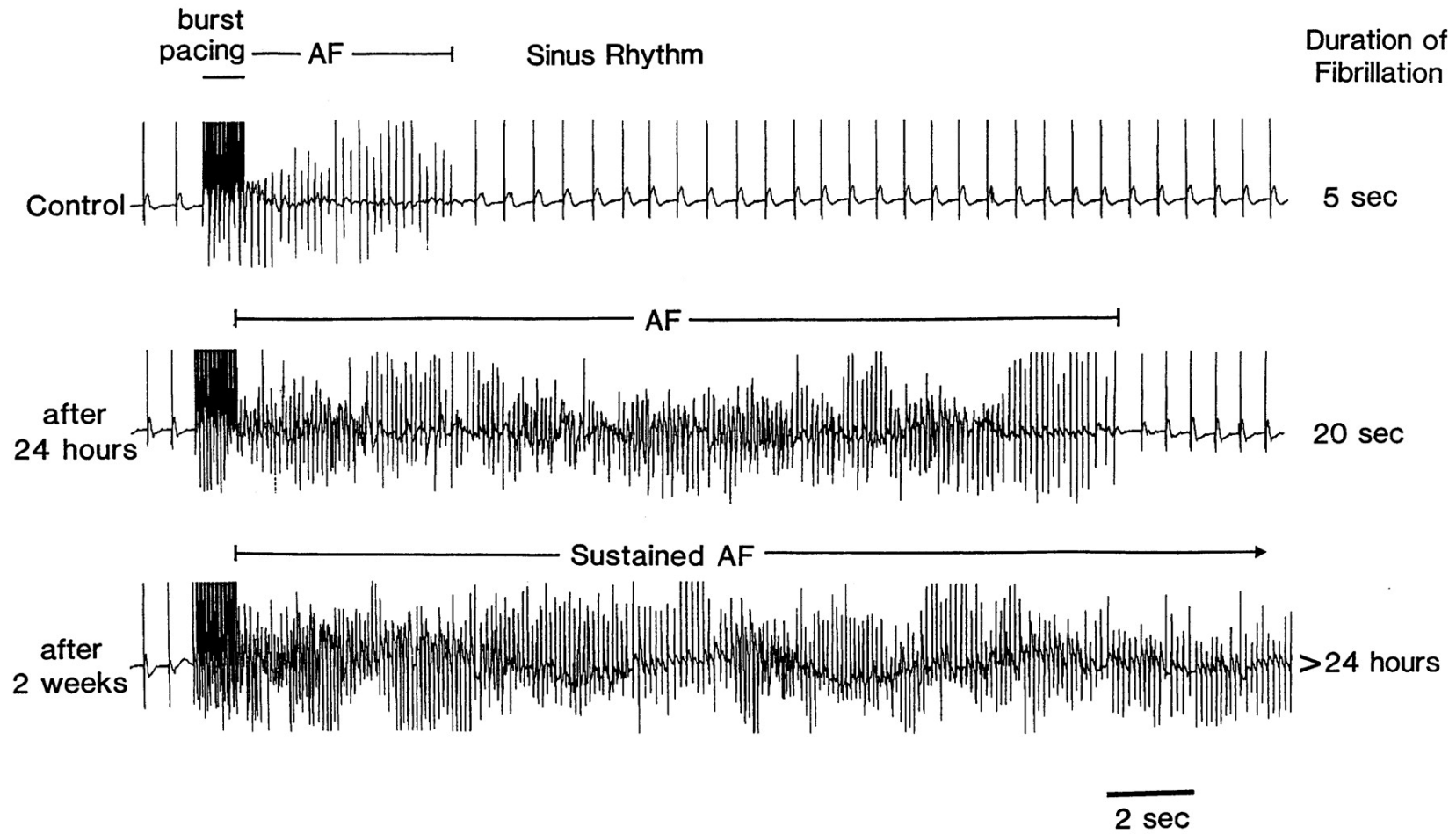


Allessie MA. *Cardiac Electrophysiology and Arrhythmias* 1985:265
Haissaguerre M. *N Engl J Med* 1998; 339:659-666



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ATRIAL FIBRILLATION BEGETS AF

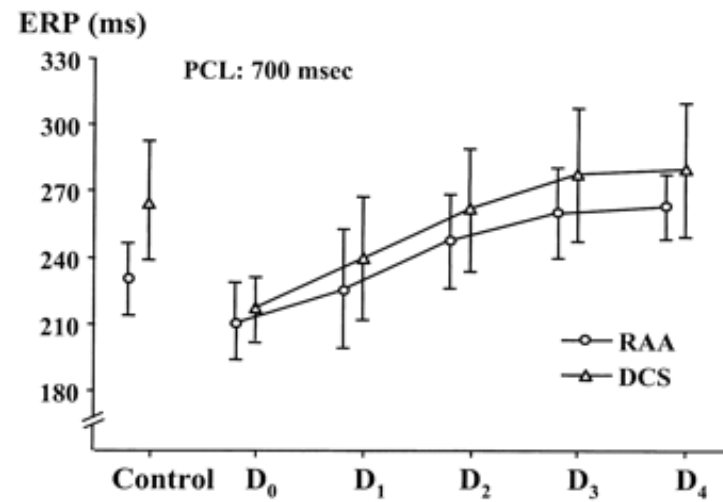
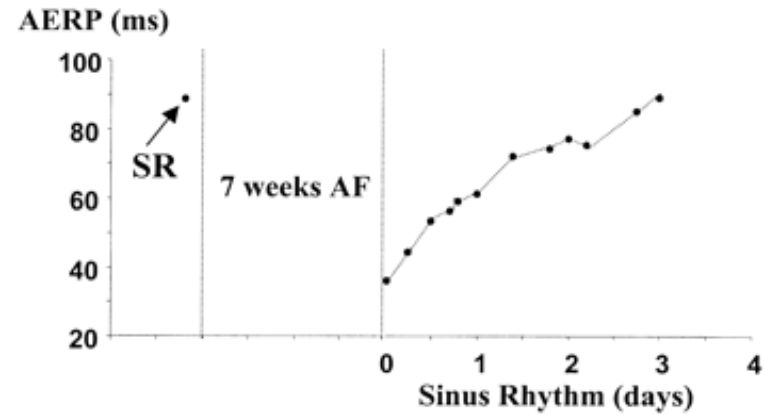


Circulation. 1995 Oct 1;92(7):1954-68

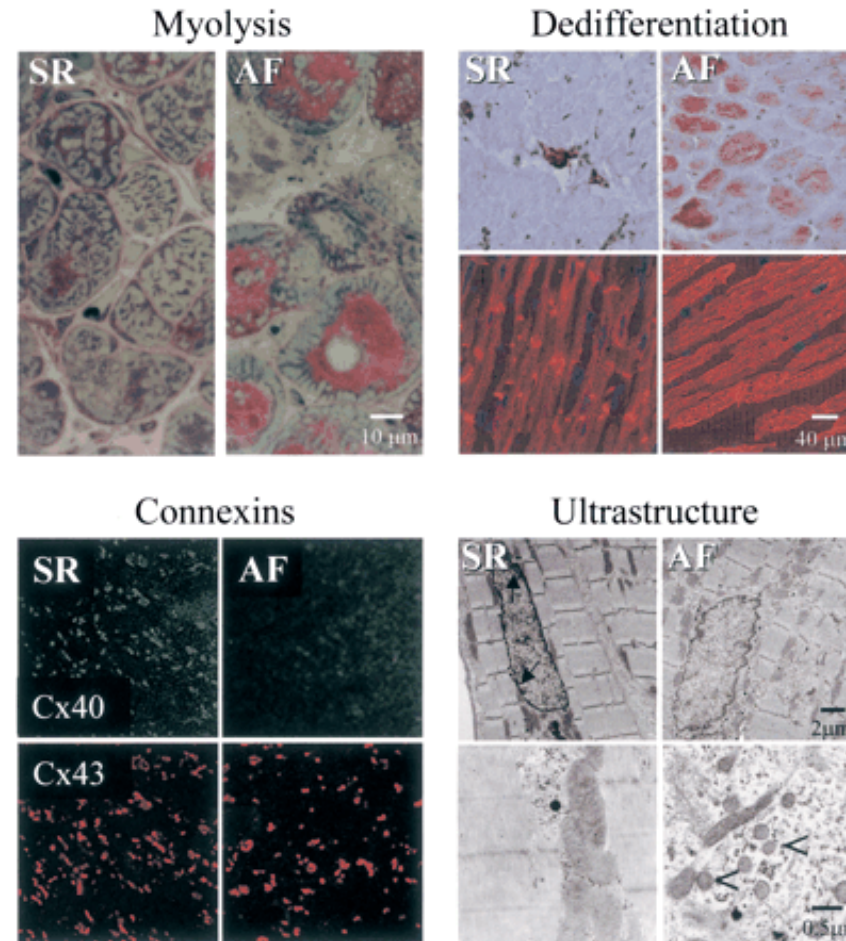


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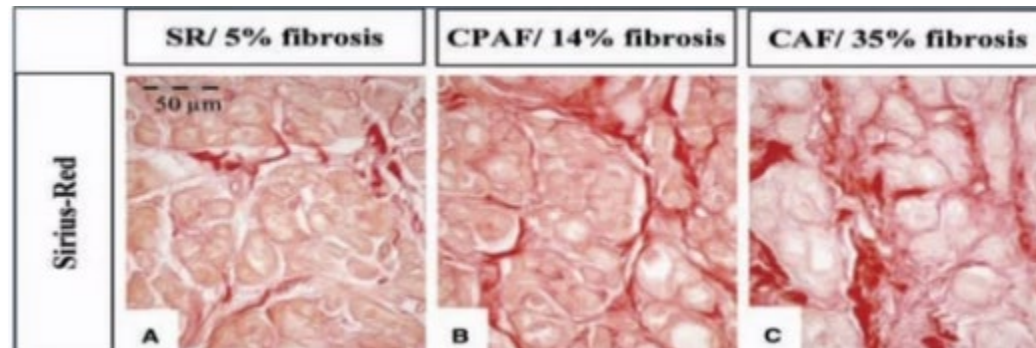
REVERSE REMODELING OF THE ATRIAL EFFECTIVE REFRACTORY PERIOD (AERP) AFTER CONVERSION



STRUCTURAL REMODELING OF ATRIAL MYOCYTES AFTER 4 MONTHS OF AF IN THE GOAT.



ATRIAL FIBROSIS INCREASES WITH DURATION OF AF



146 pts undergoing CTS
RAA excised and analyzed

*Gramley F et al. J
Cardiovasc Electrophysiol
2007;18:1076*

Paroxysmal → Persistent → Permanent

Trigger

APDs/AT from pulmonary veins
Non-PV triggers
PSVT
Atrial flutter

Substrate

Electrical remodeling
Neurohormonal changes
Atrial fibrosis
Atrial dilation



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GOALS OF CLINICAL MANAGEMENT

CLINICAL PRACTICE GUIDELINE: FULL TEXT

2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation

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

2019 AHA/ACC/HRS Focused Update of the 2014
AHA/ACC/HRS Guideline for the Management of
Patients With Atrial Fibrillation

CLINICAL PRACTICE GUIDELINES

2023 ACC/AHA/ACCP/HRS Guideline for the Diagnosis and
Management of Atrial Fibrillation: A Report of the American
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Committee on Clinical Practice Guidelines



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GOALS OF CLINICAL MANAGEMENT

- *Reduce Risk of Thromboembolism*
- *Preserve Ventricular Function*
- *Minimize Symptoms*
- *Maximize Quality of Life*

JACC VOL . 64, NO. 21, 2014
Heart Rhythm, online May 2017
Circulation. 2019;140:e125–e151

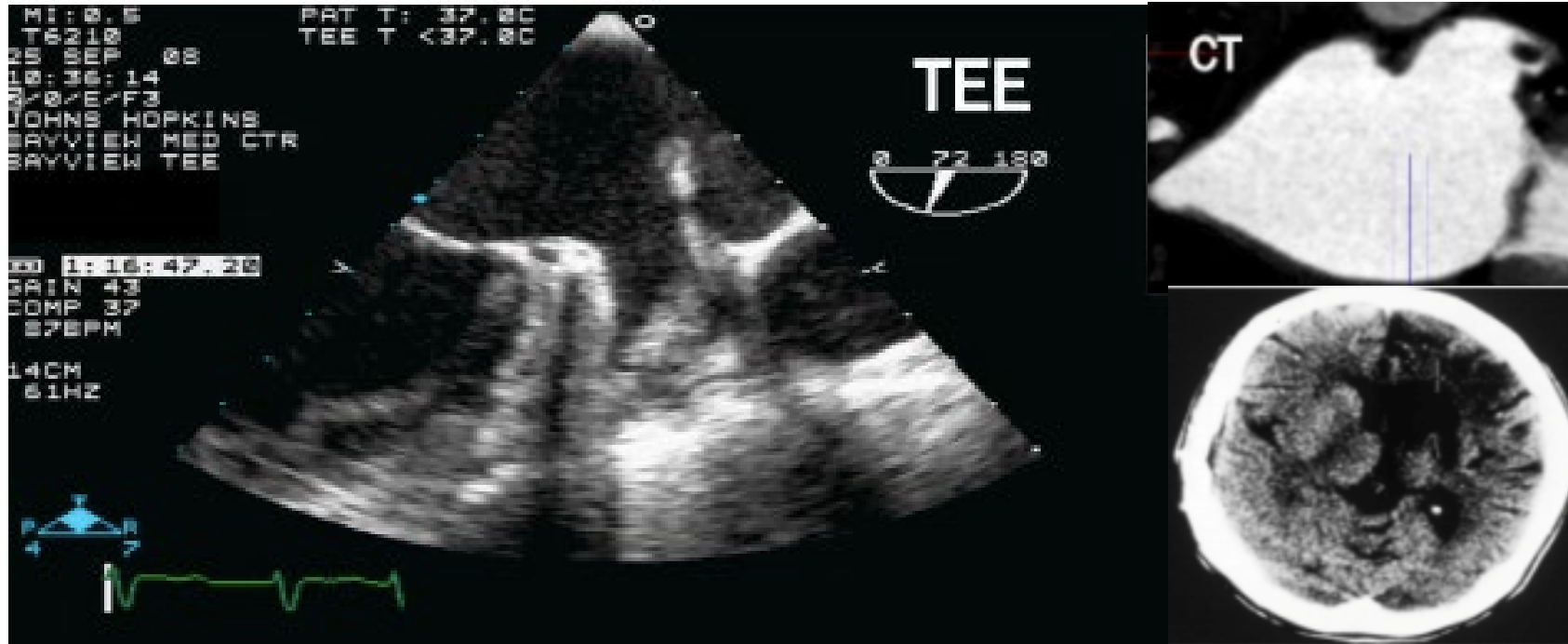


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PREVENTION OF THROMBOEMBOLISM



- LA Thrombus (most in LAA); stasis, endothelial dysfunction, hypercoagulability
- Embolize to brain (CVA) ; also to intestine, extremities, coronary artery
- 2-5% / year

ANTICOAGULATION FOR AF: ACC/AHA/GUIDELINES

Risk factor	Score
Congestive heart failure/LV dysfunction	1
Hypertension	1
Age \geq 75 ans	2
Diabetes mellitus	1
Stroke/TIA/thrombo-embolism	2
Vascular disease*	1
Age 65-74	1
Sex category [i.e. femal sex]	1
Maximum score	9

CHA2DS2-VASc score

- 0: No anti-thrombotic therapy
- 1: May be considered, Class II
- \geq 2: Oral anticoagulation

Considerations:

