



Contemporary management of Atrial Fibrillation for the Hospitalist

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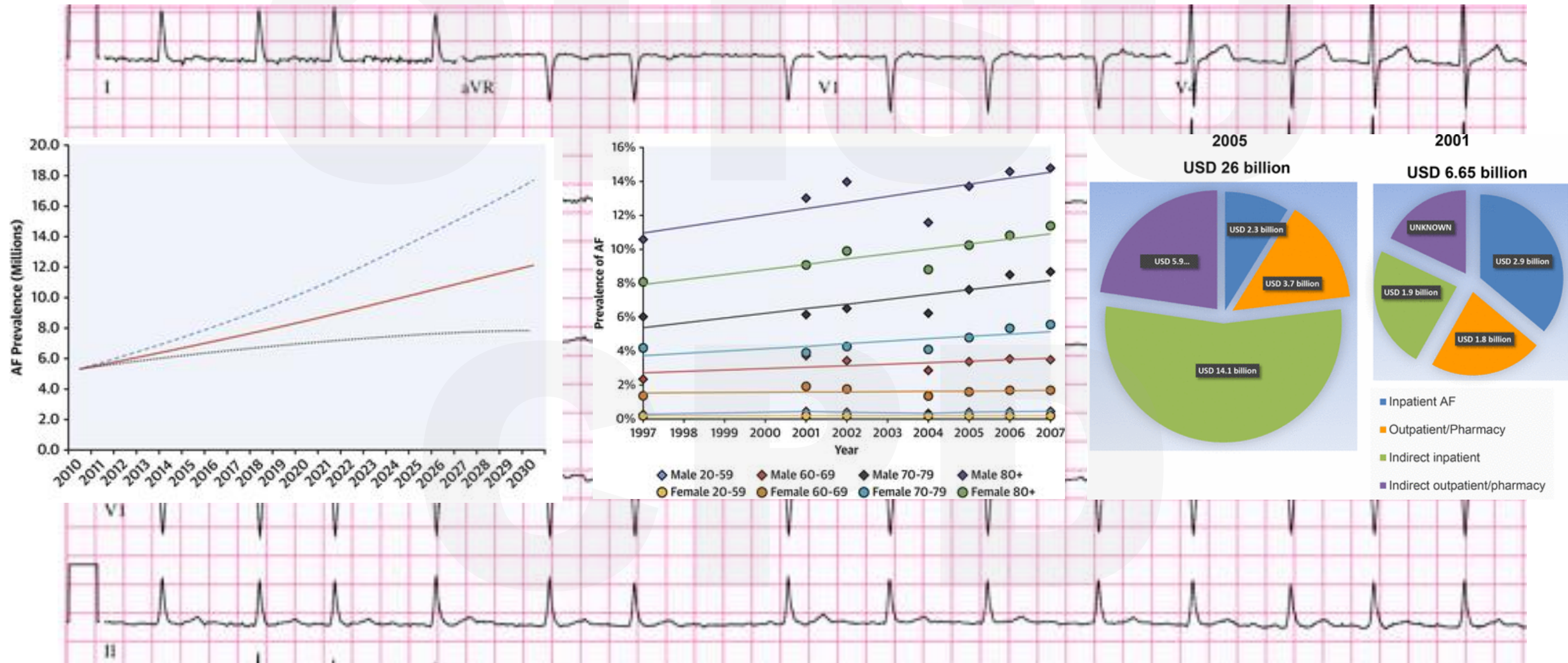
Disclosure

- None relevant

Overview

- Understand key updates from the 2023 ACC/AHA/ACCP/HRS guidelines
- Perform rapid hospital-based evaluation and initial management of AF
- Apply stroke-risk and anticoagulation recommendations
- Know when to involve electrophysiology (ablation, cardioversion, device therapy)

Public enemy #1



2023 ACC/AHA/ACCP/HRS Guideline for the Diagnosis and Management of Atrial Fibrillation

A Report of the American College of Cardiology/American Heart Association
Joint Committee on Clinical Practice Guidelines

*Developed in Collaboration With and Endorsed by the American College of Clinical Pharmacy
and the Heart Rhythm Society*



- 170 pages
- 1616 references

Writing
Committee
Members*

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SOCIETAL STATEMENT

2023 Atrial Fibrillation Guideline-at-a-Glance



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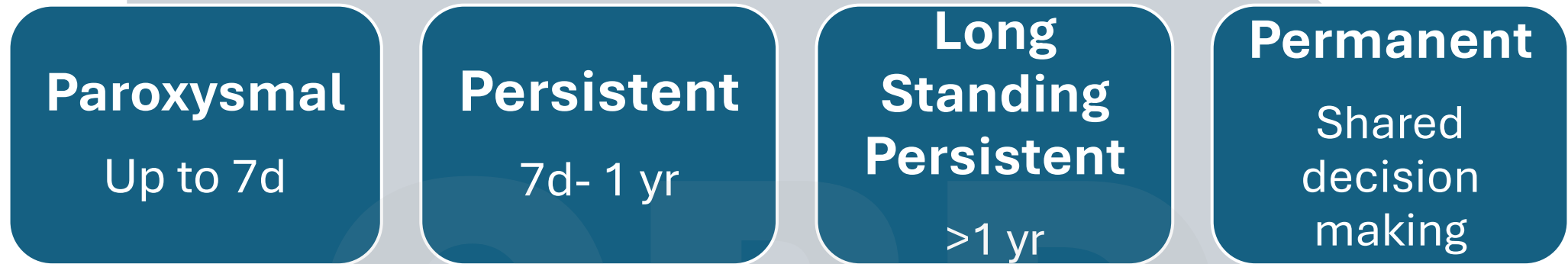
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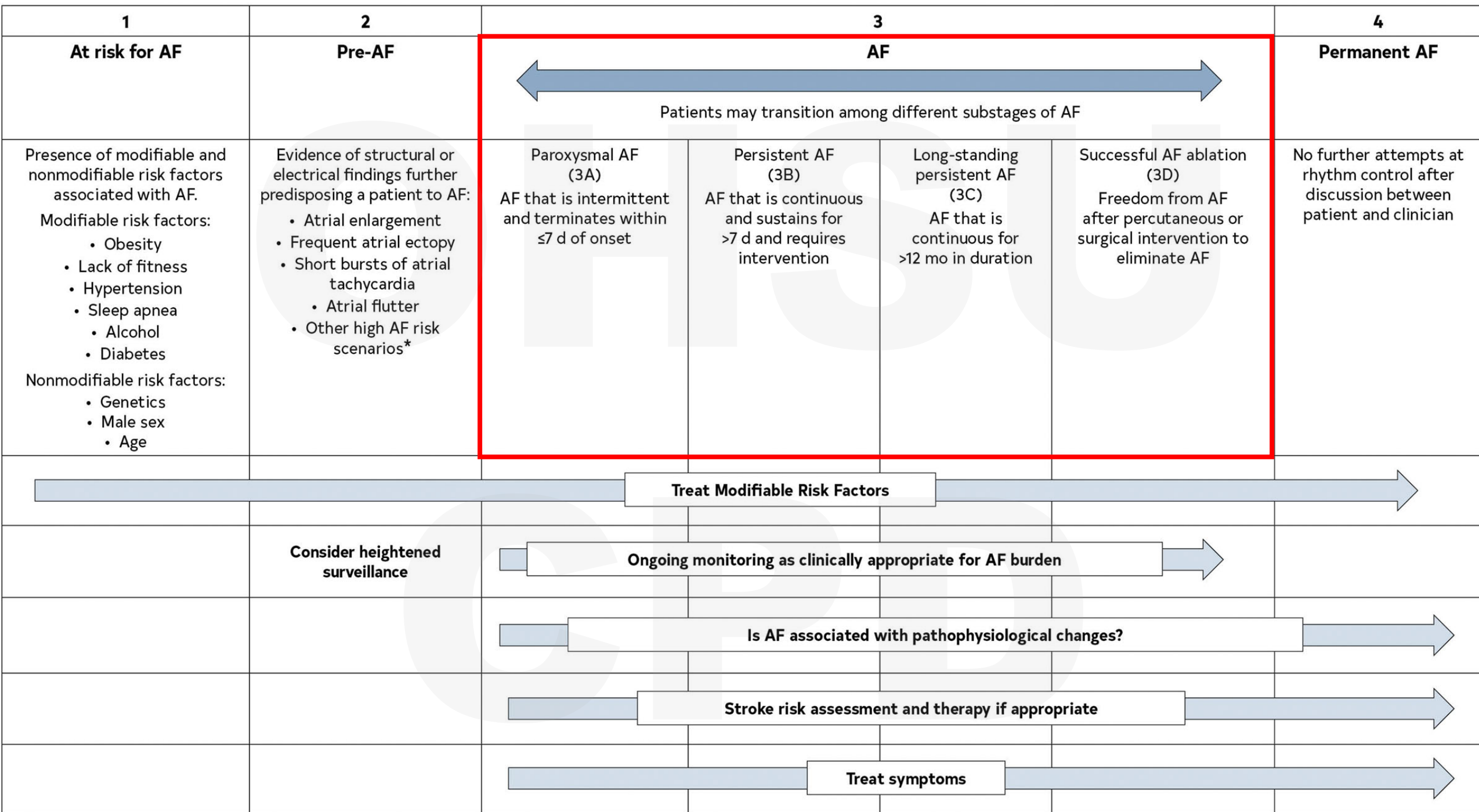
¶Heart Rhythm Society representative.

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**ACC/AHA Joint Committee on Clinical Data Standards liaison.

Natural History of AF





Primary AF vs. secondary to medical causes

- Rapid rates secondary to medical conditions (usually pre existent AF) e.g. sepsis, Heart failure, bleeding, PE
 - Treat underlying cause
 - CV only after primary condition is addressed
 - Lenient rate control
- Primary arrhythmia i.e. sudden onset AF/AFL

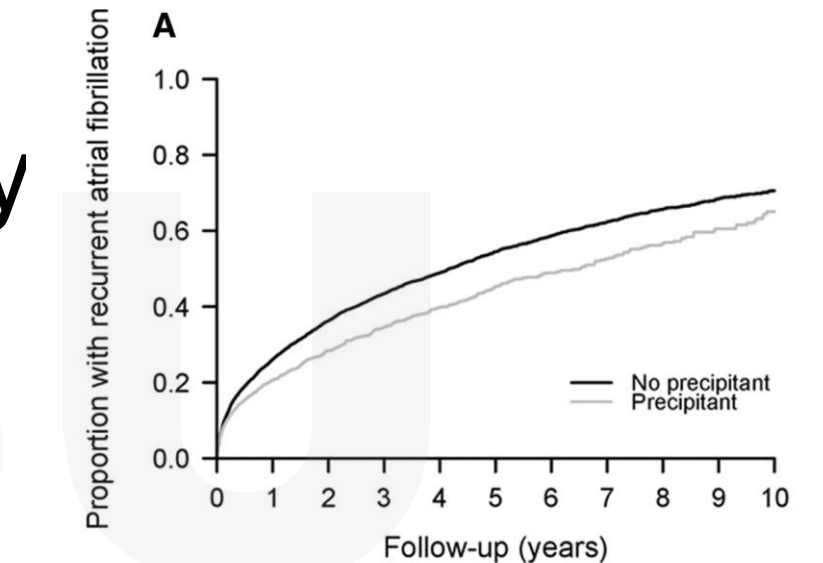
Acute Medical Illness or Surgery



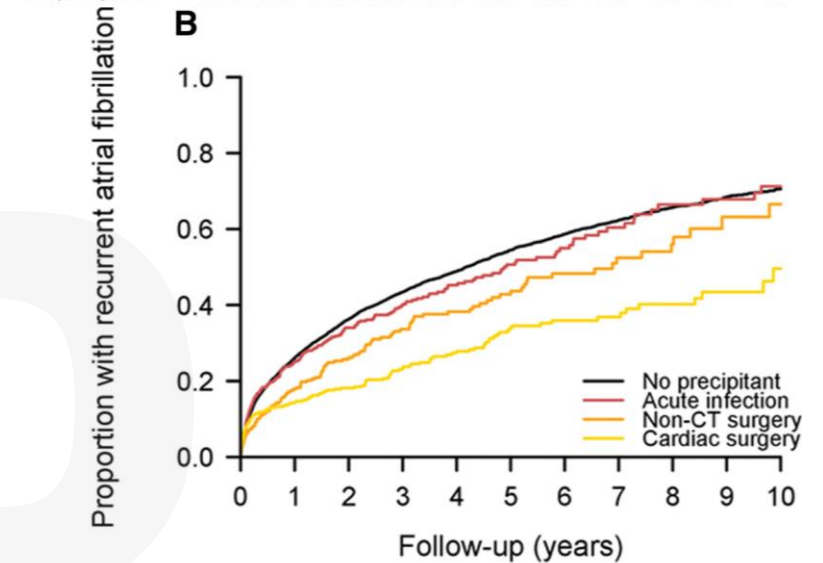
2. In patients with AF who are identified in the setting of acute medical illness or surgery, outpatient follow-up for thromboembolic risk stratification and decision-making on OAC initiation or continuation, as well as AF surveillance, can be beneficial given a high risk of AF recurrence.⁴⁻⁹



