

Ine Arrhythmias going to get Vou

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Disclosures

- Relationship with Novartis Pharmaceuticals Corporation, Amgen, Amarin, Bayer, Pfizer, Lexicon Pharmaceuticals, and Idorsia that includes consulting or advising.
- Relationship with Janssen that includes research grant funding paid directly to the research department

Objectives

- Review the most common arrhythmia, Atrial Fibrillation.
- Discuss screening and diagnosis
- Review and discuss the acute/chronic management through lifestyle
- Discuss implications of pharmacologic treatment





Case

- Sheryl, a <u>66-year-old woman</u>, is a well-established patient who presents with a 3-month history of being "tired a lot more." She has had moments where "my heart beats fast," and this causes her to feel "dizzy and lightheaded." She is on losartan-HCT 25-12.5 mg and amlodipine 5 mg, "I've had high blood pressure for years." No fever, chills, or sweats. Does not report any abnormal bleeding.
- PastHx: <u>Hypertension</u> "for years." Menopause at age 55.
- MEDS: As above.
- Vitals: BP 130/80, HR 103, SaO2 96%, T 98.9, Wt. 165 Ht. 5'6" BMI 26.6
- LABS: Serum Cr 1.1; AST 23; ALT 32; A1c 5.8%; TSH 2.23
- She has an <u>irregularly irregular</u> rhythm.



What is Atrial Fibrillation?

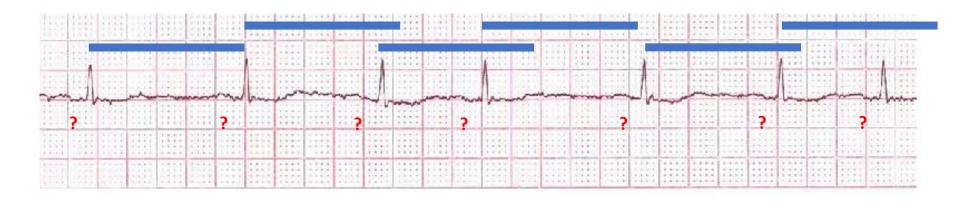
 Atrial Fibrillation is a common heart rhythm disorder characterized by irregular and often rapid heartbeats.



Atrial Fibrillation (AF)

Initial gold-standard detection

- Electrocardiogram (EKG) relatively cheap, efficient, and ubiquitous.
 - Provides the diagnosis of AF
- Findings:
 - Irregularly Irregular R-R Interval
 - No discernible P waves or related p-wave/QRS complexes



Basic Clinical Evaluation – Newly Diagnosed AF

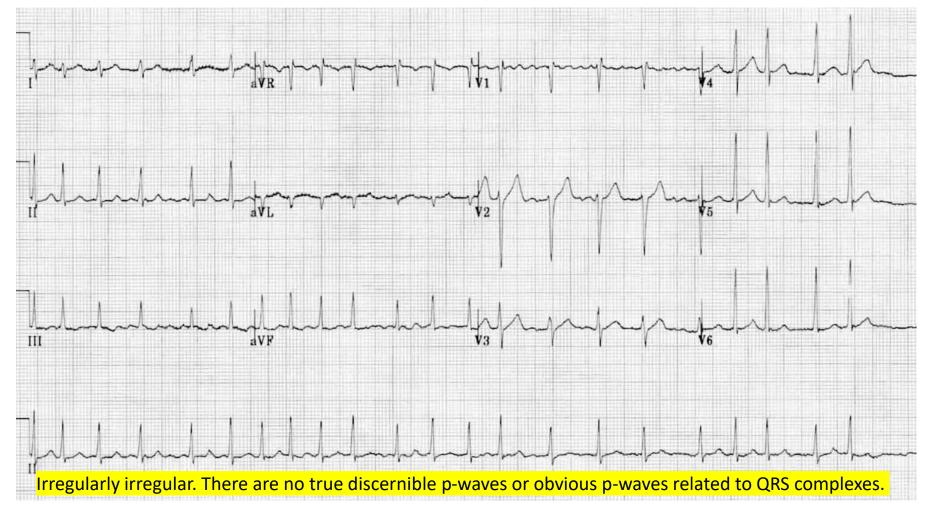
<u>Do</u>

- Transthoracic Echo
- CBC, BMP, TSH w/ Reflex T4
- Targeted testing to assess other medical conditions associate with AF to determine stroke and bleeding risk factors.

Don't

 Protocolized testing for ischemia, ACS and PE unless there are additional signs and symptoms to indicate those disorders.

Recommendations for Basic Clinical Evaluation Referenced studies that support the recommendations are summarized in the Chains Basis Supplication.							
COR	LOE	Recommendations					
1	B-NR	 In patients with newly diagnosed AF, a transthoracic echocardiogram¹⁻⁴ to assess cardiac structure, laboratory testing to include a complete blood count, metabolic panel, and thyroid function,⁵⁻⁷ 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	 In patients with newly diagnosed AF, protocolized testing for ischemia, acute coronary syndrome (ACS), and pulmonary embolism (PE) should not routinely be performed to assess the etiology of AF unless there are additional signs or symptoms to indicate those disorders.⁸⁻¹⁰ 					



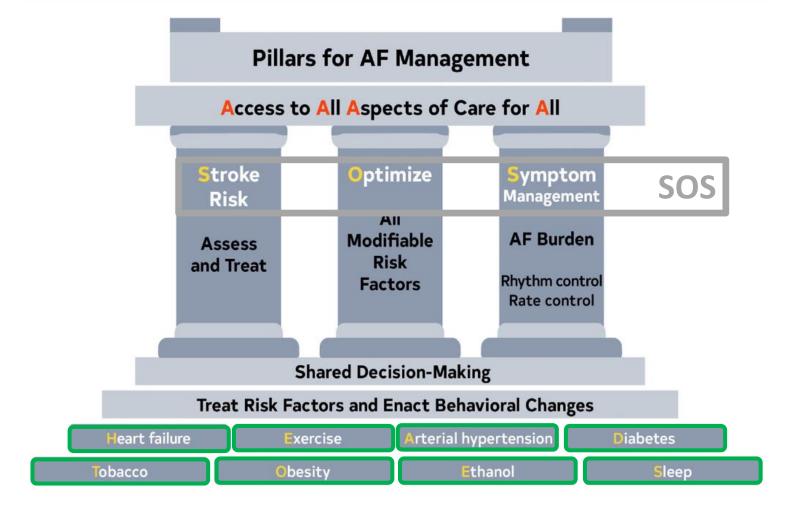
Atrial Fibrillation. A medical emergency?

Not always and not usually.

- 1. Often identified incidentally, e.g., annual wellness exam, pre-surgical exam, while being seen for other acute but non-emergent events (e.g., viral illness presentation, UTI, etc.), etc.
- 2. Deserves well-intentioned work-up and consideration for anti-coagulation in those with elevated risk score for embolism (e.g., CHADS2VASC) or being referred for cardioversion.
- 3. Discuss the early path of rhythm vs rate, and that anti-coagulation is a separate management feature.

Keys for urgent/emergent

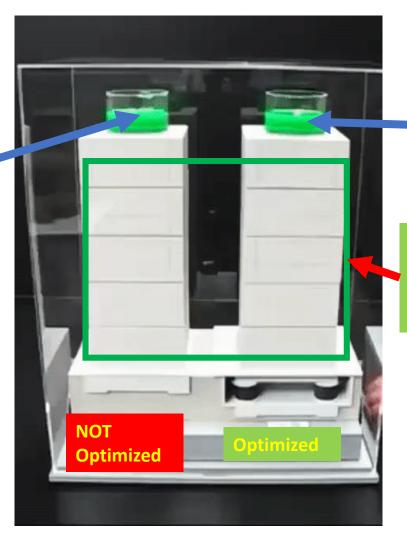
- 1. Symptomatic. With or without AF and rapid ventricular rate (RVR; Heart rate >100). Consider
 - a) Hemodynamic compromised or stable
 - b) Will they remain stable or become hemodynamically compromised
 - c) Is there a high suspicion of frailty, multiple co-morbid conditions, etc.



