The Management of Atrial Fibrillation

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No relevant disclosures

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Objectives

1. Appreciate the 3 Pillars of Atrial Fibrillation Management
2. Describe Who Should be Anticoagulated and Why
3. How to Choose Between Rate and Rhythm Control and Intervention

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NEJM, 1998

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.

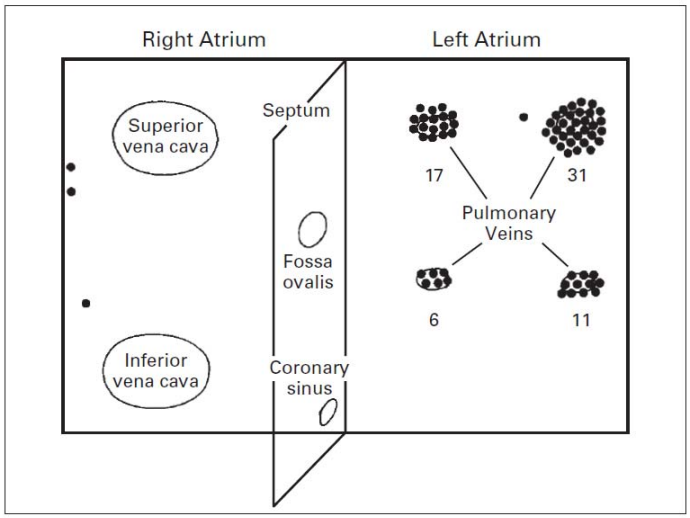


Figure 1. Diagram of the Sites of 69 Foci Triggering Atrial Fibrillation in 45 Patients.
Note the clustering in the pulmonary veins, particularly in both superior pulmonary veins. Numbers indicate the distribution of foci in the pulmonary veins.

In patients with paroxysmal AF, the vast majority of atrial premature beats **originate in the pulmonary veins** (94% of all triggers).

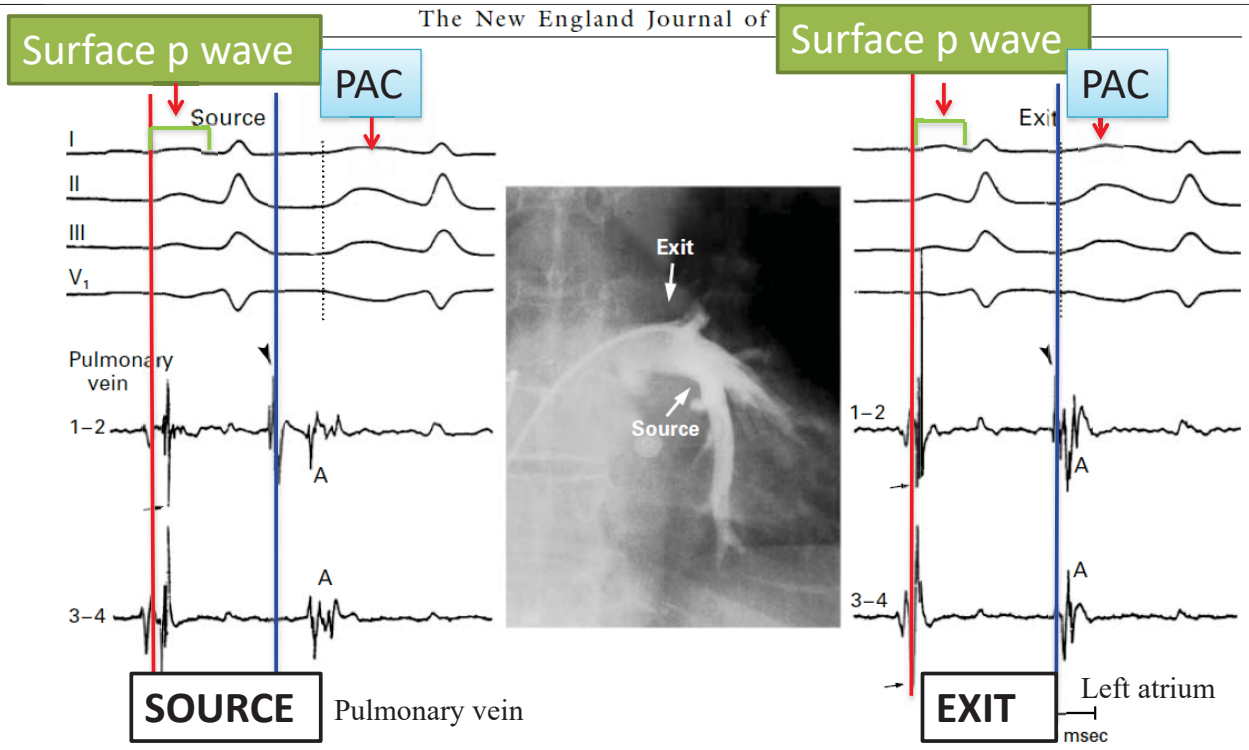
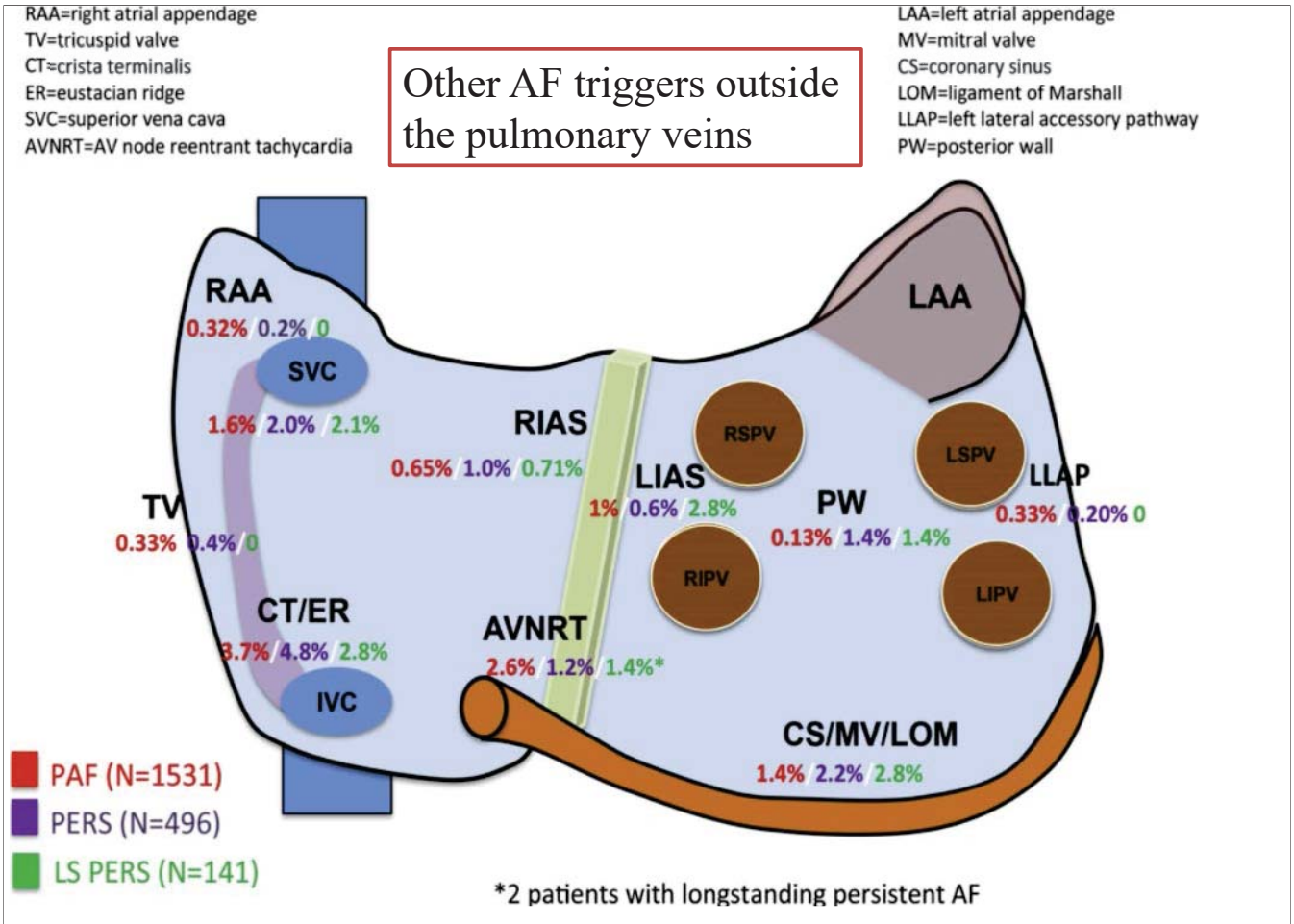


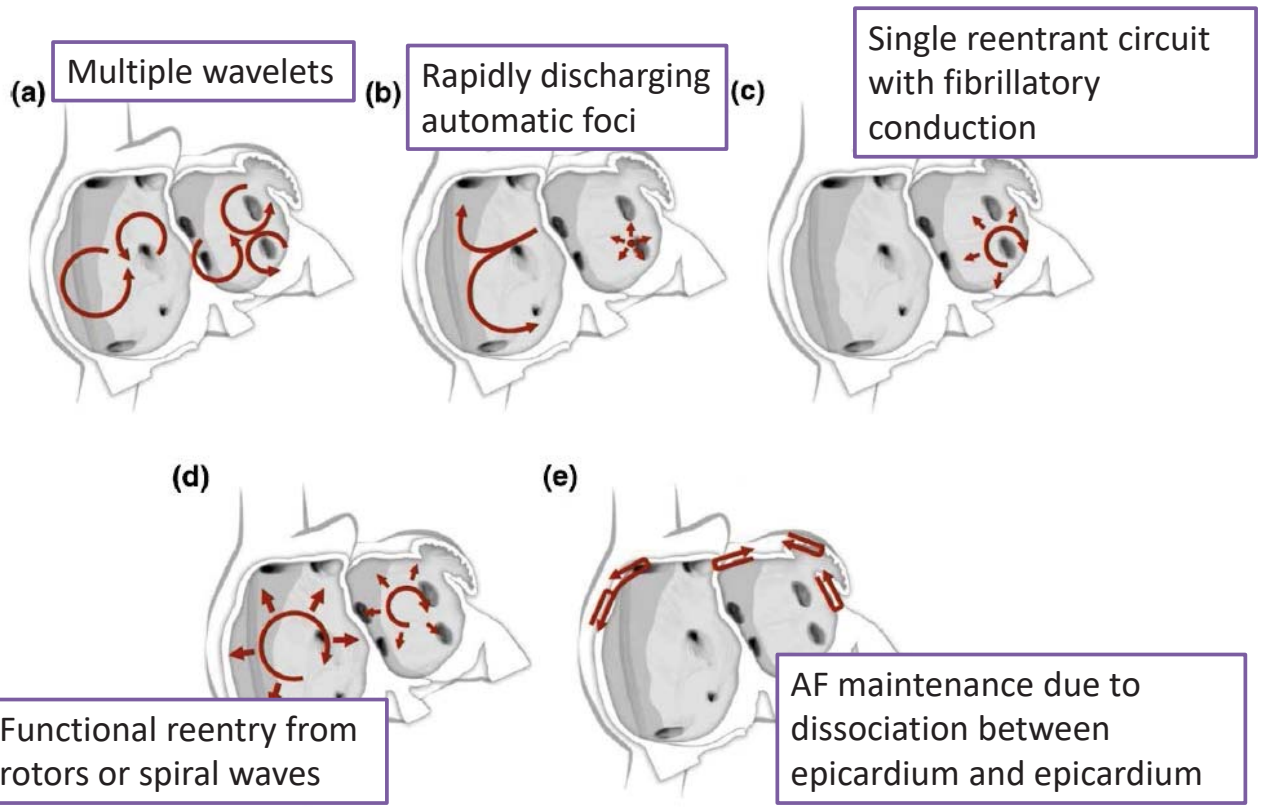
Figure 2. Angiogram of a Left Inferior Pulmonary Vein Depicting the Source and Exit of Ectopic Activity.

The electrogram showed characteristic changes in timing depending on the position of the recording catheter in the specific pulmonary vein. With an increasingly distal catheter position (toward the source), the spike was recorded progressively later during sinus rhythm (left-hand panel, arrows) and correspondingly earlier during ectopic activity (arrowhead). Conversely, in a proximal position at its exit into the left atrium (right-hand panel), the spike was not as delayed during sinus rhythm (arrows) nor as precocious during ectopic activity (arrowhead). The application of radio-frequency energy at the source of ectopic activity eliminated the local spike during sinus rhythm and ectopic beats and atrial fibrillation on a short-term basis. The dotted lines mark the onset of the ectopic P wave, and 1–2 and 3–4 are bipolar recordings from the distal and proximal poles of the mapping catheter. A indicates near-field atrial activity. The radiograph (center panel) shows the position of electrographic recordings inside the pulmonary vein at the source and exit.