4. In patients who develop postoperative AF after cardiac surgery, it is reasonable to administer anti-coagulation when deemed safe in regard to surgical bleeding for 60 days after surgery unless complications develop and to reevaluate the need for longer term anticoagulation at that time.^{5,7}



No. at risk	8634	5543	4042	2944	2149	1513	1070	705	496	347	245
No precipitant											



No. at risk	8634	5543	4042	2944	2149	1513	1070	705	496	347	245
Absent											
Acute infection	637	367	235	163	112	82	54	37	25	21	15
Non-CT surgery	321	217	174	121	89	67	47	33	23	12	8
Cardiac surgery	459	348	279	216	164	116	81	60	40	29	15

*Lubitz et al. Circ 2015

Basic evaluation after initial diagnosis

COR	LOE	Recommendations
1	B-NR	1. In patients with newly diagnosed AF, <u>a transthoracic echocardiogram¹⁻⁴ to assess cardiac structure,</u> <u>laboratory testing to include a complete blood count, metabolic panel, and thyroid function,⁵⁻⁷</u> and when clinical suspicion exists, targeted testing to assess for other medical conditions associated with AF are recommended to determine stroke and bleeding risk factors, as well as underlying conditions that will guide further management.
3: No benefit	B-NR	2. In patients with newly diagnosed AF, <u>protocolized testing for ischemia, acute coronary syndrome (ACS), and pulmonary embolism (PE) should not</u> routinely be performed to assess the etiology of AF unless there are additional signs or symptoms to indicate those disorders. ⁸⁻¹⁰

Is the patient unstable

- Instability due to primary AF is uncommon except for AF with WPW
 - Ischemia
 - Heart Failure
 - Pulmonary edema
 - Sepsis
- **Urgent CV**

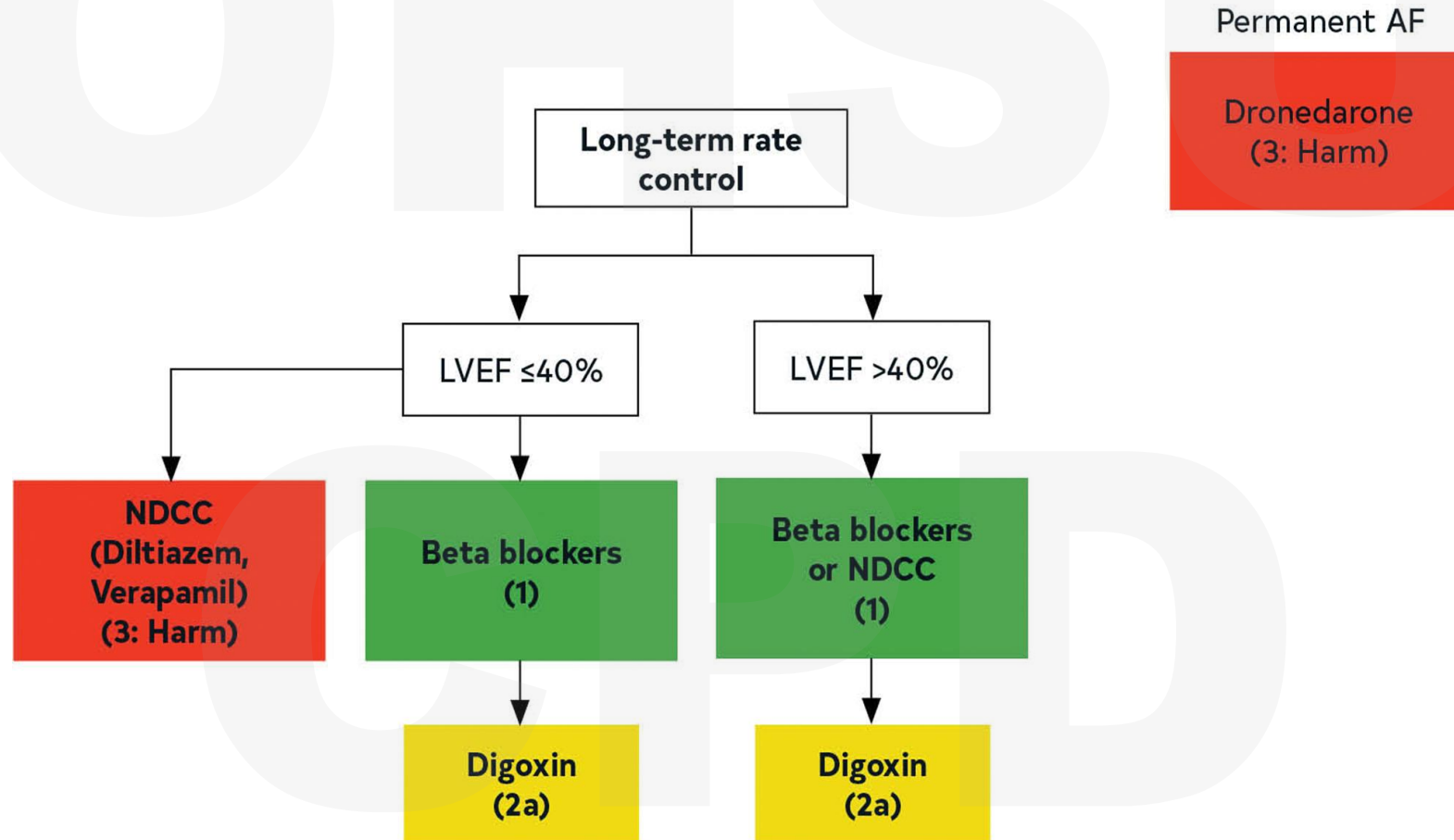
Is it safe to cardiovert?

- Adequately anticoagulated for 3 weeks
- If NOT anticoagulated for 3 weeks, it is safe to cardiovert IF-
 - Onset within 48 hrs
 - No thrombus by TEE or CTA
- Unstable

Rate control for select patients

- Calcium channel blockers and beta blockers 1st line
 - - Consider iv digoxin
- Calcium channel blocker- *avoid if heart failure*
 - Diltiazem
 - Verapamil
- Beta blocker- iv metoprolol
- Digoxin is 2nd line (does not cause hypotension)
- Average Heart Rate target <110 bpm in general

Rate control at discharge



Acute Rhythm Control Pharmacology

- Procainamide
- Ibutilide
- PO Flecainide
- Amiodarone- not recommended (delayed and inconsistent)

****Consider CV*****

Patient preference

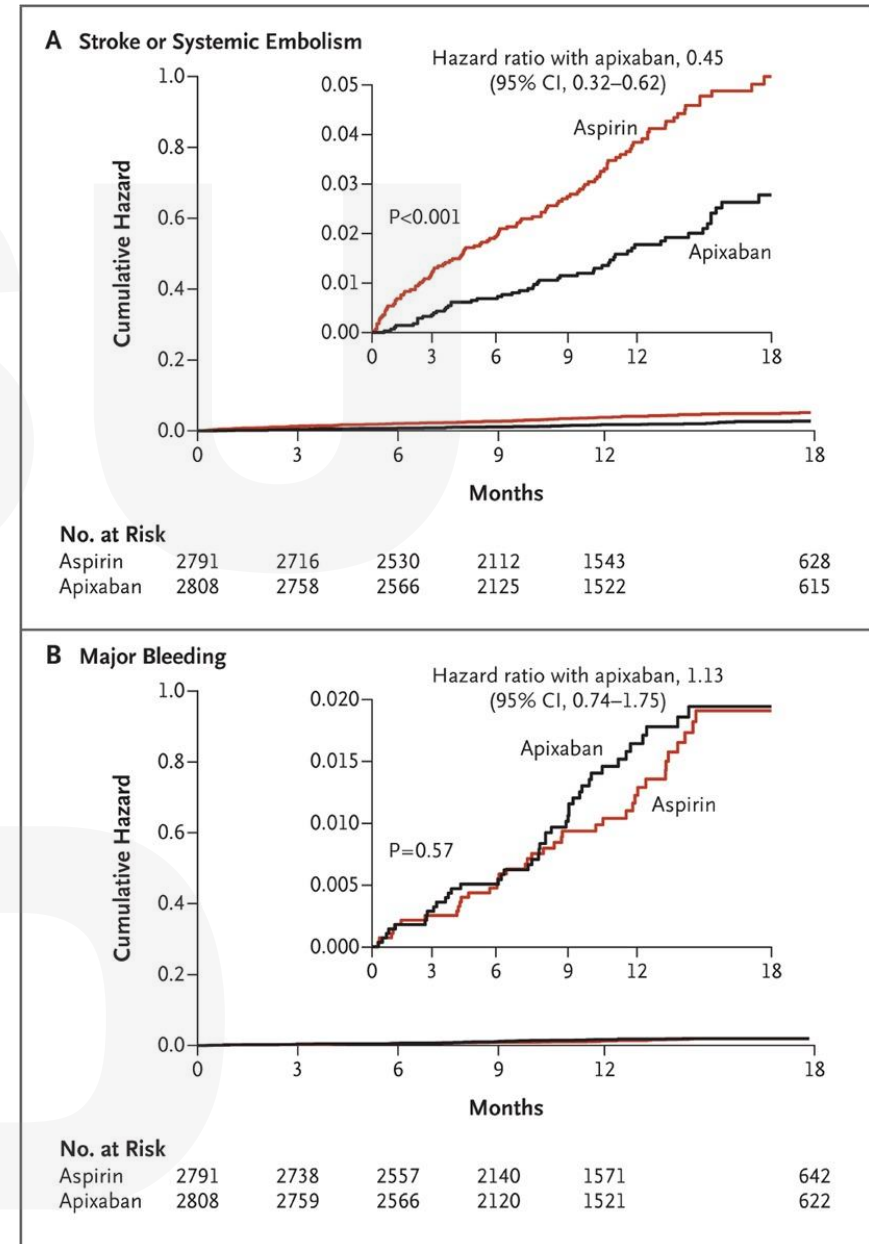
Pre- excited AF (WPW)

- Urgent CV
- IV procainamide /ibutilide
- Avoid AV nodal agents
- EP emergency!



Anticoagulation- who?