- Bleeding risk
- Anti-coagulate HCM, rheumatic MS



CHA ₂ DS ₂ -VASc score	Patients (n = 73538)	Stroke and thromboembolism event rate at 1 year follow-up (%)
0	6369	0.78
1	8203	2.01
2	12771	3.71
3	17371	5.92
4	13887	9.27
5	8942	15.26
6	4244	19.74
7	1420	21.50
8	285	22.38
9	46	23.64

- Provide greater stratification in lower risk groups that CHADS2
- Endorsed by ESC, AHA/ACC/HRS, CCS



Table 11. Additional Risk Factors That Increase Risk of Stroke Not Included in CHA₂DS₂-VASc

Higher AF burden/Long duration

Persistent/permanent AF versus paroxysmal

Obesity (BMI, ≥ 30 kg/m²)

HCM

Poorly controlled hypertension

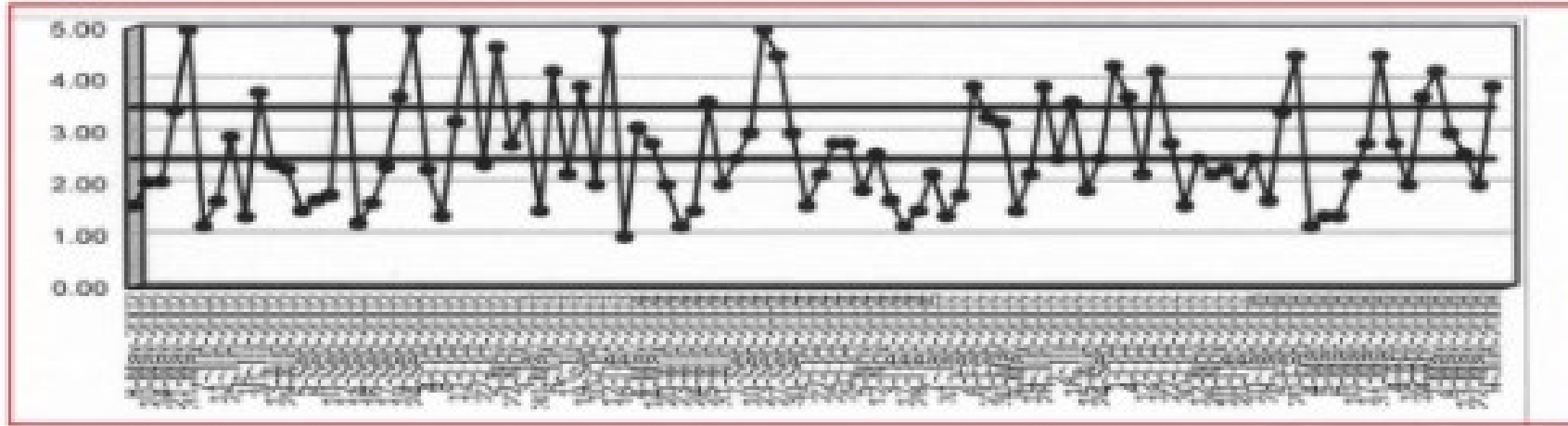
eGFR (<45 mL/h)

Proteinuria (>150 mg/24 h or equivalent)

Enlarged LA volume (≥ 73 mL) or diameter (≥ 4.7 cm)



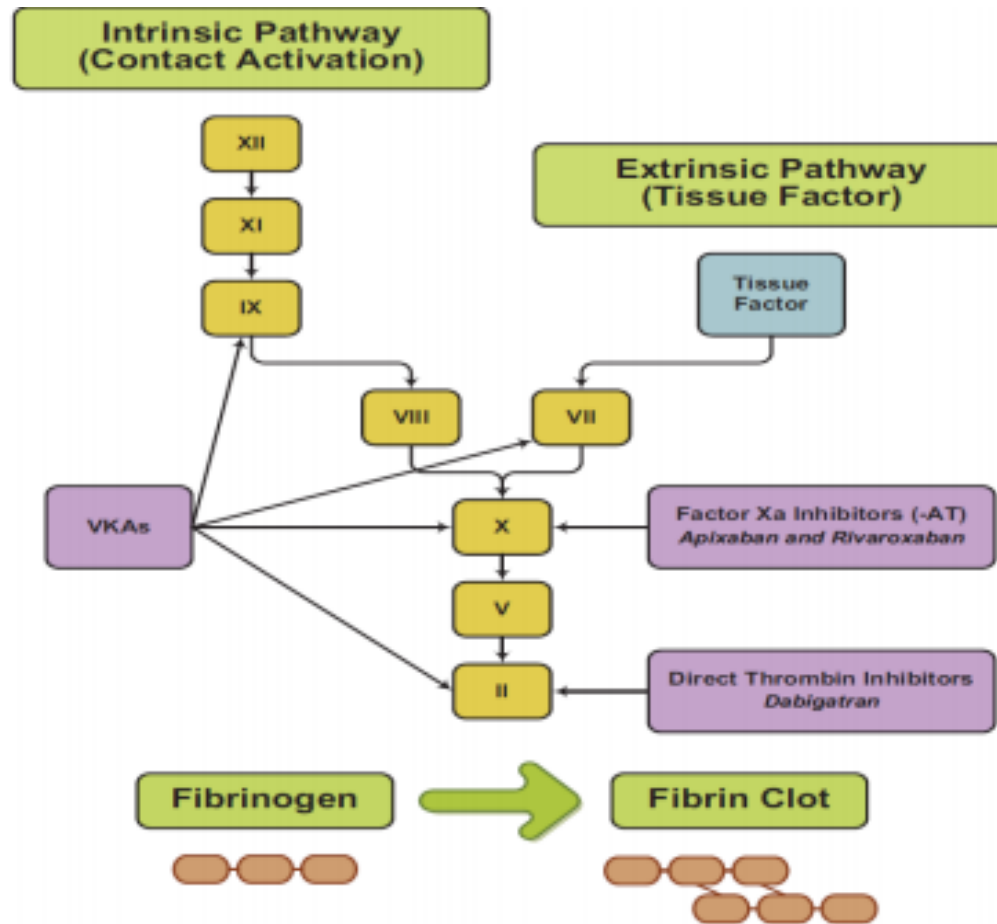
LIMITATIONS OF WARFARIN



- Difficulty maintaining target INR: TTR 60-70% even in optimal circumstances
- Cost and inconvenience
- Risk of hemorrhage
- Breakthrough thromboembolism
- 50-60% of appropriate OAC candidates receive warfarin
- Actual/perceived bleeding risk leading cause of withholding OAC



TARGET SPECIFIC ORAL ANTICOAGULANTS



Direct-acting thrombin inhibitors

- Dabigatran (Pradaxa)

Factor Xa inhibitors

- Rivaroxaban (Xarelto)
- Apixaban (Eliquis)
- Edoxaban (Savaysa)

January CT, et al. JACC 2014;65:e1-76



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COMPARISONS OF NOACS

	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
Mechanism	Thrombin inhibitor	Fxa inhibitor	Fxa inhibitor	Fxa inhibitor
Experience	8 years	7 years	6 years	3.5 years
Half-life	12-14 hrs	5-13 hrs	8-15 hrs	9-14 hrs
Dosing	Twice daily	Once daily	Twice daily	Once daily
Increased GI bleeding	Y	Y	N	Y (w/60 mg)
Renal excretion	80%	50%	25%	50%
Pivotal AF trials	1	1	2	1
Other indications	VTE	VTE	VTE	VTE
Drug interactions	P-gp inducers (rifampin) and inhibitors (ketoconazole)	P-gp+ strong CYP3A4 inhibitors (azoles, ART), inducers	Strong dual P-gp+CYP3A4 inhibitors (azoles, ART) and inducers	P-gp inducers (Rifampin)

Avoid anti-platelet agents (ASA) unless strongly indicated
Do not use with mechanical heart valves



SPECIFIC OAC ISSUES: RENAL DYSFUNCTION

	Warfarin	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
Normal (CrCl>50)	INR 2-3	150 mg BID	20 mg with evening meal	5 mg or 2.5 mg BID*	60 mg daily (if CrCl≤95)
Mod. CKD (CrCl 30-50)	INR 2-3	150 mg BID	15 mg with evening meal	5 mg or 2.5 mg BID*	30 mg daily
Severe CKD (CrCl 15-30)	INR 2-3	75 mg BID	15 mg with evening meal	5 mg or 2.5 mg BID*	30 mg daily
ESRD not on dialysis (CrCL <15)	INR 2-3	Not recommended	Not recommended	No recommendation	Not recommended
ESRD on dialysis	INR 2-3	Not recommended	Not recommended	No recommendation	Not recommended

Apixaban 2.5 mg BID if 2/3 present: Age \geq 80 yrs, BW \leq 60 kg, Cr \geq 1.5 mg/dl



SPECIFIC OAC ISSUES: REVERSAL

Warfarin: Vitamin K, FFP, PCC

Dabigatran: Dialysis, PCCs

- Idarucizumab (Praxbind, anti-dabigatran Fab fragment, approved (Pollack CV, et al. NEJM 2015; 373:511

Rivaroxaban/Apixaban/Edoxaban

Andexanet (Andexxa)- specific reversal agent approved May 2018

Connolly SJ, et al. NEJM 2016; 375:1131

Not dialyzable, PCCs reverse anticoagulant effect in animals

Prior to surgery/interventions: Hold NOAC 1-5 days depending on agent, type of surgery, renal function

- Special care with spinal/epidural procedures
- **No benefit to routine heparin bridging for warfarin in BRIDGE trial**
Douketis JD, et al. NEJM 2015; 373:823



AF GUIDELINE UPDATE: KEY CHANGES

1. Female sex downgraded as CVA risk factor

CHA2DS2-VASc 2 men/ 3 women -> OAC

CHA2DS2- VASC 1 men/2 women-> OAC or no anti-thrombotic therapy

2. No recommendation for ASA

3. DOACs preferred agents over warfarin unless moderate-severe MS or a mechanical heart valve



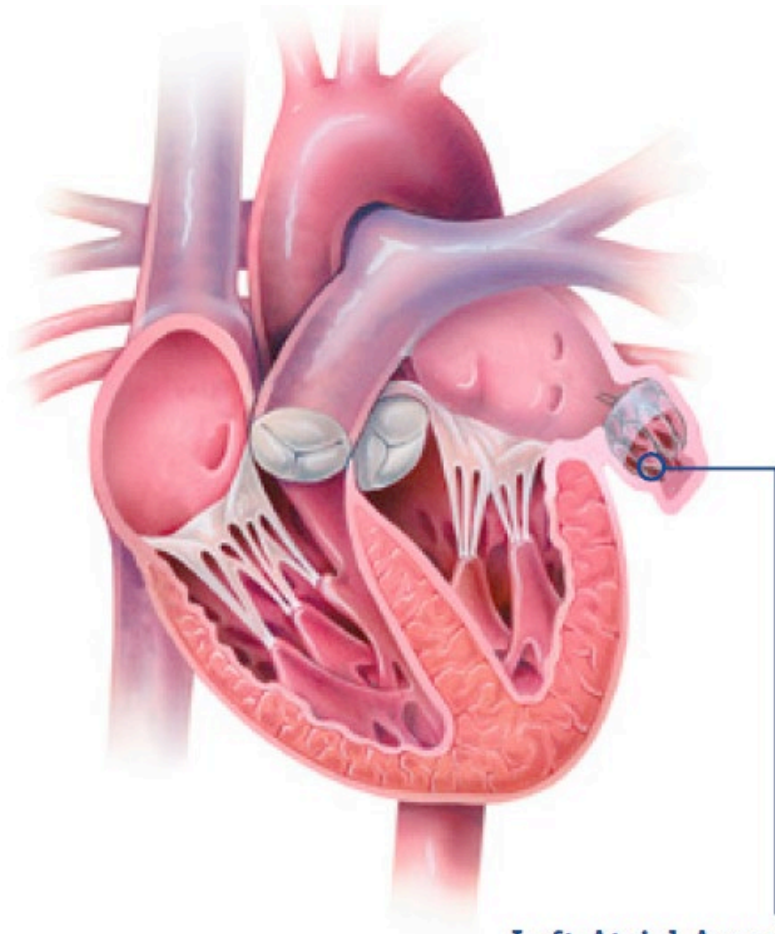
BLEEDING RISK ASSESSMENT; HAS-BLED SCORE

Letter	Clinical characteristic*	Points awarded
H	Hypertension	1
A	Abnormal renal and liver function (1 point each)	1 or 2
S	Stroke	1
B	Bleeding	1
L	Labile INRs	1
E	Elderly (e.g. age > 65 years)	1
D	Drugs or alcohol (1 point each)	1 or 2
		Maximum 9 points

Generally, do not withhold AC for minor bleeding or perceived fall risk



LAA EXCLUSION



Left Atrial Appendage
with WATCHMAN™ device implanted



AtriClip being positioned onto LAA base prior to deployment.



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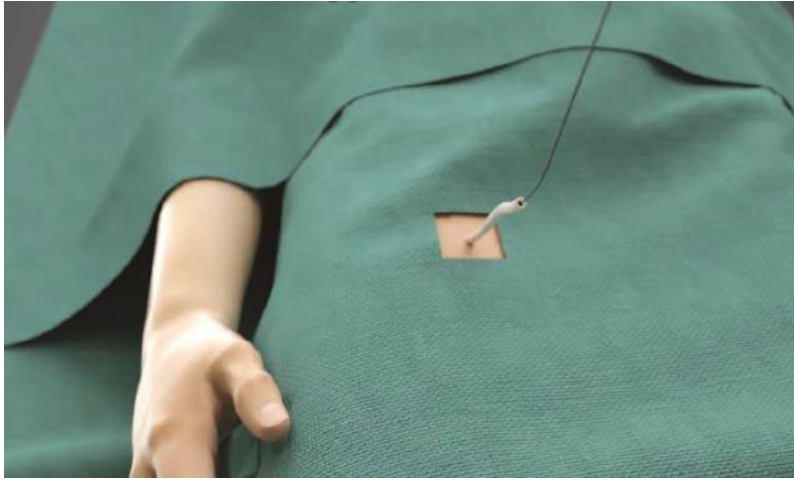
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GRAND NANILOA HOTEL

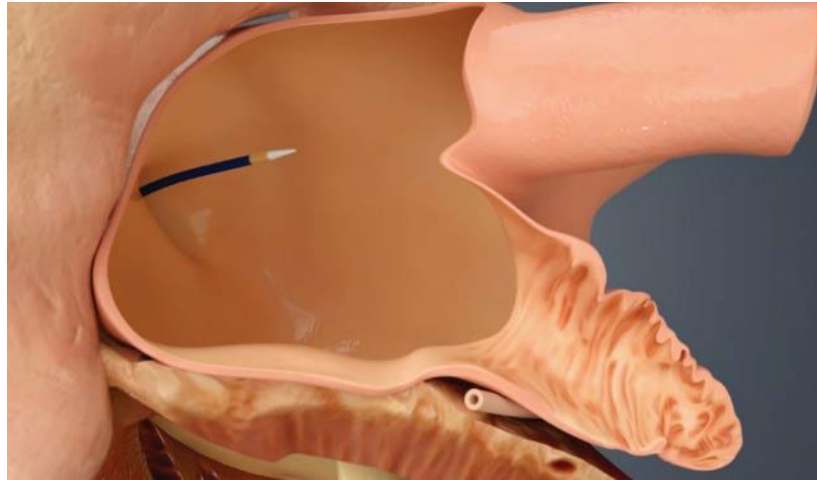
In non-valvular AF, > 90% of stroke-causing clots that come from the left atrium are formed in the LAA³



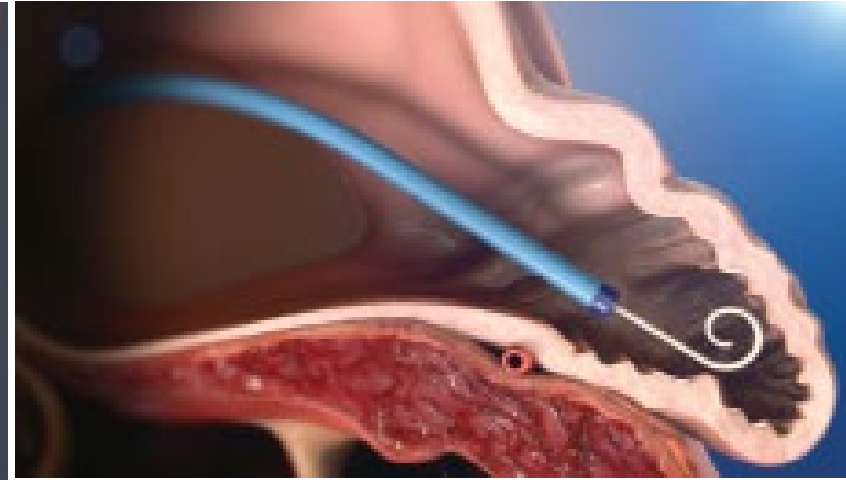
WATCHMAN FLX™



1. Using a standard percutaneous technique, a guidewire and vessel dilator are inserted into the femoral vein.



2. The implant procedure is performed with fluoroscopy and transesophageal echocardiography (TEE). The interatrial septum is crossed using a standard transseptal access system.



