Atrial Fibrillation in the Office

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McGill University
Health Centre

No disclosures

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Objectives

1. Identify the sick patient: who to send to the ED vs who can wait for outpatient referral

2. Learn how to and in who to initiate rate and rhythm controlling medication

3. Identify patients who might benefit from further intervention

4. Understand the different oral anticoagulants available for your patients

McGill University Health Centre

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.

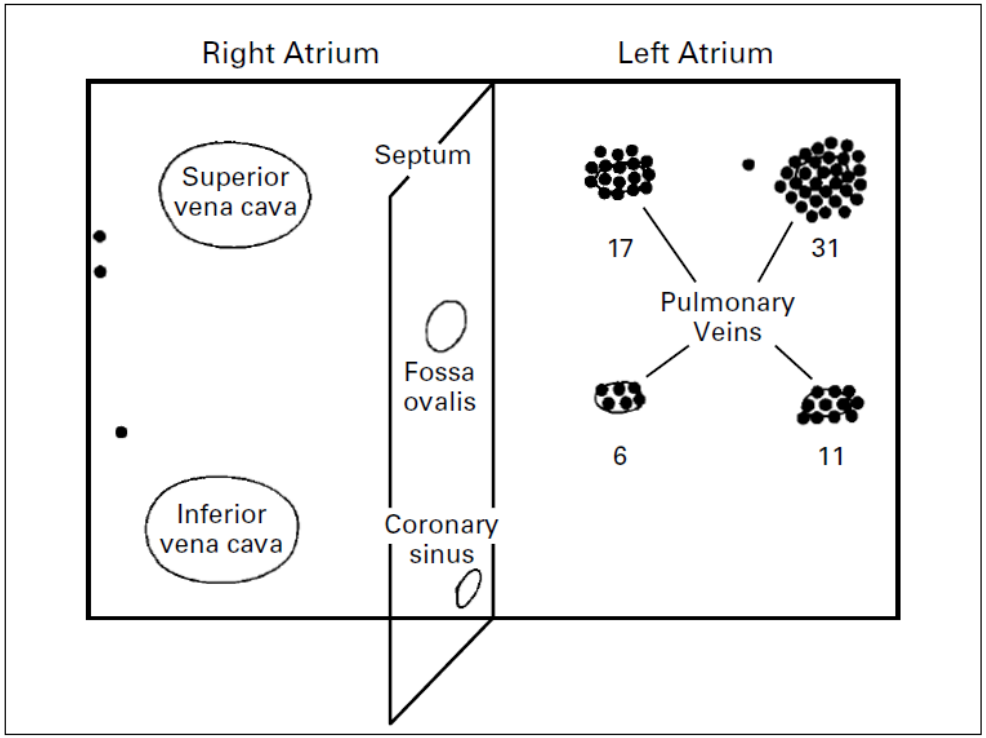


Figure 1. Diagram of the Sites of 69 Foci Triggering Atrial Fibrillation in 45 Patients.
Note the clustering in the pulmonary veins, particularly in both superior pulmonary veins. Numbers indicate the distribution of foci in the pulmonary veins.

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

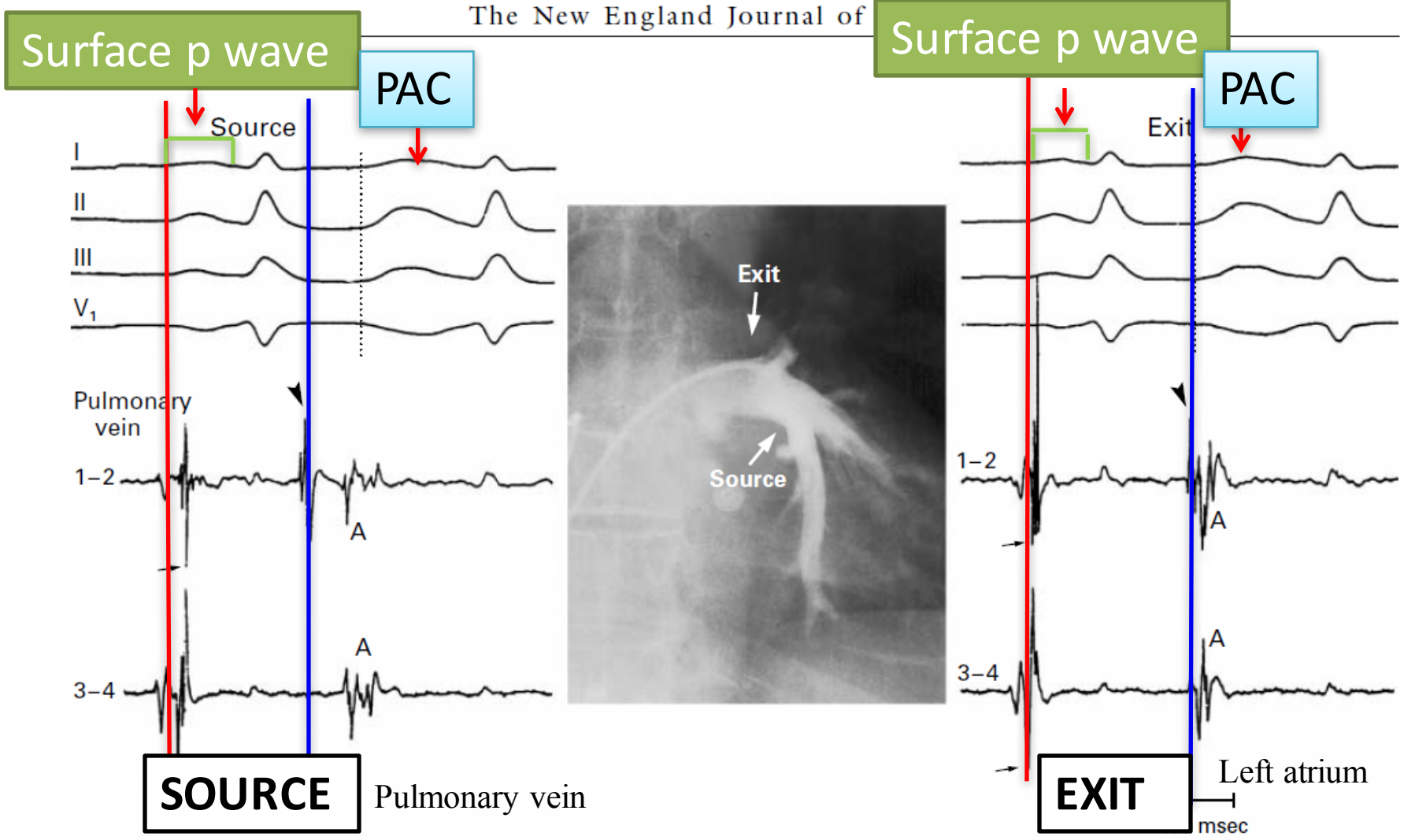


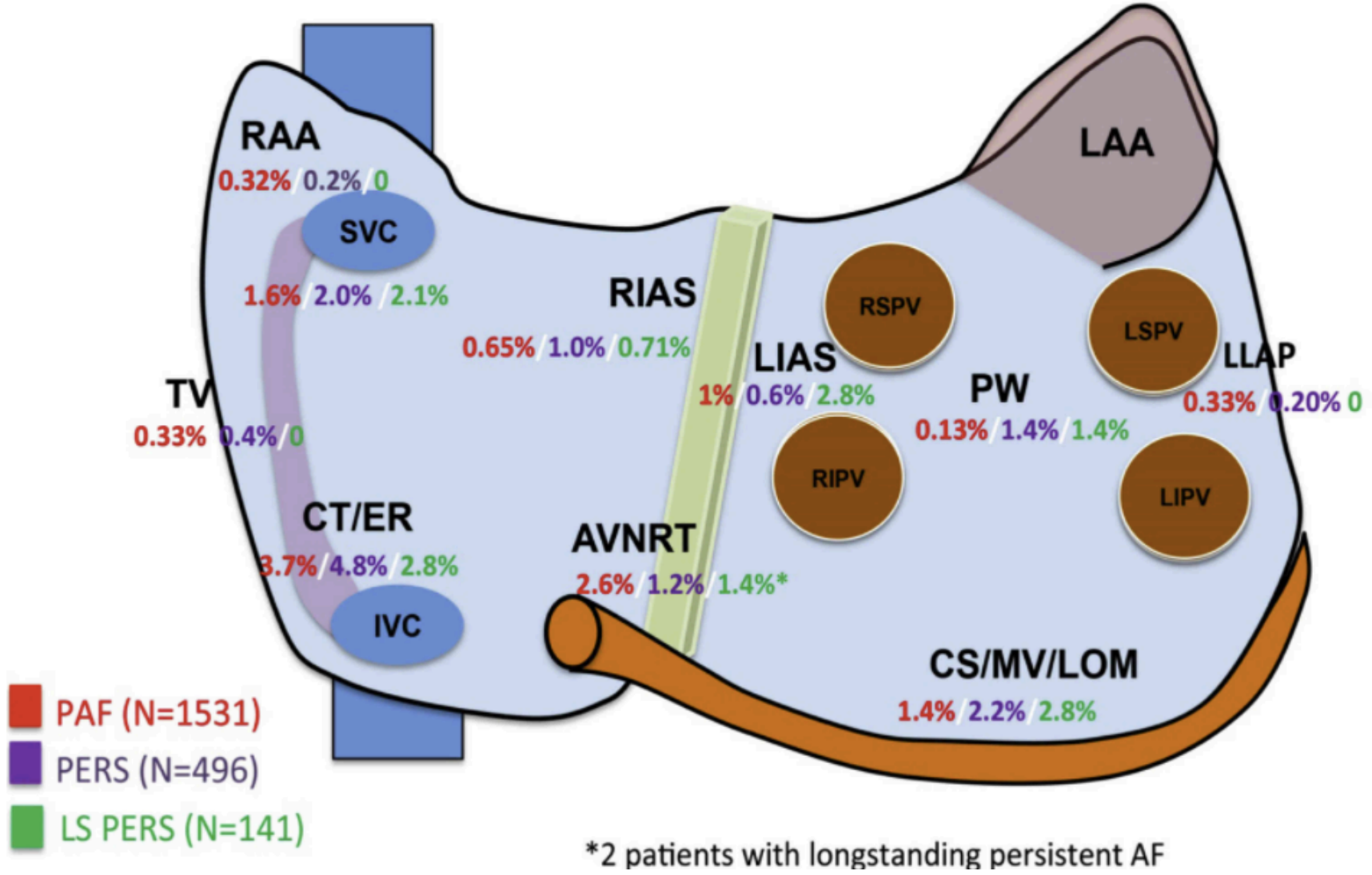
Figure 2. Angiogram of a Left Inferior Pulmonary Vein Depicting the Source and Exit of Ectopic Activity.

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.

RAA=right atrial appendage
TV=tricuspid valve
CT=crista terminalis
ER=eustacian ridge
SVC=superior vena cava
AVNRT=AV node reentrant tachycardia

Other AF triggers outside the pulmonary veins

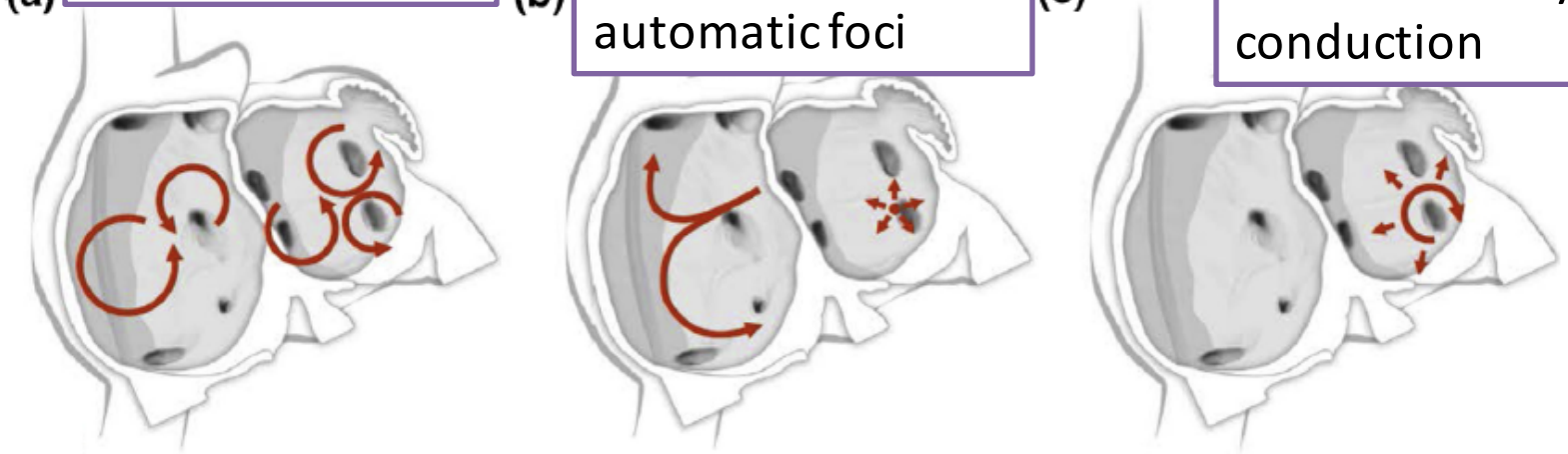
LAA=left atrial appendage
MV=mitral valve
CS=coronary sinus
LOM=ligament of Marshall
LLAP=left lateral accessory pathway
PW=posterior wall

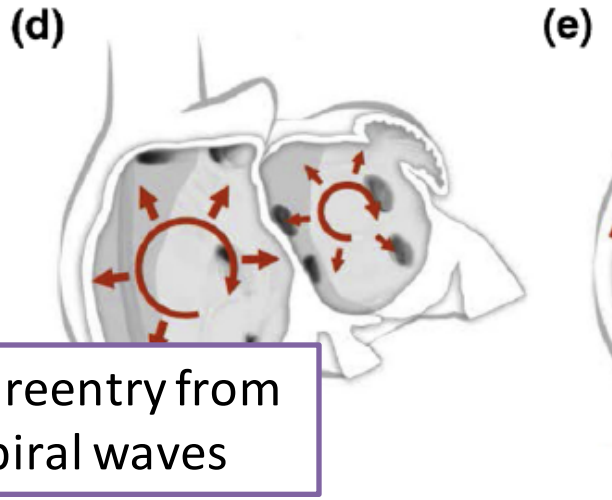


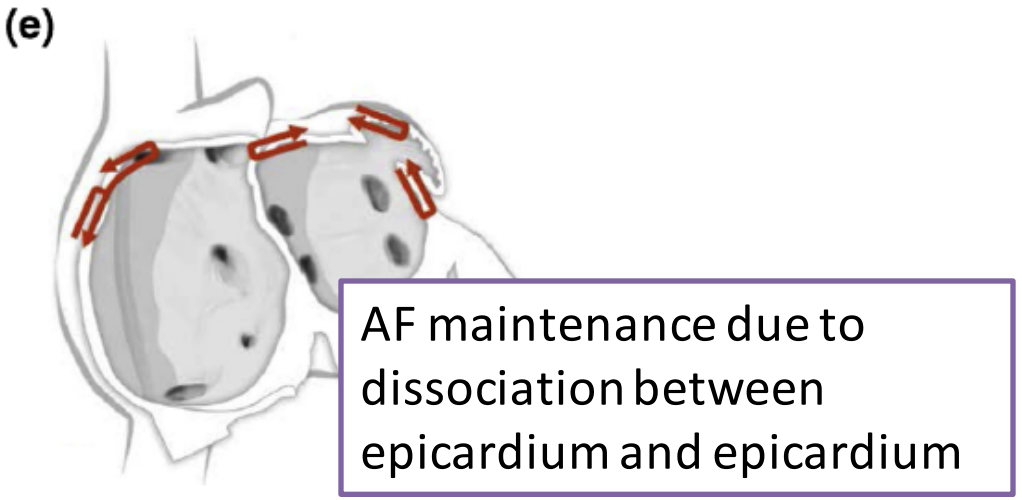
*2 patients with longstanding persistent AF

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

Hypotheses regarding mechanisms of atrial fibrillation

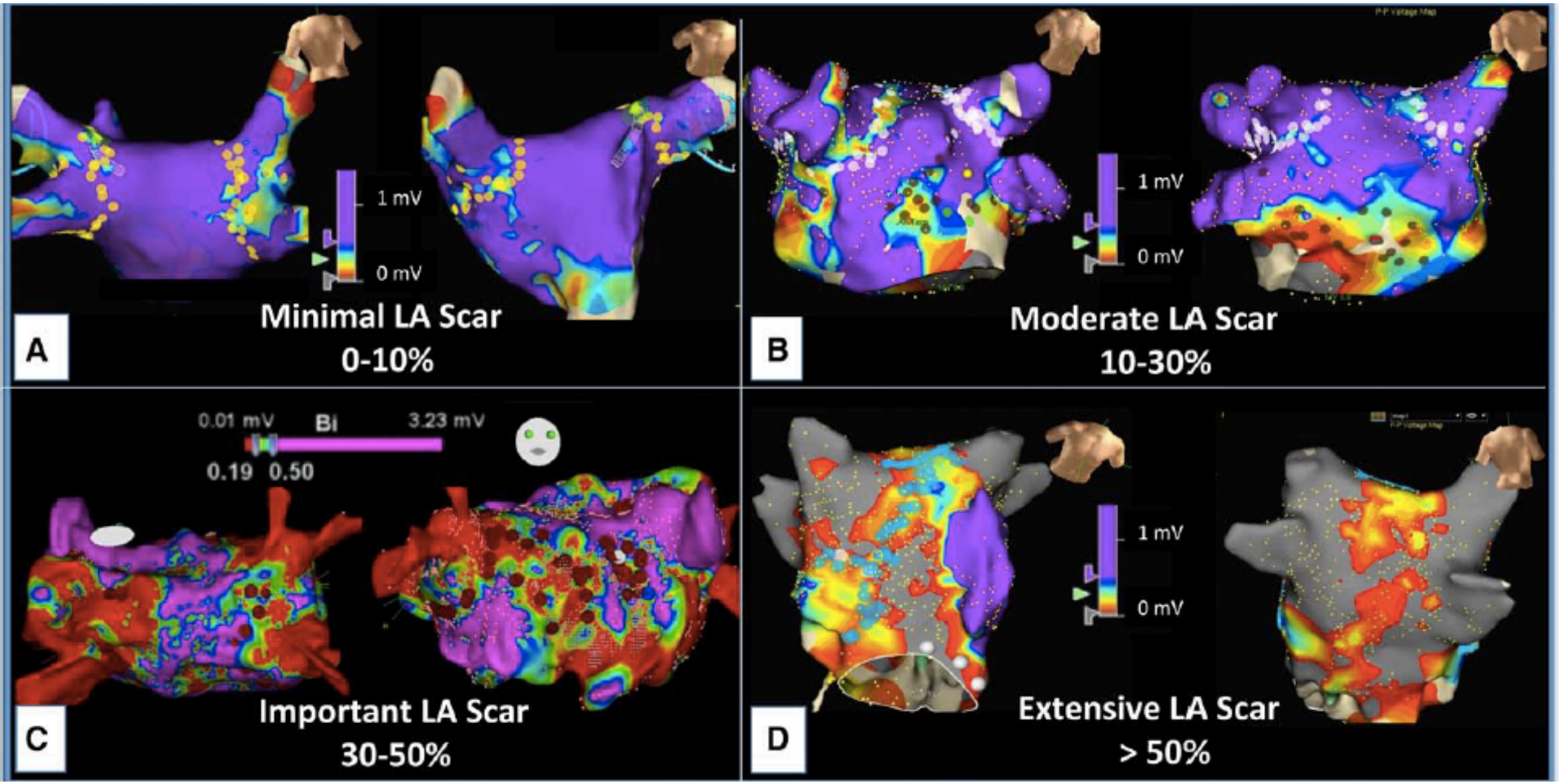






2017 HRS expert consensus statement on catheter and surgical ablation of atrial fibrillation. J Interv Card Electrophysiol (2017) 50:1-55

Atrial Fibrosis: AF is a progressive disease

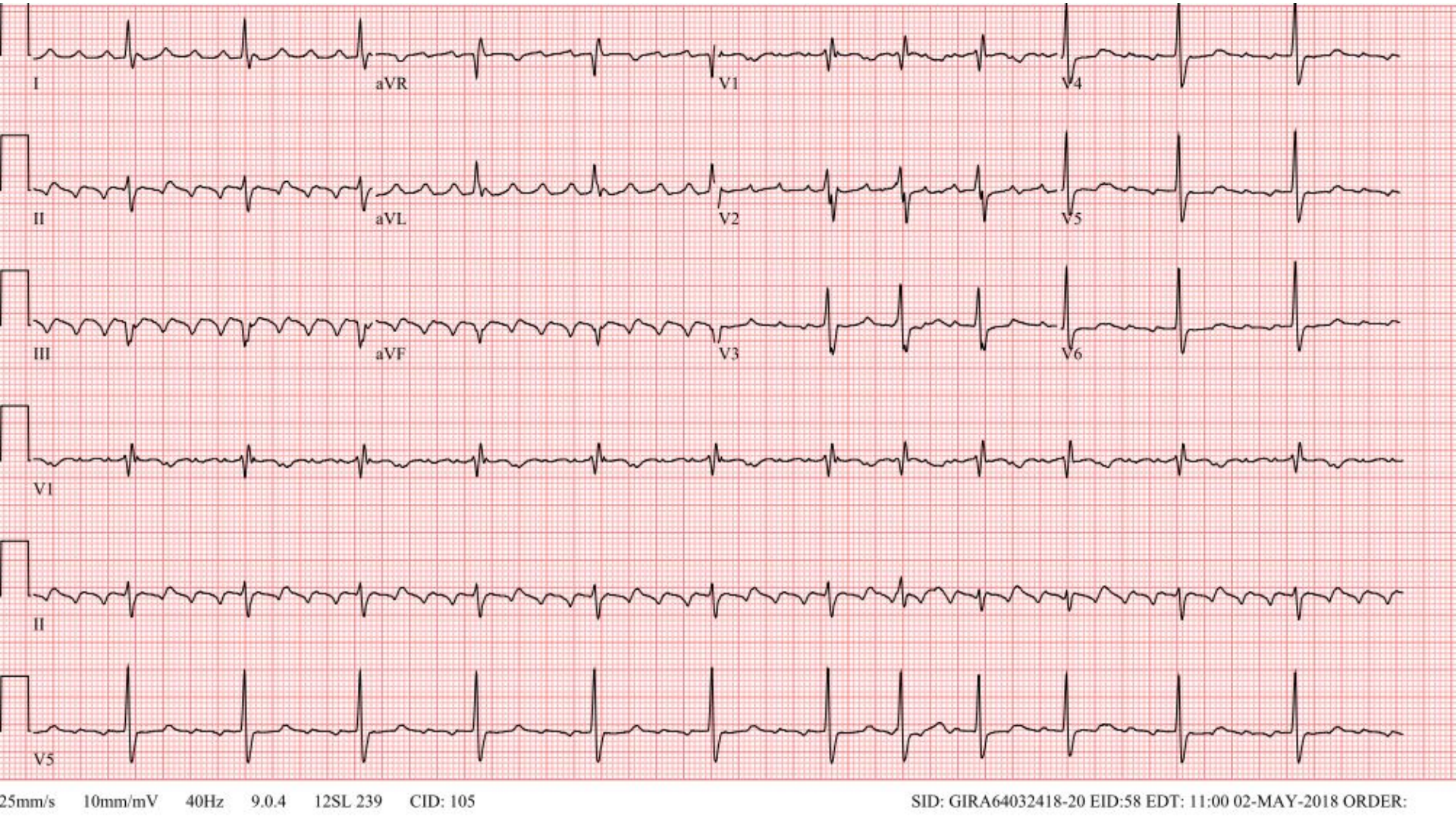


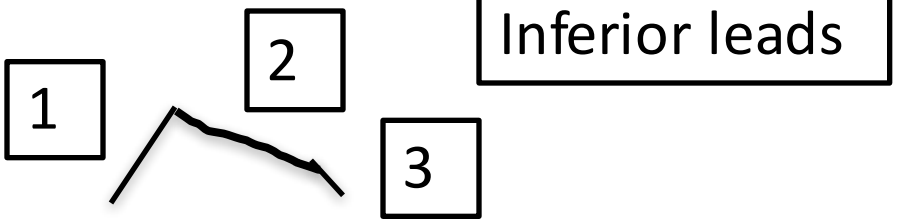
-Electroanatomic mapping allows direct contact with endocardial tissue and can reveal presence of scar (low voltage areas), not detectable by any imaging method

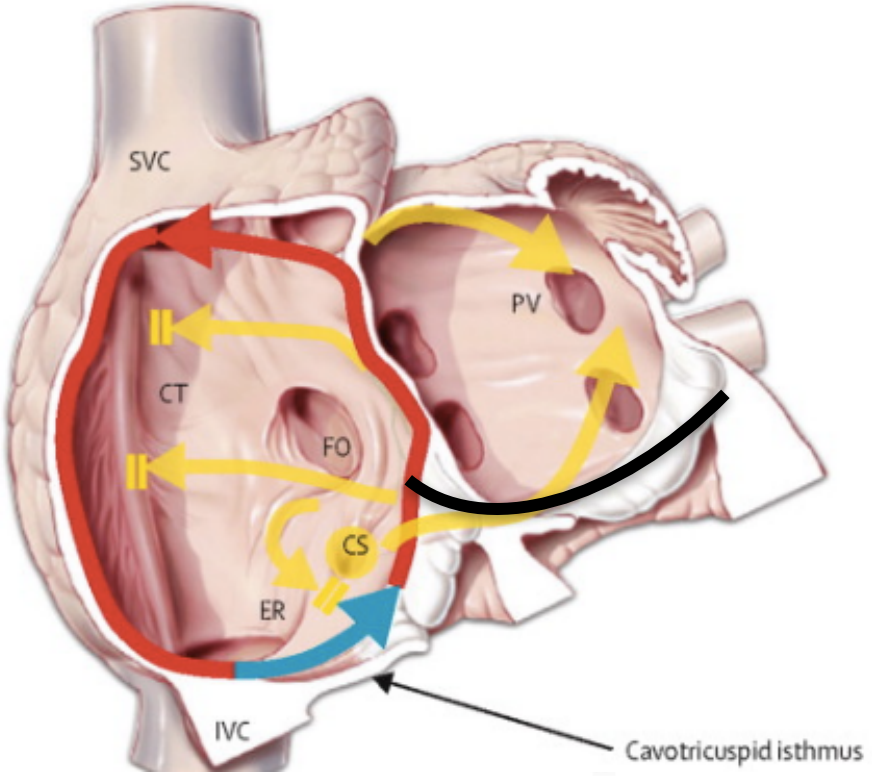
-In contrast to paroxysmal AF, an important proportion of patients with persistent AF have regional increase in atrial fibrosis that is associated with greater frequency of AF

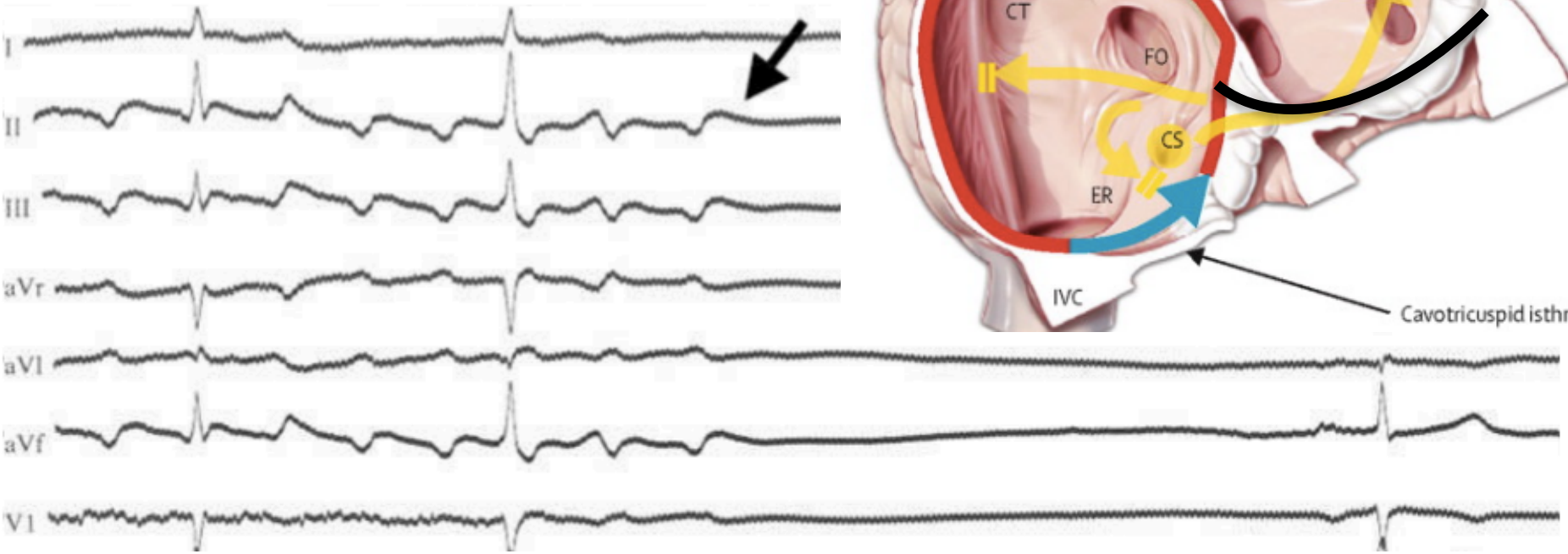
Arentz, Circulation Arrhythmia and Electrophysiology. 2016.