- Valvular AF- moderate-severe mitral stenosis, mechanical valve
- Hypertrophic Cardiomyopathy
- Non valvular atrial fibrillation:
 - CHA2DS2Vasc- 0- **No**
 - CHA2DS2Vasc- 1 (not gender) – **Maybe, Class IIa**
 - CHA2DS2Vasc ≥ 2 – **Yes, Class I**
- 4 weeks post CV
- Aspirin- reduced efficacy with similar bleeding



January et al JACC 2014
Connolly et al NEJM 2011

Table 8. Three Validated Risk Models for Stroke

Risk Factor	CHA ₂ DS ₂ -VASc ²	ATRIA ¹	GARFIELD ³
Age ≥85 y		6	0.98
Age ≥75 y	2	5	0.59
Age 65-74 y	1	3	0.20
Female sex	1	1	
Hypertension	1	1	0.16
Renal disease		1	0.35
Diabetes	1	1	0.21
Current smoking			0.48
Congestive heart failure	1	1	0.23
Previous stroke or TIA	2	2-8*	0.80
Vascular disease	1		0.20
Dementia			0.51
Previous bleeding			0.30
Proteinuria		1	
Low risk score	0	0-5	0-0.89
Intermediate risk score	1	6	0.90-1.59
High risk score	≥2	7-15	≥1.60
C-index (11)	0.63	0.66	-
C-index (13)	0.67	-	0.71

*8 points if age <65 y; 4 points if age 65-74 y; 2 points if age 75-84 y; and 3 points if ≥85 y.

ATRIA indicates Anticoagulation and Risk Factors in Atrial Fibrillation: anemia, renal disease, elderly (age ≥75 y), any previous bleeding, hypertension; CHA₂DS₂-VASc, indicates congestive heart failure, hypertension, age ≥75 y (doubled), diabetes mellitus, prior stroke or transient ischemic attack or thromboembolism (doubled), vascular disease, age 65 to 74 y, sex category; GARFIELD-AF, Global Anticoagulant Registry in the Field-Atrial Fibrillation; and TIA, transient ischemic attack.

CHA2DS2Vasc

Pros:

- Widely used
- Well validated
- Simple
- Clinical Trials

Cons:

- Poor performance in CKD
- Gender!
- Omits other risk factors:
 - Burden
 - LA size
 - Proteinuria
 - Obesity

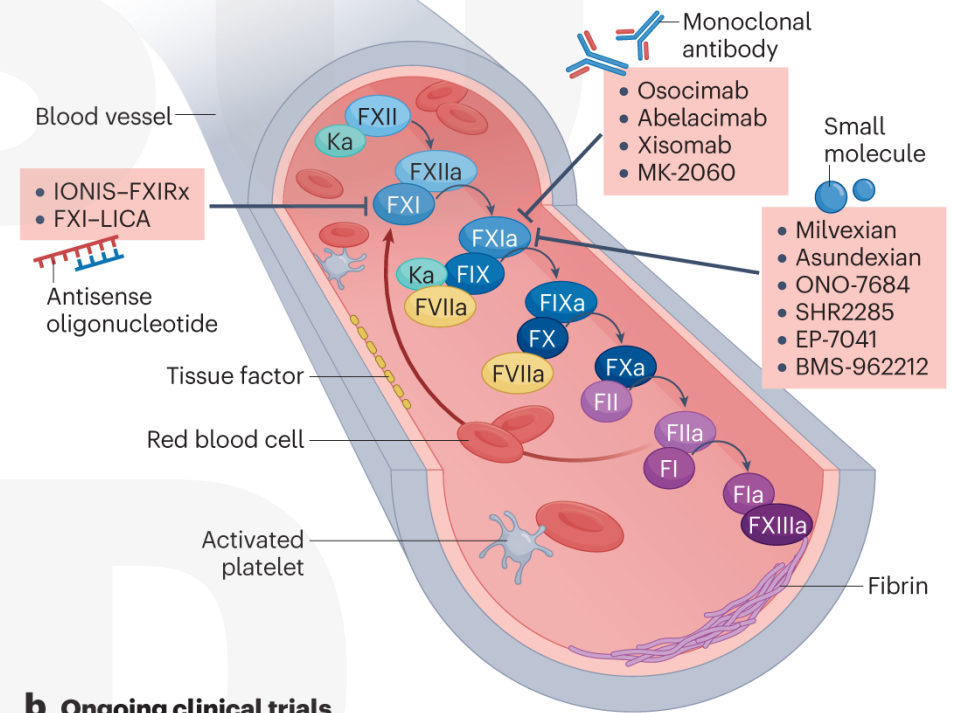
<1%/yr
1-2%/ yr
>2%/yr

Anticoagulation- What?

- NOACs > Warfarin- 1A recommendation
- Factor Xa inhibitors
 - Apixaban
 - ARISTOTLE- Slightly lower CVA and major bleeding
 - Rivaroxaban
 - ROCKET AF- Similar CVA and bleeding
 - Edoxaban
 - ENGAGE AF TIMI 48- Similar CVA but lower bleeding
- Direct thrombin inh
 - Dabigatran
 - RELY- Similar CVA and bleeding

FUTURE- TARGET FACTOR XI

a FXI inhibition and the coagulation cascade



b Ongoing clinical trials

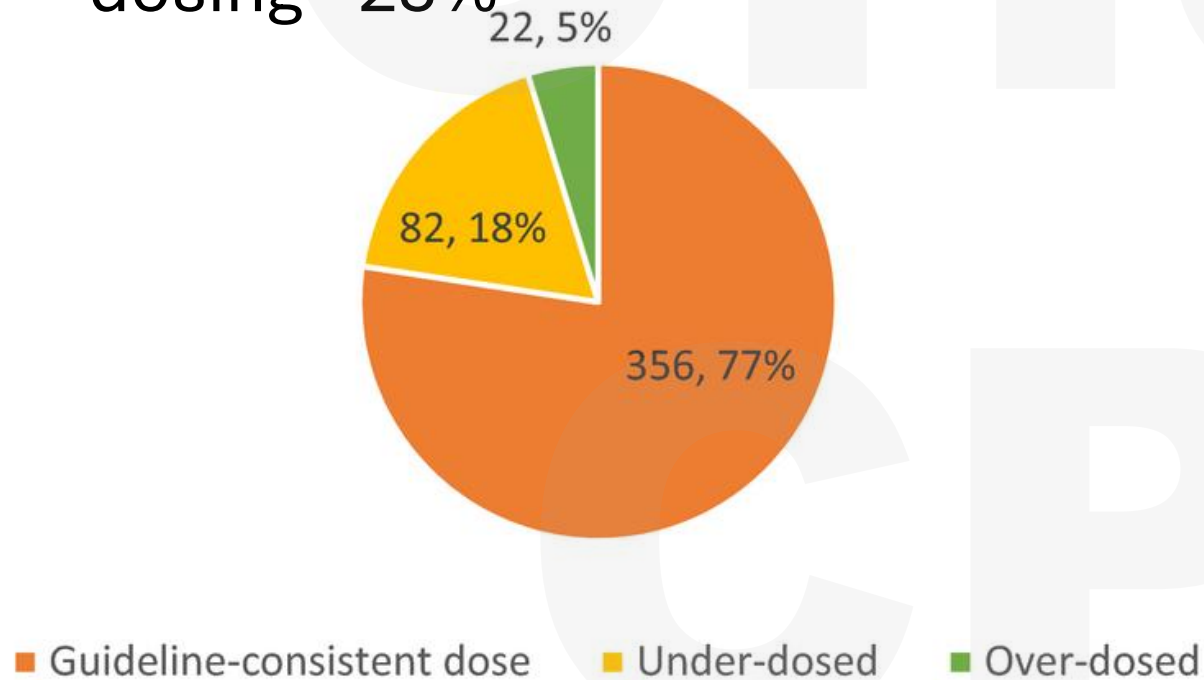
- Prevention of cardioembolic stroke in patients with AF
- Prevention of recurrent non-cardioembolic stroke
- Prevention of major adverse cardiovascular events in patients with ACS
- Safety in patients with ESRD

c Future therapeutic indications

- Valvular AF; mechanical valve
- APS
- Impaired liver function
- Obesity
- Sarcopenia
- Heart failure

Dose reduction has implications

- Frequency of inappropriate dosing ~25%



- Increased stroke
- Increased all cause mortality
- No difference in bleeding

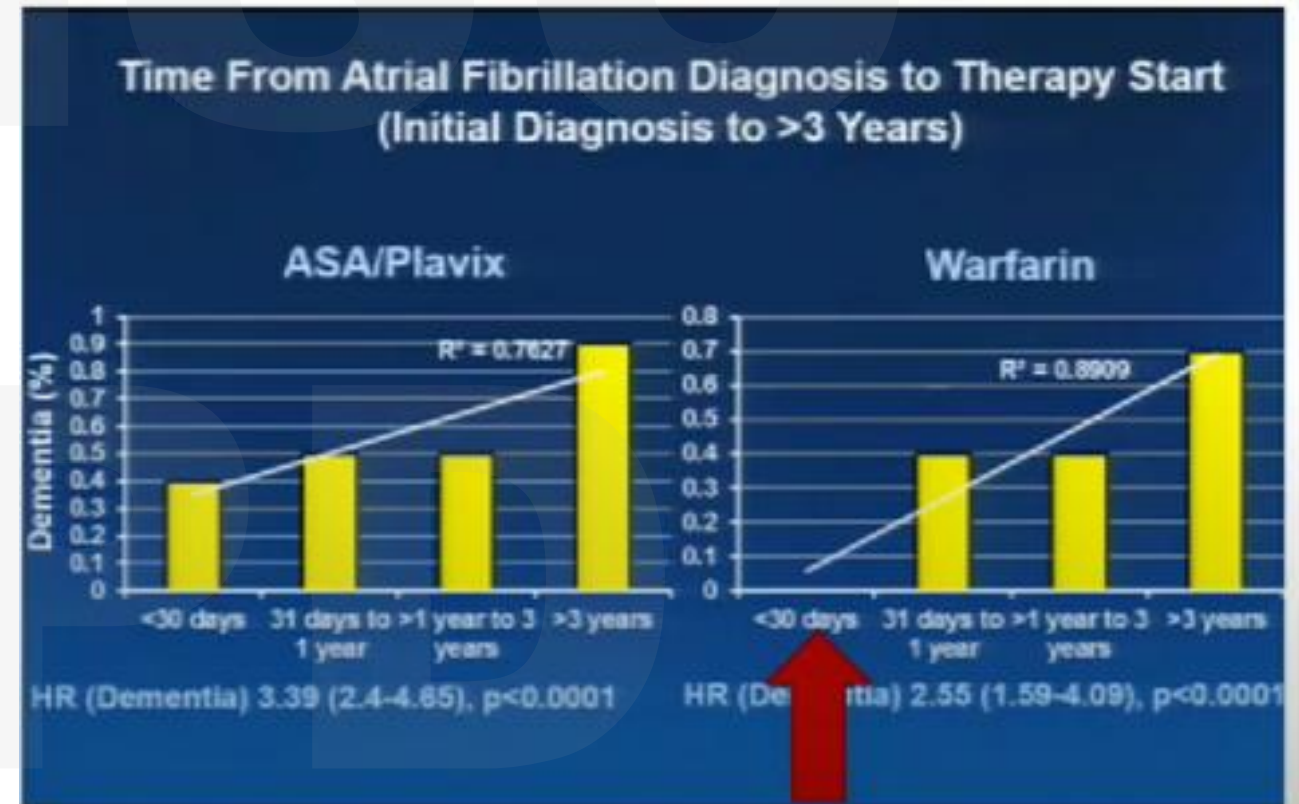
- Sanghai et al. JAHA 2020
- Ashraf et al AHJ 2021
- Sugrue et al. AMJ 2021