3. The access sheath is advanced over the guidewire into the left atrium and then navigated into the distal portion of the LAA over a pigtail catheter.



4. WATCHMAN FLX is then deployed and released in the LAA.



5. Heart tissue grows over the WATCHMAN FLX Implant, and the LAA is permanently sealed. Patients remain on OAC for at least 45 days post-procedure. TEE is used to confirm seal.

WATCHMAN included in AF Guidelines

2019 ACC/AHA/HRS Focused Update on Atrial Fibrillation

4.4. Nonpharmacological Stroke Prevention

4.4.1. Percutaneous Approaches to Occlude the LAA

Recommendation for Percutaneous Approaches to Occlude the LAA		
Referenced studies that support the new recommendation are summarized in Online Data Supplement 4 .		
COR	LOE	Recommendation
Ib	B-NR	1. Percutaneous LAA occlusion may be considered in patients with AF at increased risk of stroke who have contraindications to long-term anticoagulation (S4.4.1-1–S4.4.1-5). NEW: Clinical trial data and FDA approval of the Watchman device necessitated this recommendation.

“Oral anticoagulation remains the preferred therapy for stroke prevention for most patients with AF and elevated stroke risk. However, **for patients who are poor candidates for long-term oral anticoagulation (because of the propensity for bleeding or poor drug tolerance or adherence)**, the Watchman device provides an alternative.”

PHARMACOLOGIC THERAPY

RATE CONTROL



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Lenient versus Strict Rate Control in Patients with Atrial Fibrillation

Isabelle C. Van Gelder, M.D., Hessel F. Groenveld, M.D., Harry J.G.M. Crijns, M.D., Ype S. Tuininga, M.D., Jan G.P. Tijssen, Ph.D., A. Marco Alings, M.D., Hans L. Hillege, M.D., Johanna A. Bergsma-Kadijk, M.Sc., Jan H. Cornel, M.D., Otto Kamp, M.D., Raymond Tukkie, M.D., Hans A. Bosker, M.D., Dirk J. Van Veldhuisen, M.D., and Maarten P. Van den Berg, M.D., for the RACE II Investigators*

- Defined lenient as resting HR < 110 bpm
- Strict control <80 bpm at rest and <110 with moderate exercise
- Primary outcome: composite of death from CV causes, CHF hospitalization, stroke, systemic embolism, bleeding, and life-threatening arrhythmic events.
- Follow-up was at least 2-3 years

NEJM. 2010;362:1363–73



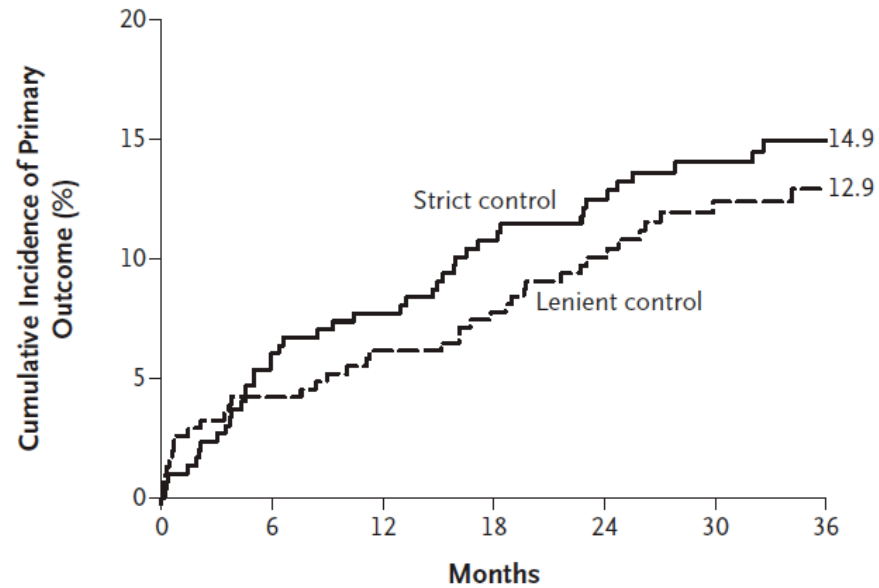
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RESULTS

Variable	Lenient Rate Control (N = 311)	Strict Rate Control (N = 303)	P Value
Rate-control target or targets achieved — no. (%)	304 (97.7)	203 (67.0)	<0.001

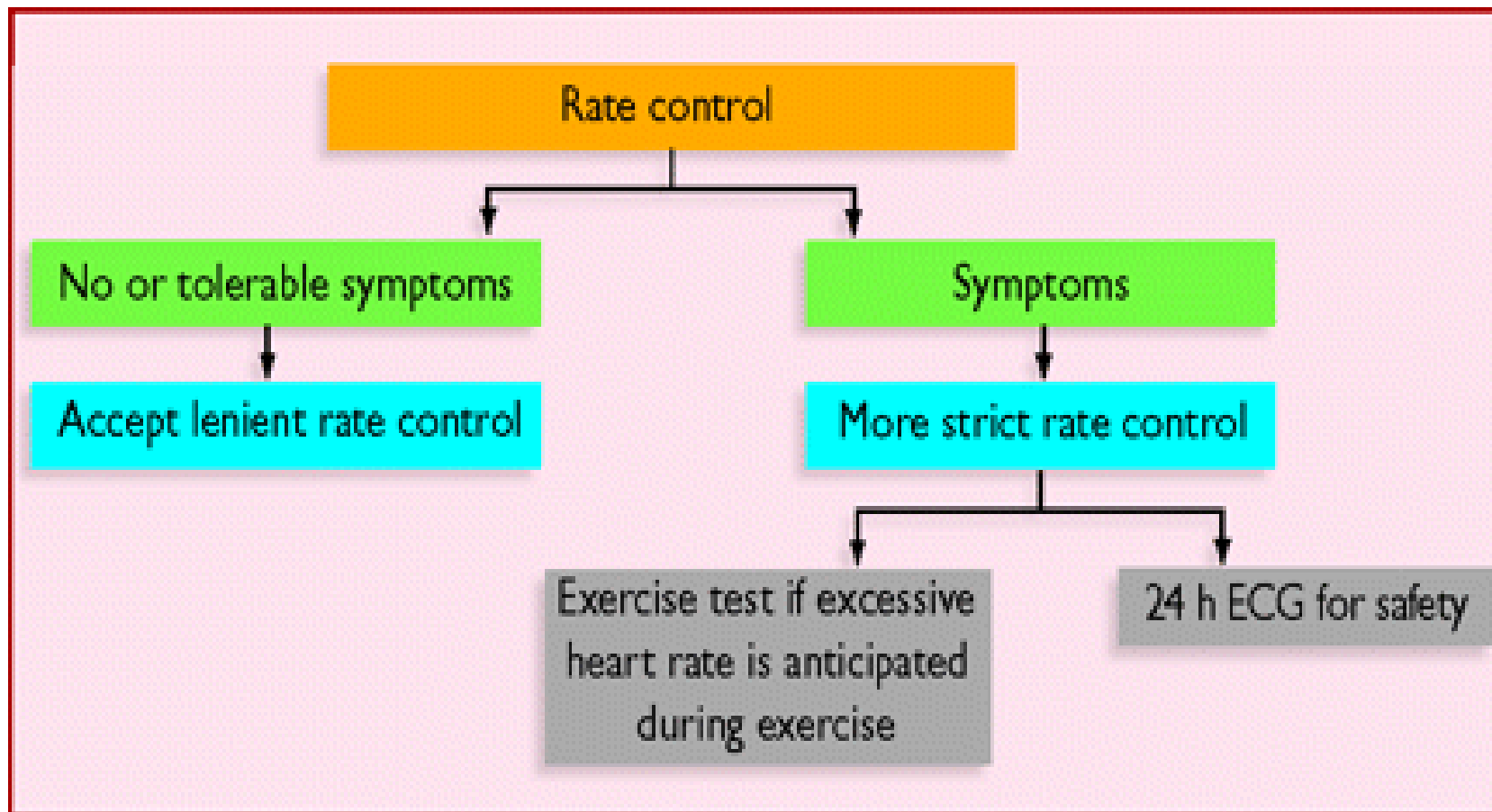


No. at Risk		0	6	12	18	24	30	36
Strict control	303	282	273	262	246	212	131	
Lenient control	311	298	290	285	255	218	138	

NEJM. 2010;362:1363–73



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RHYTHM CONTROL

ANTIARRHYTHMIC THERAPY



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NEW ANTIARRHYTHMIC DRUGS FOR AF



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Anti-arrhythmic drugs:

Class IA Quinidine, Procainamide, Disopyramide

Class IC **Flecainide, Propafenone** **always with nodal blocker therapy**

Class III **Sotalol, Dofetilide, Dronedaronone, Amiodarone**, Ibutilide (IV, acute use only)

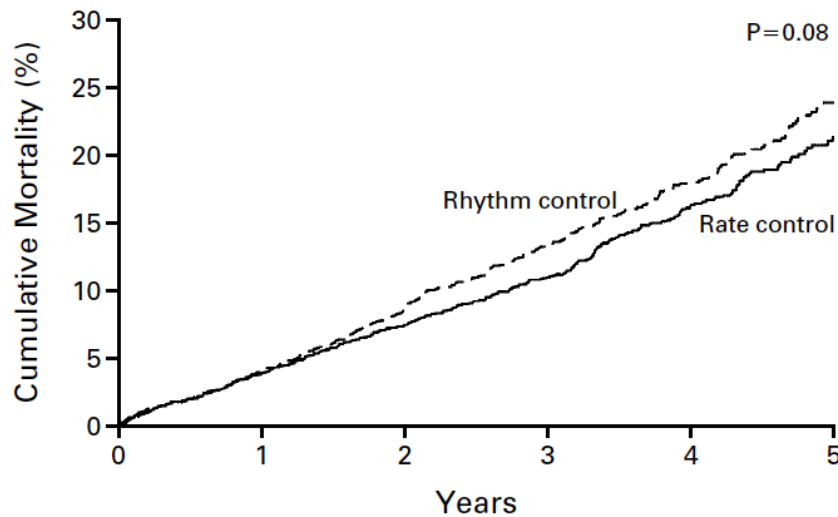


RATE CONTROL VS. RHYTHM CONTROL AFFIRM TRIAL

*Note that AFFIRM compared AADs with rate control

- Ablation was not in the Rhythm Control Arm

- Most strokes occurred in those who stopped OAC



No. OF DEATHS	number (percent)					
Rhythm control	0	80 (4)	175 (9)	257 (13)	314 (18)	352 (24)
Rate control	0	78 (4)	148 (7)	210 (11)	275 (16)	306 (21)

Figure 1. Cumulative Mortality from Any Cause in the Rhythm-Control Group and the Rate-Control Group.

Time zero is the day of randomization. Data have been truncated at five years.

NEJM 2002. Vol. 347, No. 23



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TABLE 1. BASE-LINE CHARACTERISTICS OF THE PATIENTS.*

CHARACTERISTIC	OVERALL (N=4060)	RATE-CONTROL GROUP (N= 2027)	RHYTHM-CONTROL GROUP (N= 2033)	P VALUE
Age — yr	69.7±9.0	69.8±8.9	69.7±9.0	0.82
Female sex — no. (%)	1594 (39.3)	823 (40.6)	771 (37.9)	0.08
Ethnic minority group — no. (%)	461 (11.4)	241 (11.9)	220 (10.8)	0.28
Predominant cardiac diagnosis — no. (%)				0.29
Coronary artery disease	1059 (26.1)	497 (24.5)	562 (27.6)	
Cardiomyopathy	194 (4.8)	99 (4.9)	95 (4.7)	
Hypertension	2063 (50.8)	1045 (51.6)	1018 (50.1)	
Valvular disease	198 (4.9)	98 (4.8)	100 (4.9)	
Other	42 (1.0)	23 (1.1)	19 (0.9)	
No apparent heart disease	504 (12.4)	265 (13.1)	239 (11.8)	
History of congestive heart failure — no. (%)	939 (23.1)	475 (23.4)	464 (22.8)	0.64
Duration of qualifying atrial fibrillation ≥2 days — no. (%)	2808 (69.2)	1406 (69.4)	1402 (69.0)	0.80
First episode of atrial fibrillation (vs. recurrent episode) — no. (%)†	1391 (35.5)	700 (35.8)	691 (35.3)	0.74
Any prerandomization failure of an antiarrhythmic drug — no. (%)	713 (17.6)	364 (18.0)	349 (17.2)	0.51
Size of left atrium normal — no. (%)‡	1103 (35.3)	549 (35.3)	554 (35.3)	0.98
Left ventricular ejection fraction — %§	54.7±13.5	54.9±13.1	54.6±13.8	0.74
Normal left ventricular ejection fraction — no. (%)‡	2244 (74.0)	1131 (74.9)	1113 (73.2)	0.29



ANTIARRHYTHMIC DRUG THERAPY

- The goal of antiarrhythmic therapy for AF is to improve symptoms and QoL
- No AA drug is expected to have 100% efficacy. The goal is to reduce AF burden and frequency
- AF recurrence on an AAD therapy should not be considered a “failure”. For infrequent recurrences, cardioversion can be performed without dose adjustment
- Anticoagulation should be continued, if indicated, regardless of perceived maintenance of sinus rhythm



ABLATIVE THERAPY



MEETING OF
SOCIETY OF
SPECIALISTS

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CABANA – CATHETER ABLATION VS. ANTIARRHYTHMIC DRUG FOR ATRIAL FIBRILLATION

- Randomized study of RF ablation to medical management
- Primary Endpoint: Total mortality, stroke, bleeding or cardiac arrest