Atrial rhythm

Atrial Fibrillation:

- De Novo
- Paroxysmal
- Persistent
- Recurrent post AF Ablation



Atrial rhythm

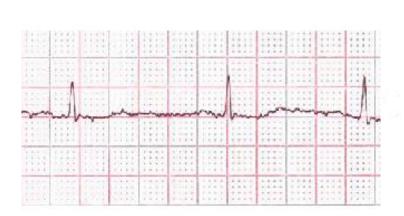
Sinus rhythm

RISK Factors:

Heart Failure, Exercise, Arterial
Hypertension, Diabetes, Tobacco, Obesity,
Ethanol, Sleep

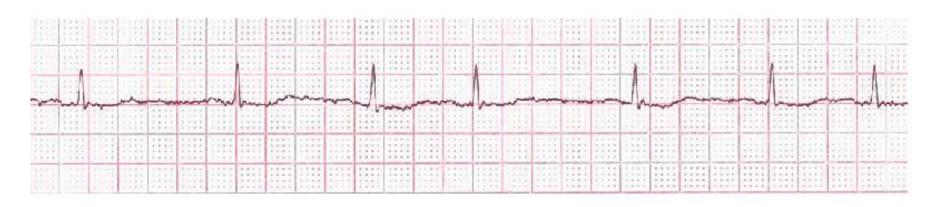
Atrial Fibrillation (AF)

Loaded diagnosis that brings fear. We need to be more precise about AF "BURDEN" – how often occurring, for how long, intermittent or continuous, requiring interve





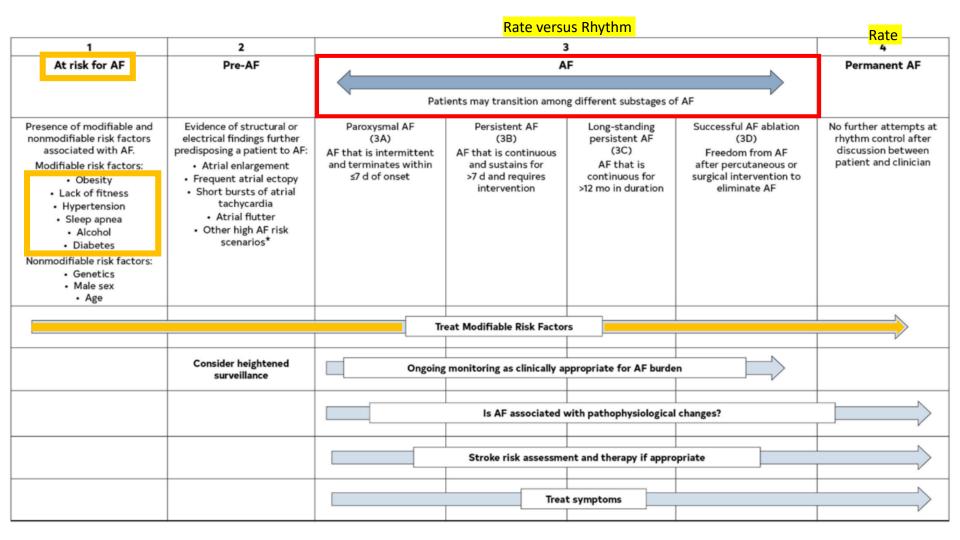
Atrial Fibrillation (AF)



We can diagnose Sheryl with AFib.

However, we don't know BURDEN—how often it occurs, and for how long?

Consider initial monitoring for evaluation of burden, e.g., patch, Holter, etc.



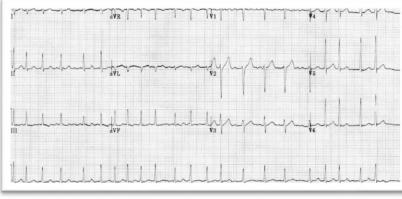
Case

• Sheryl, a <u>66-year-old</u> <u>woman</u>, is a well-established patient who presents with a 3-month history of being "tired a lot more." She has had moments where "my heart beats fast," and this causes her to feel "dizzy and lightheaded." She is on losartan-HCT 25-12.5 mg and amlodipine 5 mg, "I've had high blood pressure for years." No fever, chills, or sweats. Does not report any abnormal bleeding.

What AF stage is Sheryl in?

- Stage 1, "At risk for AF"
- Stage 2, "Pre-AF"
- Stage 3, "AF"
- Stage 4, "Permanent AF"





- Etiology and Risk Factors (the how will help with the why, e.g., valve dz → AF)
 - More prevalent in men, but only a little.
 - More prevalent with advancing age.
 - Hypertensive heart disease and Coronary Artery Disease are the two most common conditions that increase risk in developed countries.
 - Rheumatic Heart Disease is a strong risk factor, although less common in developed nations now. Still a strong factor in developing nations.
 - Other cardiac conditions associated with A-Fib include Valvular Heart Disease (especially Mitral disease), Dilated Cardiomyopathy, Hypertrophic Cardiomyopathy, Heart Failure, and Congenital Heart Diseases (especially atrial septal defect).

- Etiology and Risk Factors (continued)-
 - A-Fib can also occur in patients with otherwise healthy hearts with the following conditions or situations (acute, self-limited vs. more chronic impact):
 - Acute alcohol excess Usually transient, self-limited
 - Holiday Heart Related to sudden withdrawal ("holiday")
 - Pericarditis
 - Chest trauma or thoracic surgery
 - Thyroid disorders (thyrotoxicosis)
 - Obstructive Sleep Apnea
 - Pulmonary Embolism
 - COPD
 - Obesity
 - Some medications (theophylline, adenosine, digitalis, etc.)
 - A-Fib can rarely occur in patients with healthy hearts with no known cause.

Etiology and Risk Factors (continued)-

Highest attributable risk factors (ARIC Study) in order:

- Hypertension (22% of all AF cases, adjusted for age, too)
- BMI (~28% risk with each increase of 5 kg/m2, nonlinear though)
- Smoking (~32% for current, 9% former, 21% ever dose/response too)
- Cardiac Disease (all those above lumped together)
- Diabetes (~28% DM, 20% pre-DM)

- Pathophysiology-
 - Stretch Cardiomyocyte tissue = electrical issues
 - It will become apparent when discussing pulmonary veins.



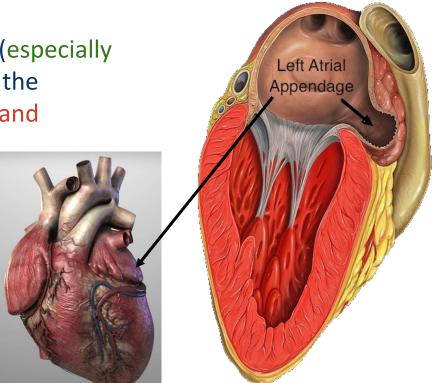


- Pathophysiology-
 - Regardless of the underlying risk factors, the underlying pathology is anatomic and electrophysiologic changes occuring in the atrial myocardium (hence, there is commonly an underlying heart disease).
 - Most commonly, it has to do with atrial enlargement, increase in atrial pressure, or atrial inflammation/infiltration.
 - These conditions cause increased atrial cell automaticity or increased trigger activity due to injury.
 - Several firing cells mean there are several areas of the atria trying to act as the pacemaker, overriding the SA node

Pathophysiology (continued)-

During A-Fib, stasis within the atria (especially the left atrial appendage) increases the propensity for thrombus formation and subsequent embolization.

This can result in cerebral infarction (stroke) or infarction of peripheral extremities



- General Classification or types of A-Fib- (Think, when do you encounter AF?)
 - O Any of the forms below can be "subclinical," meaning asymptomatic
 - Paroxysmal AF: Terminates spontaneously or with intervention within 7 days of onset (can recur).
 - Persistent AF: Fails to self-terminate within 7 days. Often requires pharmacologic or electrical cardioversion to restore NSR.
 - Long-Standing Persistent AF: Has lasted for more than 12 months.
 - Successful AF ablation: Successful termination of AF by catheter or surgical means
 - Permanent AF: Those individuals with persistent AF who, in a joint decision between provider and patient, are no longer pursuing a rhythm control strategy.

- Signs and Symptoms-
 - Many patients are asymptomatic estimated to be over 50%
 - If symptoms are present, they are variable and often vague.
 - Presentation may involve:
 - **Palpitations**
 - Tachycardia
 - Hypotension
 - Fatigue (common) or weakness
 - Dizziness/lightheadedness
 - Dyspnea
 - **Angina**
 - Presyncope or (infrequently) syncope



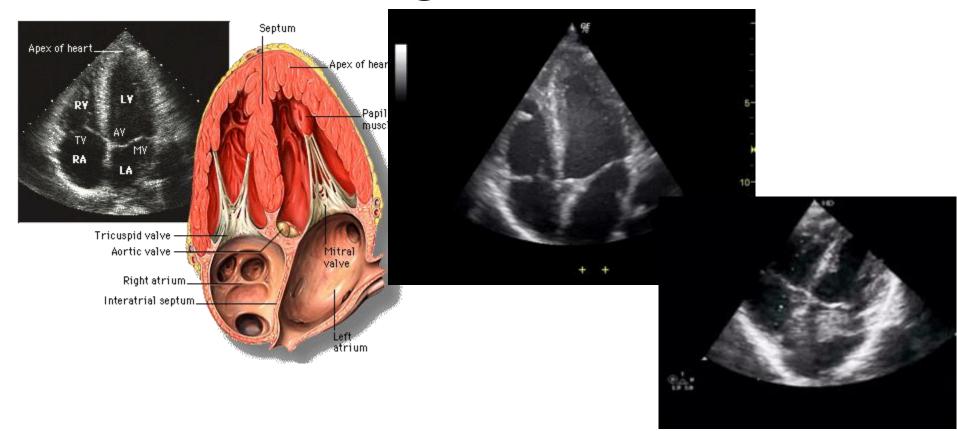
- Signs and Symptoms (continued)-
 - A-Fib can present with slow, normal, or fast rates; If the HR is greater than 100, we would call it A-Fib with Rapid Ventricular Response (RVR).
 - If sufficiently rapid, can cause hypotension, MI, or tachyinduced myocardial dysfunction
 - Although the HR can range from slow to extremely rapid, it is almost always irregular (except in complete heart block or ventricular pacer).
 - Because of varying diastolic filling duration, not all ventricular beats produce a palpable pulse (especially with fast HR).
 - Pulse deficit difference between apical rate and pulse rate