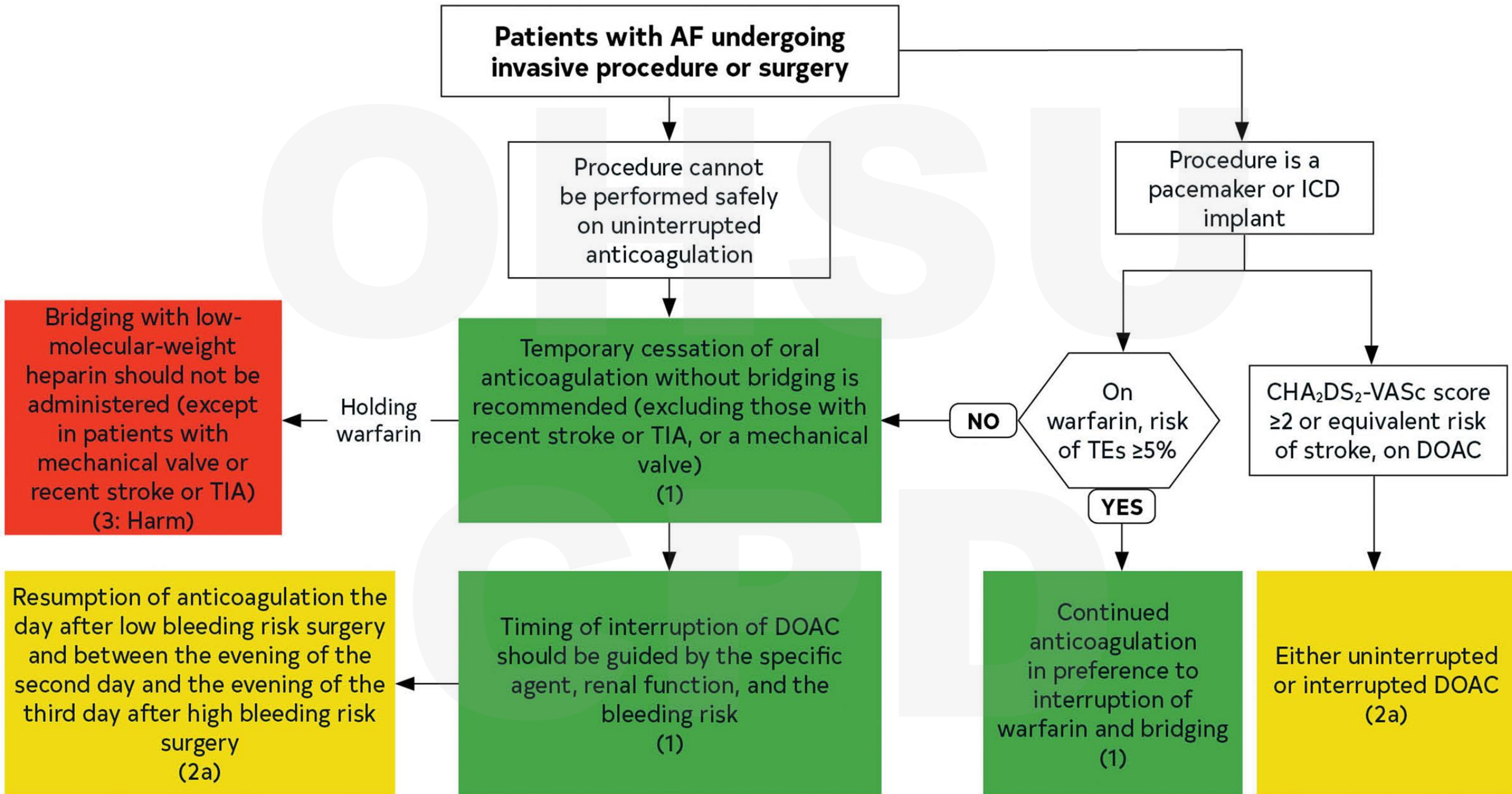
Anticoagulation- when to start?

Table 1:

Delays in Initiation of Antithrombotic Therapies in Patients with Newly Diagnosed AF

Time to Initiation	Acetylsalicylic acid/clopidogrel (n=21,781)	Warfarin (n=4,408)
General population		
≤30 days	48.0%	5.2%
31 days to 1 year	10.5%	12.4%
>1 year to 3 years	13.1%	17.1%
>3 years	28.4%	65.3%
CHA₂DS₂-VASc 2-4		
≤30 days	50.7%	4.8%
31 days to 1 year	10.2%	12.5%
1 year to 3 years	13.6%	17.9%
>3 years	25.5%	64.8%
CHA₂DS₂-VASc >5		
≤30 days	67.1%	7.9%
31 days to 1 year	8.8%	18.4%
1 year to 3 years	10.9%	25.4%
>3 years	13.2%	48.3%





Long term OAC considerations

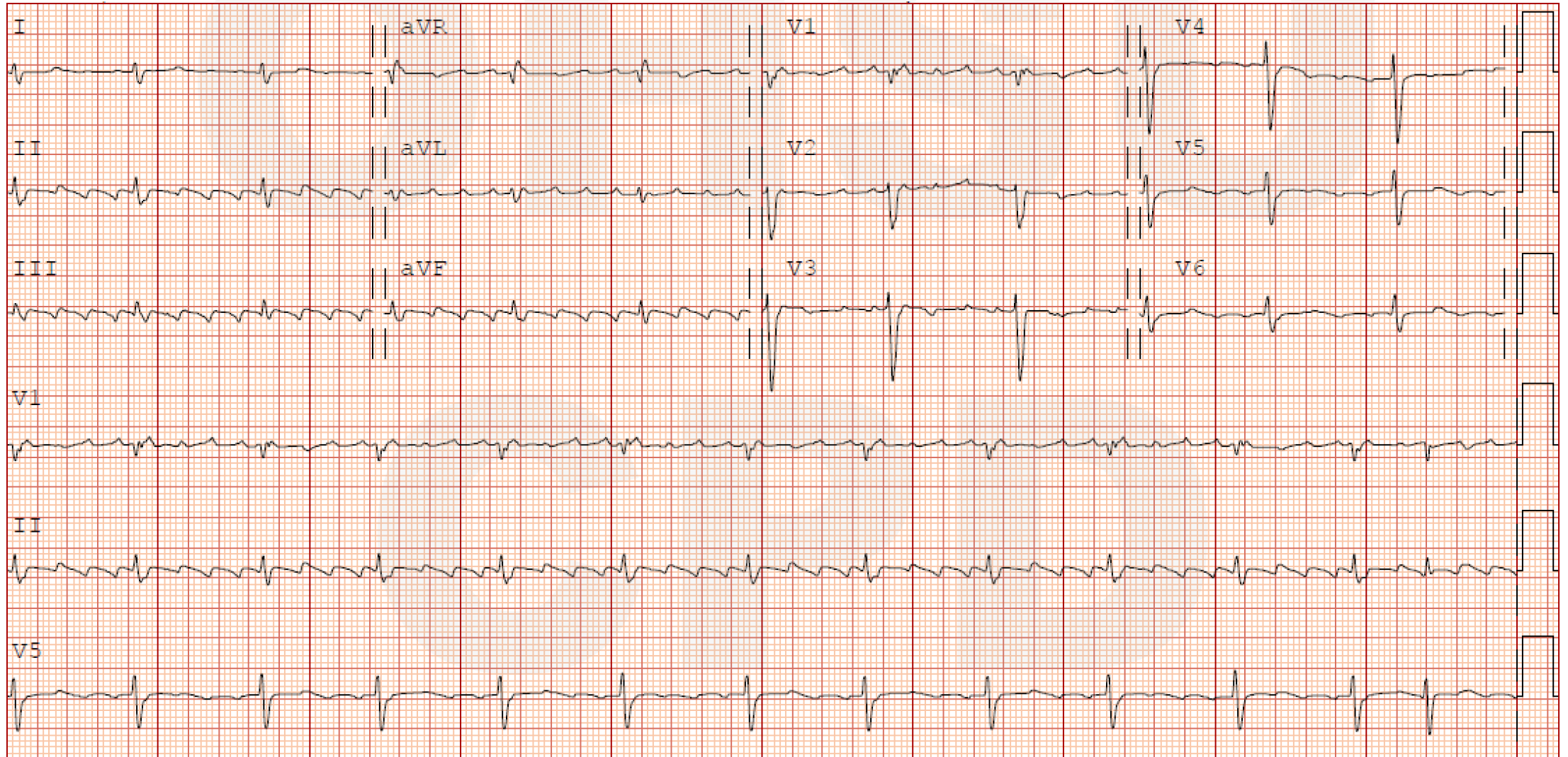
Long term AC Contraindicated

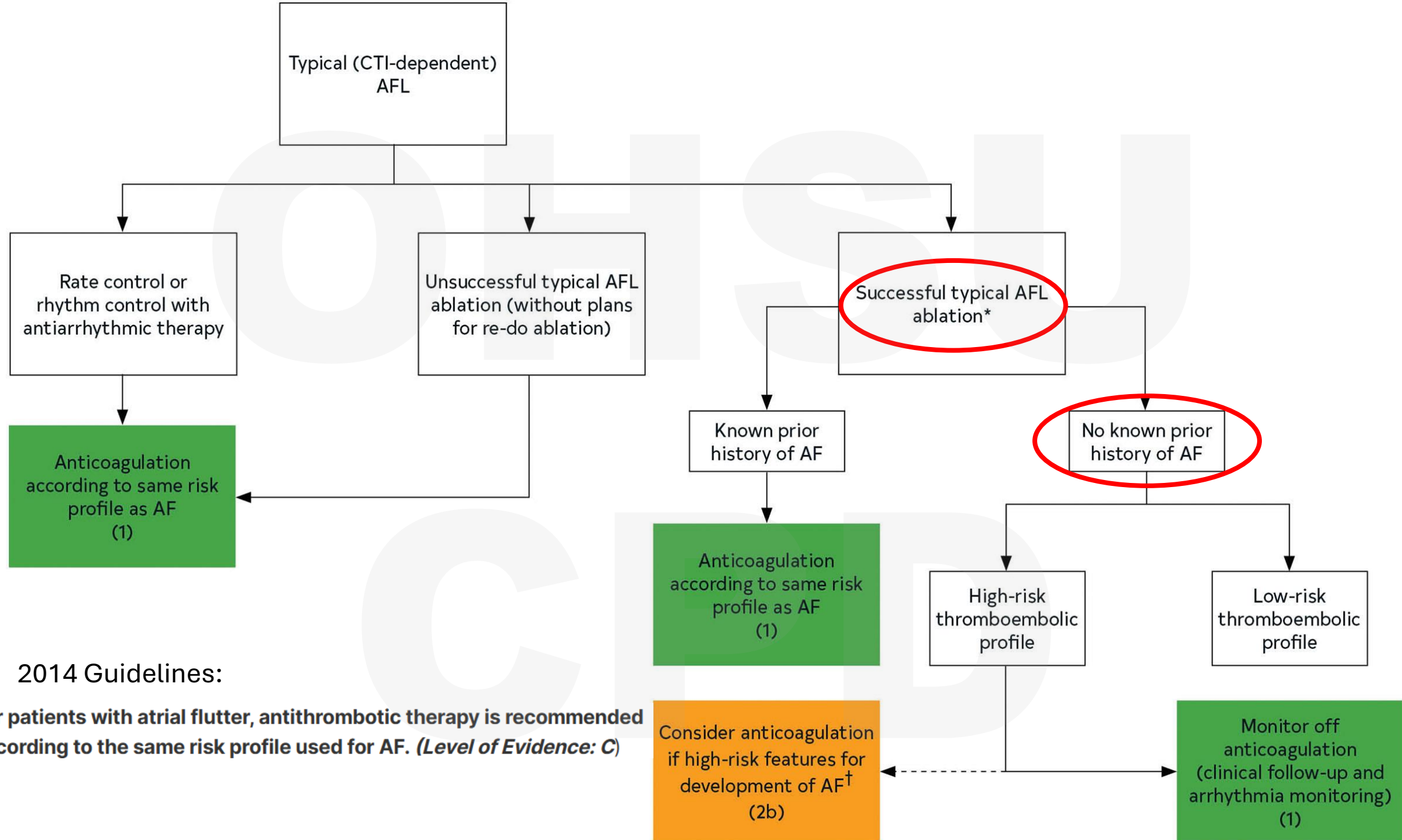
- Severe bleeding from no-reversible causes- GI, pulmonary, GU
- Spontaneous IC or intraspinal
- Serious bleeding related to recurrent falls when falls are not treatable