JAMA April 2, 2019 Vol 321, Number 13

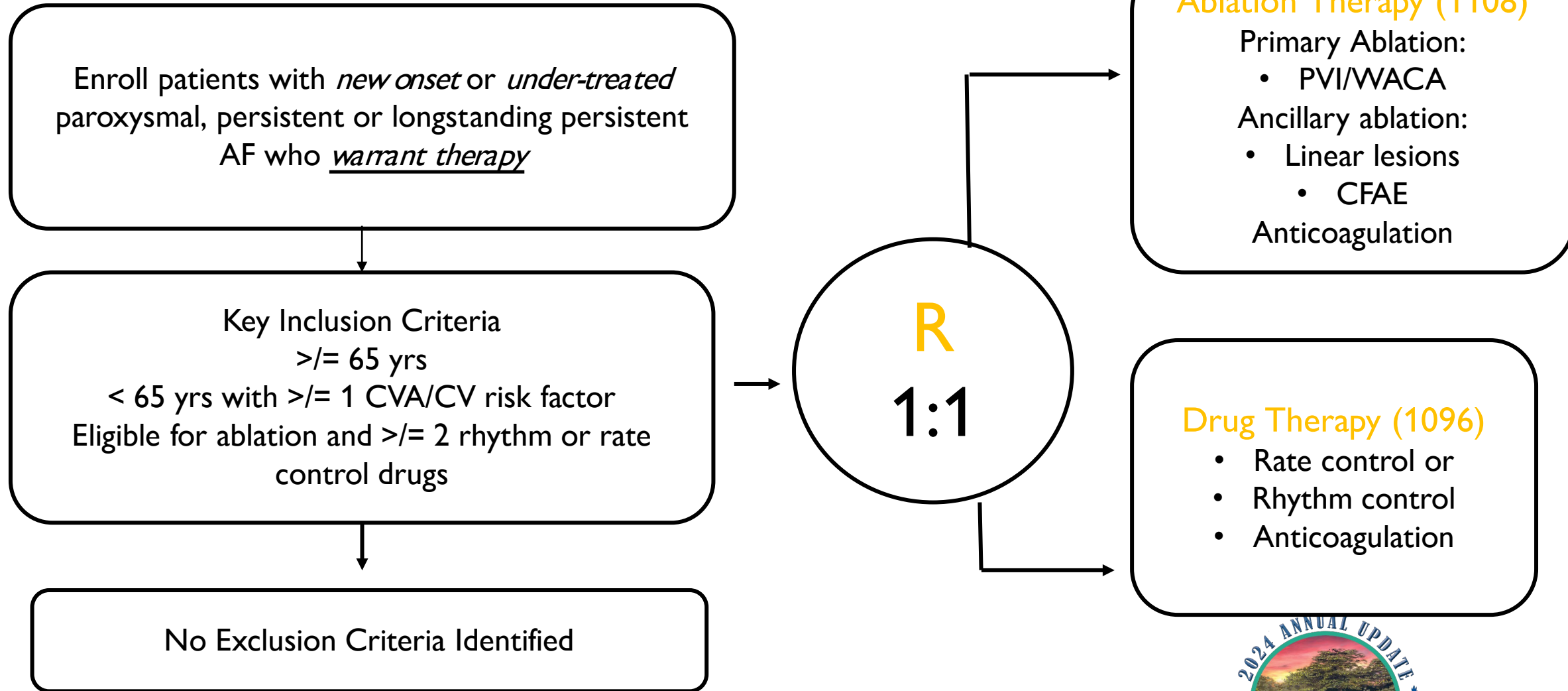


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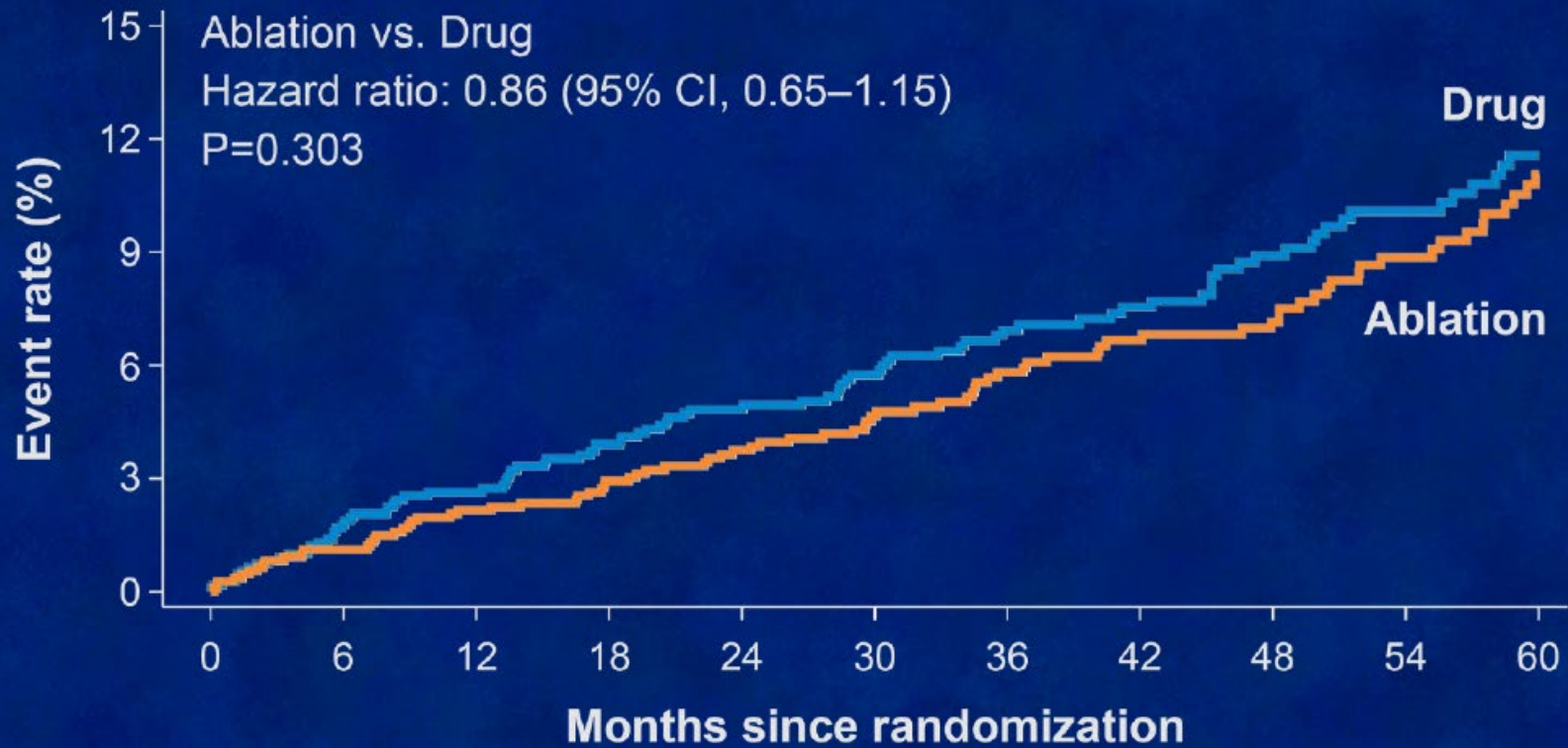
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CABANA TRIAL DESIGN





Primary Endpoint (Death, Disabling Stroke, Serious Bleeding, or Cardiac Arrest) (ITT)



Number at risk

Drug	1096	1036	1006	970	880	763	652	578	499	418	312
Ablation	1108	1045	1021	996	915	793	700	614	535	432	309



Duke Clinical Research Institute



National Heart, Lung, and Blood Institute



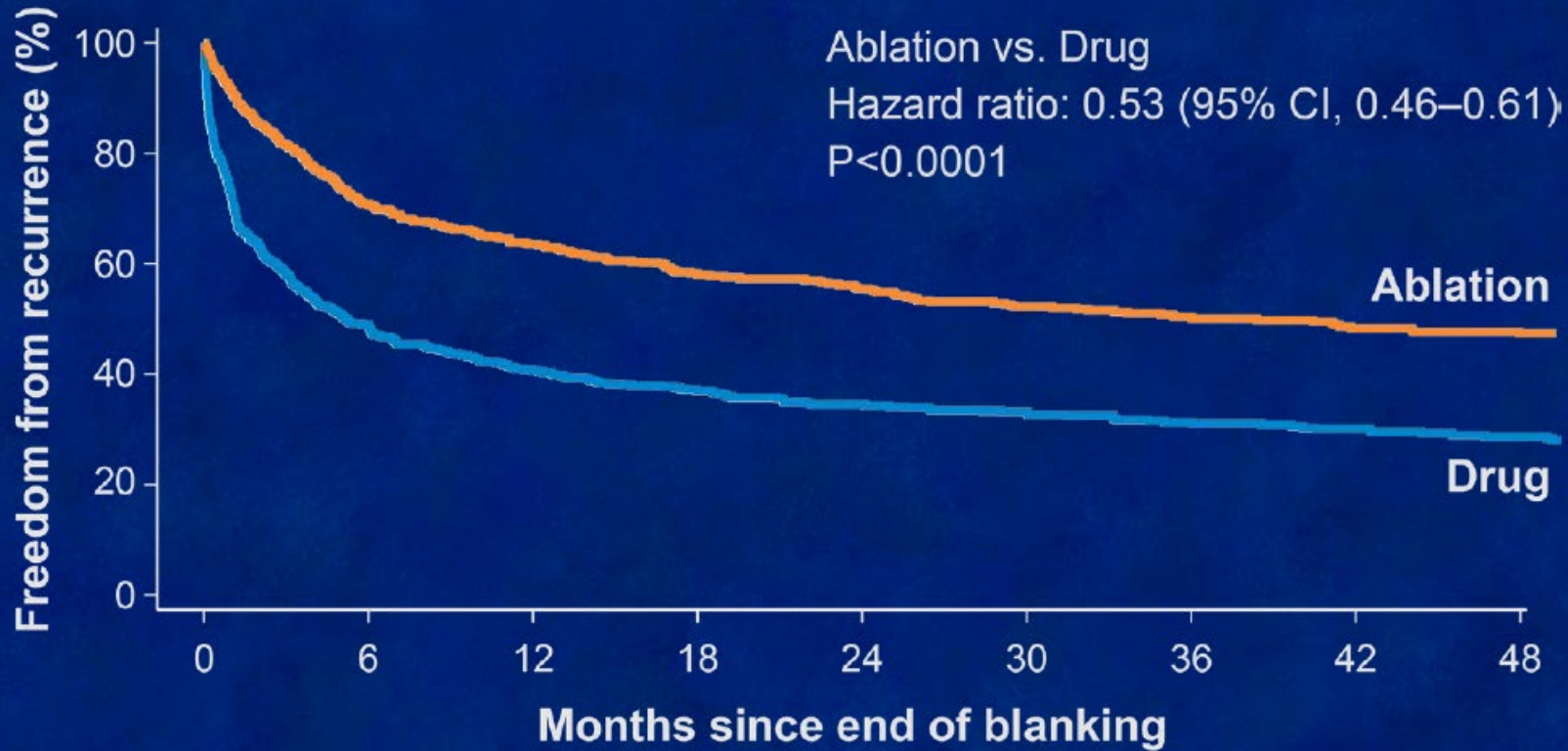
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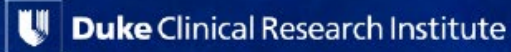


First Recurrence AF – Post Blanking* (ITT)



Number at risk

Drug	629	303	251	211	180	156	130	114	93
Ablation	611	430	380	327	290	239	199	162	133



*Using CABANA Monitors



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Primary and Secondary Outcomes (Treatment Received)*

	Ablation (N = 1307)	Drug (N = 897)	Hazard Ratio (95% CI)	P- Value
Primary Outcome	92 (7.0%)	98 (10.9%)	0.67 (0.50, 0.89)	0.006
Secondary Outcomes				
All-cause mortality	58 (4.4%)	67 (7.5%)	0.60 (0.42, 0.86)	0.005
Death or CV hospitalization	538 (41.2%)	672 (74.9%)	0.83 (0.74, 0.94)	0.002



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and Blood Institute

*pre-specified



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Radiofrequency ablation vs. antiarrhythmic drug therapy as first line treatment of symptomatic atrial fibrillation: systematic review and meta-analysis

Antti Hakalahti^{1*}, Fausto Biancari², Jens Cosedis Nielsen³, and M.J. Pekka Raatikainen^{4,5}

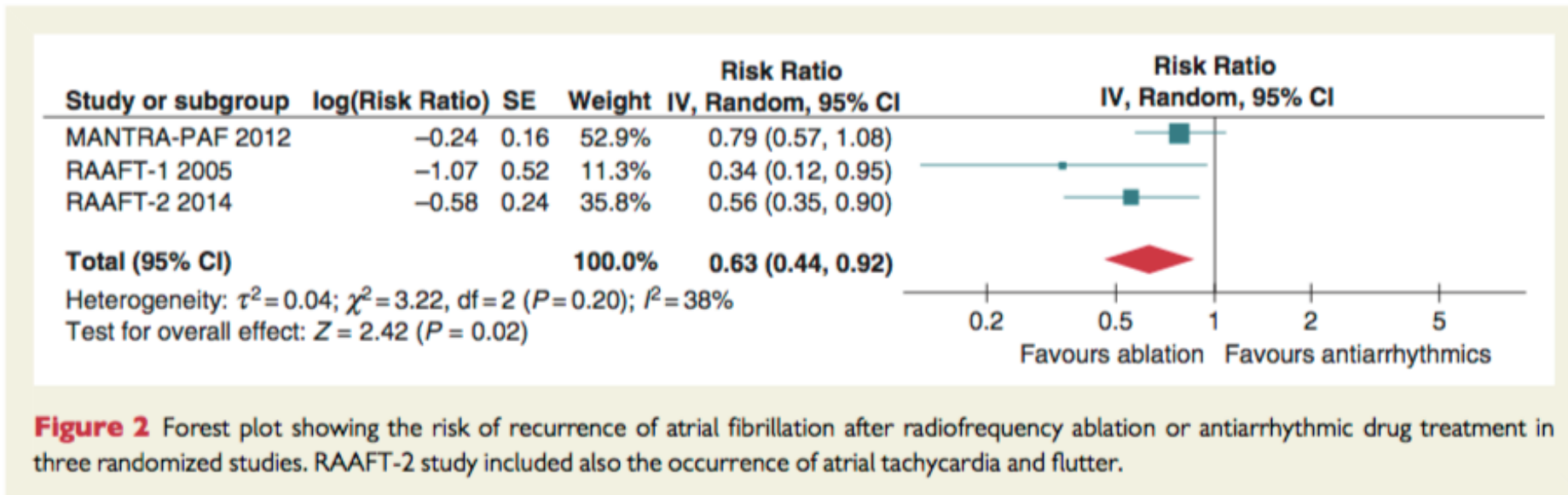


Figure 2 Forest plot showing the risk of recurrence of atrial fibrillation after radiofrequency ablation or antiarrhythmic drug treatment in three randomized studies. RAAFT-2 study included also the occurrence of atrial tachycardia and flutter.

Europace, 2015. 17(3): p. 370-8.