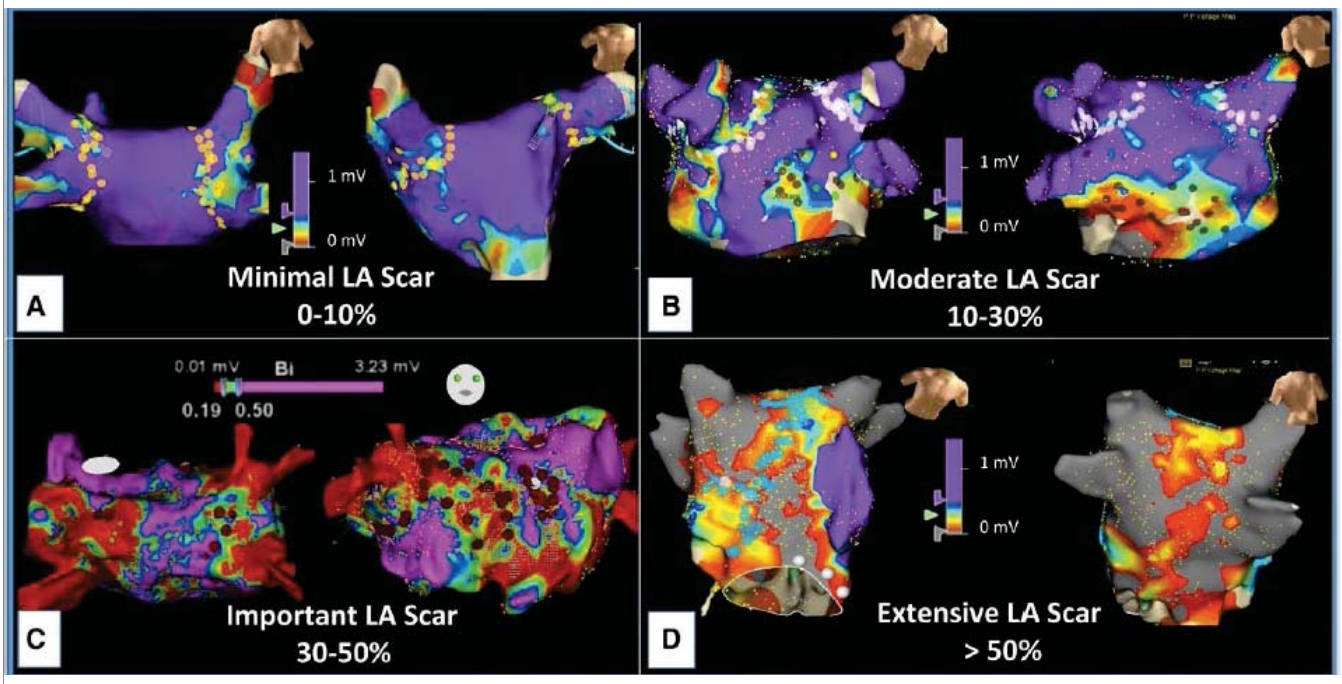
Santangeli et al. Heart rhythm July 2017. 14;7. 1087

Hypotheses regarding mechanisms of atrial fibrillation



2017 HRS expert consensus statement on catheter and surgical ablation of atrial fibrillation. J Interv Card Electrophysiol (2017) 50:1-55

Atrial Fibrosis: AF is a progressive disease



-Electroanatomic mapping allows direct contact with endocardial tissue and can reveal presence of scar (low voltage areas), not detectable by any imaging method

-In contrast to paroxysmal AF, an important proportion of patients with persistent AF have regional increase in atrial fibrosis that is associated with greater frequency of AF

Arentz, Circulation Arrhythmia and Electrophysiology. 2016.

Atrial Fibrillation Classification

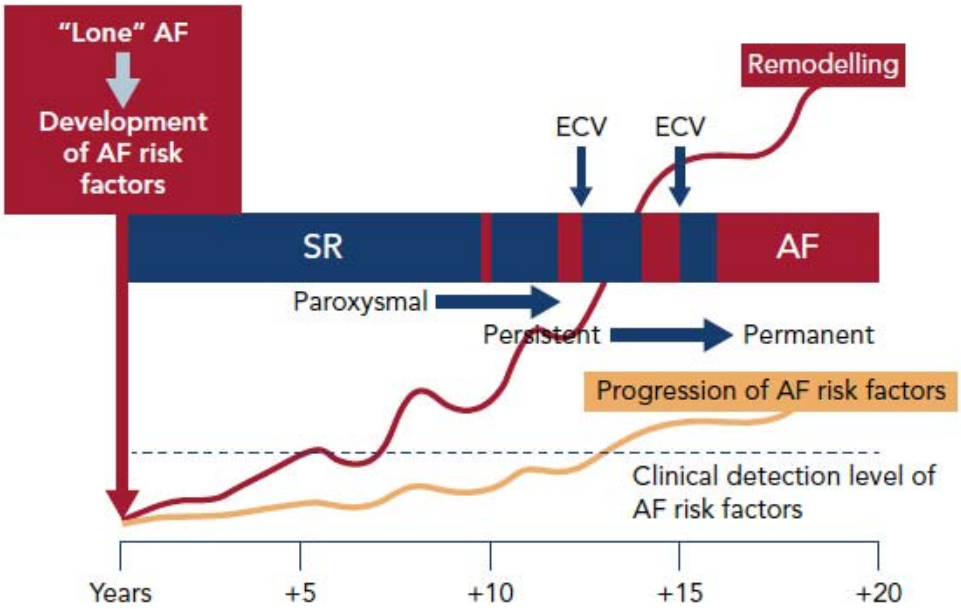
Paroxysmal: AF lasting more than 30 seconds, but < 7days

Persistent: Continuous AF episode >7 days, but < 1 year

Longstanding Persistent: Continuous AF episode ≥ 1 year, but where rhythm control is being pursued

Permanent AF: Continuous AF for which a therapeutic decision has been made not to pursue sinus rhythm restoration

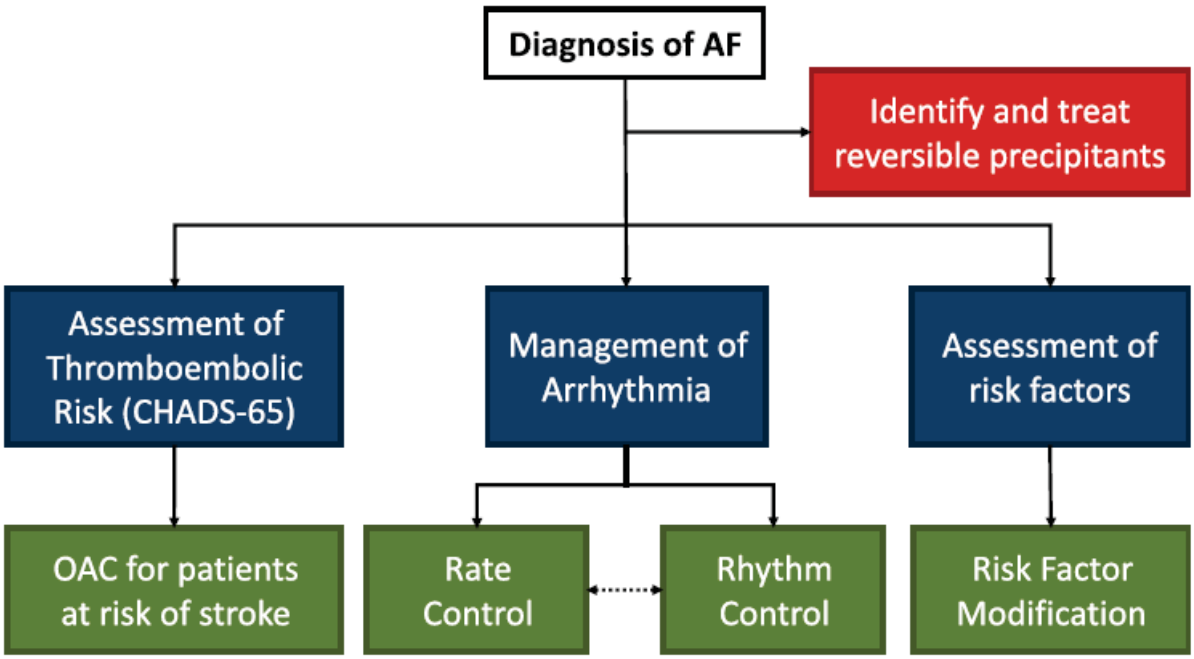
Figure 2: Time-dependent Atrial Remodelling and Development of Atrial Fibrillation



A hypothetic construct over time indicating the interrelationship between time, risk factors for atrial fibrillation (AF), atrial remodelling, detection of risk factors for atrial remodelling and progression from sinus rhythm (SR) through paroxysmal and persistent to permanent AF. ECV = electrical cardioversion. Source: J Am Coll Cardiol, 63, Wyse DG, Van Gelder IC, Ellinor PT, et al, Lone atrial fibrillation: does it exist?, 1715–23, 2014, with permission from Elsevier.[45]

The 3 pillars of Treatment

1. Risk Factor Modification
2. Arrhythmia Management: Drug Therapy (Rate or Rhythm Control) vs Interventional Therapy
3. Stroke Prevention

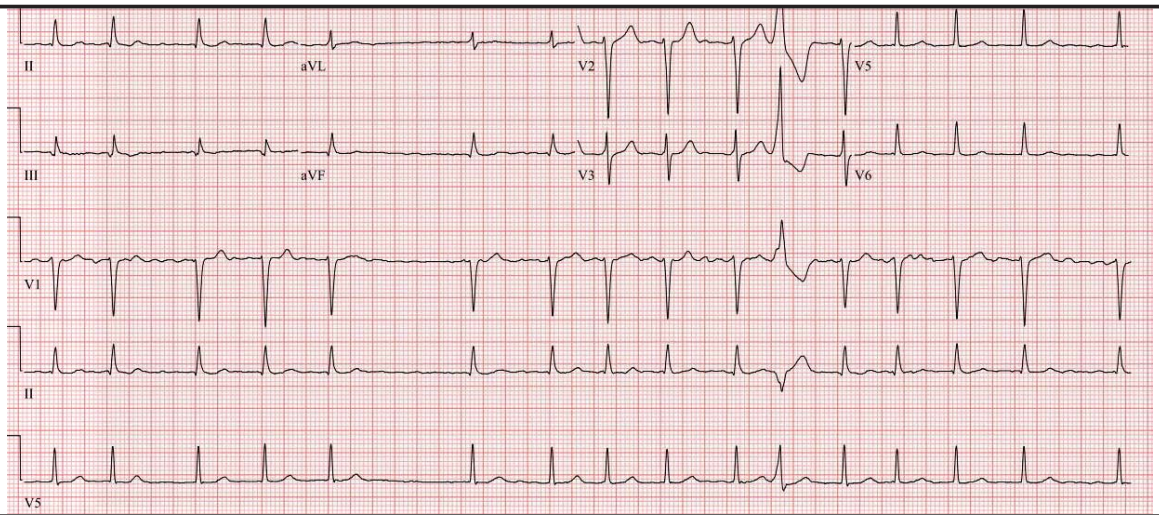


Major Goals of AF Management	Anticipated Outcome
Prevent stroke or systemic thromboembolism	Improvement in survival
Cardiovascular Risk Reduction	
Improve symptoms, functional capacity, and QOL	Reduction in healthcare utilisation (e.g. ED visits or hospitalizations)
Prevent complications (e.g. LV dysfunction, falls)	

2020 Canadian Guidelines: Atrial Fibrillation; CJC vol 36

Case 1:

55M presents with dyspnea on exertion for the last several months (he has stopped exercising due to Covid)
PMHx: hypertension x 5 years, dyslipidemia
Medications: HCTZ 25mg Qd, Norvasc 5mg po Qd, crestor 10mg Qd



Case 1:

Questions:
1. Is he symptomatic? Is he dyspneic from the atrial fibrillation?
2. Is his AF paroxysmal? Persistent?
3. Is his heart structurally normal? Ie. is EF normal, and no valve disease?

Investigations needed:
1. Bloodwork: CBC, electrolytes, creatinine, thyroid
2. Transthoracic echo: rule out valvular disease, assess EF, assess left atrial size
3. Holter monitor: What is the rate in atrial fibrillation? Is it truly persistent, or is this paroxysmal?
4. Consider an exercise stress test (for dyspnea), and CXR

Case 1:

Questions:

1. Is he symptomatic? dyspneic from the atrial fibrillation?
2. Is his AF paroxysmal? Persistent?
3. **What are his modifiable risk factors?**
4. Management decisions: 3

1. Modifiable risk factors:
   -Is BP well controlled?
   -Evaluate EtOH intake
   -Weight..
   -Does he have obstructive sleep apnea?
   -Is he a smoker?