Long term AC still reasonable

- Bleeding that is treatable
- Bleeding from isolated trauma
- Bleeding related to procedural complications

59 yo man with dyspnea on exertion



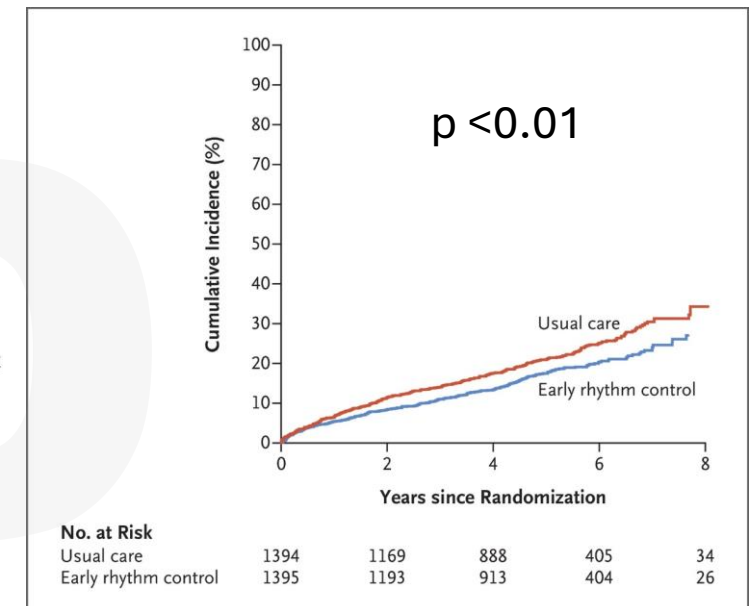
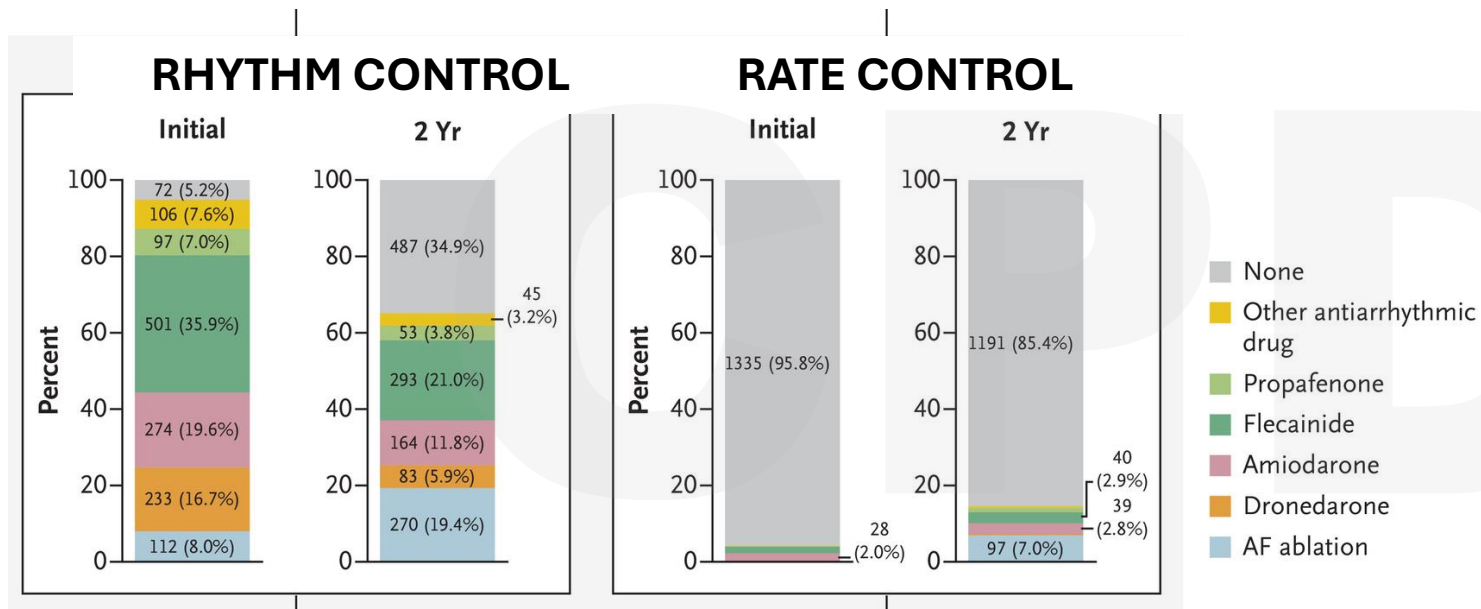


Rate vs Rhythm control- everyone deserves a chance at Sinus Rhythm?

- RCT 2789 patients with early AF
- Randomized to rate vs rhythm control
- Outcome: Composite of death, stroke, serial adverse events related to rhythm control

Table 2. Efficacy Outcomes.*

Outcome	Early Rhythm Control	Usual Care	Treatment Effect
First primary outcome — events/person-yr (incidence/100 person-yr)	249/6399 (3.9)	316/6332 (5.0)	0.79 (0.66 to 0.94)†
Components of first primary outcome — events/person-yr (incidence/100 person-yr)			
Death from cardiovascular causes	67/6915 (1.0)	94/6988 (1.3)	0.72 (0.52 to 0.98)‡
Stroke	40/6813 (0.6)	62/6856 (0.9)	0.65 (0.44 to 0.97)‡
Hospitalization with worsening of heart failure	139/6620 (2.1)	169/6558 (2.6)	0.81 (0.65 to 1.02)‡
Hospitalization with acute coronary syndrome	53/6762 (0.8)	65/6816 (1.0)	0.83 (0.58 to 1.19)‡



* Kirchhof et al. NEJM 2020

But AFFIRM concluded Rate = Rhythm control?

EAST AF 2020

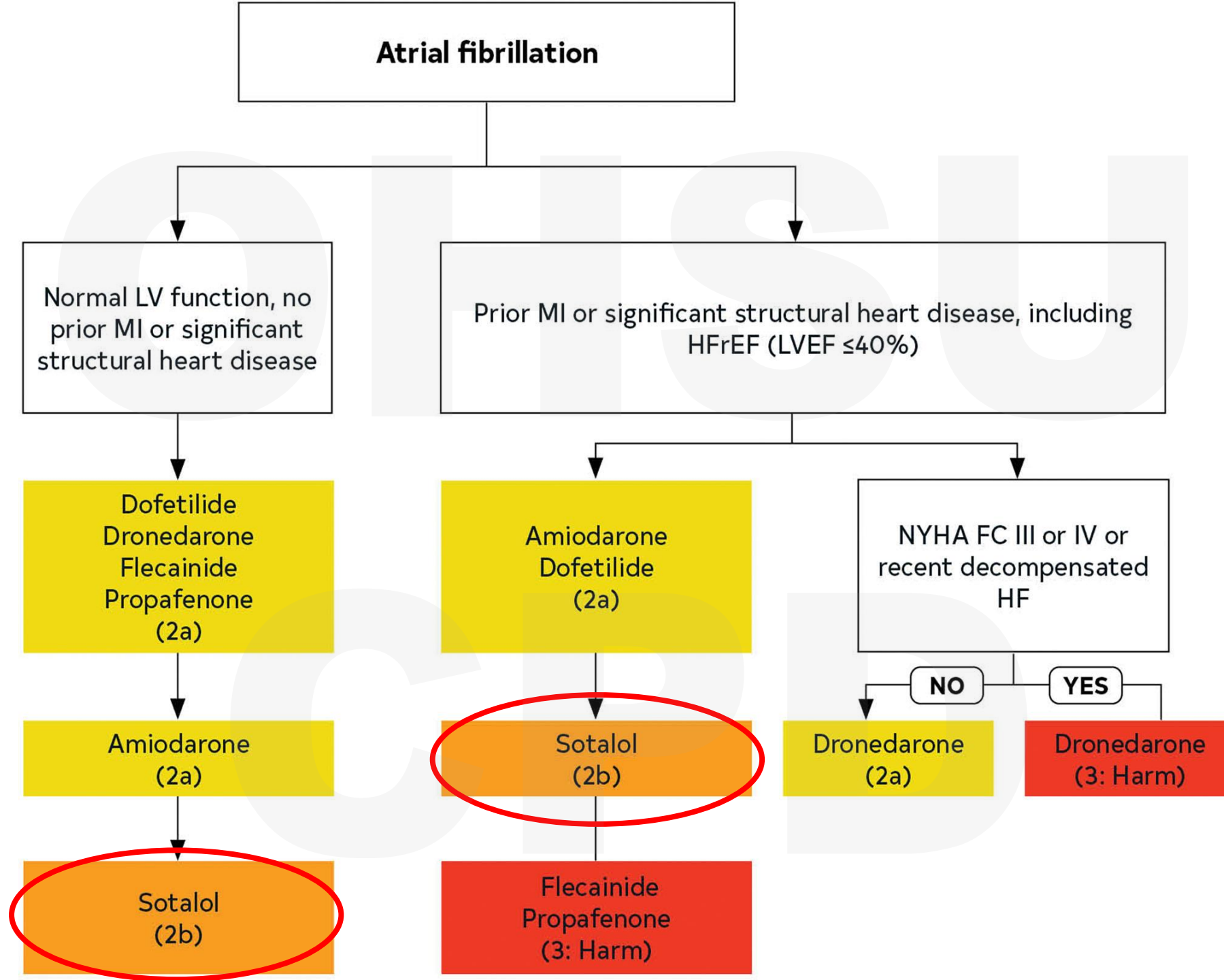
- 80% after 1st AF episode
- Class Ic, dronedarone
- Intense focus on SR maintenance (82% at 2 years)
- High OAC use (90%, mostly DOAC)
- Reasonable rate of AF ablation (20% by 2 years)

AFFIRM 2002

- 36% after 1st AF episode
- 2/3 received amiodarone/sotalol
- At 2 years, only 63% in NSR (35% in control arm)
- OAC use was limited (70% on warfarin), discontinuation in SR
- No ablation

*Wyse et al. NEJM 2002

*Kirchhof et al. NEJM 2020



Catheter Ablation for AF

1	A	1. In patients with symptomatic AF in whom anti-arrhythmic <u>drugs have been ineffective, contra-</u> <u>indicated, not tolerated or not preferred,</u> and continued rhythm control is desired, cath- eter ablation is useful to improve symptoms. ¹⁻¹⁰
1	A	2. In selected patients (<u>generally younger with</u> <u>few comorbidities</u>) with symptomatic parox- <u>ysmal AF in whom rhythm control is desired,</u> <u>catheter ablation is useful as first-line therapy</u> to improve symptoms and reduce progression to persistent AF. ¹¹⁻¹⁶

AF ablation philosophy

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., MÊLÈZE 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.