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CLINICAL PRACTICE GUIDELINES

2023 ACC/AHA/ACCP/HRS Guideline for the Diagnosis and Management of Atrial Fibrillation: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines

COR	LOE	Recommendations
1	A	1. In patients with symptomatic AF in whom antiarrhythmic drugs have been ineffective, contra-indicated, not tolerated or not preferred , and continued rhythm control is desired, catheter ablation is useful to improve symptoms
1	A	In selected patients (generally younger with few comorbidities) with symptomatic paroxysmal AF in whom rhythm control is desired, catheter ablation is useful as first-line therapy to improve symptoms and reduce progression to persistent AF



RHYTHM CONTROL IN AF

- RACE- **no** mortality benefit to rhythm control
- STAR – **no** mortality benefit to rhythm control
- AFFIRM – **no** mortality benefit to rhythm control
- CABANA – **no** ITT mortality benefit to rhythm control



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*

Table 2. Primary and Secondary Clinical End Points.*

End Point	Ablation (N=179)	Medical Therapy (N=184)	Hazard Ratio (95% CI)	P Value	
				Cox Regression	Log-Rank Test
	<i>number (percent)</i>				
Primary†	51 (28.5)	82 (44.6)	0.62 (0.43–0.87)	0.007	0.006
Secondary					
Death from any cause	24 (13.4)	46 (25.0)	0.53 (0.32–0.86)	0.01	0.009
Heart-failure hospitalization	37 (20.7)	66 (35.9)	0.56 (0.37–0.83)	0.004	0.004
Cardiovascular death	20 (11.2)	41 (22.3)	0.49 (0.29–0.84)	0.009	0.008
Cardiovascular hospitalization	64 (35.8)	89 (48.4)	0.72 (0.52–0.99)	0.04	0.04
Hospitalization for any cause	114 (63.7)	122 (66.3)	0.99 (0.77–1.28)	0.96	0.96
Cerebrovascular accident	5 (2.8)	11 (6.0)	0.46 (0.16–1.33)	0.15	0.14

N ENGL J MED 378;5

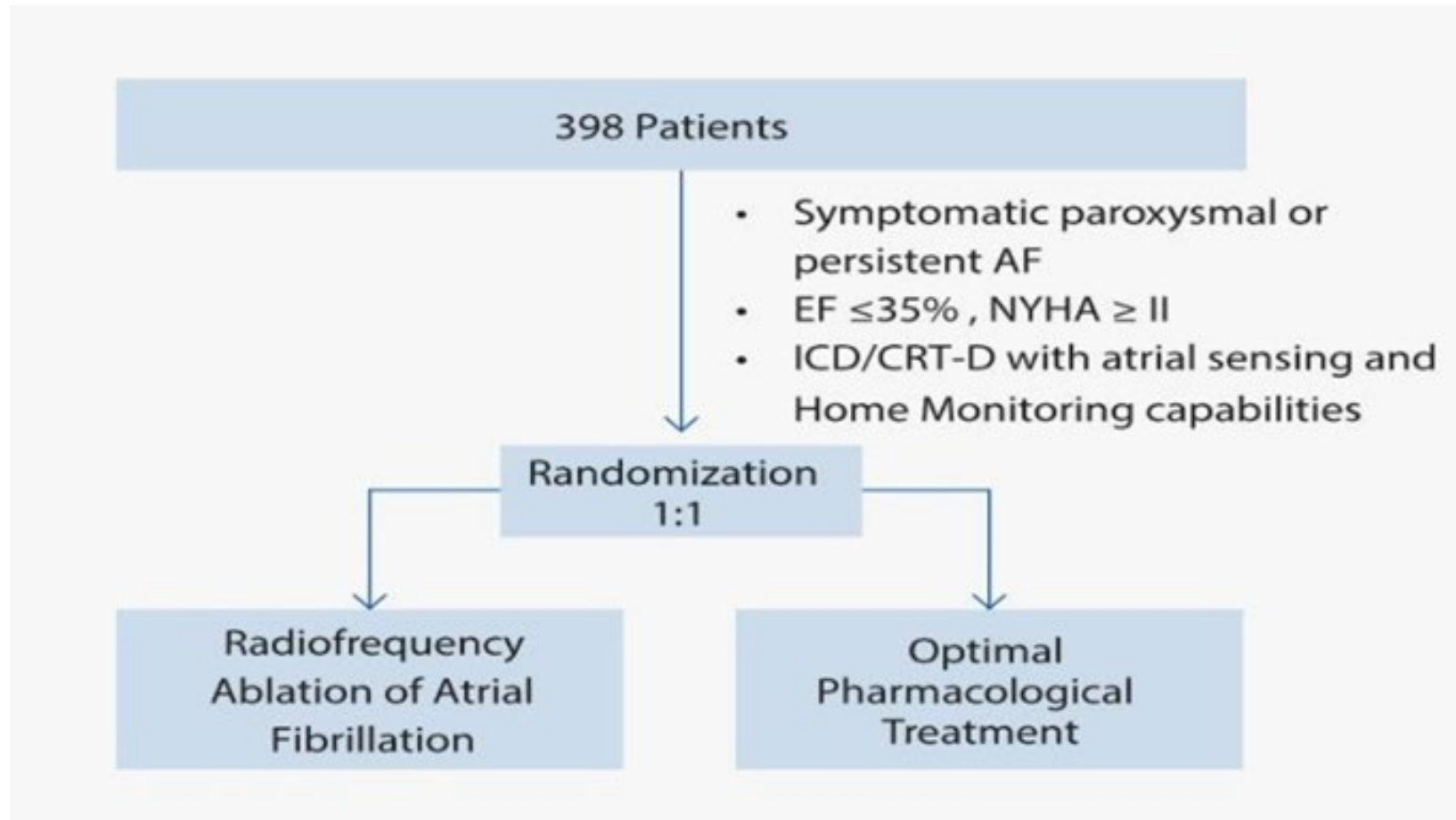


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CASTLE AF



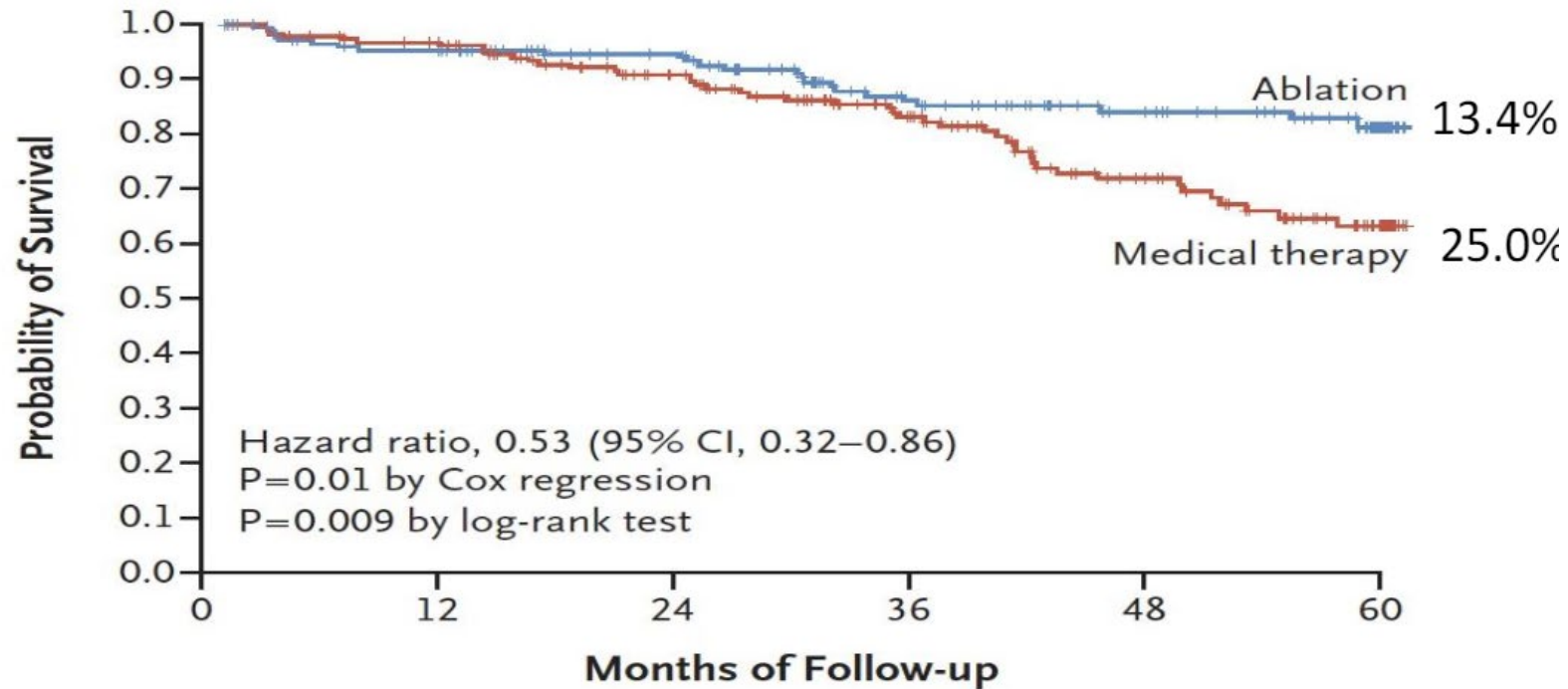
Primary endpoint: All-cause death or unplanned hospitalization due to worsening of heart failure

Marrouche et al. NEJM 2018 378(5):417.427.



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Overall Mortality



No. at Risk

Ablation	179	154	130	94	71	27
Medical therapy	184	168	138	97	63	19

Marrouche et al. NEJM 2018 378(5):417.427.



HAWAII ACADEMY OF
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Recommendations for Management of AF in Patients With HF*

Referenced studies that support the recommendations are summarized in the [Online Data Supplement](#).

COR	LOE	Recommendations
1	B-NR	1. In patients who present with a new diagnosis of HFrEF and AF, <u>arrhythmia-induced cardiomyopathy</u> should be suspected, and an early and aggressive approach to AF rhythm control is recommended. ^{1,2}
1	A	2. In appropriate patients with AF and HFrEF who are on GDMT, and with reasonable expectation of procedural benefit (Figure 24), catheter ablation is beneficial to <u>improve symptoms, QOL, ventricular function, and cardiovascular outcomes</u> . ³⁻¹³