"Enter into a Partnership: You do your part, and I will do mine"

Aggressive Risk Factor Management

Weight management and Exercise

- Diet Plan
- Initial target: >10% weight loss. Final target BMI <27kg/m2
- Avoid weight fluctuation
- Exercise: >30min for 3-3-5/week
- Increase type and duration of activity to 250 min/wk
- Resistance ex 2-3 d/week
- Flexibility exercises 10min/day 2

Hypertension: Major risk factor. Data supports tighter control

- Home BP Diary
- Reduce salt
- Suggest ACEi or ARB
- Target preferred: SBP<130/80

Obstructive Sleep Apnea

- Among AF pts, prevalence is >50%
- Screen for OSA (stopBang)
- Overnight sleep study
- Check adherence

Alcohol

- Linear dose-response with 8% increase in RR of AF with each standard drink/day
- Established RF + EtOH = higher rates of progression and less response to treatment
- Limit to <=1 standard drink/d

Diabetes

- 1.5x increased risk of AF
- 13% increased risk with each 1% increase in HbA1c

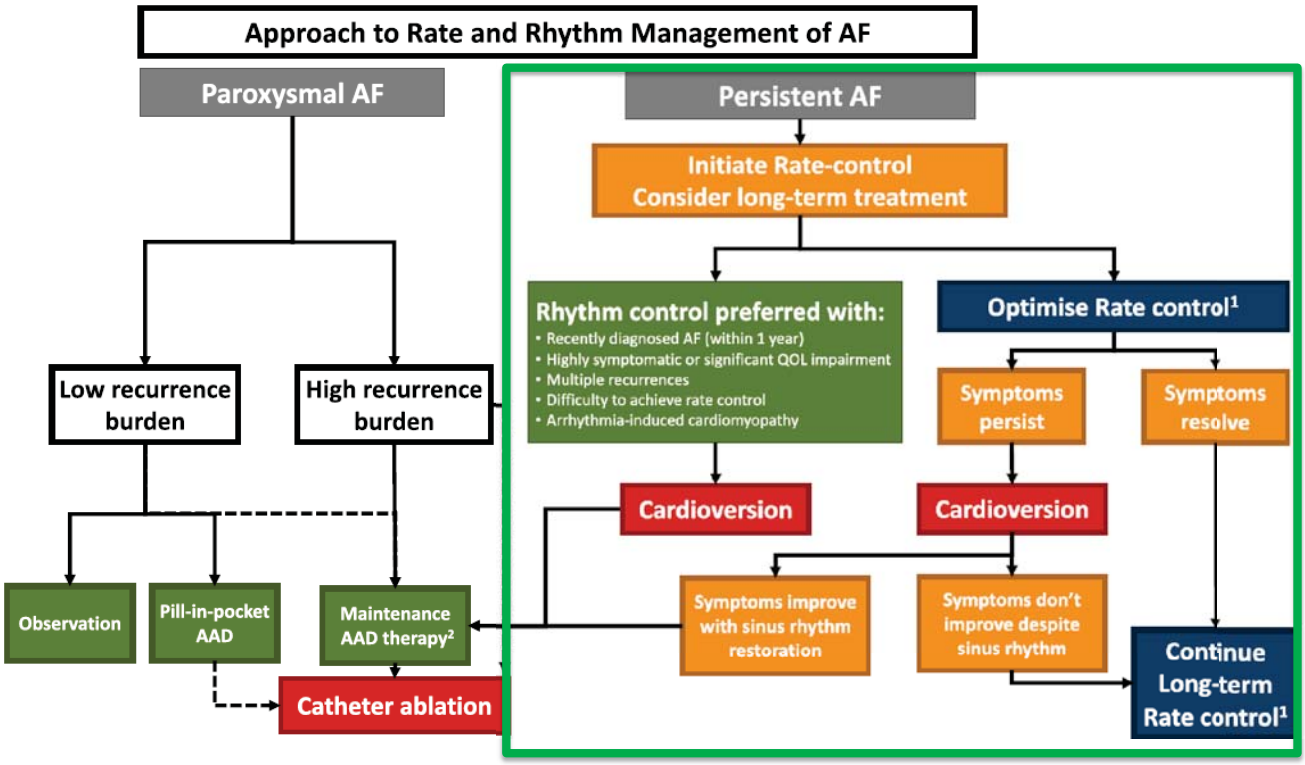
Case 1: Rate or Rhythm Control?

2. Rate vs Rhythm?
Options:
    1. Rate control: Add beta blocker or calcium channel blocker
    OR
    2. Rhythm control: Cardioversion + start on anti-arrhythmic

Rate control (or until cardioversion):
Ejection fraction >40%: b-blocker or Ca-channel blocker E.g. verapamil SR 180mg Qd or diltiazem CD 180mg po Qd
-BB are effective, but assoc. with higher S/E such as fatigue and exercise intolerance. CCBs have favourable dose-response characteristic. Consider CCB if htn or reactive airway disease vs. BB with coronary disease.

Ejection fraction<40%: bisoprolol, carvedilol, or metoprolol as 1st line. Eg. Metoprolol 25mg po BID, and up-titrate

Volume 36 2020



Patient is young, symptomatic, and likely relatively new-onset
(Each of these factors is independently important to the decision)

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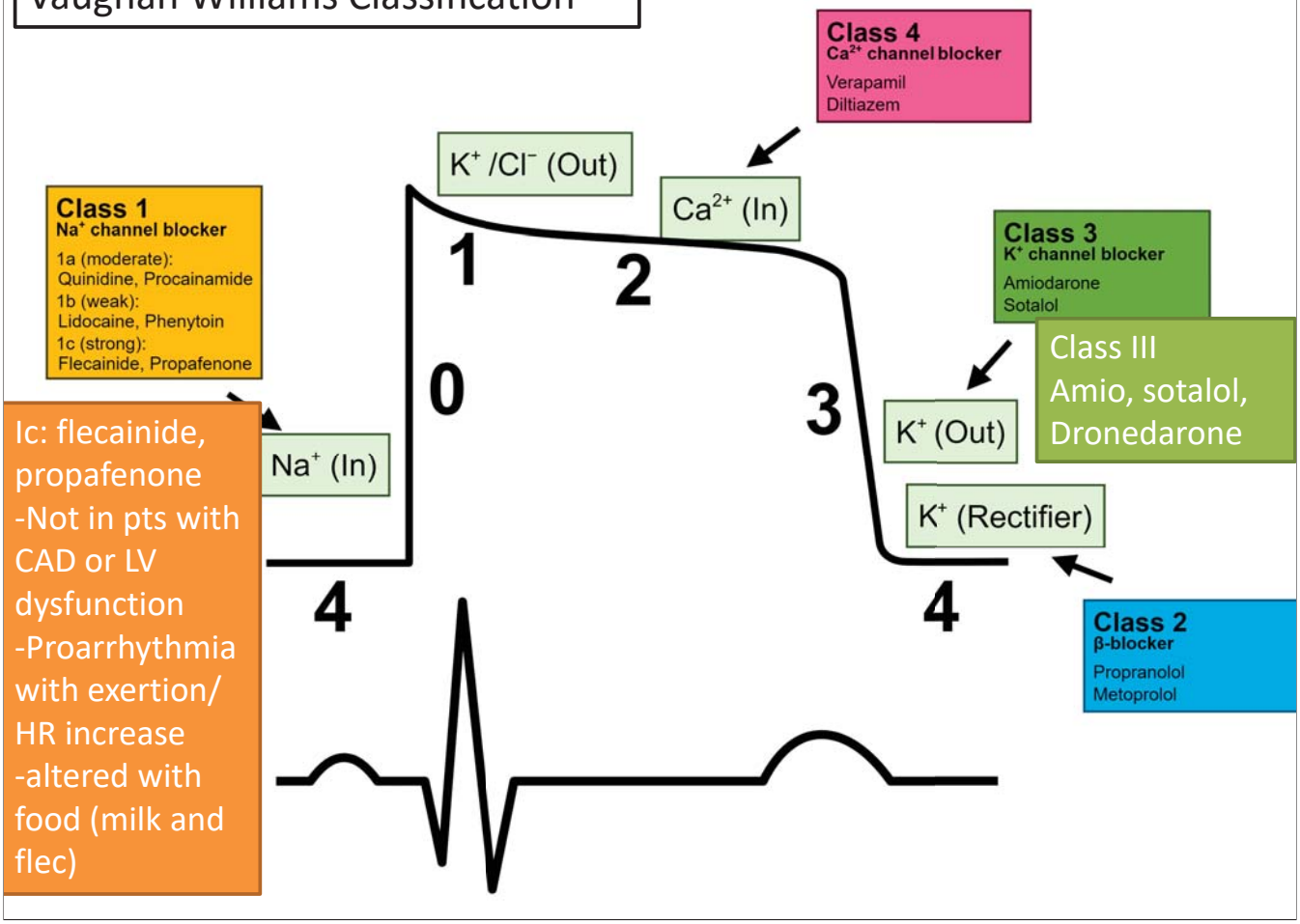
Rhythm Control

Goal: symptom relief, improving functional capacity and QOL, with reduction in healthcare utilization

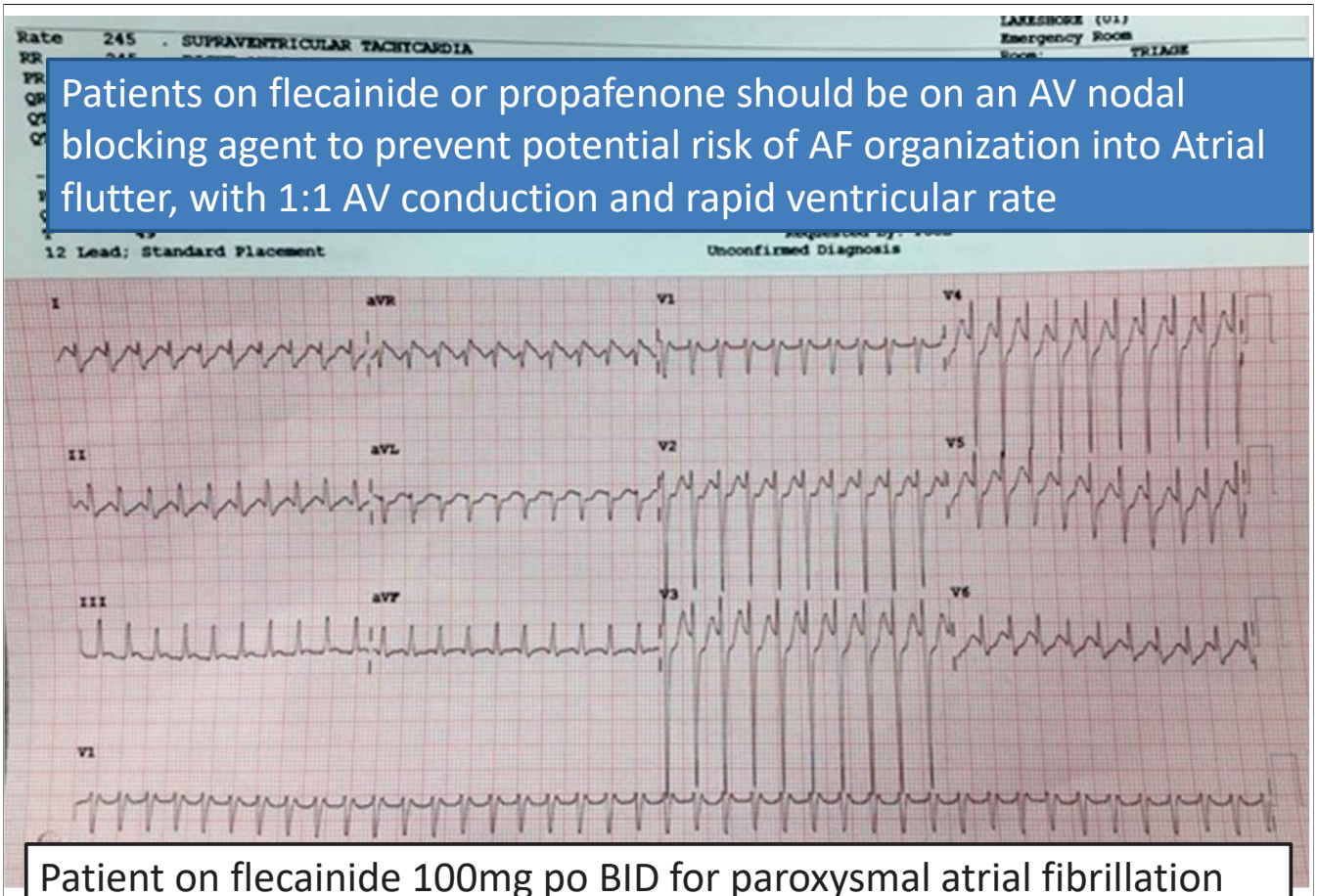
Issue: potential adverse drug effects and longterm inefficacy of antiarrhythmic drugs (AADs)

What is the efficacy of antiarrhythmic medications?
Amiodarone
Sotalol
Flecainide
Propafenone
Dronedarone

Vaughan Williams Classification

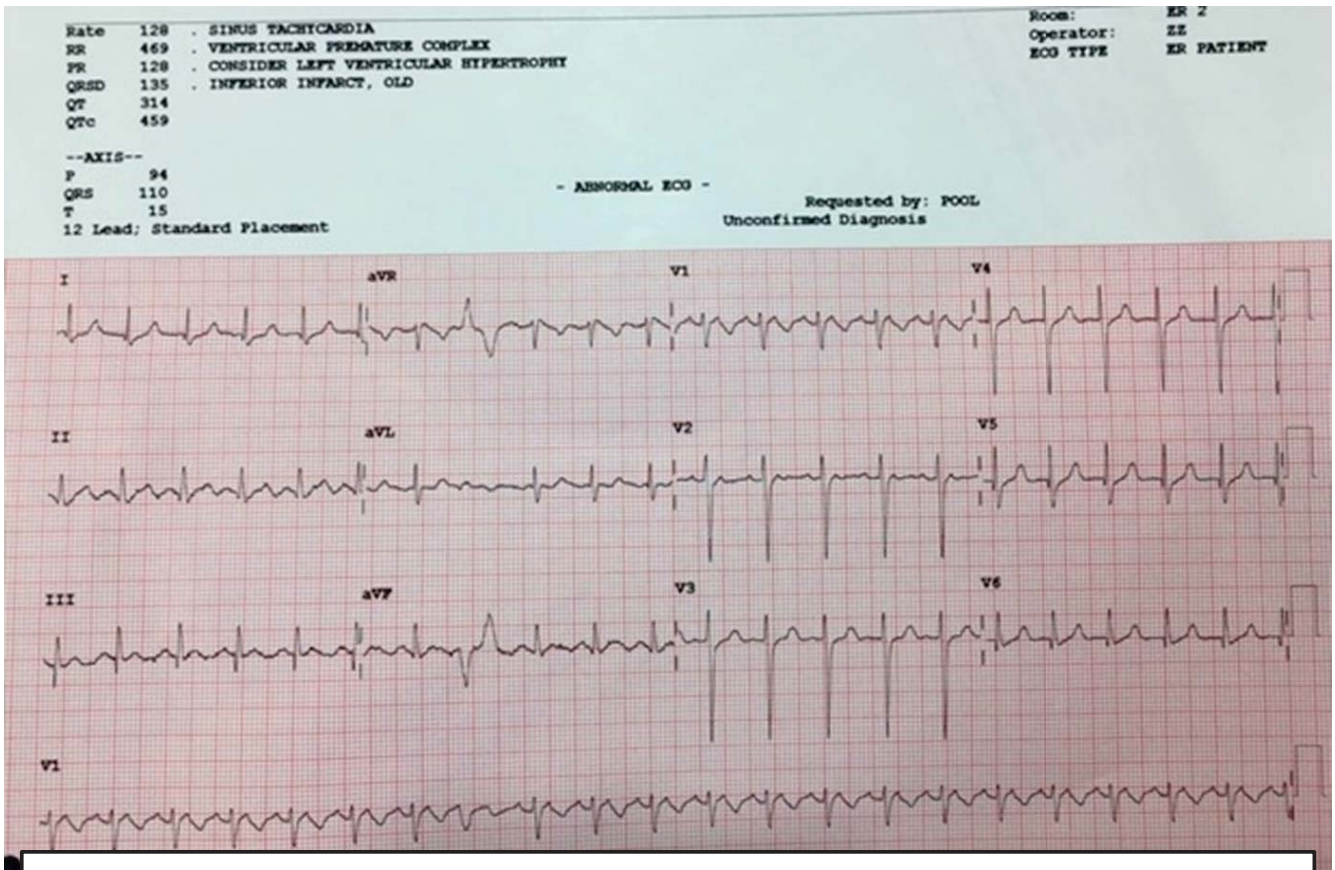


Ic: flecainide, propafenone
-Not in pts with CAD or LV dysfunction
-Proarrhythmia with exertion/ HR increase
-altered with food (milk and flec)