- 45 patients
- Ectopic beats
 - Single → 29 (69)
 - Two sites → 9
 - Three → 6
 - Four → 1
- Location: PV 2-4cm inside os
- f/u 8 months → 62% pts free of AF

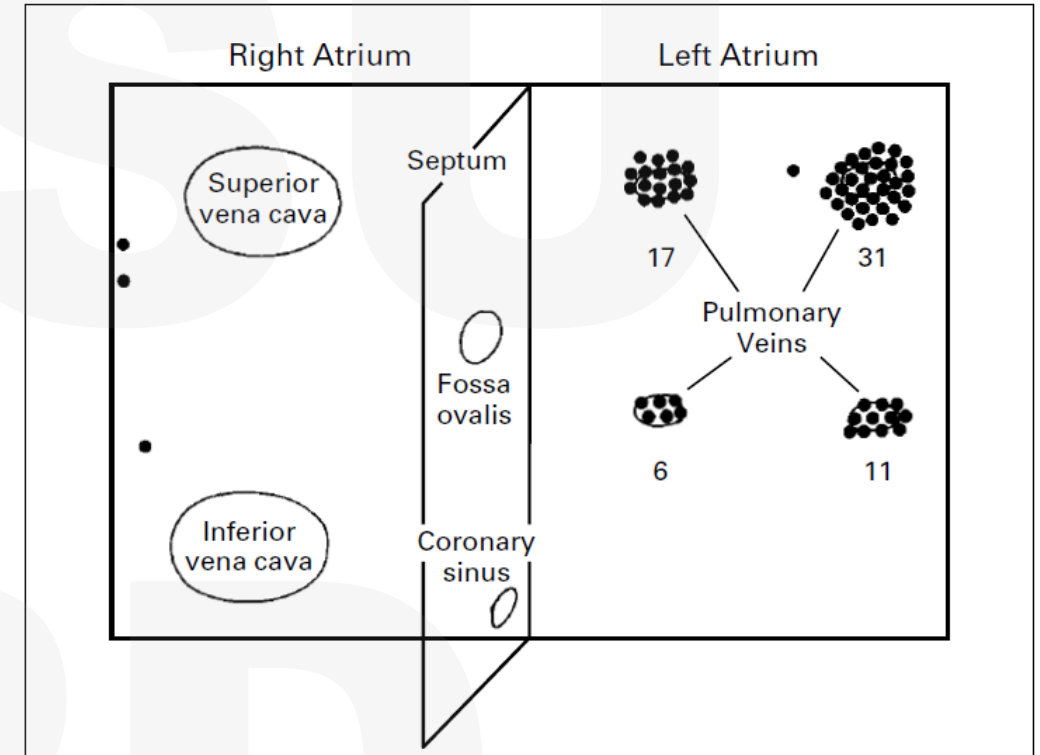
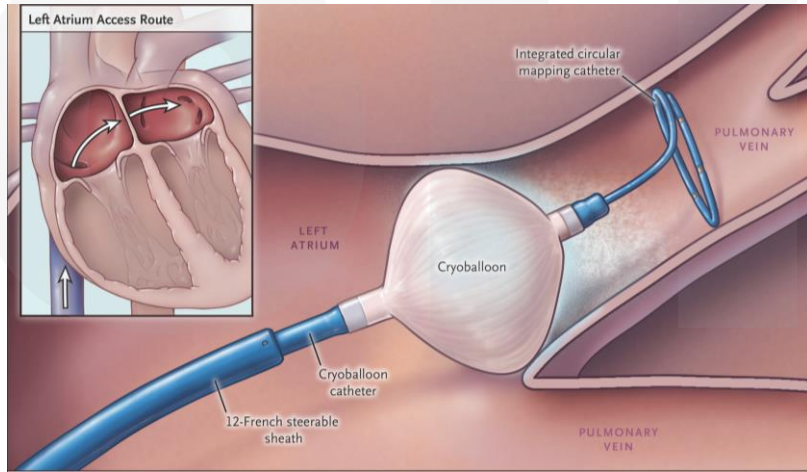
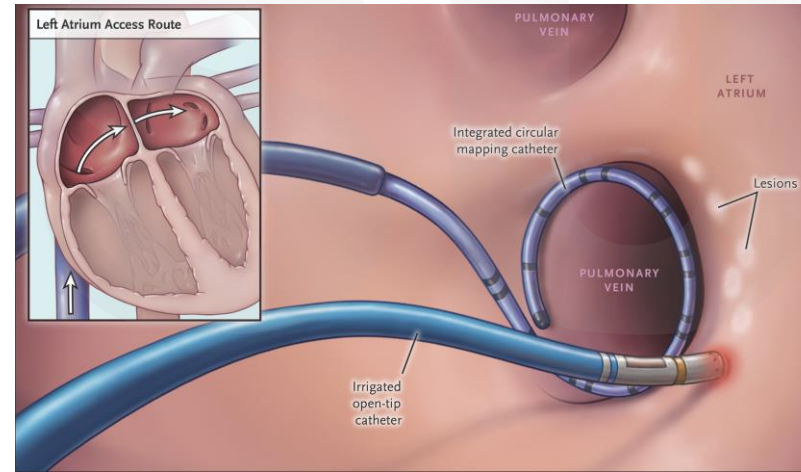


Figure 1. Diagram of the Sites of 69 Foci Triggering Atrial Fibrillation in 45 Patients. Note the clustering in the pulmonary veins, particularly in both superior pulmonary veins. Numbers indicate the distribution of foci in the pulmonary veins.

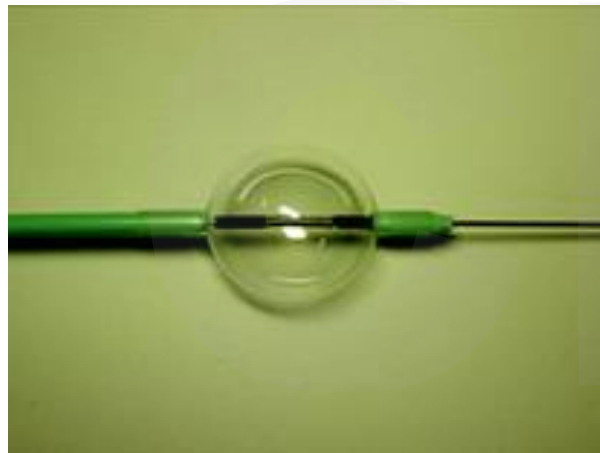
Ablation Technologies



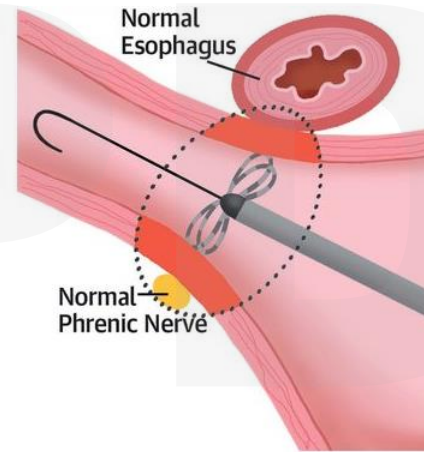
CRYOBALLOON



RADIOFREQUENCY



LASER BALLOON



PULSED FIELD

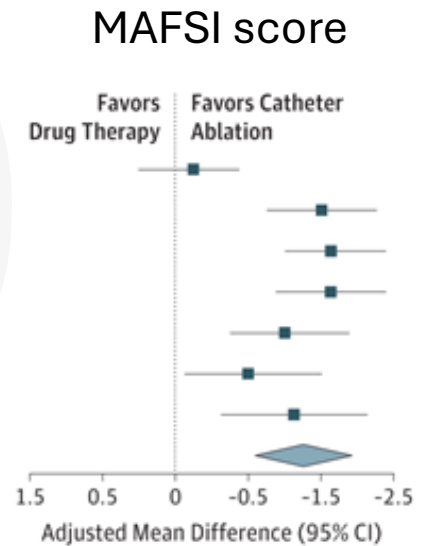
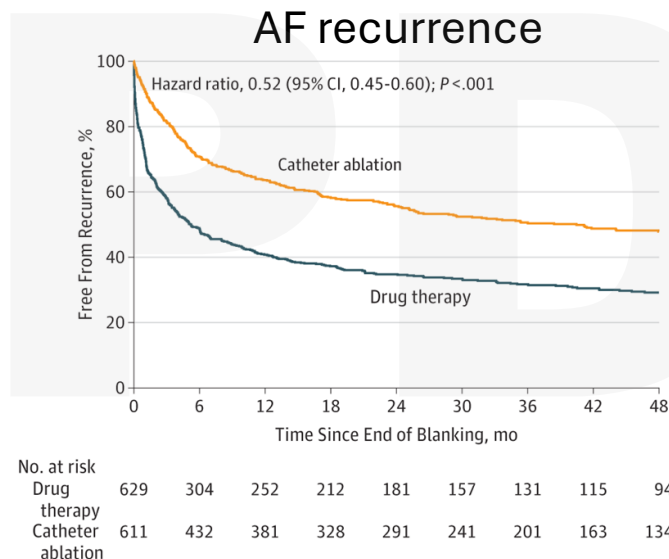
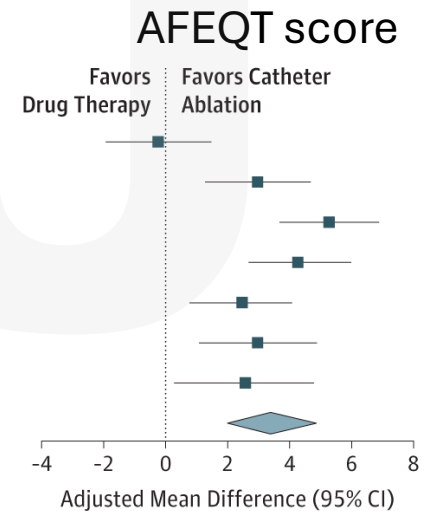
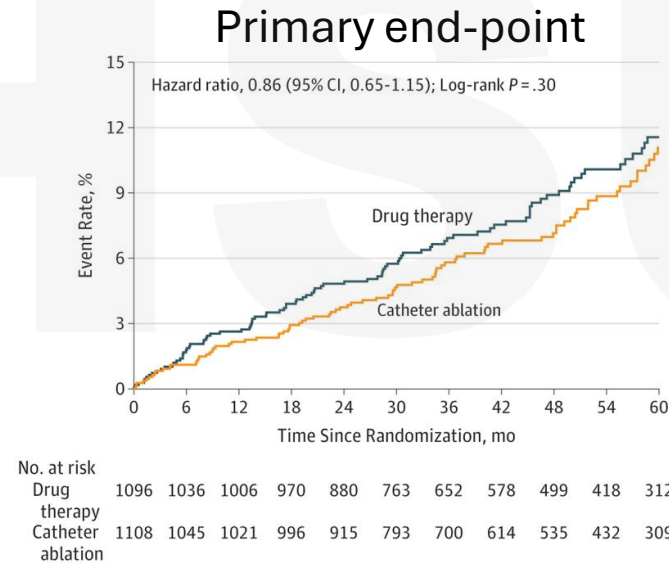
*Kuck et al. NEJM 2016