- Diagnostic Evaluation (continued)-
 - EKG also provides information about the ventricular response.
 - A-Fib often presents with Rapid Ventricular Response, with a ventricular heart rate of up to 180 bpm (commonly around 120)
 - Echocardiogram provides valuable information about the size and function of the atria and ventricles. Order for all cases of new A-Fib.
 - It can also detect valvular disease, ventricular hypertrophy, and pericardial disease
 - Transthoracic Echo (TTE) is more commonly ordered.
 - Transesophageal Echo (TEE) is more sensitive for detection of thrombi formation in the left atrium or left atrial appendage

- Diagnostic Evaluation (continued)-
 - Ambulatory Cardiac Monitoring with holter monitors or implantable loop monitors can be used to find intermittent A-Fib (if clinically suspected but not captured on a routine, in-office 12-lead).
 - Baseline Laboratory Testing is also important to rule out or evaluate for metabolic causes of A-Fib. This includes:
 - TSH and fT4
 - CBC
 - CMP or BMP
 - HgbA1C

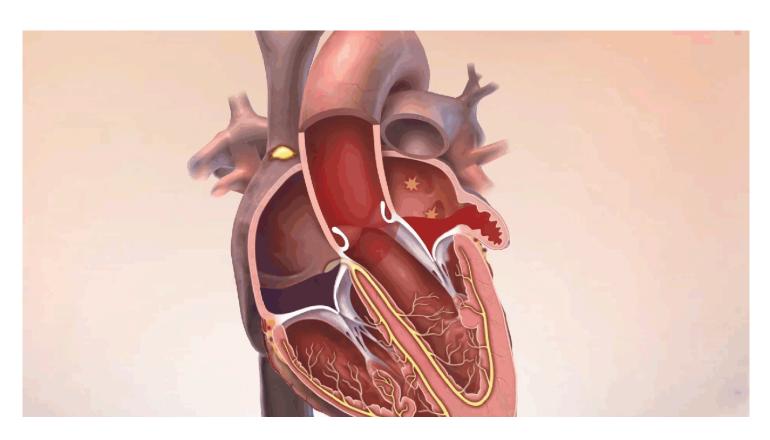


Echocardiogram



- Treatment/Management-
 - Clinical management of A-Fib can be complicated and multifactorial.
 - The plan is tailored to the patient in the context of stability
 - For all those with A-Fib, the three principal goals of treatment are...
 - Control of symptoms
 - Prevention of thromboembolism
 - **■** Reduce recurrence or progression via optimizing risk factors

Atrial Fibrillation and Stroke



Anti-coagulants – When to consider?

Paroxysmal, Persistent, Long-standing Persistent, and Permanent AF.

LOF

- Any patient with AF where the annual risk of stroke is >2%
- If not started, reassess patient risk and desire (shared decision-making) to start
- Use risk calculators: Chads2, Atria, Chads2vasc, Garfield etc.

DECOMMENDATIONS

Recommendations for Risk-Based Selection of Oral Anticoagulation: Balancing Risks and Benefits Referenced studies that support the recommendations are summarized in the Online Data Supplement.

	COIL	LOL	RECOMMENDATIONS			
	1	B-R	1. In patients diagnosed with AF who have an estimated annual risk of stroke or thromboembolic events ≥2%, selection of therapy to reduce the risk of stroke should be based on the risk of thrombo-			
_			embolism, regardless of whether the AF pattern is paroxysmal, persistent, long-standing persistent, or permanent. ¹⁻³			
	1	B-NR	 In patients with AF at risk for stroke, reevaluation of the need for and choice of stroke risk reduction therapy at periodic intervals is recommended to reassess stroke and bleeding risk, net clinical benefit, and proper dosing.^{4,5} 			
			proper dusting.			

COD

Anti-coagulants – When to consider?

Paroxysmal, Persistent, Long-standing Persistent, and Permanent AF.

- Any patient with AF where the annual risk of stroke is ≥2%
- Annual stroke ≥1 and <2% may **consider** anticoagulation
- DOACs > VKA if there is NO moderate or severe rheum mitral stenosis or mechanical heart valves

Recommendations for Antithrombotic Therapy Referenced studies that support the recommendations are summarized in the Online Data Supplement.

COR	LOE	RECOMMENDATIONS
1	Α	 For patients with AF and an estimated annual thromboembolic risk of ≥2% per year (eg, CHA₂DS₂-VASc score of ≥2 in men and ≥3 in women), anticoagulation is recommended to prevent stroke and systemic thromboembolism.¹⁻⁷
1	A	 In patients with AF who do not have a history of moderate to severe rheumatic mitral stenosis or a mechanical heart valve, and who are candidates for anticoagulation, DOACs are recommended over warfarin to reduce the risk of mortality, stroke, systemic embolism, and ICH.¹⁻⁷
2a	Α	 For patients with AF and an estimated annual thromboembolic risk of ≥1% but <2% per year (equivalent to CHA₂DS₂-VASc score of 1 in men and 2 in women), anticoagulation is reasonable to prevent stroke and systemic thromboembolism.^{1,3}
3: Harm	B-R	4. In patients with AF who are candidates for anticoagulation and without an indication for antiplatelet therapy, aspirin either alone or in combination with clopidogrel as an alternative to anticoagulation is not recommended to reduce stroke risk. ^{8,9}
3: No Benefit	B-NR	 In patients with AF without risk factors for stroke, aspirin monotherapy for prevention of thromboembolic events is of no benefit.^{10,11}

*J Am Coll Cardiol. Nov 30, 2023. Epublished DOI: 10.1016/j.jacc.2023.08.017

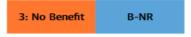
Anti-coagulants – When to consider?

Paroxysmal, Persistent, Long-standing Persistent, and Permanent AF.

- In AF, who are candidates for anticoagulation, without indication for antiplatelet (aspirin or p2y12i, e.g., clopidogrel)
 → It is NOT recommended to use alone or in combination to reduce stroke. i.e., they are NOT alternatives to DOACs/VKA!
- If there is no risk of stroke, ASA alone is of NO BENEFIT



4. In patients with AF who are candidates for anticoagulation and without an indication for antiplatelet therapy, aspirin either alone or in combination with clopidogrel as an alternative to anticoagulation is not recommended to reduce stroke risk.^{8,9}



5. In patients with AF without risk factors for stroke, aspirin monotherapy for prevention of thromboembolic events is of no benefit.^{10,11}



Anticoagulants – When to consider?

Paroxysmal, Persistent, Long-standing Persistent, and Permanent AF.

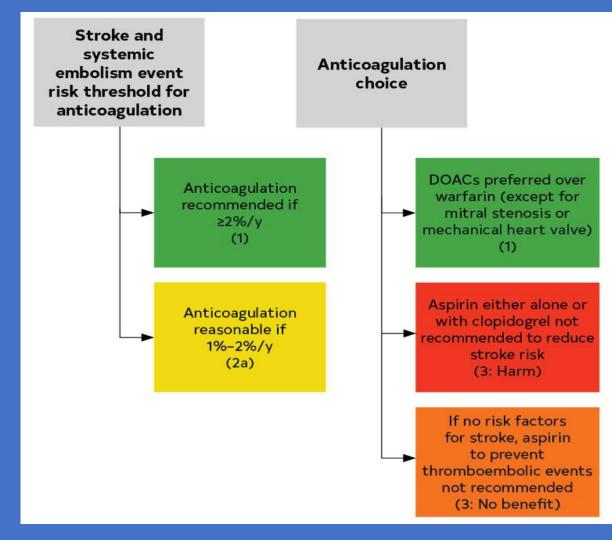
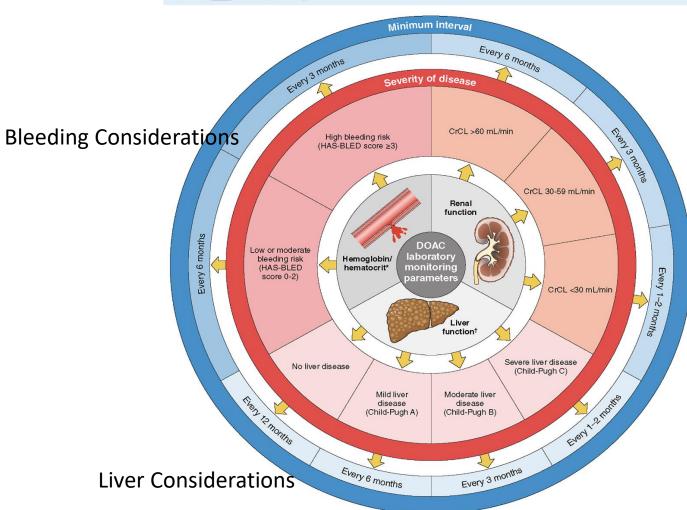