Patients on flecainide or propafenone should be on an AV nodal blocking agent to prevent potential risk of AF organization into Atrial flutter, with 1:1 AV conduction and rapid ventricular rate

Patient on flecainide 100mg po BID for paroxysmal atrial fibrillation



Carotid sinus massage

Rhythm Control

Class Ic: Flecainide/Propafenone

- Needs concomitant use of AV nodal blocking agent
- Avoid in pts with evidence of AV block (2nd or 3rd degree)
- Avoid in LBBB or RBBB with fascicular block
- Avoid where LVEF <40%
- Avoid in severe LVH
- Avoid in severe hepatic or severe renal impairment (GFR<35)
- Avoid in ischemic heart disease: active or history of Mi
- Suggest formal ischemia assessment (e.g. Stress test) in those older than 50 years or with significant risk factors for CAD
- ECG baseline and after initiation: increase in QRS duration >25% = proarrhythmic

Rhythm Control

Class III:

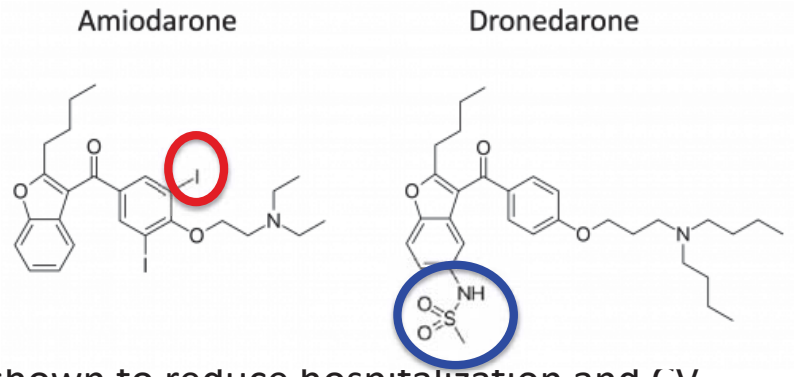
Sotalol: "Reverse Use dependence Ikr inhibition": ie. at lower doses, the Beta blocker effects predominate whereas class III effects emerge with higher doses

- QT prolongation and risk of torsades de pointes:
- Avoid in long QT, high-degree AV block, GFR<40, LVEF <40%, women>65 with concomitant diuretics
- Repeat ECG 48-72hrs after initiation to monitor QTc interval

Rhythm Control

Class III:

Dronedarone:



-Only antiarrhythmic shown to reduce hospitalization and CV mortality in pts with paroxysmal or persistent AF

-Avoid in permanent AF (this drug is NOT for rate control)

-Avoid in high degree AV block

-Avoid if prior lung or liver injury due to amio use

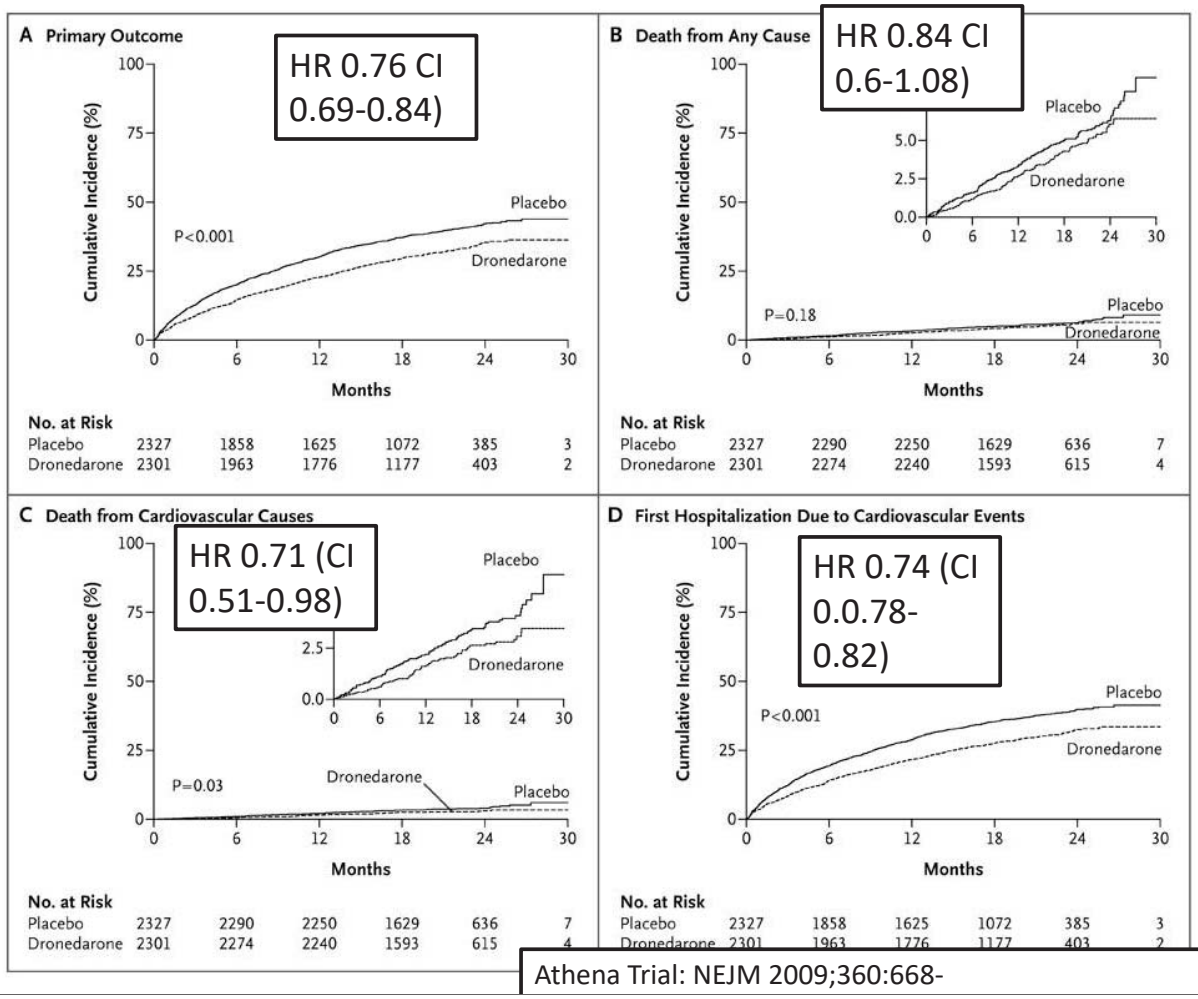
-Avoid if preexisting long QT

-Avoid in severe hepatic impairment: perform LFTs q3 months for 1st year, then q6months.

Table 2. Study Outcomes.

Outcome	Dronedarone (N=2301)	Placebo (N=2327)	Hazard Ratio for Dronedarone (95% CI)	P Value
Primary outcome — no. (%)	734 (31.9)	917 (39.4)	0.76 (0.69–0.84)	<0.001
First hospitalization due to cardiovascular events — no. (%)	675 (29.3)	859 (36.9)	0.74 (0.67–0.82)	<0.001
First hospitalization — no. (%)				
For atrial fibrillation	335 (14.6)	510 (21.9)	0.63 (0.55–0.72)	<0.001
For congestive heart failure	112 (4.9)	132 (5.7)	0.86 (0.67–1.10)	0.22
For acute coronary syndrome	62 (2.7)	89 (3.8)	0.70 (0.51–0.97)	0.03
For syncope	27 (1.2)	32 (1.4)	0.85 (0.51–1.42)	0.54
For ventricular arrhythmia or nonfatal cardiac arrest	13 (0.6)	12 (0.5)	1.09 (0.50–2.39)	0.83
Death from any cause — no. (%)	116 (5.0)	139 (6.0)	0.84 (0.66–1.08)	0.18
From noncardiovascular causes	53 (2.3)	49 (2.1)	1.10 (0.74–1.62)	0.65
From cardiovascular causes	63 (2.7)	90 (3.9)	0.71 (0.51–0.98)	0.03
From nonarrhythmic cardiac causes	17 (0.7)	18 (0.8)	0.95 (0.49–1.85)	0.89
From cardiac arrhythmia	26 (1.1)	48 (2.1)	0.55 (0.34–0.88)	0.01
From noncardiac vascular causes (including stroke)	20 (0.9)	24 (1.0)	0.84 (0.47–1.52)	0.57
Any hospitalization due to any cardiovascular event or death from any cause — no. (%) (no. of events per 100 patient-yr)	1253 (32.4)	1668 (42.6)	0.76 (0.68–0.84)	<0.001

Athena Trial: NEJM 2009;360:668-



Athena Trial: NEJM 2009;360:668-

Rhythm Control

Class III:

Amiodarone:

-Loading dose is 10-12g

-Maintenance ≤ 200mg Qd is recommended

-In hospital, can give oral and IV at same time (oral loading much faster)

-liver and thyroid tests q6months

-annual CXR

-sun protection

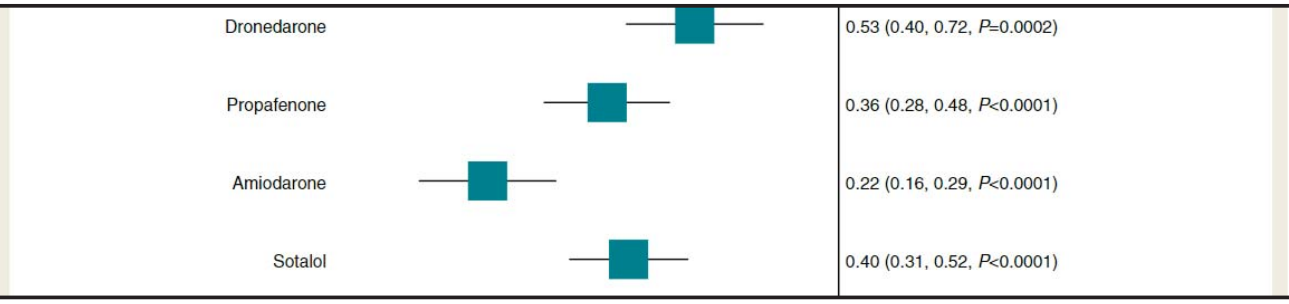
Europace (2011) **13**, 329–345
doi:10.1093/europace/euq450

Mixed treatment comparison of dronedarone, amiodarone, sotalol, flecainide, and propafenone, for the management of atrial fibrillation

Nick Freemantle[1], Carmelo Lafuente-Lafuente[2], Stephen Mitchell[3], Laurent Eckert[4]*, and Matthew Reynolds[5]

- Meta-analysis of 39 RCTs examining amiodarone, dronedarone, flecainide, propafenone, sotalol, or placebo for the treatment of AF

AF Recurrence: Amiodarone best: OR 0.22.



