Atrial Fibrillation: Clinical Considerations and the Pharmacist's Role in Management

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Conflict of Interest Disclosure

Emily Farina discloses the following relationship:

- Stockholder, Pfizer Inc.

Objectives

1

Define the etiology and risk factors related to the development of atrial fibrillation.

2

Identify the treatment for atrial fibrillation, including special populations and clinical decision making.

3

Describe the pharmacist's role in the treatment of atrial fibrillation.

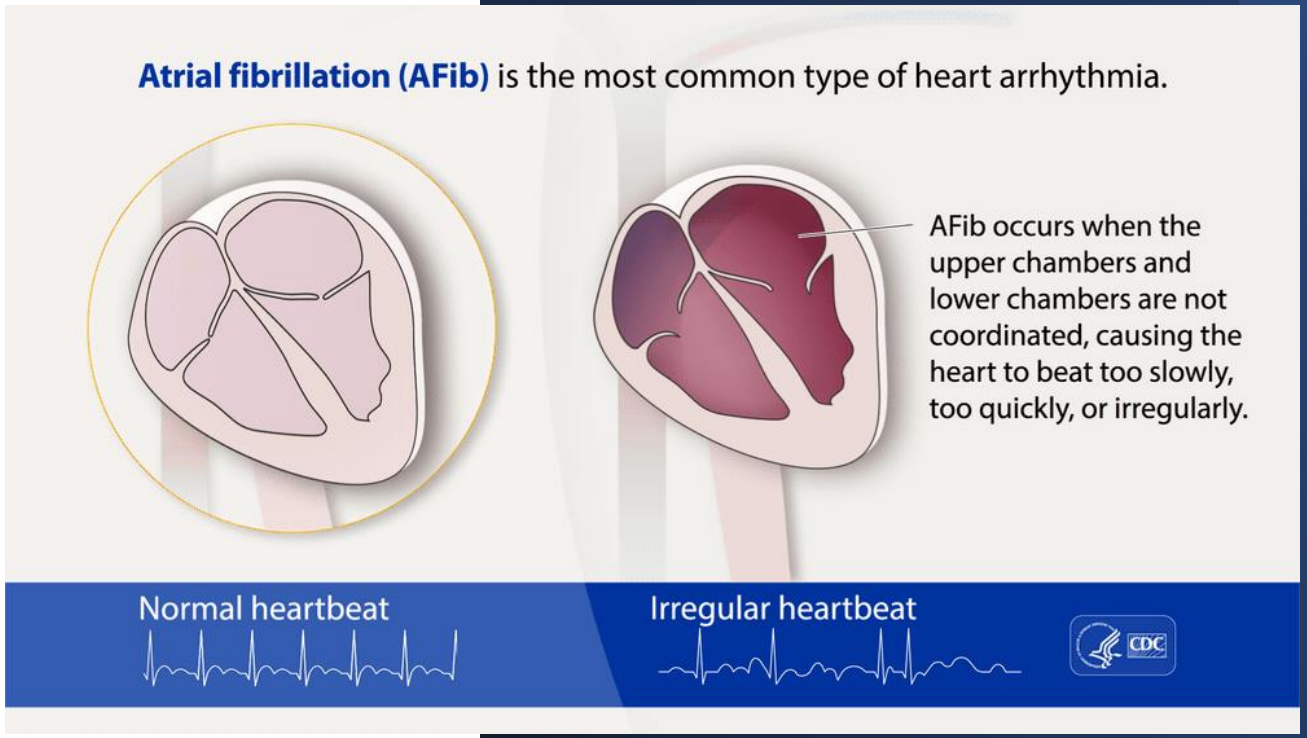
Abbreviations

- AF: Atrial Fibrillation
- AFL: Atrial Flutter
- NSR: Normal Sinus Rhythm
- ECG: Electrocardiogram
- CHF: Congestive Heart Failure
- DOAC: Directly-Acting Oral Anticoagulant
- LMWH: Low Molecular Weight Heparin
- HFrEF: Heart Failure with reduced Ejection Fraction
- ESRD: End-stage renal disease
- TTE: Transesophageal echocardiography
- ISTH: International Society on Thrombosis and Haemostasis

Introduction

What is AF?