TABLE 13 OACs I	Pharmacokinetic (Characteristics and Dosing			
Class	VKA	Direct Thrombin Inhibitor		Factor Xa Inhibitor	
Name	Warfarin	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
Metabolism	S-isomer: CYP2C9 R-isomer: CYP1A2, CYP2C19, CYP3A4	Minimal	CYP3A4/5	СҮРЗА4	Minimal CYP3A4
P-glycoprotein substrate	No	Yes	Yes	Yes	Yes
Excretion	O% renal; very little warfarin excreted unchanged in urine	80% renal	66% renal, 28% feces	27% renal, 73% biliary and intestinal	50% renal, 50% liver and biliary/intestinal
Half-life	20-60 h	12-17 h	5-9 h	12 h	10-14 h
Renal dosing adjustment based on	N/A	CrCl >30 mL/min 150 mg twice daily	CrCl >50 20 mg daily with the mL/min biggest meal*	5 mg twice daily	CrCl >50-≤95 60 mg mL/ min once daily
actual body weight		CrCl 15-30 mL/ 75 mg twice min daily	CrCl 15-50 15 mg daily with the mL/min biggest meal*	If any 2 of the following: age ≥80y, body weight ≤60 kg, SCr ≥1.5 mg/dL	CrCl 15-50 30 mg mL/min once daily
Drug interaction management based on concomitant therapy of CYP3A4 inhibitors/ p-glycoprotein inhibitors	Adjust dose based on INR trends	CrCl 30-50 mL/min with concomitant use of dronedarone or systemic ketoconazole: 75 mg twice daily CrCl <30 mL/min: avoid dabigatran use concomitantly with dronedarone or systemic ketoconazole		In patients receiving apixaban 5 mg twice daily reduce dose to 2.5 mg twice daily when combined p-glycoprotein and strong CYP3A4 inhibitors (eg, itraconazole, systemic ketoconazole, ritonavir) are used concomitantly If patients already receiving apixaban 2.5 mg twice daily, avoid apixaban use if combined p-glycoprotein and strong CYP3A4 inhibitors are concomitantly used	No dose adjustment is required
Drug interaction management based on concomitant therapy of p-glycoprotein/ CYP3A4 inducers (eg, carbamazepine, phenytoin, rifampin, St. John's wort)	Adjust dose based on INR trends	Avoid use	Avoid use	Avoid use	Avoid use with rifampin. No study evaluated the effect of other p-glycoprotein/ CYP3A4 inducers on edoxaban drug levels
Appropriate use based on liver function (Child-Pugh score)†	Not mentioned in the labeling	No dose adjustment needed	No dose adjustment needed	No dose adjustment needed	No dose adjustment needed
Child-Pugh A (mild)					
Child-Pugh B (moderate)		Use with caution	Avoid use	Use with caution	Use with caution
: 10.1016/j.jacc. (severe)		Avoid use	Avoid use	Avoid use	Avoid use

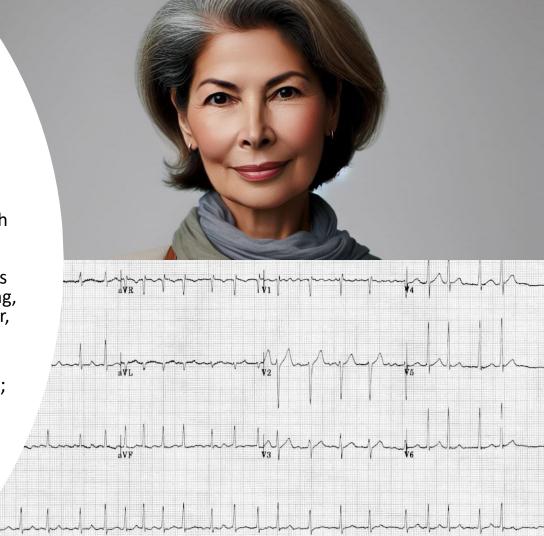


Kidney Considerations

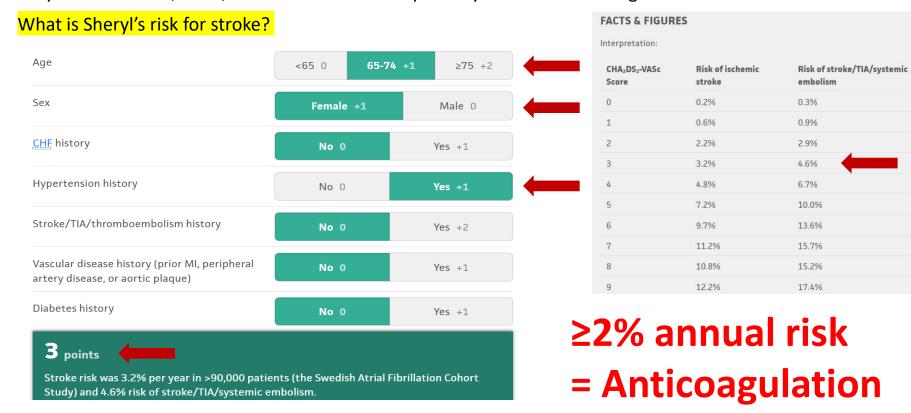
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LABS: Serum Cr 1.1; AST 23; ALT 32; A1c 5.8%; TSH 2.23

What is Sheryl's risk for stroke?



Sheryl, a <u>66-year-old woman</u>, is a well-established patient who presents with a 3-month history of being **"tired a lot more."** She has had moments where **"my heart beats fast,"** and this causes her to feel **"dizzy and lightheaded."** She is on losartan-HCT 25-12.5 mg and amlodipine 5 mg, "I've had high blood pressure for years." No fever, chills, or sweats. Does not report any abnormal bleeding.



Age 66; HTN; Serum Cr 1.1; AST 23; ALT 32; A1c 5.8%; TSH 2.23

HAS-BLED SCORING	USING THE SCORE		
Each checkmark = 1 point:	Score = 0–1: Low risk		
➡ Hypertension (SBP >160 mm Hg)	Score = 2: Moderate risk		
Abnormal: ☐ Kidney function: serum creatinine >2.26 ☐ Liver function: Bili > 2X ULN <u>and</u> LFTs > 3X LN	Score = 3: High risk		
□ Stroke history	For patients at high bleeding		
☐ B leeding history or predisposition	risk, consider:		
□ Labile INRs: TTR 60%	☐ Optimizing blood pressure control		
■ Elderly: > 65 years	☐ More frequent INRs in first 3 months		
Drugs: ☐ ETOH abuse	of warfarin		
☐ ASA or NSAID use	☐ Anticoagulation clinic management		
	☐ Fall prevention interventions, if needed		
	☐ Use of NOAC		

	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
Class	Antithrombin	Factor Xa inhibitor	Factor Xa inhibitor	Factor Xa inhibitor
Bleeding risk compared to warfarin	Less intracranial bleeding Higher incidence of gastrointestinal bleeding	Less intracranial bleeding Higher incidence of gastrointestinal bleeding	Substantially lower risk of major bleeding Less intracranial bleeding	Lower risk of major bleeding Less intracranial bleeding
Dosage	110 mg twice daily 150 mg twice daily	20 mg once daily (give with food)	5 mg twice daily	60 mg once daily
Dosage adjustments	75 mg twice daily for creatinine clearance 15–30 mL/min (approved in the United States but not tested in clinical trials)	15 mg once daily for creatinine clearance < 50 mL/min	2.5 mg twice daily for patients with at least two of three risk factors: 1. Age ≥ 80 years 2. Body weight ≤ 60 kg 3. Serum creatinine ≥ 1.5 mg/dL	30 mg once daily for creatinine clearance ≤50 mL/min FDA recommends not to use if creatinine clearance >95 mL/min

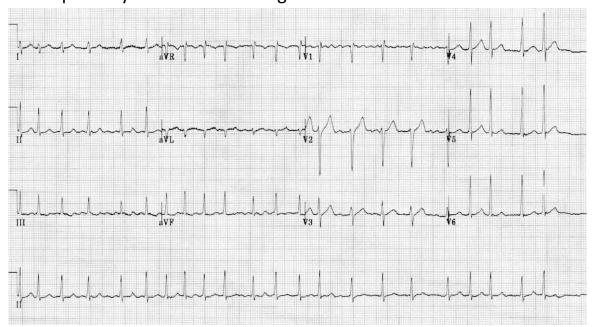


Sheryl, a <u>66-year-old woman</u>, is a well-established patient who presents with a 3-month history of being **"tired a lot more."** She has had moments where **"my heart beats fast,"** and this causes her to feel **"dizzy and lightheaded."** She is on losartan-HCT 25-12.5 mg and amlodipine 5 mg, "I've had high blood pressure for years." No fever, chills, or sweats. Does not report any abnormal bleeding.

She is Stage 3 – AF.

Not sure yet whether it is <u>Paroxysmal</u>, <u>Persistent</u>, or <u>Long-standing Persistent</u>.

She meets guideline criteria at CHADS2Vasc 3, for stroke prophylaxis (anticoagulant).



Caveats for anticoagulation

Remember, "Atrial Fibrillation" needs to have patient context, duration/burden, and symptom context

ATRESIA

Sub-clinical AF – "Atrial High Rate Episodes" by implanted devices (e.g., pacemaker, defibrillator, loop recorder) ≥6 to ≤24 minutes

EXCLUDED: Afib by EKG, telemetry or Holter > 6 min regardless of symptoms.

ARTESIA



HEALEY, J.S., ET AL. APIXABAN FOR STROKE PREVENTION IN FIBRILLATION. N ENGL J MED. 2024;390:170-1.