Right-sided CTI Atrial flutter is not Atrial Fibrillation, but still needs anticoagulation



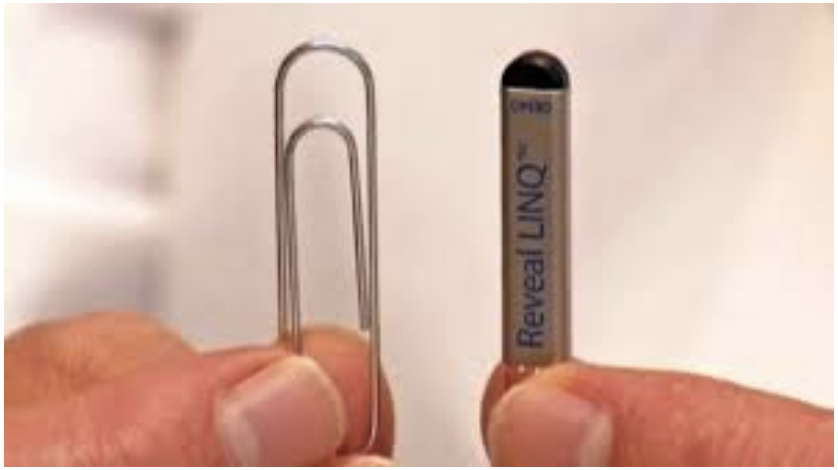


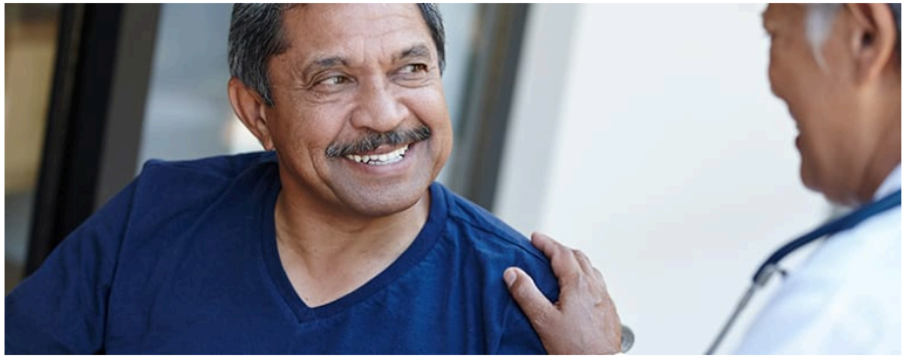




-During cavo-tricuspid isthmus ablation, the tachycardia terminates during the initial gradual downslope of the p wave indicating that this is the isthmus

Patient Populations: Who is at Risk for AF?





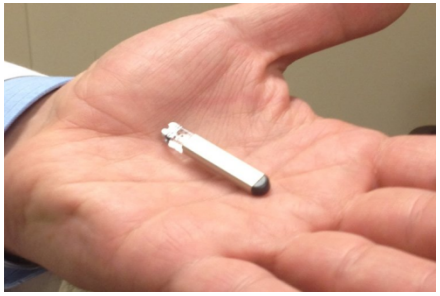
REVEAL LINQ INSERTABLE CARDIAC MONITOR

Fainting (Unexplained)

What is an event monitor?

Patient Populations: Who is at Risk for AF?

REVEAL-AF study: 385 patients with no history of AF (CHADS2 score of ≥ 3 or 2 with 1 extra risk factor) underwent LINQ monitor implant



29% detection rate of AF lasting ≥ 6 min. AF would have gone undetected in most pts had monitoring been limited to 30 days. AF incidence was higher in older and more obese patients

Table 2. Predictive Value of Baseline Characteristics for Atrial Fibrillation Onset

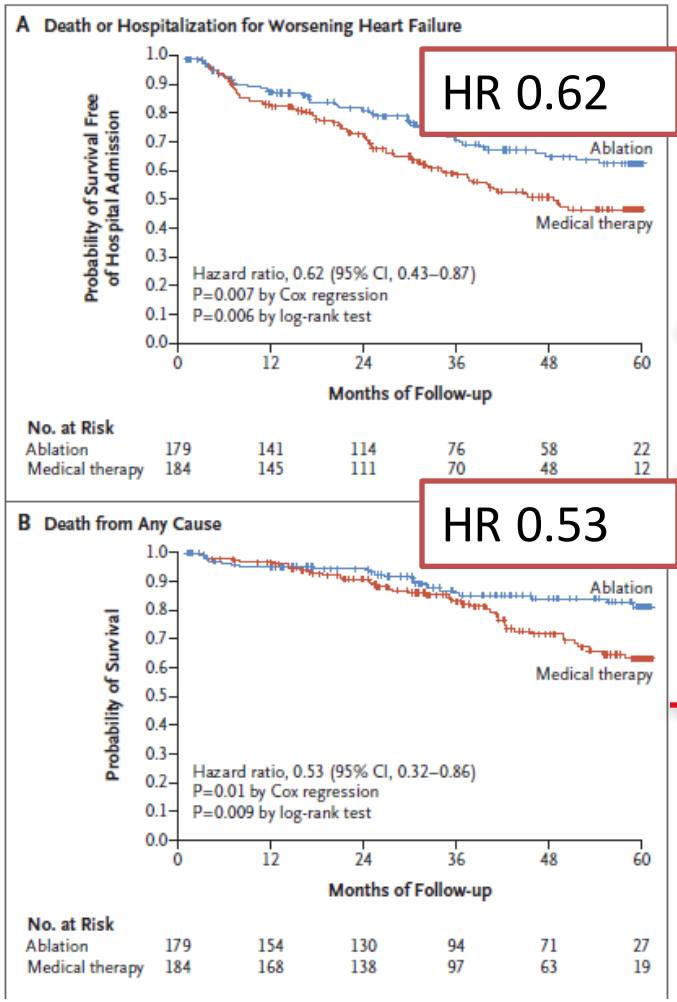
Characteristic	Hazard Ratio (95% CI)[a]	*P* Value
Age, y	1.08 (1.05-1.11)	<.001
Body mass index	1.04 (1.01-1.08)	.02
Male sex	1.11 (0.77-1.61)	.56
Diabetes	1.09 (0.74-1.59)	.66
Heart failure	1.08 (0.69-1.69)	.73
Hypertension	1.23 (0.58-2.60)	.58
Renal impairment	0.92 (0.64-1.32)	.65
Chronic obstructive pulmonary disease	0.73 (0.45-1.20)	.22
Stroke	0.86 (0.54-1.38)	.53
Coronary artery disease	0.78 (0.53-1.15)	.21
Sleep apnea	0.72 (0.45-1.17)	.19
Family history of atrial fibrillation	1.97 (0.76-5.14)	.16
Vascular disease	0.89 (0.56-1.43)	.63

[a] Obtained from the Cox proportional hazards model.

Reiffel et al. *JAMA Cardiol*. 2017;2(10):1120-1127

Special Patient Populations Undergoing AF Ablation

CASTLE-AF: 398 heart failure pts with ICDs were enrolled
Randomized to medical therapy vs ablation



HR 0.62

HR 0.53

Table 1. Characteristics of the Patients at Baseline.*

Characteristic	Treatment Type	
	Ablation (N=179)	Medical Therapy (N=184)
Age — yr		
Median	64	64
Range	56–71	56–73.5
Male sex — no. (%)	156 (87)	155 (84)
Body-mass index†		
Median	29.0	29.1
Range	25.9–32.2	25.9–32.3
New York Heart Association class — no./total no. (%)		
I	20/174 (11)	19/179 (11)
II	101/174 (58)	109/179 (61)
III	50/174 (29)	49/179 (27)
IV	3/174 (2)	2/179 (1)
Cause of heart failure — no. (%)‡		
Ischemic	72 (40)	96 (52)
Nonischemic	107 (60)	88 (48)
Type of atrial fibrillation — no. (%)		
Paroxysmal	54 (30)	64 (35)
Persistent	125 (70)	120 (65)
Long-standing persistent (duration >1 year)	51 (28)	55 (30)
Left atrial diameter		
Total no. of patients evaluated	162	172
Median — mm	48.0	49.5
Interquartile range — mm	45.0–54.0	5.0–55.0
Left ventricular ejection fraction		
Total no. of patients evaluated	164	172
Median — %	32.5	31.5
Interquartile range — %	25.0–38.0	27.0–37.0
CRT-D implanted — no. (%)§	48 (27)	52 (28)
ICD implanted — no. (%)§	131 (73)	132 (72)

Significant reduction in composite outcome of death and hospitalization for heart failure and in all-cause mortality alone

Treatment of AF

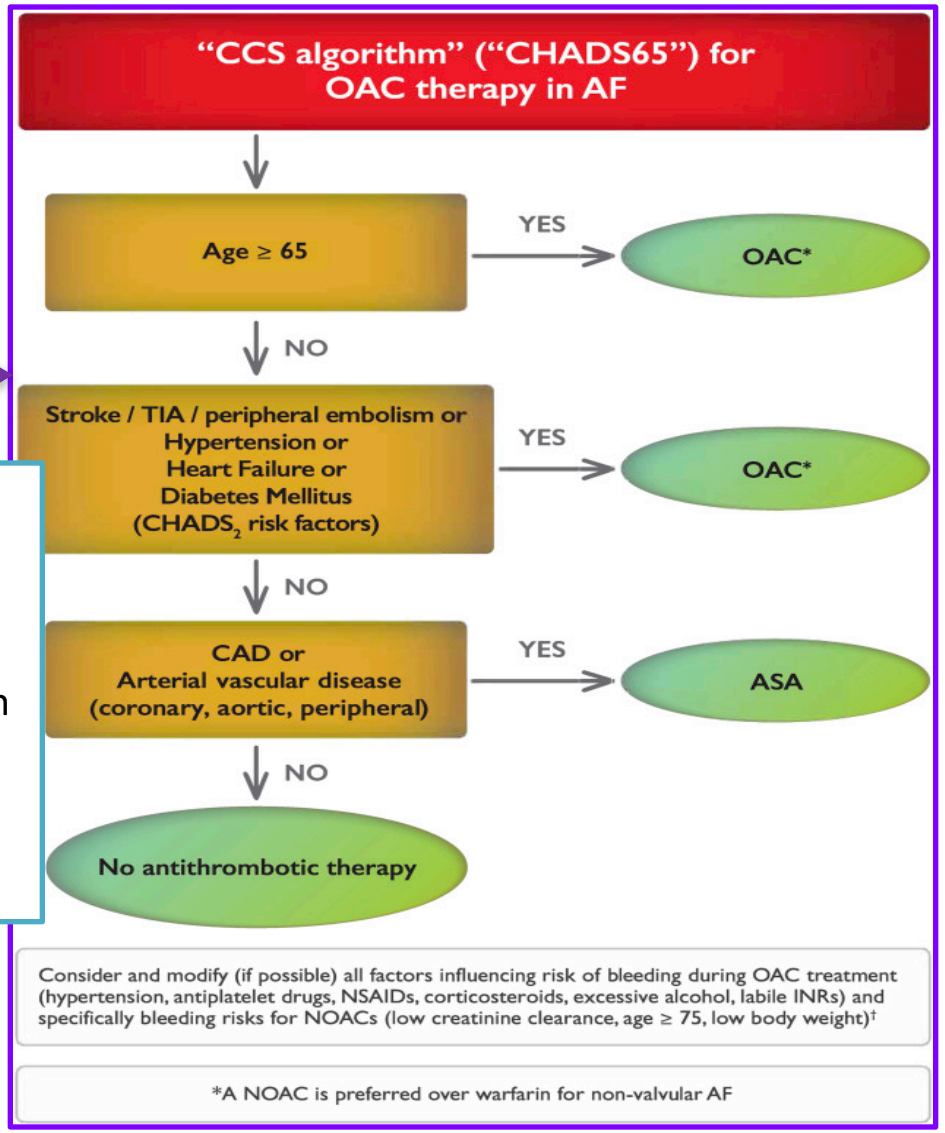
1. Risk Factor modification
2. Heart rate control : goal
resting HR < 110bpm
3. Rhythm Control
4. Anticoagulation

-Flecainide/propafenone: class Ic (Na channel blockers)
-Sotalol: class III (K+ ch blocker + BB)
-Amiodarone: class III – reserved for pts with significant HF/systolic dysf'n EF <35%
-Dronedarone: class III
-Dofetilide: class III (blocks Ikr)

II b

Ablation

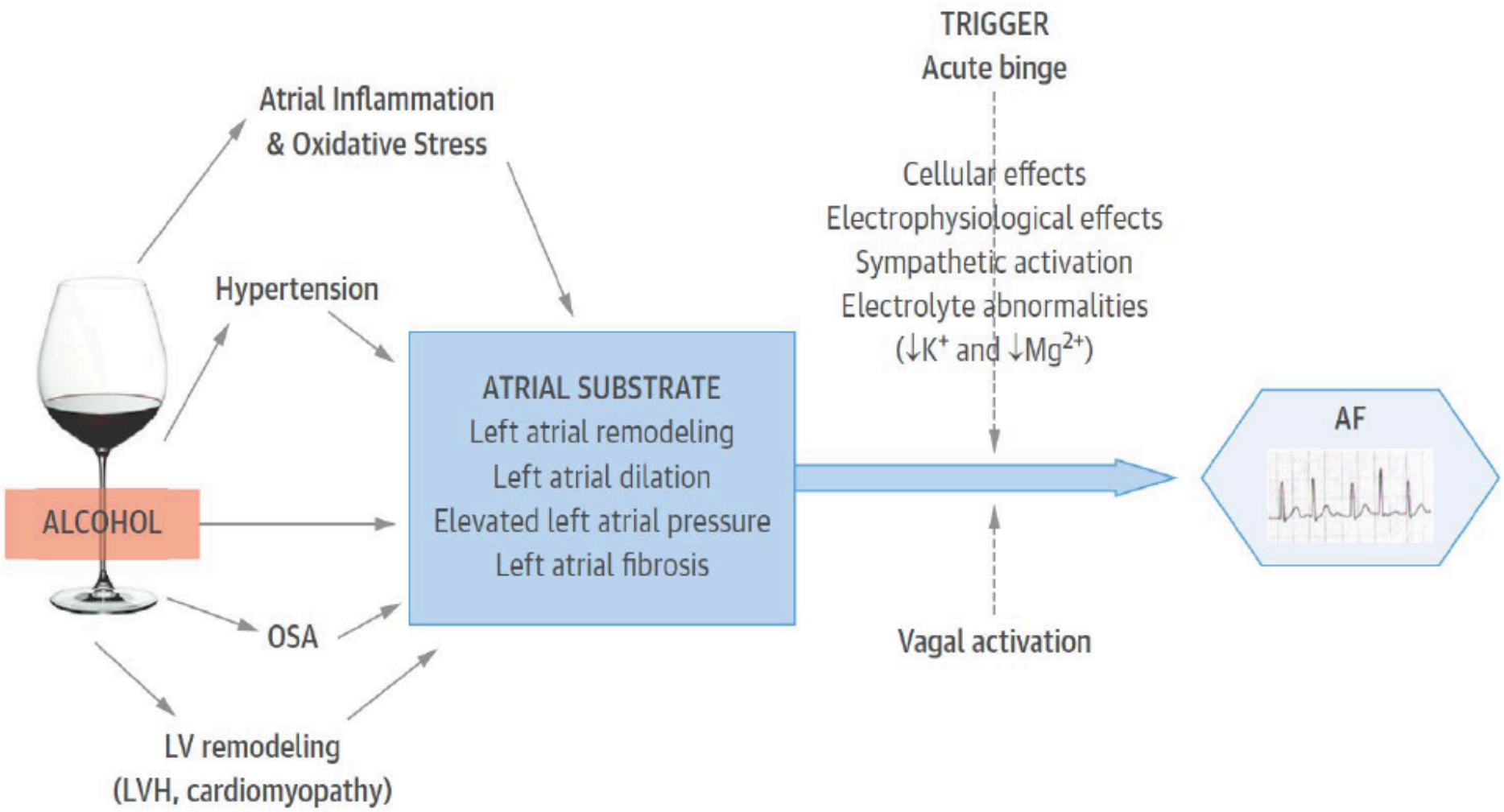
I (PAF) IIa (persistent) IIb (longstanding



2016 Focused Update of the Canadi nes for the Management of Atrial Fibrillation. CJC 32 (2016) 1170-1185

Modifiable Risk Factors

Weight
Alcohol intake
OSA
(the classics: DLP, htn, CAD)



Voskoboinik et al. JACC 2016;68:2567

Alcohol-AF Trial

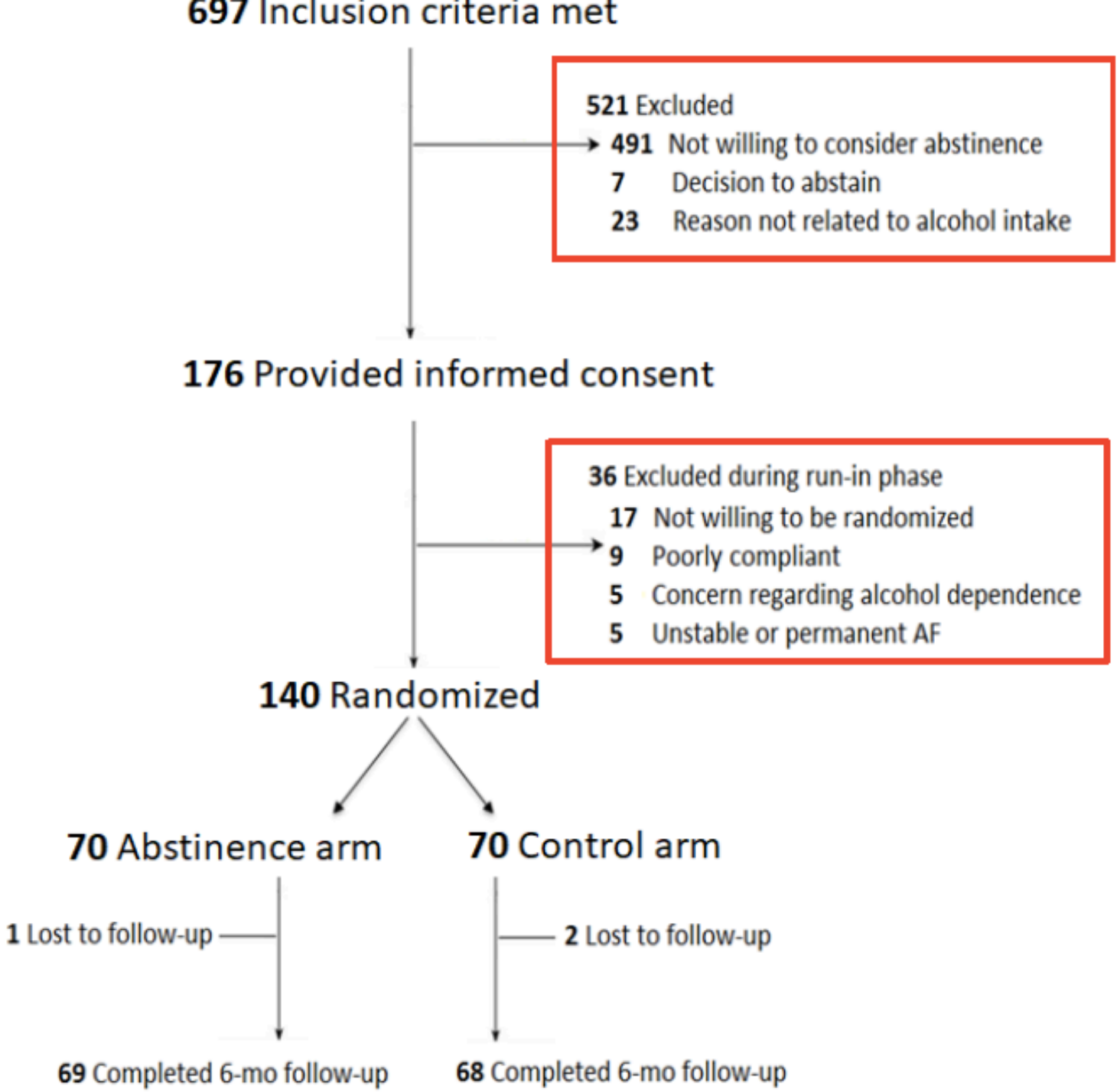
Inclusion: patients with paroxysmal AF (minimum 2 episodes in last 6 months), or persistent AF requiring cardioversion

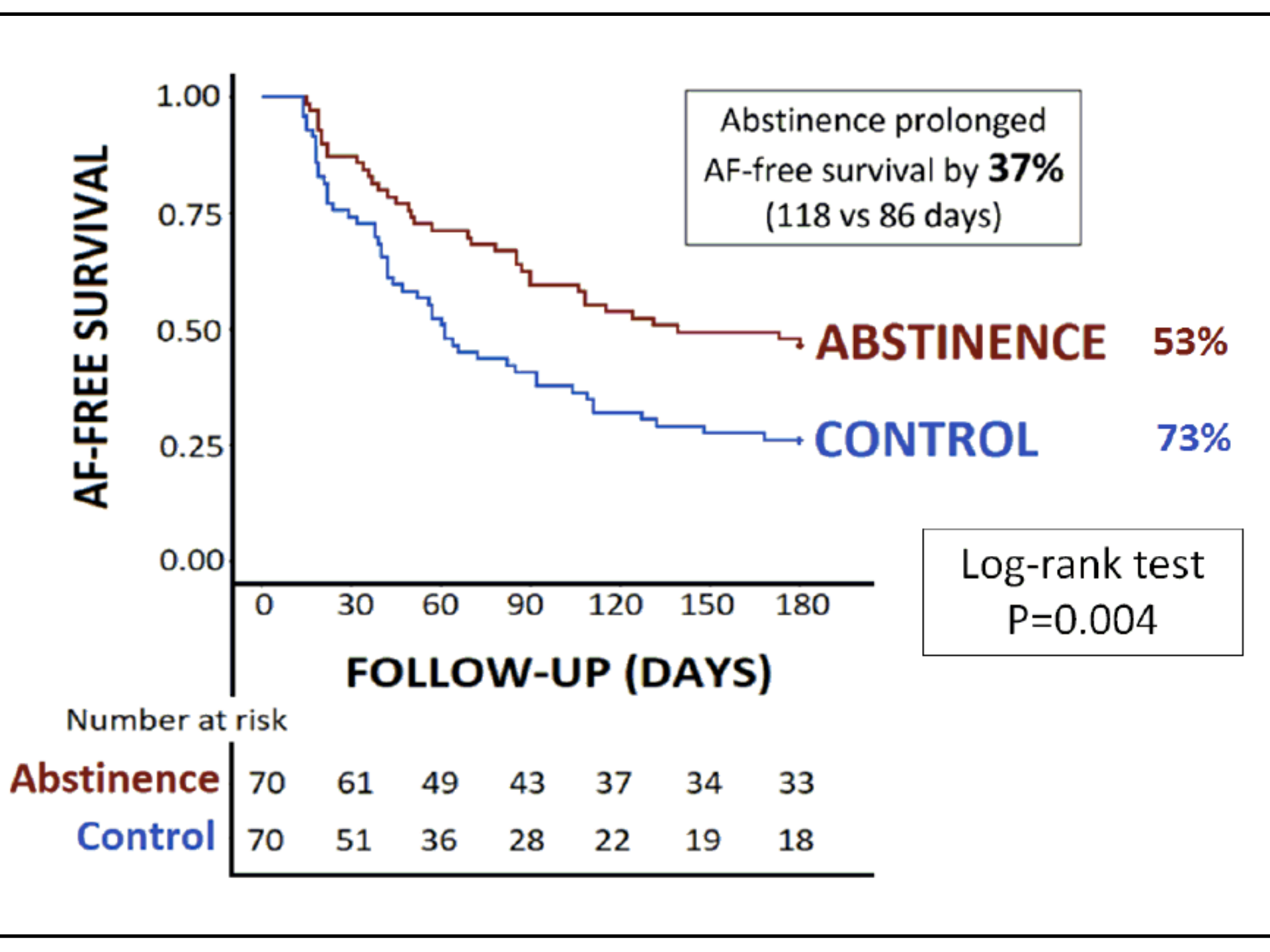
Average alcohol intake >=10 standard drinks per week
Exclusions: permanent AF, LVEF < 35%, alcohol dependence or psychiatric comorbidity, liver cirrhosis

Multicenter, prospective, open-label randomized controlled trial at 6 Australian hospital
Randomized 1:1 to undertake abstinence or continue consumption
Monitoring: Implantable loop monitor or existing pacemaker or twice daily Alive Cor mobile phone app in conjunction with holter monitoring

Follow-up 6 months

Abstinence arm: counsellors, urine testing, positive reinforcement by study investigators.