Serious adverse events: Amiodarone the worst OR 2.41

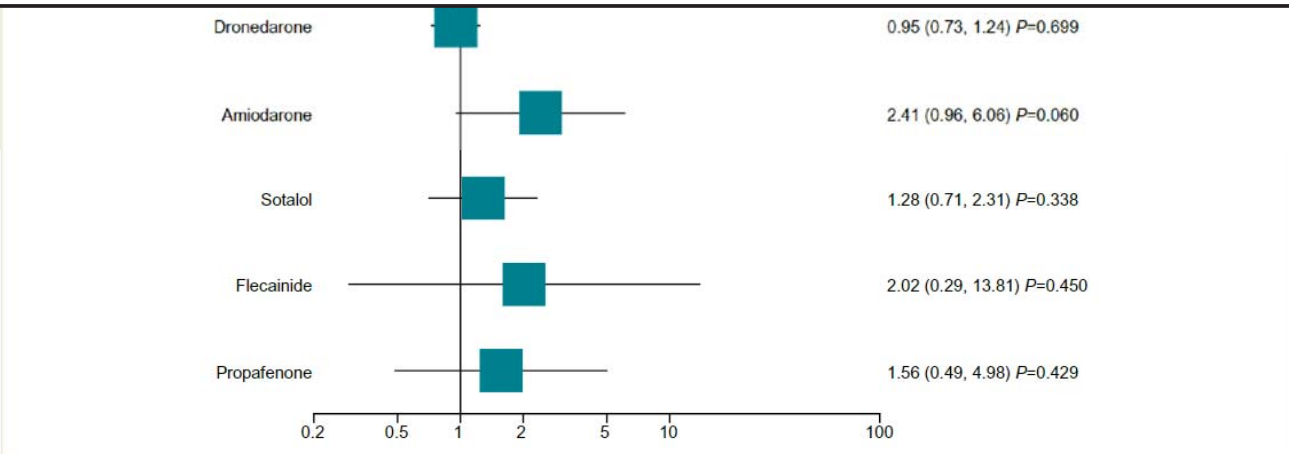
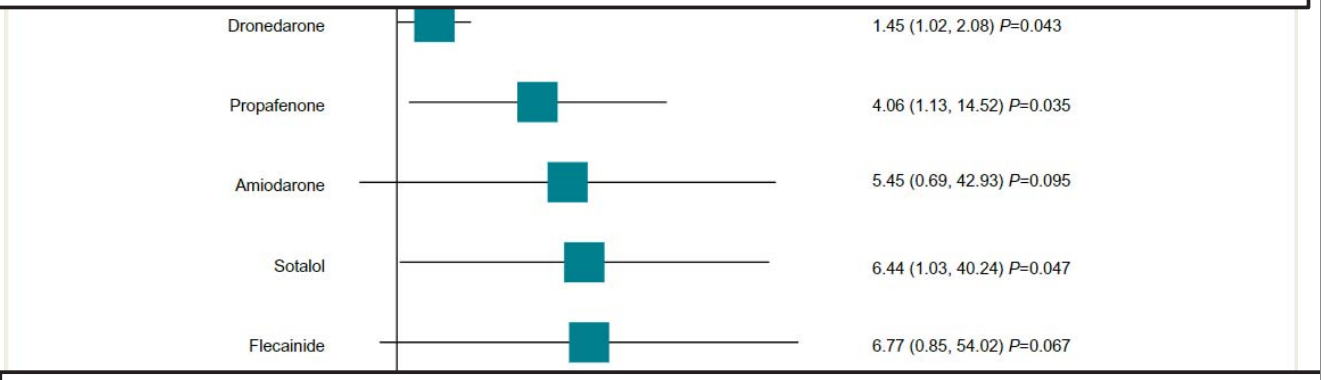


Figure 8 Mixed treatment comparison analysis: effect of anti-arrhythmic drugs on incidence of serious adverse events. Odds ratios and 95% confidence intervals. Note—odds ratio lower than 1 describes a lower rate of serious adverse events for the active treatment.

Dronedarone the least proarrhythmic (including bradycardia) OR 1.45



Dronedarone significantly lowered the risk of stroke OR 0.69 (1 study)

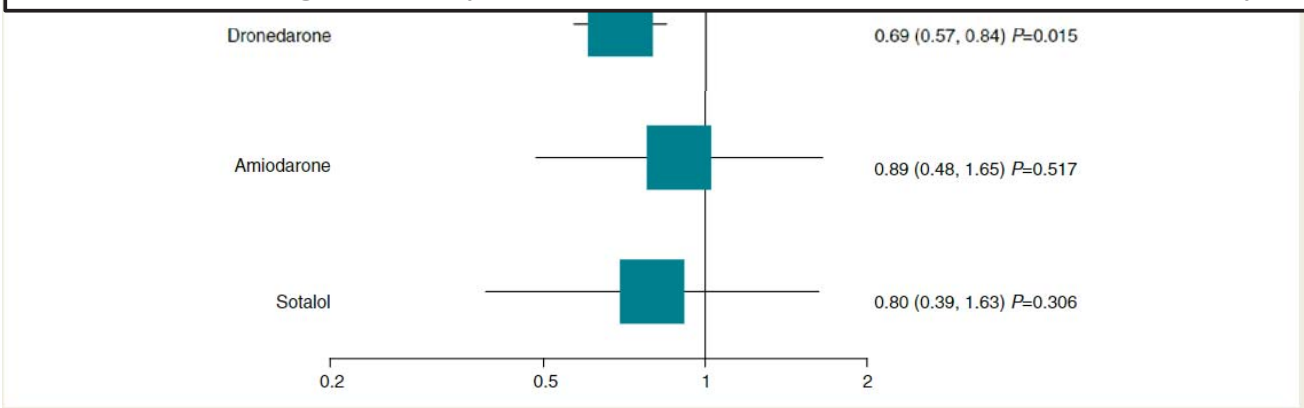


Figure 4 Mixed treatment comparison analysis: effect of anti-arrhythmic drugs on stroke. Odds ratios and 95% confidence intervals. Note—odds ratio lower than 1 describes a lower rate of stroke for the active treatment.

Trends toward increased mortality for sotalol and amiodarone, stronger when only studies >100 patients were included

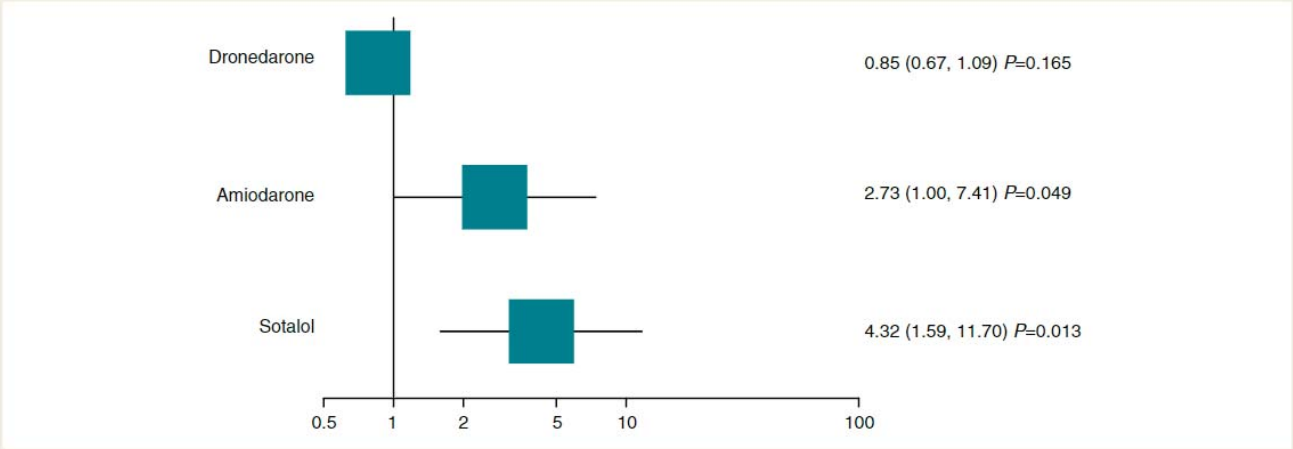


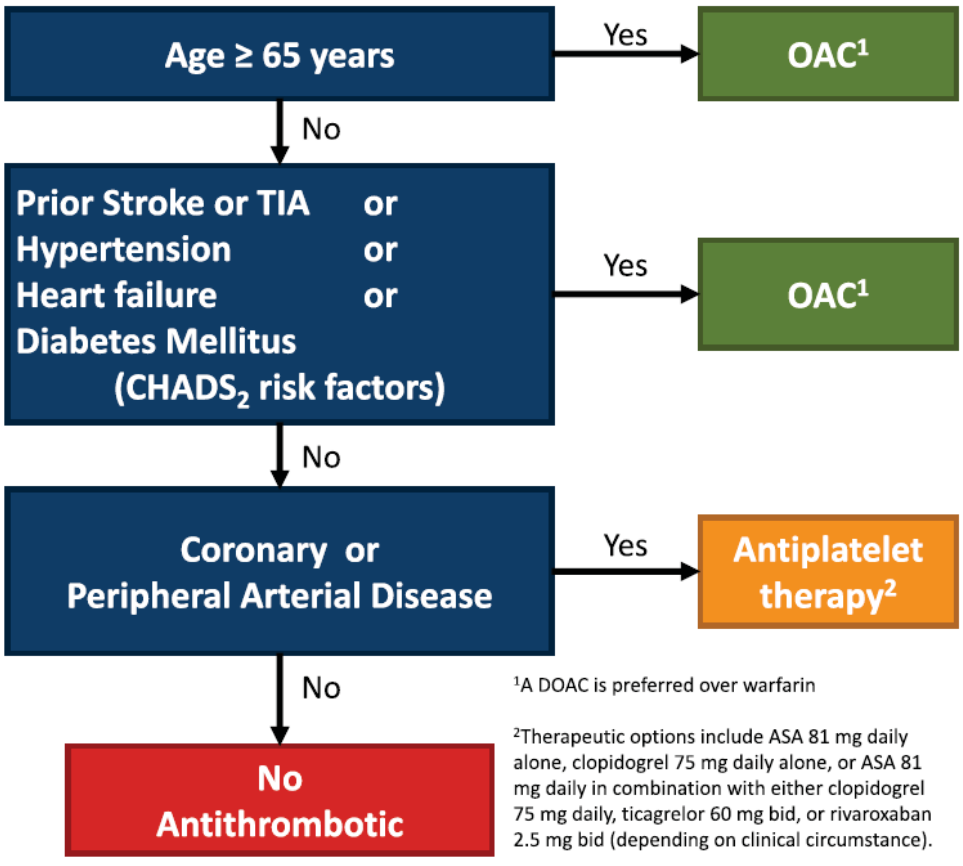
Figure 3 Mixed treatment comparison analysis: effect of anti-arrhythmic drugs on all-cause mortality in studies involving >100 patients in either arm. Odds ratios and 95% confidence intervals. Note—odds ratio smaller than 1 indicates a benefit (lower mortality) for the active agent.

Case 1:

Questions:

1. What are his modifiable risk factors?
2. Rate vs rhythm control
3. **Stroke prevention**

Can patients only take their oral anticoagulant when they have an AF episode?



2020 Canadian Guidelines: Atrial Fibrillation; CJC vol 36

Risk of Thromboembolism

Table 2. Event rates (95% CI) and hazard ratios for hospital admission and death due to thromboembolism according to components of CHA2DS2-VASc score at 5-years follow-up

Risk Factor	Annual Risk (95% CI)	Hazard Ratio (95% CI)	*P*
CHA_2DS_2-VASc = 0	0.69 (0.59-0.81)	1.0	
CHA_2DS_2-VASc = 1			
- **Heart failure**	2.35 (1.30-4.24)	3.39 (1.84-6.26)	< 0.0001
- **Diabetes mellitus**	2.28 (1.42-3.66)	3.31 (2.00-5.46)	< 0.0001
- **Hypertension**	1.60 (1.26-2.01)	2.32 (1.75-3.07)	< 0.0001
- **Age 65-74**	2.13 (1.85-2.46)	3.07 (2.48-3.80)	< 0.0001
- **Vascular disease**	1.40 (0.91-2.15)	2.04 (1.29-3.22)	0.002
- **Female sex**	0.86 (0.70-1.06)	1.25 (0.96-1.63)	0.10

CHA_2DS_2-VASc, Congestive Heart Failure, Hypertension, Age (≥75 years), Diabetes, Stroke/Transient Ischemic Attack, Vascular Disease, Age (65-74 years), Sex (Female); CI, confidence interval. Modified from Olesen et al.[22] with permission from BMJ Publishing Group Ltd.

Oral anticoagulant therapy is justified when the annual risk of stroke exceeds 1.5%

Patients age 65+ without other RF, annual risk of stroke decreases to 0.7%, which increase in major bleeding 0.5%/year to 1%

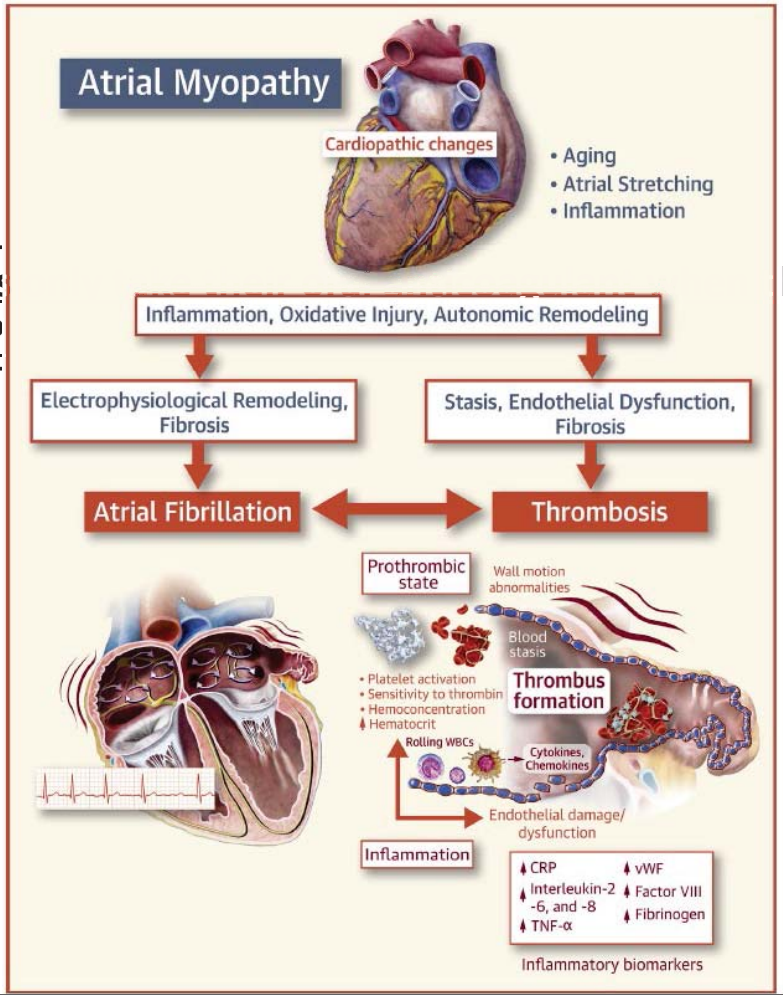
2016 Focused Update of the Canadian Cardiovascular Society Guidelines for the Management of Atrial Fibrillation. CJC 32 (2016) 1170-1185