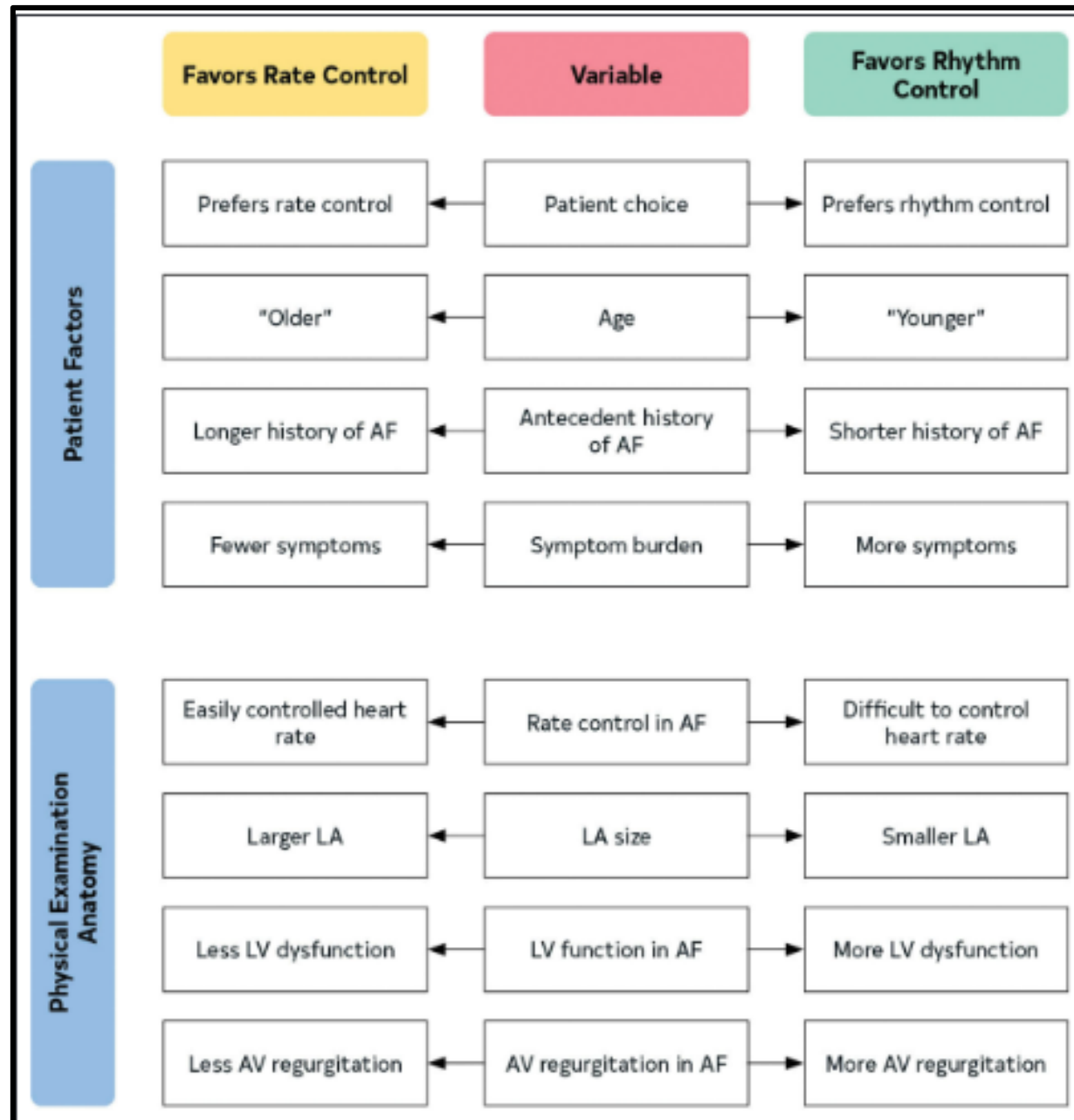


HRS/EHRA/ECAS 2017 AF GUIDELINES

B. 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





ABLATION STRATEGY

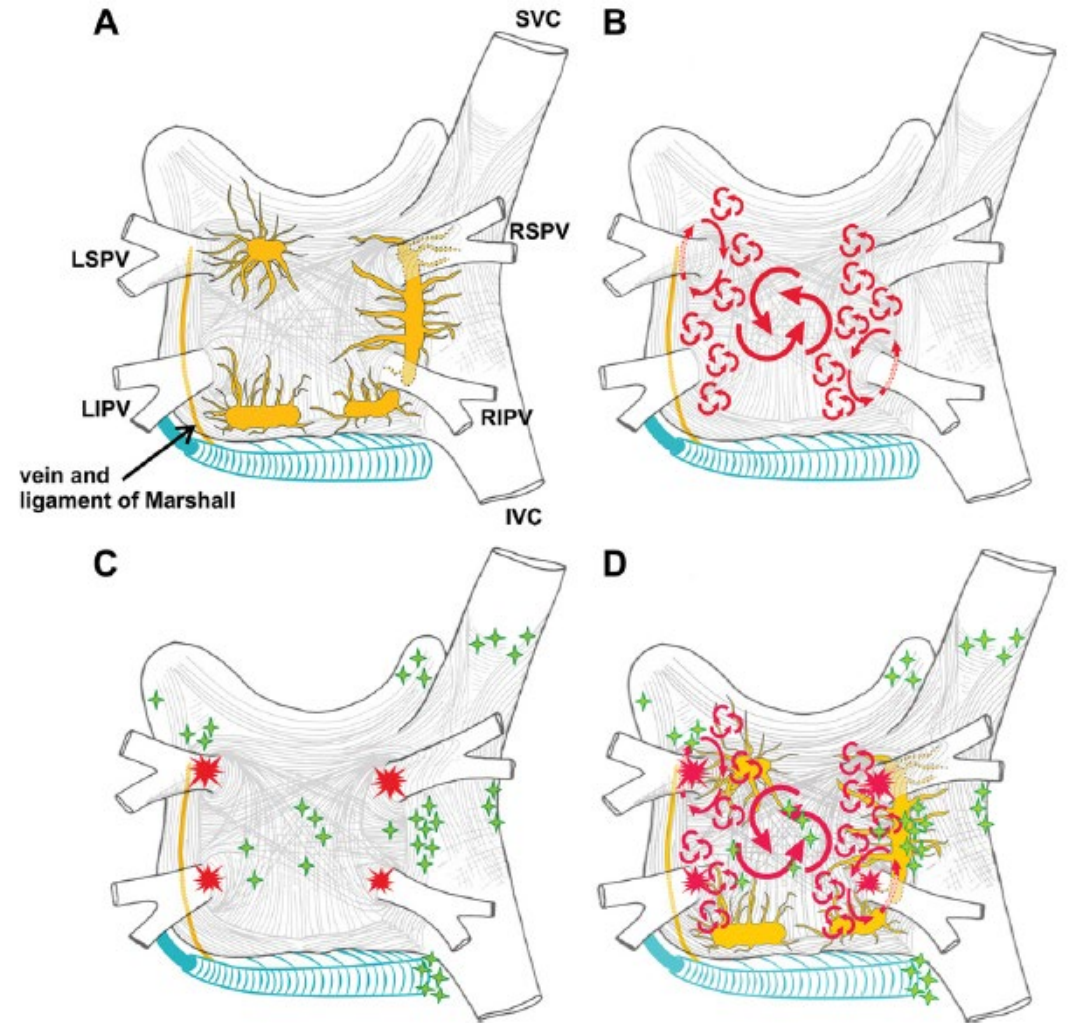


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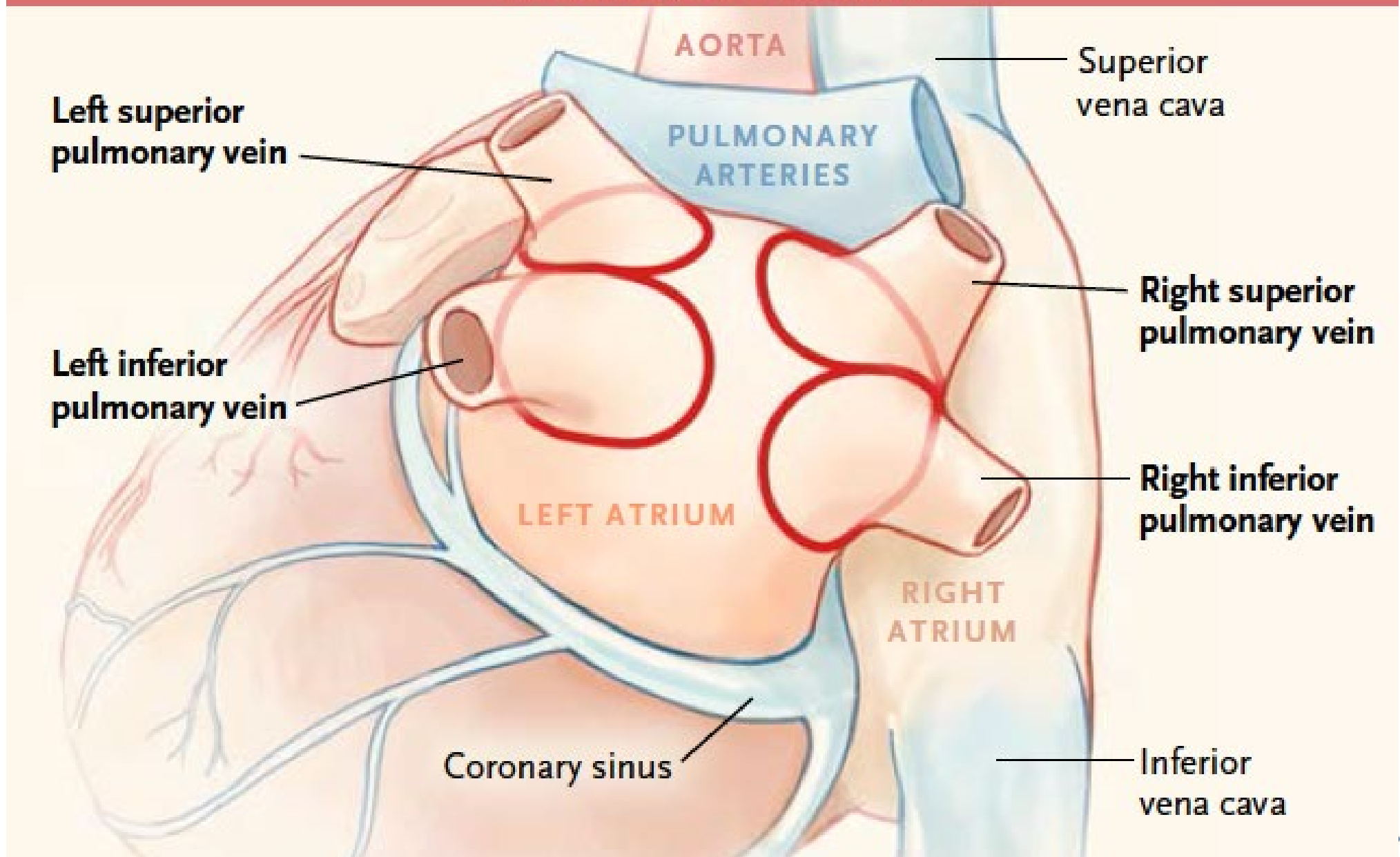
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- PV Triggers
- Left atrial autonomic ganglionic plexi
- Coronary Sinus
- Vein of Marshall
- Multiple wavelets and rotors
- Non-PV Triggers (green)



Heart Rhythm, Vol 8, No 1, January 2011

Pulmonary-vein isolation



ABLATION TECHNOLOGY

- Cryo-balloon ablation
- Radiofrequency ablation
- Pulse Field Ablation

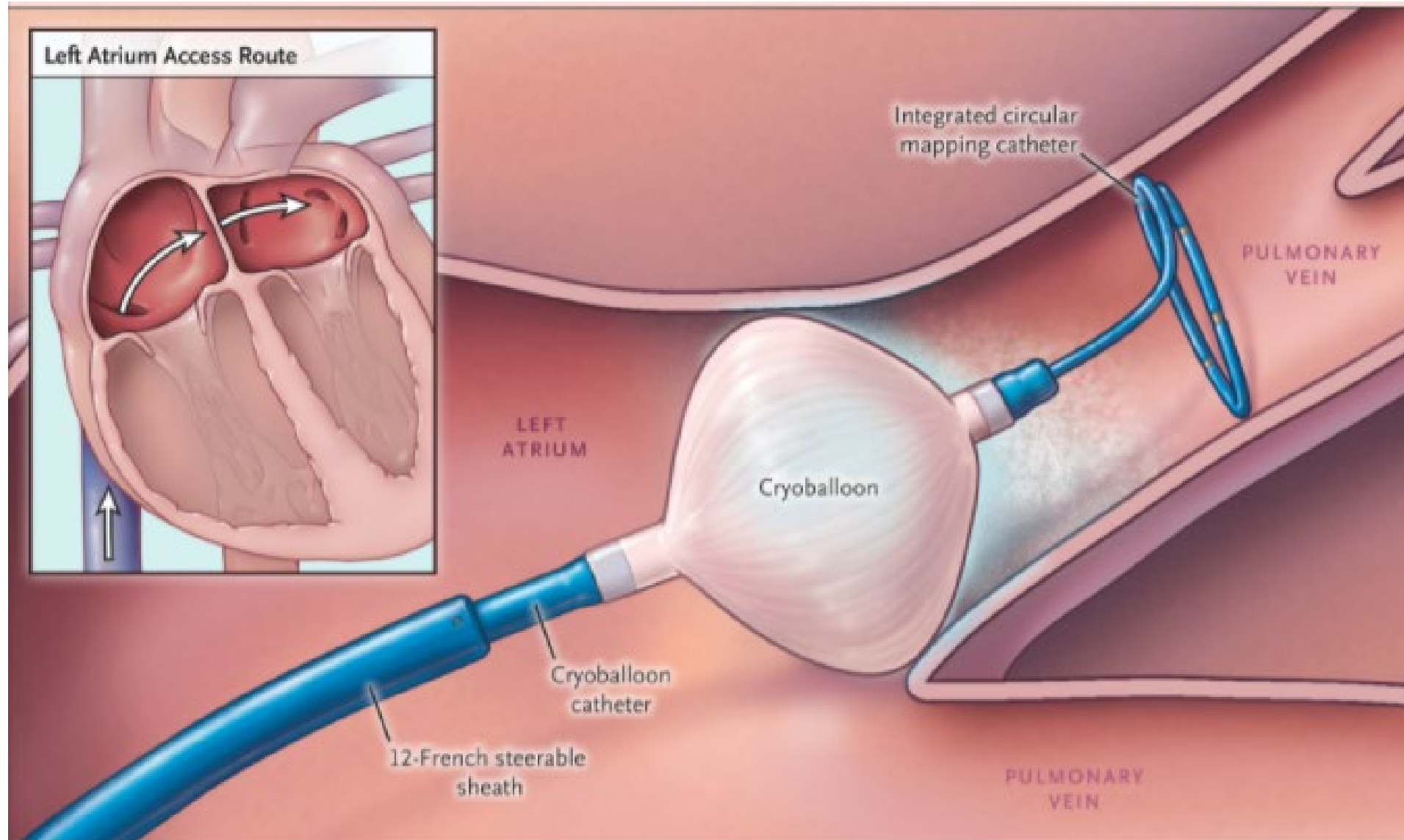


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CRYO-BALLOON ABLATION



UPDATE

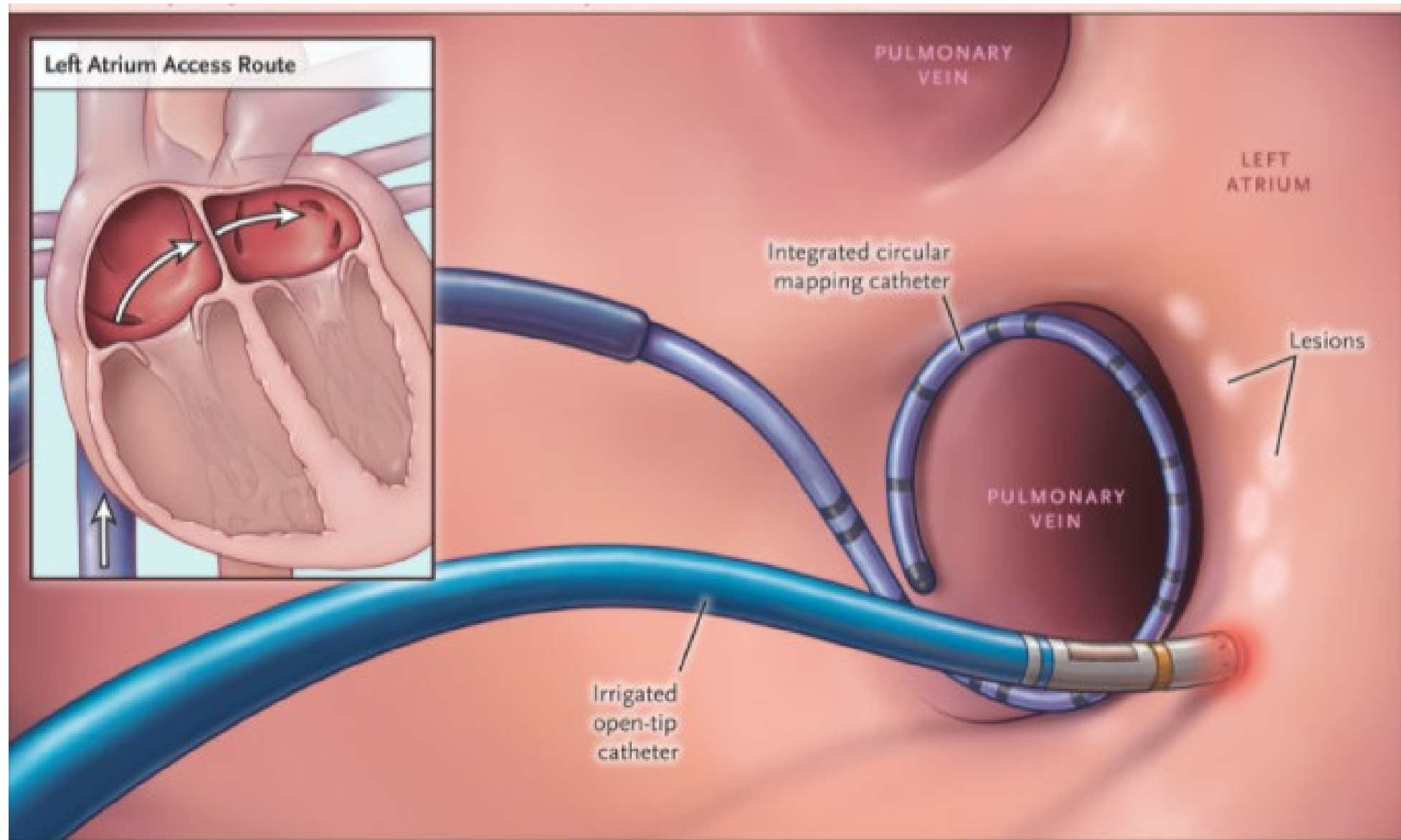
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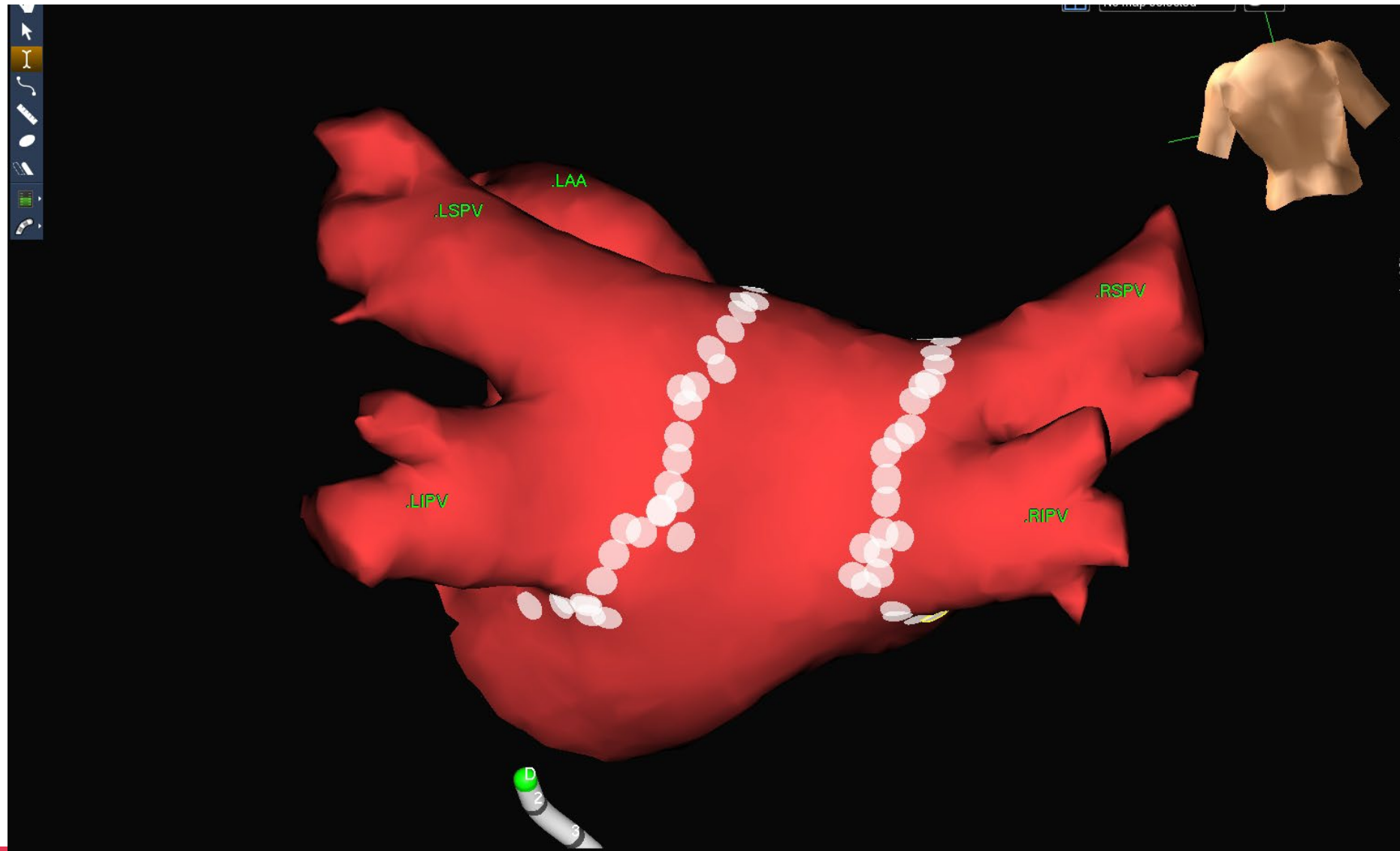