697 Inclusion criteria met
521 Excluded
491 Not willing to consider abstinence
7 Decision to abstain
23 Reason not related to alcohol intake
176 Provided informed consent
36 Excluded during run-in phase
17 Not willing to be randomized
9 Poorly compliant
5 Concern regarding alcohol dependence
5 Unstable or permanent AF
140 Randomized
70 Abstinence arm
70 Control arm
1 Lost to follow-up
2 Lost to follow-up
69 Completed 6-mo follow-up
68 Completed 6-mo follow-up

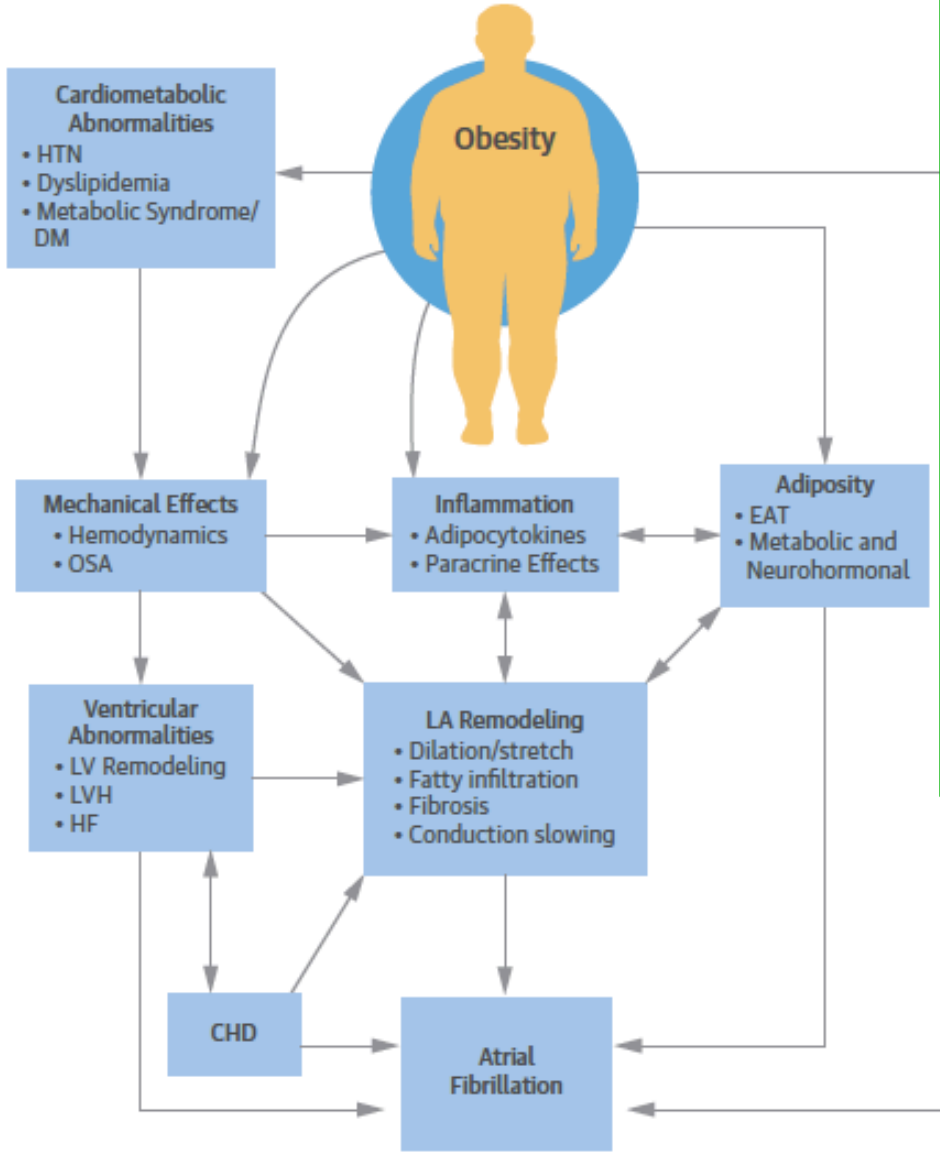

AF-FREE SURVIVAL
1.00
0.75
0.50
0.25
0.00
0
30
60
90
120
150
180
FOLLOW-UP (DAYS)
Abstinence prolonged
AF-free survival by 37%
(118 vs 86 days)
ABSTINENCE
53%
CONTROL
73%
Log-rank test
P=0.004
Number at risk
Abstinence 70 61 49 43 37 34 33
Control 70 51 36 28 22 19 18

	Abstinence			Control		
Cardiac MRI	Baseline	Follow-up	p value	Baseline	Follow-up	p value
LA area (cm^2)	29.5±4.9	27.1±4.5	<0.01	31.7±6.0	31.9±7.2	0.84
LAVI (mL/m^2)	56.7±11.9	53.7±6.4	0.09	56.0±16.7	50.0±4.4	0.40
LA emptying fraction (%)	42±14	50±8	0.02	38±11	41±5	0.27
Epicardial fat area (cm^2)	4.3±2.4	3.9±1.8	0.19	4.3±3.7	5.5±3.0	0.07
LVEF (%)	58.3±10.5	58.8±9.8	0.30	60.0±6.0	56.6±9.8	0.39

- Abstinence associated with significant reductions in:
  - **Blood pressure**
  - **Weight**
  - **Body mass index**

	Abstinence			Control		
	Baseline	Follow-up	P	Baseline	Follow-up	P
Blood pressure						
Systolic BP (mmHg)	138±16	126±17	<0.001	133±17	131±15	0.40
Diastolic BP (mmHg)	78±10	75±12	0.03	77±10	76±11	0.62
Mean BP (mmHg)	98±10	92±12	<0.001	96±11	95±10	0.48
Weight (kg)	90±16	87±14	<0.001	89±13	91±14	0.04
BMI	28.4±4.4	27.7±3.8	<0.001	28.5±4.5	28.9±4.9	0.03

FIGURE 2 Obesity and AF



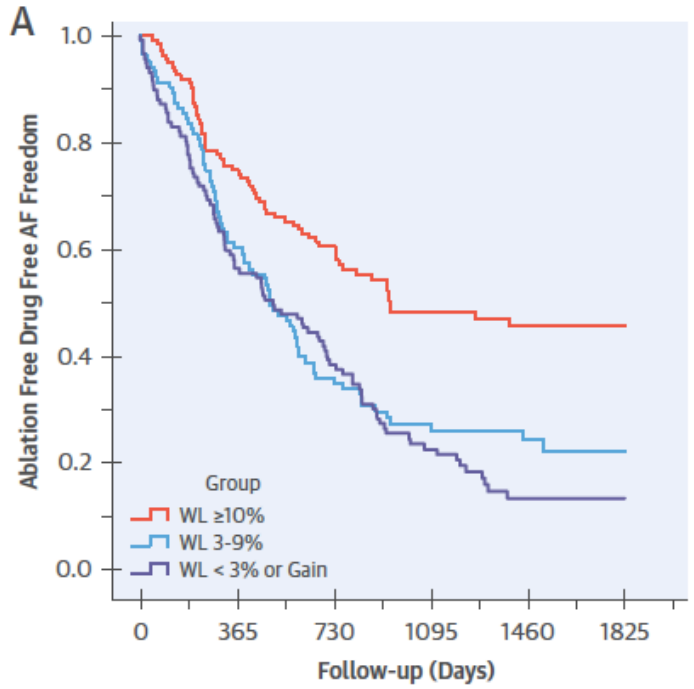
Proposed mechanisms explaining the increased risk of atrial fibrillation in obesity. CHD = coronary heart disease; DM = diabetes mellitus; EAT = epicardial adipose tissue; HF = heart failure; HTN = hypertension; LVH = left ventricular hypertrophy; OSA = obstructive sleep apnea; other abbreviations as in Figure 1.

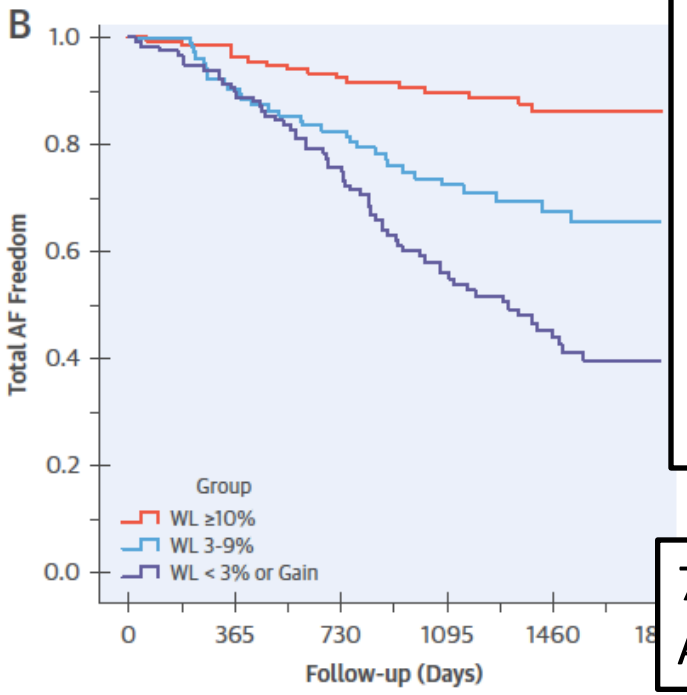
Mechanisms: AF and obesity

1. Hemodynamics: LA and systolic BP increase with LV diastolic dysfn and resultant atrial stretch/fibrosis
2. Adipose tissue: hypoxic state is proinflammatory; pericardial fat (conduction heterogenity)
3. Activation of RAAS, TGF-b, connective tissue GF: ↑collagen deposition
4. Autonomic dysregulation; OSA.

LEGACY Study

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.

355 pts BMI ≥ 27
Paroxysmal /persistent AF
-primary outcome AF burden

7-day holters, AFSS score

Limitations: Confounding by indication and residual confounding between groups

- Cluster effect of obesity and weight loss on other CV risk factors
- Prevalence of OSA much higher in this study – 50% vs ORBIT –AF 18%
- Same population demonstrated decreased AF if exercise tolerance improved

Pathak...Sanders. Weight management and AF. JACC Vol. 65, No 20. 2015.

Anticoagulation

Non-valvular AF: Definition

Atrial Fibrillation in the absence of mechanical heart valves, rheumatic mitral stenosis, or moderate to severe nonrheumatic mitral stenosis.

2018 Focused Update of the Canadian Cardiovascular Society Guidelines for the Management of Atrial Fibrillation. CJC (2018)

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%

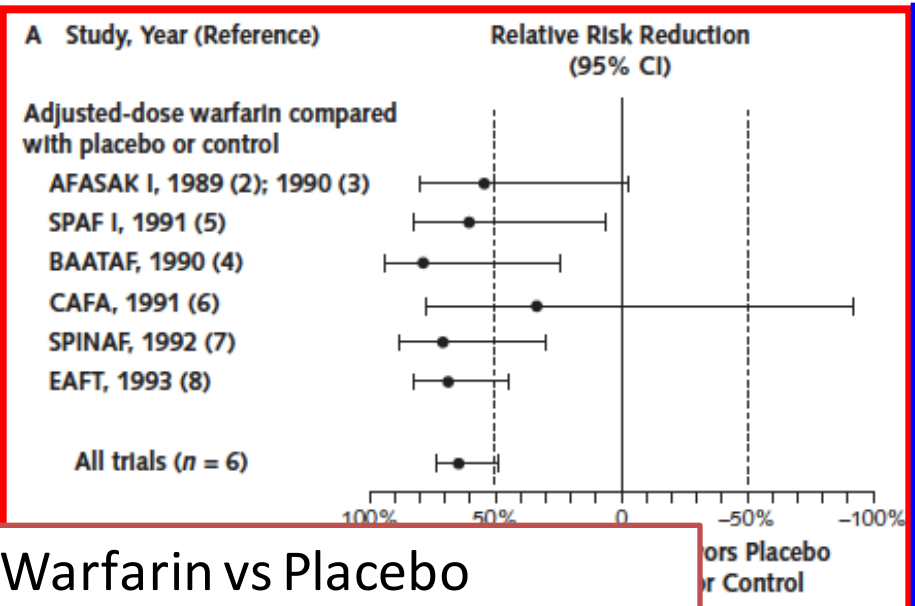
OAC for patients age ≥ 65 (even without other criteria)

ASA for patients with vascular disease (? questions remain)

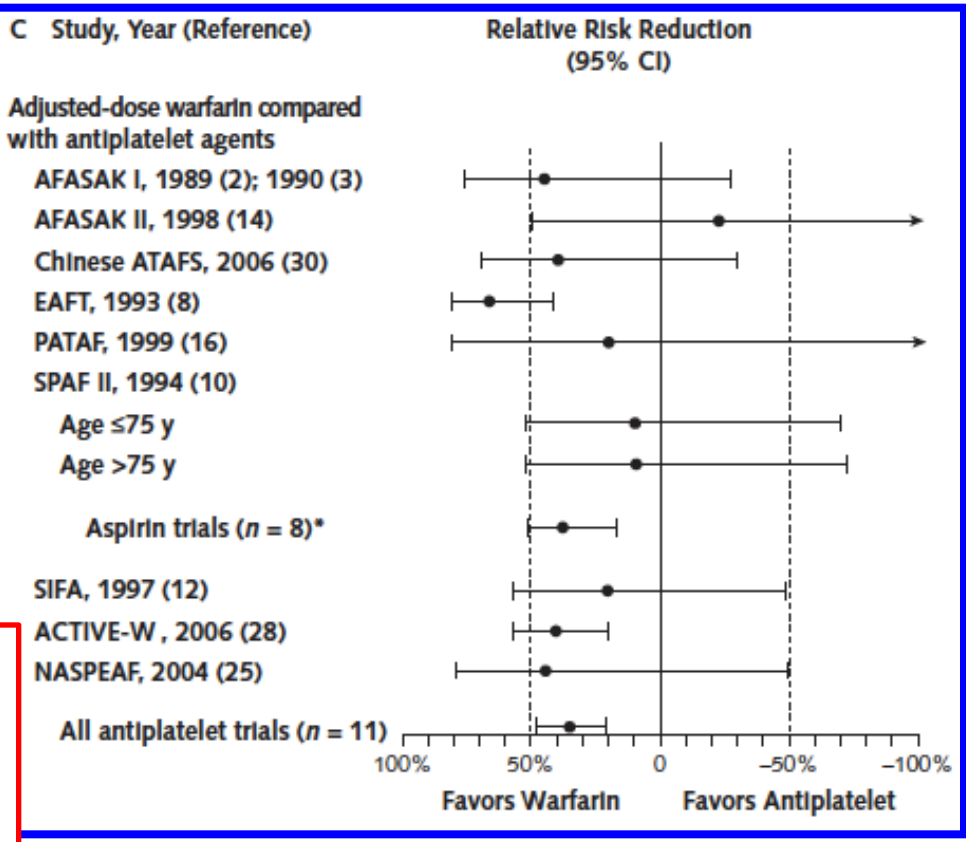
2016 Focused Update of the Canadian Cardiovascular Society Guidelines for the Management of Atrial Fibrillation. CJC 32 (2016) 1170-1185

Meta-analysis: Antithrombotic Therapy to Prevent Stroke in Patients Who Have Nonvalvular Atrial Fibrillation

Robert G. Hart, MD; Lesly A. Pearce, MS; and Maria I. Aguilar, MD



Warfarin vs Placebo



ischemic stroke ↓ by 67% (95% CI 54-77)

Hemorrhagic stroke ↓ by 64% (95% CI 49-74)

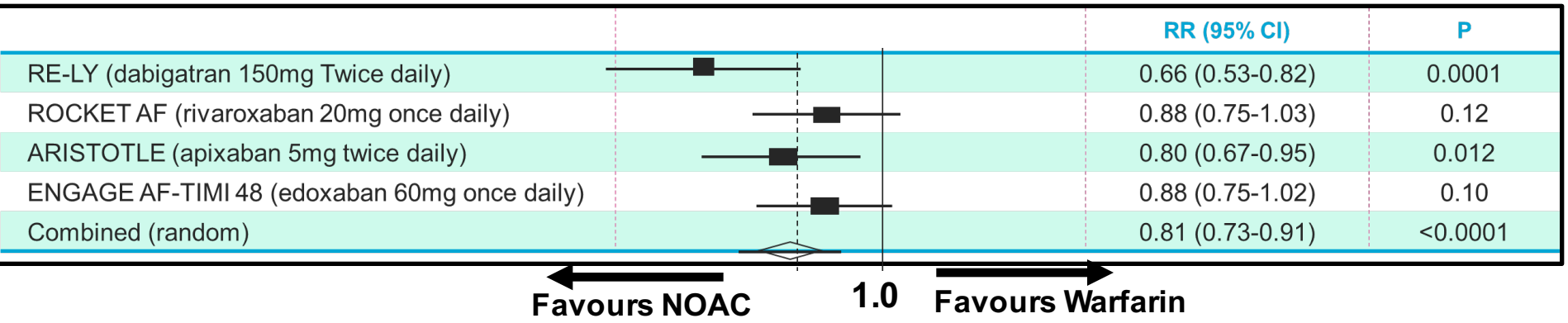
Death: ↓ by 26% (95% CI 3-45)

NNT to prevent 1 stroke is 37
(secondary prevention = 12)

Hart et al. Ann Intern Med. 2007;146:857-867

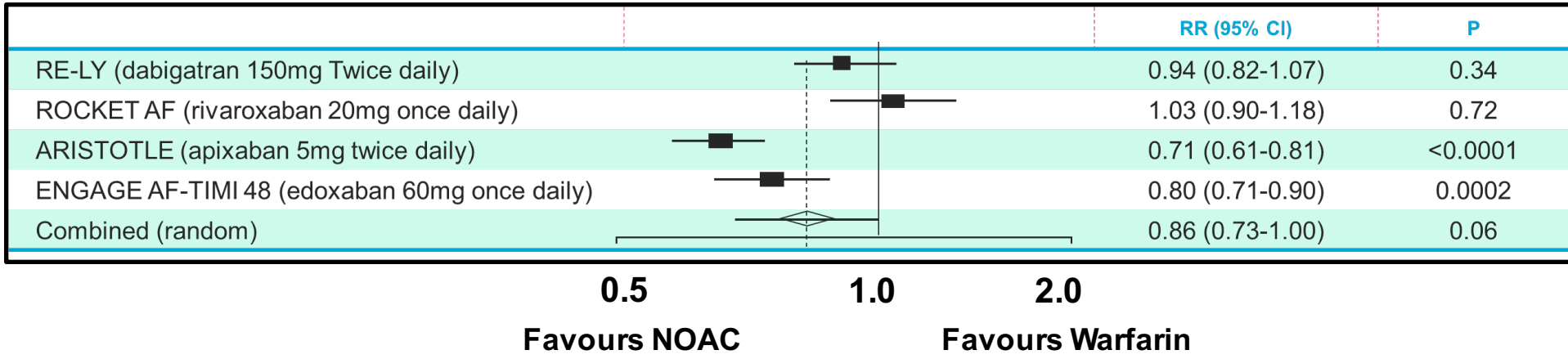
	Apixaban	Dabigatran	Edoxaban	Rivaroxaban
Mechanism of action	Direct Factor Xa inhibitor	Direct thrombin inhibitor	Direct Factor Xa inhibitor	Direct Factor Xa inhibitor
Oral bioavailability	~50%	~6.5%	62%	80-100% (when taken with food)
Food effect	No	No	No	Yes (needs to be taken with food*)
Pro-drug	No	Yes	No	No
Renal clearance	~27%	85%	50%	36%
Mean half-life ($t_{½}$)	~12 h	11-17 h	10-14 h	5-13 h
T_{max}	3-4 h	0.5-2 h	1-2 h	2-4 h
Standard dosage	5 mg	150 mg	60 mg	20 mg
Dosing frequency	Twice daily	Twice daily	Once daily	Once daily
CYP metabolism	Yes	No	Minimal <4%	Yes

Stroke or Systemic Embolic Event



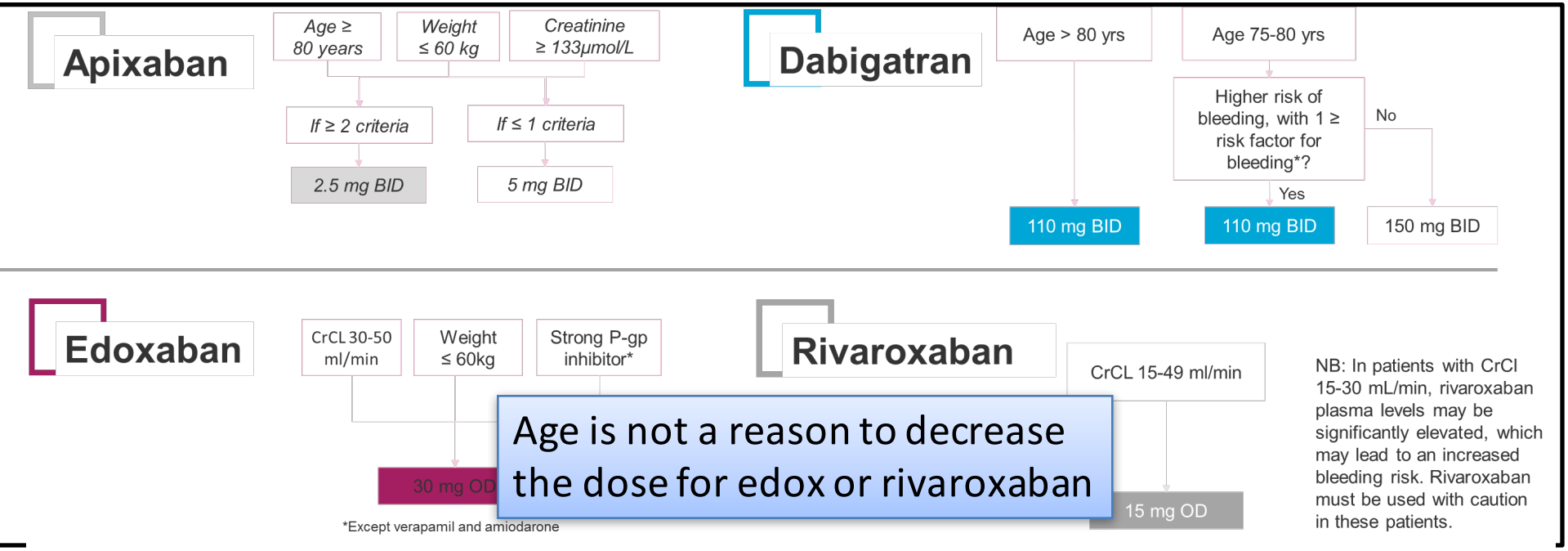
Overall stroke or systemic embolic event was reduced by the DOACs compared to warfarin (RR 0.81, 95% CI 0.73-0.91)

Major Bleeding



Trend towards reduced major bleeding risk (RR 0.86 95% CI 0.73-1.00)

Ruff CT, et *al. Lancet* 2014;383:955-62



CrCl: creatinine clearance; P-gp: P-glycoprotein

*e.g. Renal impairment, extensive cerebral infarction (haemorrhagic or ischemic) within the last 6 months, active peptic ulcer disease with recent bleeding

Edoxaban:

-Increased INR can be seen, the INR is not valid in interpreting level of anticoagulation

-limited data in patients with severe renal impairment (CrCl<30 mL/min) or on dialysis (in US and Europe, Edoxaban is approved to CrCl >15mL/min).

-The absorption of edoxaban is mediated by P-glycoprotein (P-gp). Interaction specifically with cyclosporine, dronedarone, erythromycin, quinidine, and ketoconazole (no dose reduction with amiodarone and verapamil).