- Supraventricular tachyarrhythmia
- Uncoordinated atrial activation + ineffective atrial contraction
- ECG Characteristics:
  - Irregular R-R intervals
  - Absence of distinct, repeating P waves
  - Irregular atrial activity



https://www.cdc.gov/heartdisease/atrial_fibrillation.htm

Source: January CT, et al. *J Am Coll Cardiol.* 2014;64(21):e1-e76.

Definitions

Paroxysmal AF

Terminates spontaneously or within 7 days onset after intervention

Persistent AF

Sustained > 7 days

Long-standing persistent AF

Sustained > 12 months

Permanent AF

Patient & clinician discontinue attempt to restore and maintain NSR

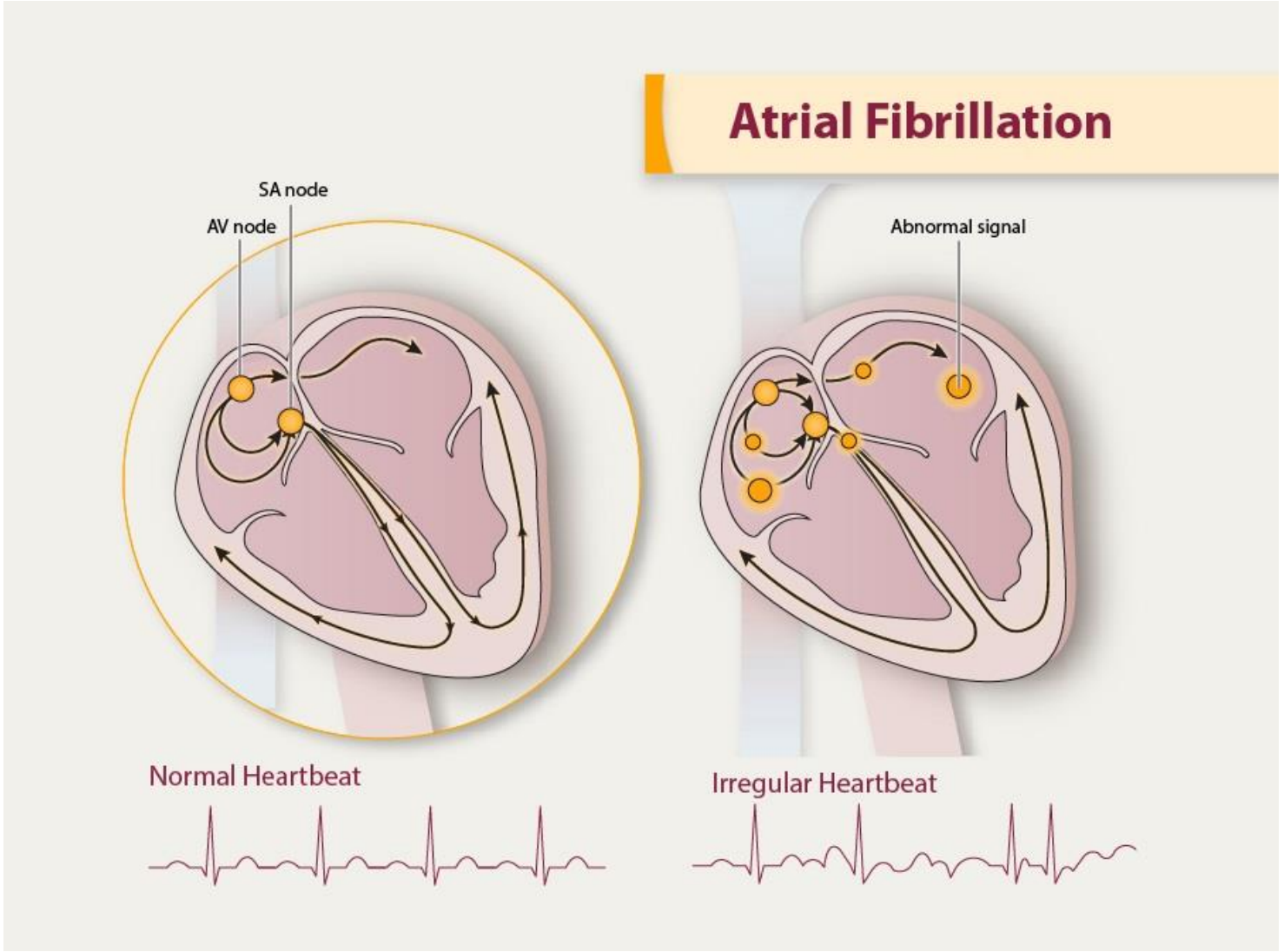
Source: January CT, et al. *J Am Coll Cardiol.* 2014;64(21):e1-e76.