*Dukkipatti et al. JACC EP 2016

*Reddy et al. JACC EP 2019

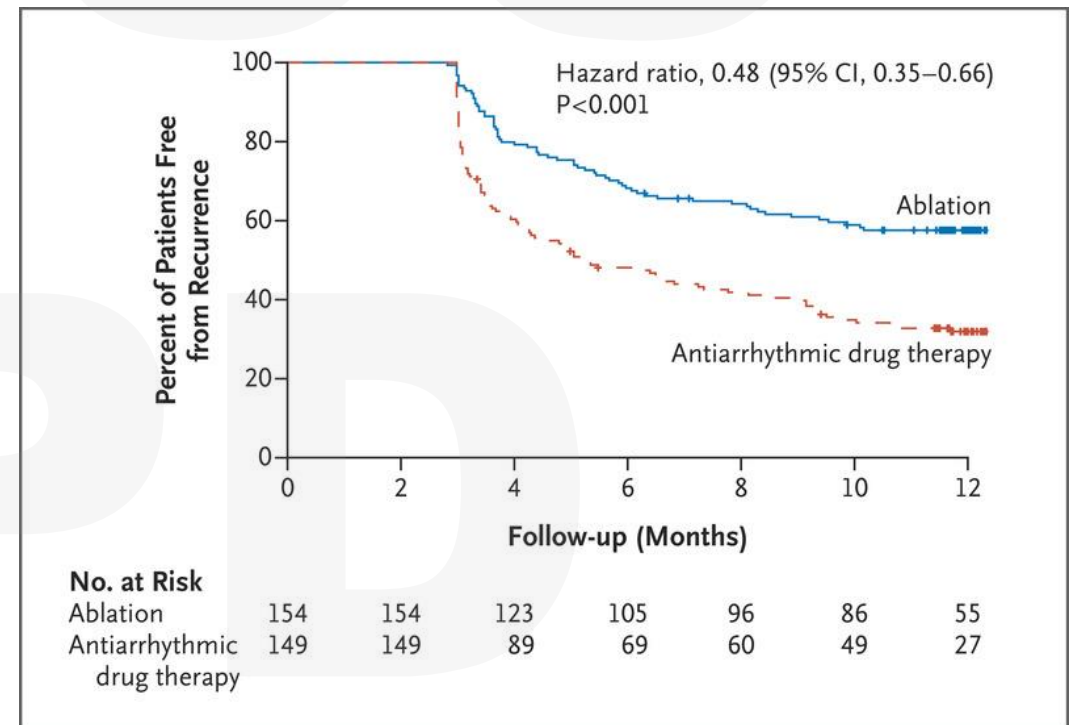
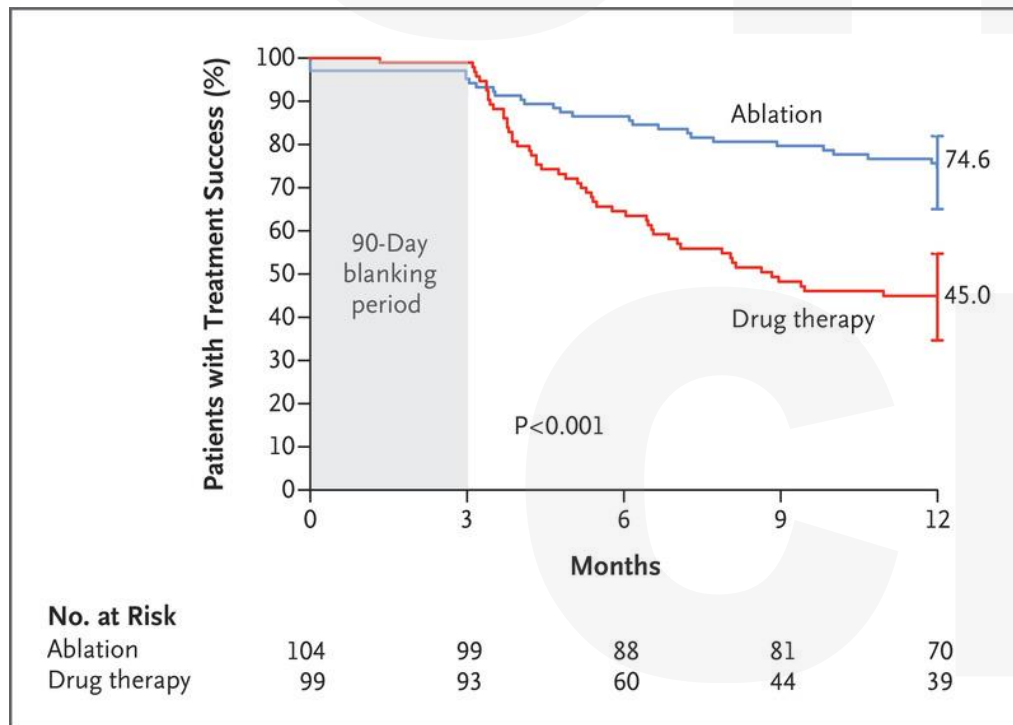
Does Catheter Ablation Improve Outcomes?

- 2204 patients with AF randomized- ablation vs drugs
- Median Age-68 y, 43% paroxysmal AF
- Primary end point- composite of death, disabling stroke, serious bleeding or cardiac arrest
- 30% crossover
- Follow up: median 48.5 m



Ablation as 1st line - STOP AF and Early AF

- Paroxysmal AF
- Ablation vs drug therapy for Rhythm control



*Andrade et al. NEJM 2021

*Wazni et al. NEJM 2021

What to expect during/after ablation?

1. Outpatient procedure with same day discharge/ overnight stay
2. General anesthesia, radial arterial line +/-, Foley, IV heparin
3. R or bilateral femoral venous access
4. One week recovery
 - no exercise
 - mild pleuritic chest pain
 - mild groin discomfort
5. Occasional recurrences during the first 90 days

Ablation Success

**Paroxysm
al**

Up to 7d

Persistent

7d- 1 yr

**Long
Standing
Persistent**

>1 yr

Permanent

Shared
decision
making

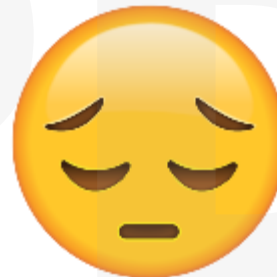
Ablation
success
(off drug):

70-80%

50-60%

40-50%

EP's
enthusiasm:



Ablation complications

<div> <div> <p>JAMA Original Investigation</p> <p>Effect of Catheter Ablation vs Antiarrhythmic Drug Therapy on Mortality, Stroke, Bleeding, and Cardiac Arrest Among Patients With Atrial Fibrillation</p> <p>The CABANA Randomized Clinical Trial</p> <p>Douglas L. Packer, MD, Daniel B. Mark, MD, MPH, Richard A. Reddy, PhD, Kristi H. Monahan, RN, Tietram D. Bahnsen, MD, Jeanne E. Poole, MD, Peter A. Noseworthy, MD, Yves D. Rosenberg, MD, MPH, Neal Jaffe, PhD, L. Brent Mitchell, MD, Greg C. Flaker, MD, Eugeny Pokushalov, MD, Alexander Romanov, MD, T. Jared Bunch, MD, Georg Noellner, MD, Andrey Ardashev, MD, Amiran Revishvili, MD, David J. Wilber, MD, Riccardo Cappato, MD, Karl-Heinz Kuck, MD, Gerhard Hindricks, MD, D. Wyn Davies, MD, Peter R. Kowey, MD, Gerald V. Naccarelli, MD, James A. Heffelf, MD, Jonathan P. Piccini, MD, MHS, Adam P. Silverstein, MS, Hussein R. Al-Khalid, PhD, Kerry L. Lee, PhD, for the CABANA Investigators</p> </div> <div> <p>The NEW ENGLAND JOURNAL of MEDICINE</p> <p>ESTABLISHED IN 1822 JANUARY 28, 2021 VOL. 384 NO. 4</p> <p>Cryoablation or Drug Therapy for Initial Treatment of Atrial Fibrillation</p> <p>Jason G. Andrade, M.D., George A. Wells, Ph.D., Marc W. Dewell, M.D., Matthew Bennett, M.D., Vidal Esszag, M.D., Ph.D., Jean Champagne, M.D., Jean-François Roux, M.D., Derek Fung, M.D., Alan Skanes, M.D., Yusef Khatib, M.D., Carlos Morillo, M.D., Unmet Joly, M.D., Paul Hozak, M.D., Ryan Lockwood, M.D., Gop Amik, M.D., Paul Anguiano, M.D., Joon Seop, M.D., Stephen Warden, M.D., Sandra Luedi, Ph.D., Laurent Macic, M.D., and Abul Verma, M.D., for the EARLY-AF Investigators¹</p> </div> <div> <p>ORIGINAL ARTICLE</p> <p>Cryoballoon Ablation as Initial Therapy for Atrial Fibrillation</p> <p>Oussama M. Wazni, M.D., Gopi Dandamudi, M.D., Nitesh Sood, M.D., Robert Hoyt, M.D., Janet Tyler, M.D., Sarfraz Durrani, M.D., Mark Niebauer, M.D., Kevin Makati, M.D., Blair Halperin, M.D., Andre Gauri, M.D., Gustavo Morales, M.D., Mingyuan Shao, Ph.D., Jeffrey Cerkenvenik, M.S., Rachelle E. Kaplan, Ph.D., and Steven E. Nissen, M.D., for the STOP AF First Trial Investigators²</p> <p>ABSTRACT</p> </div> </div>				
	CABANA ¹	EARLY-AF ²	STOP-AF First ³	Combined
# ablation patients	1006	154	104	1264
Vascular (n (%))	38 (3.8)	1 (0.6)	1 (1)	40 (3.2%)
-Hematoma	23 (2.3)	1 (0.6)		
-Pseudoaneurysm	11 (1.1)	0		
-AV fistula	4 (0.4)	0		
Tamponade	8 (0.8)	0	2 (1.9)	10 (0.7%)
Stroke	0	0	0	0
TIA	3 (0.3)	0	1 (1)	4 (0.3%)
Phrenic injury	1 (0.1)	3 (1.9)	2 (1.9)	6 (0.5%)
Pulm vein stenosis	1 (0.1)	0	0	1 (0.1%)
Atrio-esophageal fistula	0	0	0	0

**Lower now
with U/S
access**

1. Packer DL, et al. JAMA 2019.
2. Andrade JG, et al. NEJM 2021
3. Wazni OM, et al. NEJM 2021

Rate vs Rhythm Control in HF

2014 AHA/ACC/HRS Guidelines

Focus on rate control (Class I)

Class 2a Rec:

Patients with chronic HF who remain symptomatic from AF despite a rate-control strategy, it is reasonable to use rhythm-control strategy (LOE: C)

2019 Focused Update
Class 2a

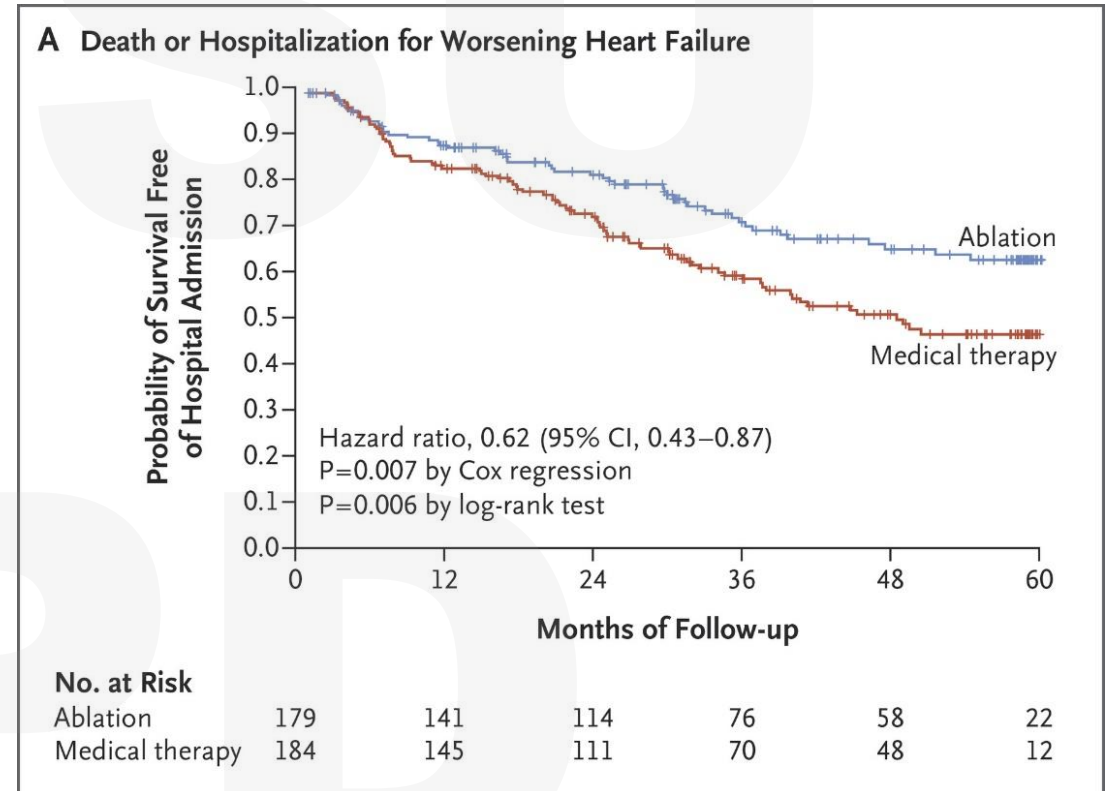
2023 Guidelines

Recommendations for Management of AF in Patients With HF*
Referenced studies that support the recommendations are summarized in the [Online Data Supplement](#).