NOAC Dose Modification for BMI

NOAC	Weight-related Contraindication / Dose Adjustments
Apixaban	If patient weighs ≤60 kg AND has another dose-reduction criterion (Age ≥80 years or creatinine ≥133 µmol/L), use 2.5 mg b.i.d. dose
Dabigatran	None
Edoxaban	If patient weighs ≤60 kg, use 30 mg q.d. dose
Rivaroxaban	None

None of the NOACs are contraindicated or require dose adjustment for high BMI

From Current Canadian Product Monographs.

Percentage of Obese Patients in the ENGAGE-AF TIMI 48 Trial

- 10% had a BMI 35-40 and 5.5% BMI > 40

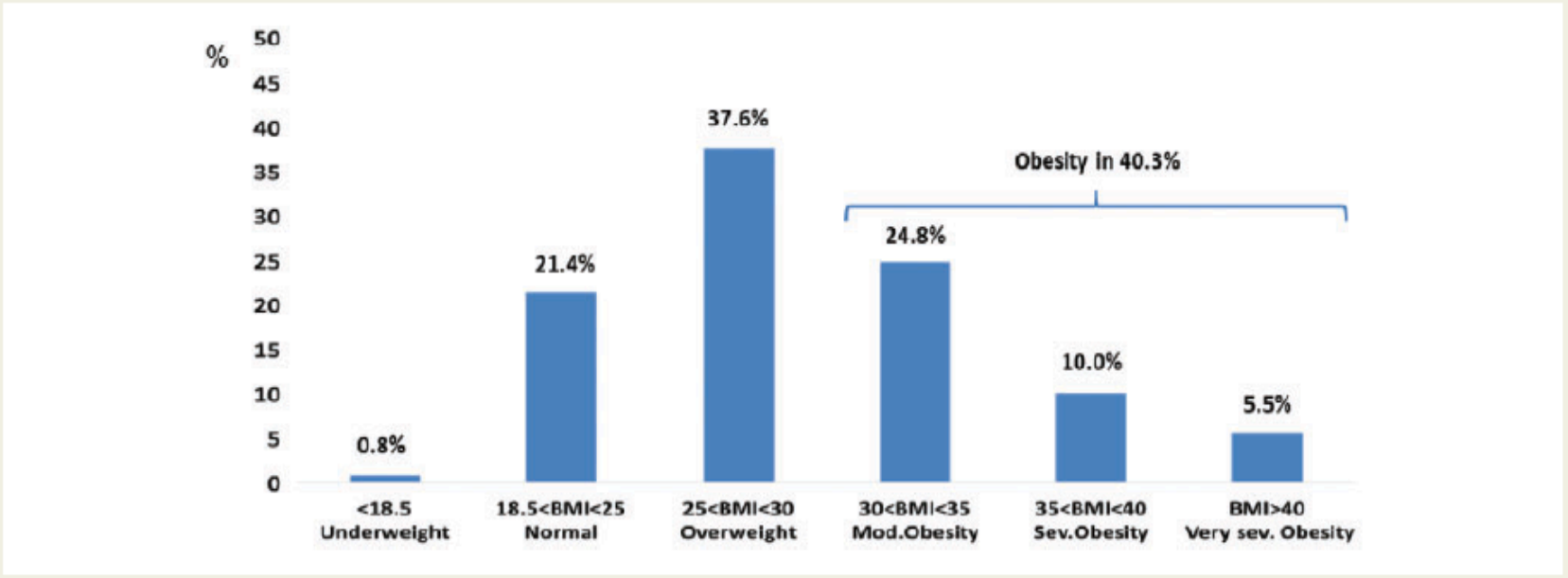


Figure 1 Distribution of body mass index (kg/m^2) in the ENGAGE AF-TIMI 48 population. Groups are shown according to body weight in kg/m^2. BMI, body mass index; Mod., Moderate; Sev., Severe.

Table 2 Concentration and anti-Factor Xa activity at trough with the higher-dose edoxaban regimen according to body mass index categories in the sample of patients who fulfilled (top) and not fulfilled (bottom)[a] the criteria for edoxaban dose reduction

Body mass index (kg/m^2)		Underweight (<18.5)	Normal (18.5 to <25)	Overweight (25 to <30)	Moderately obese (30 to <35)	Severely/very severely obese (≥35)	P-value for trend
Patients with edoxaban dose reduction at randomization							
Trough edoxaban concentration	*N* patients	25	369	268	119	39	
(ng/mL)	Median	27.0	25.3	29.9	28.4	27.5	0.17
	25–75 percentile	23.4–61.1	14.0–42.4	14.7–48.1	14.4–44.6	18.0–50.2	
Trough anti-Factor Xa activity	*N* patients	15	136	108	46	19	
(IU/mL)	Median	0.45	0.47	0.53	0.60	0.54	0.77
	25–75 percentile	0.11–1.30	0.29–0.81	0.30–0.87	0.30–0.85	0.31–0.82	
Patients without edoxaban dose reduction at randomization							
Trough edoxaban concentration	*N* patients	1[a]	304	950	761	479	
(ng/mL)	Median	N/A	34.9	37.6	36.2	33.0	0.28
	25–75 percentile	N/A	19.9–60.4	20.4–62.0	19.3–61.9	16.7–62.7	
Trough anti-Factor Xa activity	*N* patients	0	97	433	358	238	
(IU/mL)	Median	N/A	0.78	0.62	0.66	0.64	0.73
	25–75 percentile	N/A	0.42–1.17	0.37–1.06	0.36–1.15	0.37–1.16	

[a]Only one patient with BMI <18.5 was not dose-reduced and data are not shown.

Trough anti-Factor Xa

Trough Anti-Xa levels remained the same across BMI groups

Table 3 Outcomes from a multivariable model according to body mass index categories (adjusted analysis)

Body mass index (kg/m^2)	Normal (18.5 to <25) N. of events (%)	Overweight (25 to <30) HR[a] (95% CI)	Moderately obese (30 to <35) HR[a] (95% CI)	Severely obese (35 to <40) HR[a] (95% CI)	Very severely obese (≥40) HR[a] (95% CI)	*P* for trend
Stroke/SEE	273 (2.3)	0.91 (0.78–1.07)	0.82 (0.68–1.00)	0.68 (0.52–0.89)	0.54 (0.35–0.83)	<0.001
Ischaemic Stroke/SEE	229 (2.0)	0.91 (0.77–1.09)	0.80 (0.65–0.98)	0.70 (0.52–0.94)	0.48 (0.30–0.77)	<0.001
Mortality	629 (5.2)	0.79 (0.71–0.87)	0.77 (0.68–0.88)	0.75 (0.63–0.9)	0.78 (0.62–0.98)	0.037
Major bleeding	283 (2.9)	1.03 (0.88–1.20)	1.12 (0.94–1.34)	1.18 (0.94–1.48)	1.28 (0.96–1.70)	0.045
Net outcome[b]	987 (8.7)	0.91 (0.83–0.98)	0.92 (0.83–1.01)	0.87 (0.77–1.00)	0.95 (0.80–1.12)	0.44
Major or clinically relevant non-major bleeding	1014 (11.8)	1.05 (0.97–1.14)	1.10 (1.00–1.20)	1.17 (1.04–1.32)	1.27 (1.10–1.47)	<0.001
Any bleeding	1234 (15.0%)	1.04 (0.97–1.12)	1.06 (0.97–1.15)	1.15 (1.04–1.28)	1.23 (1.08–1.40)	<0.001

BMI, body mass index; CI, confidence interval; HR, hazard ratio; SEE, systemic embolic event.

[a]Adjusted hazard ratio with normal BMI as the referent. The model is adjusted for treatment group, $CHADS_2$ score at screening, verapamil or quinidine use at screening, paroxysmal vs. non-paroxysmal AF, sex, region, age, previous use of vitamin K antagonist for ≥60 days, baseline use of aspirin, thienopyridine agents, amiodarone, digoxin or digitalis preparations, smoking status, history of hypertension, stroke or TIA, CHF, diabetes, and creatinine at baseline.

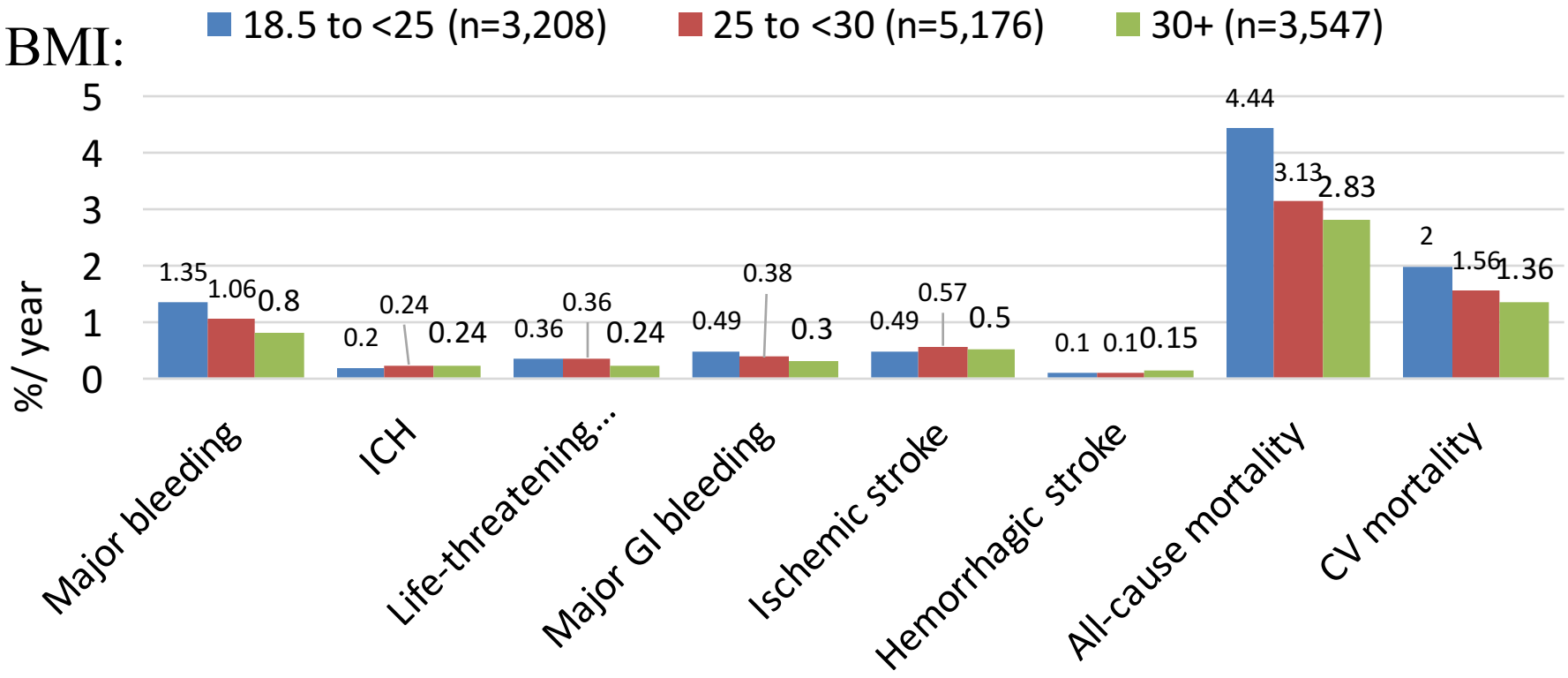
[b]Net outcome: composite of stroke, systemic embolic event, major bleeding, or death.

-Higher BMI was independently associated with lower risks of stroke and of death.
-Higher BMI was associated with an increased risk of bleeding, despite good control of INR in the warfarin group and no difference in edoxaban concentrations or anti-Factor Xa activity, as the BMI increased.

Take-home:
-The efficacy and safety profiles of edoxaban relative to well-managed warfarin were similar across BMI groups. The similar pharmacokinetic and pharmacodynamic results with edoxaban across the range of BMIs support the clinical observations.

Real-life Use of Edoxaban: Outcomes by BMI Range

Data from the European arm of the Global ETNA-AF Programme (N=11,931)



Conclusions: Within the ranges tested, BMI did not affect 1-year efficacy or severe bleeding outcomes with edoxaban

Rhythm Control

Channel Blockers	Class I *(Na^+ channel blockers)*	Procainamide Flecainide Propafenone (Vernakalant)
	Class II *(β blockers)*	Atenolol Metoprolol Carvedilol
	Class III *(K^+ channel blockers)*	Amiodarone Ibutilide Sotalol Dronaderone (Vernakalant)
	Class IV *(Ca^{2+} channel blockers)*	Verapamil Diltiazem

Sotalol is also a beta-blocker Amiodarone has Class I, II, III & IV activity

Rhythm Control Strategy in the ED

Table 1. Characteristics of antiarrhythmic medications used for acute pharmacological cardioversion

Medication	Dose	Time to conversion	Risks
Class Ia			
Procainamide	15-18 mg/kg I.V. over 30-60 minutes	Approximately 60 minutes	Hypotension Bradycardia Ventricular proarrhythmia
Class Ic			
Flecainide	300 mg PO (> 70 kg) 200 mg PO (≤ 70 kg)	2-6 hours	Hypotension Bradycardia and conversion pauses
Propafenone	600 mg PO (> 70 kg) 450 mg PO (≤ 70 kg)	2-6 hours	1:1 Conduction of atrial flutter*
Class III			
Ibutilide	1 mg I.V. over 10 minutes May repeat once	30-60 minutes	QT prolongation Torsades de pointes† Hypotension
Amiodarone	150 mg I.V. bolus then 60 mg/h for 6 hours then 30 mg/h for 18 hours	8-12 hours	Bradycardia Atrioventricular block Torsades de pointes Phlebitis
Vernakalant	3 mg/kg I.V. over 10 minutes, followed by 2 mg/kg I.V. if no conversion	12-30 minutes	Hypotension Bradycardia Nonsustained ventricular tachycardia‡

ACS, acute coronary syndrome; AV, atrioventricular; I.V., intravenous; PO, orally.

* Class Ic drugs (flecainide and propafenone) should be used in combination with AV nodal blocking agents (β-blockers or calcium channel inhibitors). Class Ic agents should be avoided in patients with ischemic heart disease or significant structural heart disease.

† Consider pretreating with 1-4 mg of I.V. $MgSO_4$. Ibutilide should be avoided in patients with hypokalemia, baseline QT prolongation, or significant structural heart disease.

‡ Vernakalant should be avoided in patients with hypotension, recent ACS, or significant structural heart disease.

Table 2. PIP antiarrhythmic drug therapy

Appropriate candidates for PIP	(1) Symptomatic patients (2) Sustained AF episodes (eg, ≥ 2 hours) (3) AF episodes that occur less frequently than monthly (4) Absence of severe or disabling symptoms during an AF episode (eg, fainting, severe chest pain, or breathlessness) (5) Ability to comply with instructions, and proper medication use
Contraindication to PIP	(1) Significant structural heart disease (eg, left ventricular systolic dysfunction [left ventricular ejection fraction < 50%], active ischemic heart disease, severe left ventricular hypertrophy) (2) Abnormal conduction parameters at baseline (eg, QRS duration > 120 msec, PR interval > 200 msec, or evidence of pre-excitation) (3) Clinical or electrocardiographic evidence of sinus node dysfunction, bradycardia or advanced AV block (4) Hypotension (systolic BP < 100 mm Hg) (5) Previous intolerance of any of the PIP-AAD medications
PIP administration	Immediate release oral AV nodal blocker (one of diltiazem 60 mg, verapamil 80 mg, or metoprolol tartrate 25 mg) 30 minutes before the administration of a class Ic AAD (300 mg of flecainide or 600 mg of propafenone if ≥ 70 kg; 200 mg of flecainide or 450 mg of propafenone if < 70 kg)
Initial ED monitoring	Telemetry for at least 6 hours Blood pressure monitoring every 30 minutes 12-Lead ECG monitoring every 2 hours
Determinants of initial treatment failure	(1) AF persistence > 6 hours after PIP-AAD administration or electrical cardioversion required for termination (2) Adverse events including symptomatic hypotension (systolic BP ≤ 90 mm Hg), symptomatic conversion pauses (> 5 seconds), symptomatic bradycardia after sinus rhythm restoration, proarrhythmia (conversion to atrial flutter/tachycardia, or episodes of ventricular tachycardia), severe symptoms (dyspnea, presyncope, syncope), or a > 50% increase in QRS interval duration from baseline
Instructions for subsequent out-of-hospital use	Patients should take the AV nodal agent 30 minutes after the perceived arrhythmia onset, followed by the class Ic AAD 30 minutes after the AV nodal agent. After AAD administration patients should rest in a supine or seated position for the next 4 hours, or until the episode resolves Patients should present to the ED in the event that: (1) The AF episode did not terminate within 6-8 hours (2) They felt unwell after taking the medication at home (eg, a subjective worsening of the arrhythmia after AAD ingestion, or if they developed new or severe symptoms such as dyspnea, presyncope, or syncope) (3) More than one episode occurred in a 24-hour period (patients were advised not to take a second PIP-AAD dose within 24 hours) (4) If the AF episode was associated with severe symptoms at baseline (eg, significant dyspnea, chest pain, pre-syncope, or symptoms of stroke), even in the absence of PIP-AAD use

AAD, antiarrhythmic drug; AF, atrial fibrillation; AV, atrioventricular; BP, blood pressure; ECG, electrocardiogram; ED, emergency department; PIP, "pill-in-the-pocket."

2018 Focused Update of the Canadian Cardiovascular Society Guidelines for the Management of Atrial Fibrillation. CJC (2018)

Cardioversion

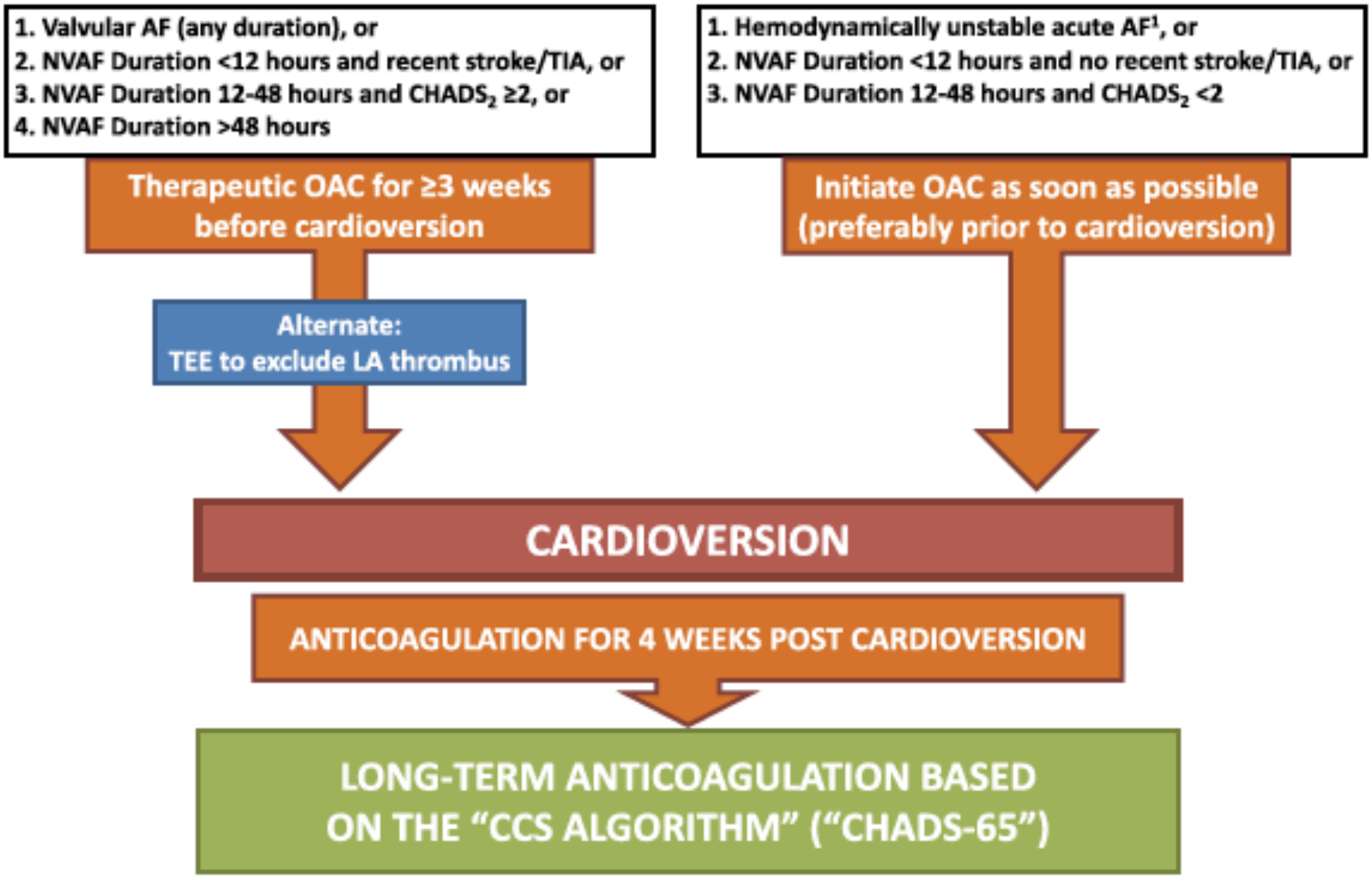
Risk and Mechanisms of Thromboembolism post cardioversion

- 1-month risk of stroke or systemic embolism after cardioversion = 0.46% for those treated with warfarin and 0.31% for those treated with NOAC (ie. double the risk of a patient not undergoing cardioversion)
- In patients not receiving anticoagulation, the risk of a thromboembolic event is 1.9%

<u>Mechanisms</u>

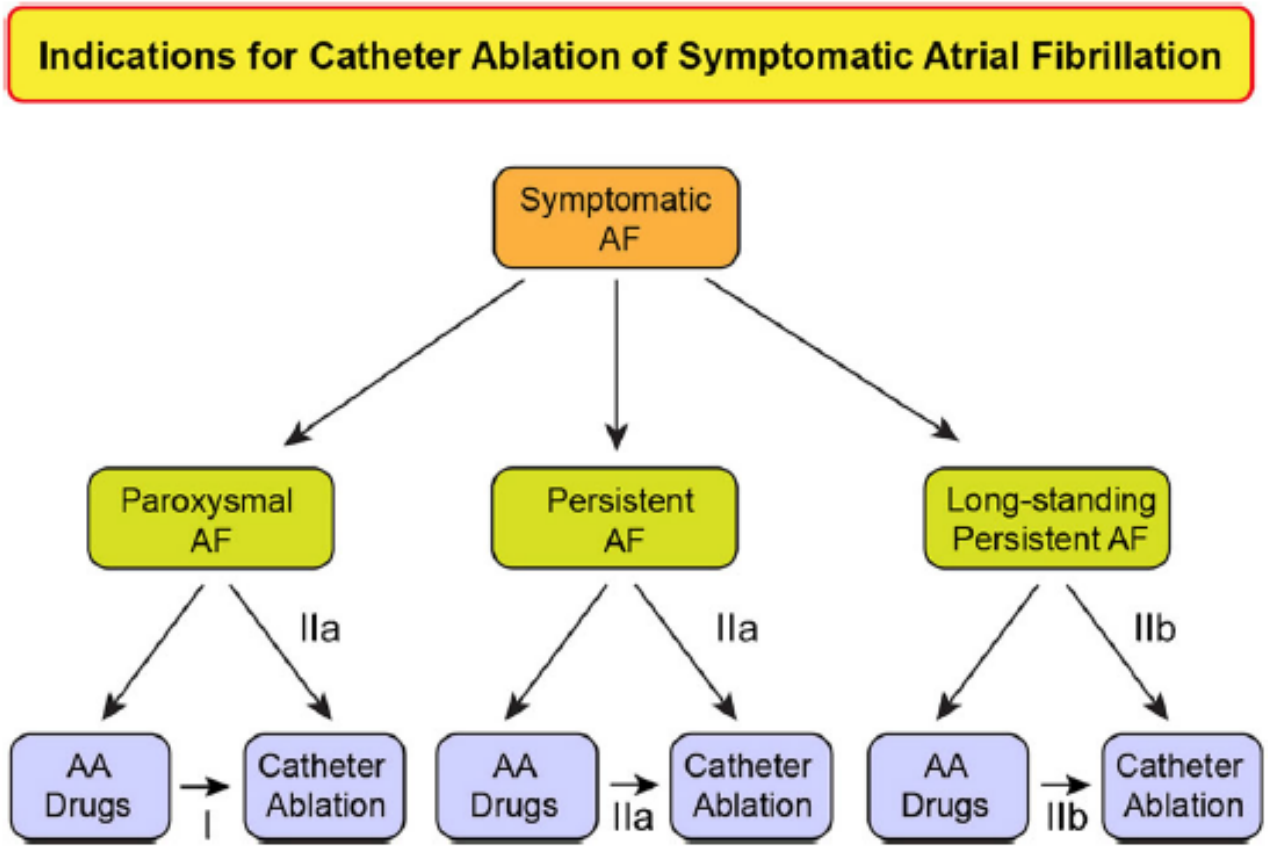
1. Generation of thrombi during the atrial fibrillation episode with embolization after sinus rhythm is achieved

2. Atrial stunning: development of new thromboemboli post cardioversion as a result of atrial dysfunction



2018 Focused Update of the Canadian Cardiovascular Society Guidelines for the Management of Atrial Fibrillation. CJC (2018)

Indications for AF ablation



Paroxysmal:
AF terminates with intervention or spontaneously within 7 days of onset