CrCl	Warfarin	Apixaban	Dabigatran	Edoxaban	Rivaroxaban
CrCl >50 mL/min	Dose adjusted for INR 2.0-3.0	5 mg BID†	150 mg BID*	60 mg daily∞	20 mg daily
CrCl 30-49 mL/min	Dose adjusted for INR 2.0-3.0	5 mg BID†	Consider 110 mg BID	30 mg daily	15 mg daily
CrCl 15-29 mL/min	No RCT Data**	Very limited RCT Data§	No RCT Data¶	Very limited RCT Data¶	No RCT Data
CrCl <15 mL/min (or on dialysis)	No RCT Data‡	Very limited RCT Data¶	No RCT Data¶	No RCT Data¶	Very limited RCT Data¶

Ok: 2021

BID, twice daily; CrCl, creatinine clearance, INR, international normalized ratio; RCT, randomized clinical trial.
*Dabigatran 110 mg po BID is recommended if age ≥80 years, or ≥75 years with other bleeding risk factors including CrCl 30-50mL/min
†Apixaban 2.5 mg po BID is recommended if 2 of the 3 following criteria are present: 1) age ≥80 years, 2) body weight ≤60 kg, or 3) serum creatinine ≥133 μmol/L
∞Consider Edoxaban 30mg daily if weight ≤60 kg or concomitant potent P-Gp inhibitor therapy EXCEPT amiodarone or verapamil
**Dose adjusted warfarin has been used, but data regarding safety and efficacy is conflicting
‡Dose adjusted warfarin has been used, but observational data regarding safety and efficacy is conflicting and suggests harm.
§The ARISTOTLE trial included a small number of patients with a CrCl as low as 25 mL/min
¶Product monographs suggest the drug is contraindicated for this level of renal function.

Can patients **hey have an AF episode?**



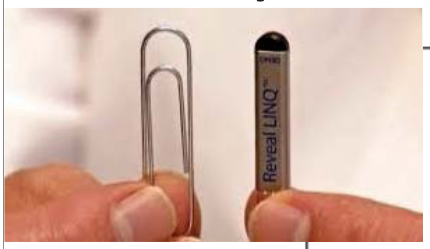
Shen et al. JACC Basic Trans Science 2019;4(5):640-)

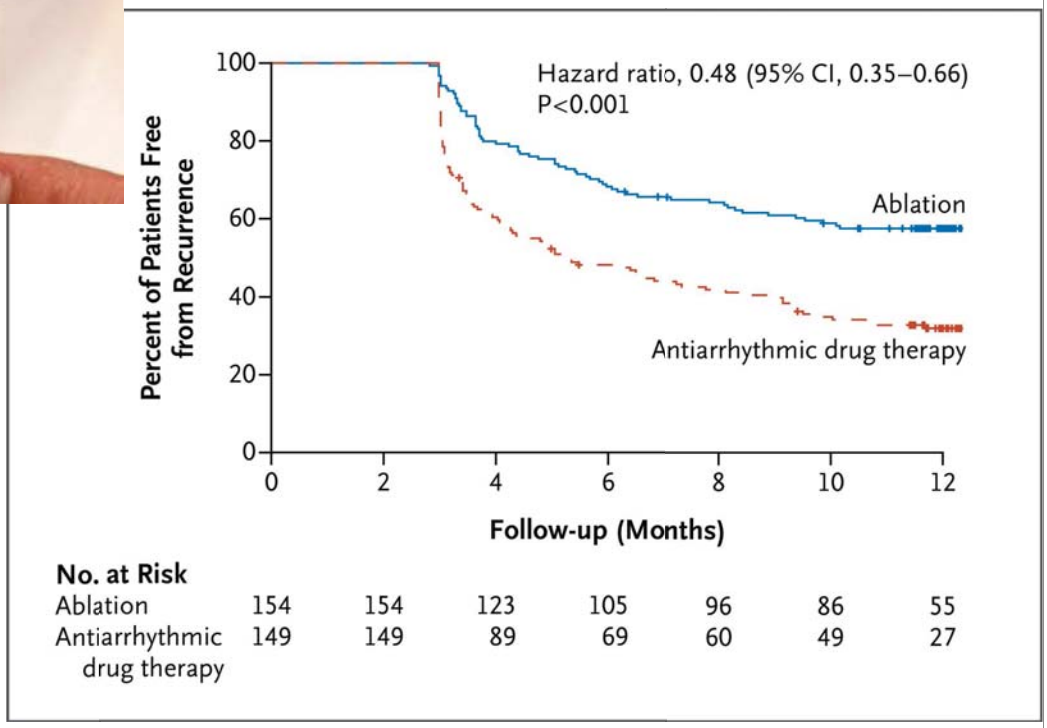
Case 1:

55M presents with dyspnea on exertion
PMHx: hypertension x 5 years, dyslipidemia
Medications: HCTZ 25mg Qd, Norvasc 5mg po Qd, crestor 10mg Qd

- Risk Factor modification
- Started him immediately on metoprolol 25mg po BID and DOAC (Apixaban or Edoxaban preferred)
- Echo revealed normal EF, and dyspnea likely as a result of AF
- Cardioverted, and flecainide 100mg po BID added to metoprolol
- Sent for exercise stress test several weeks after flecainide initiation to rule out CAD (given history)
- If feels better in sinus rhythm, will put on list for AF ablation

Why Early Adoption of Ablation?

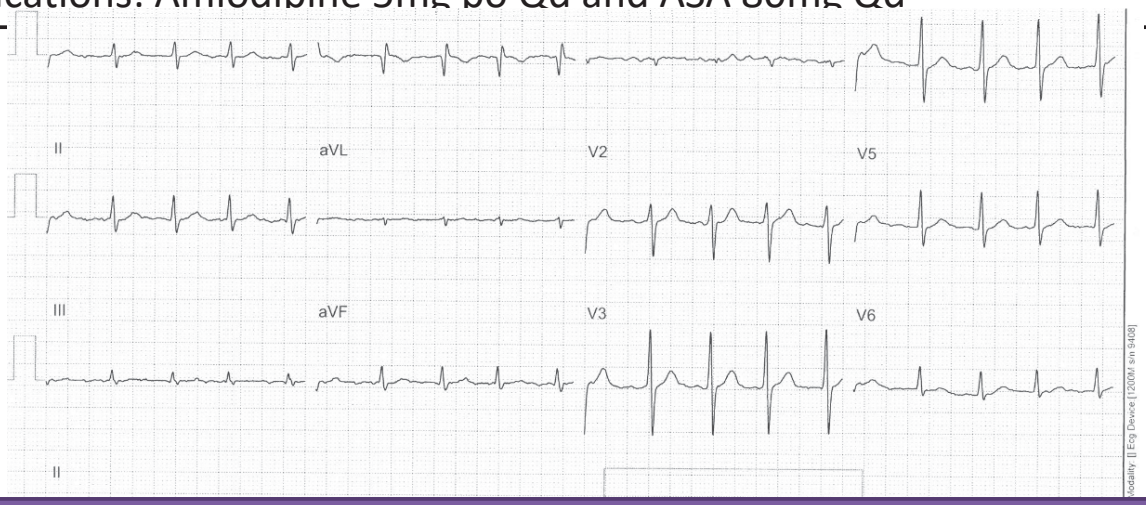




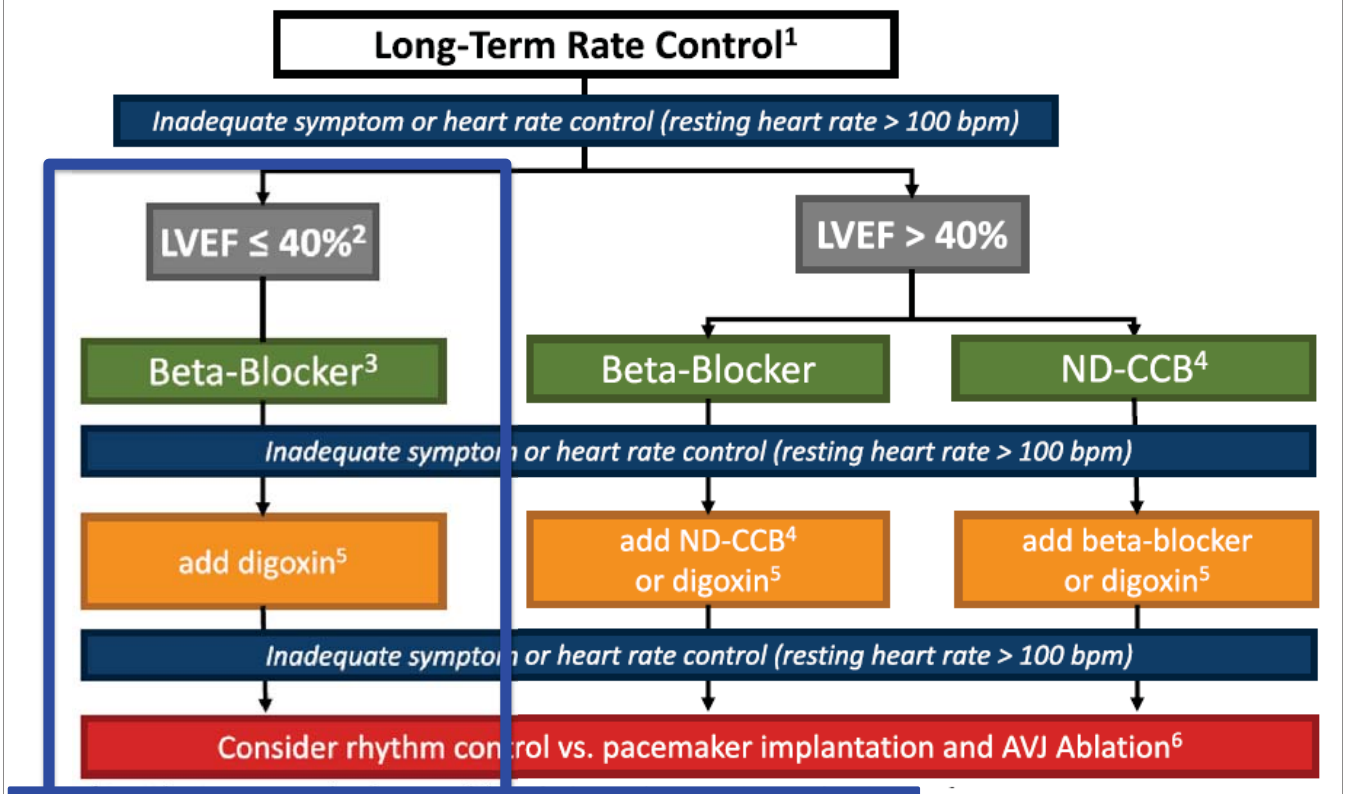
Andrade et al. Early AF. NEJM 2021; 384:305-315

Case 2: 78F

78F presents with palpitations
PMHx: hypertension x 2 years
Medications: Amlodipine 5mg po Qd and ASA 80mg Qd



1. Modifiable risk factors? Hypertension: 24 hour BP monitor
2. Rate vs Rhythm control?
3. Stroke prevention: Discontinue ASA and start DOAC



In patients with reduced LVEF, strongly consider ablation if risks of ablation are not elevated

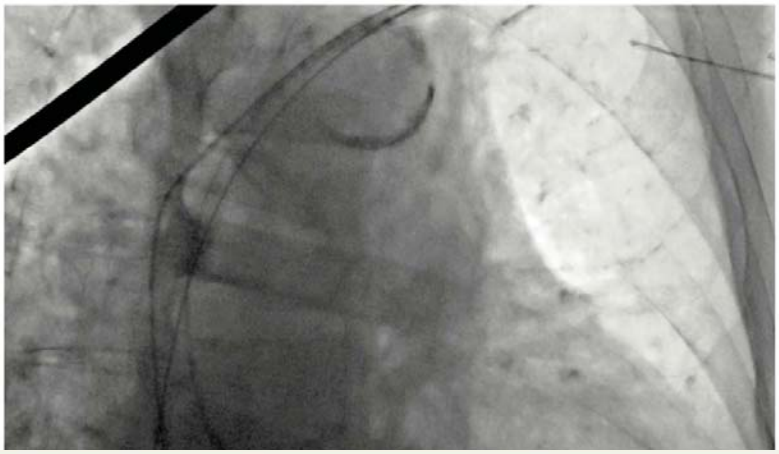
Case 2: 78F

LVEF 50% in AF, severely enlarged left atrium
Patient now on metoprolol 100mg po BID and Cardizem CD 240mg po Qd (Norvasc discontinued). ECG still demonstrates a heart rate in AF at 100bpm and patient continues to complain of palpitations. What is next step?

1. Can add digoxin. Consider drug monitoring in patients at higher risk of adverse events (female sex with low body weight and impaired renal function). Trough levels 0.6-0.9ng/mL = significant decrease in all-cause mortality and hospitalizations compared with levels ≥ 1.0ng/mL. Optimal level is unknown.