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RADIO-FREQUENCY ABLATION



RADIOFREQUENCY ABLATION LESION SET



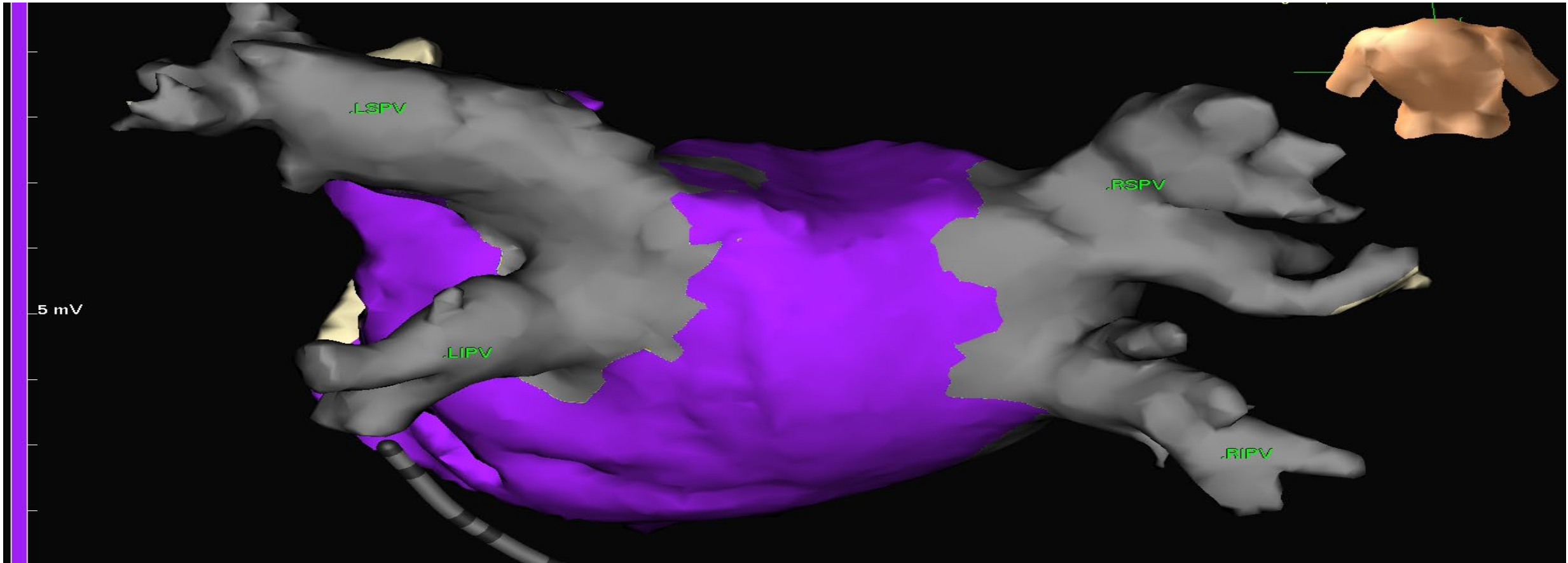
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VOLTAGE MAP AFTER ABLATION

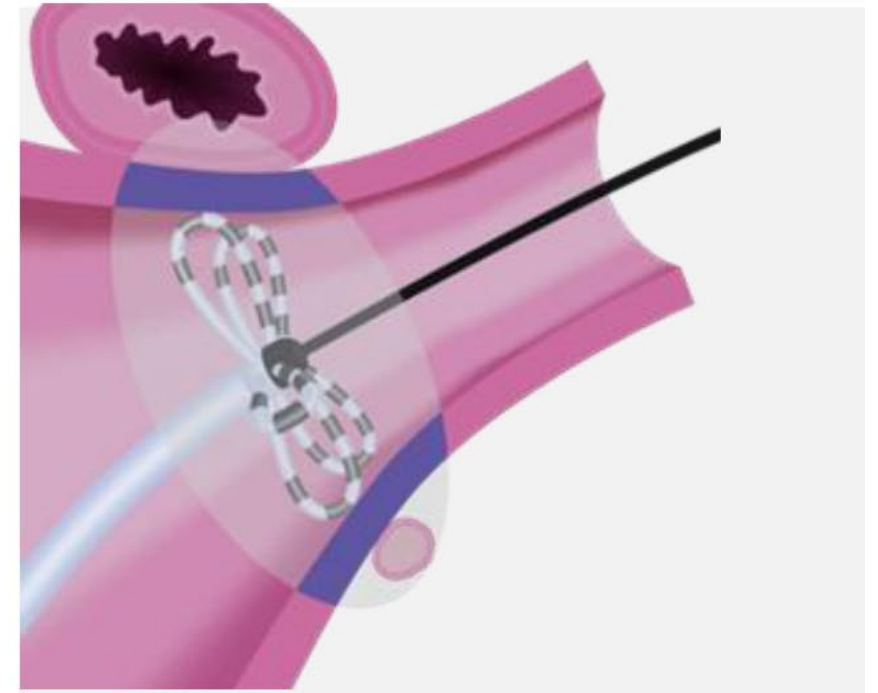
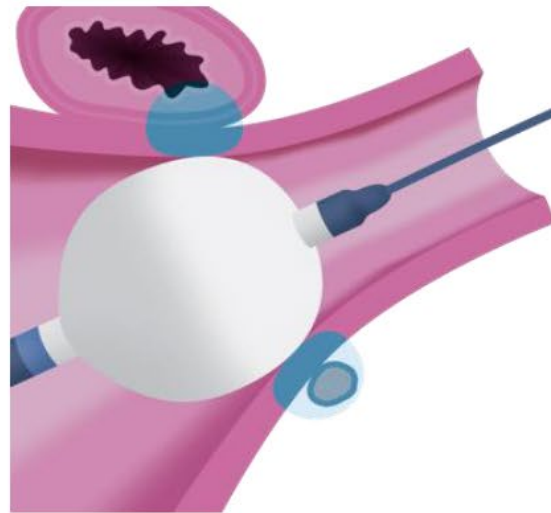
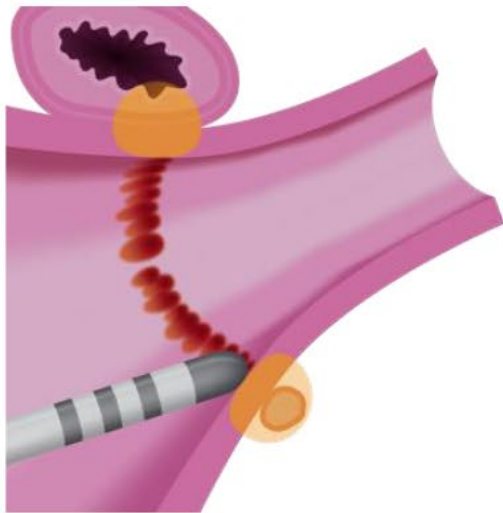


COMING DOWN THE PIKE...

Radiofrequency Ablation

Cryoballoon Ablation

Pulsed Field Ablation



¹Reddy VY et al. J Am Coll Cardiol. 2019;74(3): 315-26

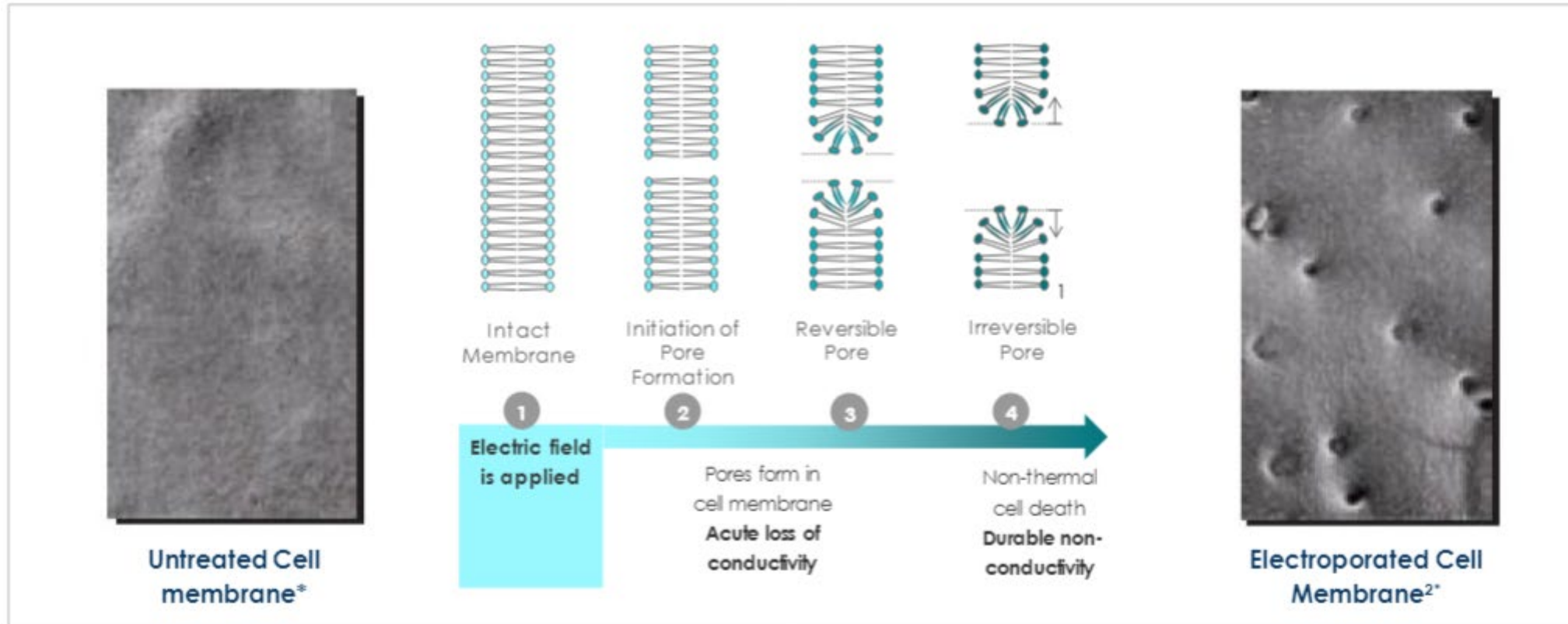


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PULSE FIELD ABLATION



T. Kotnik et al, IEEE Electrical Insulation Magazine, Vol. 28, No. 5 p. 14-23, 2012



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ABLATION STRATEGIES IN PERSISTENT ATRIAL FIBRILLATION; ADDITIONAL TARGETS BEYOND PVI

Non-PV triggers:

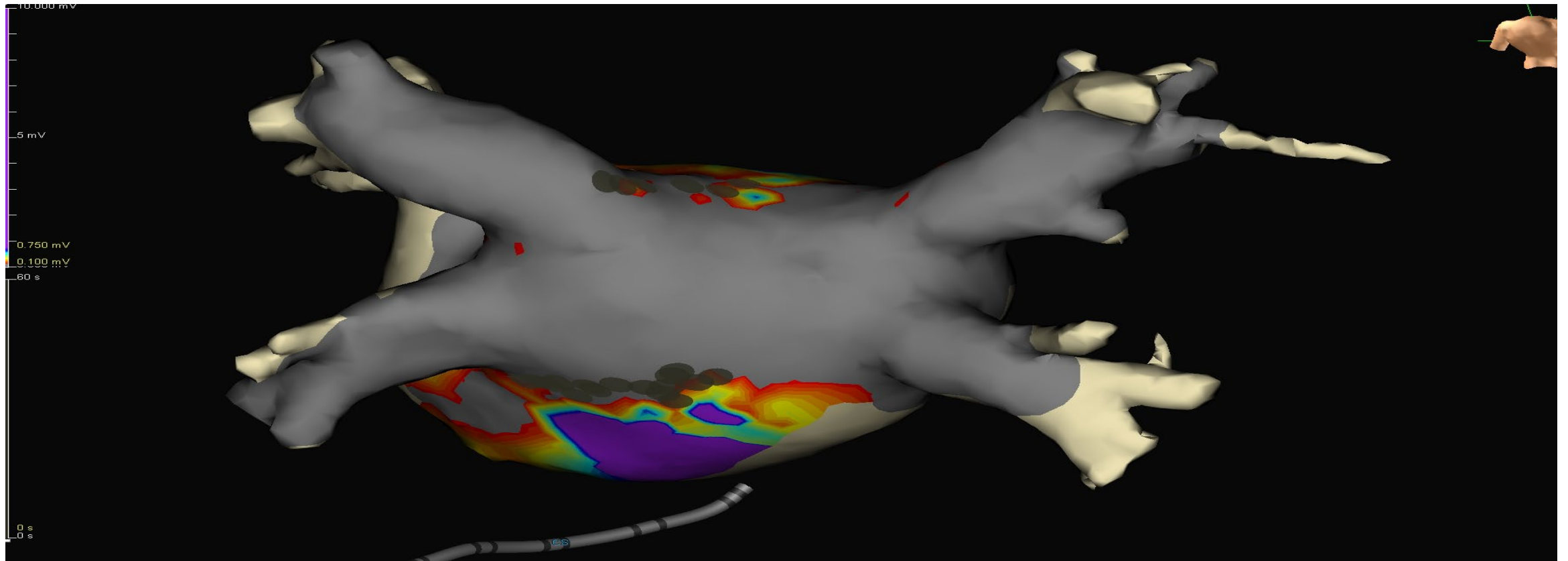
- Other thoracic veins (SVC, CS)
- Left atrial appendage isolation

Substrate modification:

- Linear Ablation (LA roof, mitral isthmus)
- Posterior LA wall isolation
- Complex Fractionated Atrial Electrograms
- EtOH ablation of VOM
- Signal processing guided approaches to target rotors/drivers