Persistent:
AF that is sustained beyond 7 days but < 3 months

Longstanding persistent:
Continuous AF > 12 months duration

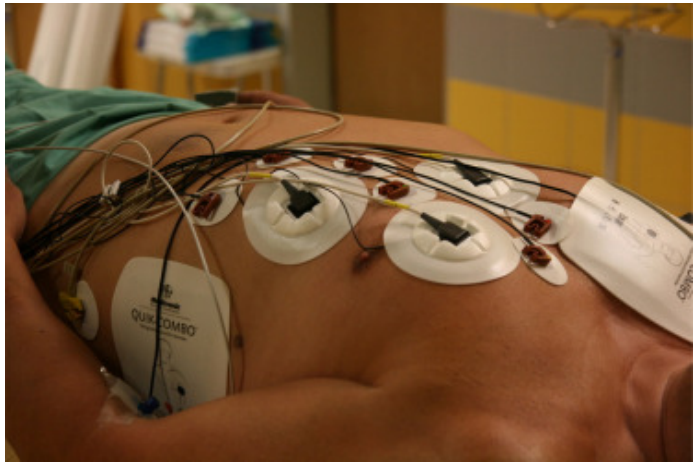
Success rate in maintaining sinus rhythm:

catheter ablation: 66-89%
antiarrhythmics: 9-58%

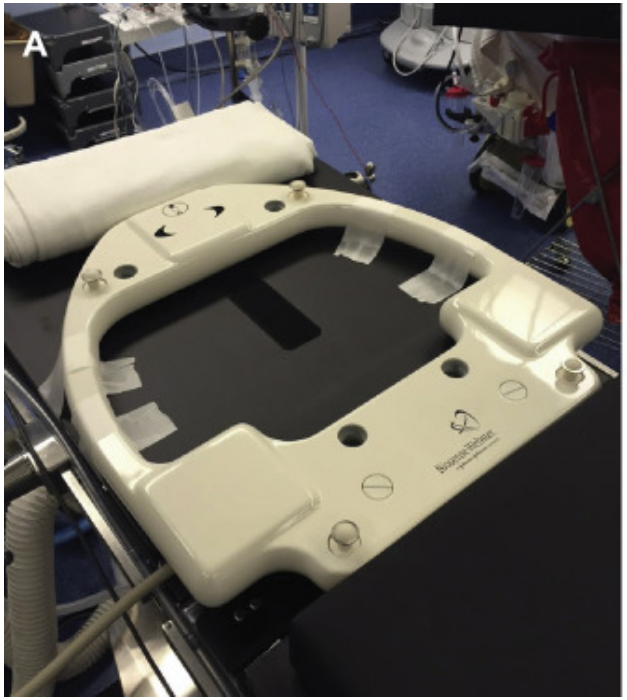
2017 HRS expert consensus statement on catheter and surgical ablation of atrial fibrillation. J Interv Card Electrophysiol (2017) 50:1-55
Contemporary AF managemenet. Andrade et al. CJC 33 (2017) 965-976

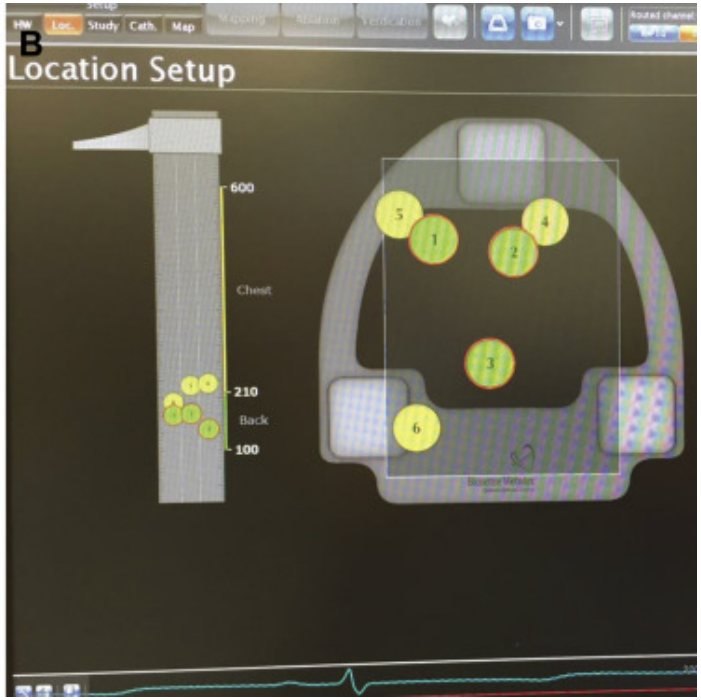
AF Ablation Procedure

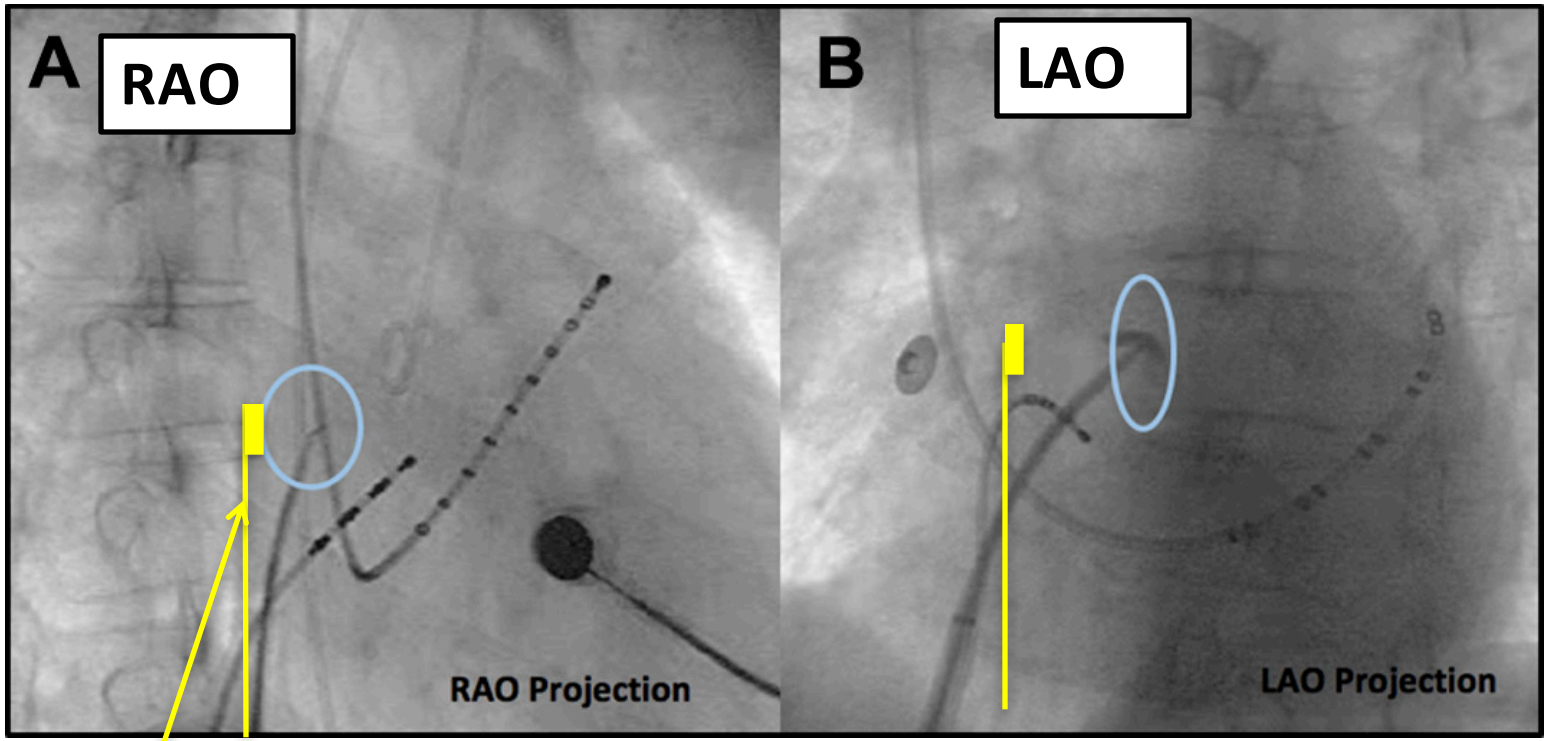
AF Ablation Procedure

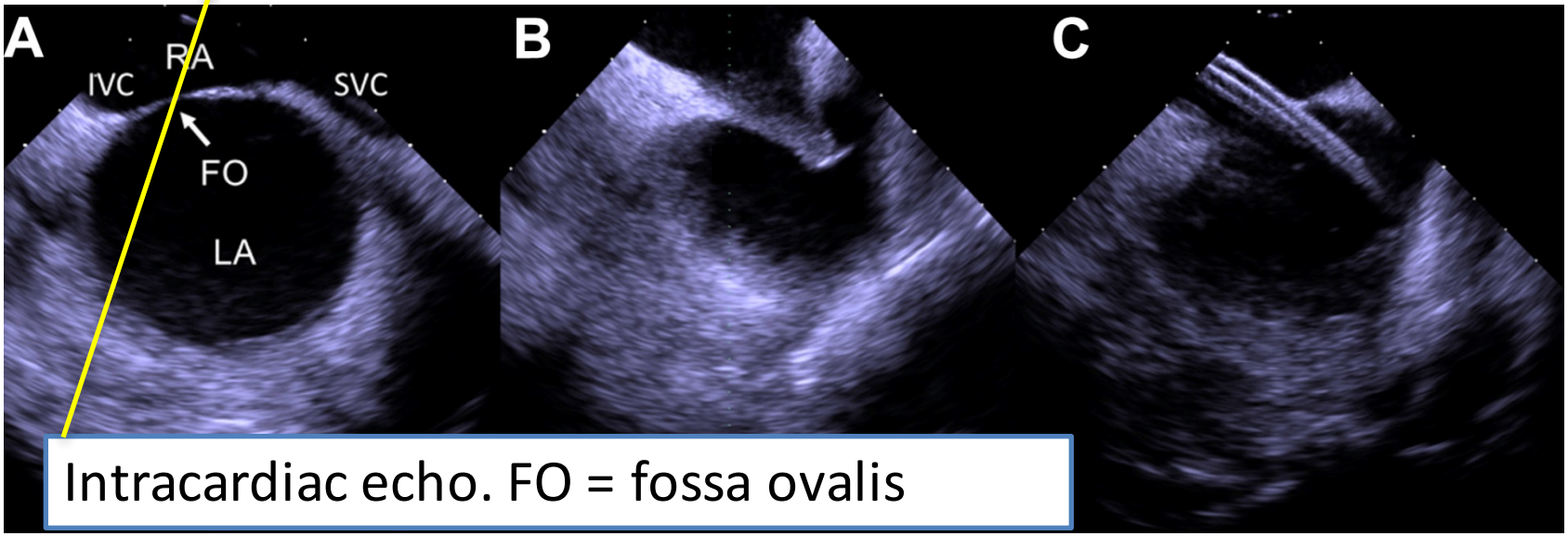


The mapping and ablation catheters have magnetic sensors that link to patches on the patient's front and back with a reference under the table/at torso level.





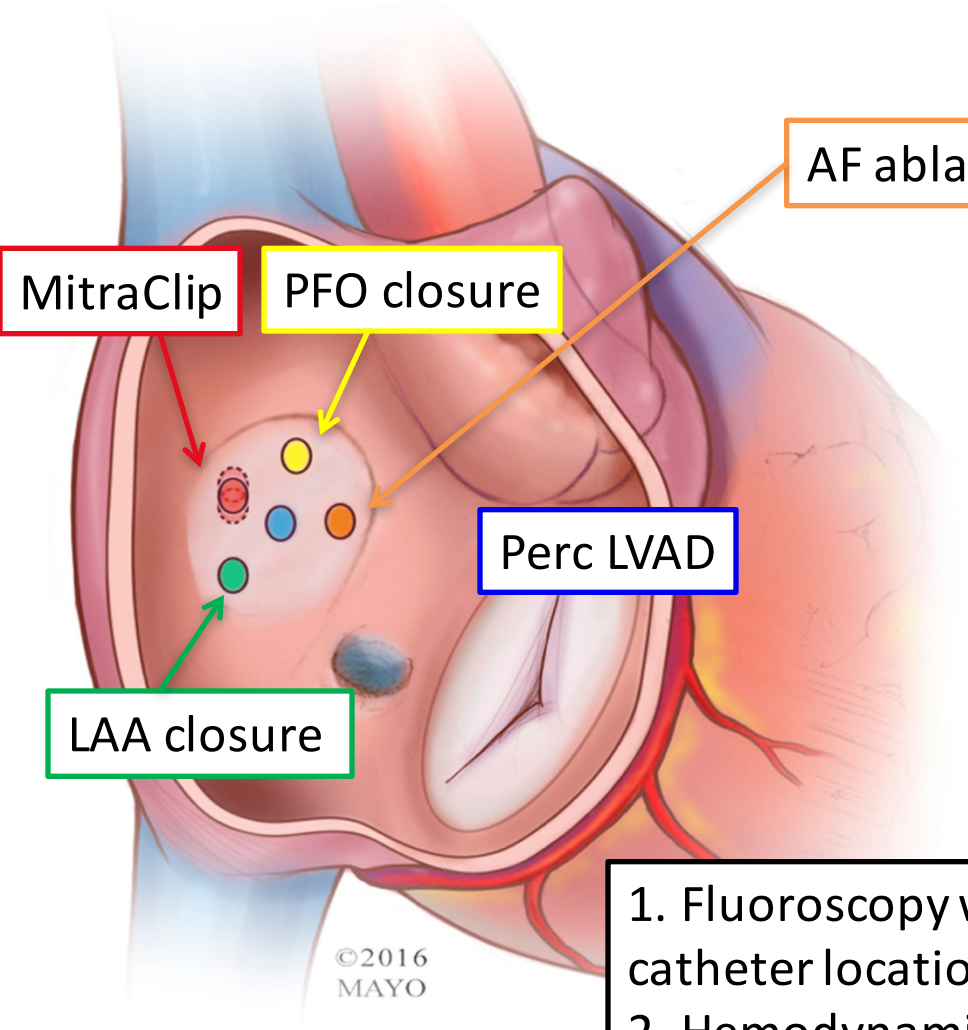


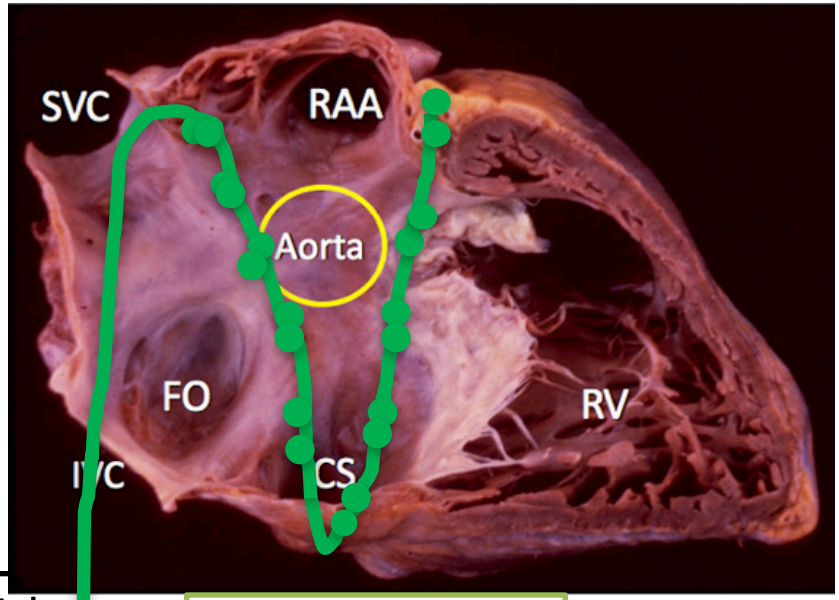


Intracardiac echo. FO = fossa ovalis

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

Site-Specific Transseptal Puncture for Various Intracardiac Interventions



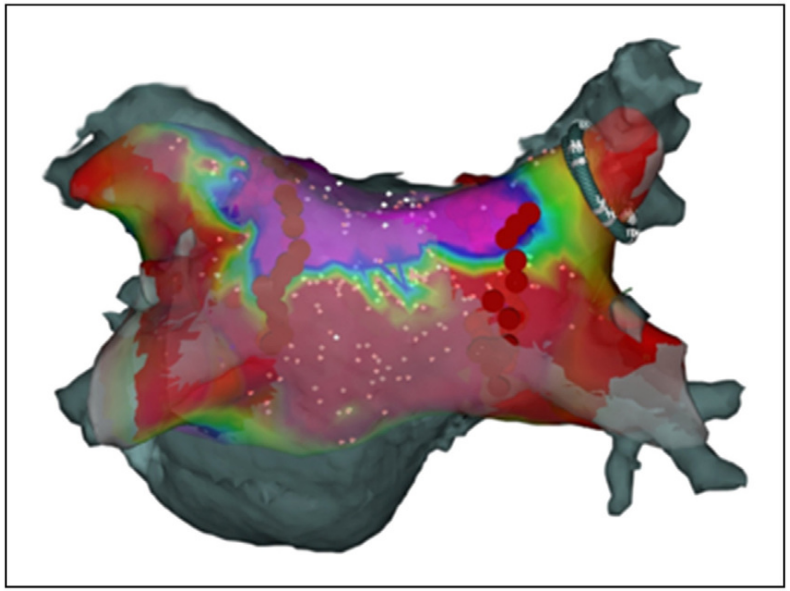


1. Fluoroscopy with catheter location
2. Hemodynamics
3. TEE
4. Intracardiac echo (ICE)

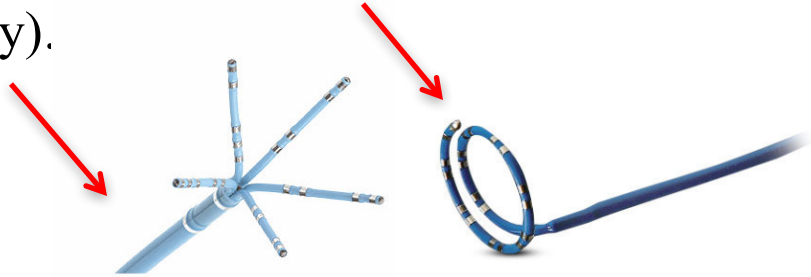
Coronary sinus catheter

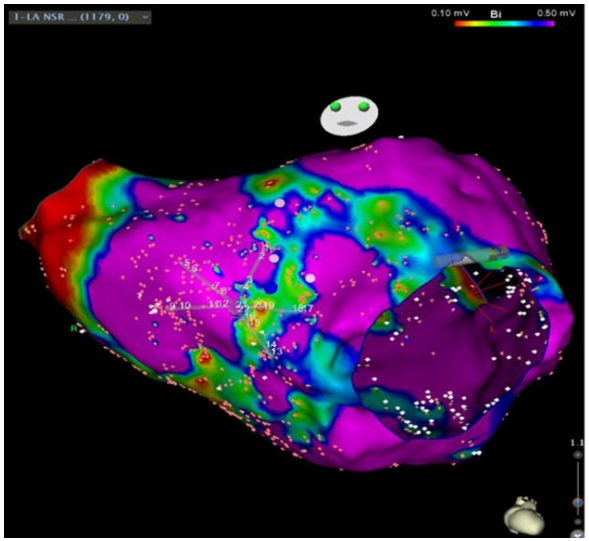
Alkhouli et al. JACC Volume 9, 24 (2016), 2465-2480

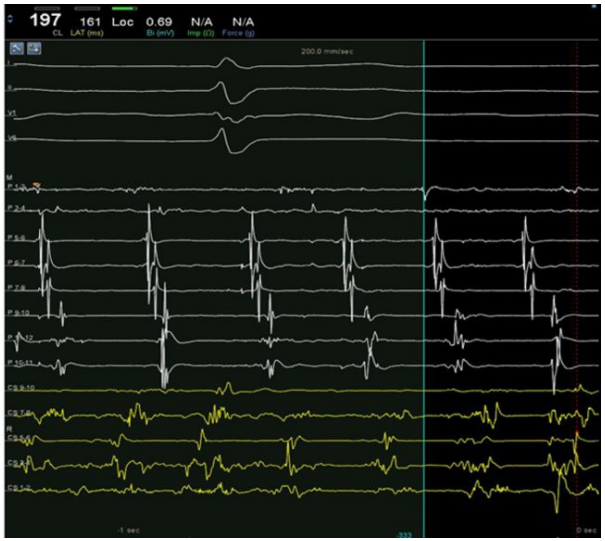
AF Ablation Procedure: Mapping

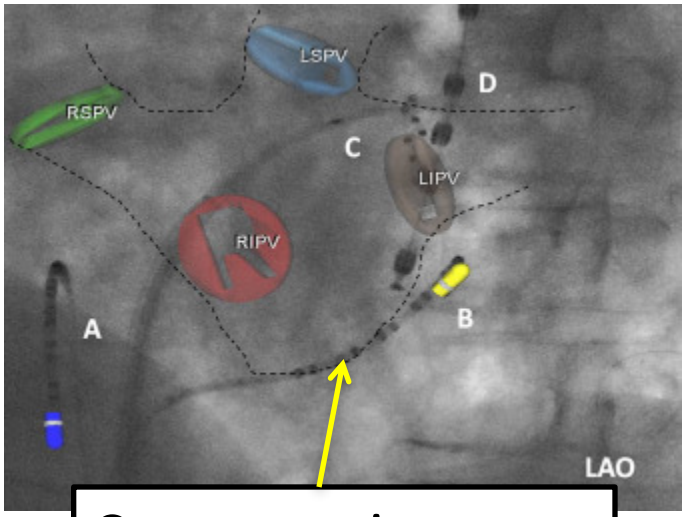


A left atrial electroanatomic map is created using a multielectrode mapping catheter (lasso or pentaray).