COR	LOE	Recommendations
1	B-NR	1. In patients who present with a new diagnosis of HFrEF and AF, arrhythmia-induced cardiomyopathy should be suspected, and an <u>early and aggressive approach to AF rhythm control</u> is recommended. ^{1,2}
1	A	2. In appropriate patients with AF and HFrEF who are on GDMT, and with reasonable expectation of procedural benefit (Figure 24), <u>catheter ablation is beneficial to improve symptoms, QOL, ventricular function, and cardiovascular outcomes.</u> ^{3–13}
2a	B-NR	3. In appropriate <u>patients with symptomatic AF</u> and <u>HFpEF</u> with reasonable expectation of benefit, catheter ablation can be useful to improve symptoms and improve QOL. ^{14,15}

What about patients with heart failure?

- CASTLE-AF RCT
- 363 patients with AF and LVEF $\leq 35\%$, NYHA II-III
- Persistent 70%
- Follow up 37 ± 20 months
- Class I rec for rhythm control now*



* Marrouche et al. NEJM 2018

Catheter Ablation in Heart Failure

Likely to benefit from ablation

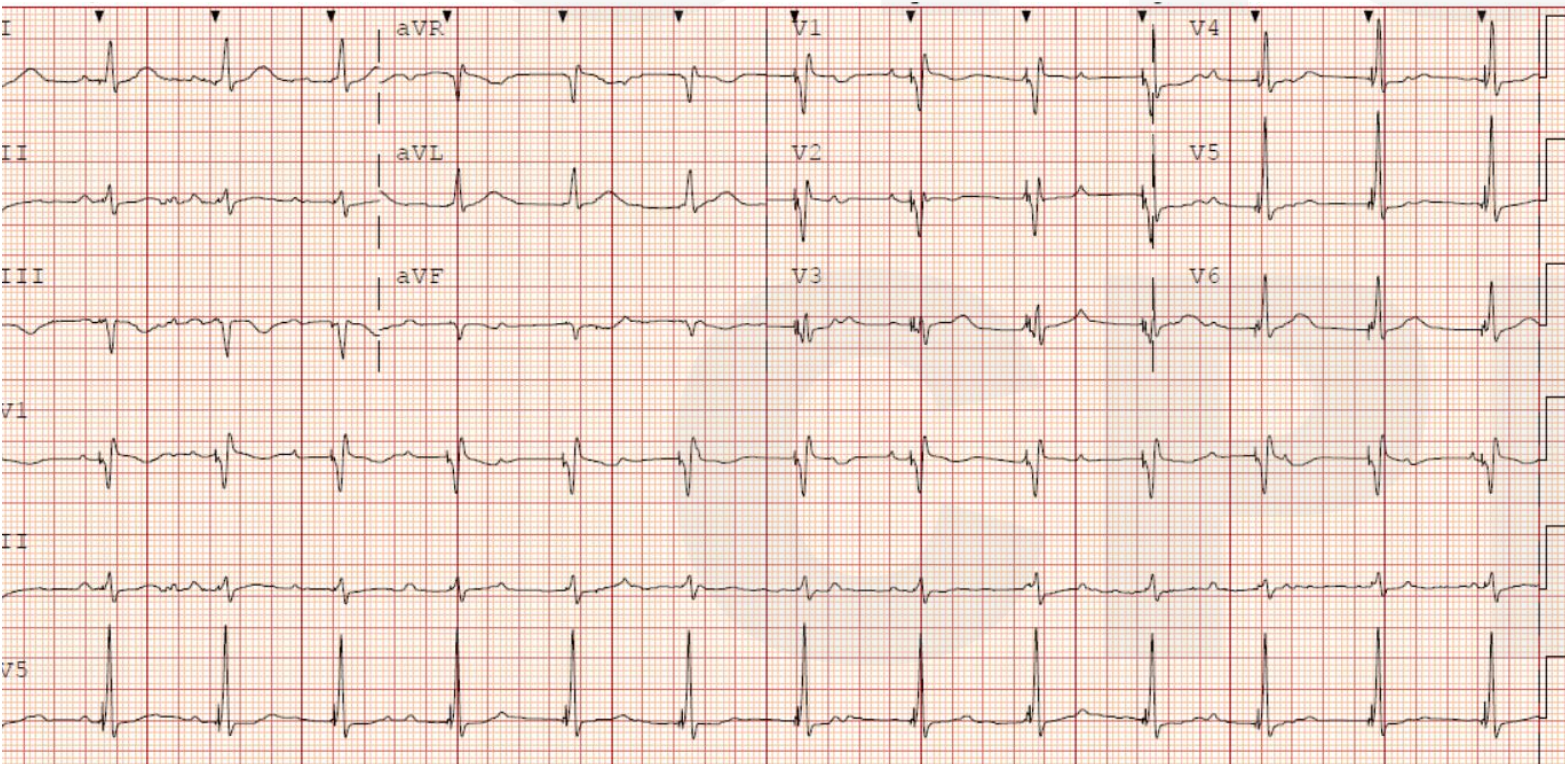
- AF mediated CM suspected
- Early stage of HF
- No LGE on CMR
- No or mild atrial myopathy
- Paroxysmal or early persistent
- Younger

Less likely to benefit

- Advanced HF
- Significant LGE
- Severe atrial myopathy
- Long standing persistent
- Prior failed ablations
- Multiple comorbidities

AV node ablation + PPM

- 84 yo with persistent AF & CM
- Prior failed ablation
- Amiodarone thyrotoxicity and breakthrough



Recommendations for AVNA

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

COR	LOE	Recommendations
1	C-LD	1. In patients with AF and a persistently rapid ventricular response who undergo AVNA, initial pacemaker lower rate programming should be 80 to 90 bpm to reduce the risk of sudden death. ^{1,2}
2a	B-R	2. In patients with AF and uncontrolled rapid ventricular response refractory to rate-control medications (who are not candidates for or in whom rhythm control has been unsuccessful), AVNA can be useful to improve symptoms and QOL. ³⁻⁶
1	B-NR	3. In patients with AF who are planned to undergo AVNA, implantation of a pacemaker before the ablation (ie, before or same day of ablation) is recommended to ensure adequacy of the pacing leads before performing ablation. ⁷⁻⁹
2b	C-LD	4. In patients with AF with normal EF undergoing AVNA, conduction system pacing of the His bundle ¹⁰⁻¹³ or left bundle area ^{12,13} may be reasonable.

Hospitalist checklist — practical orders & documentation

- 1) Hemodynamic assessment (stable vs unstable)
- 2) Labs: electrolytes, TSH, troponin if indicated, renal function, CBC, Echo
- 3) Anticoagulation decision documented (CHA2DS2-VASc and rationale)
- 4) Rate-control meds ordered with monitoring plan
- 5) EP referral if considering rhythm control/ablation or complex care
- 6) Discharge plan: anticoagulation plan, follow-up with cardiology/EP, risk-factor referrals

OHSU

THANK YOU

CPD

The OHSU AF clinic Approach

Anticoagulation

- CHADSVASC ≥ 2
- CHADSVASC 1 (not gender) \rightarrow SDM
- Surgical LAAO for all AF pts getting cardiac sx
 - Post op imaging
- Endovascular LAAO for OAC c/i

Early Rhythm Control

- Young, symptomatic
 - CV for symptom assessment
- Cardiomyopathy

- **Ablation- 1st line in select**
- **Class Ic - flecainide**
- **IV sotalol/Dofetilide**
- **Amiodarone**
- **AV node ablation + Physiologic Pacing**

Risk Factor Modification

- Referral for HAT
- Counselling for substance use
- Exercise counselling
- HTN/DM mgt with PCP
- Genetic for all <45 yr

Key references & guideline sources

- Major guideline sources:
 - 1) 2023 ACC/AHA/ACCP/HRS Guideline for the Diagnosis and Management of Atrial Fibrillation. (Circulation / JACC summaries).
 - 2) Heart Rhythm Society resources summarizing the 2023 guideline updates.
 - 3) ACC practical primer and guideline-at-a-glance resources (focus on EP applications).
 - 4) Professional slide summaries and AHA/ACC clinical updates.

DOAC Dosing (nonvalvular AF)

DOAC	Standard Dose	Renal Adjustment
Apixaban	5 mg BID	2.5 mg BID if ≥ 2 of: age ≥ 80 , wt ≤ 60 kg, Cr ≥ 1.5
Rivaroxaban	20 mg daily with food	15 mg daily if CrCl 15–49
Dabigatran	150 mg BID	75 mg BID if CrCl 15–30
Edoxaban	60 mg daily	30 mg daily if CrCl 15–50 or wt ≤ 60 kg

IV Rate-Control Agents — Inpatient Use

Agent	IV Dose (initial)	Notes
Metoprolol tartrate	2.5–5 mg IV q5min up to 15 mg	Avoid in acute decompensated HF
Diltiazem	0.25 mg/kg IV bolus, then 5–15 mg/hr infusion	Avoid in HFrEF
Verapamil	5–10 mg IV over 2 min	Avoid in HFrEF
Digoxin	0.25 mg IV q2h up to 1.5 mg/24h	Useful if hypotension; renal adjust

ESC 2020 guidelines- Dose reduction criteria

	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
Standard dose	150 mg b.i.d.	20 mg o.d.	5 mg b.i.d.	60 mg o.d.
Lower dose	110 mg b.i.d.			
Reduced dose		15 mg o.d.	2.5 mg b.i.d.	30 mg o.d.
Dose-reduction criteria	Dabigatran 110 mg b.i.d. in patients with: <ul style="list-style-type: none"> • Age ≥ 80 years • Concomitant use of verapamil, or • Increased bleeding risk 	CrCl 15–49 mL/min	At least 2 of 3 criteria: <ul style="list-style-type: none"> • Age ≥ 80 years, • Body weight ≤ 60 kg, or • Serum creatinine ≥ 1.5 mg/dL (133 $\mu\text{mol/L}$) 	If any of the following: <ul style="list-style-type: none"> • CrCl 15–50 mL/min, • Body weight ≤ 60 kg, • Concomitant use of dronedarone, ciclosporin, erythromycin, or ketoconazole