QUESTION

INCLUSION CRITERIA

- 1. Patients with subclinical atrial fibrillation detected by cardiac monitor with at least one episode lasting 6 min but no
- 2. CHADSCVASC of 3 or higher
- 3. Age ≥ 55 years

EXCLUSION CRITERIA

- 1. History of major bleeding within the last 6 months
- 2. Creatinine clearance < 25 mL/min
- 3. Treatment w/ other DOAC

RANDOMIZATION

Mean follow up: 3.5 +/- 1.8 years



N = 4012



*Anticoagulation was permanently discontinued if there was development of atrial fibrillation lasting > 24hrs



PRIMARY OUTCOME

STROKE OR SYSTEMIC EMBOLISM



Apixaban





SAFETY OUTCOME



Apixaban



95% CI 1.26 to 2.57



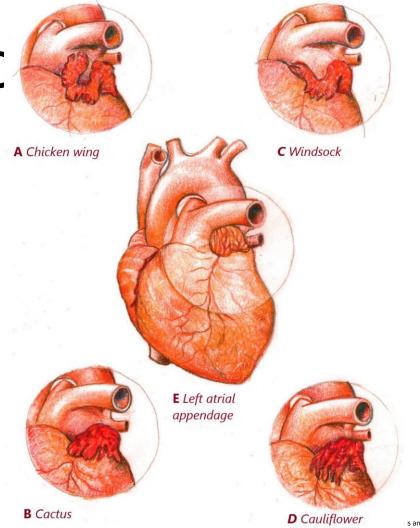
CONCLUSION

In patients with subclinical atrial fibrillation, patients randomized to apixaban had a lower risk of stroke or systemic embolism than aspirin but a higher risk of major bleeding.

Atrial Fibrillatic

What about devices to reduce stroke in AF?

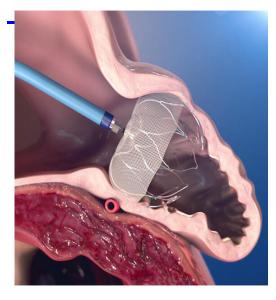
The left atrial appendage

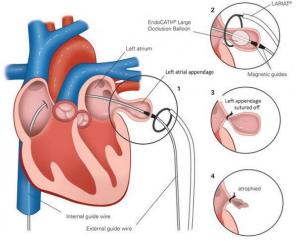


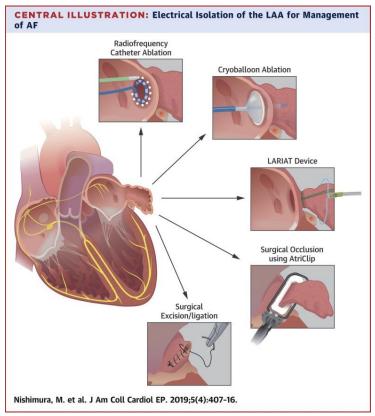
Atrial Fibrillation

What about devices to reduce stroke in AF?

Lariat







RATE VS RHYTHM – No clear choice, but some variables to help decide

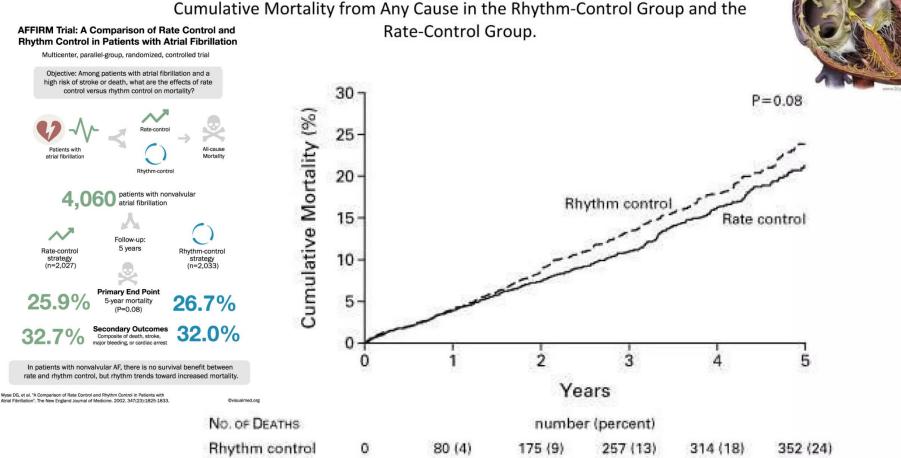


Randomized Control Trial	Population	Treatments	Outcomes
AFFIRM (2002)	Patients with AF and additional	Rate: BB, CCB, digoxin	No difference in survival
	stroke risk factors	Rhythm: amiodarone, sotalol,	 Lower risk of adverse drug
	• n = 4060	propafenone, procainamide,	effects with rate control
		quinidine, flecainide,	
		disopyramide, moricizine	
RACE (2002)	Persistent AF after previous	Rate: digoxin, BB, CCB, or	Rate control non-inferior to
	electrical cardioversion	combination	rhythm control
	• n = 522	Rhythm: cardioversion, sotalol,	
		flecainide, amiodarone	

AFFIRM, PMID 12466506; **RACE**, PMID 12466507 Abbreviations: AF = atrial fibrillation; BB = beta blocker; CCB = calcium channel blocker

Rate control

Cumulative Mortality from Any Cause in the Rhythm-Control Group and the



78 (4)

148 (7)

210 (11)

275 (16)

306 (21)

TABLE 2. DRUGS USED IN THE RATE-CONTROL GROUP AND THE RHYTHM-CONTROL GROUP.*

Drug	RATE-CONTROL GROUP		RHYTHM-CONTROL GROUP	
At least 10%, up to 20% use of rhythm control agent at any time in the 5 years, no idea for how long or if in the same patient	USED DRUG FOR INITIAL THERAPY	USED DRUG AT ANY TIME no. of pati	USED DRUG FOR INITIAL THERAPY	USED DRUG AT ANY TIME
Rate control				
Data available Digoxin Beta-blocker Diltiazem Verapamil Rhythm control	1957 949 (48.5) 915 (46.8) 583 (29.8) 187 (9.6)	2027 1432 (70.6) 1380 (68.1) 935 (46.1) 340 (16.8)	1266 417 (32.9) 276 (21.8) 198 (15.6) 56 (4.4)	2033 1106 (54.4) 1008 (49.6) 610 (30.0) 204 (10.0)
Data available Amiodarone Sotalol Propafenone Procainamide Quinidine Flecainide Disopyramide Moricizine Dofetilide	1265 2 (0.2)† 1 (0.1)† 2 (0.2)† 0 2 (0.2)† 0 0 0	2027 207 (10.2) 84 (4.1) 45 (2.2) 30 (1.5) 14 (0.7) 29 (1.4) 7 (0.3) 2 (0.1) 5 (0.2)	1960 735 (37.5) 612 (31.2) 183 (9.3) 103 (5.3) 92 (4.7) 88 (4.5) 42 (2.1) 14 (0.7) 0	2033 1277 (62.8) 841 (41.4) 294 (14.5) 173 (8.5) 151 (7.4) 169 (8.3) 87 (4.3) 35 (1.7) 13 (0.6)

RATE VS RHYTHM — I may sneak off with rhythm control first though...;)





EAST-AFNET 4 TRIAL



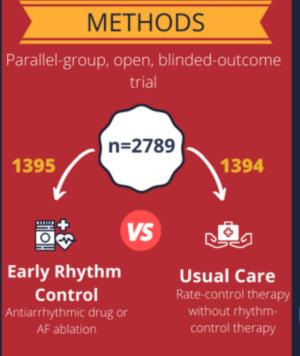
Kirchhof P. et al. Early Rhythm-Control Therapy in Patients With Atrial Fibrillation. N Engl J Med 2020;383:1305-16..

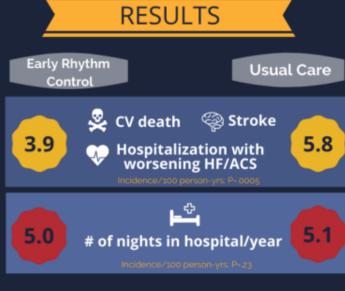
OBJECTIVE

? Is Early Rhythm-Control
? Therapy associated with lower risk of CV Outcomes in patients with early AFIB?

Rhythm control strategies: antiarrhythmic drugs or ablation and/or cardioversion of persistent AF

Both groups were in their first year of AFib diagnosis with at least two CV conditions





Safety outcome: Serious adverse events related to

rhythm-control therapy occurred in 4.9% vs 1.4% of

the patients assigned to usual care

Conclusion: Early rhythm control was associated with a lower risk of CV outcomes than usual care among patients with early AF and CV conditions