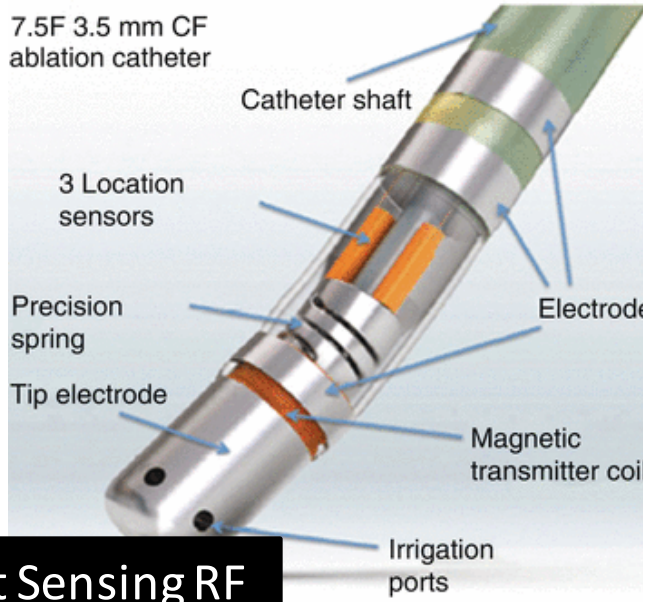




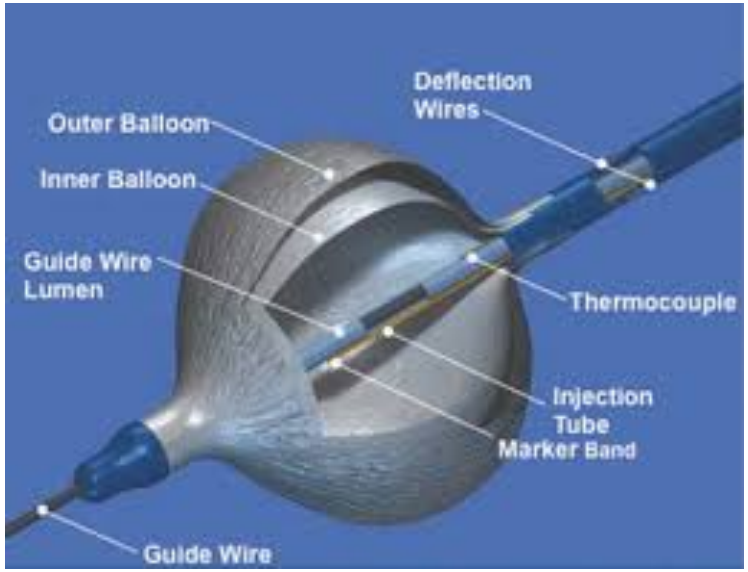


Coronary sinus catheter

Radiofrequency

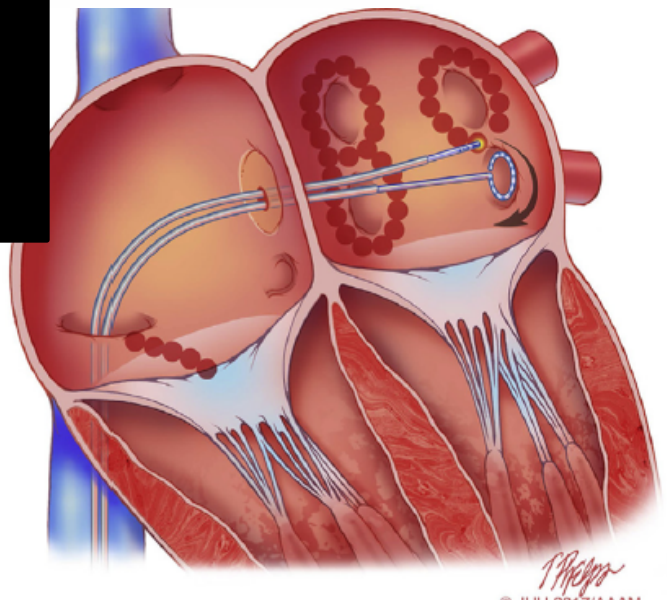


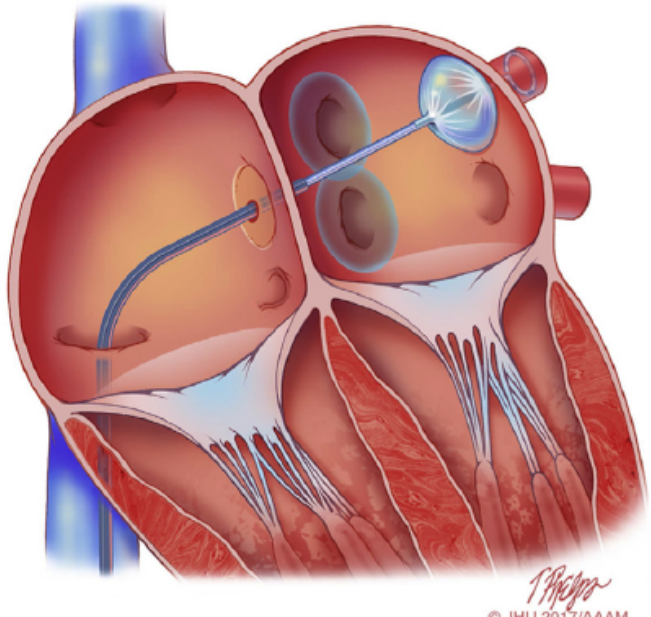
Cryoablation



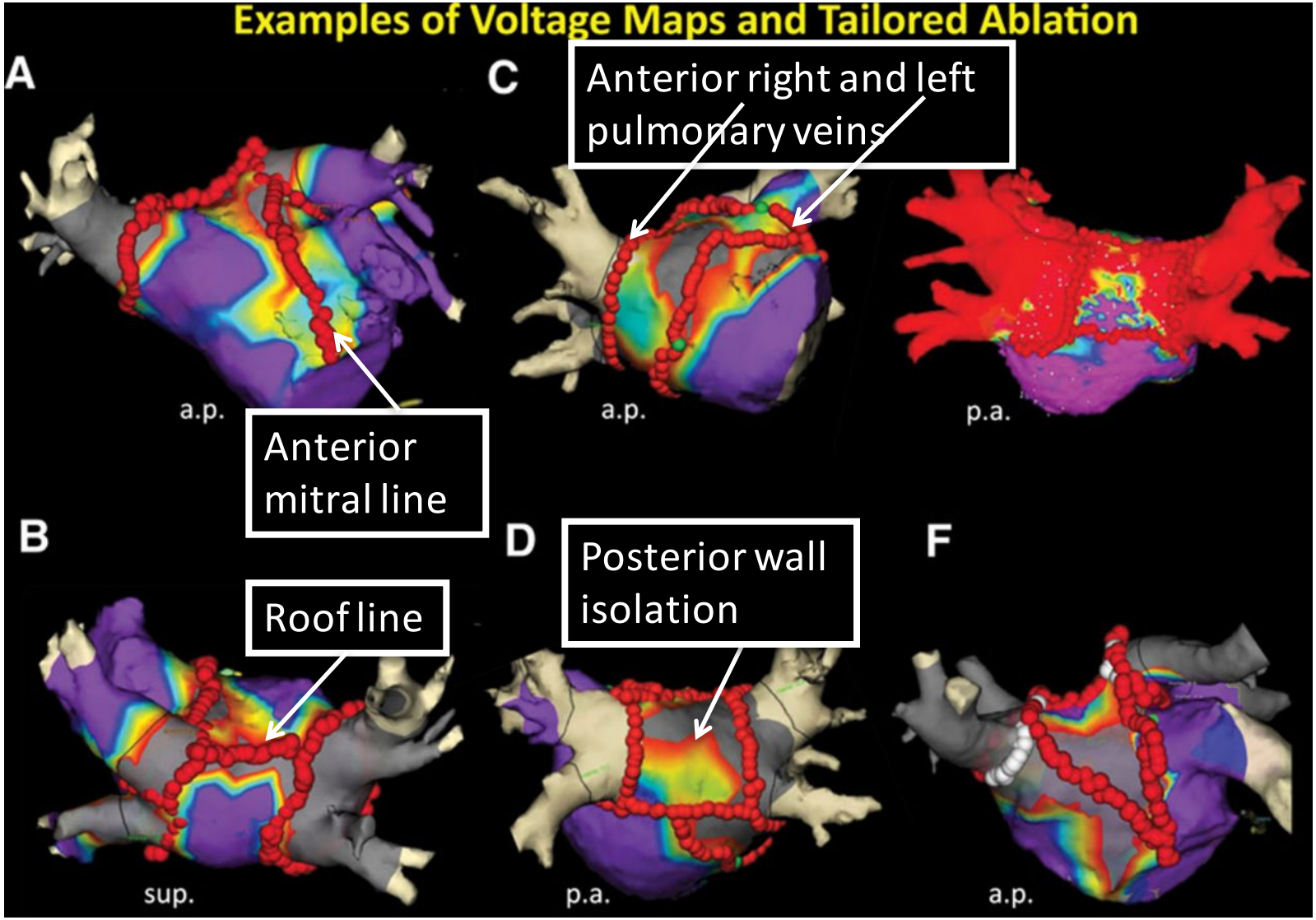
Contact Sensing RF catheters since 2014 = more efficacious lesions and safer procedure

(b)

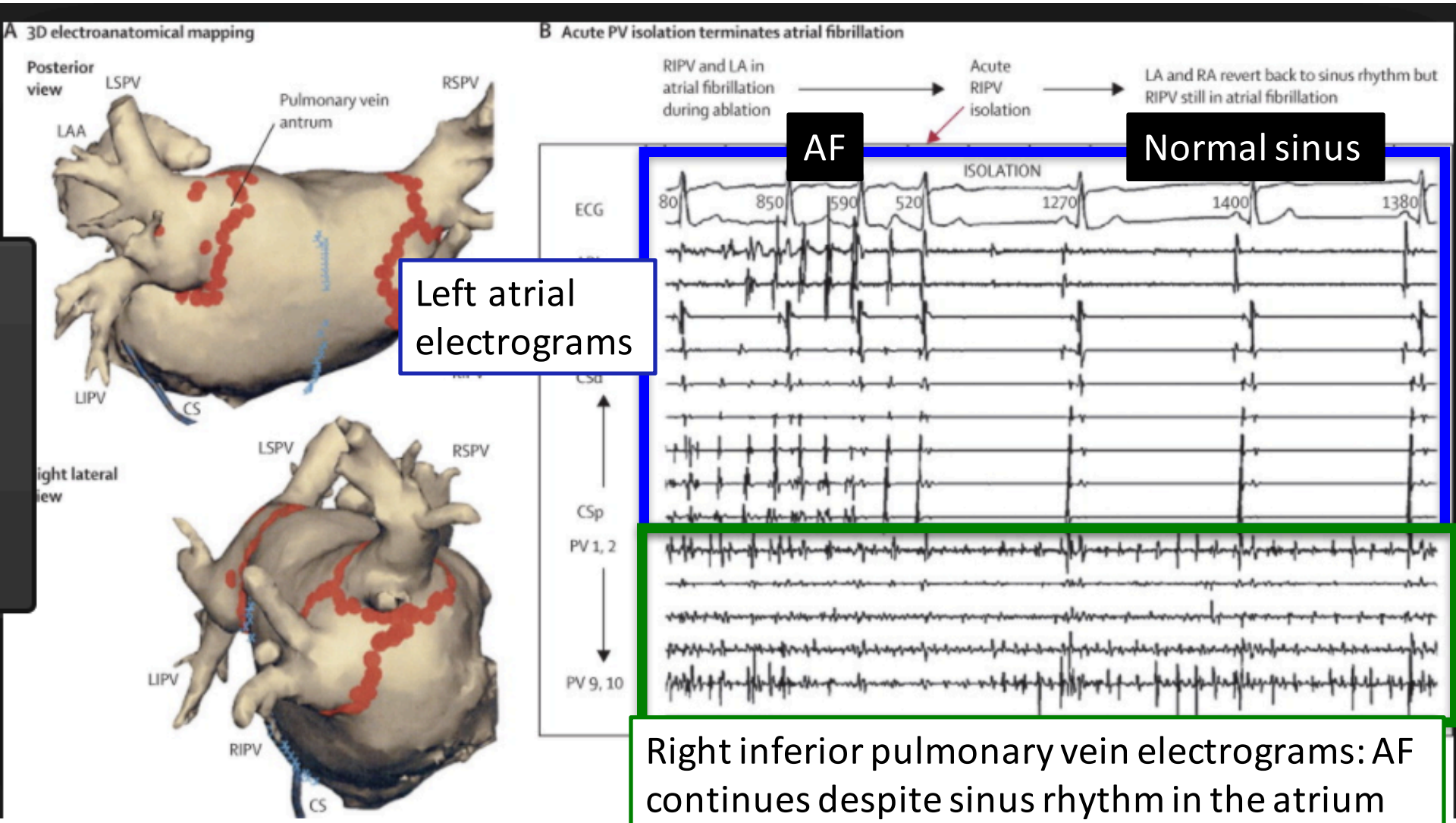




Radiofrequency Lesion Sets



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


A 3D electroanatomical mapping
Posterior view
LSPV
RSPV
Pulmonary vein antrum
LAA
LIPV
CS
ight lateral iew
LSPV
RSPV
LIPV
RIPV
CS
B Acute PV isolation terminates atrial fibrillation
RIPV and LA in atrial fibrillation during ablation
Acute RIPV isolation
LA and RA revert back to sinus rhythm but RIPV still in atrial fibrillation
AF
Normal sinus
ISOLATION
ECG
80
850
590
520
1270
1400
1380
CSp
PV 1, 2
PV 9, 10
Left atrial electrograms
Right inferior pulmonary vein electrograms: AF continues despite sinus rhythm in the atrium

Cases:

Anticoagulation concerns

CASE: 90 year-old Female

90F with a dual-chamber pacemaker

-PMHx: hypertension, osteoarthritis.
-Medications: norvasc 5mg po Qdaily, gabapentin, ecASA 80mg Qd
-Lives alone with caregiver, uses a cane/walker.
-Needs help with most ADLs/IADLs
-She was known to have AF in the past, but due to her high risk of falls, so she was started on ASA alone.

On pacemaker interrogation, found to be in AF 40% of the time since last follow-up 6 months ago

90 year-old Female with Asymptomatic AF on Pacemaker

Weight 70kg; Creat Cl 60mlmin; no valvular disease on echo

Do you:

A. Continue her ASA: her fall risk is too high

B. Start a DOAC with dose reduction?

C. Start DOAC without a dose reduction?

D. Start warfarin

Should frail patients at risk of falls receive a lower dose of a DOAC?

Prior History of Falls and Risk of Outcomes in Atrial Fibrillation: The Loire Valley Atrial Fibrillation Project

Amitava Banerjee, MPH, DPhil,[a] Nicolas Clementy, MD,[b] Ken Haguenoer, MD,[b] Laurent Fauchier, MD, PhD,[b,1] Gregory Y.H. Lip, MD[a,1]

[a]*University of Birmingham Centre for Cardiovascular Sciences, City Hospital, Birmingham, UK;* [b]*Service de Cardiologie, Pôle Coeur Thorax Vasculaire, Centre Hospitalier, Universitaire Trousseau et Faculté de Médecine, Université François Rabelais, Tours, France.*

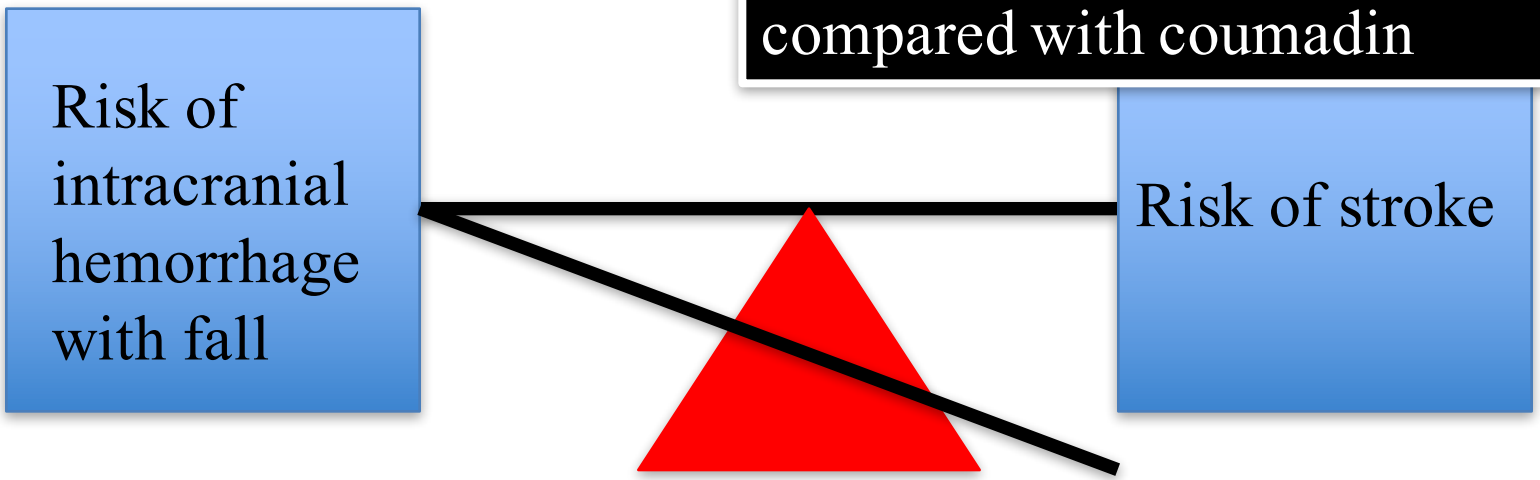
	Prior History of Falls n = 76		No History of Falls n = 7080		
	Events	**Event Rate**	**Events**	**Event Rate**	**P-Value***
Ischemic stroke	9	1.18 (0.54-2.25)	353	0.50 (0.45-0.55)	.01
Ischemic stroke/thromboembolism	12	1.58 (0.82-2.76)	533	0.75 (0.68-0.83)	.01
Hemorrhagic stroke	3	0.39 (0.08-1.15)	98	0.14 (0.11-0.17)	.09
Bleeding	8	1.05 (0.45-2.07)	542	0.77 (0.77-0.83)	.38
All-cause mortality	20	2.63 (1.61-4.06)	827	1.17 (1.07-1.27)	<.0001

-Among 7156 patients with AF, prior fall history was uncommon (1.1%)
-higher risk scores for stroke/thromboembolism, but not for bleeding
-In multivariable analyses, prior hx of falls was independently associated with increased risk of stroke/thromboembolism (HR 5.19), major

Adapted from Banerjee A, et al. *Am J Med.* 2014; 127(10):972-8.

Increased risk of intracranial hemorrhage with falling
vs.
the baseline risk of stroke in this higher-risk population

DOACs have consistently been linked with an approximately 50% reduced risk for intracranial bleedings as compared with coumadin



Pre-specified Analysis of Risk of Falls: No Significant Impact of Fall Risk on Efficacy of Edoxaban 60/30 mg (ENGAGE AF-TIMI 48)

Patients were categorized as having an increased risk of falling if they had any of the following 8 criteria at randomization:

Prior history of falls	Orthostatic hypotension
Lower extremity weakness	Use of psychotropic drugs
Poor balance	Severe Arthritis
Cognitive impairment	Dizziness

900 patients (4.3%) were judged at randomization to be at increased risk of falling

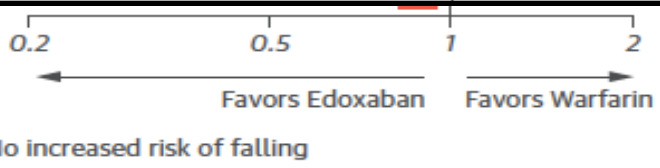
-overall older, more often female, and higher incidence of comorbidities (CAD, DM2, moderate renal insufficiency).

-Higher stroke risk, and more frequently a history of stroke or TIA

Steffel J, et al. *J Am Coll Cardiol* 2016; 68:1169-78.

FIGURE 1 Efficacy of HDER Versus Warfarin in Patients With and Without Increased Risk of Falls at Baseline

Endpoint	HDER (n= 310)	Warfarin (n= 307)	Hazard Ratio (HDER vs Warf)	p-int
Stroke / SEE	22 (2.81%)	22 (2.85%)	0.96 (0.53-1.75)	0.74
	274 (1.51%)	315 (1.76%)	0.86 (0.73-1.01)	
All cause death / Stroke / SEE	73 (9.27%)	78 (9.98%)	0.92 (0.67-1.26)	0.96
	876 (4.83%)	968 (5.38%)	0.90 (0.82-0.98)	
Stroke	20 (2.55%)	20 (2.58%)	0.97 (0.52-1.81)	0.76
	261 (1.44%)	297 (1.66%)	0.87 (0.74-1.03)	
Fatal Stroke	5 (0.63%)	6 (0.75%)	0.84 (0.26-2.70)	0.82
	75 (0.41%)	80 (0.44%)	0.93 (0.68-1.28)	
Primary Hemorrhagic Stroke	3 (0.38%)	8 (1.01%)	0.37 (0.10-1.41)	0.55
	46 (0.25%)	82 (0.45%)	0.56 (0.39-0.80)	
Primary Ischemic Stroke	17 (2.17%)	14 (1.78%)	1.18 (0.58-2.41)	0.63
	219 (1.21%)	221 (1.23%)	0.98 (0.82-1.19)	
All-cause death	58 (7.14%)	64 (7.79%)	0.91 (0.64-1.29)	0.90
	715 (3.86%)	775 (4.2%)	0.92 (0.83-1.02)	
Cardiovascular death	34 (4.18%)	41 (4.99%)	0.83 (0.53-1.30)	0.82
	496 (2.67%)	570 (3.09%)	0.87 (0.77-0.98)	
Myocardial infarction	7 (0.89%)	7 (0.88%)	0.99 (0.35-2.83)	0.91
	126 (0.69%)	134 (0.74%)	0.94 (0.73-1.19)	



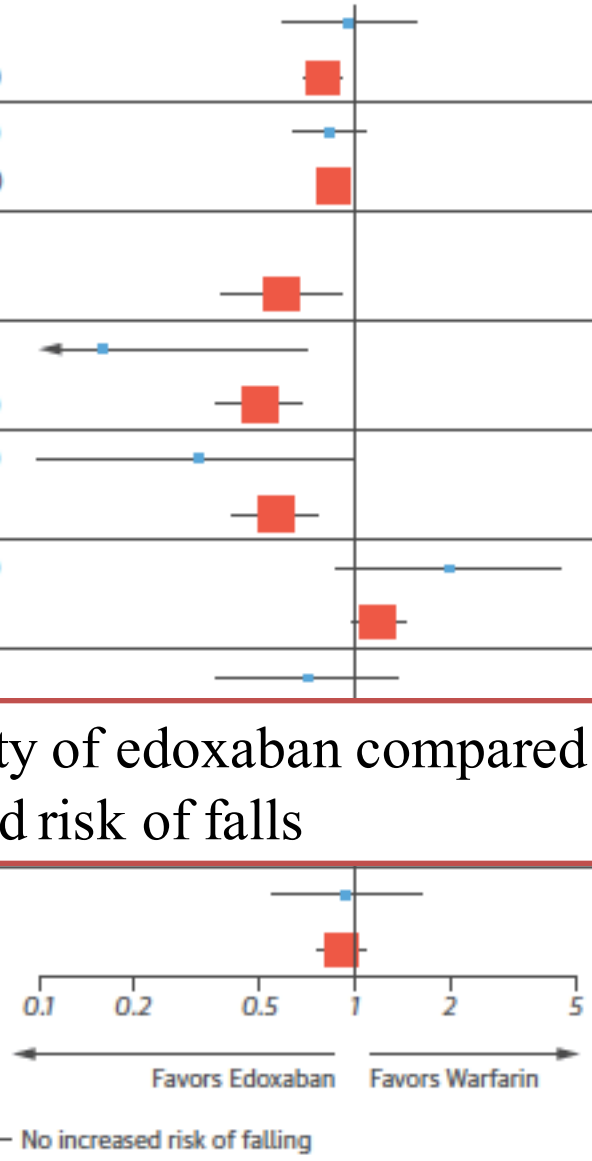
Steffel J, et al. *J Am Coll Cardiol* 2016; 68:1169-78.

FIGURE 2 Safety of HDER Versus Warfarin in Patients With and Without Baseline Increased Risk of Falls

Endpoint	HDER (n= 310)	Warfarin (n= 307)	Adjusted HR (HDER vs Warf)	p-int
Major bleed	31 (5.43%)	34 (5.55%)	0.96 (0.59-1.56)	0.45
	413 (2.77%)	523 (3.5%)	0.79 (0.70-0.90)	
Major / CRNM bleed	103 (21.74%)	127 (26%)	0.83 (0.64-1.08)	0.76
	1472 (10.92%)	1683 (12.72%)	0.86 (0.80-0.93)	
Fatal bleed	0 (0%)	4 (0.64%)		---
	32 (0.21%)	55 (0.36%)	0.59 (0.38-0.91)	
Intracranial hemorrhage	2 (0.33%)	13 (2.08%)	0.16 (0.04-0.71)	0.13
	59 (0.39%)	119 (0.78%)	0.50 (0.37-0.68)	
Life-threatening bleed	4 (0.67%)	13 (2.08%)	0.32 (0.10-0.98)	0.34
	63 (0.41%)	114 (0.74%)	0.56 (0.41-0.76)	
Major gastro-intestinal bleed	17 (2.91%)	9 (1.46%)	1.98 (0.88-4.46)	0.23
	223 (1.48%)	189 (1.24%)	1.19 (0.98-1.45)	
Death or intra-	15 (2.5%)	22 (3.52%)	0.71 (0.37-1.37)	

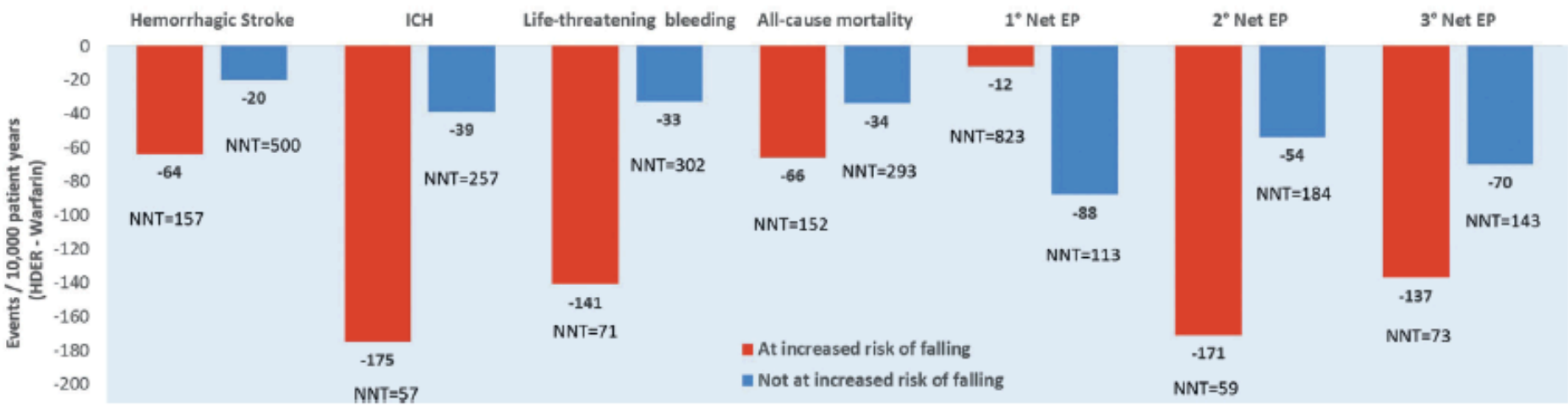
Consistent relative efficacy and safety of edoxaban compared with warfarin in patients with an increased risk of falls

Bone Fracture Due to Falling	25 (4.38%)	27 (4.48%)	0.94 (0.55-1.61)	0.90
	232 (1.55%)	256 (1.7%)	0.91 (0.76-1.09)	



Steffel J, et al. *J Am Coll Cardiol* 2016; 68:1169-78.

CENTRAL ILLUSTRATION **Absolute Risk Reduction of Higher Dose Edoxaban Regimen Compared With Warfarin in Patients at Increased Fall Risk Versus Not at Increased Fall Risk**



Steffel, J. et al. J Am Coll Cardiol. 2016;68(11):1169-78.

EP = endpoint; ICH = intracranial hemorrhage; life-threatening bleeding = ICH or bleeding associated with hemodynamic compromise requiring intervention; NNT = number needed to treat; SEE = systemic embolic event; 1° net clinical EP = death/stroke/SEE/major bleed; 2° net EP 2 = death or disabling stroke or life-threatening bleed; 3° net EP = death or stroke or SEE or life-threatening bleed.

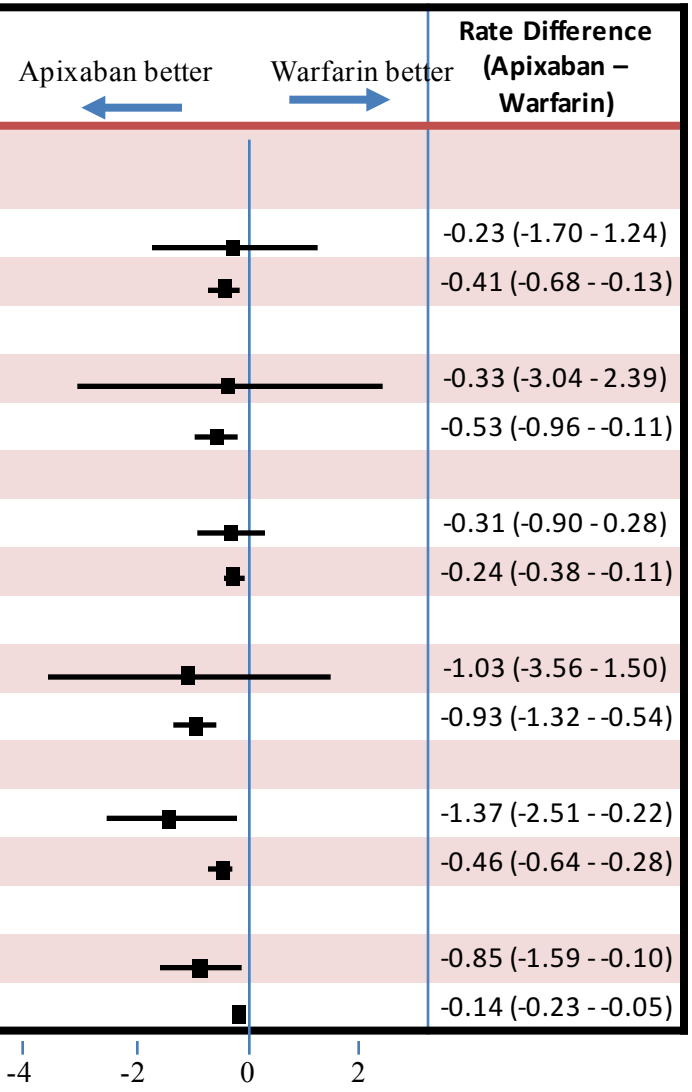
-Because patients at increased risk of falling demonstrate a higher risk of events, treatment with high dose edoxaban resulted in a greater ARR for the most severe bleeding events (i.e., intracranial, life-threatening, or fatal bleeding as compared with patients not at increased risk of falls).