Why Are We Concerned About AF?

- 12.1 million people in the U.S. may have AF by 2030
- AF mentioned on 183,321 death certificates in 2019
- Associated with 5-fold ↑ risk of acute ischemic stroke
  - AF causes 1 in 7 strokes

Source: CDC. Atrial Fibrillation. 2021. https://www.cdc.gov/heartdisease/atrial_fibrillation.htm

Pathophysiology



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Risk Factors

Nonmodifiable

- Age
- Male gender
- European ancestry
- Family history
- Heart failure
- Myocardial infarction

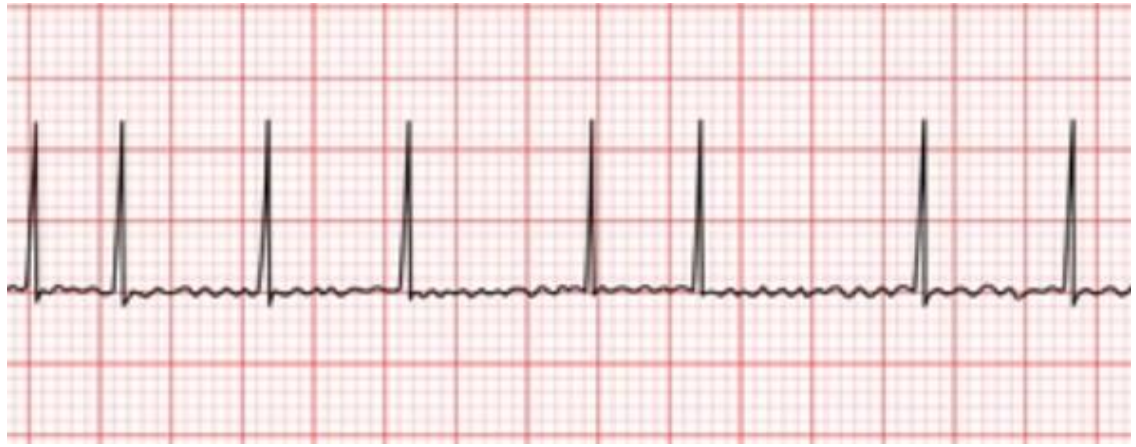
Modifiable

- Sedentary Lifestyle
- Smoking
- Obesity
- Obstructive sleep apnea
- Diabetes
- Hypertension

Source: Staerk L, et al. *Circ Res*. 2017;120(9):1501-1517.; Lau DH, et al. *Circulation*. 2017;136(6):583-596.

Diagnosis

- ECG
- Ambulatory rhythm monitoring
- Implanted loop recorders
- Pacemakers or defibrillators



https://www.shutterstock.com/search/ecg+atrial+fibrillation

Source: January CT, et al. *J Am Coll Cardiol.* 2014;64(21):e1-e76.