CV death



🗐 Stroke



Hospitalization with worsening HF/ACS

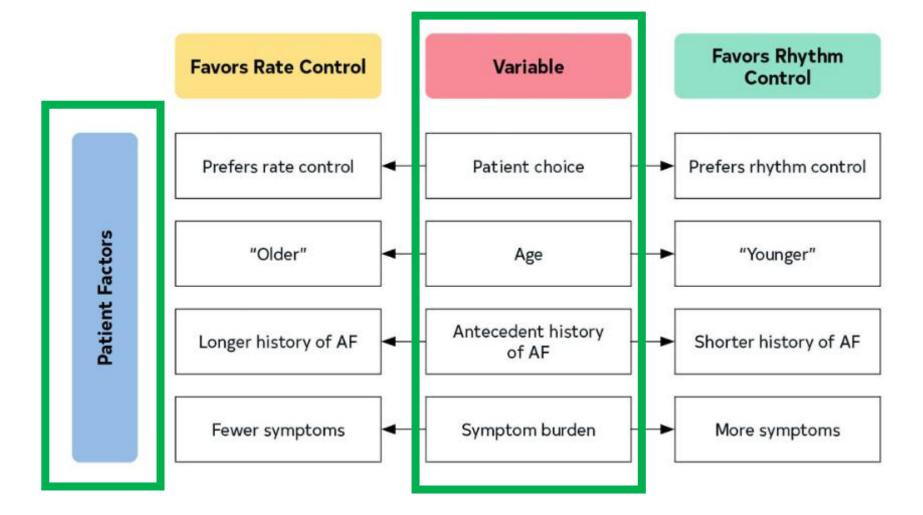
5.8

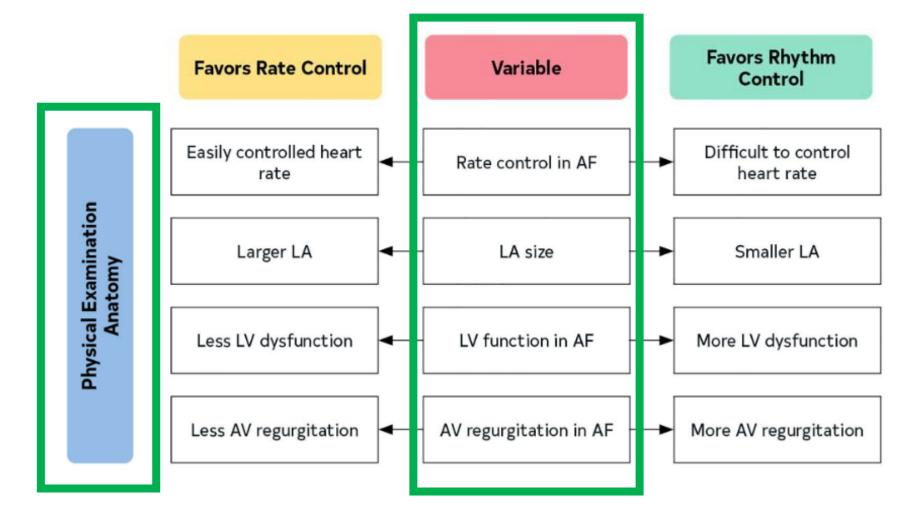
Incidence/100 person-yrs: P-.0005





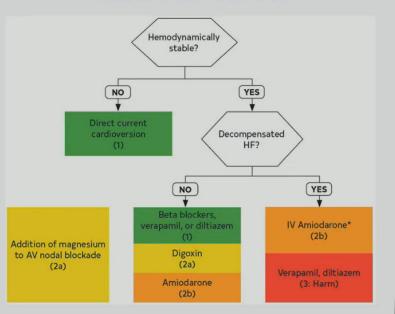
of nights in hospital/year





Atrial Fibrillation Management – Rate Control

Acute Rate Control





Atrial Fibrillation

Newly diagnosed A-Fib: initial management depends on whether they are hemodynamically unstable or stable.

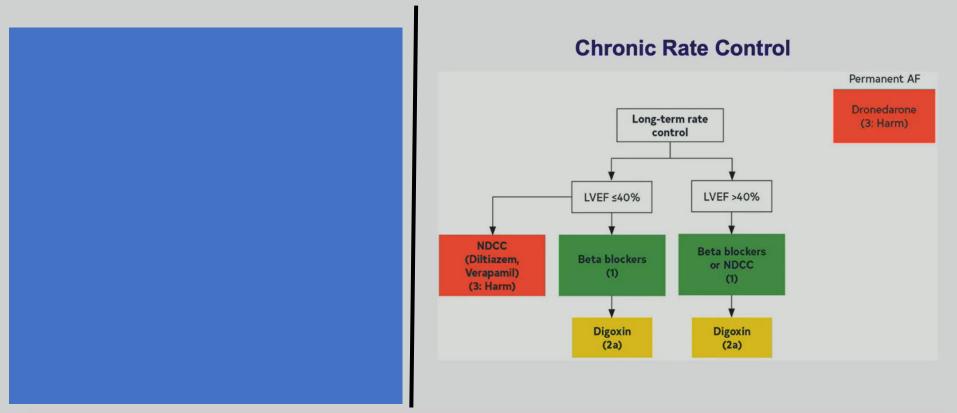
- Hemodynamically Unstable Patient-
 - Hospitalization and immediate treatment of A-Fib are required.
 - Instability is generally a result of rapid ventricular rate or associated cardiac or noncardiac conditions.
 - In the acute setting, IV beta blockers (ie. Metoprolol) or IV calcium channel blockers (ie. Diltiazem) are usually effective at rate control.
 - What about urgent electrical cardioversion?
 - indicated in patients with shock/severe hypotension, pulmonary edema, or ongoing MI/ischemia.

Atrial Fibrillation

Newly diagnosed A-Fib: initial management depends on whether they are hemodynamically unstable or stable.

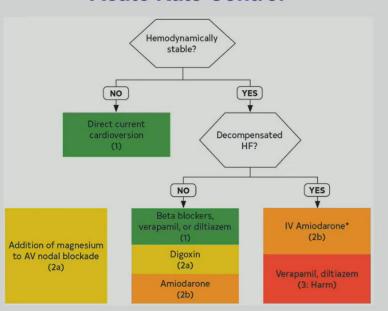
- Hemodynamically Stable Patient-
 - If the newly diagnosed patient is clinically stable and at least relatively asymptomatic, hospitalization is generally not necessary.
 - A strategic approach to rate control and anticoagulation is appropriate.
 - This is true whether the condition that precipitated the A-Fib is likely to persist or might resolve spontaneously over hours to days
 - In stable patients, IV or PO beta blockers or calcium channel blockers are considered first-line agents for controlling ventricular rate.
 - Up to 66% of those with acute onset (< 36 hrs) of A-Fib spontaneously revert to NSR without cardioversion; If A-Fib has been present for more than a week, spontaneous conversion is unlikely.

Atrial Fibrillation Management – Rate Control

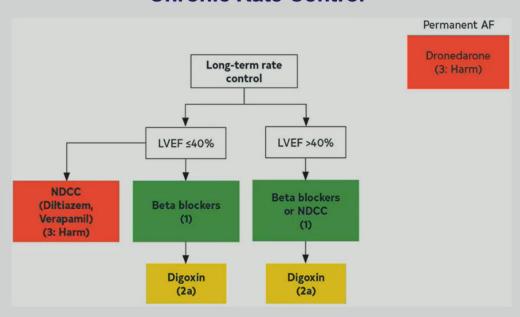


Atrial Fibrillation Management – Rate Control

Acute Rate Control



Chronic Rate Control



Rate Control – What heart rate parameters?

Paroxysmal, Persistent, Long-standing Persistent, and Permanent AF.

- A decision to remain in AF also means reasonable heart rate parameters to avoid tachycardic cardiomyopathy or avoidable symptoms from tachycardia.
- Absent a co-morbid diagnosis of Heart Failure, resting heart rates of <100 to 110 is reasonable

Recommendations for Broad Considerations for Rate Control
Referenced studies that support the recommendations are summarized in the Online Data Supplement.

COR	LOE	RECOMMENDATIONS
1	B-NR	 In patients with AF, SDM with the patient is recommended to discuss rhythm- versus rate-control stra- tegies (taking into consideration clinical presentation, comorbidity burden, medication profile, and pa- tient preferences), discuss therapeutic options, and for assessing long-term benefits.¹⁻³
2a	B-R	 In patients with AF without HF who are candidates for select rate-control strategies, heart rate target should be guided by underlying patient symptoms, in general aiming at a resting heart rate of <100 to 110 hnm.^{2,4-6}

Rate Control – What heart rate parameters?

Paroxysmal, Persistent, Long-standing Persistent, and Permanent AF.

Recommendations for Long-Term Rate Control

Referenced studies that support the recommendations are summarized in the Online Data Supplement.

COR	LOE	RECOMMENDATIONS
1	B-NR	 In patients with AF, beta blockers or nondihydropyridine calcium channel blockers (diltiazem, verapamil) are recommended for long-term rate control with the choice of agent according to underlying substrate and comorbid conditions.^{1,2}
2a	B-NR	2. For patients with AF in whom measuring serum digoxin levels is indicated, it is reasonable to target levels <1.2 ng/mL. ³⁻⁶
2a	B-R	3. In patients with AF and HF symptoms, digoxin is reasonable for long-term rate control in combination with other rate-controlling agents, or as monotherapy if other agents are not preferred, not tolerated, or contraindicated. ⁷⁻⁹
3: Harm	C-LD	4. In patients with AF and LVEF <40%, nondihydropyridine calcium channel-blocking drugs should not be administered given their potential to exacerbate HF. ^{10,11}
3: Harm	B-R	 In patients with permanent AF who have risk factors for cardiovascular events, dronedarone should not be used for long-term rate control.¹²



Atrial Fibrillation Management – AV Node Ablation

7.3. Atrioventricular Nodal Ablation (AVNA)

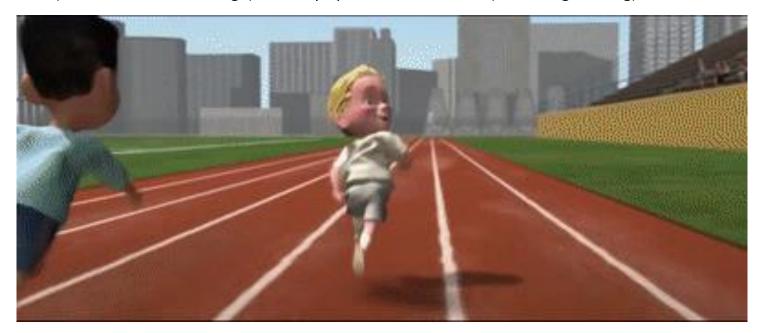
Recommendations for AVNA Referenced studies that support the recommendations are summarized in the Carlina Batta Supplement.				
COR	LOE	Recommendations		
1	C-LD	In patients with AF and a persistently rapid ventricular response who undergo AVNA, initial pacemaker lower rate programming should be 80 to 90 bpm to reduce the risk of sudden death. ^{1,9}		
2a	B-R	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 OOL. ⁹⁻⁶		
1	B-NR	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	 In patients with AF with normal EF undergoing AVNA, conduction system pacing of the His bundle¹⁰⁻¹³ or left bundle area^{12,13} may be reasonable. 		