-Fewer than 6 pts would need to be treated for 10 years with edoxaban vs warfarin to prevent either an ICH or occurrence of death, disabling stroke or life-threatening bleeding.

Steffel J, et al. *J Am Coll Cardiol* 2016; 68:1169-78.

No Significant Impact of Fall Risk on Efficacy of Apixaban (ARISTOTLE)

	Apixaban	Warfarin	Rate Difference (Apixaban – Warfarin)
Stroke/Systemic embolism			
History of falls	1.76 (12)	1.99 (13)	-0.23 (-1.70 - 1.24)
No history of falls	1.23 (177)	1.63 (234)	-0.41 (-0.68 - -0.13)
Death from any cause			
History of falls	6.41 (45)	6.74 (45)	-0.33 (-3.04 - 2.39)
No history of falls	3.17 (469)	3.71 (546)	-0.53 (-0.96 - -0.11)
Hemorrhagic stroke			
History of falls	0.14 (1)	0.45 (3)	-0.31 (-0.90 - 0.28)
No history of falls	0.23 (3/)	0.47 (68)	-0.24 (-0.38 - -0.11)
Major bleeding			
History of falls	4.35 (26)	5.38 (31)	-1.03 (-3.56 - 1.50)
No history of falls	2.07 (274)	3.00 (389)	-0.93 (-1.32 - -0.54)
Intracranial bleeding			
History of falls	0.33 (2)	1.69 (10)	-1.37 (-2.51 - -0.22)
No history of falls	0.32 (43)	0.78 (103)	-0.46 (-0.64 - -0.28)
Subdural bleeding			
History of falls	0.00 (0)	0.85 (5)	-0.85 (-1.59 - -0.10)
No history of falls	0.07 (9)	0.21 (27)	-0.14 (-0.23 - -0.05)



Benefits of apixaban over warfarin preserved: 80% reduction in intracranial bleeding;

Rao MP, et al. *Am J Med* 2018; 131:269-75.

"Frail patients at risk of falls should receive the lower dose of NOACs."

Conclusion:

There is no compelling evidence to support this statement. Indeed, the number needed to treat to prevent thromboembolic events with appropriately dosed NOACs appears to be substantially lower among patients with increased risk of falls compared to those without such risk.

90 year-old Female with Asymptomatic AF on Pacemaker

Weight 70kg; Creat Cl 60mlmin; no valvular disease on echo

Do you:

A. ~~Continue her ASA: her fall risk is too high~~

B. Start a DOAC with dose reduction?

C. Start DOAC without a dose reduction?

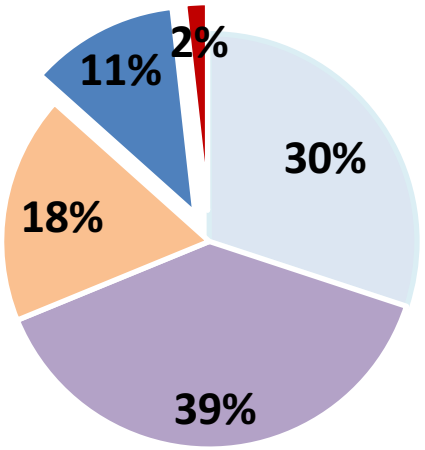
D. ~~Start warfarin~~

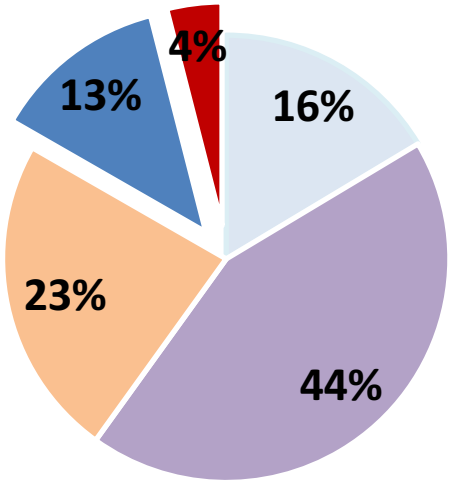
It Depends…

NOAC benefits clearly outweigh risks in very elderly people (over 80 years old and even over 85 years).

Proportion of Patients ≥80 and ≥85 Years in Major NOAC Trials

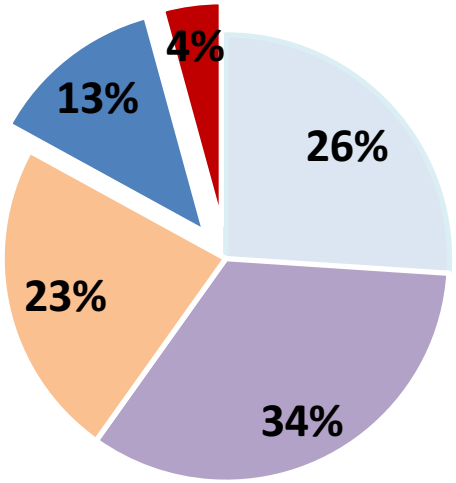
ARISTOTLE
Apixaban
N=18,201
≥80 yrs: n=2,436
≥85 yrs: n=322

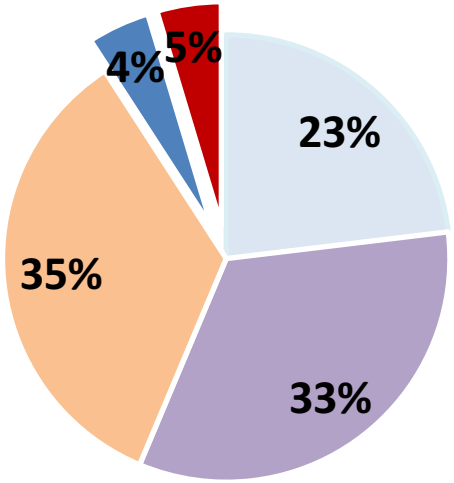




RE-LY
Dabigatran
n=18,113
≥80 yrs: n=3,027
≥85 yrs: n=722

ENGAGE AF-TIMI 48
Edoxaban
n=21,105
≥80 yrs: n=3,591
≥85 yrs: n=899





ROCKET-AF
Rivaroxaban
n=14,624
≥80 yrs: n=1,305
≥85 yrs: n=622

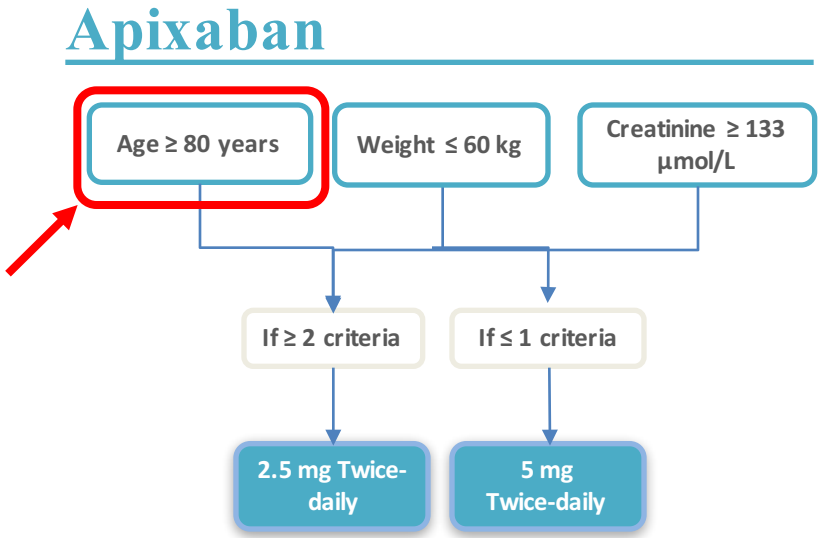
Adapted from Kato ET, et al. *Ageing Res Rev* 2019; 49:115-24.

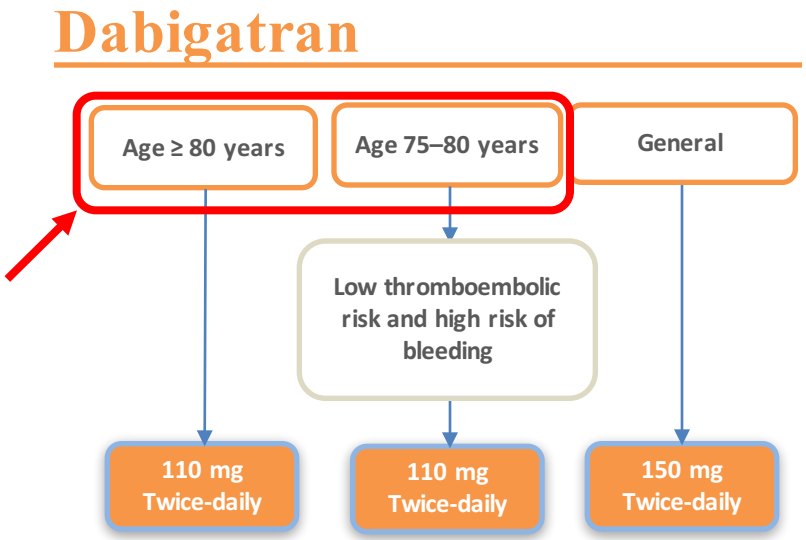
Numbers of Patients ≥80 and ≥85 Years in Major NOAC Trials

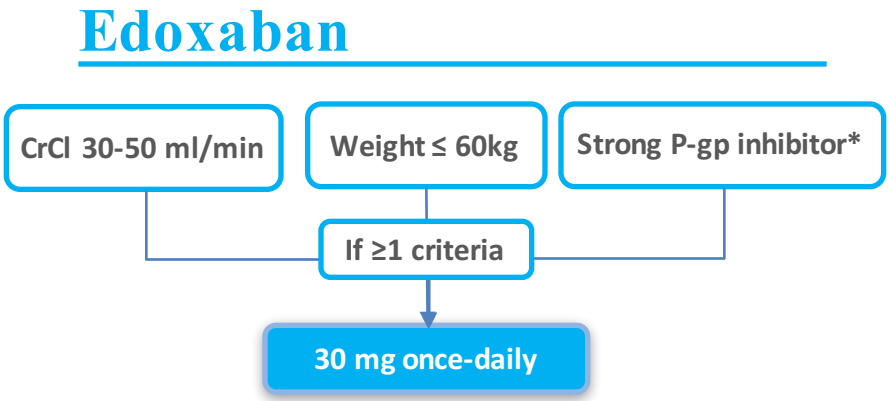
Study	Total N	n ≥80 Years	n ≥85 Years
ARISTOTLE (apixaban)	18,201	2,436	322
RE-LY (dabigatran)	18,113	3,027	722
ENGAGE AF-TIMI 48 (edoxaban)	21,105	3,591	899
ROCKET-AF (rivaroxaban)	14,624	1,305	622
Total, 4 studies	**72,043**	**10,359**	**2,565**

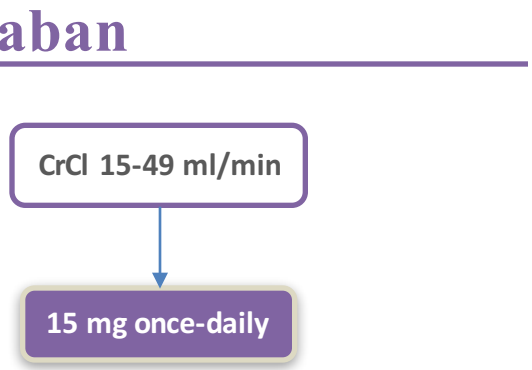
Adapted from Kato ET, et al. *Ageing Res Rev* 2019; 49:115-24.

No Specific Frailty / Fall Criteria for NOAC Dose Reduction



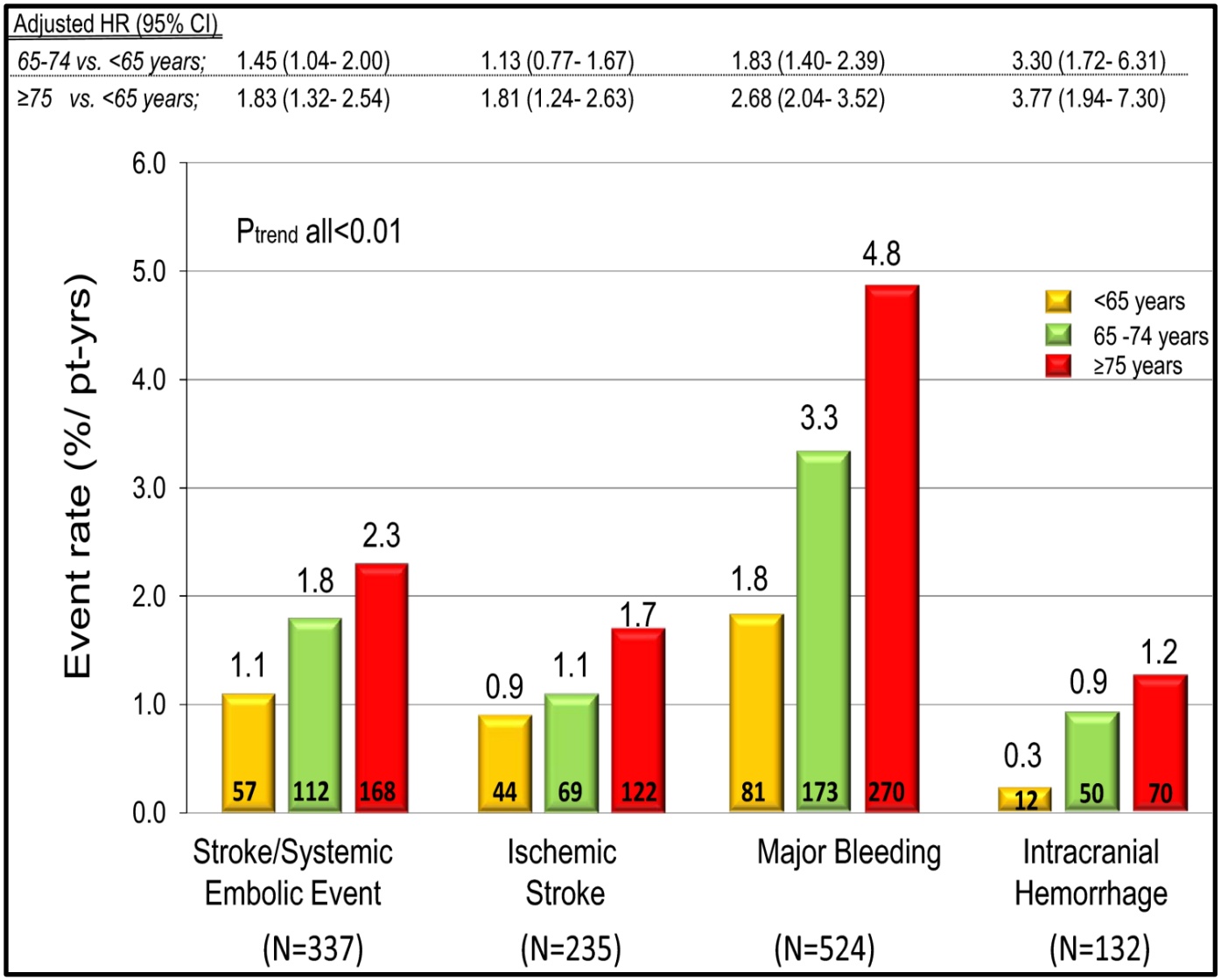






CrCl: creatinine clearance; P-gp: P-glycoprotein - *Except verapamil and amiodarone
From current Canadian product monographs.

Efficacy and Safety of Edoxaban in Elderly Patients With Atrial Fibrillation in the ENGAGE AF–TIMI 48 Trial



Kato ET, et al. *J Am Heart Ass*

Efficacy and Safety of Edoxaban in Elderly Patients With Atrial Fibrillation in the ENGAGE AF–TIMI 48 Trial

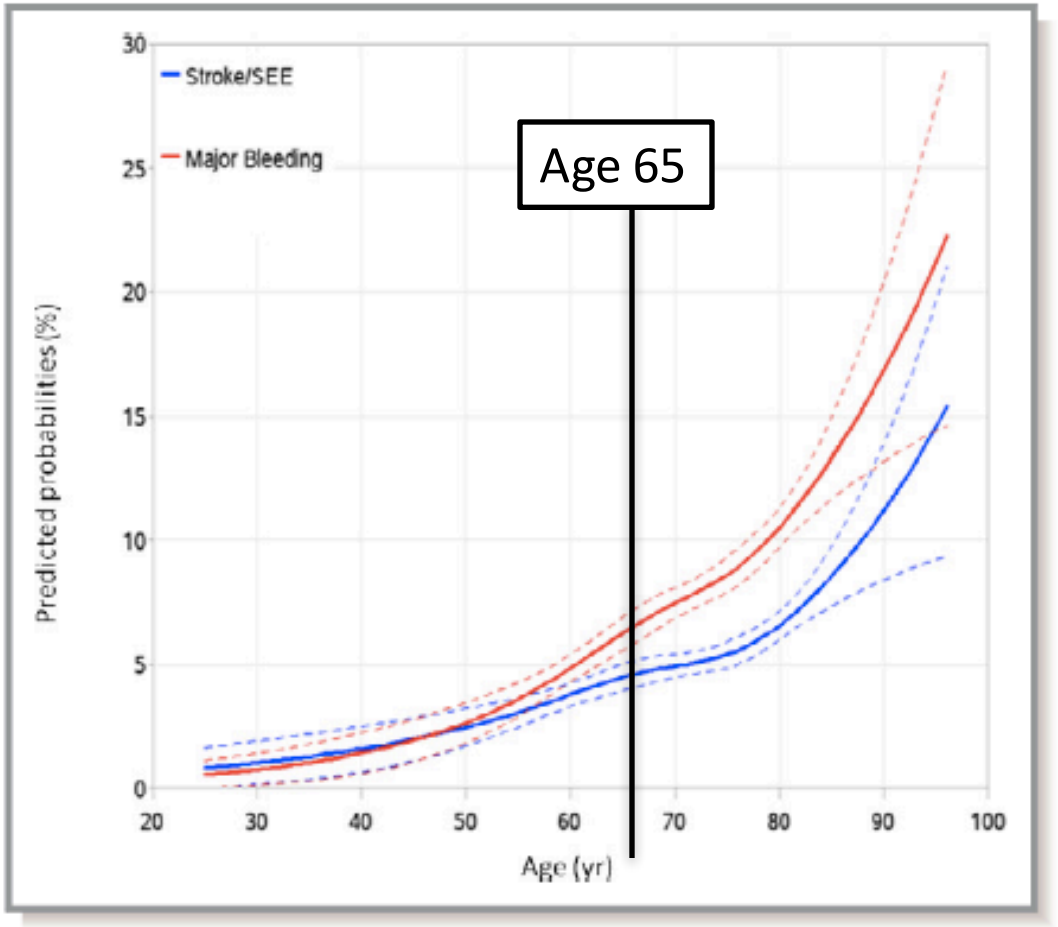


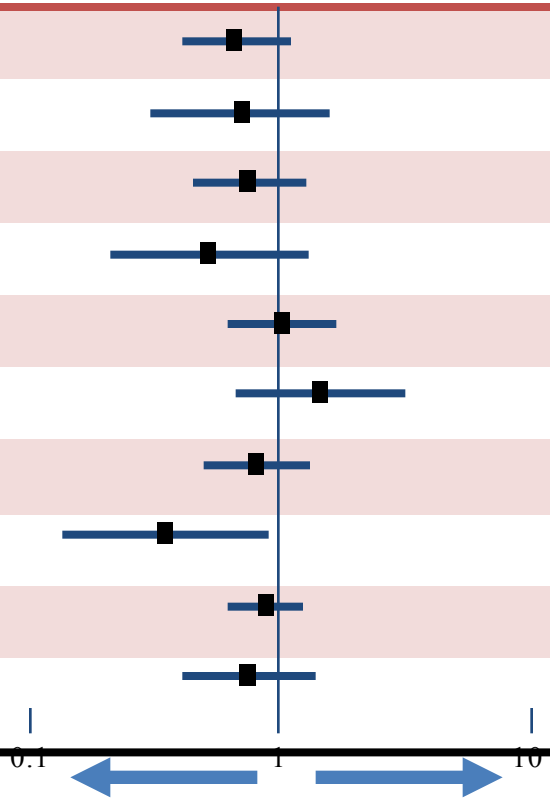
Figure 2. Calculated probabilities by continuous age. The outcomes were analyzed by age as a continuous variable for stroke or SEE (blue line) and major bleeding (red line). The dotted lines represent the 95% CI. SEE indicates systemic embolic event.

-Age has a greater impact on bleeding: as age increases, the slope for major bleeding increases more sharply than the corresponding slope for stroke, particularly > age 75

Kato ET, et al. *J Am Heart Ass*

Antithrombotic Efficacy (Stroke/SEE) of NOACs vs. Warfarin in Subgroups 80-84 and ≥85 Years in Major NOAC Trials

Trial	Age (yrs)	HR (95% CI)	$P_{interaction}$ *
RE-LY (150 mg)	80-84	0.67 (0.41, 1.10)	0.996
	≥85	0.70 (0.31, 1.57)	
RE-LY (110 mg)	80-84	0.75 (0.46, 1.23)	0.39
	≥85	0.52 (0.21, 1.29)	
ROCKET AF	>80	0.91 (0.60, 1.40)	0.31†
	≥85	0.92 (0.34, 2.47)	
ARISTOTLE	≥80	0.81 (0.51, 1.29)	0.74 §
	≥85	0.35 (0.14, 0.89)	NA
ENGAGE AF-TIMI48 (60/30mg)	≥80	0.88 (0.64, 1.20)	0.39 §
	≥85	0.73 (0.40, 1.33)	0.68¶

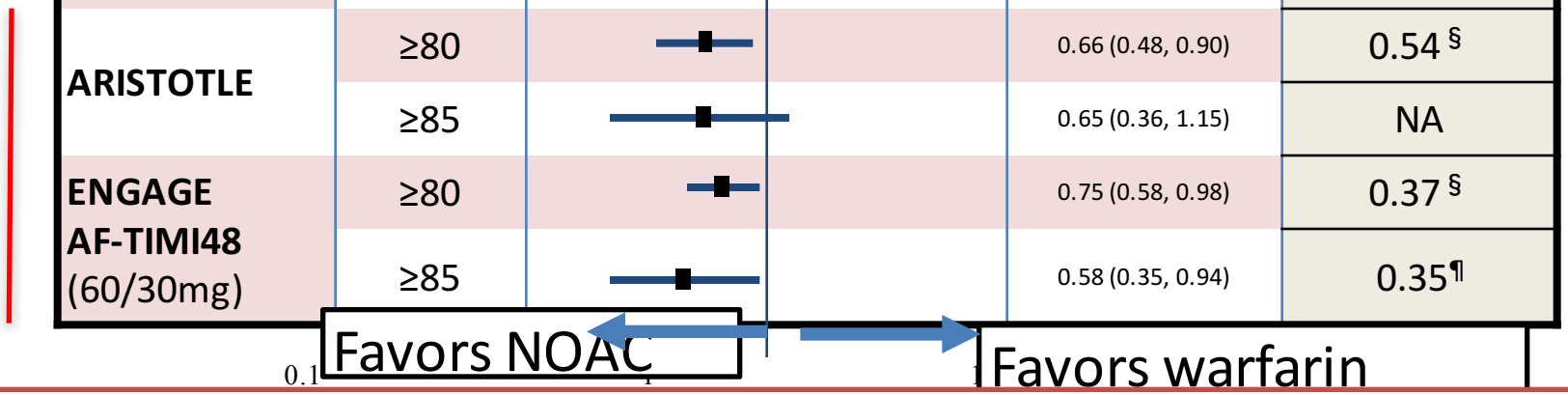


*$P_{interaction}$ represents interaction between age and treatment. †indicates $P_{interaction}$ between age (age cut point at 75 years) and treatment, ‡indicates $P_{interaction}$ between age (age cut point at <65 years, 65–74 years, and ≥75 years) and treatment, §indicates $P_{interaction}$ between age (age cut point at 80 years), and ¶indicates $P_{interaction}$ between age (age cut point at 85 years). Otherwise, $P_{interaction}$ represents interaction between age and treatment at the shown age cut points.

Adapted from Kato ET, et al. *Ageing Res Rev* 2019; 49:115-24.