POSTERIOR BOX LESION SET



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ABLATION OF PERSISTENT AND LONG-STANDING PERSISTENT AF



Concept credited to Fred Morady, MD

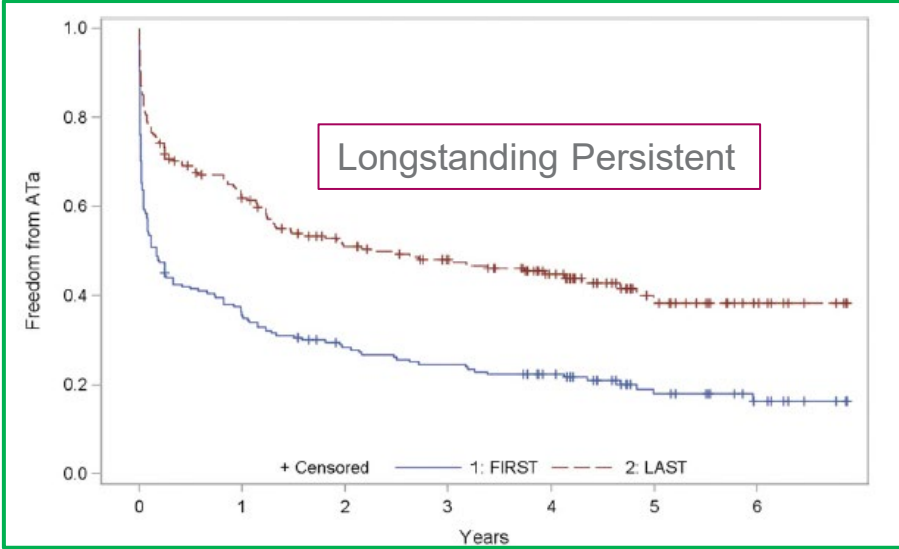
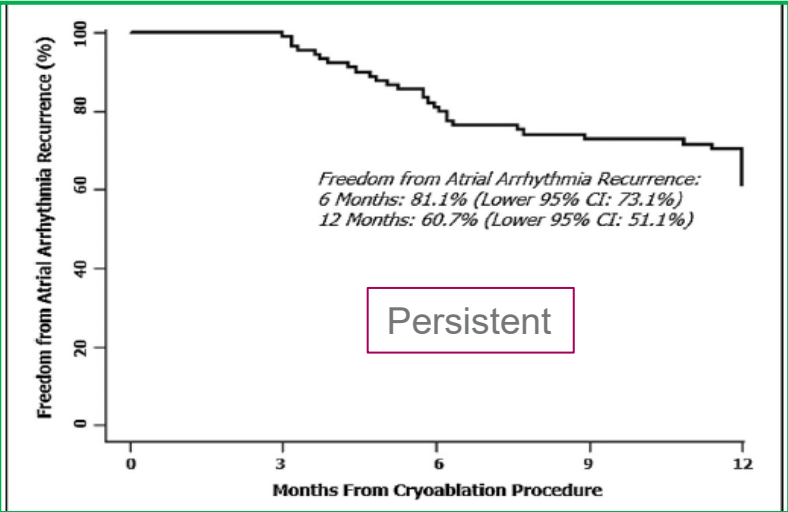
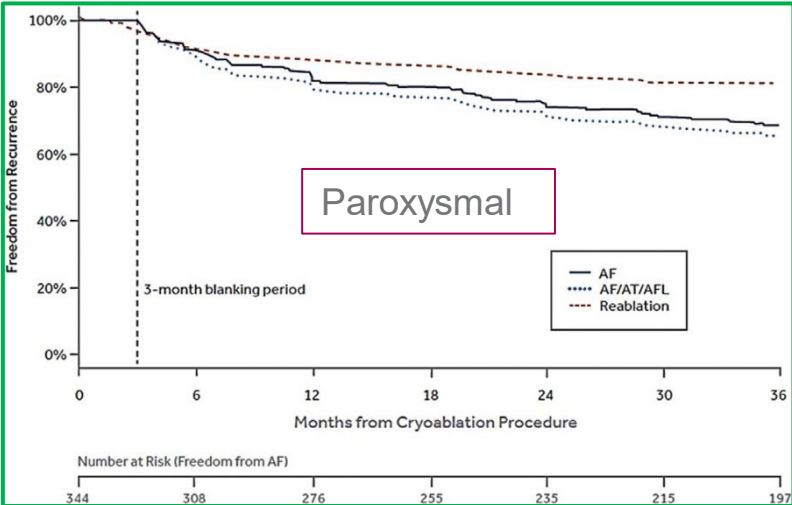


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OUTCOMES OF AF ABLATION BY DURATION OF AF



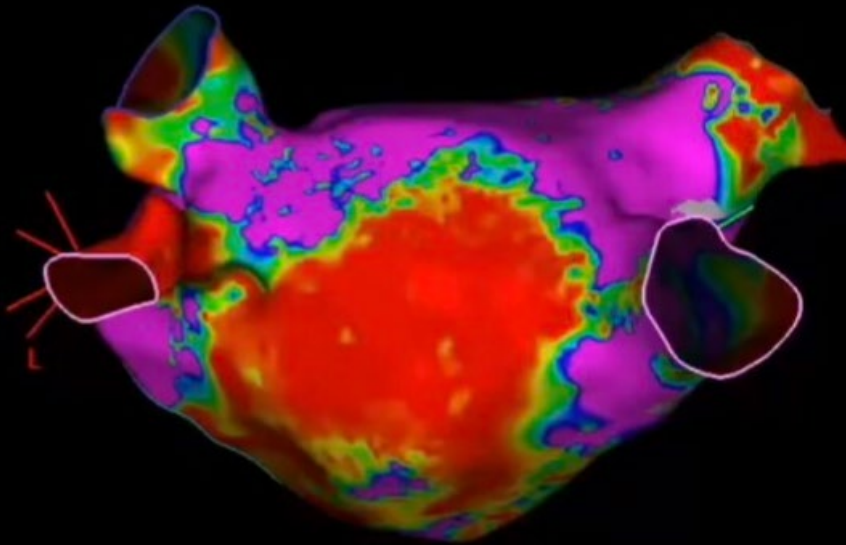
JACC 2012
 JACC EP 2019
 JACC EP 2018



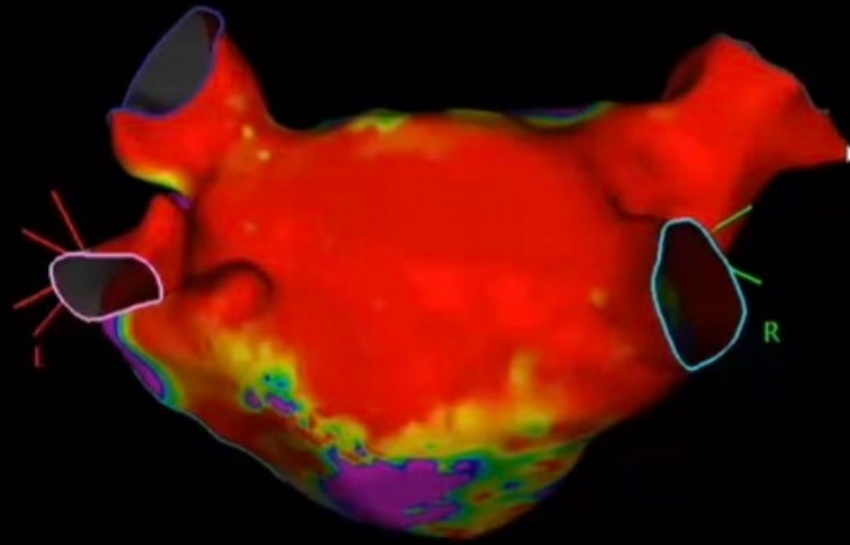
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HYBRID/CONVERGENT AF ABLATION

EPICARDIAL ABLATION



ENDOCARDIAL ABLATION



1.33



1.33



AMERICAN SOCIETY OF
FAMILY PHYSICIANS

FEBRUARY 16-18

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Recommendations for Surgical Ablation

Referenced studies that support the recommendations are summarized in the [Online Data Supplement](#).

COR	LOE	Recommendations
2b	B-R	3. For patients with symptomatic, persistent AF refractory to antiarrhythmic drug therapy, a hybrid epicardial and endocardial ablation might be reasonable to reduce the risk of recurrent atrial arrhythmia. ⁵⁻⁷



COMPLICATIONS

- Pericardial effusion/tamponade
- Stroke/embolic events
- Pulmonary vein stenosis
- LA-esophageal fistula
- Vascular complications



Table 7. Major Complications in the Overall Population

Type of Complication	No. of Patients	Rate, %
Death	25	0.15
Tamponade	213	1.31
Pneumothorax	15	0.09
Hemothorax	4	0.02
Sepsis, abscesses, or endocarditis	2	0.01
Permanent diaphragmatic paralysis	28	0.17
Total femoral pseudoaneurysm	152	0.93
Total artero-venous fistulae	88	0.54
Valve damage/requiring surgery	11/7	0.07
Atrium-esophageal fistulae	6	0.04
Stroke	37	0.23
Transient ischemic attack	115	0.71
PV stenoses requiring intervention	48	0.29
Total	741	4.54

Updated Worldwide Survey on the Methods, Efficacy, and Safety of Catheter Ablation for Human Atrial Fibrillation

Riccardo Cappato, MD; Hugh Calkins, MD; Shih-Ann Chen, MD; Wyn Davies, MD; Yoshito Iesaka, MD; Jonathan Kalman, MD; You-Ho Kim, MD; George Klein, MD; Andrea Natale, MD; Douglas Packer, MD; Allan Skanes, MD; Federico Ambrogi, PhD; Elia Biganzoli, PhD

Electrophysiol. 2010;3:32-38



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Rhythm-Symptom Correlation in Patients on Continuous Monitoring After Catheter Ablation of Atrial Fibrillation

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TABLE 2

Symptom-Rhythm Correlation Based on Symptoms Reported by Patients

	Overall Follow-Up Period			Excluding the First 3 Months of Follow-Up			
	Total	Symptomatic Patients	Asymptomatic Patients	Total	Always Symptomatic Patients	Always Asymptomatic Patients	Symptomatic-Asymptomatic Patients
Global							
Patients with any AF recurrence \geq 6 minutes	98 (69%)	53 (54%)	45 (46%)	46 (32%)	15 (33%)	21 (46%)	10 (22%)
Patients without AF recurrence	45 (31%)	15 (29%)	32 (71%)	97 (68%)	39 (40%)	45 (46%)	2 (2%)
Based on duration of AF recurrence							
Patients with AF >6 minutes <1 hour	24 (17%)	9 (38%)	15 (62%)	17 (12%)	6 (35%)	9 (53%)	2 (12%)
Patients with AF >1 hour <12 hours	31 (22%)	16 (52%)	15 (48%)	17 (12%)	5 (29%)	7 (41%)	5 (29%)
Patients with AF >12 hours <24 hours	19 (13%)	13 (68%)	6 (32%)	4 (3%)	1 (25%)	0 (0%)	3 (75%)
Patients with AF \geq 24 hours	24 (17%)	15 (63%)	9 (37%)	8 (6%)	3 (38%)	5 (63%)	0 (0%)



FINAL POLL QUESTION

A 76 year old man with HTN and paroxysmal atrial fibrillation has pulmonary vein isolation by cryo- ablation. At his six month follow-up, he is free of any arrhythmia related symptoms. Given his successful ablation, it is now reasonable to discontinue anticoagulation in exchange for ASA 325mg daily.

1. True
2. False



FINAL POLL QUESTION

A 76 year old man with HTN and paroxysmal atrial fibrillation has pulmonary vein isolation by cryo-ablation. At his six month follow-up, he is free of any arrhythmia related symptoms. Given his successful ablation, it is now reasonable to discontinue anticoagulation in exchange for ASA 325mg daily.

1. True
2. **False**



SUMMARY

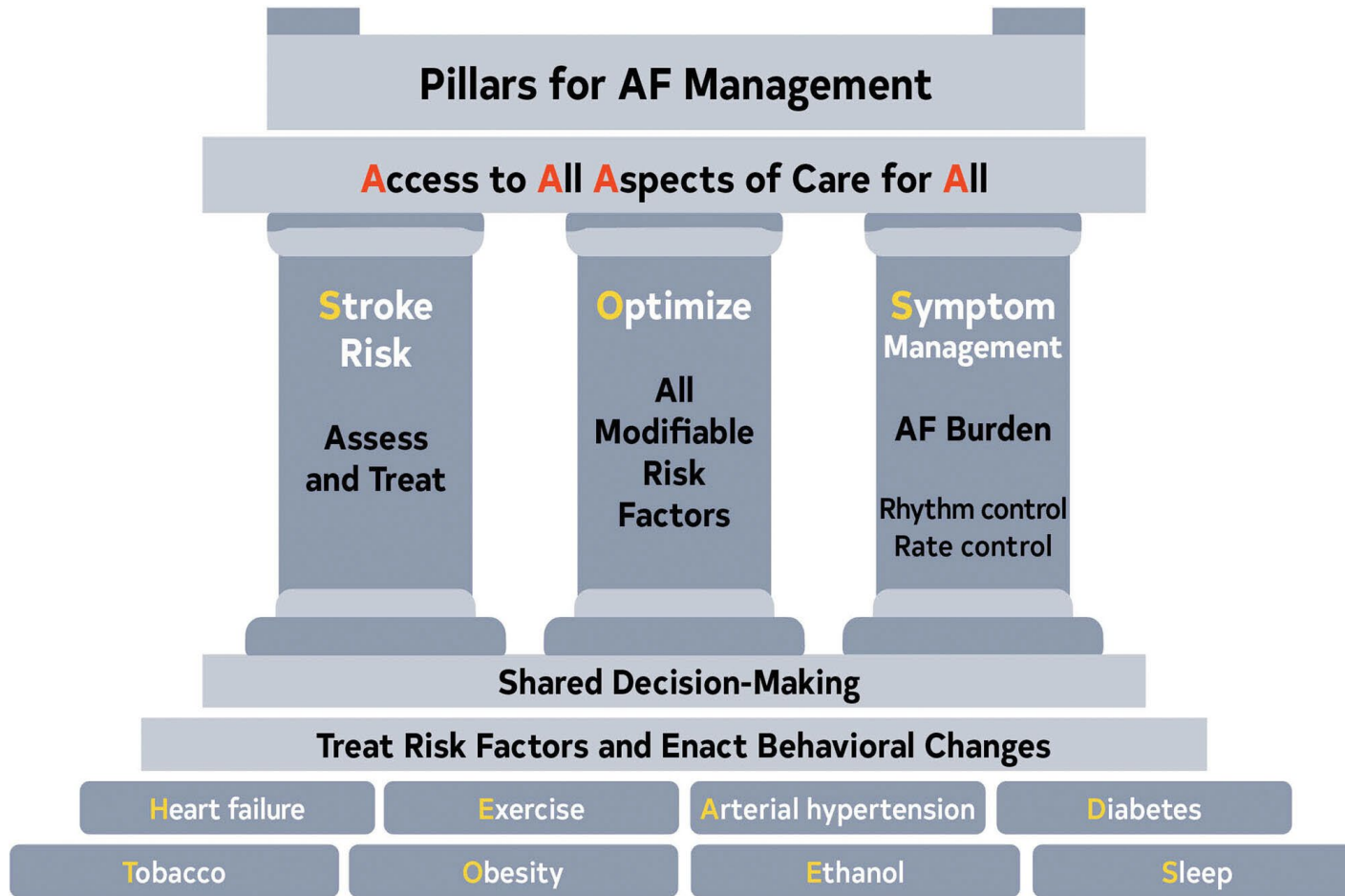
- *AF is triggered by PV firing and maintained by focal firing (sympathetic) and reentry (parasympathetic) mechanisms*
- *AF tends to promote more AF through structural (fibrosis) and electrical (shortening APD) remodeling*
- *Lifestyle modifications reduce burden of AF and improve symptoms*
- *Use NOAC for CHA₂DS₂ VASc > 0 (or 1 in selected cases)*



SUMMARY (...CONTD.)

- *Use rhythm control approach to minimize symptoms and maximize QoL*
- *Cornerstone of AF ablation is PV isolation*
- *AAD risks/benefit should be carefully considered and used to improve symptoms and minimize adverse effects*
- *While no mortality benefit to SR maintenance, several studies have documented lower mortality with ablation in AF + CHF*





José A. Joglar. Circulation. 2023 ACC/AHA/ACCP/HRS Guideline for the Diagnosis and Management of Atrial Fibrillation: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines, Volume: 149, Issue: 1, Pages: e1-e156, DOI: (10.1161/CIR.0000000000001193)

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**THANK
YOU**



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