Pharmacotherapy

- Anticoagulation
- Conduction abnormality control
  - Rate control
  - Rhythm control

Assessing Stroke Risk: CHA_2DS_2-VASc

C	H	A_2	D	S_2	V	A	Sc
CHF	Hypertension	Age ≥75	Diabetes	Stroke/TIA	Vascular Disease	Age 65-74	Female Sex Category
1	1	2	1	2	1	1	1

	Men	Women
Anticoagulation indicated	≥ 2	≥ 3

Source: January CT, et al. *J Am Coll Cardiol.* 2014;64(21):e1-e76.; January CT, et al. *J Am Coll Cardiol*. 2019;74(1):104-132.

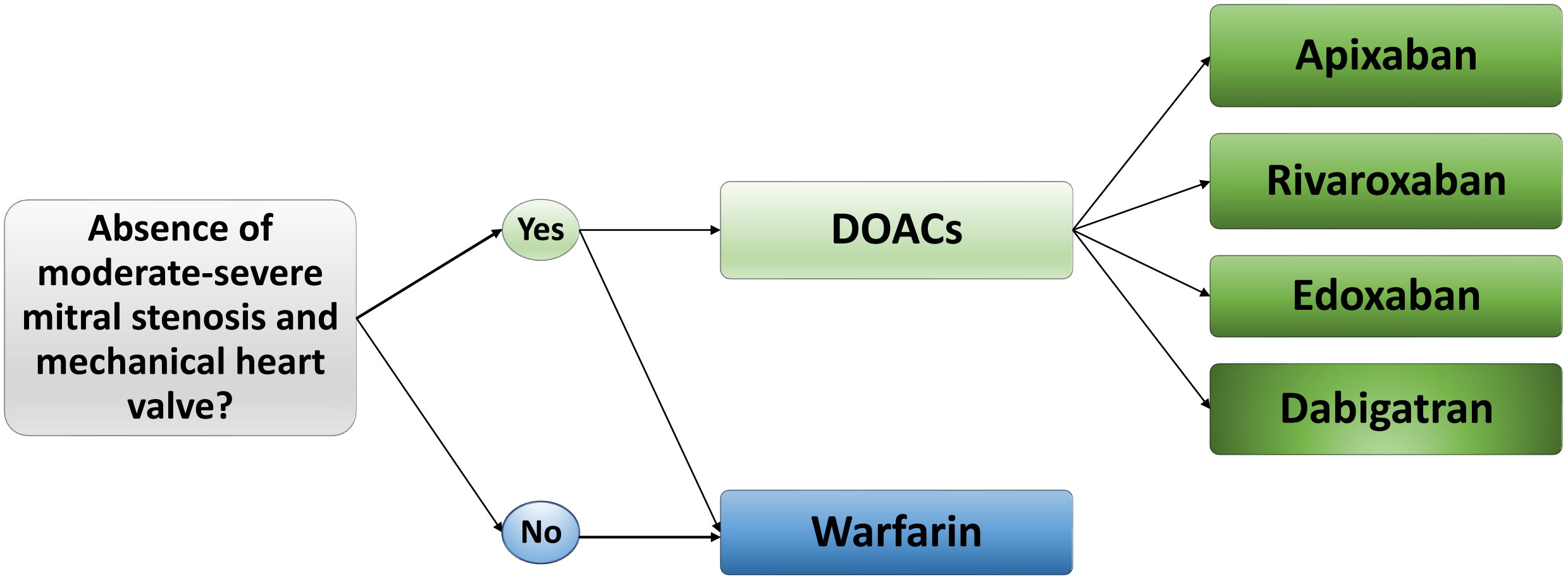
Assessing Bleeding Risk: HAS-BLED

H	A	S	B	L	E	D
Hypertension	Abnormal renal/liver function	Stroke	Bleeding history or predisposition	Labile INR	Elderly (Age ≥ 65)	Drugs/alcohol concurrently
1	1	1	1	1	1	1

0	1 – 2	≥ 3
Low risk	Moderate Risk	High risk

Source: Zhu W, et al. *Clin Cardiol*. 2015;38(9):555-561.