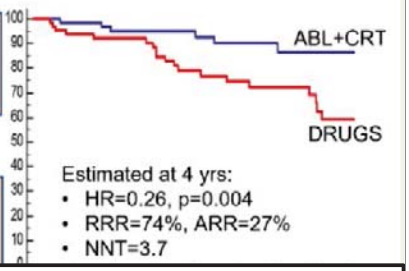
2. Pacemaker implantation and AV node ablation: "Pace and Ablate" Then discontinuation of rate-controlling medications

1. Pacemaker implant (single ventricular wire vs both RV and LV wires (CRT))
2. Ablation of the AV node



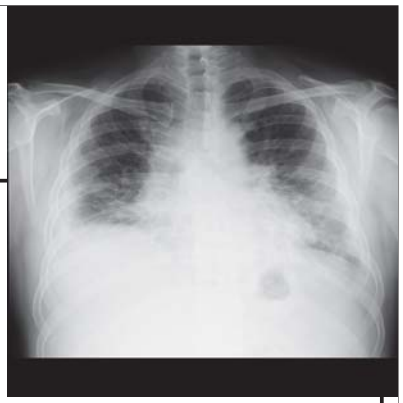
AV junction ablation and cardiac resynchronization for patients with permanent atrial fibrillation and narrow QRS: The APAF-CRT Mortality Trial. ***Brignole M et al.***

Trial population	Randomization	Optimization	Death from any cause (ITT analysis)
133 pts with: • Permanent AF • Narrow QRS • ≥1 HF hospitalization • Severe symptoms	**63** Rate control **ABL+CRT**	HR = **70** bpm	**11%** (7 pts)
	70 Rate control **DRUGS**	HR = **82** bpm	**29%** (20 pts)



Brignole et al. APAF-CRT: EHJ 2021. 42, 4731-)

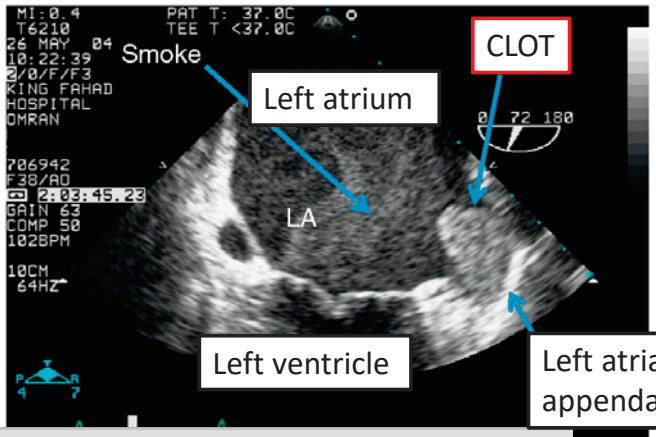
Case 3

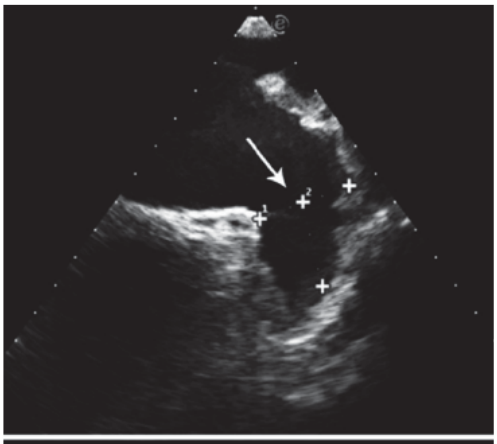


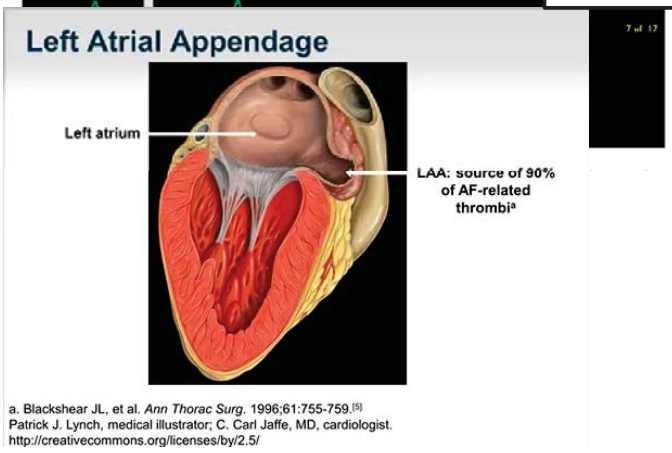
68F presents with dyspnea on exertion to ED x 2 months, but worse over last week.
ECG: rapid atrial fibrillation in the 160's with
BP 90/60mmHg
CXR demonstrates pulmonary edema
Echo reveals an LVEF of 20%.
Cath: normal coronary arteries

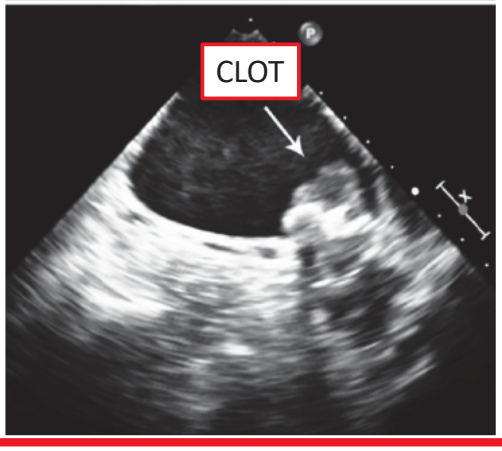
Presumed diagnosis: Tachy-mediated cardiomyopathy

Plan: Transesophageal echo to rule out left atrial appendage thrombus, then cardioversion and start amiodarone.



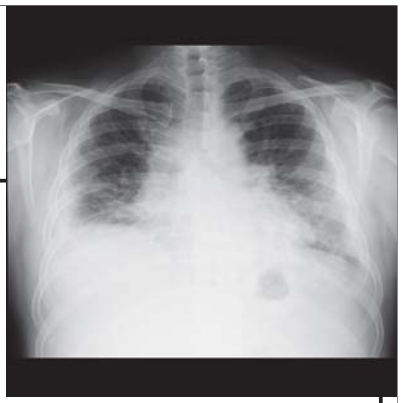






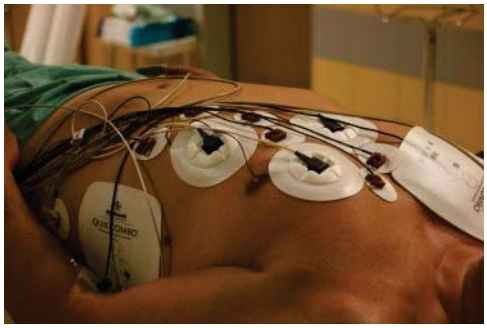
During atrial fibrillation blood clots can form within left atrial appendage; these can break off and cause stroke and systemic emboli

Case 3

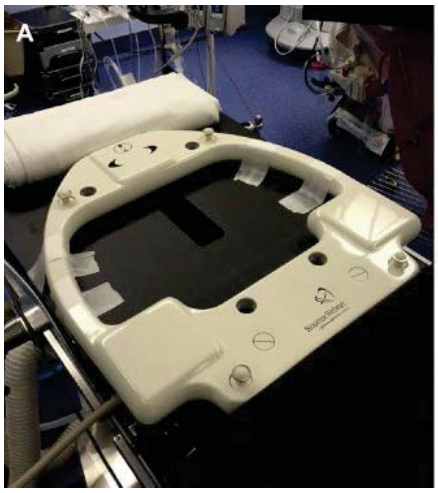


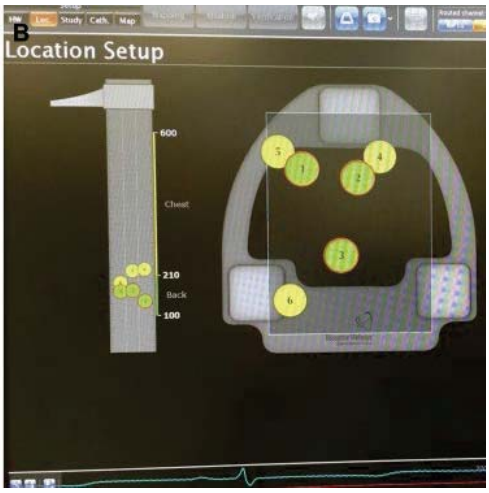
- Started on a DOAC
- Rate-control therapy attempted
- 6 weeks later, repeat TEE performed. No clot
- What next?

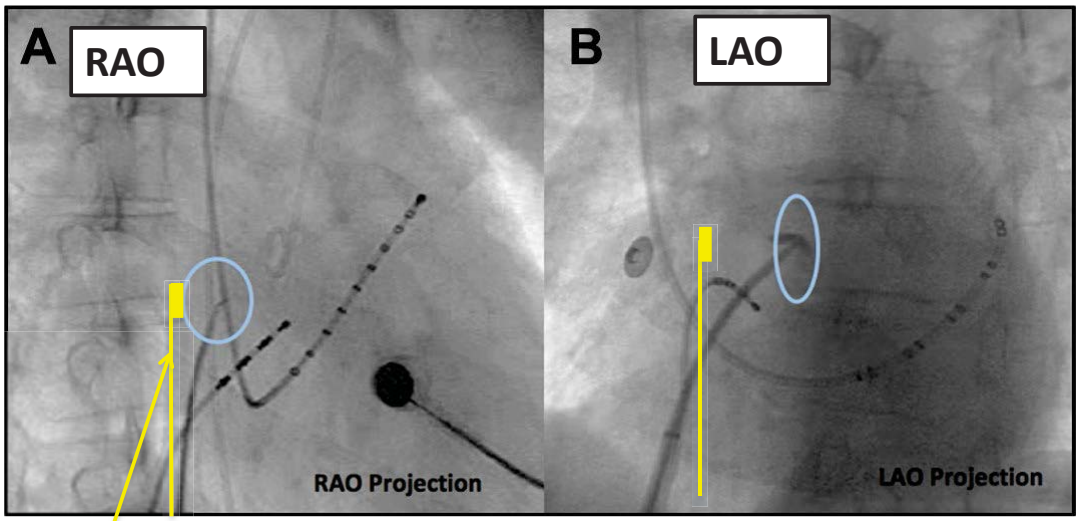
AF Ablation Procedure

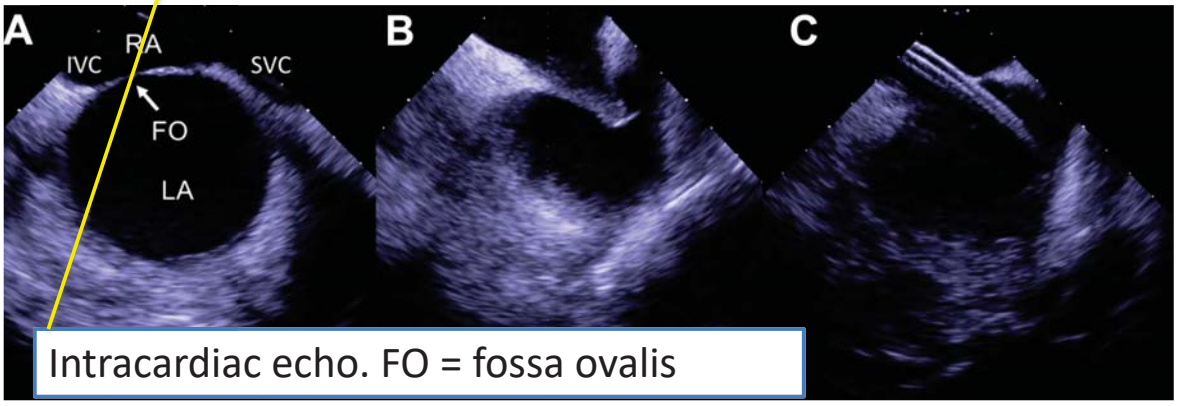


The mapping and ablation catheters have magnetic sensors that link to patches on the patient's front and back with a reference under the table/at torso level.