- AV node ablation can be useful to improve symptoms and quality of life in patients with AF and uncontrolled rapid ventricular response refractory to medical management (Level 2a)
- Patients with AF and plan for AV node ablation, implantation of a pacemaker before the ablation is recommended to ensure adequacy of pacing leads prior to ablation. (Level 1)
- Initial pacemaker lower rate programming should be 80 to 90 bpm to reduce the risk of sudden death. (Level 1)
- Conduction system pacing may be reasonable in AF patients with normal LVEF undergoing AV node ablation.

Rate Control – What heart rate parameters?

Paroxysmal, Persistent, Long-standing Persistent, and Permanent AF.

- Tachy-Brady Syndrome Be careful of the iatrogenic variety of bradycardia
- Too slow (rate control dose too high), <60 + symptomatic; or too fast (not enough dosing), >110 sustained



Rhythm Control

Paroxysmal, Persistent, Long-standing Persistent, and Permanent AF.

Recommendations for Goals of Therapy With Rhythm Control
Referenced studies that support the recommendations are summarized in the Online Data Supplement.

All very reasonable, laudable even, goals. Clinical trials have not addressed these directly to date

COR	LOE	RECOMMENDATIONS
1	B-R	 In patients with reduced LV function and persistent (or high burden) AF, a trial of rhythm control should be recommended to evaluate whether AF is contributing to the reduced LV function.¹⁻⁶
2a	B-R	2. In patients with symptomatic AF, rhythm control can be useful to improve symptoms. ⁷⁻¹¹
2a	B-R	3. In patients with a recent diagnosis of AF (<1 year), rhythm control can be useful to reduce hospitalizations, stroke, and mortality. ¹²⁻¹⁴
2a	B-R	 In patients with AF and HF, rhythm control can be useful for improving symptoms and improving out- comes, such as mortality and hospitalizations for HF and ischemia.¹⁵⁻¹⁹
2a	B-NR	5. In patients with AF, rhythm-control strategies can be useful to reduce the likelihood of AF progression. 20-27
2b	C-LD	 In patients with AF where symptoms associated with AF are uncertain, a trial of rhythm control (eg, cardioversion or pharmacological therapy) may be useful to determine what if any symptoms are attributable to AF.²⁸⁻³²
		7. In patients with AF, rhythm-control strategies may be useful to reduce the likelihood of development of

dementia or worsening cardiac structural abnormalities. 33-45

2b

B-NR

Rhythm Control

Paroxysmal, Persistent, Long-standing Persistent, and Permanent AF.

For rhythm control

- If HFrEF ≤40% = amiodarone or dronedarone
- Uncomplicated AF = flecainide or propafenone
- 3) Uncomplicated AF = if failed flecainide or propafenone, consider dofetilide, amiodarone, or sotalol

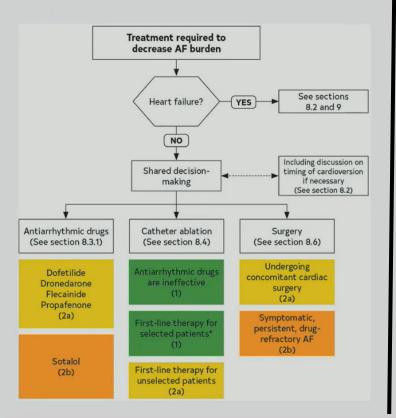


Recommendations for Specific Drug Therapy for Long-Term Maintenance of Sinus Rhythm
Referenced studies that support the recommendations are summarized in the Online Data Supplement.

COR	LOE	RECOMMENDATIONS
2a	A* B-NR†	 For patients with AF and HFrEF (≤40%), therapy with dofetilide*1 or amiodarone†2 is reasonable for long-term maintenance of sinus rhythm.
2a	A	 For patients with AF and no previous MI, or known or suspected significant structural heart disease, or ventricular scar or fibrosis, use of flecainide³⁻⁵ or propafenone⁵⁻¹² is reasonable for long-term mainte- nance of sinus rhythm.
2a	A	 For patients with AF without recent decompensated HF or severe LV dysfunction, use of dronedarone^{5,13-15} is reasonable for long-term maintenance of sinus rhythm.
2a	Α	4. For patients with AF without significant baseline QT interval prolongation or uncorrected hypokalemia or hypomagnesemia, use of dofetilide ^{1,5,16} 5-7,10,17,18 is reasonable for long-term maintenance of sinus rhythm, with proper dose selection based on kidney function and close monitoring of the QT interval, serum potassium and magnesium concentrations, and kidney function.
2a	А	5. For patients with AF and normal LV function, use of low-dose amiodarone (100-200 mg/d) is reasonable for long-term maintenance of sinus rhythm ^{2,5,17-22} but, in view of its adverse effect profile, ^{5,23,24} should be reserved for patients in whom other rhythm control strategies are ineffective, not preferred, or contraindicated.
2b	А	6. For patients with AF without significant baseline QT interval prolongation, hypokalemia, hypomagne- semia, or bradycardia, use of sotalol ^{5-7,10,17,18} may be considered for long-term maintenance of sinus rhythm, with proper dose selection based on kidney function and close monitoring of the QT interval, heart rate, serum potassium and magnesium concentrations, and kidney function.
3: Harm	B-R	 In patients with previous MI and/or significant structural heart disease, including HFrEF (LVEF ≤40%), flecainide and propafenone²⁵ should not be administered due to the risk of worsening HF, potential proarrhythmia, and increased mortality.^{26,27}
3: Harm	B-R	For patients with AF, dronedarone should not be administered for maintenance of sinus rhythm to those with NYHA class III and IV HF or patients who have had an episode of decompensated HF in the past 4

weeks, due to the risk of increased early mortality associated with worsening HE 28

Atrial Fibrillation Management – Rhythm Control

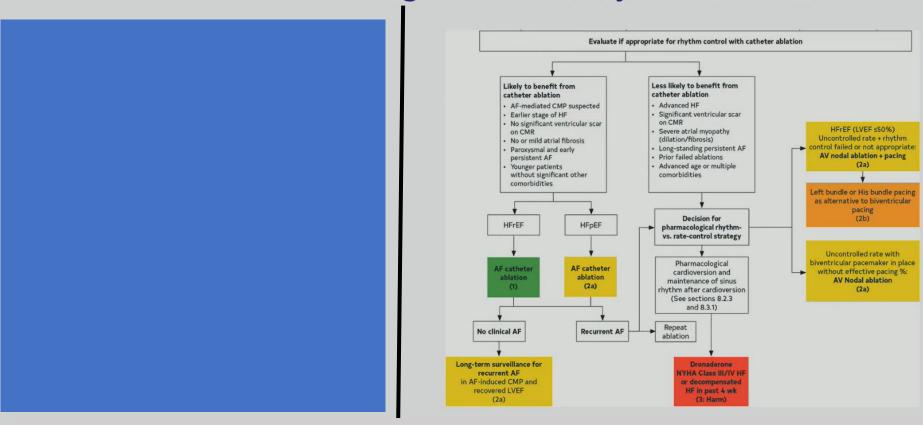




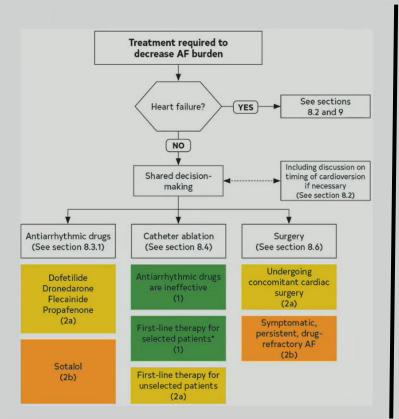
Rate vs Rhythm Control

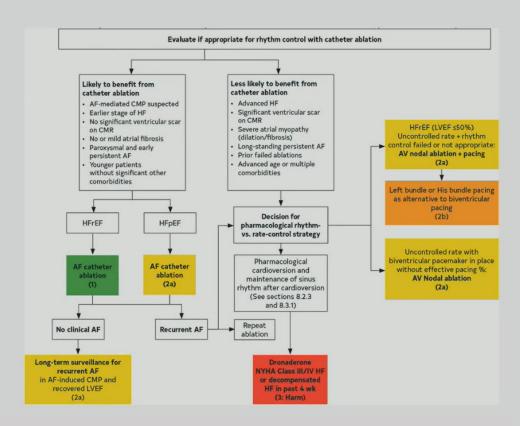
- Basic principles of the Rhythm Control strategy:
 - Initial conversion to normal sinus may involve antiarrhythmic medications or external electrical therapy.
 - AKA pharmacological or electrical cardioversion
 - STOP. THINK. -> What is the most pressing issue/complication of atrial fibrillation if you are going to "cardiovert" a patient?
 - If unknown onset of AF, initiate anticoagulation before cardioversion. In the least, perform immediate TEE prior to attempted chemical or electrical cardioversion. See anticoagulation guidelines.