Anticoagulation Options



Source: January CT, et al. *J Am Coll Cardiol.* 2014;64(21):e1-e76.; January CT, et al. *J Am Coll Cardiol*. 2019;74(1):104-132.

Comparison of Anticoagulants

	Apixaban (Eliquis®)	Rivaroxaban (Xarelto®)	Edoxaban (Savaysa®)	Dabigatran (Pradaxa®)	Warfarin (Coumadin®)
AF dose	5mg BID	20mg daily with PM meal	60mg daily	150mg BID 110mg BID^	2.5 – 5mg daily
Renal insufficiency	2.5mg BID*	CrCl 15 – 50 mL/min: 15mg CrCl < 15 mL/min: Avoid use	CrCl >95, <15 mL/min: Avoid use CrCl 15 – 50mg: 30mg	CrCl 15 – 30 mL/min: 75mg BID CrCl < 15 mL/min: Avoid use	Avoid with CRRT
Hepatic impairment	Not recommended with severe	Not recommended with moderate to severe		No recommendations	

*If ≥ 2 of the following: Scr ≥ 1.5 mg/dL, weight ≤ 60 kg, age ≥ 80
^Increased risk of bleeding (off-label)

Source: Eliquis (apixaban) [prescribing information]. 2021.; Xarelto (rivaroxaban) [prescribing information]. 2021.; Savaysa (edoxaban) [prescribing information]. 2021. ;Pradaxa (dabigatran) [prescribing information]. 2019.; Warfarin [prescribing information]. 2017.

Preventing Thromboembolism During Cardioversion

AF/AFL ≥ 48h or unknown

- Planned cardioversion
  - Anticoagulation ≥ 3 weeks before and 4 weeks after
- Immediate cardioversion
  - Anticoagulate ASAP and ≥ 4 weeks after
- May perform TEE and convert if no left atrial thrombus identified

AF/AFL < 48h + ↑ stroke risk

- Recommend anticoagulation before & immediately after
- Follow up with long-term anticoagulation

Source: January CT, et al. *J Am Coll Cardiol.* 2014;64(21):e1-e76.

Rate vs. Rhythm Control

AFFIRM

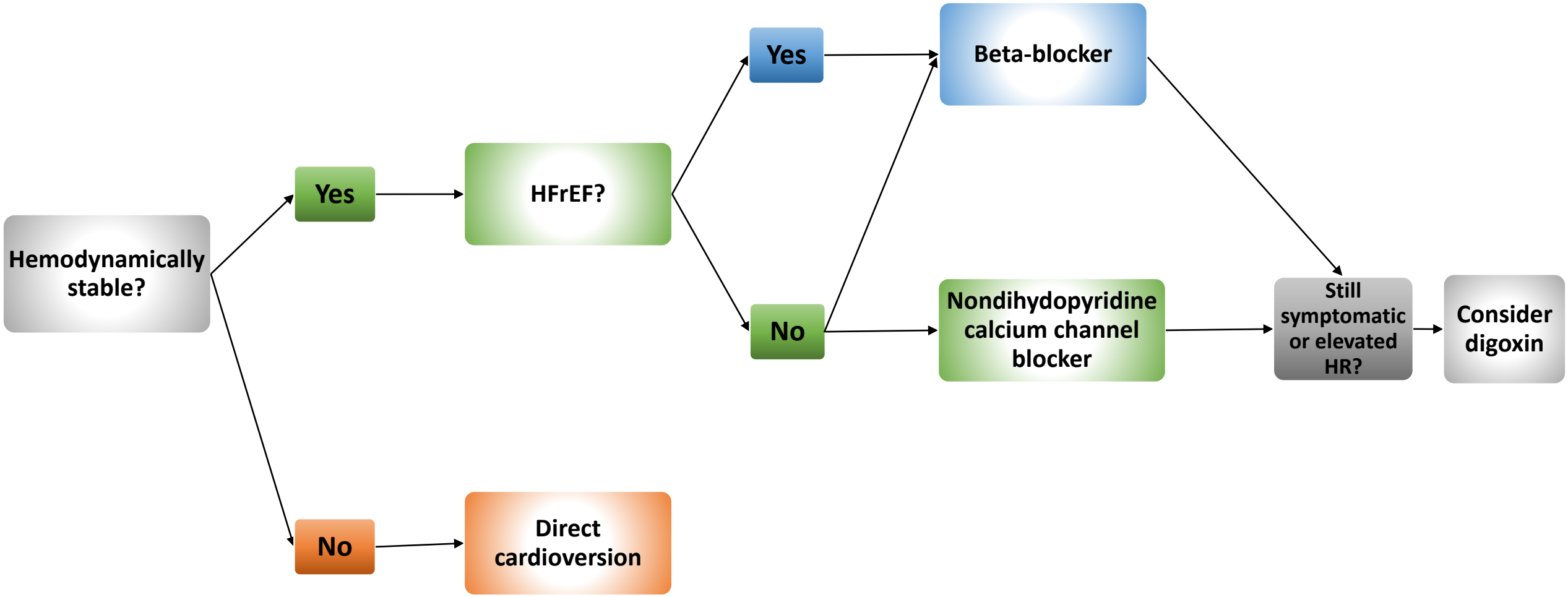
- 4060 participants
- ≥ 65 years
- Rhythm control found to have no survival benefit over rate control
- Limitations:
  - Selection bias
  - Anticoagulation discontinued in rhythm control group