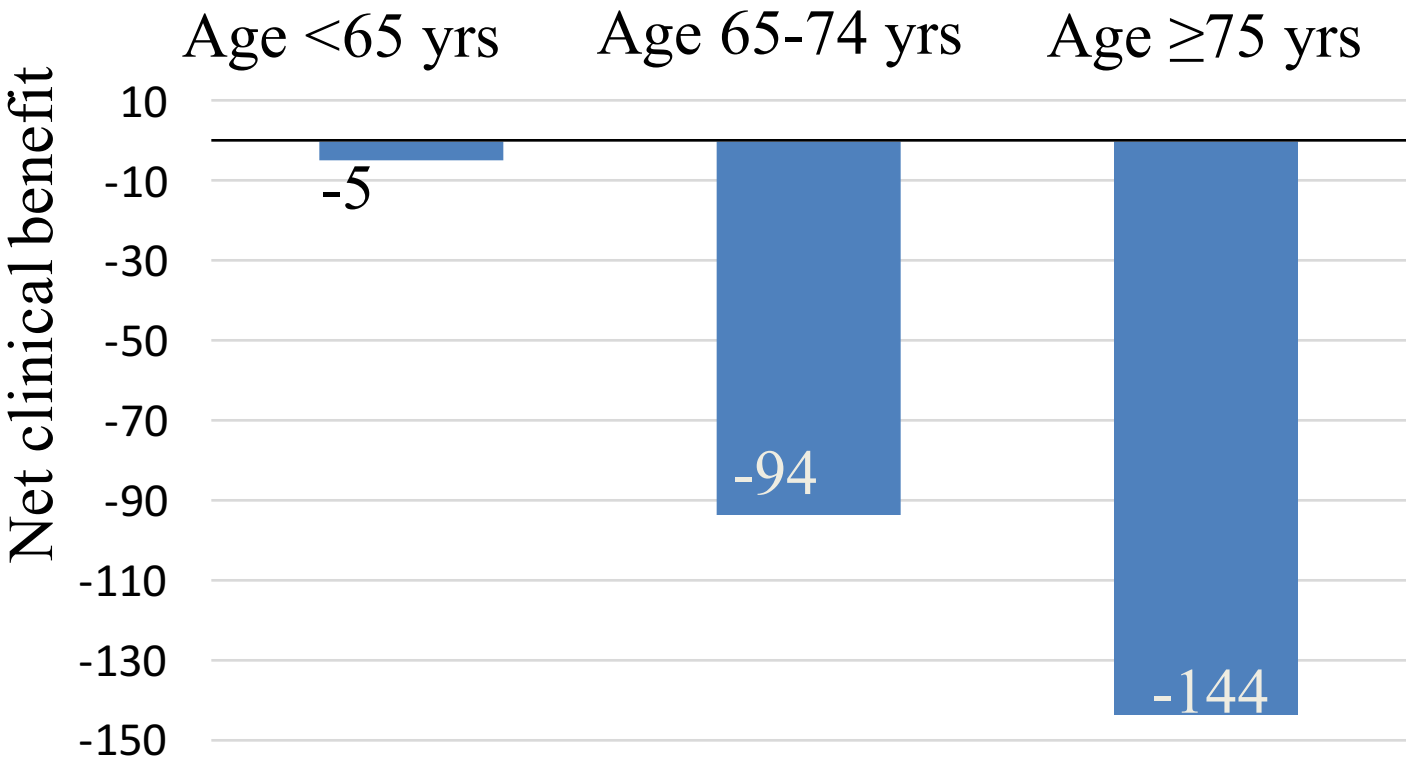
Safety (Major Bleeding) of NOACs vs. Warfarin in Subgroups 80-84 and ≥85 Years in Major NOAC Trials

Trial	Age (yrs)	HR (95% CI)	$P_{interaction}$ *
RE-LY (150 mg)	80-84	1.41 (1.02, 1.94)	0.001
	≥85	1.22 (0.74, 2.02)	
RE-LY (110 mg)	80-84	1.18 (0.84, 1.65)	0.006
	≥85	1.01 (0.59, 1.73)	
ROCKET AF	>80	1.20 (1.04, 1.40)	0.009†
	≥85	1.13 (0.84, 1.52)	
ARISTOTLE	≥80	0.66 (0.48, 0.90)	0.54 §
	≥85	0.65 (0.36, 1.15)	NA
ENGAGE AF-TIMI48 (60/30mg)	≥80	0.75 (0.58, 0.98)	0.37 §
	≥85	0.58 (0.35, 0.94)	0.35¶



Because a stronger association with age is observed with bleeding than with ischemic events, the net benefit of apixaban and adoxaban over warfarin is greater in elderly patients compared to younger

Greater Net Clinical Benefit* of Edoxaban in Older Age Groups in ENGAGE AF-TIMI 48



Due to the higher thromboembolic and particularly bleeding risk in the elderly as compared to younger patients, the absolute benefits of edoxaban over warfarin were more marked in older patients.

*Incorporating death, stroke; systemic embolic events, major bleeding

Kato ET, et al. *J Am Heart Assoc* 2016; 5(5).

"NOAC benefits clearly outweigh risks in very elderly people (over 80 years old and even over 85 years)."

Conclusion:

The evidence base for NOACs clearly shows a continued (and potentially even stronger) treatment effect for overall clinical benefit among older adults.

-There is a caveat that the proportion of very elderly patients in the major NOAC clinical trials was fairly low.

Case: 46M

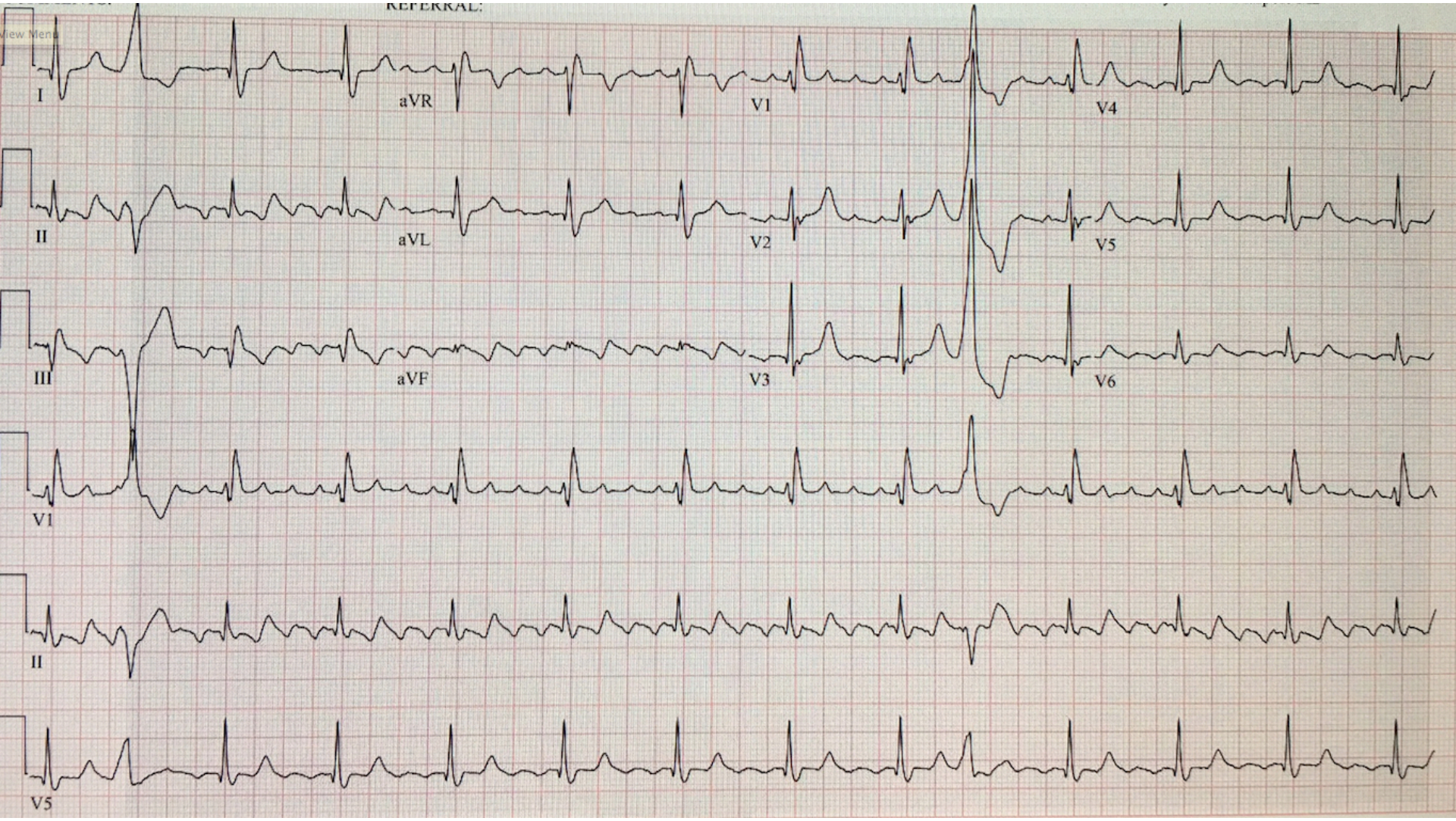
Medical history:

GI bleeding s/p right anterior hemicolectomy from infectious CMV colitis

DM-1 on insulin, htn, glaucoma, chronic renal failure

Medications: ASA 80mg Qd, rosuvastatin 10mg Qd, candesartan 8mg Qd, sevalamer, pantoprazole

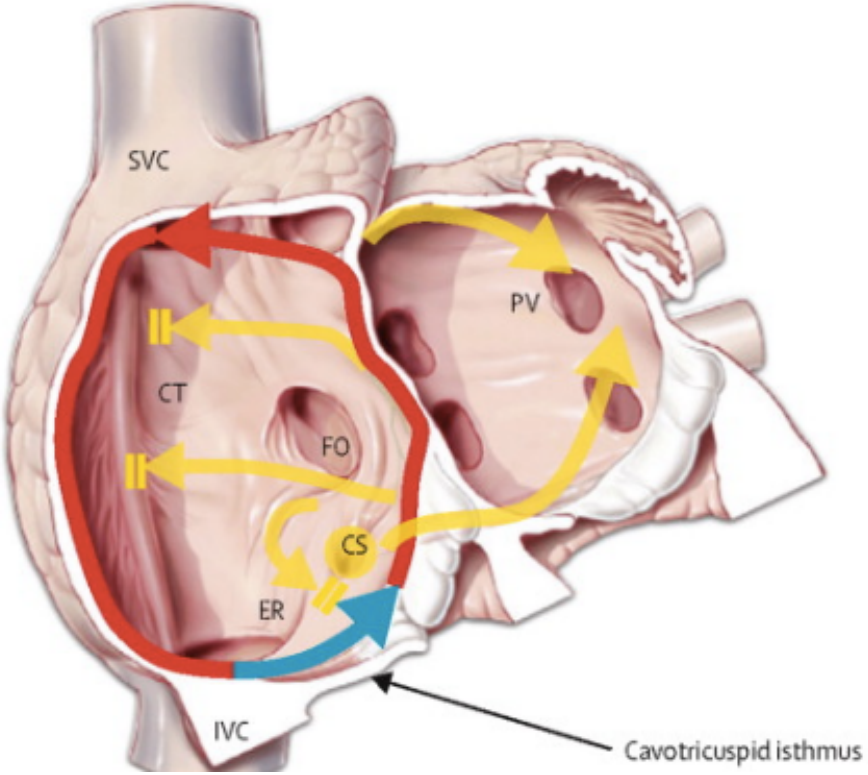
Patient has a high risk of bleeding! What next?

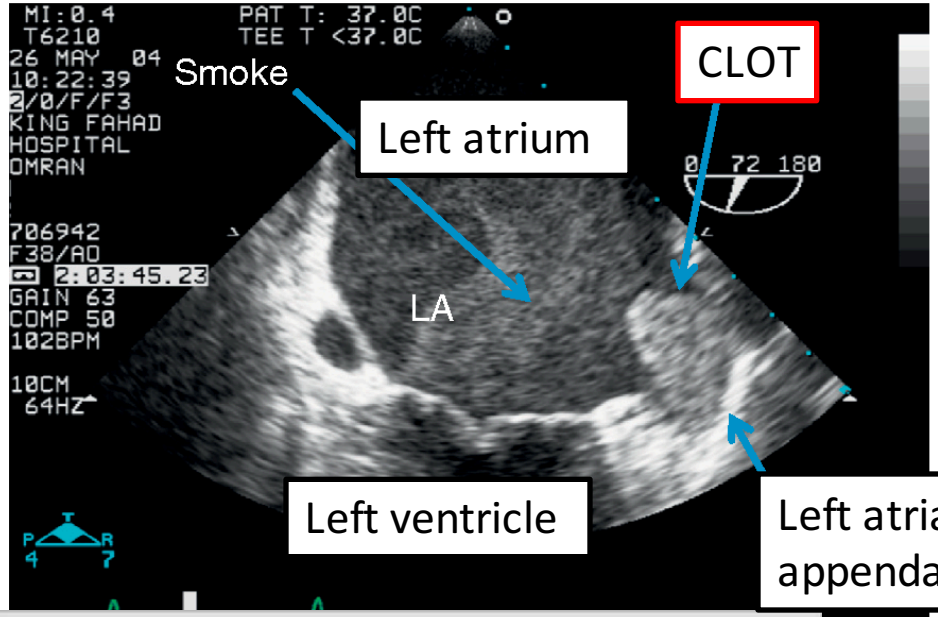

I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6
V1
II
V5

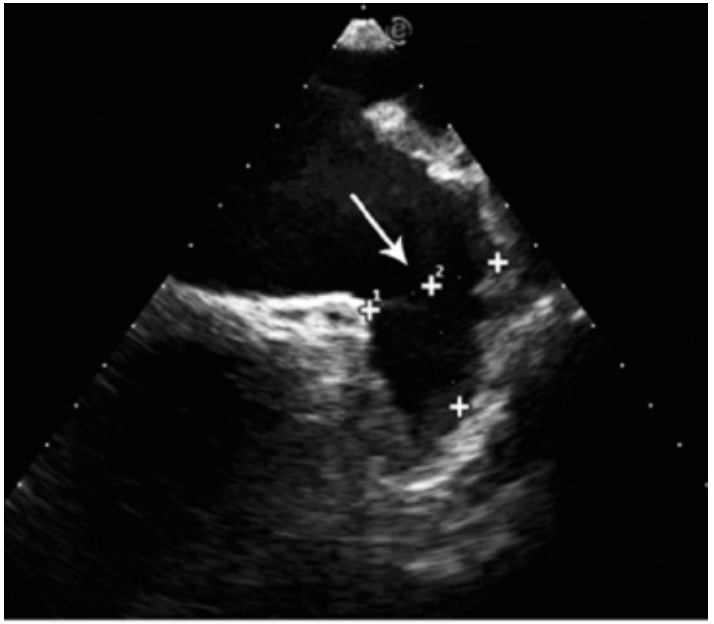
Case: 46M

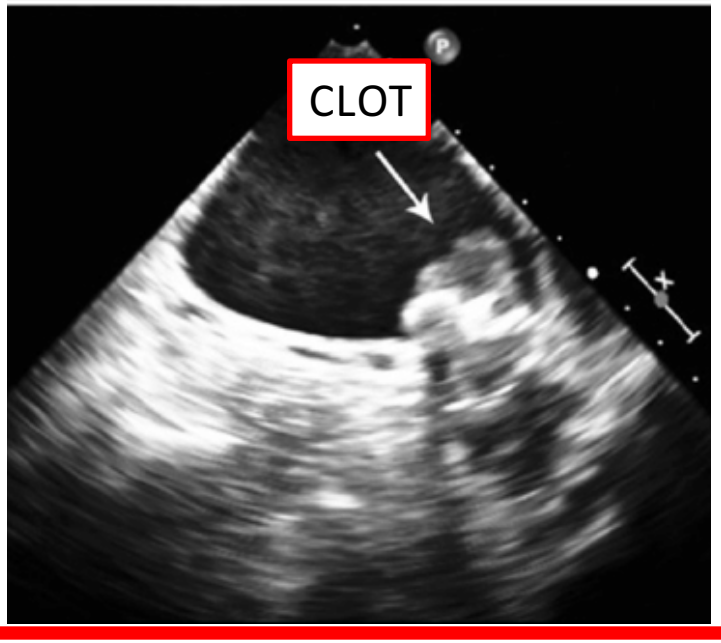
PLAN:

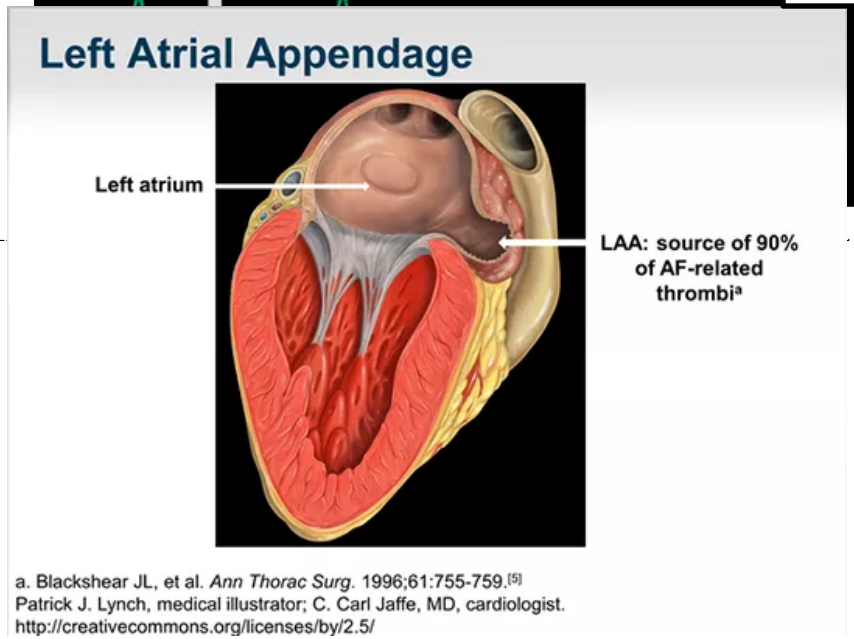
Typical Flutter ablation + Watchman Implant during same procedure



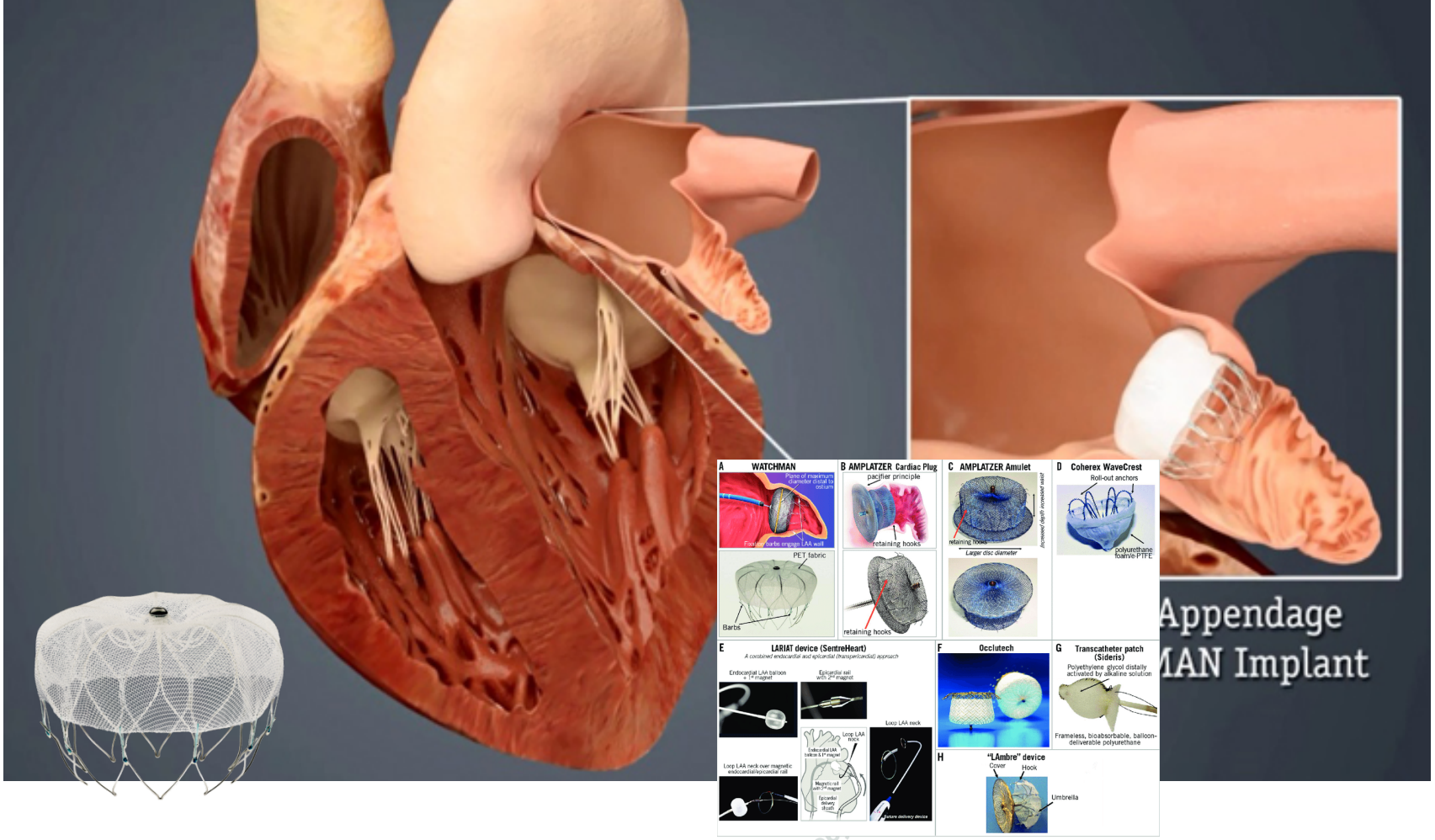








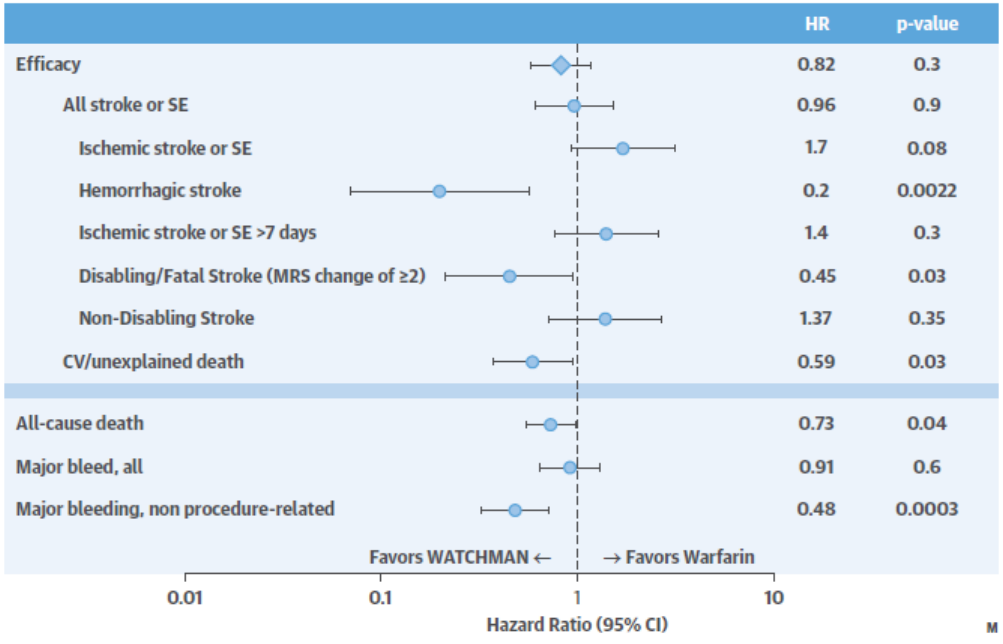
During atrial fibrillation blood clots can form within left atrial appendage; these can break off and cause stroke and systemic emboli



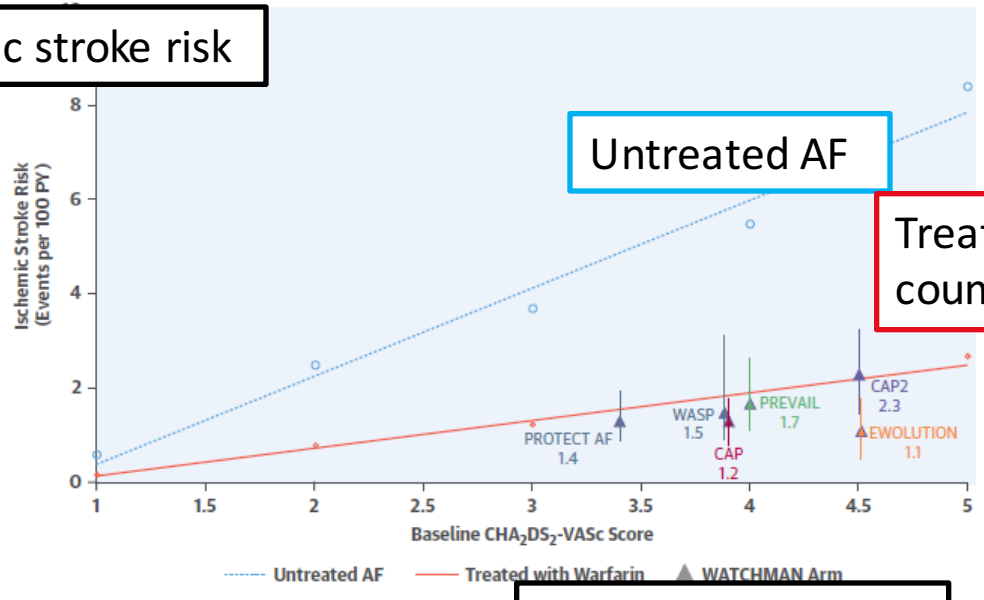
Left atrial appendage occlusion is a minimally-invasive procedure performed in the cath/EP lab.

Indicated in patients who are at increased risk for stroke (based on CHADS score) but are unable to take an oral anticoagulant.

CENTRAL ILLUSTRATION Stroke Prevention in Nonvalvular Atrial Fibrillation With LAA Closure



Ischemic stroke risk



CHA2DS2-VASc score

Reddy, V.Y. et al. J Am Coll Cardiol. 2017;70(24):2964–75.

5-year combined outcomes of PREVAIL and PROTECT trials

Left atrial appendage closure provides stroke prevention in nonvalvular AF comparable to warfarin, with additional reductions in major bleeding (particularly hemorrhagic stroke) and mortality

TABLE 2. AVERAGE DISCOUNTED LIFETIME COST OF STROKE PREVENTION TREATMENTS IN AF	
Warfarin	$21,429
Dabigatran	$25,760
LAA occlusion	$27,003
Note: Analysis performed from perspective of Ontario Ministry of Health and Long Term Care, the third-party payer for insured health services in Ontario, Canada.	