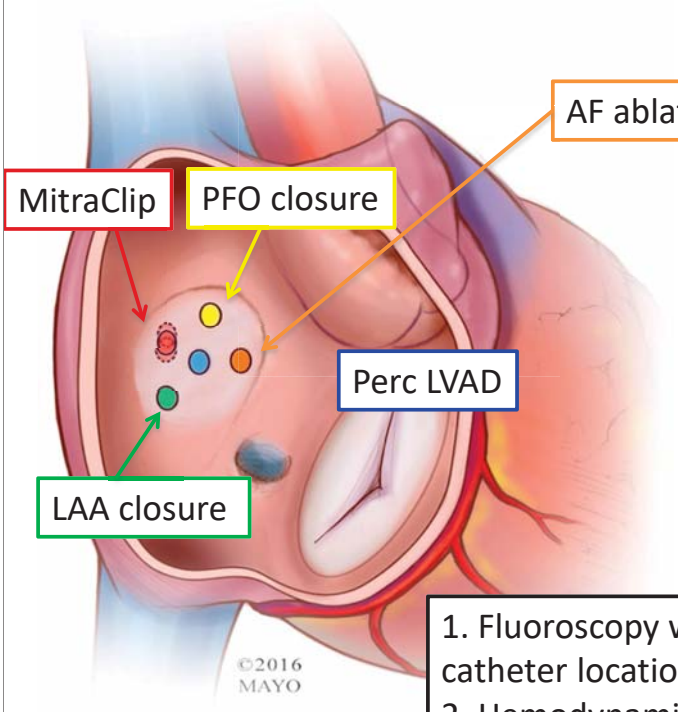


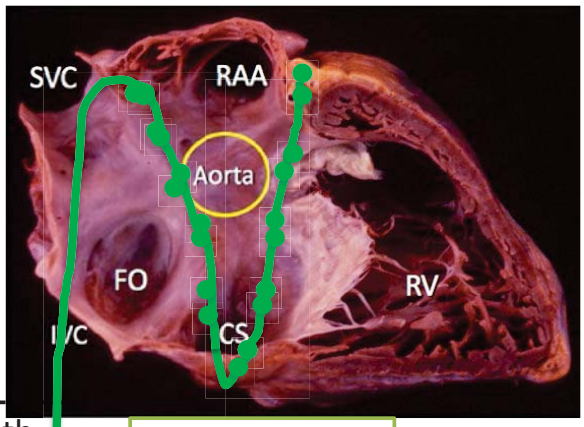




Alkhouli et al. JACC Cardiovascular Interventions. Volume 9, 24 (2016), 2465-2480

Site-Specific Transseptal Puncture for Various Intracardiac Interventions



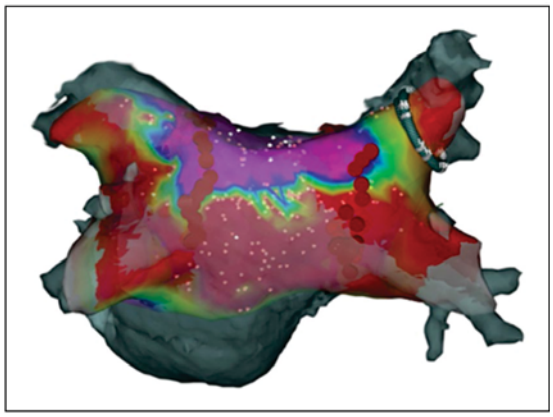


1. Fluoroscopy with catheter location
2. Hemodynamics
3. TEE
4. Intracardiac echo (ICE)

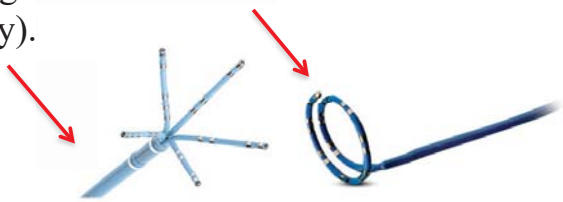
Coronary sinus catheter

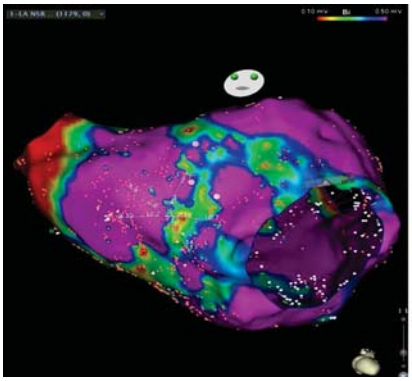
Alkhouli et al. JACC Volume 9, 24 (2016), 2465-2480

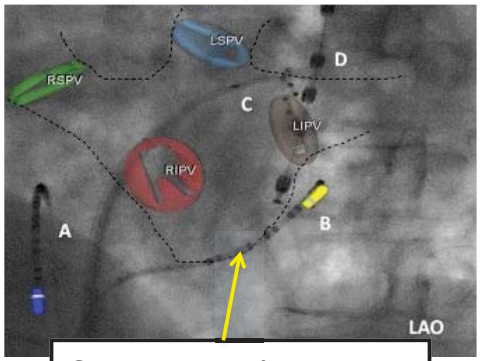
AF Ablation Procedure: Mapping



A left atrial electroanatomic map is created using a multielectrode mapping catheter (lasso or pentaray).

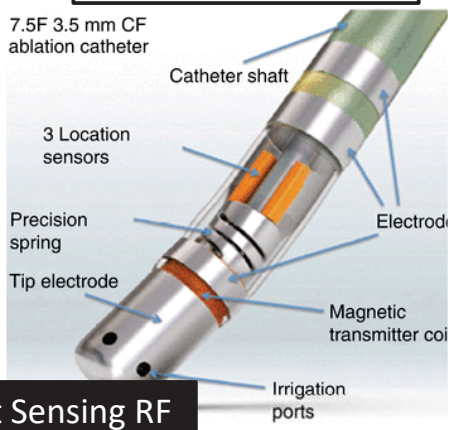




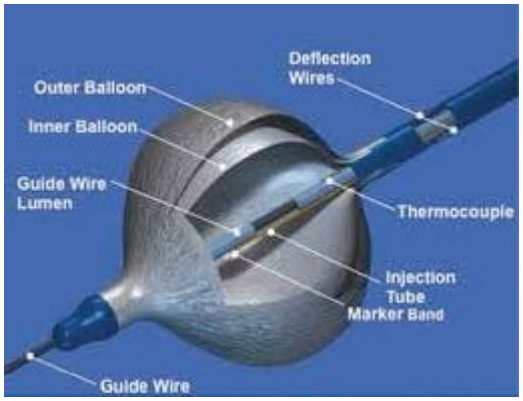


Coronary sinus catheter

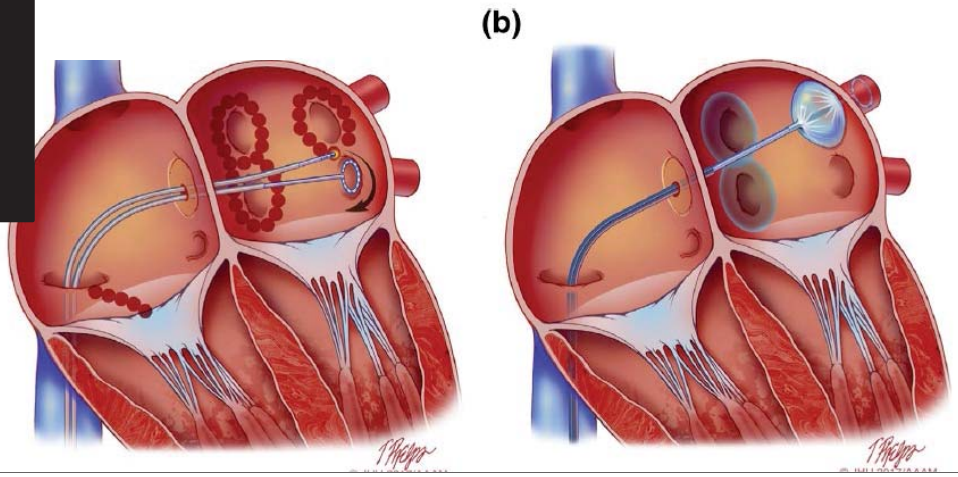
Radiofrequency



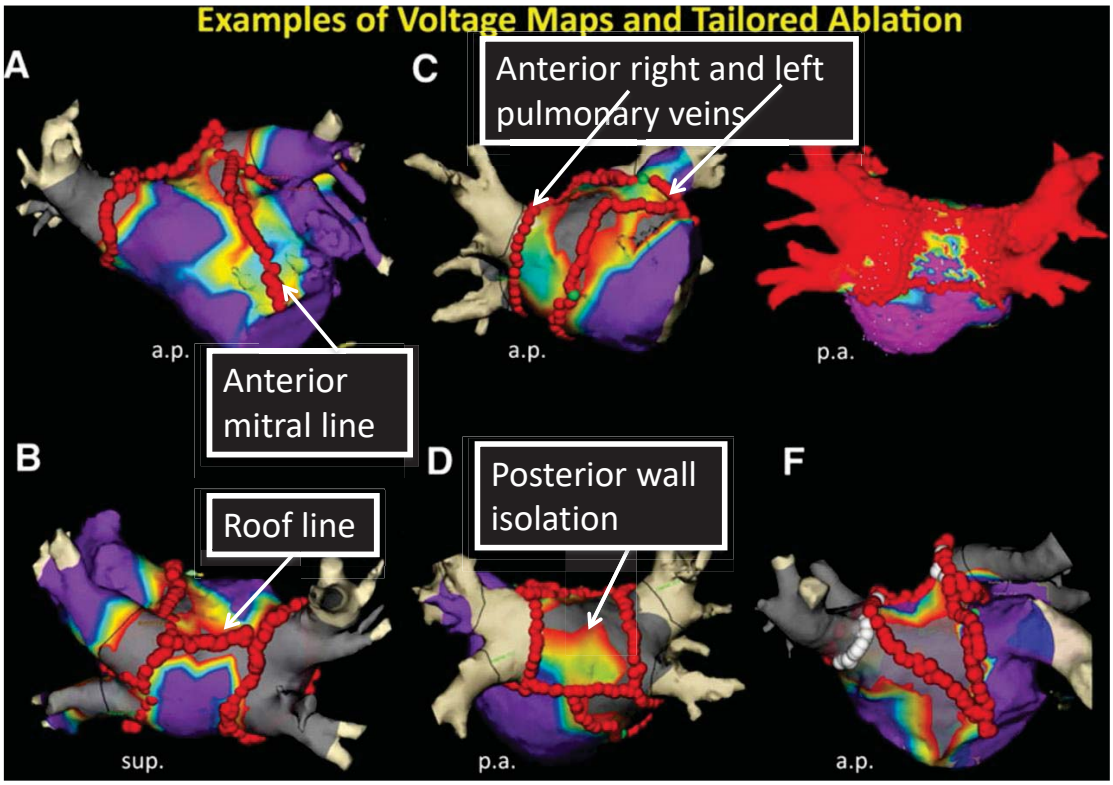
Cryoablation



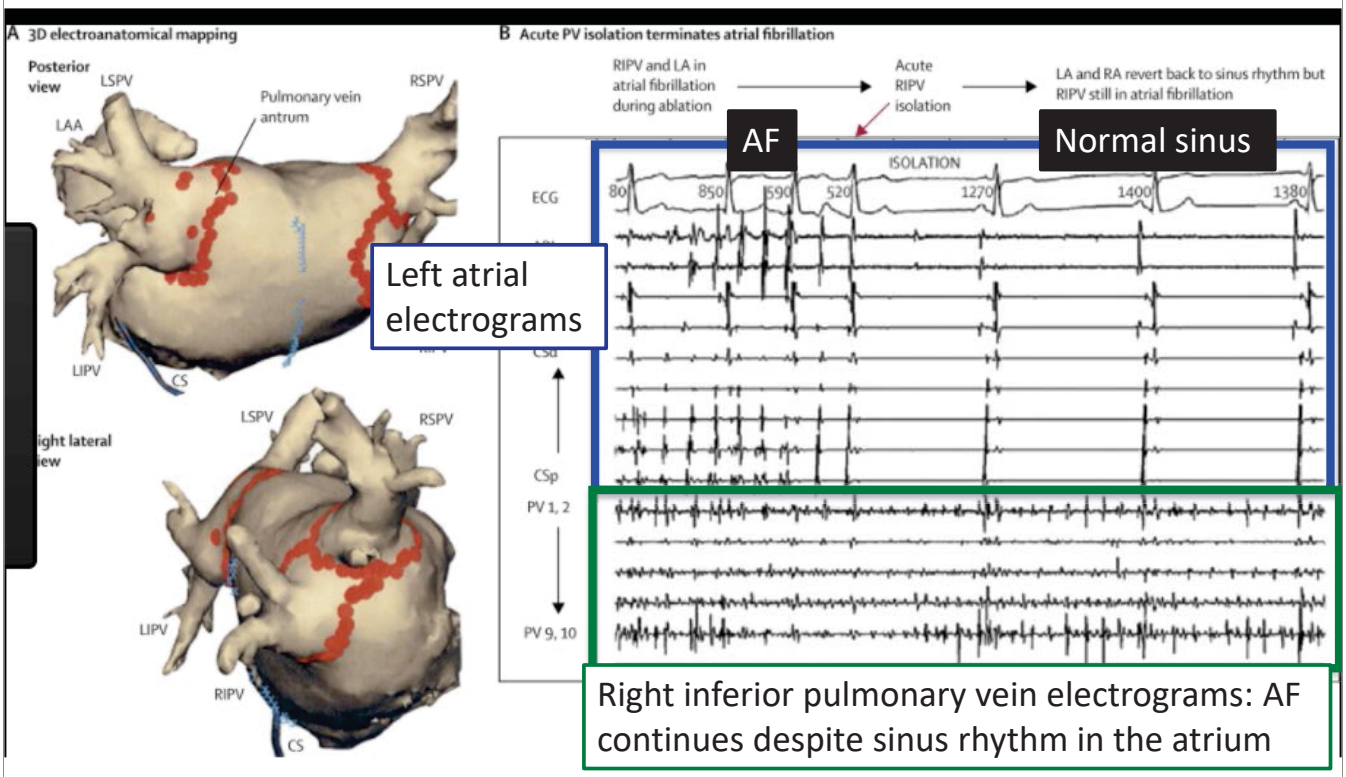
Contact Sensing RF catheters since 2014 = more efficacious lesions and safer procedure



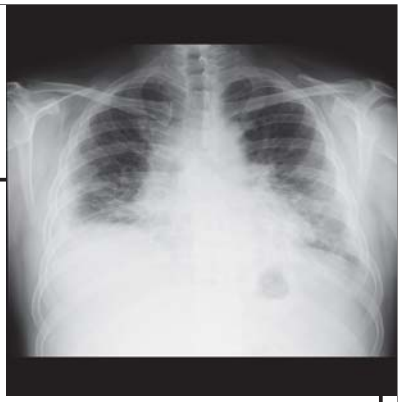
Radiofrequency Lesion Sets



Different lesion sets are created depending on location of scar, persistent vs paroxysmal AF, recurrent atrial tachycardias/flutters (red=scar, purple=healthy)



Case 3



Post-ablation echo performed at 3 months

LVEF normalized.

Plan: lifelong DOAC and beta blocker

Conclusion

The 3 Pillars of Atrial Fibrillation Management:

- Risk Factor Modification
- AF Management: rate vs rhythm control
- Stroke prevention

McGill University
Health Centre