EAST-AFNET-4

- 2789 participants
- ≥ 18 years
- ↓ risk of adverse CV outcomes with early rhythm control
- Limitations:
  - Did not assess specific agents
  - Early diagnosis

Source: Wyse DG, et al. *N Engl J Med.* 2002;347(23):1825-1833.; Kirchhof P, et al. *N Engl J Med.* 2020;383(14):1305-1316.

Rate Control



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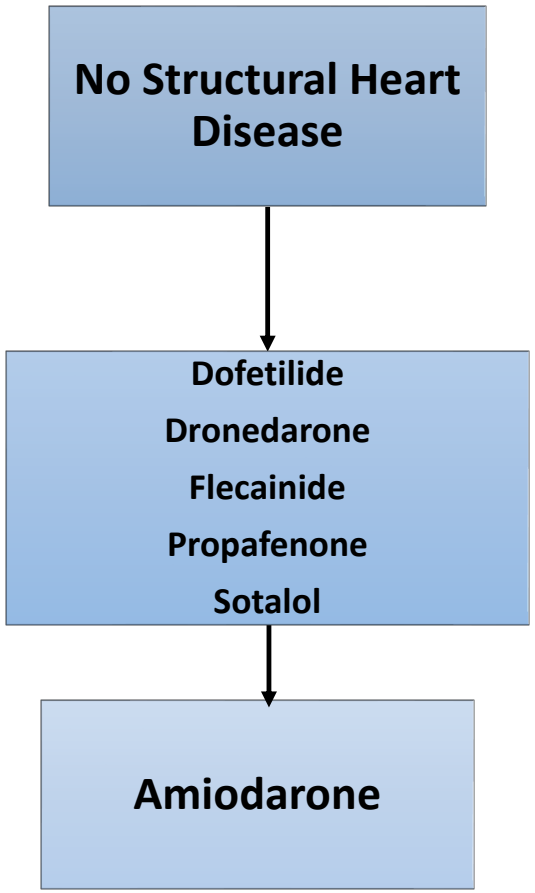
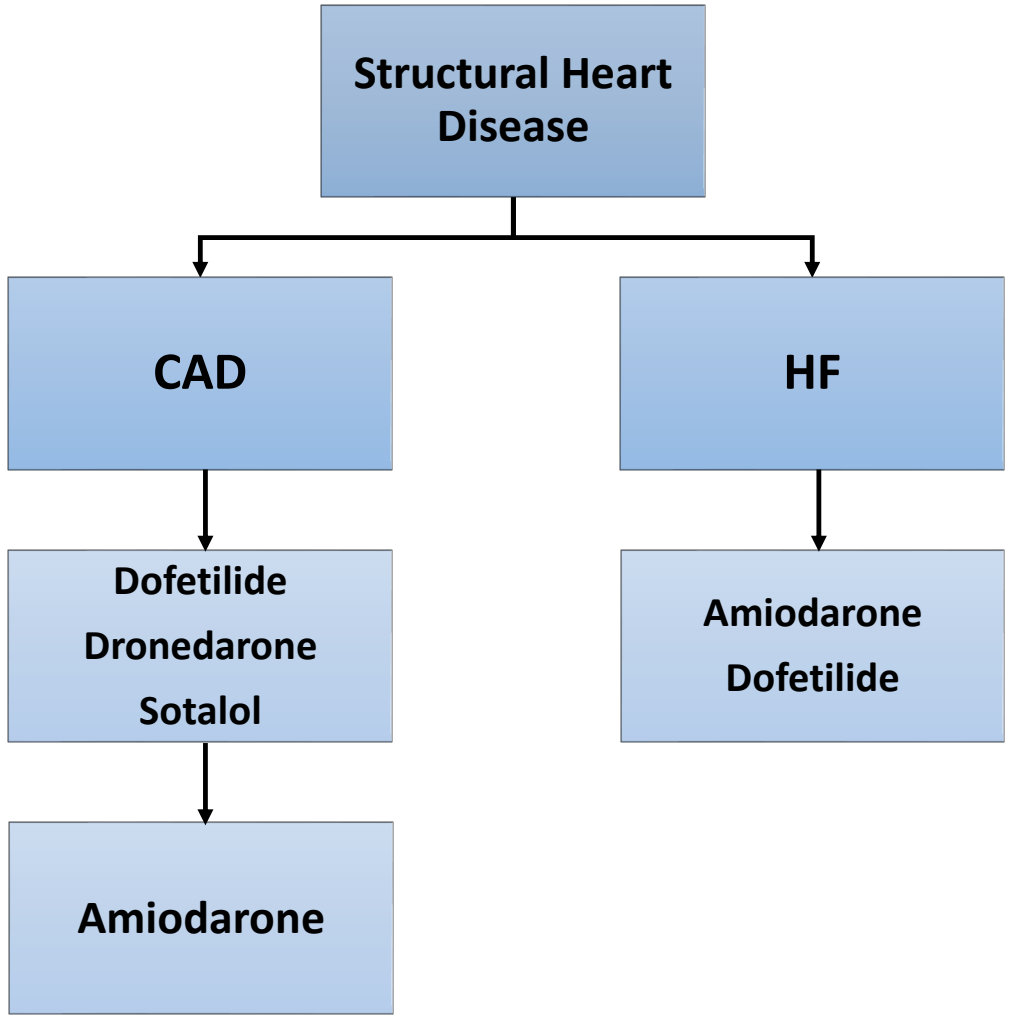
Rhythm Control





Source: January CT, et al. *J Am Coll Cardiol.* 2014;64(21):e1-e76.

Question #1

Which of the following is an appropriate treatment regimen for a patient with AF who also has a mechanical heart valve and HFrEF?

A. Apixaban + diltiazem

B. Rivaroxaban + metoprolol succinate

C. Warfarin + dofetilide

D. Warfarin + verapamil

Question #1: Answer

Which of the following is an appropriate treatment regimen for a patient with AF who also has a mechanical heart valve and HFrEF?

A. Apixaban + diltiazem

B. Rivaroxaban + metoprolol succinate

C. Warfarin + dofetilide

D. Warfarin + verapamil

Special Considerations

AF + Heart Failure

Rate Control

- Beta-blockers
- Digoxin

Rhythm Control

- Amiodarone
- Dofetilide

Source: January CT, et al. *J Am Coll Cardiol.* 2014;64(21):e1-e76.