Atrial Fibrillation Management – Rhythm Control



Atrial Fibrillation Management – Rhythm Control





EARLY-AF

Andrade JG, Wells GA, Deyell MW, et al. Cryoablation or drug therapy for initial treatment of atrial fibrillation.

New England Journal of Medicine. 2021;384(4):305-315.





Objective

Is first-line ablation more effective than antiarrhythmic drugs in preventing recurrence of atrial tachyarrhythmia?

Inclusion criteria:

>18 years of age
At least one episode of AF on ECG
in the past 24 months

Primary endpoint:

AF recurrence (after 91-365 days)

Secondary endpoints:
Free of symptomatic arrhythmias
AF burden
Quality of life
Health care utilization

Methods

Prospective, multicenter, openlabel, randomized trial

303 patients



monitor



Monitored via
Implantable cardiac

Results

Follow up: 1 year

Recurrence of AF

Ablation: Antiarrhythmic 66/154 (42.9%) 101/149 (67.8%)

HR 0.48 (0.35-0.66)

Symptomatic arrhythmia Safety endpoint

Ablation: 17/154 (11%) Ablation: 5/154 (3.2%) Antiarrhythmic: 39/149 (26%) Antiarrhythmic: 6/149 (4%)

HR 0.39 (0.22-0.68) HR 0.81 (0.25-2.59)

Conclusion:

Catheter cryoballoon ablation was associated with a significantly lower rate of AF recurrence when used as initial treatment for symptomatic paroxysmal AF compared to antiarrhythmic therapy.

Recurrence of AF

Ablation: Antiarrhythmic 66/154 (42.9%) 101/149 (67.8%)

HR 0.48 (0.35-0.66)

Symptomatic arrhythmia

Safety endpoint

Ablation: 17/154 (11%) Antiarrhythmic: 39/149 (26%) Ablation: 5/154 (3.2%) Antiarrhythmic: 6/149 (4%)

HR 0.39 (0.22-0.68)

HR 0.81 (0.25-2.59)

STOP AF

Wazni OM, Dandamudi G, Sood N, et al. Cryoballoon ablation as initial therapy for atrial fibrillation. New England Journal of Medicine. 2021;384(4):316-324.





Objective

Is first-line cryoballoon ablation more effective than antiarrhythmic drugs in restoring sinus rhythmm in patients with symptomatic paroxysmal AF?

Inclusion criteria:

18-80 years of age **Recurrent symptomatic** paroxysmal AF

Primary endpoint: Treatment success*

Secondary endpoints: Quality of life

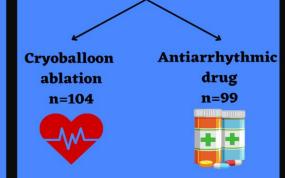
Safety endpoints (specific procedural complications)

*freedom from initial failure of the procedure or atrial arrhythmia recurrence after a 90-day blanking period to allow recovery from the procedure or drug dose adjustment, evaluated in a Kaplan-Meier analysis

Methods

Parallel, multicenter, openlabel, randomized trial

203 patients



Monitored via 12-lead EKG at 1, 3, 6, 12 mo. 24-hr holter at 6 & 12 mo

Results

Follow up: 1 year

Treatment success

Ablation: 78/104 (74.6%)

Antiarrhythmic 48/99 (45%)

P<0.001

Arrhythmia Reoccurrence

Serious Adverse event

Ablation: 21/104 (20%)

Ablation: 15/104 (14%)

Antiarrhythmic: 35/99 (35%) Antiarrhythmic: 14/99 (14%)

Conclusion:

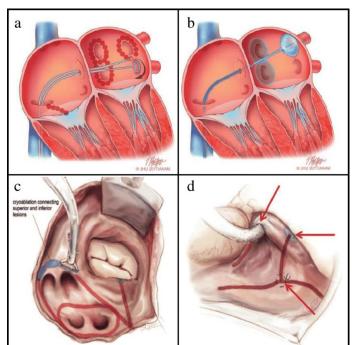
Cryoballoon ablation as initial therapy was superior to drug therapy for the prevention of atrial arrhythmia recurrence in patients with symptomatic paroxysmal AF

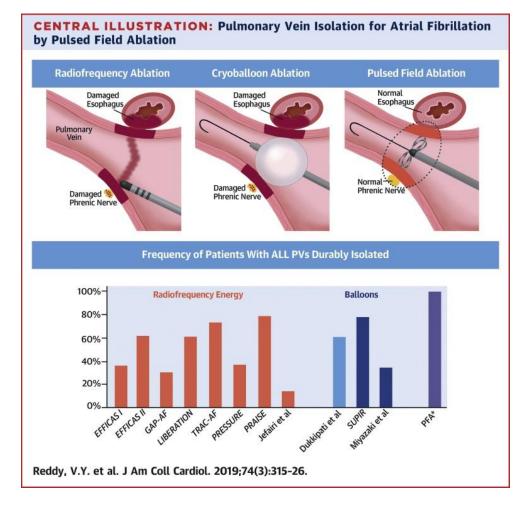
Treatment success Ablation: Antiarrhythmic 78/104 (74.6%) 48/99 (45%) P<0.001

Arrhythmia Serious Reoccurrence Adverse event

Ablation: 21/104 (20%) Ablation: 15/104 (14%) Antiarrhythmic: 35/99 (35%) Antiarrhythmic: 14/99 (14%)

Radiofrequency and cryoablation (Pulmonary Vein Isolation)







Sheryl, a <u>66-year-old woman</u>, is a well-established patient who presents with a 3-month history of being "tired a lot more." She has had moments where "my heart beats fast," and this causes her to feel "dizzy and lightheaded." She is on losartan-HCT 25-12.5 mg and amlodipine 5 mg, "I've had high blood pressure for years." No fever, chills, or sweats. Does not report any abnormal bleeding.

Rate or Rhythm control for Sheryl?

- A. Rate
- B. Rhythm
- C. No idea yet need to assess her goals/preferences and the context of her AF (symptoms, length of time, etc.) and anatomical features (large atrium, LV function, etc.).



Sheryl, a <u>66-year-old woman</u>, is a well-established patient who presents with a 3-month history of being **"tired a lot more."** She has had moments where **"my heart beats fast,"** and this causes her to feel **"dizzy and lightheaded."** She is on losartan-HCT 25-12.5 mg and amlodipine 5 mg, "I've had high blood pressure for years." No fever, chills, or sweats. Does not report any abnormal bleeding.

After the discussion, she chose to start apixaban 5 mg twice daily.

At her echocardiogram, her atria sizes are normal and she has mild concentric LVH (long-standing hypertension), and EF 55% ("normal" 50-75%) and is in NSR, ventricular rate 65.

She is now anticoagulated (stroke prophylaxis). Appear to have Paroxysmal AF (comes and goes).

Rate versus Rhythm control? Perhaps we need more data – expensive single assessment Holter, Ambulatory Telemetry Monitoring (ATM)...

OR Patient owned continuous and ongoing FDA cleared wearables?



Sheryl, a <u>66-year-old woman</u>, is a well-established patient with a 3-month history of being **"tired a lot more."** She has had moments where **"my heart beats fast,"** and this causes her to feel **"dizzy and lightheaded."** She is on losartan-HCT 25-12.5 mg and amlodipine 5 mg, "I've had high blood pressure for years." No fever, chills, or sweats. Does not report any abnormal bleeding.

She has AF stage 3, paroxysmal. She is now on apixaban 5 mg twice daily. She has metoprolol tartrate 50 mg $\frac{1}{2}$ to 1 tab PRN for heart rates >110. Her heart anatomy suggests that the rhythm control strategy is reasonable.

In the absence of LV dysfunction and symptomatic coronary disease, she elects flecainide 50 mg po BID. She likes the idea of using a wearable to identify whether symptomatic palpitations are AF.



Sheryl, a <u>66-year-old woman</u>. She has stage 3 AF, paroxysmal AF. She is now on apixaban 5 mg twice daily. She has metoprolol tartrate 50 mg ½ to 1 tab PRN for heart rates >110. Her heart anatomy suggests rhythm control strategy is reasonable.

In the absence of LV dysfunction and symptomatic coronary disease, she elects flecainide 50 mg po BID (100 mg daily) and likes the idea of using a wearable to identify whether symptomatic palpitations are AF.

Potential INSTRUCTIONS:

- 1. For AF recurrences, if HR >110, may use a ½ tab Metoprolol tartrate 50 mg.
- 2. May use an extra tab of flecainide 50 mg (up to 300 mg daily maximum) to "chemically cardiovert"
- Sheryl is provided contact numbers of the clinic and specific RN/Mas supporting me and has my direct cell for texts/calls for clarification.
- 4. Always, she is directed that ED is reasonable when symptoms are severe.

Summary

- 1. Identify and reduce elevated stroke risk with anti-coagulation. Use risk calculators WITH your patient.
- Patient-owned devices can help assess the burden of AF and help inform the choice for rate or rhythm control strategies.
- 3. Additionally, A rate or rhythm control strategy can leverage patient-owned devices to improve therapeutics' choice and "success" to achieve mutually agreed-upon goals.
- 4. Patient-owned devices may help guide patients on PRN delivery of therapeutics on top of chronic daily medications.
- 5. Patient-owned devices may help patients become more engaged and improve patient understanding of their disease and the therapies they are using.

QUESTIONS?