AF + Renal Insufficiency

Anticoagulation

- Warfarin or apixaban in ESRD
  - Apixaban: DOAC least reliant on kidneys

Rate control

- Lower digoxin doses initially

Rhythm control

- Amiodarone
- Dronedarone
- Ibutilide
- Propafenone

Source: January CT, et al. *J Am Coll Cardiol.* 2014;64(21):e1-e76.; January CT, et al. *J Am Coll Cardiol*. 2019;74(1):104-132.; Hu A, et al. *Semin Nephrol*. 2018;38(6):618-628.

AF + Obesity & Anticoagulation

Warfarin

- BMI > 40 kg/m^2 associated with higher weekly requirements

DOACs

- ISTH recommends to avoid in:
  - BMI > 40 kg/m^2
  - Weight > 120 kg
- Study found rivaroxaban Cmax & AUC unaffected by weight > 120 kg

Source: Vyas V, Lambiase P. *Arrhythm Electrophysiol Rev*. 2019;8(1):28-36.; Kubitza D, et al. *J Clin Pharmacol*. 2007;47(2):218-226.; Martin K, et al. *J Thromb Haemost.* 2016;14(6):1308-1313.

AF + Pregnancy

Anticoagulation

- Warfarin = teratogenic
- Enoxaparin

Rate control

- Beta-blockers
- Digoxin

Rhythm control

- Sotalol
- Flecainide

Source: Fischer AJ, et al. *Herzschrittmacherther Elektrophysiol.* 2021;32(2):145-151.; Georgiopoulos G, Tet al. Expert Opin Pharmacother. 2019;20(13):1625-1636.

Question #2

Which antiarrhythmic is safe to use in a patient with CKD stage 4 WITHOUT the need for dose adjustment?

A. Amiodarone

B. Dofetilide

C. Flecainide

D. Sotalol

Question #2: Answer

Which antiarrhythmic is safe to use in a patient with CKD stage 4 WITHOUT the need for dose adjustment?

A. Amiodarone

B. Dofetilide

C. Flecainide

D. Sotalol

Clinical Updates

Summary: What's new?

- Antithrombotic → anticoagulant
- Term "nonvalvular" eliminated
- Edoxaban added for anticoagulation
- DOACs > warfarin when eligible
- Warfarin or apixaban use in ESRD
- Idarucizumab for dabigatran reversal
- Andexanet alfa for apixaban & rivaroxaban reversal

Source: January CT, et al. *J Am Coll Cardiol*. 2019;74(1):104-132.

The Pharmacist’s Role

Patient Education

- Adherence
- Monitoring
- Warfarin dosing
- Weight loss
- Smoking cessation

Source: Morrissey E, et al. *Heart* 2016;**102:**A25.

QTc Monitoring

Electrolytes

Drug interactions

Dose adjustment

Source: Tisdale JE. *Can Pharm J.* 2016;149(3):139-152.

Question #3

Which of the following is NOT a way pharmacists can help and educate patients with AF?

A. Assisting in improving adherence

B. Allowing patient non-adherent to INR checks to be lost to follow-up

C. Offering nicotine replacement therapy when appropriate

D. Assisting provider in dosing warfarin for a patient with labile INRs

Question #3: Answer

Which of the following is NOT a way pharmacists can help and educate patients with AF?

A. Assisting in improving adherence

B. Allowing patient non-adherent to INR checks to be lost to follow-up

C. Offering nicotine replacement therapy when appropriate

D. Assisting provider in dosing warfarin for a patient with labile INRs

Additional References & Resources

CDC AF resources:
www.cdc.gov/heartdisease/atrial_fibrillation.htm

Medications affecting the QTc:
www.crediblemeds.org

AHA/ACC 2019 AF Guideline Update:
www.ahajournals.org/doi/10.1161/CIR.0000000000000665

Conclusions

AF causes ↑ morbidity & mortality for patients

Treatment consists of anticoagulation, rate control, and/or rhythm control depending on the patient

Care must be taken when treating special populations

Pharmacists play a large role in optimizing AF treatment

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Thank you!

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